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Lightening talks: Autoinflammatory and bone disease

O001

CLINICAL FEATURES AND OUTCOMES IN STING-ASSOCIATED VASCULOPATHY WITH ONSET IN INFANCY (SAVI)

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Introduction: STING-Associated Vasculopathy with Onset in Infancy (SAVI) is a rare autoinflammatory interferonopathy caused by gain-of-function mutations in *STING1*, characterized by peripheral vasculopathy and interstitial lung disease
Objectives: Describe the clinical and immunological manifestations of SAVI
Methods: Clinical information on 30 patients with SAVI, based on NIH evaluation (n=15) or on records and samples provided by collaborators (n=15), were retrospectively reviewed. All patients were enrolled in an IRB-approved natural history protocol. The IFN score was calculated as previously described [1]. Features of lung inflammation and damage on Computed Tomography (CT) were scored by a single radiologist (LF)
Results: 11/30 (37%) patients were female. SAVI was sporadic in 77% and familial in 23%. It was due to heterozygous mutations in 80%; only one mutation, p.R281W, present in 6 patients from 4 families, needs homozygosity to be disease-causing. The p.N154S and p.V155M mutations were most common (27% each). Disease symptoms presented in the first year of life (78%), with rash (14/27), respiratory symptoms (11/27) and fever (10/27). Median age at last evaluation was 12.6 years (range 0.4-54), 4 patients had no peripheral vasculopathy and 4 had no lung involvement. Compared to the other genotypes, the p.V155M mutation was more commonly associated with severe lung involvement (100% vs 47.6%, *p=0.01*). Table 1 lists clinical and laboratory features in SAVI. Patients failed a mean of 2.2 DMARDs or biologic, 73% received steroids; 7 patients died at a mean age of 7 years, mostly due to respiratory failure. 23 patients were treated with a JAK-inhibitor (baricitinib n=14, tofacitinib n=6, ruxolitinib n=6), for a median of 1.6 years (range 0.1-5.7). Skin ulcers improved in 9/9 patients, but recurred. Over an average of 2.6 years (range 1.1-3.9), chest CT inflammatory features improved in 6/7, with stable/improved damage in 6/7.

Clinical features	n (%)	**Laboratory features**	n (%)	**Outcomes and complications**	n (%)
Rash/chilblains	26/29 (89.7%)	Elevated inflammatory markers	22/26 (84.6%)	Death	7/30 (23.3%)
Lung disease	26/30 (86.7%)	Anemia	21/27 (78%)	Lung fibrosis	12/16 (75%)
Failure to thrive/ Growth failure	22/28 (78.6%)	Thrombocytosis	15/21 (74%)	Respiratory insufficiency	11/28 (39.3%)
Fever	19/25 (76%)	Lymphopenia	12/22 (55%)	Pulmonary hypertension	4/26 (15.4%)
Clubbing	11/20 (55%)	Elevated IgG	17/24 (70.8%)	Nasal septum perforation	7/27 (25.9%)
Arthralgia/arthritis	10/27 (37%)	Elevated IgA	16/24 (67%)	Amputations	6/30 (20%)
Myositis	5/27 (18.5%)	Autoantibodies	25/27 (92.6%)	Pathologic fractures	4/16 (25%)
Basal ganglia calcifications	2/12 (16.7%)	Elevated IFN Score	17/17 (100%)*	Short stature	15/24 (62.5%)

* In 4 patients IFN score was positive only in PBMCs
Conclusion: SAVI is a severe early-onset interferonopathy, that is sporadic in 77%. SAVI can present with isolated pulmonary involvement and should be suspected in patients with interstitial lung disease even in the absence of vasculopathy. The p.V155M mutation is associated with severe lung disease. Rarely, the IFN score can be negative in whole blood and positive in PBMCs. Treatment with JAK inhibitors halted progression of lung damage over an average of 2.3 years, but only partially controlled peripheral vasculopathy and did not normalize IFN score

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Funding for this study was provided by the Division of Intramural Research, NIAID, NIH

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Disclosure of Interest: None declared

O002

COMPARISON OF CLINICAL AND IMAGING FEATURES BETWEEN CHRONIC NONBACTERIAL OSTEOMYELITIS AND ITS MIMICKERS: A MULTI-NATIONAL 450 CASE-CONTROL STUDY

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Introduction: Chronic nonbacterial osteomyelitis (CNO)/chronic recurrent multifocal osteomyelitis (CRMO) predominantly affects children and young adults. Classification criteria are not available and diagnostic criteria that were suggested have not been validated. We previously identified candidate items for the development of classification criteria.
Objectives: To refine candidate items for pediatric classification criteria for CNO by comparing clinical, laboratory and imaging features of CNO against mimicking conditions.
Methods: International multicentre collection of clinical and investigational features of cases with CNO or mimicker diseases with at least 12 months follow-up was conducted through a REDCap online database. Prevalence ratios of each collected item between CNO and mimickers were calculated. A p value of <.05 was considered significant.
Results: 450 cases were collected from 20 centers in 7 countries and 4 continents. Cases were filtered based on indicated confidence levels of diagnosis for CNO or mimickers using a cut-off of +/- 2 (moderately confident). 264 (59%) CNO cases and 145 (32%) mimicker controls were used for analysis. 41 (9%) cases were excluded. When compared to mimicker diagnoses, CNO patients were predominantly female, more frequently exhibited intermittent versus continued pain (especially of neck, back and upper torso), but less commonly had fever. Clavicular swelling was more common in CNO, while active arthritis was less common as compared to controls. CNO patients more frequently had whole body imaging (usually whole-body MRI). Symmetric patterns of bone lesions were more common in CNO. CNO frequently involved the thoracic spine, clavicle, sternum/manubrium, pelvic bones, bilateral femur, bilateral tibia, unilateral fibula, and foot bones. Imaging features concerning for infection or malignancy were less common in CNO. Lastly, complete and sustained response to antibiotic treatment is less frequent in CNO patients.
Conclusion: Using a case-based approach, key features of CNO were identified to support the development of classification criteria. Next steps will include expert panel discussions and a 1000Minds exercise.
Disclosure of Interest: Y. Zhao Consultant for: Novartis, R. Naden Consultant for: ACR/EULAR, M. Oliver: None declared, Z. Wang: None declared, E. Wu: None declared, C. Aguiar: None declared, J. Akikusa: None declared, O. Basaran: None declared, K. Cain: None declared, M. Capponi: None declared, N. Donaldson: None declared, E. Fox: None declared, A. Insalaco: None declared, A. Jansson: None declared, U. K. Akca: None declared, T. Lee: None declared, E. Marrani: None declared, K. Mahmood: None declared, E. Murray: None declared, F. Nuruzzaman: None declared, K. Onel: None declared, M. Pardeo: None declared, L. Potts: None declared, N. Rogers: None declared, A. Schnabel: None declared, G. Simonini Speaker Bureau of: Abbvie/Novartis, J. Soep: None declared, S. Stern: None declared, A. Theos: None declared, Y. Zhang: None declared, P. Ferguson Consultant for: Novartis, C. Hedrich Consultant for: Novartis, F. Dedeoglu Consultant for: Novartis, H. Girschick Consultant for: Novartis, R. Laxer Consultant for: Eli Lily Canada/Novartis/Sanofi, S. Ozen Consultant for: Novartis/SOBI

O003

DEMOGRAPHIC FEATURES IN A COHORT OF 101 CHILDHOOD ONSET FMF PATIENTS WITH RENAL AMYLOIDOSIS

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Introduction: AA Amyloidosis is the most severe complication of Familial Mediterranean Fever (FMF). Untreated amyloidosis is always progressive and typically leading to organ failure and death. Recently the rate of AA amyloidosis was reported as 8.6% in patients with a large cohort of FMF from Turkey.
Objectives: The primary aim of this study was to describe demographic, clinical, laboratory and genetic features of the patients with AA amyloidosis in a large number of childhood onset FMF patients.
Methods: In this case cohort study, patients were recruited from the nephrology and rheumatology outpatient clinics at GSM between September 2003 and February 2020. Patients who had AA amyloidosis were followed by a comprehensive patient-based registry. FMF-related AA amyloidosis was diagnosed with the positive staining pattern with Congo red dye.
Results: There were 195 patients diagnosed as amyloidosis in our registry. In total, 101 (65 males, 64.4%) of 195 patients with FMF related AA amyloidosis were diagnosed as FMF before 18-year-old.
Median age of FMF diagnosis was 13.0 (5.0-17.0) years, median age for diagnosis of amyloidosis was 21.0 (13.0-31.0) years and median age of the patients were 35.0 (20.0-49.0) years. Median (95% CI) elapse time between amyloidosis and diagnosis of FMF was 10.0 (9.3-10.6) years. Median follow up duration for our patients was 92.0 (65.0-101.0) months. Family history of FMF and amyloidosis were positive in 45 patients (44.6%) and 34 patients (33.7%), respectively.
The most common symptoms associated with the FMF episodes were fever (n=87, 86.1%), abdominal pain (n=72, 71.3%), arthritis (n=70, 69.3%), chest pain (n=65, 64.4%), vomiting (n=30, 29.7%), and mood disorder (n=26, 25.7%). Median serum hs-CRP level was 18 (9-95) mg/L (normal range <5mg/L) and median urine protein excretion was 5140 (3090-17000) mg/24 hours at the time of diagnosis for AA amyloidosis. A kidney biopsy was performed in all patients. Genetic screening showed that M694V (n=118, 61.4%) was the most common allele and M694V/M694V (n=48, 50%) was the most common mutation in our cohort. Eleven patients (10.9%) were died during the follow up due to myocardial infarction (n=9) and arrythmia (n=2). Five patients (5%) had kidney transplantation and two patients (2%) were on dialysis. All patients had used colchicine but only 72 patients (71.3%) are on colchicine treatment currently. Twenty-eight patients were treated with biologic DMARDs (Anakinra in 12 patients (11.9%), Canakinumab in 16 patients (15.8%).
Conclusion: To the best of our knowledge, our cohort is the largest number of childhood onset FMF patients who developed AA amyloidosis. The positive family history of FMF and amyloidosis, presence of arthritis, high M694V allele frequency and elevated hs-CRP level are the most prominent findings in our cohort. FMF related AA amyloidosis is still major problem especially in the countries where the disease has high prevalence such as Turkey, Israel.
Disclosure of Interest: None declared

O004

EVALUATION OF THE NEW CLASSIFICATION CRITERIA FOR PFAPA SYNDROME

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Introduction: Periodic Fever, Aphthous stomatitis, Pharyngitis and Cervical Adenitis (PFAPA) syndrome is characterized by regularly recurrent fever flares of early onset, accompanied by pharyngitis, cervical lymphadenopathy and oral aphthous ulcers. The diagnosis was based on the modified Marshall's criteria proposed in 1999. PFAPA is not a well-defined disease and shows a clinical overlap with inherited periodic fevers (IPF), such as Familial Mediterranean Fever (FMF), Tumor necrosis factor receptor-associated periodic syndrome (TRAPS) and Mevalonate kinase deficiency (MVK) and Cryopyrine associated periodic syndrome (CAPS), for which a causative gene is well established. Recently new classification criteria for PFAPA and IPF have been developed during a consensus conference in Genoa in March 2017.

Objectives: To evaluate the performance of the new clinical criteria for PFAPA, FMF, MDK, TRAPS and CAPS on our cohort of patients with recurrent fever.

Methods: In the first part, we selected all patients with PFAPA, FMF, MDK, TRAPS, CAPS and UPF from 5 participating centers, and applied the new classification criteria for PFAPA. In the second part, we applied the five new sets of clinical criteria on a population of PFAPA and UPF patients from 2 centers. In the last part, we considered the 121 patients from our Swiss consultation and evaluated the clinical outcome.

Results: In the first part, we included 417 patients (187 PFAPA, 63 UPF, 12 MKD, 114 FMF, 29 TRAPS, 12 CAPS): 42% of them met 7 out of the 8 criteria to be classified as PFAPA. Based on these results, we calculated for the new PFAPA criteria a sensitivity of 80.2% and a specificity of 89.1%, and a good positive predictive value (85.7%). In the second part, we evaluated the overlap between PFAPA and the monogenic AID. We applied the five sets of criteria to 288 patients, classified by the clinician as PFAPA (n=195) and UPF (n=93).

PFAPA (N=195)	41% PFAPA only	36% PFAPA + MKD	10% MKD only	5% No criteria	3% FMF only	2% FMF+ MKD	1% PFAPA + FMF	1% PFAPA+ MKD+FMF	1% PFAPA+ MKD+CAPS
UPF (N=93)	7% PFAPA only	14% PFAPA + MKD	24% MKD only	27% No criteria	13% FMF only	3% FMF+ MKD	1% PFAPA + FMF	3% PFAPA+ MKD+FMF	3% TRAPS only

In the third part, we evaluated the outcome in 121 patients followed in Lausanne for PFAPA (n=85) or UPF (n=36). In the PFAPA group, 88.1% had a remission of flares, 7.1% were stable and 4.8% had a flare increase. In the UPF group, 85.2% had a remission of flares, 7.4% were stable and 7.4% had a flare increase. Among all the different groups defined by the classification criteria there were no significant difference of the evolution.

Conclusion: The new criteria for PFAPA syndrome showed, when applied to a cohort of real-life patients, good sensitivity and specificity, and a good predictive value. However, when applying the 5 sets of clinical criteria to PFAPA and UPF patients, we found a large diagnostic overlap mainly between PFAPA and MKD. In the second part, we prove that when applied to patients of our cohort, the new clinical criteria were unable to distinguish PFAPA from MKD in about a third of our cohort. Clinical progression in patients with recurrent non-monogenic fever is generally favorable and is not different between the clusters.

Disclosure of Interest: None declared

O005

GUT MICROBIOTA PROFILING OF CHILDREN AFFECTED BY CHRONIC NONBACTERIAL OSTEOMYELITIS (CNO): A POTENTIAL ROLE IN THE PATHOGENESIS

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Introduction: Chronic non-bacterial osteomyelitis (CNO) is classified among autoinflammatory bone disorders but the exact etiology and pathogenesis are currently under investigation. The interplay between genetics, immunological and enviromental factors has been recognized as a possible causative factor so far. Emerging studies are suggesting that an altered ecology and function of microbiota (known as dysbiosis) can contribute to the occurrence or progression of a range of inflammatory diseases, affecting the balance between pro and anti-inflammatory immune responses. In a mouse model of CNO (cmo) dietary manipulation was accompanied with significant alterations of gut microbiome and significantly decreased of pro-IL-1β expression by distant neutrophils, thus resulting in protection from bone inflammation (gut-microbiota axis inflammasome).

Objectives: To assess the composition of gut microbiota in a cohort of CNO patients compared to healthy controls in order to assess its potential contribution to the pathogenesis of the disease.

Methods: In an observational cohort study, fecal samples were collected during follow up from 15 CNO patients (9 males) with a median age of 14.1 years (IQR 11.7-17.3). Four of them presented active disease at time of microbiota analysis. Microbiome maps were compared to samples from geographically- and age-matched healthy children. Gut microbiota ecology was determined by 16S ribosomal RNA-based metagenomics. Data were analyzed for their α- and β-diversity and differences in bacterial distribution were investigated by Mann Whitney and LEfSe assays.

Results: Microbiota richness, in terms of rare operational taxonomic units (OTUs), measured by the Shannon index, showed increased richness compared to healthy controls. In particular, ecological analysis revealed the presence of two distinct subjects' clusters, represented by CNO patients and healthy controls. The CNO group was characterized by a decrease of Verrucomicrobia and an increase of Actinobacteria. Especially, *Bacteroides*, *Odoribacter* and *Flavobacterium* were identified as potential microbial biomarkers for CNOs. Remarkably, the presence of *Prevotella* was only associated to the CTRL group.

Conclusion: This is the first study regarding the microbiome in CNO patients and our findings show evidence for clear dysbiosis and a distinct beta-diversity profile in the CNO patients. The dysbiosis could actually lead to a pro-inflammatory status through the selection of specific bacterial strains associated with gut inflammation and immune response activation. These findings highlight the possibility of studying bacterial biomarkers associated with this disorder and might led to novel potential therapeutic strategies.

Disclosure of Interest: None declared

O006

CHARACTERISATION OF A GROUP OF PATIENTS WITH PSTPIP1-ASSOCIATED INFLAMMATORY SYNDROME

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Introduction: PSTPIP1-associated inflammatory syndrome (PAID) results from mutations in the *PSTPIP1* gene and is characterized by a range of clinical phenotypes and variable expressivity. Most mutations of *PSTPIP1* lead to pyogenic phenotype. Yet, mutation c.748G>A(p.E250K) often leads to hematological symptoms associated with a variable degree of autoinflammation. Complex pathogenesis of PAID and its diverse clinical features lead to diagnostic and therapeutic challenges.

Objectives: To analyze clinical features, laboratory data and response to therapy of a group of patients with c.748G>A(p.E250K) *PSTPIP1* mutation.

Methods: We characterize 9 patients (4 females, 5 males, median age 14 years (range 3–42 years) from 6 unrelated families with the c.748G>A(p.E250K) *PSTPIP1* heterozygous mutation identified via customized panel next generation sequencing (NGS) and confirmed by Sanger sequencing.

Results: Median age at disease onset was 1 years (range birth–10 years). Most patients had various manifestations characteristic of autoinflammatory syndrome: 7/9 patients had recurrent fever; 6/9 – osteoarticular symptoms (arthralgia, arthritis, osteomyelitis, synovitis), 7/9 – dermatological symptoms (abscesses, acne, gangrenous pyoderma, vasculitis), 7/9 - lymphoproliferation, 2/9 - hepatomegaly and 4/9 - gastrointestinal symptoms. All patients had increased laboratory inflammatory markers. Yet, most patients also had a variety of hematologic abnormalities: anemia was present in 2/9 patients, neutropenia – in 1/9, pancytopenia – in 4/9, anemia and neutropenia – in 2/9, myelodysplastic syndrome - 1/9, hemophagocytic lymphohistiocytosis – in 1/9.

Tumor necrosis factor-α (TNF) inhibitor therapy was successful in 1/7 cases, had partial effect in 5/7 cases and no effect – in 1/7 cases. In responders TNF inhibitors alleviated the inflammatory symptoms but not hematologic features (Table 1). IL-1 inhibitors, steroids, JAK inhibitors were not effective in any of the patients treated. Combination of an IL-6 inhibitor and JAK inhibitor had partial effect in two patients.

Hematopoietic stem cell transplantation (HSCT) was performed in 3 patients. Two patients are now 2 and 2,5 years post-HSCT, with mostly donor chimerism and complete absence of the disease symptoms, one patient had early graft rejection, and is 42 days after second HSCT, with full donor chimerism and alleviation of the disease symptoms.

Table.1. Treatment of patients with PSTPIP1-associated inflammatory syndrome

Therapy	patient (n)	Response		
		Full	Partial	No effect
Steroids	4	0	0	4
Anti-TNFα (adalimumab, infliximab)	6	1	4	1
Anti-TNFα (infliximab)+ Steroids	1	0	1	0
Anti-IL1 (anakinra)	1	0	0	1
Anti-IL6 (tocilizumab)	3	0	0	3
IVIG	4	0	2	2
Methotrexat	2	0	1	1
Sirolimus	3	0	2	1

Conclusion: Patients with p.E250K *PSTPIP1* mutation have frequent hematological manifestation different from the rest of the PAID patients and represent a therapeutic challenge. HSCT might be a viable treatment option.

Disclosure of Interest: None declared

O007

BASELINE CHARACTERISTICS OF AN INTERNATIONAL LONGITUDINAL COHORT OF 1012 FMF PATIENTS FROM THE EUROFEVER REGISTRY

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Introduction: A new classification of pathogenicity of genetic variants associated to hereditary recurrent fevers[1] is available. The new Eurofever/PRINTO classification criteria (EPCC)[2] combine clinical manifestations with genotype.

Objectives: To describe the baseline characteristics of a longitudinal international cohort of familial Mediterranean fever (FMF) patients (pts) enrolled in the Eurofever registry and to evaluate the impact of EPCC criteria and new classification criteria for the pathogenicity of MEFV variants

Methods: We reviewed baseline demographic, genetic and clinical data of FMF pts included in the Eurofever registry. EPCC criteria were applied to the population. All MEFV variants were classified according to ref. 1.

Results: Since November 2009, 1175 FMF pts from 119 centers were enrolled in the registry. Clinical information was available for 1012 pts (532 males/480 females, 827 children/185 adults). For 125 pts clinical and genetic data mandatory for the application of EPCC were missing. Among the 887 remaining pts 623 (70.2%) satisfied EPCC (EPPC+), while 264 (29.8%) did not (EPPC-). Most of the EPCC- pts (172, 65.1%) displayed negative or non-informative genetics (monoallelic or biallelic benign variants, monoallelic VOUS). Eighty-nine (33.7%) and 3 (1.1%) pts with monoallelic and biallelic pathogenic variants respectively lacked FMF-associated clinical manifestations for EPCC

The differences in clinical manifestations between the EPCC+ and EPCC- pts are shown in Table 1. In EPPC+ group, the frequency of South-east Mediterranean ethnicity was higher.

At baseline 68.5% pts were treated with colchicine (438 EPCC+, 212 EPCC-). NSAIDs and steroids on demand were used in 30.8% and 16.9% in EPCC- and in 21.1% and 8.3% in EPPC+ pts respectively. Anti-IL1 treatment was used in 41 (4.1%) pts , without significative differences between the two groups.

Table 1. Clinical features

	Whole FMF population (887 pts)	**EPCC+ (623)**	**EPCC- (264)**	**p**
High risk ethnicity (South-East Mediterranean)	360	297 (47.7%)	63 (23.9%)	< 0.0001
Duration of episodes, median (25^{th} – 75^{th} p)	3 (2-3)	3 (2-3)	4 (2-4)	< 0.0001
Abdominal pain	845 (83,4%)	589 (94,5%)	166 (62,9%)	< 0.0001
Chest pain	373 (36,9%)	308 (49,8%)	39 (14,8%)	< 0.0001
Arthritis	246 (24,3%)	186 (29,9%)	38 (14,4%)	< 0.0001
Arthro-myalgia	527 (52,1%)	355 (45,1%)	355 (56,9%)	NS
Erysipela-like rash	85 (8,4%)%	72 (11,7%)	5 (1,9%)	< 0.0001
Amyloidosis	6 (0,7%)	3 (0,05%)	3 (1,1%)	NS

Conclusion: The combination of EPCC and the new pathogenic variant classification criteria captured the majority of FMF pts in the Eurofever cohort in a homogeneous group. The longitudinal evaluation of EPCC+ and EPCC- pts will provide clues on the overall long-term outcome with particular interest for the efficacy, safety and tolerability of different treatments.

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Aknowlegments: this research was financially supported by Novartis AG.
Disclosure of Interest: M. Bustaffa: None declared, I. Koné-Paut: None declared, S. Ozen: None declared, G. Amaryan: None declared, E. Papadopoulou-Alataki: None declared, R. Gallizzi: None declared, M. Carrabba: None declared, Y. Butbul Aviel: None declared, L. Cantarini: None declared, M. Alessio: None declared, J. Anton Consultant for: Novartis, Sobi, Speaker Bureau of: Novartis, Sobi, L. Obici: None declared, F. Gok: None declared, E. Batu: None declared, E. Moreno: None declared, P. Brogan: None declared, M. Trachana: None declared, G. Simonini Speaker Bureau of: Abbvie, Novartis, D. Rigante: None declared, M. Gattorno Consultant for: Novartis, Sobi, Speaker Bureau of: Novartis, Sobi, L. Rossi-Semerano : None declared

O008

THE LEVEL OF INTERFERON ALPHA PROTEIN IN DISTINCT INTERFERONOPATHIES PROVIDES CLUES TO THE OBSERVED DIFFERENTIAL TISSUE INVOLVEMENT

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Introduction: Whilst, by definition, up-regulation of type I interferon (IFN) signalling is common to the type I interferonopathies (T1Is), disease expression varies across this set of diseases, the basis of which remains unclear.
Objectives: To compare the levels of IFN-alpha in the cerebrospinal fluid (CSF) and serum in distinct IFN-related diseases.
Methods: We collected CSF and serum from patients with the known T1Is Aicardi-Goutières syndrome (AGS) and STING-associated vasculopathy with onset in infancy (SAVI), from individuals with presumed monogenic T1Is (pT1I), from cases of childhood-onset neuropsychiatric systemic lupus erythematosus (nSLE), and from children with non-IFN related auto-inflammation (AI) and non-inflammatory hydrocephalus (as controls). We measured IFN-alpha protein using digital-ELISA.
Results: Eighty-four and 60 measurements were recorded respectively in CSF and serum of 42 patients and 6 controls. In an intergroup comparison of the CSF data (taking one sample per analysed individual), the median level of CSF IFN-alpha was elevated in AGS, SAVI, pT1I and nSLE compared to AI and controls, with levels highest in AGS compared to all other groups. In AGS, CSF IFN-alpha concentrations were higher than in paired serum samples. In contrast, serum IFN was consistently higher compared to CSF levels in SAVI, pT1I and nSLE.
Conclusion: Whilst IFN-alpha is present in the CSF and serum of all IFN-related diseases studied here, the primary sites of IFN production in AGS and SAVI are, respectively, the CNS and the periphery. These data likely reflect tissue specificity in the expression, or biological redundancy, of the mutated gene, and/or in the generation of the endogenous self-nucleic acid ligands presumed to trigger the observed IFN response.
We thank ImmunoQure AG for sharing antibodies.
Disclosure of Interest: L. Lodi: None declared, I. Melki: None declared, V. Bondet: None declared, L. Seabra: None declared, G. I. Rice: None declared, E. Carter: None declared, A. Lepelley: None declared, M. J. Martin-Niclós: None declared, B. Al-Adba: None declared, B. Bader-Meunier: None declared, M. Barth: None declared, T. Blauwblomme: None declared, C. Bodemer: None declared, O. Boespflug-Tanguy: None declared, R. Dale: None declared, I. Desguerre: None declared, C. Ducrocq: None declared, F. Dulieu: None declared, C. Dumaine: None declared, P. Ellul: None declared, A. Hadchouel: None declared, V. Hentgen: None declared, M. Hié: None declared, M. Hully: None declared, E. Jeziorski: None declared, R. Lévy: None declared, F. Mochel: None declared, B. Neven: None declared, S. Orcesi: None declared, S. Passemard: None declared, M. Pouletty: None declared, P. Quartier: None declared, F. Renaldo: None declared, R. Seidl: None declared, S. Blanche: None declared, D. Duffy: None declared, Y. J. Crow Consultant for: Y.J.C discloses consultancy work with Biogen on behalf of the University of Edinburgh, M.-L. Frémond: None declared

O009

STANDARDIZING CARE AND FOSTERING SYSTEMIC AUTOINFLAMMATORY DISEASE (SAID) RESEARCH THROUGH THE CARRA AUTOINFLAMMATORY DISEASE NETWORK

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Introduction: International registries have significantly enhanced the understanding of the genetics, phenotype, prognosis, and treatment of Systemic Autoinflammatory Diseases (SAIDs) but largely lack a genetically heterogeneous Northern American cohort.

Objectives: To explore developing a Childhood Arthritis and Rheumatology Research Alliance (CARRA) Autoinflammatory Disease Network.

Methods: A team within CARRA of rheumatologists, ID physicians, immunologists, otolaryngologists, geneticists, parents/patients, and members of the Autoinflammatory Alliance met in person and via teleconferences to discuss the benefits of SAIDs networks. A literature search using keywords such as “EuroFever”, “pharmacosurveillance”, and “autoinflammatory registry” was reviewed to identify stakeholders and methods for establishing clinics. Physicians who were involved in establishing SAIDs programs shared their experiences. To explore the feasibility of and need for this network, 17 physicians from different sites approximated total patient numbers seen in their programs, as determined by ICD-10 codes when available.

Results: The workgroup participants agreed by consensus that a CARRA Autoinflammatory Disease Network would be instrumental to improve clinical care, enhance research, facilitate international collaboration, and improve patient and family involvement in research planning. The literature search highlighted the benefits of this approach in rare diseases in preventing diagnostic delay, understanding the epigenetics of SAIDs, and providing an opportunity for pharmacosurveillance in a cohort of patients exposed to biologics in a real world setting. Data was collected from 17 sites in the US, Canada, Israel, and Ukraine, to assess the number of potential patients this network could reach. Collectively these sites (~10% of CARRA sites) care for 2493 SAID patients, including 1029 coded with periodic fever syndromes, 81 with CAPS, 786 with other defined SAIDs (including PFAPA), 160 with undefined SAIDs, and 437 with CNO/CRMO. We found significant variability in how ICD-10 codes were utilized among this small survey of US centers. ICD-10 codes were not necessarily in concordance with the physicians’ diagnosis.

Conclusion: CARRA physicians manage thousands of patients in North America with SAIDs, which emphasizes the need for a CARRA Autoinflammatory Disease Network to facilitate earlier diagnoses, education, and access to expert and multidisciplinary quality care. This network will also create an infrastructure for clinical and translational research. Future work will focus on characterizing the patients seen across CARRA Registry sites. Given the genetically diverse populations in North America, an autoinflammatory network built around the CARRA Registry would facilitate collaborations with international colleagues to benefit patients worldwide.

Disclosure of Interest: G. Schulert Consultant for: Novartis and SOBI, J. Cherion: None declared, T. Wampler Muskardin Consultant for: Novartis and Regeneron, M. Twilt: None declared, S. Akoghlanian: None declared, G. Amarilyo: None declared, D. Dissanayake: None declared, K. Durrant: None declared, P. Ferguson Consultant for: Novartis, M. Gutierrez: None declared, L. Harel: None declared, J. Hausmann: None declared, M. Heshin-Bekenstein: None declared, R. Laxer: None declared, A. Lenert: None declared, S. Li: None declared, G. Licameli: None declared, G. Lionetti: None declared, I. Michelow: None declared, L. Moorthy: None declared, E. Propst: None declared, V. Saper: None declared, H. Srinivasalu: None declared, A. Thatayatikom: None declared, L. Tucker: None declared, P. Wright: None declared, C. Yildirim-Toruner: None declared, F. Dedeoglu Consultant for: Novartis, S. Lapidus: None declared

O010

EVALUATION OF THE THYROID DISORDERS IN CHILDREN WITH FAMILIAL MEDITERRANEAN FEVER

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Introduction: Autoimmune thyroid diseases is the most frequent organ-specific autoimmune disease. Although it is well-known that autoimmune thyroid diseases are more common in most of the autoimmune connective tissue diseases, the relationship between autoinflammatory diseases like familial Mediterranean fever (FMF) and autoimmune thyroid diseases has not well-evaluated yet and still remains unclear.

Objectives: The objective of this study was to evaluate the frequency of autoimmune diseases of the thyroid gland in children with FMF.

Methods: A total of 133 children aged <18 years with FMF and 70 healthy controls were included in the study. Thyroxine (fT4), thyroid stimulating hormone (TSH), thyroid peroxidase (TPO) and thyroglobulin (TG) antibodies, and thyroid ultrasound findings of all participant were evaluated.

Results: One hundred thirty-three patients with FMF [72 female and 61 male] and 70 healthy controls (n=40 female/30 male) were enrolled in the study. The mean free T4 levels of the patients and control groups were 1.25 ± 0.13 ng /ml and 1.35 ± 0.27 ng / mL, respectively (p=0.20). The mean TSH levels were 2.86 ± 1.72 mcU / mL in patients group and 3.1 ± 1.55 mcU / mL in control group. There was no statistical difference in TSH values between two groups (p=0.76) (**table1**)

There were five patients with increased levels of antibodies (2 of them positive for anti TPO and 3 of them positive for both of the antibodies) in patients with FMF and all of them were euthyroid. Four of these patients with high autoantibodies were pubertal and 1 of them were prepubertal. Two cases of control group had positive thyroid antibodies and they were euthyroid, too. Heterogeneity in thyroid parenchyma was observed in 1 of 5 patients with high autoantibodies in patients with FMF and 1 of 2 patients with high autoantibodies of the control. Thus, the frequency of Hashimoto's thyroiditis was 0.7 % in the cases with FMF and 1,2 % in control group.

In the FMF group, one patient had overt hypothyroidism and 5 patients had subclinical hypothyroidism. In the control group, subclinical hypothyroidism was detected in 3 patients and overt hypothyroidism was detected in 2 patients. The antibodies of the patients with overt and subclinical hypothyroidism in both groups were negative and the ultrasound findings were normal.

Table 1: The comparison of the thyroid function tests and the ultrasound findings of the patient group and the healthy controls.

	Patient group (n=133) (mean ± SD) / n (%)	Control group (n=70) (mean ± SD) / n (%)	p value
Mean age (years)	11.09 ± 4.19	10.4 ± 4.4	0,776
Thyroid stimulating hormone (mcU / mL)	2.86 ± 1.72	3.1 ± 1.55	0,76
Free thyroxine (ng /ml)	1.25 ± 0.13	1.35 ± 0.27	0,20
Anti-TPO† or/and Anti-Tg‡ positivity	5 (3.7)	2 (2.8)	0,718
Mean volume of right lobe	3,39±0,92	2,84±1,1	0,125
Mean volume of left lobe	2,8±1,2	2,6±0,78	0,431
Subclinical hypothyroid	5 (3,7%)	1 (1,25%)	0,340
Overt hypothyroid	3 (2,25%)	2 (2,5%)	0,916

Conclusion: Although the relationship between thyroid abnormalities and FMF has been reported before, we did not find a deterioration in thyroid functions in children with FMF. Our results suggest that there is no need for routine screening of serum thyroid function tests and thyroid antibody levels in patients with FMF in the absence of clinical symptoms or family history.

Disclosure of Interest: None declared

O011

GALECTIN-3: A NEW BIOMARKER FOR DIFFERENTIATING PFAPA (PERIODIC FEVER, ADENITIS, PHARYNGITIS, APHTHOUS STOMATITIS) SYNDROME FROM FAMILIAL MEDITERRANEAN FEVER

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Introduction: Periodic fever, aphthosis, pharyngitis, and adenitis (PFAPA) syndrome is an autoinflammatory recurrent fever syndrome of early childhood. In regions endemic for familial Mediterranean fever (FMF), differentiating PFAPA syndrome from FMF could be challenging in some cases. Galectin-3 is a lectin with regulatory functions in apoptosis and inflammation.
Objectives: We aimed to test whether galectin-3 could be a biomarker for differentiating PFAPA syndrome from FMF.
Methods: Patients with PFAPA syndrome, FMF, cyropyrin-associated periodic syndrome (CAPS), and streptococcal pharyngitis were included in this cross-sectional study along with healthy controls. Serum galectin-3 levels were measured using enzyme-linked immunosorbent assay.
Results: Ninety-three patients (42 patients with PFAPA, 39 with FMF, 8 with CAPS, and 4 with streptococcal pharyngitis) and 17 healthy controls were included. Blood samples were drawn during attacks from 23 PFAPA and 7 FMF patients, and during attack-free periods from 24 PFAPA, 35 FMF, and 8 CAPS patients. The median serum galectin-3 level in the PFAPA attack group (1.117 ng/ml) was significantly lower than the levels in healthy control (2.367 ng/ml), streptococcal pharyngitis (3.021 ng/ml), FMF attack (2.402 ng/ml), and FMF-attack-free groups (2.797 ng/ml) ($p=0.005$, 0.04, 0.01, and <0.001, respectively). PFAPA attack-free group also had lower galectin-3 levels compared to FMF attack-free group (1.571 vs. 2.797 ng/ml, respectively; $p=0.008$). Serum galectin-3 levels did not differ significantly between CAPS patients and attack-free PFAPA patients (1.439 ng/ml vs. 1.571 ng/ml, respectively; $p=0.78$).
Conclusion: Galectin-3 may serve as a biomarker to differentiate PFAPA syndrome from FMF. Further studies with larger number of patients could validate its role as a biomarker.
Disclosure of Interest: None declared

O012

LONG-TERM EFFECTIVENESS OF CANAKINUMAB IN AID – INTERIM ANALYSIS OF THE CAPS SUBGROUP FROM THE RELIANCE REGISTRY

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Introduction: In the treatment of monogenic autoinflammatory diseases (AID), a heterogeneous group of diseases with excessive interleukin (IL)-1ß release and severe systemic and organ inflammation, the anti-IL-1 inhibitor canakinumab (CAN) has been associated with rapid remission of symptoms in clinical trials as well as in real-life[1,2].

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[1]Lachmann et al. N Engl J Med. 2009;360(23):2416-25
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Objectives: The aim of the Reliance registry is to explore long-term effectiveness and safety of CAN under routine clinical practise conditions in pediatric and adult patients with CAPS (cryopyrin-associated periodic syndromes, including Muckle-Wells syndrome (MWS), familial cold autoinflammatory syndrome (FCAS), neonatal onset multisystem inflammatory disease (NOMID)/chronic infantile neurological cutaneous and articular syndrome (CINCA), FMF (familial Mediterranean fever), TRAPS (tumor necrosis factor receptor-associated periodic syndrome) and HIDS/MKD (hyperimmunoglobulinemia D syndrome/mevalonate kinase deficiency).

Methods: This prospective, non-interventional, observational study is based in Germany with a 3-year follow-up and enrolls pediatric (from 2 years) and adult patients with clinically confirmed diagnoses of CAPS, FMF, TRAPS and HIDS/MKD routinely receiving CAN. In 6-monthly visits, clinical data and patient-reported outcomes are assessed. Study endpoints are long-term effectiveness and safety of CAN. Here, the CAPS cohort was analyzed.

Results: This 18-month interim-analysis includes 78 CAPS patients (49% females) enrolled by September 2019. Mean age at baseline was 25 years and mean duration of prior CAN treatment was 5.7 years. 64 patients (82%) had MWS, 2 FCAS, 7 NOMID/CINCA, 3 atypical CAPS and 2 lacked subtype diagnosis. Disease activity, fatigue and social impairment by patients' assessment, days absent from school/work, inflammatory markers, and remission by physician assessment were evaluated at 6-monthly intervals starting at baseline with last update at 18 months of follow-up (table 1). The results demonstrate sustained remission and disease control as evaluated parameters remained stable over time. Serious adverse events were reported for 10 patients including papillitis, pyrexia, chest pain, tonsillitis, appendicitis, circulatory collapse, skin disorders, TIA, and preterm delivery.

	Baseline	6 months	12 months	18 months
Number of patients, N	78	51	42	29
Mean age, years (SD)	25 (4; 79)	22 (4; 79)	20 (4; 58)	22 (4; 54)
Patient's assessment of disease activity 0-10, mean (min; max)	2.2 (0; 7)	1.8 (0; 7)	2.4 (0; 7)	2.8 (0; 8)

Patient's assessment of fatigue 0-10	2.9 (0; 9)		2.4 (0; 8)		2.8 (0; 8)		1.7 (0; 7)	
Number (%) of patients without impairment of social life by disease	16 (49)		29 (76)		20 (61)		14 (67)	
Number (%) of patients with days absent from school/work	25 (32.5)		11 (22)		14 (34)		15 (52)	
Inflammatory markers, CRP/SAA, mean (mg/dL)	0.4	3.2	0.4	2.1	0.3	0.8	0.2	0.5
Number (%) of patients in disease remission (physician assessment)	55 (72)		38 (76)		29 (71)		22 (76)	

Conclusion: The 18-month interim analysis of the RELIANCE study, the longest running real-life CAN registry, demonstrates that long-term CAN treatment is safe and effective in CAPS patients.

Disclosure of Interest: J. Kuemmerle-Deschner Consultant for: Novartis, AbbVie, SOBI, Speaker Bureau of: Novartis, AbbVie, Sobi, B. Kortus-Götze Speaker Bureau of: Novartis, M. Borte: None declared, I. Foeldvari Consultant for: Novartis, G. Horneff Speaker Bureau of: Abbvie, Chugai, Roche, Novartis, Pfizer, MSD, Bayer, A. Janda: None declared, T. Kallinich Speaker Bureau of: SOBI, Roche, CSL, Novartis, P. Oommen: None declared, C. Schuetz: None declared, F. Weller-Heinemann Speaker Bureau of: Novartis, J. Weber-Arden Employee of: Novartis, N. Blank Speaker Bureau of: SOBI, Novartis

O013

CLINICAL, DIAGNOSTIC AND THERAPEUTIC FEATURES OF CHILDREN WITH CHRONIC NON-BACTERIAL OSTEOMYELITIS (CNO) – AN ANALYSIS OF THE GERMAN NATIONAL PEDIATRIC RHEUMATOLOGIC DATABASE 2009-2018

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Introduction: An analysis of data was performed, investigating clinical, diagnostic and therapeutic features of juvenile patients with CNO.

Objectives: The objective of this investigation was to collect data of clinical and diagnostic features of patients with CNO during the first year of disease course.
Methods: Patients with diagnosis of CNO, disease duration < 13 months and a first registration into the National Pediatric Rheumatologic Database (NPRD) between 2009 and 2018 were included in this cross-sectional analysis. The data analyzed, included age, gender and routine laboratory parameters. Skin involvement as well as clinical and radiological data was documented in addition to therapeutics applied. Well-being and pain were assessed via numerical rating scales (NRS) and the functional ability by the C-HAQ.
Results: Of 774 documented patients, 62.8 % are female with a median age of 11 years. Symptoms at first visit included fever (>38°C) in 77/593 patients (13.0 %) and CRP > 1 mg/dl in 107/593 patients (18.0 %). HLA-B27 was positive in 48 patients (7.4 %), while the mean ESR was 12 mm/h. 14.8 % of the patients showed skin involvement, most of them psoriasiform. In 406 cases, X-ray was performed at the first visit, showing osteosclerosis/ -lysis in 34 % and hyperostosis in 14.5 % of the cases. In 177/406 patients, no changes were detected in conventional X-rays. MRI scan was performed in 648 cases, and 81.5 % showed a positive T2 signal. In 589 patients, clinical active lesions were documented, most frequently affected sites were tibia (29,7 %), pelvis (28,0 %) and femur (27,8 %). The spine was affected in 96 individuals (16.3 %). 48.2 % showed monofocal lesions, 6.5 % presented with 6 or more. In most patients, radiologically active lesions corresponded to the clinical sites. Main locations were tibia, pelvis and femur in 36,5 %, 32,5 %, and 31,2 %, respectively. Therapeutically, 78.2 % of the patients received non-steroidal anti-inflammatory drugs (NSAIDs), 6.2 % glucocorticoid treatment, 10.8 % of the patients (71/657) obtained disease modifying anti-rheumatic drugs (DMARDs) (methotrexate 4.4 %, sulfasalazine 3.7 %, etanercept 1.4 %) and 5.2 % bisphosphonates at the time of documentation. The evaluation of the patient`s questionnaire showed pain VAS (0-10) of 2.0, C-HAQ (range 0-3) of 0.13 and overall well-being (NRS 0-10) of 2.0. Diagnostic criteria for enthesitis-related arthritis are fulfilled in 16/672 patients (2.4 %).
Conclusion: To our knowledge, the NPRD cohort presents the largest cohort of children suffering from CNO. Clinical and diagnostic parameters of these patients at disease-onset and in the first year of disease course were analyzed. At initial presentation one third of the patients presented with clinical symptoms (fever, local redness and/or elevated inflammatory markers (CRP, ESR)). Conventional X-ray scans did not show any changes in almost 50 %, but more than 80% showed positive T2-signaling in the MRI. Most patients were treated with NSAIDs, only a small group received additional therapies like conventional or biological DMARDs, steroids or bisphosphonates.
In contrast to adult SAPHO patients during the first year of treatment, pediatric patients did not present with diagnostic criteria consistent with enthesitis-related arthritis (ERA). Evaluating the patients' questionnaires concerning QoL, no strong impairment due to CNO could be shown.
Disclosure of Interest: None declared

O014

PAEDIATRIC SARCOIDOSIS: PHENOTYPE OF A RETROSPECTIVE COHORT OF BIOPSY-PROVEN PATIENTS

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Introduction: Paediatric sarcoidosis is a multisystemic inflammatory condition characterised by the formation of non-caseating granulomata that may lead to end-organ damage. Diagnosis is challenging as a compatible clinical-radiographic presentation with histopathologic confirmation is needed. Caution must be exercised to exclude granulomata of infectious aetiology as well as those seen in immunodeficiencies associated with immune dysregulation. Little is known about this rare disease's presentation and outcome in children. We report a retrospective cohort of children with biopsy-confirmed sarcoidosis.
Objectives: To describe the phenotype of children with biopsy-proven sarcoidosis, their treatment and the course of the disease on various treatments.
Methods: Patients' notes were reviewed retrospectively, and multisystem involvement identified. We included patients with biopsies consistent with sarcoidosis or granulomatous inflammation which were performed or reviewed at our centre between 2010 and 2020. Excluded were gut biopsies, samples suggestive of an infectious diagnosis and immunodeficiencies with immune dysregulation.
Results: We identified 42 children with biopsy-proven sarcoidosis. Mean age at diagnosis was 9.4 years; male to female ratio 0.68. Twenty-seven patients were of Afro-Caribbean descent, 7 Asian, 5 Caucasian and 1 of mixed race. Tissues biopsied included lymph node, skin, kidney, liver, lung, submandibular, lacrimal and salivary gland, eye, spleen, bone, brain and synovium.
28 patients had lymphadenopathy, 16 glandular involvement (13 parotid, 16 other glands including submandibular, lacrimal, thyroid), 17 liver, 17 pancreas, 13 renal (including 3 with nephrocalcinosis), 11 spleen, 27 skin, 14 lung involvement, 11 arthritis, 4 tenosynovitis, 3 hearing loss, 2 bone, 1 cerebral, and 25 eye involvement (including 19 with uveitis).
Remarkable laboratory findings were as follows: 9 patients had hypercalcaemia, 16 raised amylase, 4 raised lipase and 30 raised ACE levels; 12 patients had abnormal renal function, 13 abnormal liver function. 13 patients were tested for NOD2 mutations, which were present in 5.
38 patients received treatment for sarcoidosis. Of those, 37 received steroids, 16 intravenous followed by oral steroids, 18 oral steroids only and 18 received steroid eye drops; 36 patients received disease-modifying antirheumatic drugs (DMARDS) including 26 methotrexate, 11 mycophenolate mofetil and 10 azathioprine; 4 patients received hydroxychloroquine, 5 cyclophosphamide; 10 received biologic therapy including 9 anti-TNF, 2 interleukin-1 blockade, one JAK inhibitor, one IL-6 blocker and 1 rituximab.
All patients had a good response to steroids, and most responded to methotrexate. The treatment of a subset of patients was escalated to include anti-TNF treatment, owing to grumbling disease activity. Although most of the patients were able to wean off regular steroids, the majority remained on long-term DMARDS to maintain disease control.
Conclusion: Our study suggests that non-necrotizing granulomatous inflammation on biopsy, multiorgan involvement, response to steroids and chronic course appear to be the hallmarks of paediatric sarcoidosis. DMARDs, in particular methotrexate, were used with efficacy. When response was partial, addition of an anti-TNF was efficacious at controlling the disease, particularly in ocular sarcoidosis. Additional organ involvement occurs over time when the disease is not fully controlled. However, no biomarkers are available to assess disease activity apart from ACE, which does not appear sensitive enough. Prospective cohort studies are needed to define this rare paediatric disease.
Disclosure of Interest: None declared

LB006

RISK FACTORS OF PERSISTENTLY ACTIVE DISEASE AMONG FILIPINO CHILDREN WITH SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS: 10-YEAR STUDY IN A TERTIARY HOSPITAL

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Introduction: Systemic Juvenile Idiopathic Arthritis (SJIA) is one of the most common subtypes of arthritis among children in Southeast Asia with higher progression of disease activity. Unsuccessful control of the disease may lead to long-term disability resulting to functional limitations that would affect the productivity of the individual.
Objectives: The study determined the risk factors for persistently active disease among Filipino children aged 2 weeks to 18 years diagnosed with SJIA seen in the Section of Pediatric Rheumatology of University of Santo Tomas Hospital (USTH) from June 2009 to June 2019.
Methods: A retrospective cohort study was done involving chart review of both clinical division and private division patients. The following parameters were determined: sex, age at diagnosis, time elapsed from symptom onset to diagnosis, joint involvement, inflammatory markers, and extra-articular manifestation. Statistical analysis included frequencies, percentages, and logistic regression for the risk factors of interest.
Results: One hundred twenty-seven patients with SJIA who were appropriately treated for at least 3 years were included. Among which, 88 (69%) developed a persistently active disease. Among them, 36 (41%) were diagnosed at 1-5 years old. Many were diagnosed (n=54, 61%) after 5 weeks. The most commonly affected joints were the wrists, knees, and ankles. Most common contracture noted involved the cervical joint. Only 33 (26%) patients received biologic agents. Risk factors identified for the development of persistent disease activity were low hemoglobin levels at the time of diagnosis and after 1 month of treatment, elevated platelet count after a month, substantial joint count after 3 months, and increased ESR after 6 months.
Conclusion: The change or improvement of the joint count and in hemoglobin, platelet count, and ESR levels after appropriate treatment may determine risk for persistently active disease in Filipino children with SJIA.
Consent: I have obtained written consent
Disclosure of Interest: None declared

Lightening talks: Treatment

O015

TRANSITION READINESS ASSESSMENT FROM PEDIATRIC TO ADULT SERVICES IN RHEUMATIC DISEASES

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Introduction: Pediatric rheumatic diseases are chronic illness, which requires special and continuity of health care throughout adulthood. The transition of care should be developed and adjusted according to the readiness of each child, so the individualized readiness assessment should be performed before transferring patients to adult care. Transition Readiness Assessment Questionnaire (TRAQ) is one of the validity and reliability tools, which is used for the assessment of transition-related skills in patients with chronic illness. Although TRAQ had been used in previous studies in European countries, there is limited data in pediatric rheumatic diseases especially in Asian countries, where cultural differences. Therefore, the development of a validated and reliable tool in the Thai language is needed.
Objectives: To cross-culturally adapt and validate Thai version of TRAQ and assess transition readiness in pediatric rheumatic diseases in Thailand.
Methods: This is a cross-sectional study design. TRAQ was translated into the Thai language and adapted to Thai culture and lifestyle. Forward translation and backward translation were performed by three different translators. After completing the translation process, the TRAQ was validated for the final version. Then the TRAQ Thai version was completed by participants aged 15 – 24-year-old, who was diagnosed with rheumatic diseases. The demographic data, including age, sex, socioeconomic status, diagnosis, duration of disease, medication, and disease activity were reviewed from medical records. Descriptive analysis and logistic regression analysis were used in this study.
Results: A total of 123 participants were included in this study. The mean age was 17.81 ± 2.19 years. The mean TRAQ score was 3.90 ± 0.68. There were significantly higher TRAQ scores in participants, who involved these parameters; 1) aged more than 18 years, 2) education in a Bachelor's degree program, 3) a transition clinic attendance, 4) a transition discussion with the doctor, and 5) an independent clinic visit (table 1). In multivariate analysis, a higher education level and an independent clinic visit were predictors for a higher TRAQ score with OR 4.64, 95%CI (1.68 – 12.80) and 4.07, 95%CI (1.35 – 12.22), respectively. The appointment keeping and tracking health issues were two domains in the questionnaire that had a lower score than others. Inactive disease status and dependent visit were factors that associated with participants, who had lower scores in these 2 domains, with OR 5.60, 95%CI (1.20 – 26.14) and 4.13, 95%CI (1.60 – 10.67), respectively.

Table 1 Comparison of TRAQ score in different parameters

Parameters	TRAQ score (mean ± SD)		*P* value
	Yes	No	
Age ≥ 18 years	4.26 ± 0.42	3.70 ± 0.71	< 0.01
Education in a Bachelor's degree program	4.30 ± 0.35	3.76 ± 0.71	< 0.01
Transition clinic attendance	4.30 ± 0.50	3.85 ± 0.69	0.03
Receiving transition discussion	4.15 ± 0.56	3.80 ± 0.69	0.04
Independent clinic visit	4.32 ± 0.53	3.78 ± 0.67	< 0.01

Conclusion: The Thai version of TRAQ was validated in rheumatic disease populations with good performance. Patients, who had a higher education level and visited the clinic on their own, had a higher chance of successful transit to adult care.
Disclosure of Interest: None declared

O016

EARLY IMPLEMENTATION OF TREATMENT WITH ETANERCEPT INCREASES THE LIKELIHOOD TO ACHIEVE REMISSION

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Introduction: Juvenile idiopathic arthritis (JIA) is the most common chronic inflammatory rheumatic disease in children and adolescents. A consistent therapy is required to avoid consequential damage and permanent loss of function. Biologic disease modifying anti-rheumatic drugs (bDMARDs) provide a well-accepted option for treatment of patients with a severe course of JIA. Etanercept (ETA) is still the most commonly prescribed bDMARD for JIA in Germany.
Objectives: To analyze adherence to treatment with ETA with special attention on discontinuation after achieving an inactive disease and recurrence of active disease after ETA withdrawal.
Methods: Data from two ongoing prospective, multicenter, non-interventional registries BiKeR and JuMBO were used for the analysis. JuMBO is the follow-up study to BiKeR and follows patients who have reached the age of 18. Both registers provide treatment data, individual trajectories of clinical data and outcomes from childhood into adulthood in JIA patients treated with bDMARDs and csDMARDs. Clinical disease characteristics, such as disease activity, were reported by the rheumatologists in addition to patient-reported outcomes at each six-months follow-up. Start and end dates for DMARDs as well as reasons for discontinuation were reported by the rheumatologists. Remission was defined as inactive disease defined by the Wallace Criteria.
Results: Data from 2,500 patients who were included in BiKeR and had an age ≥18 at the time of analysis were considered. A subset of 1,535 were enrolled in JuMBO. The mean follow-up was 8.6 (SD 4.2) years for the JuMBO patients. The majority of them had polyarthritis (35%), followed by enthesitis-related arthritis (20%). A total of 1,779 (68.8% of 2,584) patients were ever treated with ETA, providing 2,178 ETA treatment courses. There were 1,724 (67%) patients with first, 338 patients with a second and 54 with a third course of ETA treatment course. 710 (41.2%) discontinued ETA by ineffectiveness in the first course with similar rates of discontinuation due to ineffectiveness in the first and second course. A total of 332 (+/-MTX, 19.3%) discontinued ETA after achieving remission in the first ETA course. Among those, 129 (38.9%) patients did not require treatment with any other bDMARD subsequently until last follow-up (3.9 years, SD 3.5), while 169 (50.9%) re-started treatment with ETA, 14 (4.2%) with adalimumab and 4 with other bDMARDs. The likelihood of discontinuing ETA due to an inactive disease was positively associated with a younger age (hazard ratio (HR) 1.08, $p<0.001$), persistent oligoarthritis (HR 1.89, $p=0.004$), a shorter duration between JIA onset and ETA start (HR 1.10, $p<0.001$) as well as a good response to therapy within the first six months of treatment (HR 1.11, $p<0.001$). 209 (of 332) had ETA monotherapy at withdrawal. Of those, 77% (n=161) experienced recurrence of disease with a mean time to flare of 12.1 (SD 13.7) months. 129 patients restarted bDMARD therapy (n=117 ETA). We could not identify any correlates for the risk of flare. 70% re-achieved remission and 20% again discontinued therapy thereafter.
Conclusion: The study confirms the good effectiveness of ETA, even in the re-treatment of patients with JIA. Our data highlight the association of an early bDMARD treatment with a higher likelihood to achieve an inactive disease indicating a window of opportunity.
Disclosure of Interest: None declared

O017

SAFETY OF BIOLOGICALS IN JUVENILE IDIOPATHIC ARTHRITIS: A RISK ANALYSIS FROM THE BIKER REGISTER

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Introduction: The pharmacotherapy with biologicals is characterized by a high efficiency with comparatively good safety.
Objectives: Using large patient numbers from the BIKER register even rare risks can be detected as well as influencing factors .
Methods: The BIKER database was used to identify adverse events of special interest (AESI). A cohort of biologic-naïve JIA patients treated with methotrexate (MTX) was used as control. The influence of biographical factors, comorbidities, pre- and concomitant therapy and disease activity was analysed univariate and multivariate.
Results: 2856 non-systemic polyarticular JIA patients with a total of 2808 treatment courses with biologics (Etanercept n=1816, Adalimumab n=633, Tocilizumab n=178, Abatacept n=74, Golimumab n=60, Infliximab n=47) and 970 control patients were included. NSAIDs were used in 2930 (78%) treatment courses, systemic steroids in 1241 (33%), MTX in 2815 (65%), other DMARDs in 349 (9%). Pre-existing comorbidities were more frequent in the biologics cohort (1007 (36%) vs. 203 (20%); p<0.001). There were 2265 adverse events (AE) with biologics (81% of courses) compared to 832 in the control cohort (86%; p<0.001). Of these, 232 AE were classified as serious (SAE) in the biologics (8.3%) compared to 34 (3.5%) in the control cohort (p<0.001).
AESI with biologics were medically important infection n=106, opportunistic infection n=28, uveitis n=100, cytopenia n=31, hepatic event n=26, inflammatory bowel disease n=18, anaphylaxis n=14, depressive disorder n=14, evolving psoriasis n=12, other autoimmunopathy n=11, bleeding event n=5 and pregnancy n=5. Univariate analysis revealed a number of factors significantly associated with the occurrence of AESI: Anaphylaxis n=14, cytopenia n=10, hepatic event n=14, serious infection n=28, opportunistic infection n=13, Uveitis n=24, Psoriasis, n=15, IBD n=15,Depression, n=7. Results of multivariate analysis: association with serious infections are outlined in table 1.
Table 1: Significant factors in multivariate analysis for 8 Adverse Events of Special Interest. Odd's ratio (95% CI) is given.

Anaphylaxis	Cytopenia	Hepatic event	Serious infection	Uveitis	Psoriasis	IBD	Depression
Infliximab 57.8 (15.1-222)	Endocrine comorbidity 4.7 (1.6-13.9)	Tocilizumab 4,1 (1.5-11.1	Golimumab 4.7 (1.5-14.8)	Previous uveitis 4.8(3.2-7.3)	Premedication Abatacept 7.4 (1.5-51)	Infliximab 20.7 (1.8-241)	Vascular events 18.5 (2.1-161)
Respiratory comorbidity 7.2 (1.4-38)	Tocilizumab 3.7 (1.6-6.7)	Systemic steroids 3.7 (1.6-8.7)	Gastrointest. comorbidity 3.7 (1.2-11.4)	ESR 1.2 (1.1-1.3)#	Premedication Adalimumab 7.4 (1.4-40)	Hepatic comorbidity 15.9 (1.6-156)	Pretreatment MTX 1.4 (1.1-1.8)
Premedication i.a. steroids 7.1 (2.3-22.3)	Pretreatment with Steroids 3.2 (1.3-7.6)	BMI 1.5 (1.1-2.2)*	Adalimumab 2.7 (1.4-5.3)	Active joint count 0.8 (0.6-0.9)*	Adalimumab 7.1 (2.0-26)	Gastrointest. comorbidity 8.8 (1.6-48)	
Tocilizumab 5.9 (1.2-29.5)		Age 0.4 (0.3-0.3/*	Etanercept 2.22 (1.3-3.8)	BMI 0.7 (0.5-0.9)*	Psoriatic arthritis 5.9 (1.7-20)	Etanercept 7.4 (1.7-32.3)	
Age 0.5 (0.3-0.9)*			JADAS 10 1.2 (1.2-1.4)*	Age 0.6 (0.4-0.8)*	Premedication i.a. steroids 4.3 (1.4-13.5)	Cardial comorbidity 6.4 (1.1-36.9)	Physician global VAS 0.8 (0.6-1.0)
			Age 0.6 (0.5-0.8)*			Premedication I.a. steroids 2.6 (1.0-6.8)	
			ANA positive 0.6 (0.4-0.9)				

increment for each 10 mm (ESR); *increment for each 5 years (age), each 5kg/m2, each 5 joints or 5 points (JADAS)
Conclusion: Various AESIs were associated with several patient characteristics, comorbidities, pretreatment and the kind of biologic used. Interestingly, protective factors also were defined such as older age and ANA positivity for serious infections

and higher active joint count and higher age for uveitis. The knowledge of these influencing factors enables an individual risk assessment and can significantly influence the choice of the biological agent.
Disclosure of Interest: None declared

O018

VACCINATION WORKING PARTY OF PRES- PAST, PRESENT AND FUTURE

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Introduction: Vaccination WP has its first meeting at PRES congress in Athens 2017. Officially it was established in 2018 PRES congress in Lisbon, Portugal. One of the main reasons for establishing this WP was low level of evidence on which recommendation for vaccination in children with rheumatic diseases (RD) was based and it was concluded that in following years we need more solid evidence to answer numerous remaining questions. The first task was to create the platform for future multicentre studies. We gathered data from 25 countries about the variability of vaccination practices across the globe and presented it as the first Vaccination WP poster. There were considerable qualitative and quantitative differences amongst countries in their vaccination programmes, coverage and in parent obligation to vaccinate the child.

Objectives: The group identified many problems in this field including vaccine coverage in children with RD, the attitude of physicians towards vaccinations, the hesitancy of parents to vaccinate their children and among other the main issue was safety and immunogenicity of live attenuated vaccines, in particular MMR and varicella vaccine in children treated with different immunosuppressive and anti-inflammatory drugs including the ‘biologics’. Another unanswered question was also long term immunogenicity of vaccines in children with RD.

Methods: We created on line data collection on vaccine coverage, on attitude of physicians towards vaccinations in children with RD and on safety of booster MMR/V vaccine in children with RD on immunosuppressive therapy.

Results: In the 2019 PRES congress the group presented 2 abstracts: Live attenuated vaccines in pediatric rheumatic diseases are safe: Multicenter, retrospective data collection that was presented in YIM and in the congress plenary session as oral presentation by Veronica Moshe and An international survey on approaches towards immunization in children with rheumatic diseases: a report of the PReS Vaccinations Working Group in YIM and congress as poster presenation by Elena Moraitis. Recently, the article »Live attenuated MMR/V booster vaccines in children with rheumatic diseases on immunosuppressive therapy are safe: Multicenter, retrospective data collection” was published in Vaccine.

In 2020 we collected the data on Influenza vaccine uptake which was low in majority of participating countries.

Conclusion: The main task for the future is prospective study on MMR/V safety and immunogenicity in children with RD on immunosuppressive therapy.

In conclusion we believe that there are many tasks in front of us. Infections remain the main adverse event of immunosuppressive drugs that we use with great success for treatment of children with RD. And even more so in this terrible time of corona epidemics when we realised again how endanger can we be because of infection and that vaccine can be the only solution to the problem in such times.

Disclosure of Interest: None declared

O019

ATTAINMENT OF INACTIVE DISEASE FOLLOWING DISCONTINUATION OF ADALIMUMAB MONOTHERAPY IN PATIENTS WITH ERA

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Introduction: Enthesitis Related Arhtritis (ERA) is one of the most challenging JIA subtypes in terms of drug management and duration of treatment.
Objectives: We present the results of a retrospective study regarding clinical remission sustainment and potential relapse-associated factors in children with ERA treated with TNF-inhibitor (adalimumab -ADA).
Methods: This was a retrospective case study including patients with ERA (based on ILAR criteria) who received ADA from January 2012 to December 2017. All subjects had clinically inactive disease (clinical remission on medication (CRM) and Juvenile Spondylarthritis Disease Activity (JSpADA) remission criteria) for at least 2 years on treatment. Demographics, clinical, laboratory parameters as well data on medication exposure and clinical outcome were documented. Data were analyzed using STATA 15.
Results: In a total of 35(17 girls) patients with inactive ERA(median age 12.5 years), ADA treatment was discontinued. Median treatment duration was 2.8 years. Median time to achieve clinically inactive disease was 5.2 months (range 3.8-7.8). Discontinuation was gradual; in 40% of patients we performed gradual dose reduction while dose spacing was performed in 60% of patients. In 29 patients ADA treatment was successfully ceased. Out of these 29 patients, 3 (10%) developed a single episode of peripheral mono-arthritis managed by intra-articular joint injection while 3 (10%) had a flare of anterior uveitis managed with topical steroids; the rest remained in flare-free clinical remission (>2 years). 6(19%) patients considerably flared during the follow-up period and were restarted on ADA. Median duration of remission following ADA withdrawal was 5 months (range 3.6-11.6). Subgroup analysis showed that patients with unilateral (92%) vs bilateral (74%) sacroiliitis (p=0.06) and patients with shorter disease duration (0.5 vs 1.1 years, p=0.03) had a higher chance of successful withdrawal. In addition, patients with accompanying uveitis were more prone to require drug re-initiation(p=0.04). Time to achieve clinically inactive disease, rise of inflammatory markers at initiation of ADA, presence of enthesitis, peripheral arthritis as well as the tender joint count at diagnosis did not affect the primary outcome. Relapse rate decreased proportionally to time [66.5% relapse(< 6m) vs 33.5%(>6m), p=0.07]. The relapse percentages were identical in the dose-reduction versus gradual spacing mode of discontinuation groups. Age, gender, range of inflammatory markers at diagnosis did not affect clinical outcome.
Conclusion: This was a retrospective study regarding discontinuation of ADA used as monotherapy in patients with ERA (and associated sacroiliitis), following attainment of clinical disease remission, showing optimistic results. TNFi are generally effective in inducing and maintaining remission in ERA and ankylosing spondylitis(AS) patients and therefore long-term therapy is recommended. Overall, biologic-naïve patients demonstrate a swift and sustained response to TNFi; however majority of studies also ensue a synthetic DMARD. Our study demonstrated that ADA withdrawal is feasible in a significant proportion of ERA patients, provided anti-TNFi is initiated promptly. Patients with shorter disease duration and unilateral sacroiliitis showed a higher chance of attaining long-term remission. Prolonging the duration of treatment in clinical remission before discontinuation may show favorable results in contrast to other studies endeavoring earlier discontinuation.
Disclosure of Interest: None declared

O020

CANAKINUMAB, ON A REDUCED DOSE OR A PROLONGED DOSE INTERVAL WITHOUT CONCMITANT CORTICOSTEROIDS AND METHOTREXATE, MAINTAINS CLINICAL REMISSION IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS PATIENTS

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Introduction: Treatment with canakinumab (CAN), a selective, human anti-IL-1β monoclonal antibody, has shown sustained therapeutic effect along with corticosteroid dose reduction/discontinuation in patients with systemic juvenile idiopathic arthritis (SJIA), in a long-term extension study (NCT00891046).
Objectives: To evaluate the efficacy and safety of 2 different canakinumab tapering regimens in SJIA patients who were in clinical remission (NCT02296424).
Methods: This Phase 3b/4 study had two parts. In Part I 182 patients, n=84 with inactive disease from the extension study1 (cohort 1) and n=96 CAN-naïve patients (cohort 2) with active disease were administered subcutaneous CAN 4 mg/kg q4w. Per protocol titration off corticosteroids and/or methotrexate was attempted during Part I. Eligible patients (inactive disease for 24 consecutive weeks and being corticosteroid- and methotrexate-free for at least 4 weeks) advanced to Part II. Patients were randomised to either a 3-step CAN dose reduction regimen (2mg/kg/q4w, followed by tapering to 1 mg/kg/q4w and then discontinuation) or dose interval prolongation regimen (4mg/kg q8w, followed by tapering to 4 mg/kg/q12w and then discontinuation); patients advanced to the next tapering step if inactive disease was maintained for 24 weeks. The primary objective was to evaluate if at least 40% of patients were able to maintain inactive disease status for at least 24 consecutive weeks on either 2mg/kg q4w or 4mg/kg q8w.
Results: In Part II, a total of 75 patients were randomised to a dose reduction (n=38) or dose interval prolongation (n=37) CAN tapering regimen. The proportion of patients who maintained inactive disease for 24 consecutive weeks significantly exceeded the predefined threshold of 40% of Step 1 in both treatment arms: CAN reduced dose (71%; 2 mg/kg q4w) and in prolonged dose interval (84%; 4 mg/kg q8w). A total of 68% (26/38) and 79% (30/37) of the dose reduction and interval prolongation arms, respectively were successful in Step 2, while only 33% (25/75) of patients successfully discontinued CAN and maintained inactive disease for 24 consecutive weeks. Adverse events (AEs) and serious AEs observed within the 2 treatment cohorts and across Parts I and II were similar without any specific pattern or relationship to patients' disease status at baseline or treatment regimen. The most frequent AEs were common infections such as nasopharyngitis, upper respiratory tract infection, and pharyngitis followed by SJIA-related events such as rash, pyrexia and arthralgia. Clinical laboratory abnormalities were consistent with expected findings in patients with active SJIA and the known safety profile of CAN.
Conclusion: SJIA patients who are able to maintain inactive disease status on CAN monotherapy can successfully taper CAN by either reducing the dose or prolonging the dosing interval. However, only a minority of patients successfully discontinued CAN treatment for 24 weeks. The safety profile for both CAN titration regimens was similar and consistent with other CAN SJIA studies. No new safety signals were identified.
Disclosure of Interest: P. Quartier Consultant for: AbbVie, Chugai-Roche, Lilly, Novartis, Novimmune, Sanofi,SOBI, Speaker Bureau of: AbbVie, BMS, Chugai-Roche, Novartis, Pfizer, SOBI, E. Alexeeva: None declared, C. Wouters Consultant for: GSK, Roche, Pfizer, I. Calvo: None declared, T. Kallinich Speaker Bureau of: Sobi, Roche, Novartis, CLB, B. Magnusson: None declared, N. Wulffraat Consultant for: Novartis, X. Wei Employee of: Novartis, A. Martini: None declared

O021

LONG-TERM SAFETY PROFILE OF ANAKINRA IN PATIENTS WITH SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Systemic juvenile idiopathic arthritis (sJIA) is characterized by extra-articular manifestations, as fever and rash, and rarely associated by a potentially lethal complication as macrophage activation syndrome (MAS). Anakinra is a recombinant human interleukin (IL)-1 receptor antagonist whose efficacy and safety profile has been studied for patients with sJIA.
Objectives: To evaluate the long-term safety profile of anakinra in patients with sJIA in current clinical practice.
Methods: Data from patients with sJIA treated with anakinra and enrolled in Pharmachild registry before 30 September 2018 was retrospectively analyzed (EUPAS28378). The study endpoints were the occurrence of non-serious adverse events (AEs) of at least moderate severity and serious AEs (SAEs), including MAS; the duration of anakinra treatment and reasons for discontinuation. All endpoints were analyzed overall and stratified by 6 months time windows.
Results: 306 patients were enrolled with both genders equally represented. Anakinra was administered at the median age of 8.0 years and after a median of 0.6 years from the disease onset. Almost half of the patients (n=146; 46%) were continuously treated with anakinra for at least 12 months, 34.0% for at least 18 months and 28.1% for at least 24 months. A total of 201 AEs was reported during a total of 509.3 patient years (py) of treatment with an overall incidence rate (IR) of 39.5 (95% CI 30.8-50.6) per 100 py, mostly represented by infections (52 events, 25.9%; IR 10.2/100 py). 56 SAEs were reported (IR 11.0/100 py; 95% CI 7.9-15.2), whereof 13 infections (23.2%; IR 2.6/100 py), and 11 MAS episodes (19.6%; IR 2.2/100 py). The IR/100 py of AEs was higher during the first 6 months of treatment and gradually decreased over time. Ten patients (3.3%) had a history of MAS before anakinra start, 9 of these patients did not experience any new MAS episode after anakinra start. 8 patients developed MAS several months after anakinra discontinuation. Discontinuation of treatment occurred at least once in 233 patients (76%) more often during the first 6 months and decreased over time and reasons were overall secondary to inefficacy (43%), remission (31%) or AEs and intolerance (15.0%). No deaths occurred during anakinra treatment while 3 deaths occurred after anakinra discontinuation (5 months, 3 years, and 5 years after discontinuation, respectively). No malignancies were reported neither during treatment with anakinra nor after discontinuation.
Conclusion: The results of the present study confirm the long-term safety profile of anakinra in sJIA patients without any new safety findings. Long-term treatment with anakinra in sJIA patients was well tolerated, with a decreasing overall incidence rate of AEs.
Disclosure of Interest: G. Giancane: None declared, R. Papa: None declared, S. Vastert Consultant for: SOBI and Novarts + unrestricted research grant from SOBI in collaboration with a public private funding opportunity of the Dutch National Science Organisation, F. Bagnasco: None declared, J. Swart: None declared, E. Alexeeva Speaker Bureau of: Novartis and has received research grants from Roche, Pfizer, Centocor, Novartis, P. Quartier Consultant for: AbbVie, Bristol-Myers Squibb, Chugai-Roche, Lilly, Novartis, Novimmune, Sanofi and Swedish Orphan Biovitrum, I. Kone-Paut Consultant for: AbbVie, Pfizer, Roche, CHUGAI, Novartis, Sobi, Novimmune, J. Anton Consultant for: Sobi, Novartis, Roche, Speaker Bureau of: Sobi, Novartis, Roche, S. Sawhney: None declared, F. Sztajnbok: None declared, S. Kamphuis: None declared, T. Herlin: None declared, V. Panaviene: None declared, R. Cuttica Consultant for: Bristol Myers Squibb, Centocor, Glaxo Smith Kline, Janssen, Lilly, Novartis, Pfizer, Roche, Sanofi Aventis., W. M. Saad Suwairi: None declared, H. Sanner: None declared, C. Pallotti: None declared, K. Franck-Larsson Employee of: Sobi, H. Malmström Employee of: Sobi, S. Cederholm Employee of: Sobi, N. Wulffraat: None declared, N. Ruperto Consultant for: NR has received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, Astrazeneca-Medimmune, Aurinia, Biogen, Boehringer, Bristol Myers and Squibb, Centrical Global, Domain Therapeutics, Eli-Lilly, EMD Serono, Glaxo Smith and Kline, Hoffmann-La Roche, Idorsia, Janssen, Merck, Novartis, Pfizer, R-Pharma, Sanofi, Servier, Sinergie, and Sobi.

O022

EARLY TREATMENT AND IL1RN SNPS AFFECT RESPONSE TO ANAKINRA IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Systemic juvenile idiopathic arthritis (sJIA) represents 10-20% of all chronic arthritis during childhood. The interleukin 1 (IL-1) plays a pivotal role in the pathogenesis of the disease. Indeed, several studies confirmed the therapeutic efficacy of anakinra (recombinant IL-1 receptor antagonist) in a significant portion of patients with sJIA, especially in the first phase of disease. The use of anakinra as first-line therapy can benefit from the so-called "window of opportunity", for which the evolution of the disease can be modified preventing the onset of chronic arthritis. Despite a good response to anakinra in a high percentage of patients, there is a subset of non-responders. The early identification of non-responder patients is of primary importance to avoid the progression towards chronic arthritis. Some single nucleotide polymorphisms (SNPs) in *IL1RN* gene have been found associated with sJIA, and recently, a cluster of SNPs in the *IL1RN* non-translated region has been suggested as a possible predictor of non-response to anakinra.
Objectives: The aim of this study was to evaluate the impact of early treatment and genetic variants in *IL1RN* gene on the response to anakinra in sJIA.
Methods: Response to anakinra was considered as clinically inactive disease (CID) at 6 months, without glucocorticoids treatment. Demographic, clinical and laboratory characteristics of 56 patients were analyzed in univariate and multivariate analysis as predictors of response to treatment. Six SNPs in *IL1RN* gene were genotyped by qPCR or Sanger sequencing. Haplotype mapping was performed with Haploview software and *IL1RN* mRNA expression in whole blood from patients before anakinra initiation was assessed by qPCR.
Results: After 6 months of treatment, 73.2% of patients met the criteria for CID off glucocorticoids. In univariate analysis the variable strongly related with the response was disease duration from onset to anakinra initiation, with an optimal cut-off at 3 months. Patients who started anakinra after 3 months from disease onset had an 8-fold higher risk of non-response at 6 months. We confirmed that the 6 *IL1RN* SNPs were inherited as a common haplotype in our cohort of patients. We found that homozygosity for at least one high expression SNP correlates with higher *IL1RN* mRNA levels and was associated with a 6 fold higher risk of non-response, independently of disease duration.
Conclusion: Our results confirm the important role of early IL-1 inhibition and suggest that genetic *IL1RN* variants predict non-response to therapy with IL-1 blockade in patients with sJIA.

Disclosure of Interest: None declared

O023

PHARMACOKINETICS-PHARMACODYNAMICS OF HYDROXYCHLOROQUINE IN CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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Introduction: Childhood-onset systemic lupus erythematosus (cSLE) is a chronic, autoimmune multisystem inflammatory disease that is associated with sizable morbidity and mortality. Hydroxychloroquine (HCQ) is an antimalarial agent given to patients with systemic lupus erythematosus (SLE) as first-line therapy with accumulating evidence on its role in reducing mortality and morbidity. HCQ is known to alleviate cSLE skin and musculoskeletal disease, along with decreasing disease activity and flare. Despite longstanding use of HCQ in children patients, the effect of HCQ in pediatric population and the potential need for dose adjustments remains unknown.
Objectives: To study the pharmacokinetics/ pharmacodynamics relationships of HCQ in cSLE
Methods: We performed a population-pharmacokinetic analysis using samples from patients' medical records in Necker-Enfants-malades Hospital and Robert-Debré hospital from 2016 to 2018. cSLE flares were defined using the SLE Disease Activity Index (SLEDAI); flare was denoted by a SLEDAI score of > 6. Hydroxychloroquine blood concentration was measured using high-performance liquid chromatography with fluorometric detection. Population pharmacokinetic/pharmacodynamic parameters were estimated using the nonlinear mixed-effects modelling software Monolix (version 2019R2).
Results: 144 results of blood samples were obtained from 48 child patients (45 girls). The mean age was 15.2 ±2.3 years; the median body weight was 56.1 ± 18.2 kg. Most subjects took HCQ as 400 mg per day (300 ± 113 mg/d). We found large interindividual variations in blood HCQ concentrations; the mean HCQ blood concentration was 685 ng/mL, range [100-2509]. HCQ apparent blood clearance CL/F was dependent on patients body weight (positive effect according to the allometric rule) and platelet count (negative effect). The mean SLEDAI score war 4.2 [0 -19]. Patients with active cSLE had a lower mean blood HCQ concentration than patients with inactive cSLE (536 ± 294 vs 758 ± 490 ng/mL, $p < 0.05$). When considering blood HCQ concentration ≥ 1000 ng/mL, 42/48 of patients had inactive cSLE. The joint model for HCQ concentration and probability of active disease status confirmed that HCQ concentration and treatment duration were significant predictors of disease status
Conclusion: We developed the first population-pharmacokinetic/pharmacodynamic model for hydroxychloroquine in childhood-onset systemic lupus erythematosus. Whole blood HCQ concentrations are associated with cSLE disease activity. To confirm these results, a prospective pharmacokinetic / pharmacodynamic analysis is necessary
Disclosure of Interest: None declared

O024

'IT GIVES THE TREATMENT STRUCTURE': PATIENT AND PARENTAL PERSPECTIVES ON TREATING TO TARGET IN JUVENILE-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS TREAT

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Introduction: 'Treat to target' (T2T), in which treatment is adjusted or escalated until a specific target is achieved, is now part of routine clinical care in many areas of medicine. It has been proposed as a strategy to improve management of juvenile-onset systemic lupus erythematosus (JSLE), using existing treatments in a more structured way. The TARGET LUPUS research programme; 'Targeting disease, Agreeing Recommendations and reducing Glucocorticoids through Effective Treatment, in LUPUS' has been established in order to develop a JSLE T2T study. There is currently little guidance on JSLE patient/parental views on the concept of T2T.
Objectives: To explore, in-depth, the views of JSLE patients and parents on the treatment targets, outcome measures and study designs for T2T being considered by TARGET LUPUS, in light of their previous treatment and care.
Methods: Topic guided semi-structured interviews explored what it means to JSLE patients to be 'well', and their views on potential T2T study targets e.g. Lupus Low Disease Activity State (LLDAS). As part of the interviews, patients and parents completed health-related quality of life (HRQOL) and fatigue tools and were then asked about their views of the tools and how well these captured their experiences. The concept of T2T was also explored, and patient and parental views on the proposed study and potential study designs were sought. Analysis of audio recorded interviews was informed by thematic approaches.
Results: 24 semi-structured interviews were conducted with 12 JSLE patients (aged 9-18 years) and 12 parents from six UK hospitals. Most patients reported feeling very well at the time of the interview, with several commenting that they felt completely back to normal. Most parents also classed their children as feeling well. However, several parents rated their child's wellbeing as worse than their child had themselves. Both patients and parents tended to class joint pain, muscle aches/weakness and rash as consistent with low disease activity. When asked about symptoms/signs that had not previously experienced during their disease course patients and parents often regarded as these signifying high disease activity. Of the three HRQOL questionnaires assessed, both patients and parents favoured the Peds QL Rheumatology Module, as they felt it provided the clearest picture of both wellbeing and functioning. Almost all patients and parents thought it was important to have a specific questionnaire focusing on fatigue. Most families felt that reducing corticosteroids would be a good treatment target. Almost all families liked the idea of a T2T approach to treatment, commenting that it would structure their treatment and enable more frequent clinic visits where needed. However, some were concerned about the impact of increased visits on schooling and parental work and suggested holding monthly visits until medication is stable, and then visits could become less frequent.
Conclusion: This study has provided insights on patient and parental perspectives on treatment targets, outcomes measures and indicated that the concept of T2T is acceptable to families in principle. These findings will be shared with JSLE experts, including patients and families during future international consensus meetings on further defining a treatment target and treatment strategy which is acceptable to both patients, families and clinical teams.
Disclosure of Interest: None declared

O025

A NATIONAL MULTICENTRE STUDY ON SEVERE PAEDIATRIC RECURRENT IDIOPATHIC PERICARDITIS TREATED WITH IL-1 BLOCKERS: APPROPRIATENESS OF THE STANDARD OF CARE AND PROS AND CONS OF ANTI-IL-1 TREATMENTS.

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Introduction: Recurrent pericarditis (RP) is a rare cause of morbidity in children. Non-steroidal anti-inflammatory drugs (NSAIDs), glucocorticoids and colchicine are the standard of care in adults. Recently, anakinra has been proven to be effective in patients with steroid-dependence and colchicine resistance.

Objectives: To analyse, in a cohort of paediatric patients with RP undergoing to anti-IL-1 treatment for resistance to standard treatments, the appropriateness of the first line treatments, the long-term efficacy of different IL1-blockers and the percentage of patients achieving a drug-free remission.

Methods: Paediatric patients with RP pericarditis followed by Italian centers of paediatric rheumatology or cardiology and treated with IL1 inhibitors were included in the study. The efficacy of treatment with IL1-blockers was evaluated trough an annualized relapse. A bivariate logistic regression analysis wad used to identify variables associated to an increased probability to withdraw the biological treatment without relapses.

Results: 58 patients were enrolled in the study. Overall, NSAIDS, colchicine and steroids were used in 56, 49 and 48 patients, respectively. 8/18 and 6/38 patients without a complete response to treatment with NSAIDs and colchicine, respectively, were not receiving an adequate dosage according to ESC guidelines. 4/48 patients treated with glucocorticoids were receiving the proper dosage of < 0,5 mg/kg/day of prednisone or equivalent. Steroidal-dependence was observed in 45 patients.

Anakinra and canakinumab were used in 57 and 6 patients respectively. In 57 patients treated with anakinra the annualized relapse rate (ARR) before treatment was of 3.05 and 0.28 ($p < 0.0001$) during daily treatment; however, an increase in the number of relapses was then observed after the reduction or discontinuation of treatment (ARR=0.83, $p < .0001$). In the 6 patients treated with canakinumab he ARR was 2.3 and 1.46, before and during treatment, respectively.

At last follow-up, only 9 patients had withdrawn all treatment. None of the variables analysed were associated with a statistically significance between the group of these patients and those 49 in which the withdrawal was not possible, due to recurrence of the disease.

Conclusion: This study confirm the effectiveness of IL-1 blockade in paediatric patients with recurrent pericarditis; however, most of the patients require prolonged treatment to maintain relapse-free remission. In our cohort of patients the rate of response was higher for anakinra then for canakinumab.

Disclosure of Interest: R. Caorsi Consultant for: Sobi, Novartis, A. Insalaco: None declared, F. Bovis: None declared, G. Martini: None declared, M. Cattalini: None declared, M. Chinali: None declared, A. Rimini: None declared, C. Longo: None declared, S. Federici: None declared, C. Celani: None declared, G. Filocamo: None declared, R. Consolini: None declared, C. Maggio: None declared, G. Fadanelli: None declared, F. Licciardi: None declared, M. Romano: None declared, B. Teruzzi: None declared, A. Taddio: None declared, A. Miniaci: None declared, F. La Torre: None declared, A. De Fanti: None declared, G. Cavalli: None declared, B. Bigucci: None declared, R. Gallizzi: None declared, M. Chinello: None

declared, A. Brucato: None declared, M. Imazio: None declared, R. Cimaz: None declared, F. De Benedetti: None declared, M. Gattorno Consultant for: Sobi, Novartis

O026

EVALUATION OF FLARE RATE AND TAPERING STRATEGIES IN JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Biological treatment (BT) has changed the perspectives of Juvenile Idiopathic Arthritis (JIA) patients, but it remains unclear the time point when and how to taper or to withdraw treatment, neither the effect of treatment withdrawal after remission is achieved.
Objectives: To assess the course of the disease after tapering or stopping BT in a cohort of JIA patients. Tapering strategies and median time to flare were analyzed.
Methods: A retrospective, descriptive study was conducted in a cohort of JIA patients followed up in a Pediatric and Transition Unit of a referral hospital and who had received BT between 2000 and 2019. All JIA patients with at least one attempt of tapering were included. Remission was defined according to Wallace criteria for remission.
Results: 131 JIA patients and 219 BT were reviewed. 198 de-escalations in 108 (49,3%) BT in 95 (72,5%) JIA patients were identified and included. 67,7% of the patients were female. The median age at JIA diagnosis was 5 years [IQR (2-12)] and the median age at the beginning of tapering was 17 years [IQR (11,8-26)]. Patients were in remission a median of 9 months [IQR (6-17)]. Main BT tapered were: TNF inhibitors (76,3%), IL6 inhibitors (15,2%) and IL1 inhibitors (6,5%). Conventional DMARDs (cDMARDs) were administrated in combination with BT in 40,4% of the deescalations. Regarding JIA categories: 44 (22,2%) were Oligoarticular Persistent, 36 (18,2%) were Oligoarticular Extended, 32 (16,2%) were Systemic JIA, 31 (15,7%) were Enthesitis related Arthritis, 19 (16,2%) were Psoriatic Arthritis, 16 (8,1%) were Polyarticular Rheumatoid Factor positive, 16 (8,1%) were Polyarticular Rheumatoid Factor negative and 5 (2,5%) were Undifferentiated. 8 (6,3%) patients were lost in follow-up.
The 171/198 (86,3%) cases started a de-escalation. The most frequent tapering strategy was prolonged interval between applications (90,6%), combined strategy (5,8%) and lower dosage (3,5%). The median remaining dose administrated was 50% [IQR (50, 75)].

Twenty-seven (13,6%) cases withdrawn BT abruptly. The main causes of abrupt BT withdrawal were: remission (33,3%), pregnancy (29,6%), active infection (14,8%) and vaccination (14,8%).
Forty-five (26,3%) cases stopped BT after tapering. Median time to withdrawal was 11 months [IQR (6-22)]. The main causes of withdrawal after tapering were remission (66,7%), pregnancy (11,1%), infections (6,7%) and vaccination (4,4%).
There was no difference in remission rates after withdrawal among cases with previous tapering or abrupt discontinuation [Median time of remission on withdrawal after tapering 5 +-(1,1), median time of remission among abrupt withdrawal 7 +-(2,6), Log rank=0,946]. After 6 months of withdrawal 48,1% of cases that stopped abruptly and 56,1% of cases that stopped after tapering had presented a flare. 10/72 (13,8%) cases are currently on remission without BT during follow-up, 9,7% without any treatment and 4,1% with cDMARDs.
BT was tapered without withdrawal in 126 (63,6%) cases. Remission rates during tapering are specified in table 1. 40 (20%) cases continue tapered without a flare after a median of 77 months [IQR (36,3-111,3)] of follow-up.

Time, months	Cases on remission, n %
6	101 (79,8)
12	86 (68,1)
24	60 (47,4)
Currently on remission	40 (31,8)

Table 1: Remission rates among cases tapered without withdrawal during follow-up.. n=126.

Conclusion: - There was no difference in remission rates among patients that discontinuated BT after tapering or after abrupt discontinuation. After 6 months of withdrawal 48,1% of cases that stopped abruptly and 56,1% of cases that stopped after tapering had presented a flare.
- Tapering without withdrawal is safe: 79,8% of cases at 6 months and 47,4% of cases at 24 months that tapered without withdrawal remained on sustained remission.
Disclosure of Interest: None declared

O027

SHOULD ETANERCEPT BE AVOIDED IN CERTAIN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS DUE TO RISK OF DEVELOPING INFLAMMATORY BOWEL DISEASE ?

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Introduction: Inflammatory bowel disease is a relatively rare comorbidity in patients with juvenile idiopathic arthritis but is known to have an important negative impact on quality of life. It is suggested that IBD development is associated with use of etanercept but due to its low incidence, thus far this has not been proven.

Objectives: The aim of this study was to determine risk factors for developing IBD in JIA patients and evaluate the possible relationship between medication and IBD development.

Methods: In this study, Pharmachild, the largest international JIA registry was used. Enrollment of patients was facilitated by members of the Paediatric Rheumatology INternational Trials Organisation (PRINTO). Risk factors for IBD where identified both before and after adjustment for confounders. A prediction model was developed using multivariable logistic regression analysis in a backward procedure based on likelihood ratio tests. To identify associations between drugs of interest and IBD development, patients who developed IBD were matched to similar controls based on the variables in the prediction model. Odds ratios were calculated using conditional logistic regression analysis.

Results: 8,942 patients were included in this study of which 48 (0.5%) developed IBD. Age at JIA onset was significantly higher in patients with IBD (8.94 years vs 5.33 years p=0.000) and there was a lower female predominance in the IBD group (52.1% vs 68.0% p=0.029). Family history was significantly more positive for autoimmune disease in IBD patients (43.8% vs 29.0% p=0.037) and enthesitis-related arthritis (ERA) was more frequently observed (39.6% vs 10.8% p=0.000). The model with the best discriminative performance included the variables age, gender, ERA and the total number of first and second degree relatives with a history of autoimmune disease and had an AUC of 0.721 (95% CI 0.646-0.796). Analyses on IBD patients with available onset date (n =27) matched to non-IBD controls (n =129) showed that patients treated with ETN had a 6.88 and 7.45 times higher odds for developing IBD within 3 and 6 months respectively, compared to control patients that did not receive ETN at similar disease duration (Table 1). In addition, both patients using ETN and MTX dual therapy and patients using ETN without MTX had higher odds for developing IBD. Use of other biologicals and MTX without ETN were not significantly associated with IBD.

Table 1: Odds ratios for the development of IBD

	3 months before IBD OR (95% CI)	**6 months before IBD OR (95% CI)**	**>6 months before IBD OR (95% CI)**
Drug therapy			
Methotrexate	**2.87 (1.16 – 7.07)**	**3.15 (1.24 – 8.03)**	2.93 (0.66 – 13.05)
MTX without ETN	1.11 (0.40 – 3.10)	1.02 (0.37 – 2.83)	0.57 (0.21 – 1.56)
Etanercept	**6.88 (2.51 – 18.81)**	**7.45 (2.75 – 20.16)**	2.38 (0.92 – 6.12)
ETN without MTX	**3.13 (1.08 – 9.03)**	**3.6 (1.12 – 11.08)**	-
ETN + MTX	**7.12 (2.03 – 25.01)**	**6.46 (2.06 – 20.27)**	**2.73 (1.07 – 6.99)**
Infliximab	9.21 (0.83 – 102.62)	9.21 (0.83 – 102.62)	2.27 (0.49 – 10.48)
Adalimumab	2.24 (0.14 – 35.9)	1.49 (0.13 – 17.34)	0.8 (0.18 – 3.46)

Conclusion: In this study, ERA patients were at an increased risk of developing IBD. The most important risk factors for developing IBD were age, gender, ERA subtype and family history of autoimmune disease. In addition, patients using ETN had higher odds of developing IBD while we did not find a protective role of MTX for the development of IBD. Therefore, we recommend to prescribe other biologicals than ETN to JIA patients with a higher risk of developing IBD.

Disclosure of Interest: None declared

O028

EARLY START OF BIOLOGICAL TREATMENT IN JUVENILE IDIOPATHIC ARTHRITIS: DOES A THERAPEUTIC WINDOW EXIST IN REAL LIFE?

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Introduction: Biological therapy (BT) has changed the treatment and perspectives of JIA patients but little is known about when is the best moment to start BT and the impact of this prompt initiation.
Objectives: To analyse the response to BT of Juvenile Idiopathic Arthritis (JIA) patients according to the time when the BT was started
Methods: A retrospective, descriptive study was conducted on JIA patients followed up in a referal hospital that started BT up to 24 months after diagnosis from 2000 to 2018. Disease activity was measured, at 2 years after diagnosis, according to Wallace criteria for remission (absence of: active arthirits, active uveitis, fever, rash or any other manifestation attributable to JIA, normal CRP and ESR, PGA indicating no active disease) for at least 6 months.
Results: 55 JIA patients that started BT up to 24 months from diagnosis were analyzed. 69,1% were girls with a median age at diagnosis of 8 years old [IQR(3-13)], median age at the start of BT of 9 years old [IQR(3-13)]. Regarding JIA categories: 25,5% were Oligoarticular Persistent (OligP), 18,2% Systemic JIA (sJIA), 16,4% Entesitis related Arthritis (ERA), 12,7% Psoriatic Arthritis (APso) and Polyarticular RF- (PolyRF-), 5,5% Oligoarticular Extended (OligE) and Polyarticular RF+ (PolyRF+), 3,6% Undifferentiated (Und). 20% of patients had uveitis during followup. Conventional DMARD (cDMARD) was indicated in 83,6% of patients (95,7% Methotrexate) at diagnosis [median 0 months IQR(0-2,3)]. At the end of followup (2 years) only 30,9% of patients continued with cDMARDs. The main causes of discontinuation were: adverse events (46,7%), remission (36,7%). TNF inhibitors were precribed in 81,8% of patients and 18,2% of patients recieved two BT during the first 2 years from diagnosis. 54,5% of BT were indicated during the first 6 months from diagnosis, 27,3% from 7 to 12 months, 12,7% from 13 to 18 months, 5,5% from 19 to 24 months.

After 2 years from diagnosis, 78,2% of patients were on remission and 21,8% active. Among patients with active disease: 75% had arthritis, 16,7% had uveitis and 8,3% had both. There were no differences regarding disease activity among patients with uveitis and neither taking cDMARDs. Regarding JIA categories: 66,7% of OligE, 57,1% of PolyRF- and 57,1% of APso patients were active at 2 years from diagnosis when compared to the other categories (p=0.004).

Patients on remission at 24 months from diagnosis started sooner the BT than active patients [CI 95% (0,46-8,29) p=0,029]. The time when the BT was started was correlated to the activity at 2 years (K= 0,294 p=0,029). When the BT was prescribed after 7,5months from diagnosis it was correlated, in a COR curve, with a higher probability of active disease at 2 years(S= 0,67 E= 0,63). There was a correlation, among patients on remission at 2 years, between prompt start of BT and less time to reach remission (K= -0,345 p=0,024). Patients with active disease at 2 years, regardless of moment of BT iniciation, required more BT during follow-up (p=0,002).
Conclusion: Prompt iniciation of BT was correlated with a better outcome. JIA patients that started BT early after diagnosis had a higher probability of remission after 2 years. Starting BT after 7,5 months was correlated with a higher probability of active disease at 2 years. Active disease at 24 months was correlated with presistent active disease during follow-up.
Disclosure of Interest: None declared

O029

AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION IN RHEUMATOLOGIC DISEASES: THE EXPERIENCE OF A THIRD-LEVEL HOSPITAL IN MEXICO.

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Introduction: Autologous hematopoietic stem cell transplantation (AHSCT) is an alternative treatment for patients with refractory rheumatologic disease (RD). AHSCT can re-establish immunological tolerance and induce complete remission of the disease.
Objectives: To report our experience of AHSCT in patients with refractory RD [diffuse cutaneous systemic sclerosis (dcSSc) and systemic juvenile idiopathic arthritis (sJIA)] at the Hospital Infantil de México Federico Gómez.
Methods: We included pediatric patients from 0 to 16 years with refractory dcSSc and sJIA, whom underwent AHSCT. We carried out a retrospective analysis of these cases.
Results: The present study was carried out from January 2018 to December 2019. We report 6 patients. 33% of patients with dcSSc and 67% sJIA. 83% were female. The mean age at the time of diagnosis was 12.8. The median time interval from diagnosis to AHSCT was 52 months. Regarding the dcSSc patients, received an average of 4 nonbiologic disease-modifying antirheumatic drugs (DMARDs) and 1 biologic agent prior to AHSCT. The sJIA patients received an average of 1.5 nonbiologic DMARDs and 2 biologic agents prior to AHSCT. The peripheral stem cells were mobilized with cyclophosphamide (CYC) and granulocyte colony-stimulating factor and harvested by leukapheresis and subsequently selected for CD34+ cells, on day 0 were infused, after compliance with the conditioning adjustment (CYC was given on days -8, -7 and -6 and antithymocyte globulin on days -5, -4, -3, -2 y -1). All patients received acyclovir, cefepime and fluconazole for infection prophylaxis. We follow-up the patients a median of 28.5 weeks. Patients with dcSSc experienced resolution of dyspnea, digital ulcers, decrease 33% the mRss and the number of Raynaud's phenomenon events. There were no significant changes in lung function tests, HRCT of the lungs and EGDS in dcSSc. All patients with JIAs had 0 joints with active arthritis, we documented a decrease of CRP 95% and VSG 64% after AHSCT. The cHAQ score improved 98% and the DAS 28 score 61%. The total of patients with dcSSc are in complete remission. Of the patients with AIJs, 66% have complete remission and 33% partial remission. No mortality has been reported.

Table 1. Baseline characteristics of the patients with refractory rheumatologic disease

Gender	Age (years)	Diagnosis	Time (month)	Damaged organ	Pre-transplant treatment	Post-transplant treatment	Complications	Status	
F	11	dcSSc	26	Skin + Lung + Digestive	HCQ + MTX + MMF + CYC	HCQ	Catheter-related sepsis	Complete remission	
F	17	dcSSc	31	Skin + Lung + Digestive	HCQ + MTX + MMF + CYC + RTX	HCQ	Malabsorption Syndrome	Complete remission	
F	16	sJIA	73	MAS	MTX + LFN + TOCI + IVIG + HLH-2004	HCQ	Catheter-related sepsis + CMV infection	Complete remission	
F	8	sJIA	65	-----	MTX + LFN + TOCI + ABA + ETA	LFN	-----	Partial remission	
M	14	sJIA	33	MAS	MTX + TOCI + ETA + IVIG + HLH-2004	MTX + TOCI	Catheter-related sepsis + Septic shock + Anaphylaxis + Adenovirus-induced hemorrhagic cystitis	Partial remission	

F	11	sJIA	84	-----	MTX + TOCI + ETA	HCQ	-----	Complete remission	

Conclusion: To our best knowledge, this is the first study in Mexico that describes the use of AHSCT in patients with refractory dcSSc and sJIA. AHSCT is a viable, effective and safe procedure in dcSSc and sJIA. AHSCT can slow the progression of rheumatologic disease, however, it does not reverse established damage. We must investigate poor prognosis factors that allow us to recognize patients with a high probability of rapid disease progression in order to select them for the AHSCT in a timely manner.

Disclosure of Interest: None declared

LB005

CANAKINUMAB IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS: CLINICAL INACTIVE DISEASE RATE AND SAFETY IN ITALIAN PATIENTS

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Introduction: Systemic juvenile idiopathic arthritis (sJIA) accounts for 10-20% of all patients with JIA. The demonstration of a key role of IL-1 and IL-6 in the pathogenesis of the disease, led to consider sJIA an autoinflammatory disease: this explain the successfully use of IL-1 and IL-6 inhibitors. While the efficacy and safety of anakinra in sJIA is widely documented, there are no reports on large series of patients treated with canakinumab outside of the setting of clinical trials.

Objectives: The aim of this study was to evaluate clinical response rate and disease course of canakinumab in Italian cohort of patients with sJIA.

Methods: This is a retrospective multicenter study. Demographic features, previous medical history and therapies was evaluated for each patients. Clinical features, laboratory parameters and adverse events were collected at baseline and after 6 months from starting canakinumab. Clinically inactive disease (CID) was defined according to Wallace criteria.

Results: We enrolled 82 (50 F) patients with sJIA treated with canakinumab from 2006 to 2020; 75 of them reached a follow up of 6 months. At baseline 49 patients (59.8%), of which 36 in active disease (AD) and 13 in CID, were previously treated with anakinra, while 33 patients in AD (40.2%) were naïve. At 6 months of follow-up 51/75 patients (68%) met criteria of CID off-glucocorticoids, including all 13 patients in CID at baseline, 19 patients in AD previously treated with anakinra and 19 patients naïve. Twenty-four patients (32%) maintained AD. To evaluated if the response to canakinumab might be related to the baseline features we excluded 13 patients in CID at baseline; we divided the 62 patients in responders (38/62, 61.3%) and non-responders (24/62, 38.7%). There were no significant differences between the two groups regarding demographic, clinical and laboratory parameters, except for a higher number of active joints ($p=0.021$) and for a greater use of disease-modifying antirheumatic drugs (DMARDs) ($p<0.0001$) in non-responders patients (Table). No major adverse events nor cases of macrophage activated syndrome were recorded.

Conclusion: Canakinumab was able to induce CID in patients in AD at baseline (both in naïve patients and in patients previous treated with anakinra) and to maintain clinical remission achieved with anakinra. The percentage of clinical response is in keeping with what reported in literature, even if we did not found predictive factors of response.

Trial registration identifying number:

The study was performed after approval by the ethics committee of the “Ospedale Pediatrico Bambino Gesù” with the ethics approval number 1683 OPBG 2018.

The study was performed after approval by the ethics committee of the “Ospedale Pediatrico Bambino Gesù” with the ethics approval number 1683 OPBG 2018.

Consent: I have obtained written consent

Disclosure of Interest: None declared

Lightening talks: Basic and translational science

O030

EXAMINING HEALTH OUTCOMES IN JUVENILE IDIOPATHIC ARTHRITIS- A GENETIC EPIDEMIOLOGY STUDY

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Introduction: Juvenile idiopathic arthritis (JIA) is the most common paediatric rheumatic disease, however there is limited data on other health-related outcomes in JIA patients.
Objectives: The aims of this study were to use publicly available genome-wide association study (GWAS) datasets to interrogate the genetic correlation between JIA and a broad range of health-related traits. We then sought to examine whether JIA was causally associated with any correlated traits.
Methods: We used publicly available JIA GWAS data (sample size 15872) and the LDHub platform to implement linkage disequilibrium score regression (LDSC) to explore genetic correlation (r_g) between JIA and 832 other health traits across the life course. Results were adjusted for multiple testing based on the false discovery rate (FDR). For non-autoimmune traits correlated with JIA (FDR-adjusted p value, P_{adj}, <0.05), we then conducted two sample Mendelian randomisation (2SMR) to examine evidence of causality. We employed multiple sensitivity analyses to ensure the evidence was robust. MR estimates for continuous outcomes are reported as beta coefficients and for binary outcomes are transformed onto the odds ratio scale.
Results: We found robust evidence of positive genetic correlation between JIA and seven human traits: “rheumatoid arthritis” (r_g 0.63, P_{adj} 0.029), “coeliac disease” (r_g g 0.58, P_{adj} 0.032), “systemic lupus erythematosus” (r_g 0.40, P_{adj} 0.032), “coronary artery disease” (CAD, r_g 0.42,P $6.0x10^{-3}$), “hypothyroidism/myxoedema” (r_g 0.61, P_{adj} $4.1x10^{-5}$), “number of non-cancer illnesses” (r_g 0.42, P_{adj} 0.016) and “paternal health” (r_g 0.57, P_{adj} 0.032). There was robust evidence of negative correlation with “strenuous sports” (r_g -0.52, P_{adj} 0.032). In addition, we found some evidence for genetic correlation between JIA and a number of unfavourable cardiometabolic traits. Using 2SMR we identified robust evidence for a causal relationship between genetically predicted JIA and “number of non-cancer illnesses”(2SMR causal estimate beta 0.021, 0.008-0.034). The 2SMR estimate for genetically predicted JIA and CAD (OR 1.05, 95% CI 0.98-1.12), “paternal health” (OR 1.05, 95% CI 0.98-1.13) and “strenuous sports” (OR 0.98, 95% CI 0.96-1.00) provides very little evidence of a causal relationship between these traits and JIA despite their high genetic correlation.
Conclusion: We show evidence of genetic correlation between JIA and a several novel and important long-term health outcomes, particularly coronary artery disease and other systemic and organ-specific autoimmune disorders. Although 2SMR analysis suggests the association between JIA and CAD is one of correlation rather than causation, our findings support the observational literature regarding the need for cardiovascular risk assessment and management of JIA patients, and the consideration of routine thyroid function monitoring and coeliac screening.
Disclosure of Interest: None declared

O031

PATIENTS WITH PERIODIC FEVER, APHTHOUS STOMATITIS, PHARYNGITIS AND ADENITIS (PFAPA) SYNDROME HAVE DIFFERENTIAL METHYLATION IN INTRON REGIONS OF PIK3AP1 AND SPON2 GENES

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Introduction: Periodic fever, aphthous stomatitis, pharyngitis and adenitis (PFAPA) syndrome is the most common periodic fever syndrome in children, often grouped together with hereditary periodic fever syndromes, although its cause and hereditary nature remain unexplained. Genes known to be involved in inflammation seem to contribute to a predisposition to PFAPA syndrome, suggesting complex genetic inheritance.
Objectives: We investigated whether a differential DNA methylation was present in DNA from peripheral blood mononuclear cells in patients with PFAPA versus a group of healthy young individuals.
Methods: A whole epigenome analysis (Methylated DNA Immunoprecipitation (MeDIP) and Methyl-CpG-binding domain (MBD)) was performed using pooled DNA libraries enriched for methylated genomic regions. Of identified candidate genes, two most significantly different regions were further evaluated with methylation specific restriction enzymes coupled with qPCR (MSRE-qPCR).
Results: MSRE-qPCR proved to be a quick and reliable method to confirm results from MeDIP and MBD. Differential methylation was observed in patients with PFAPA. The analysis showed that the first intron region of *PIK3AP1* (BCAP) is hypermethylated ($P<0.0001$) and that the fifth intron region of the *SPON2* (spondin-2) is differentially methylated (hypomethylated ($P=0.001$) and hypermethylated ($P=0.0191$)) in patients with PFAPA compared to healthy individuals. Both B cell adapter protein (BCAP) as PI3K binding inhibitor of inflammation and spondin-2 as a pattern recognition molecule and integrin ligand could play a role in etiology of PFAPA.
Conclusion: Our findings indicate that BCAP and spondin-2 could be involved in the pathogenesis of PFAPA, their role and the effect of changed DNA methylation in PFAPA etiology and autoinflammation need further investigation.

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Disclosure of Interest: None declared

O032

CELL DAMAGE AND PATHOGEN-ASSOCIATED TLR4 LIGANDS FUNDAMENTALLY DIFFER IN THEIR ABILITY TO INDUCE TYPE I INTERFERON EXPRESSION

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Introduction: Damage and pathogen-associated molecular patterns (DAMPs, PAMPs) can strongly activate innate immune cells via sensors such as toll-like receptors (TLRs). DAMPs are particularly important players in sterile inflammation. In diseases such as systemic juvenile idiopathic arthritis (systemic JIA) and disease-complicating macrophage activation syndrome (MAS) the TLR4-signaling DAMPs S100A8/A9 and A12 are highly overexpressed and are thought to trigger and perpetuate inflammation. However, TLR4-signaling is not exclusively pro-inflammatory. Upon receptor internalization, an alternative pathway is initiated, which induces prominent type I interferon (T1-IFN) expression.
Objectives: We recently reported on a critical role of IFNa/b in regulating IL-18 expression in hyperinflammation and MAS, which results in its sensitivity to JAK/STAT-inhibition in both murine models as well as patients (Verweyen *et al.*, Am J Respir Crit Care Med, 2020). While this study was largely built on PAMP (LPS) stimulations, we next wondered whether a purely sterile inflammatory environment as in systemic JIA can be sufficient to already induce T1-IFN expression and may thus operate as driver of the high IL-18 levels observed in disease.
Methods: In human PBMCs we investigated pro-inflammatory as well as IFN-related gene expression resulting from LPS, S100A8/A9, S100A12, serum amyloid A (SAA), Apolipoprotein A1 (ApoA1), HMGB1 and type I or type II interferon-stimulations. Different concentrations and stimulation times as well as inhibitors for LPS-signaling and LPS-binding protein (LBP) were tested. Stimulation-induced TLR4-internalization was analyzed by flow cytometry.
Results: In contrast to previous results obtained from experiments built on LPS-stimulations (Verweyen *et al.*, Am J Respir Crit Care Med, 2020), we initially observed, that S100A12-treatment of primary human monocytes did not result in comparable *IL18* expression. Broadened analyses of pro-inflammatory and IFN-related gene expression in LPS, S100A12, IFNa or IFNg-treated human PBMCs revealed, that in contrast to LPS, S100A12 - even when far beyond physiological levels - failed in inducing *IFI27*, *IFI44L*, *IFIT1*, *ISG15* and *RSAD2* expression. *IL1A*, *IL1B*, *IL1RN* and *IL6* expression was induced at levels comparable to LPS. When investigating stimulated cells by flow cytometry, we observed no TLR4-internalization by S100A12-treated human monocytes. *Vice versa*, inhibition of LBP, which has been assigned a fundamental role in TLR4-internalization, impaired LPS-induced receptor endocytosis, which resulted in abrogation of T1-IFN-related gene expression as observed with S100A12 treatment. When testing stimulations with other TLR4-dependent DAMPs (S100A8/A9, SAA, ApoA1, HMGB1) alongside with S100A12 we universally observed pro-inflammatory but no *IFIT1*, *ISG15* and *RSAD2* expression compared to LPS.
Conclusion: In contrast to LPS, TLR4-dependent DAMPs fail to enable LBP-driven receptor internalization. In consequence, this restricts DAMP-signaling to the MyD88-dependent pro-inflammatory pathway and excludes TRIF-dependent T1-IFN expression. As T1-IFN acts as natural negative regulator of IL-1, while it is strictly required for *IL18* expression, this has fundamental consequences on how TLR4-dependent DAMPs shape a sterile inflammatory environment in diseases such as systemic JIA.

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Disclosure of Interest: None declared

O033

SEX DIFFERENCES IN JUVENILE-ONSET SLE SUSCEPTIBILITY AND CARDIOVASCULAR RISK COULD BE ASSOCIATED WITH ALTERED TREG PHENOTYPE AND LIPOPROTEIN METABOLISM

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Introduction: Males and females have altered immune responses resulting in variation in autoimmune and cardiovascular risk (CVR). Recently, these differences have played a role in the inflammatory response to COVID-19 infection. Sex differences exist in the frequency and activity of immune-cell subsets but mechanisms underlying sexual dimorphism remain unknown. Our previous work identified a link between immune cell function and lipid metabolism. We hypothesised that sex hormones could influence immune cell differentiation via changes in lipid metabolism and this could be altered in autoimmune diseases such as juvenile-onset systemic lupus erythematosus (JSLE), a disease that emerges during puberty, results in an increased CVR and has a strong female prevalence.
Objectives: We investigated sex differences in T-cell subset frequency and function during adolescence in healthy donors and JSLE patients, including the relationship with lipid metabolism and CVR.
Methods: Flow cytometry and qPCR were used to measure metabolic marker expression on 44 immune cell subsets from 39 teenage healthy controls (HCs, 17 male, 22 female, mean age 19), 35 age matched JSLE patients (12 male, 23 female, mean age 19), pre puberty HCs (10 males and 10 females, mean age 8) and individuals with gender dysphoria undergoing cross-sex hormone therapy (10 biologic males and 10 biologic females). Analysis of metabolic biomarkers, including lipoprotein composition, was performed on matching serum using nuclear magnetic resonance.
Results: HC responder (Tresp) and regulatory (Treg) T-cell subsets displayed the strongest immune profile differences by sex with significantly increased Tregs ($p= 0.036$) and reduced Tresp ($p= 0.001$) frequencies in males compared to females. HC Male Tregs had an increased suppressive capacity, IL-4 production ($p= 0.019$) (supported by increased GATA-3 expression) and plasma membrane glycosphingolipid (GSL) expression ($p= 0.038$) compared to Tregs from HC females. GSL changes were mirrored by increased expression of GSL synthesis enzyme UGCG ($p= 0.042$) in male Tregs, suggesting a sex-specific alteration in lipid metabolism related to Treg function.
Metabolomic lipoprotein analysis of matching serum revealed that teenage HC males had significantly reduced atheroprotective high density lipoprotein subsets and increased atherogenic very low density lipoprotein (VLDL) subsets compared to HC females. These differences were not observed pre-puberty but were induced appropriately by sex hormone treatment in gender dysphoria individuals; suggesting that sex hormones regulate lipid metabolism in vivo.
VLDL subsets from HC males were preferentially enriched with triglycerides and correlated positively with activated Treg subsets compared to VLDL from HC females where no such relationship was seen. Furthermore, Tregs cultured with VLDL isolated from either HC males or females recapitulated the male and female Treg phenotype respectively. Strikingly, sex differences in Treg frequency, phenotype, lipid metabolism and serum lipoproteins were lost in patients with JSLE. This loss of sexual dimorphism in JSLE patients involved the development of a more atherogenic metabolomic profile and pro-inflammatory T-cell phenotype in females.
Conclusion: Potential defects in sex hormone signalling in patients with JSLE may lead to a loss of differential male/female lipid taxonomy. Defective lipoprotein metabolism in JSLE could alter immune cell plasma membrane lipids and immune cell function and contribute to increased CVR in female JSLE patients.
Disclosure of Interest: None declared

O034

EXAMINING THE ROLE OF IFN-I AND LANGERHANS CELL ADAM17 IN LUPUS PHOTOSENSITIVITY

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Introduction: Photosensitivity resulting in inflammatory skin lesions is a hallmark of cutaneous lupus. Lesions can be disfiguring and have a negative impact on quality of life. Understanding photosensitivity is critical to developing better treatment. Our lab showed ADAM17, a metalloprotease found on Langerhans cells (LCs), is activated by UVR and is critical for limiting UVR-induced keratinocyte apoptosis and skin inflammation through cleavage and activation of epidermal growth factor receptor (EGFR) ligands. Two photosensitive SLE models showed reduced LC ADAM17 expression with evidence for dysfunction in human SLE, suggesting that photosensitivity is at least in part due to dysfunctional LCs. A prominent IFN signature has been documented in the blood and skin of SLE patients and could be an upstream mediator of ADAM17. We thus hypothesized that Type I IFN downregulates LC ADAM 17 activity resulting in photosensitive rash in SLE.
Objectives: Our primary objective was to examine gene expression patterns in non-lesional skin of human and murine lupus skin. We seek to develop an LC ADAM17- deficient gene expression signature and hypothesize the presence of a prominent IFN signature further demonstrating a potential link between interferon and ADAM17 downregulation.
Methods: Transcriptomics of non-lesional skin from discoid lupus (DLE) and healthy controls and of MRL and MRL/lpr mice were compared. Human data was gathered from unpublished data from Krueger et al (2014) using microarray in DLE lesions compared to psoriasis and healthy skin. We performed RNA seq on non-lesional skin of MRL and MRL/lpr mice. Data were analyzed in R using edgeR. Gene set analyses were performed with QuSAGE and plots were generated using a custom Shiny platform developed by the HSS Genomics Center. To examine whether LCs show an IFN-I regulated gene signature, we are currently sorting LCs from both UVR-exposed and non-exposed WT and Adam 17 fl/fl Langerin Cre mice for RNA seq. Using the IRB approved method of suction blistering to sample immune cells in the skin, our plan is to gather LCs from the skin of SLE patients to determine LC ADAM17 activity and whether this correlates with interferon signature via RNA seq.
Results: IFN-I regulated genes were among the most differentially regulated genes in non-lesional skin in both human and the MRL/lpr lupus mouse model. Many interferon regulated genes were found to be highly expressed in both (Fig 1A, D). Pathway analysis further showed that IFN-I-regulated genes were among the most differentially regulated pathways in disease vs control skin for both humans and mice (Fig 1B, E). Preliminary results from the analysis of ADAM17fl/fl Langerin Cre mice are expected in the next several months.
Conclusion: Microarray results suggest an elevated IFN signature in non-lesional skin of DLE patients with a similar IFN signature found in MRL/lpr mice via RNA sequencing. We anticipate that we will detect a reduction in ADAM17 activity in non-lesional skin of human SLE patients and find a correlation with IFN signature, supporting a potential role for IFN-I in dysregulating ADAM17 in lupus photosensitivity. These findings could help to understand why type I IFN targeted therapies are having success in SLE skin disease and may lead to targeting of ADAM17 for lupus. In the future, we hope to determine whether the gene signature associated with ADAM17 deficiency can be seen in other inflammatory skin conditions, such as dermatomyositis.
Disclosure of Interest: None declared

O035

SYNOVIAL TISSUE RESIDENT MEMORY T CELLS MEDIATE ARTHRITIS FLARES

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Introduction: Resident memory T cells (T_{RM}) are site-specific memory T cells that take up long-term residence in peripheral tissues and aid in local immune defense. T_{RM} have also been implicated in autoimmune diseases by driving localized recurrent inflammation.
Objectives: As chronic arthritis is characterized by recurrent site-specific joint inflammation, we sought to investigate the role of T_{RM} in joint-specific memory.
Methods: We performed 10x genomics droplet-based single cell RNA sequencing and immune repertoire profiling on memory T cells disaggregated from human rheumatoid arthritis synovium to evaluate transcriptomic signature. We also used Mantra multispectral immunofluorescence microscopy to evaluate T cells expressing common T_{RM} protein markers in human arthritic synovial tissue sections. To assess the functional contribution of T_{RM} cells in arthritis in vivo, we generated a novel murine model of joint-specific recurrent synovitis. We utilized adoptive transfer, in vitro metabolic and migration assays, in vivo cell labeling, and localized depletion strategies to characterize T_{RM} cells in the synovium and their functional role in arthritis flare.
Results: We identified cells with the phenotypic and transcriptomic signature of T_{RM} within human arthritic synovium. These cells were primarily CD8+ and exhibited restricted T cell receptor clonotypes as well as a pro-inflammatory gene expression profile. Adoptive transfer studies in our animal model of joint-specific recurrent inflammation confirmed that arthritis flares were mediated by antigen-specific CD8+ T cells that remained within previously inflamed joints during remission. These cells were bone fide T_{RM}, as confirmed through surface signature, failure to migrate in vivo or in vitro, preferential uptake of free fatty acids, and long-term residency. Site-specific depletion of synovial T cells during remission markedly ameliorated disease recurrence, confirming a role of synovial T_{RM} in arthritis flares.
Conclusion: Here, we demonstrate that synovial T_{RM} present in human inflamed synovium are a targetable mediator of joint-specific memory in arthritis.
Disclosure of Interest: None declared

O036

AN ACTIVE PRONGF/P75NTR AXIS IN ARTHRITIS PATIENTS INFLUENCES CYTOKINE PRODUCTION IN SYNOVIAL FIBROBLASTS

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Introduction: Inflammation has been associated with a marked increase in the basal levels of NGF in tissues, but how NGF and its immature form proNGF, regulate cell functions and mediator release during inflammatory responses is still largely unknown. In this study, we investigated the effects of proNGF, the biological active NGF precursor, on inflammatory cytokine production in synovial fibroblasts to clarify whether changes in proNGF concentration or in the expression of its specific receptor p75NTR are involved in joint inflammation.
Objectives: To investigate whether proNGF and its specific receptor p75NTR modulate distinct pro-inflammatory pathways in synovial fibroblasts of chronic arthritis patients and whether p75NTR/proNGF axis inhibition dampens inflammatory cytokine production.
Methods: NGF expressions, TrkA, p75NTR expression and signaling in synovial fibroblasts from arthritis patients were evaluated by quantitative PCR (qPCR) and Western Blot Analysis. Specific ELISA were used to analyze NGF, proNGF and cytokine production. *In vitro* inhibition of p75NTR was performed using a synthetic inhibitors (LM11A-31) that blocks the binding site of proNGF.
Results: High amounts of proNGF were detected in the synovial fluid of chronic arthritis patients. *In vitro* stimulation of patient synoviocytes with recombinant cytokines strongly enhanced the release of proNGF in conditioned media as well as the expression of p75NTR. Inhibition of p75NTR significantly decreased the release of inflammatory mediators as IL-6, Il-1β, IL-8, MCP1. To recreate *ex vivo* the condition of an inflamed synovia, synovial fibroblasts were cultured in media enriched with 30% synovial fluid (SF) obtained from active Juvenile Idiopathic Arthritis (JIA) patients and that contained high concentration of inflammatory mediators and high proNGF amounts. As expected, synoviocytes cultured in 30% SF significantly enhanced the release of IL-6 and other inflammatory cytokines in the conditioned media. The inhibition of proNGF binding to p75NTR using LM11A-31, strongly decreased inflammatory cytokines release. This reduction was even more substantial of the one obtained using monoclonal antibodies against IL-6 R (tocilizumab), IL-1β (canakinumab) and TNFα (infliximab) commonly used for arthritis treatment. The analysis of the intracellular pathways in LM11A-31 treated synoviocytes showed a decreased phosphorylation of MAPK downstream molecules like p38 and JNK, indicating that inhibition of proNGF binding to p75NTR results in a decreased activity of the pro-inflammatory cascade response.
Conclusion: Inflammatory stimuli induce both p75NTR expression and the release of proNGF in synoviocytes. Blocking the binding of proNGF to its receptor p75NTR, using LM11A-31 inhibitor, strongly reduces in synoviocytes the release of inflammatory mediators, suggesting that enhanced p75NTR expression levels might have a crucial role in the chronicity of the inflammatory response and prospect the use of p75NTR inhibitors as a new therapeutic approach to chronic arthritis.
Disclosure of Interest: None declared

O037

COEXISTENCE OF SYNOVIAL T LYMPHOCYTES DRIVING AND REGULATING CHRONIC INFLAMMATION IN JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: T lymphocytes accumulate in inflamed tissues of patients with juvenile idiopathic arthritis (JIA) and they can express pro-inflammatory cytokines upon re-stimulation in vitro. This and a significant genetic linkage of JIA to MHC genes suggest that T lymphocytes play an important role in the pathogenesis of this disease. But their role in established disease is less clear.

Objectives: We aimed to define the transcriptional and clonal identity of autoreactive memory T cells in patients with JIA.

Methods: We isolated paired samples of antigen-experienced conventional CD4+CD45RO+CD25lo T helper memory cells (T_{cons}), regulatory CD4+CD45RO+CD127loCD25hi T memory cells (T_{regs}) and cytotoxic CD8+CD45RO+ T memory cells (CTLs) by flow cytometry from the synovial fluid (SF) and the blood of seven patients with JIA. Subsequently, we performed single-cell sequencing combined with T cell receptor (TCR) sequencing on 74.891 cells to dissect their cell heterogeneity due to their transcriptional profiles and clonal repertoire. We then performed shared nearest neighbor-clustering using dimensional reduction analysis by t-distributed stochastic neighbor embedding (t-SNE).

Results: Our data reveal transcriptional heterogeneity among the different subsets of T memory cells both in peripheral blood as well as in cells derived from inflammatory tissues. TCR sequencing and gene expression of TCR signaling-induced genes enabled us to distinguish autoreactive from bystander memory T cells. Gene expression profiles of expanded recently activated clonotypes showed elevated expression of *PDCD1* (encoding for PD-1) compared to non-enriched bystander T helper memory cells from the inflamed tissue. A PD-1$^+$*TOX*$^+$*EOMES*$^+$ population of CD4$^+$ T lymphocytes expressed immune regulatory genes and genes attracting myeloid cells. A PD-1$^+$*TOX*$^+$*BHLHE40*$^+$ population of CD4$^+$, and a mirror population of CD8$^+$ T lymphocytes expressed genes driving inflammation as well as genes supporting B lymphocyte activation. This dichotomy among *PDCD1*-expressing cells represents a general, lineage-transcending signature of memory T lymphocytes in chronic inflammation, since both CD4$^+$ and CD8$^+$ T memory cells possess analogous populations. Finally, we identified autoreactive T lymphocyte clones and transcriptional signatures of recirculating SF-derived cells in the blood of JIA patients.

Conclusion: Taken together, these results might offer a basis for developing diagnostic and therapeutic strategies for patients with JIA i), by developing biomarkers on the basis of recirculating autoreactive memory T cells and ii), by treating patients with agents to selectively deplete memory T cells driving pathology in chronic inflammation.

Disclosure of Interest: None declared

O038

IDENTIFICATION OF A REGULATORY PATHWAY GOVERNING EXPRESSION OF TRAF1 VIA A JIA-ASSOCIATED NON-CODING VARIANT

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Introduction: Over the past decade, genome-wide association studies (GWAS) have identified TRAF1/C5 locus as a risk locus for rheumatoid diseases including RA and JIA(1, 2), and TRAF1 negatively regulates Toll-like receptor signaling(3). However, the exact risk variant within that locus and its underlying mechanism regulating TRAF1 expression is still not known.
Objectives: We aim to identify non-coding variant in TRAF1/C5 locus governing the expression of TRAF1 gene and its regulatory pathway.
Methods: Single-nucleotide polymorphisms (SNPs) in linkage disequilibrium (LD) with the most disease associated SNP in TRAF1/C5 locus from immunochip data (5 thousands JIA patients and 14 thousands health controls) were high-throughput screened by SNP-seq(4). Top candidates' regulatory function were further validated by Electrophoretic mobility shift assay (EMSA) and luciferase reporter assay. Then the transcriptional factor that might binds to the functional variant after validation was tested by CHIP-qPCR, oligo pulldown assay as well as supershift assay. Finally, the association between this transciptional factor and TRAF1 gene expression were analyzed by RNAi knockdown experiment.
Results: After screening by SNP-seq, EMSA and luciferase reporter assay, rs7034653 was found to be the best functional non-coding variant in TRAF1/C5 locus that is associated with JIA. EMSA shows that protein from monocyte nuclear extract has a preferential binding to protective allele A than the risk allele G of rs7034653, and that binding preference likely regulates higher gene expression as shown by luciferase reporter assay, which is consistent of existing eQTL data that shows higher expression of TRAF1 in protective allele than risk allele in human monocytes. Furthermore, this variant is found to be able to bind to AP1 transcriptional factor FRA2. Suppressed expression of FRA2 by RNAi leads to lower expression of TRAF1 after LPS stimulation in THP-1 monocytic cell line.
Conclusion: Non-coding variant rs7034653 in TRAF1/C5 locus likely regulates TRAF1 gene expression in monocytes through binding to transcriptional factor FRA2.

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Disclosure of Interest: None declared

O039

A NOVEL LOSS-OF-FUNCTION MUTATION IN LACC1 UNDERLIES HEREDITARY JUVENILE ARTHRITIS WITH EXTENDED INTRA-FAMILIAL PHENOTYPIC HETEROGENEITY

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Introduction: Recent clinical reports link early-onset hereditary JIA with likely-pathogenic homozygous variants in the *Laccase (multicopper oxidoreductase) domain-containing 1* gene - *LACC1* (*C13orf31*, *FAMIN*, MIM 613409). Interestingly, a shared *LACC1* likely-pathogenic variant was independently reported in association with either monogenic JIA or severe pediatric Crohn's disease..
Several associations studied have linked *LACC1* risk variants with increased susceptibility to leprosy and to various autoimmune disorders, including ulcerative colitis, psoriasis, Behcet and ankylosing spondylitis.

Objectives: To reports the intra-familial phenotypic heterogeneity associated with early onset Juvenile Idiopathic Arthritis (JIA) secondary to *LACC1* disruption, and to describe its effect on infalmatory pathways.
Methods: Whole exome sequencing (WES) in a consanguineous Israeli-Muslim family with autosomal recessive polyarticular JIA and extra-articular involvement including renal amyloidosis and Crohn's disease.
Expression studies of an identified homozygous truncating variant variant in *LACC1* in patient-derived macrophages (Mϕ) and Cytokine profile analysis in WT and LACC1-disrupted Mϕ.
Results: Whole exome sequencing (WES) in a consanguineous Israeli-Muslim family with autosomal recessive polyarticular JIA and extra-articular involvement including renal amyloidosis and Crohn's disease, identified a novel homozygous truncating variant (p.Glu348Ter) in *LACC1* as underlying the disease. The p.Glu348Ter variant is predicted to cause premature stop of the LACC1 protein sequences, is absent from ethnically-matched control samples and from public variation databases, and is predicted harmful by prediction software. Expression studies of p.Glu348Ter-LACC1 in patient-derived macrophages (Mϕ) indicate lack of endogenous RNA transcription and protein expression, most probably secondary to nonsense-mediated mRNA decay. Cytokine profile analysis in WT and LACC1-disrupted Mϕ indicate increased levels of pro-inflammatory chemokines and cytokines in affected as compared to WT cells, thereby implicating a role for *LACC1* disruption in pro-inflammatory molecular pathways.
All the described family members with JIA showed remarkable response to Tocilizumab therapy, causing sustained improvement of their arthritis, and resolution of amyloidosis in the affected family member.
Conclusion: Taken together, our findings reinforce the role of LACC1 disruption in autosomal recessive JIA, extend the clinical spectrum and the intra-familial heterogeneity of the disease-associated phenotype, and suggest an inhibitory role for wild-type *LACC1* on pro-inflammatory pathways.
Disclosure of Interest: None declared

O040

ROLES OF INTESTINAL BARRIER AND MICROBE-ASSOCIATED MOLECULAR PATTERNS IN THE PATHOGENESIS OF INFLAMMATORY ARTHRITIS

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Introduction: Juvenile idiopathic arthritis (JIA) is the most common childhood-onset chronic rheumatic disease. The cause of JIA remains unknown. A growing body of evidence suggest that intestinal microbiota and intestinal barrier dysfunction may play a pivotal role in the pathophysiology of JIA. Furthermore, some publications suggest a putative role of Microbe-Associated Molecular Patterns (MAMPs) for the development of murine models of arthritis. In order to develop new treatment approaches for inflammatory arthritis it is necessary to better understand the putative link between intestinal barrier dysfunction and development of inflammatory arthritis.

Objectives: To study the link between changes in the intestinal permeability, systemic translocation of microbial components and development of arthritis in mice.

Methods: We used the collagen induced arthritis (CIA)model and IL1Ra KO mice that is a spontaneous model of arthritis. Severity was assessed by a clinical score. Intestinal permeability was studied *ex vivo* using translocation of labelled marker in Ussing chambers.

Results: Oral treatment with carrageenan (CGN) increased intestinal permeability (mean 859 vs 313pmol/cm^2/h, $p<0.01$) and was associated with a more severe arthritis (mean 3.6 vs 1.3, $p<0.01$). In accordance with previous publications on intestinal-conditional HNF4aKO mice, we observed increased intestinal permeability (794 vs 379 pmol/cm^2/h, $p<0.05$). Furthermore, they exhibited a higher score of collagen-induced arthritis (1.7 vs 0.77, $p<0.05$). The worsening effect of CGN on arthritis was also confirmed in IL1RaKO mice (mean 2.7 vs 0.5, $p<0.05$). Treatment with CGN and deleting intestinal HNF4a were associated to an increased *ex vivo* translocation of muramyldipeptide (MDP) (respectively $p=0.001$ and $p=0.03$) and lipopolysaccharide (LPS)($p=0.04$ and $p=0.04$). Oral treatment with probiotic Vsl3 reduced intestinal permeability (mean 277 vs 667 pmol/cm^2/h, $p<0.05$) and decreased *ex vivo* translocation of muramyldipeptide (MDP) ($p=0.01$) and lipopolysaccharide (LPS)($p=0.01$). Furthermore, VSL3 tended to decrease the severity of arthritis in the CIA (mean 3.7 vs 11.3,$p=0.07$) and in the IL1RaKO (mean 2.2 vs 0.4, $p<0.05$) mouse models. While oral treatment with MDP and LPS did not affect the intestinal permeability, it exacerbated collagen induced arthritis (mean 3.2 vs CTRL mean 0, $p<0.01$). The worsening effect of treatment with MDP and LPS was also confirmed in the IL1RaKO arthritis model (mean 2.9 vs 0.5, $p<0.01$).

Conclusion: Changing the intestinal permeability impacted on the severity of arthritis. Bioavailable MDP and LPS contribute to the development of arthritis. Further experiments are necessary to understand how exactly systemic MAMPs leads to worsening of arthritis.

Disclosure of Interest: None declared

O041

APPLICATION OF SYSTEMS BIOLOGY-BASED IN SILICO TOOLS TO OPTIMIZE TREATMENT STRATEGY IN STILL'S DISEASE

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Introduction: Systemic Juvenile Idiopathic Arthritis (sJIA) and Adult Onset Still's Disease (AOSD) are manifestations of an autoinflammatory disorder with complex pathophysiology and significant morbidity, together also termed Still's disease.
Objectives: To investigate the optimal treat-to-target strategy for Still's disease by in silico models based on systems biology.
Methods: Molecular characteristics of Still's disease and data on biological inhibitors of interleukin (IL)-1 (anakinra, canakinumab), IL-6 (tocilizumab, sarilumab), glucocorticoids as well as conventional disease-modifying anti-rheumatic drugs (DMARDs, methotrexate) were used to construct in silico mechanisms of action (MoA) models by means of Therapeutic Performance Mapping System technology (TPMS). TPMS combines artificial neuronal networks (ANN), sampling-based methods and artificial intelligence. The models were validated with publicly available expression data from sJIA patients.
Results: Biologicals demonstrated more pathophysiology-directed efficiency than non-biological drugs. IL-1 blockade mainly acts on the innate immune system, while IL-6 signaling blockade has a weaker activity on the innate immunity and rather affects the adaptive immunity (Table 1). The MoA models showed that the IL-1β inhibitor canakinumab is more efficient than the IL-6 receptor inhibiting antibody tocilizumab in the autoinflammatory/systemic phases of Still's disease. MoA models reproduced 67% of the information obtained from expression data.
Table 1. Summary of ANN scores. A) Global Still's disease evaluation. B) Immune system component. ANN scores mean the probability of the resulted relationship is true positive: +++ correspond to values >78% (p-value<0.05); ++ correspond to values > 59% (p-values <0.15) and; + correspond to values > 38% (p-value<0.25).

A) Still's disease molecular definition		**Biologics**				**Non-biologics**	
		Anakinra	**Canakinumab**	**Sarilumab**	**Tocilizumab**	**Methotrexate**	**Prednisone**
Still's disease		+++ (81%)	+++ (86%)	+++ (85%)	+++ (85%)	- (5%)	++ (70%)
	Systemic profile	+++ (80%)	+++ (88%)	+++ (85%)	+++ (85%)	- (4%)	++ (70%)
	Rheumatic profile	+++ (87%)	+++ (92%)	+++ (81%)	+++ (81%)	- (9%)	++ (64%)
B) Immune system components		**Biologics**				**Non-biologics**	
		Anakinra	**Canakinumab**	**Sarilumab**	**Tocilizumab**	**Methotrexate**	**Prednisone**
Innate immune system deregulation		++ (71%)	++ (71%)	+ (55%)	+ (55%)	- (10%)	++ (65%)
Adaptive immune system	**T-cell response activation**	+ (45%)	- (37%)	++ (71%)	++ (71%)	- (25%)	+ (47%)
	Defective immune regulation	- (19%)	- (37%)	+ (47%)	+ (47%)	- (15%)	+ (50%)

Conclusion: Systems biology-based modelling supported the preferred use of biologics as immunomodulatory treatment strategy for Still's disease. This further encourages early IL-1β blockade in initial autoinflammatory/systemic phases of Still's Disease to prevent the development of disease or drug-related complications. Further studies are needed to determine the optimal timeframe of the window of opportunity for canakinumab treatment.
Disclosure of Interest: M. Coma Employee of: Anaxomics Biotech, C. Segú-Vergés Employee of: Anaxomics Biotech, C. Kessel: None declared, S. Smeets Employee of: Novartis, D. Foell Consultant for: Novartis, Chugai-Roche, Paid Instructor for: Novartis, Pfizer and SOBI, A. Aldea Employee of: Novartis

O042

INTERFERON-Γ DRIVES THE EXPRESSION OF T-BET IN NAÏVE B CELLS OF PATIENTS WITH PAEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS

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Introduction: Paediatric systemic lupus erythematosus (pSLE) is an autoimmune disorder of childhood characterized by the production of autoantibodies against nuclear antigens. In the last decade, several studies showed an up-regulation of genes induced by type I interferons (IFNα) in peripheral blood and tissues of pSLE patients[2]. It has been reported that the expression of this group of genes, known as the type I IFN signature, correlates with disease activity[2]. More recently, also the type II interferon (IFNγ) has been implicated in pSLE; however, its precise role has not been clarified yet[3].
Objectives: To investigate the role of IFNγ in the pathogenesis of pSLE evaluating: 1) the expression levels of IFNγ-related genes in the peripheral blood of pSLE patients; 2) the expression of T-bet in B cells of pSLE patients; the induction of T-bet in B cells by IFNγ.
Methods: Expression levels of IFNα-induced genes (IFI27, IFI44L, IFIT1, RSAD2, ISG15, SIGLEC1), IFNγ and IFNγ-induced genes (CXCL9, CXCL10, IDO1) were analysed by quantitative PCR (qPCR) in whole blood of pSLE patients and healthy donors (HDs). We developed a type II IFN score similarly to the type I IFN score described by Crow[4]. Expression of T-bet in B cells was evaluated by flow cytometry. Peripheral blood mononuclear cells (PBMCs) from 5 HDs were stimulated *in vitro* with recombinant human IFNγ and IFNα2b; expression of T-bet was evaluated by flow cytometry. Serum levels of CXCL9 were evaluated by ELISA. For each patient, SLEDAI was calculated.
Results: Expression levels of both IFNα and IFNγ-induced genes were upregulated in patients with pSLE (n=39). The type II IFN score significantly correlated with the SLEDAI (r = 0.33, P = 0.03). As previously reported, also the type I IFN score significantly correlated with SLEDAI (r = 0.50, P < 0.01). We also found increased serum levels of CXCL9 in pSLE patients compared to HDs (mean±SD HD 333±117pg/mL, SLE 2125±4885pg/mL, P=0.0003). Thus, patients with pSLE have increased activity of IFNγ .
B cells play a crucial role in the pathogenesis of SLE. In murine models of SLE, IFNγ was shown to activate B cells to make autoantibodies[4]. We evaluated the expression of T-bet (a transcription factor that is thought to be induced specifically IFNγ) in B cells: we observed a population of B cells expressing T-bet in the naïve compartment in patients with pSLE. The frequency of T-bet+ naïve B cells correlated with SLEDAI. To confirm the induction of T-bet in B cells by IFNγ, we stimulated PBMCs of HD with either IFNγ or IFNα: both chemokines induced the expression of T-bet in naïve B cells. Since it is known that IFNα can induce the expression of IFNγ, we stimulated cells with IFNα and an antibody blocking IFNγ: in this setting IFNα did not upregulate the expression of T-bet in B cells.
Conclusion: Our data suggest a potential role of IFNγ in the pathogenesis of pSLE. IFNγ-induced genes in whole blood and CXCL9 in serum were increased in pSLE patients. IFNγ specifically induced the expression of T-bet in naïve B cells. We observed an expansion of T-bet+ naïve B cells in patients with pSLE. Thus, IFNγ is hyperactiaved in SLE, inducing the aberrant expression of T-bet in naïve B cells. Further research is needed to dissect the role of IFNγ-activated B cells in pSLE.
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Disclosure of Interest: None declared

O043

IN VITRO ANALYSIS OF STANDARD OF CARE DRUGS ON THE IFN TYPE I SIGNATURE; ASPIRIN AND HYDROXYCHLOROQUINE THE OLD KIDS ON THE BLOCK

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Introduction: Childhood-onset Systemic Lupus Erythematosus (cSLE) is prototypic Interferon (IFN) driven autoimmune disease characterized by an increased expression of type-I IFN stimulated genes, known as the IFN signature. The inhibitory effects of various drugs like Hydroxychloroquine and more recently Aspirin on IFN inductions routes led to the idea that some standard of care drugs might be the cause of a low IFN score observed in a subgroup of treated patients. For this, testing these, but also other standard of care immunosuppressive agents in an *in vitro* model for their effect on IFN activation would lead to new knowledge and a broader view of the mechanisms that lead to a patient having an increased expression of the IFN signature or not.
Objectives: To study the effect of immunosuppressive medication on the type-I IFN signature in an *in vitro* model
Methods: Freshly isolated human PBMCs were stimulated with or without CpG-A or Imiquimod (IQ) or transfected with the cGAS agonist G3-YSD to induce IFN upregulation through the TLR7/9- and DNA Sensing Receptor-pathway respectively. To assess the direct role of the drugs on the downstream pathway of the IFNAR PBMCs were stimulated with IFN-a2b. Aspirin, diclofenac, HCQ, Mycophenolate Mofetil (MMF) and prednisone were added separately to these cultures followed by analysis of MxA by qPCR. Cell viability in all culture conditions was above 85%.
Results: The IFN signature induced by CpG-A, IQ, G3-YSD and IFN-a2b was significantly reduced after addition of Aspirin in three separate experiments. Addition of diclofenac showed a trend towards reduced levels in all conditions. HCQ was able to significantly reduced the CpG-A and IQ induced IFN activation while MMF and prednisone did not show an effect in any of the culture conditions.
Conclusion: The IFN signature induced through various routes was significantly reduced by Aspirin and HCQ in an in vitro model. Combining both clinical and *in vitro* data from our longitudinal cohort will elucidate the effect of different immunosuppressive drugs on the type-I IFN signature in cSLE.
Disclosure of Interest: None declared

Lightening talks: Juvenile Idiopathic arthritis and uveitis

O044

SUBCHONDRAL HIGH T2 SIGNAL IN PEDIATRIC SACROILIAC JOINT MRI: A NORMAL FINDING THAT CAN MIMIC SACROILIITIS

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Introduction: Understanding of the normal magnetic resonance imaging (MRI) appearance of the developing sacroiliac joint (SIJ) is important for distinguishing normal developmental variations from disease. Subchondral signal changes in SIJ in children can give rise to diagnostic challenges and false positive diagnoses of sacroiliitis, as they can mimic bone marrow edema (BME).
Objectives: To determine how subchondral signal intensity on T2-weighted images in SI-joints in children varies with age, sex and closure of segmental apophyses of the sacrum.
Methods: MRI of 502 SIJ in 251 children (132 girls), mean age 12.4 years (range 6.1-18.0), were obtained. Ethics committee approval was obtained, informed consent was signed by all children and parents. 127/251 had asymptomatic joints and were imaged for non-rheumatologic reasons in whom we added semi-coronal T1 and STIR of the SI joints, and 124 had low back pain but no sign of sacroiliitis on initial clinical MRI review. Before the main reading exercise, images of 10 participants (20 SIJ) who had been excluded from the study were used for multi-step calibration exercises. Three calibration rounds were conducted over 8 months. Subchondral high signal (‘flaring’) was defined as increased signal in subarticular bone on STIR images compared to normal bone marrow in the centre of S1 and S2 vertebral bodies. After calibration, three subspecialist radiologists independently scored subchondral signal changes from 0-3 in 4 locations: vertical sacral (along the lateral apophyses of the sacrum), horizontal sacral (along the intersegmental apophyses), iliac (vertically along iliac side of SIJ), and iliac crest (horizontally along iliac wing upper margin), separately for left and right sides. The degree of closure of sacral segmental apophyses was graded as well. Readers were blinded to demographic, clinical and other imaging findings. Associations between patient age, sex, signal changes and apophyseal closure were analysed.
Results: Rimlike subchondral increased T2 signal or ‘flaring’ was commonly seen in children at the margins of the SI joints, and is far more common on the sacral side (72% vs 16%, p<.001). It was symmetrical in >90% of children. Iliac flaring scores were always lower than sacral, except for 1 child. Signal changes decreased as sacral apophyses closed, and were seen in <20% of subjects with fully closed apophyses. Signal changes were more frequent in boys, and peaked in intensity later than for girls (ages 8-12 vs. 7-10). Subchondral signal in iliac crests was high throughout childhood and did not correlate with other locations. We found no significant difference between left/right side, boys/girls nor between both groups.
Conclusion: Rimlike subchondral high T2 signal 'flaring' is commonly observed at MRI of sacroiliac joints in children, and should not be confused with pathology. It is generally sacral-predominant, symmetrical, and seen in less than 1/5 of children after segmental apophyses are closed. Flaring that is asymmetrical, greater in ilium than sacrum, or intense in a teenager with closed apophyses, is unusual for normal children and raises concern for pathologic bone marrow edema. Subchondral signal in iliac crests is high throughout childhood and cannot be used for reference in diagnostic criteria. Accurately distinguishing between normal and pathologic pediatric subchondral sacroiliac joint signal changes requires understanding the patterns of normal variation, to avoid misdiagnosis of sacroiliitis.
Disclosure of Interest: None declared

O045

FOOT AND ANKLE MRI IN JIA: DEVELOPMENT AND PRELIMINARY VALIDATION OF A PAEDIATRIC-TARGETED MRI SCORING SYSTEM FOR THE ASSESSMENT OF DISEASE ACTIVITY AND DAMAGE.

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Introduction: Arthritis of the ankle occurs commonly in all subtypes of JIA and might cause considerable functional impairment. Clinical assessment of this region is often challenging due to the multiplicity of joint recesses and surrounding tendons**.**

Objectives: (1) to explore the value of MRI in the assessment of the ankle/foot; (2) to set-up a MRI scoring system to assess disease activity and damage in this region, and provide preliminary evidence of its validity in JIA patients.

Methods: 101 patients with JIA and clinical ankle/foot involvement were recruited from the Paediatric Rheumatology of Gaslini Institute and Ospedale Pediatrico Bambino Gesù between 2015 and 2018The clinically more affected ankle/foot was investigated with MRI and radiography (CR). One-year MRIs follow-up were available in 53 patients. Images were scored according to a MRI semi-quantitative score developed for the purpose, which included grading of synovitis, bone marrow oedema (BMO), bone erosions and cartilage lesions. Validation procedures included analysis of reliability, construct validity and responsiveness to change. Foot and ankle MRIs, obtained from 39 age-matched healthy controls, were included to evaluate the discriminant ability.

Results: Concordance between MRI and clinical evaluation in the assessment of disease activity was poor at the subtalar (70% of patients showed synovits on MRI whereas this joint was clinically involved in 39% of them) and talonavicular joints (54.4% of patients had synovitis on MRI versus 11% of patients with clinical active disease). MRI visualized tenosinovitis in 68.3% of patients, while clinical examination revealed tendons involvement in 19.8% of them. BMO was visualised in 49/101 (48.5%) patients. Bone erosions and cartilage damage were detected by MRI in 56/101 (56%) and 37/101 patients (36.6%), respectively. The MRI score showed an excellent inter-reader agreement for synovitis, tenosynovitis, BMO, bone erosions and cartilage damage scores (interclass-correlation coefficient>0.9 for each items). The MRI synovitis and tenosynovitis scores were moderately correlated with clinical variables reflecting disease activity, such as the total count of swollen joints (r 0.44 and r 0.54) and the JADAS-71 (r 0.46 and r 0.47). The median values of MRI bone erosion and cartilage scores were significantly higher in patients with radiographic damage compared to patients without structural damage on CR ($p<0.05$). The responsiveness to change was satisfactory for the MRI synovitis (standardized response mean (SRM) 1.09) and tenosynovitis (SRM 0.85) scores, moderate for the MRI bone erosion score (SRM 0.41) and poor for the BMO score (SRM 0.27). MRI revealed synovitis in 6/39 (15%) healthy children; one healthy child showed bone profile changes resembling bone erosion. BMO was detected in 20/40 (50%) healthy children.

Conclusion: Foot and ankle MRI is more sensitive than clinical evaluation to identify the single anatomic components that are affected by the disease, with relevant implications for therapeutic intervention. The proposed paediatric MRI score appears to be a reliable and valid tool for assessing disease activity and damage in JIA patients with foot and ankle involvement. BMO is present in a relevant percentage of healthy children, thus significantly limiting its prognostic value.

Disclosure of Interest: None declared

O046

EARLY ACHIEVEMENT OF JADAS ACCEPTABLE DISEASE ACTIVITY IS STRONGLY PREDICTIVE OF ONE-YEAR REMISSION IN ETANERCEPT-TREATED POLYARTICULAR JIA PATIENTS: RESULTS FROM A BIKER COHORT

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Introduction: Although an early onset of clinical improvement is thought to be a key factor in determining treatment success in juvenile idiopathic arthritis (JIA), the minimal early treatment response required to achieve remission remains undefined.
Objectives: We assessed Juvenile Arthritis Disease Activity Score (JADAS) and American College of Rheumatology (ACR) criteria for response to treatment at 3 months as a predictor of treatment success at one year in polyarticular JIA (pJIA) using a well-defined cohort of pJIA patients newly starting etanercept.
Methods: Patients from the German Biologics registry for Pediatric Rheumatology (BiKeR) with a diagnosis of pJIA initiating etanercept treatment were identified. Response to treatment at 3 months was determined according to JADAS improvement of disease activity[1], JADAS acceptable (ADA, JADAS≤5.4) and minimal disease activity (MDA, JADAS≤3.8), as well as to ACR improvement criteria. Primary outcome measures at one year were JADAS remission (JADAS≤1) and ACR defined inactive disease. Data were analysed using intention-to-treat.
Results: Altogether, 968 patients (758 females, 78.3%) with pJIA (491/132 RF negative/positive polyarthritis, 293 extended oligoarthritis, 52 PsA) were included. Mean age and disease duration at baseline were respectively 11.2±4.2 and 4.1±3.5 years. Achievement of JADAS improvement, ADA or MDA at 3 months correlated to 2.2 (1.5-3.3), 5.0 (3.5-7.2) and 5.4 (3.9-7.5) times higher odds to achieve JADAS remission, and to 2.6 (1.8-3.9), 3.7 (2.7-5.3) and 4.7 (3.4-6.5) times higher odds to achieve ACR inactive disease at one year compared to failure to meet these criteria, respectively. Achievement of ACR30/50/70 response at 3 months was associated to 2.3 (1.5-3.5), 2.2 (1.5-3.1) and 3.2 (2.3-4.3) times higher likelihood to achieve JADAS remission, and to 2.3 (1.6-3.5), 2.5 (1.7-3.5) and 3.1 (2.3-4.3) times higher likelihood to achieve ACR inactive disease at one year compared to failure to meet these responses, respectively. Failure to achieve a response to treatment, JADAS or ACR-defined, at 3 months showed a high negative predictive value (NPV) for attainment of JADAS remission or ACR inactive disease at one year (s. table).

	Response at 1 year							
	JADAS remission				ACR inactive disease			
Response at 3 months	Rate (%)	OR (95%CI)	P value	NPV (%)	Rate (%)	OR (95%CI)	P value	NPV (%)
JADAS impr	42	2.2 (1.5-3.3)	<0.0001	76	41	2.6 (1.8-3.9)	<0.0001	79
JADAS ADA	50	5.0 (3.5-7.2)	<0.0001	83	47	3.7 (2.7-5.3)	<0.0001	81
JADAS MDA	56	5.4 (3.9-7.5)	<0.0001	81	54	4.7 (3.4-6.5)	<0.0001	80
ACR30	42	2.3 (1.5-3.5)	<0.0001	76	41	2.3 (1.6-3.5)	<0.0001	77
ACR50	43	2.2 (1.5-3.1)	<0.0001	74	43	2.5 (1.7-3.5)	<0.0001	77
ACR70	51	3.2 (2.3-4.3)	<0.0001	75	50	3.1 (2.3-4.3)	<0.0001	76

Conclusion: Achievement of JADAS ADA / MDA at 3 months was significantly associated with better remission outcome at one year in etanercept-treated pJIA. Conversely, ACR30/50/70 and JADAS improvement did not strongly predict treatment success at one year. Our data suggest that, in a treat-to-target concept, attainment of at least JADAS ADA at 3 months may be meaningful.

References: [1] Horneff G et Becker I. Rheumatology. 2014;53:1229-34
Disclosure of Interest: G. Armaroli: None declared, A. Klein: None declared, K. Minden: None declared, I. Foeldvari Consultant for: Chugai, Novartis, A. Hospach Speaker Bureau of: Chugai, Roche, Novartis, F. Weller-Heinemann: None

declared, R. Trauzeddel: None declared, J. Kuemmerle-Deschner Consultant for: Novartis, Sobi, G. Horneff Speaker Bureau of: Pfizer, Abbvie, Chugai, Novartis

O047

PATIENT-REPORTED ADVERSE EVENTS AND TREATMENT ADHERENCE IN JIA: ANALYSIS OF TWO LARGE INTERNATIONAL COHORTS

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Introduction: Juvenile idiopathic arthritis (JIA) patients may experience significant adverse effects (AEs) from medications. AEs may negatively affect patients' well-being and reduce treatment compliance, ultimately compromising patient outcomes.
Objectives: 1) To assess the frequency of patient-reported adverse events (AEs) and their effects on well-being, health-related quality of life (HRQoL) and school activity.
2) To investigate treatment non-adherence and its determinants, focusing on the possible impact of AEs.
Methods: Data on 13704 visits of 8402 patients were obtained from two large multi-center international studies, the pharmacovigilance registry Pharmachild and The EPidemiology, treatment and Outcome of Childhood Arthritis (EPOCA) cohort. Subjects who were on medications at the time of visit were included. AEs, currently prescribed medications, root of administration, disease-related school problems, self-reported treatment adherence (as a dichotomic variable), reasons for non-compliance, patient overall well-being (PGA), physician global assessment (MD-global) and VAS-rated pain intensity were collected through the Juvenile Arthritis Multidimensional Assessment Report (JAMAR). HRQoL was assessed through a ten items Likert-type HRQoL scale encompassing a physical health (PhH) and psychosocial health (PsH) subscale, with higher scores indicating worse outcomes. The effects of AEs on PGA, PsH scale, school problems, and the determinants of therapy non-compliance were analyzed using General Linear and Generalized Mixed Effects Models with random intercepts per individual**.**
Results: AEs were reported by 29,49% of patients. Experiencing one or more AEs was associated to worse PGA (β 0.377, η^2 0.011, $p < 0.001$) and PsH score (β 0.618, η^2 0.024, $p < 0.001$) and school problems (OR 1.82, 95%CI 1.64-2.01, $p < .001$) after adjustment for MD-global, PhH and pain levels. Mood swings, sleep problems and weight gain showed the highest impact on PsH; frequency of the main AEs and regression estimates for outcomes are depicted in the table. Treatment non-adherence was reported by 9,27% of subjects. The most frequently cited reasons for non-adherence were drug refusal by the child (n=200) and fear of adverse events (n=142). Self-reported medication adherence was negatively associated to combination treatment with conventional and biologic DMARDs (OR 0.40, 95%CI 0.26-0.62, $p < .001$) and subcutaneous administration (OR 0.13, 95%CI 0.09-0.20, $p < .001$). Nausea predicted non-compliance due to fear of AEs (OR 13.93, 95%CI 5.02-38.65, $p < .001$).

AEs	Frequency (%)	PGA		PsH Scale	
		β	p	β	p
Nausea	11.4	0.061	0.221	0.065	0.279
Headache	6.5	0.155	0.010	0.385	< .001
Gastric pain	6.1	0.182	0.003	0.293	< .001
Mood swings	5.4	0.548	< .001	153.654	< .001
Vomit	4.8	0.058	0.406	0.065	0.432
Sleep problems	3.5	0.253	0.002	0.659	< .001
Injection site reaction	3.3	0.164	0.034	0.097	0.287
Weight gain	3.2	0.113	0.157	0.499	< .001

Conclusion: AEs have a substantial impact on patients' quality of life, functioning and therapy adherence in JIA. Understanding treatment-related burden is vital to achieve good therapeutic compliance and improve outcomes in JIA.
Disclosure of Interest: None declared

O048

TOFACITINIB FOR THE TREATMENT OF POLYARTICULAR COURSE JUVENILE IDIOPATHIC ARTHRITIS: PATIENT-REPORTED OUTCOMES IN A PHASE 3, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED WITHDRAWAL STUDY

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Introduction: Tofacitinib is an oral Janus kinase inhibitor that is being investigated for juvenile idiopathic arthritis (JIA).
Objectives: To evaluate the impact of tofacitinib on parent/patient-reported outcomes (PROs) in patients (pts) with polyarticular course JIA (pcJIA: extended oligoarthritis, systemic JIA without systemic features, rheumatoid factor-positive polyarthritis or rheumatoid factor-negative polyarthritis).
Methods: This was a Phase 3, randomised, double-blind (DB), placebo (PBO)-controlled withdrawal study in pts aged 2–<18 years with pcJIA, psoriatic arthritis or enthesitis-related arthritis. In the 18-week open-label (OL) phase (Part 1), pts received tofacitinib (5 mg twice daily or weight-based equivalent dose in pts <40 kg). Pts with ≥JIA ACR30 response at Week (W)18 were blindly randomised 1:1 to continue receiving tofacitinib or switch to PBO in the DB phase (Part 2; W18−44). This post hoc analysis assessed PROs in pts with pcJIA in Parts 1 and 2 including: mean values for the 3 Childhood Health Assessment Questionnaire (CHAQ) domains (Disability Index, parent/pt assessment of child pain and parent/pt assessment of child overall well-being) and mean scores for the 15 Child Health Questionnaire (CHQ) health concepts, and the CHQ physical (PhS) and psychosocial (PsS) Summary Scores.
Results: In Part 1, 184 pts with pcJIA received OL tofacitinib; of these, 142 were blindly randomised in Part 2 to continue receiving tofacitinib or switch to PBO. Improvements in the 3 CHAQ domains occurred from Part 1 baseline (BL) up to W18 with tofacitinib (Table). At W44, each CHAQ domain had improved from Part 2 BL (W18) by a numerically greater extent with tofacitinib vs PBO (Table). Mean scores for the 15 CHQ health concepts, and the PhS (Table), improved from Part 1 BL to W18 with tofacitinib, with these improvements generally sustained with tofacitinib and PBO in Part 2. The CHQ PsS was within the range of a healthy normative population (ie mean 50 [standard deviation 10]) at Part 1 BL and remained as such throughout the study (Table).
Table. CHAQ and CHQ in pts with pcJIA

	Part 1		**Part 2**			
	Tofacitinib[a]		**Tofacitinib[a]**		**PBO**	
	Part 1 BL	**W18**	**Part 2 BL**	**W44**	**Part 2 BL**	**W44**
CHAQ domain,[b] mean (SE)	**N=184**	**N=154**	**N=72**	**N=49**	**N=70**	**N=33**
Disability Index	1.01 (0.05)	0.51 (0.05)	0.47 (0.06)	0.29 (0.07)	0.48 (0.07)	0.33 (0.08)
Parent/pt assessment of child pain	5.20 (0.20)	2.07 (0.17)	1.86 (0.23)	1.02 (0.22)	1.95 (0.23)	1.71 (0.33)
Parent/pt assessment of child overall well-being	4.91 (0.19)	2.09 (0.16)	1.94 (0.22)	0.99 (0.17)	1.89 (0.23)	1.36 (0.29)
CHQ score,[b] mean (SE)	**N=182**	**N=150**	**N=71**	**N=49**	**N=67**	**N=31**
Physical Summary Score	30.24 (1.14)	43.73 (0.91)	45.28 (1.11)	48.68 (1.32)	43.97 (1.41)	44.53 (2.08)
Psychosocial Summary Score	47.82 (0.78)	52.41 (0.74)	52.49 (1.05)	52.23 (1.33)	52.30 (1.08)	54.13 (1.48)

[a]5 mg twice daily or weight-based equivalent dose in pts <40 kg
[b]Missing data not imputed
BL=baseline; CHAQ=Childhood Health Assessment Questionnaire; CHQ=Child Health Questionnaire; N=number of pts; pcJIA=polyarticular course juvenile idiopathic arthritis; PBO=placebo; pt=patient; SE=standard error; W=Week
Conclusion: In pts with pcJIA, tofacitinib demonstrated sustained improvements in PROs, as measured by the CHAQ and CHQ.
Acknowledgements: Study sponsored by Pfizer Inc. Medical writing support was provided by Emma Deeks, CMC Connect, and funded by Pfizer Inc.
Trial registration identifying number: ClinicalTrials.gov (NCT02592434)

Disclosure of Interest: N. Ruperto Grant / Research Support from: Bristol-Myers Squibb, Eli Lilly, GSK, Janssen, Novartis, Pfizer Inc, Roche and Sobi, Consultant for: AbbVie, Ablynx, AstraZeneca-MedImmune, Bristol-Myers Squibb, Biogen, Boehringer Ingelheim, Eli Lilly, EMD Serono, GSK, Janssen, Merck, Novartis, Pfizer Inc, Roche, R-Pharm, Sanofi, Servier, Sinergie, Sobi and Takeda, Speaker Bureau of: AbbVie, Ablynx, AstraZeneca-MedImmune, Biogen, Bristol-Myers Squibb, Boehringer Ingelheim, Eli Lilly, EMD Serono, GSK, Janssen, Merck, Novartis and Roche, D. J. Lovell Grant / Research Support from: AbbVie, Bristol-Myers Squibb, Janssen, Novartis, Pfizer Inc, Roche and UBC, Consultant for: Abbott, Amgen, AstraZeneca, Boehringer Ingelheim, Celgene, GSK, Novartis, Pfizer Inc, Roche, Takeda, UBC and Wyeth; and is a DSMB chairperson for NIH and Forest Research, E. Alexeeva: None declared, J. Chaitow: None declared, P. Chiraseveenuprapund Grant / Research Support from: Pfizer Inc, Consultant for: CARRA and Novartis, M. Erguven: None declared, B. Gottlieb Grant / Research Support from: AbbVie, Janssen, Pfizer Inc and UCB, S. Knupp Oliveira: None declared, M. Klein-Gitelman Grant / Research Support from: AbbVie, Bristol-Myers Squibb, CARRA, LFA, NIH, Pfizer Inc, UCB, Consultant for: AbbVie, S. Ozen Consultant for: Novartis and Pfizer Inc, Speaker Bureau of: Sobi, C. Saad Magalhaes: None declared, D. Gruben Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, R. Germino Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, H. Posner Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, R. Suehiro Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, L. Stockert Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, A. Martini Consultant for: Janssen, Novartis and Pfizer Inc, Speaker Bureau of: AbbVie, Eli Lilly, EMD Serono, Janssen, Novartis and Pfizer Inc, H. I. Brunner Grant / Research Support from: AstraZeneca-MedImmune, Bristol-Myers Squibb, Novartis and Pfizer Inc, Consultant for: AbbVie, AstraZeneca-MedImmune, Bayer, Biocon, Bristol-Myers Squibb, Boehringer Ingelheim, Eli Lilly, Janssen, Novartis, Pfizer Inc, Roche and R-Pharm, Speaker Bureau of: GSK, Novartis and Roche

O049

PREDICTORS OF CLINICAL REMISSION IN CHILDREN WITH EXTENDED OLIGOARTICULAR ARTHRITIS, ENTHESITIS-RELATED ARTHRITIS, OR PSORIATIC ARTHRITIS TREATED WITH ETANERCEPT IN THE CLIPPER STUDIES

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Introduction: CLIPPER is an ongoing, 8-year, phase 3b, multicenter, open-label study of the safety and efficacy of etanercept in the treatment of juvenile idiopathic arthritis (JIA) categorized as extended oligoarticular arthritis (eoJIA), enthesitis-related arthritis (ERA), or psoriatic arthritis (PsA).
Objectives: To identify predictors of sustained 6-month clinical remission on medication using long-term data from CLIPPER.
Methods: Previously reported baseline characteristics of the 127 children enrolled in CLIPPER (60 eoJIA [2–17 years], 38 ERA [12–17 years], and 29 PsA [12–17 years])[1] were analyzed post hoc as possible predictors of the attainment of clinical remission on medication (per the JIA ACR criteria or Juvenile Arthritis Disease Activity Score 71-joint [JADAS] criteria) sustained for 6 consecutive months using univariate logistic regression models and stepwise multivariate models. Clinical response and disease activity status after 4, 8, and 12 weeks of treatment were also evaluated as predictors. Analyses were based on observed cases in CLIPPER and 6 years of follow-up in the CLIPPER2 extension.
Results: Univariate analyses showed that baseline Patient/Parent Global Assessment score, JIA ACR inactive disease (IA) at Week 12, JADAS low disease activity (LDA) at Week 12, and JADAS IA at Week 12 were associated with the attainment of 6-month remission according to both JIA ACR criteria and JADAS criteria (**Table**). Multivariate analyses showed that age at onset and JADAS LDA at Week 12 were predictors of 6-month remission according to JIA ACR criteria, whereas JADAS LDA at Week 12 was a predictor according to JADAS criteria.

Table. Predictors of sustained 6-month clinical remission on medication during the CLIPPER studies

Univariate analyses		
	Definition of remission	
	JIA ACR (N=127)	**JADAS (N=127)**
Patient characteristic	**OR (95% CI)**	**OR (95% CI)**
Age at onset (≤7.61 years vs older)	5.17 (2.31, 11.57)	1.93 (0.90, 4.14)
Patient/Parent Global Assessment score (≤2.5 vs >2.5)	2.67 (1.13, 6.28)	2.75 (1.13, 6.67)
JIA ACR IA at Week 12 (Yes vs No)	5.06 (1.51, 16.99)	4.64 (1.24, 17.38)
JADAS LDA at Week 12 (Yes vs No)	5.83 (2.60, 13.06)	7.06 (3.02, 16.51)
JADAS IA at Week 12 (Yes vs No)	7.00 (2.14, 22.89)	4.10 (1.26, 13.29)
Multivariate analyses		
Definition of remission and patient characteristic	**OR (95% CI)**	
JIA ACR		
Age at onset (≤7.61 years vs older)	7.19 (2.71, 19.09)	
JADAS LDA at Week 12 (Yes vs No)	6.29 (2.46, 16.06)	
JADAS		
JADAS LDA at Week 12 (Yes vs No)	7.68 (3.08, 19.14)	
CI: confidence interval; IA: inactive disease; LDA: low disease activity; OR: odds ratio.		

Conclusion: JADAS LDA at Week 12 of etanercept treatment was a predictor of attaining sustained 6-month clinical remission on medication according to JIA ACR criteria and JADAS criteria during the CLIPPER studies. Younger age at onset was also a predictor according to JIA ACR criteria.

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Trial registration identifying number: NCT0962741, NCT01421069.

Disclosure of Interest: J. Vojinović: None declared, V. Chasnyk: None declared, J. Dehoorne: None declared, V. Panaviene: None declared, J. Akikusa: None declared, T. Avcin Consultant for: AbbVie, Alexion, Octapharma, and Takeda, Speaker Bureau of: AbbVie, Octapharma, and Takeda, J. Chaitow: None declared, B. Lauwerys: None declared, J. Antón Grant / Research Support from: AbbVie, Eli Lilly, GSK, Novartis, Novimmune, Pfizer, Roche, Sanofi, and Sobi, Consultant for: AbbVie, GSK, Novartis, and Sobi, Speaker Bureau of: Novartis and Sobi, I. Penades: None declared, B. Flato: None

declared, A. Boteanu: None declared, H.-I. Huppertz: None declared, J. Jaller: None declared, D. Graham Shareholder of: Pfizer, Employee of: Pfizer, C. Borlenghi Shareholder of: Pfizer, Employee of: Pfizer, B. Vlahos Shareholder of: Pfizer, Employee of: Pfizer, C. Zang Shareholder of: Pfizer, Employee of: Pfizer, N. Ruperto Grant / Research Support from: Bristol-Myers Squibb, Eli Lilly, Novartis, Pfizer, Roche, and Sobi, Consultant for: Astrazeneca-Medimmune, Aurinia, Biogen, Bristol-Myers Squibb, Centrical Global, Domain Therapeutics, Eli Lilly, EMD Serono, GSK, Idorsia, Janssen, Novartis, Pfizer, Sinergie, and Sobi

O050

EVALUATION OF ANTI-HBS AND ANTI-VZV ANTIBODY LEVELS IN JUVENILE IDIOPATHIC ARTHRITIS PATIENTS TREATED WITH CLASSICAL DISEASE MODIFYING DRUGS AND BIOLOGICS

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Introduction: Juvenile idiopathic arthritis(JIA) is the most common chronic arthritis in children. The effects of classical disease modifying anti-rheumatic drugs(DMARDs) and biological drugs on vaccine responses in patients are controversial.
Objectives: The aim of our study was to evaluate the childhood vaccine responses against hepatitis B and varicella zoster virus of patients with JIA using classical DMARDs and biologic drugs.
Methods: Our study included 95 JIA patients who received classical DMARDs (methotrexate,salazopyrin,leflunomide,cyclosporine, hydroxychloroquine), 95 JIA patients who received biological drugs(anti-TNF, anti-IL-6, anti-IL-1 and CTLA4-Ig) and 91 healthy controls between the ages of 2-19 years. All participants were vaccinated according to our country's routine vaccination program in infancy. The anti-HBs and anti-VZV IgG antibody levels of participants were evaluated. Also the patients receiving DMARDs and biologic treatments were assessed within each group separately.
Results: Anti-HBs and anti-VZV IgG titers were not different in patients with DMARDs, patients with biologics and healthy controls(p=0.094), (p=0.22) . The duration of biologic treatment was longer in patients with anti-HBs negative in biologic group(p=0.023), and was found to be a risk factor for anti-HBs negativity (OR:0.978 95%CI 0.961-0.966, p=0.012) in univariate logistic regression. However, the duration of biological treatment did not affect anti-VZV positivity(p=0,553). Significant relationship was not detected between the duration of DMARDs therapy and anti-HBs(p=0.721) and anti-VZV(p=0.560) positivity.

Table1. Comparison of the characteristics of controls, patients with DMARDs and patients with biologics

Variable	**Control (n=91)**	**Patients with DMARDs (n=95)**	**Patients with biologics (n=95)**	**p value**
Age, year (median, range)	13,0(4-18)	12,52(2,08-18,17)	13,58(2,91-19,75)	-
Gender				-
Female(n, %)	45(49.5%)	59(62.1%)	60(63.2%)	
Male(n, %)	46(50.5%)	36(37.9%)	35(36.8%)	
JIA subtypes(n, %)				-
Oligoartikülar JIA	-	59(62,1%)	31(33.7%)	
ERA	-	18(18.95%)	24(24.2%)	
RF- polyarticular JIA	-	8(8.42%)	24(25.2%)	
RF+ polyarticular JIA	-	5(5.26%)	2(2.1%)	
Systemic JIA	-	5(5.26%)	9(9.5%)	
Psoriatic arthritis	-	-	3(3.16%)	
Undifferantiated	-	-	2(2.1%)	
DMARDs duration, months (median, range)	-	15,0(1-105)	37,05(1-140)	0,000
Biologic duration, months (median, range)	-	-	30,6(1,33-115,0)	-
Anti-HBs(n, %)				
Positive(>10 IU/L)	50(54.9%)	67(70.5%)	64(67.4%)	0,065
Negative(<10 IU/L)	41(45.1%)	28 (29.5%)	31(32.6%)	
Anti-VZV IgG(n, %)	81(89%)	77(81.1%)	81(85.3%)	0,313
Positive(>110 IU/L)	10(11%)	18(18.9%)	14(14.7%)	
Negative(<110 IU/L)				
Anti-HBs titer(IU/L) (median, range) (±SD)	12,95 (2-1000) (±140,53)	19,47 (2-1000) (±205,4) 484 (0-5000) (±1426,1)	26,1 (2-1000) (±180,97) 430 (0-5000) (±1460,81)	0,094
Anti-VZV IgG titer(IU/L)				0,223

(median, range) (±SD)	916,0 (0-5000) (±1294,8)			
DMARDs, disease modifying anti-rheumatic drugs; ERA, enthesitis related arthritis; JIA, juvenile idiopathic arthritis; RF, rheumatoid factor				

Conclusion: We found that the anti-HBs and anti-VZV positivity are not different in patients with JIA from healthy controls. However, the duration of biologic therapy is a risk factor for negative anti-HBs titers.

Disclosure of Interest: None declared

O051

VALIDITY AND RELIABILITY OF FOUR PARENT/PATIENT REPORTED OUTCOME MEASURES FOR JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: In the last years, the interest in the assessment of parent- and child-reported outcomes (PCROs) in paediatric rheumatic diseases is gaining increasing importance. These measures reflect the parent and child perception of the disease course and effectiveness of therapeutic interventions and may facilitate concordance with physician's choices, improve adherence to treatment, and participation in a shared decision -making strategy. Moreover, the availability of reliable PCROs could be crucial for remote monitoring of patients when in person clinical evaluation may be difficult or even not possible.
Objectives: Aim of this work is to provide further evidence of validity and reliability for four PCRO measures included in the OMERACT JIA core domain set: the evaluation of the child's pain and of the child's level of disease activity, the assessment of the morning stiffness (MS) duration, and an active joint count for parent/patient proxy or self-assessment.
Methods: Pain and disease activity were rated on a 21-numbered circle scale corresponding to the traditional VAS (0=no pain; 10=extreme pain). MS was measured with a 5-point Likert scale. The proxy- and self-assessment of active joints was obtained by rating the presence of pain or swelling in the following joints or joint groups: cervical spine, lumbo-sacral spine, shoulders, elbows, wrists, small hand joints, hips, knees, ankles, and small foot joints. To each joint or joint group, one point was given in case of monolateral involvement, two points in case of bilateral involvement. Patients were included in a multinational dataset of patients enrolled in the Epidemiology Treatment and Outcome of Childhood Arthritis study. Criterion validity was assessed by examining the correlation of the four tested measures with physician centered measures, ESR, and composite disease activity scores. To further assess the validity of the tools correlations of the measure with the cJADAS10 were computed after grouping patients by ILAR category, by geographic area, and by education level. Reliability was assessed in a subset of subjects with Spearman correlations and intraclass correlation coefficients (ICC), comparing two visits 7-14 days apart.
Results: A total of 8,848 parents and 6,204 patients had all the evaluations available. Correlations of tested measures were in the moderate range (0.4–0-7) with physician centered measures and in the poor range (< 0.4) with ESR. The level of correlation of the tested parent measures with the cJADAS10 remained stable after grouping patients by ILAR category. In the same analysis with patients grouped in eight geographic areas, correlation levels were similar, although, on average, they were higher in Latin America and slightly lower in North America. The levels of correlation with the cJADAS10 were similar in subjects in which the level of education of the parent filling the questionnaire was elementary or lower, high school, or degree, respectively. In 442 parents and 344 children, correlations between first and second assessment was > 0.7 for all measures; ICC ranged between 0.79 and 0.87 for parents and 0.81 and 0.88 for children.
Conclusion: The four tested PCROs showed good criterion validity and excellent reliability. These tools can be considered for remote patient assessment, when in person evaluation might not be possible.
Disclosure of Interest: C. Trincianti: None declared, E. H. P. Van Dijkhuizen: None declared, S. Calandra: None declared, L. De Miglio: None declared, M. Mazzoni: None declared, F. Ridella: None declared, T. Herlin: None declared, M. Cattalini: None declared, H. Sanner: None declared, G. Susic: None declared, F. Sztajnbok: None declared, D. Maritsi: None declared, T. Constantin: None declared, N. Ruperto Consultant for: Ablynx, Astrazeneca-Medimmune, Aurinia, Biogen, Boehringer, Bristol Myers and Squibb, Centrical Global, Domain Therapeutics, Eli-Lilly, EMD Serono, Glaxo Smith and Kline, Hoffmann-La Roche, Idorsia, Janssen, Merck, Novartis, Pfizer, R-Pharma, Sanofi, Servier, Sinergie, and Sobi., Speaker Bureau of: Ablynx, Astrazeneca-Medimmune, Aurinia, Biogen, Boehringer, Bristol Myers and Squibb, Centrical Global, Domain Therapeutics, Eli-Lilly, EMD Serono, Glaxo Smith and Kline, Hoffmann-La Roche, Idorsia, Janssen, Merck, Novartis, Pfizer, R-Pharma, Sanofi, Servier, Sinergie, and Sobi., A. Ravelli: None declared, A. Consolaro: None declared

O052

LONGITUDINAL EFFECTIVENESS OF ABATACEPT IN JUVENILE IDIOPATHIC ARTHRITIS (JIA): RESULTS FROM AN ONGOING JIA REGISTRY

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Introduction: Abatacept (ABA) is a selective T-cell co-stimulation modulator approved for use in JIA. Efficacy and safety of ABA in patients (pts) with JIA has been demonstrated previously in two Phase III studies.[1,2]
Objectives: Provide data from a real-world setting for longitudinal effectiveness of IV and SC ABA in pts with JIA.
Methods: By protocol, clinical sites in the Pediatric Rheumatology Collaborative Study Group and Paediatric Rheumatology International Trial Organization enrolled pts with JIA currently taking or starting IV or SC ABA. Planned duration of follow-up (FU) is 10 yrs; data were collected up to 31 Mar 2018. Effectiveness was assessed at day of entry into registry (baseline; BL), 3 and 6 mos and 1, 2, 3, 4 and 5 yrs. Safety data were collected at each visit.
Results: 438 were enrolled; 435 were included in the analysis, 346/435 (80%) were female. At BL, 17 (4%) pts were aged 2–5 yrs and median age was 13.6 yrs; JIA disease duration was 4.4 yrs; ABA treatment duration 6.5 mos, number of active joints 1 (mean 2.7). JIA categories were systemic (2%), oligo (23%), poly RF– (55%), poly RF+ (10%), psoriatic (3%), enthesitis-related (3%) and undifferentiated (4%). Total ABA exposure was 474.0 pt-yrs. At 1-yr FU, pts had low MD Global Disease Activity, low Juvenile Arthritis Multidimensional Assessment Report scores and improved joint assessments (Table 1). A higher percentage of pts achieved clinically inactive disease after 1 yr FU vs BL (32 vs 45; Table 1). This trend continued despite low numbers of pts with 4 and 5 yrs of FU. There were 5 serious infections reported (incidence rate [IR] 0.66 /100 pt-yrs of FU, 95% CI: 0.22, 1.55; IR 0.79/100 pt-yrs on treatment, 95% CI: 0.26, 1.84). There were 15 autoimmune events (9 new onset) in 14 patients (IR 1.98/100 pt-yrs of FU, 95% CI: 0.66, 4.65; IR 2.37/100 pt-yrs on treatment, 95% CI: 0.78, 5.52). No malignancies or TB reported. There was 1 death (unrelated pre-existing cardiac problems).

Table 1. Assessment of disease activity and impact

Endpoint	**BL n=435**	**3 mos n=348**	**6 mos n=319**	**1 yr n=296**	**2 yrs n=189**	**3 yrs n=75**	**4 yrs n=21**	**5 yrs n=3**
MD Global Disease Activity[a]	2.0 (0.1)	1.6 (0.1)	1.6 (0.1)	1.2 (0.1)	1.1 (0.1)	1.0 (0.2)	1.0 (0.3)	1.0 (0.6)
Clinical inactive disease (Wallace criteria), %	32	31	37	45	49	47	48	33
No. joints with active arthritis	2.7 (0.3)	2.1 (0.2)	2.2 (0.2)	1.8 (0.2)	1.7 (0.3)	1.8 (0.5)	1.1 (0.4)	0.3 (0.3)
JAMAR functional scale[b]								
Child	5.4 (0.3)	4.7 (0.3)	4.3 (0.3)	4.1 (0.4)	3.6 (0.4)	3.8 (0.6)	4.5 (1.2)	0.7 (0.3)
Parent	6.1 (0.4)	5.7 (0.4)	4.5 (0.4)	3.8 (0.4)	3.2 (0.4)	3.8 (0.8)	4.3 (2.1)	1.0 (–)
JAMAR HRQoL[c]								
Child	7.2 (0.3)	6.0 (0.3)	5.7 (0.3)	5.2 (0.3)	4.5 (0.4)	6.2 (0.7)	7.0 (1.4)	1.0 (0.6)
Parent	7.2 (0.3)	6.4 (0.3)	6.1 (0.3)	5.3 (0.4)	4.4 (0.5)	4.7 (0.8)	6.4 (2.2)	1.0 (--)

Mean (SE), unless otherwise indicated.
[a]Visual analogue scale 0–10; 0=inactive; [b]range 0–15, 0=no functional limitation; [c]range 0–15, 0=best possible HRQoL.
HRQoL=health-related quality of life; JAMAR=Juvenile Arthritis Multidimensional Assessment Report; MD=physician.
Conclusion: In this real-world JIA cohort, abatacept was safe and well-tolerated with no new safety risks identified. This longitudinal analysis further supports the persistent effectiveness of abatacept in pts with JIA.

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Trial registration identifying number: NCT01357668
Disclosure of Interest: N. Ruperto Consultant for: Ablynx, AbbVie, AstraZeneca-Medimmune, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb Company, Eli Lilly, EMD Serono, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, Pharma, Sanofi, Servier, Sinergie, Sobi, Takeda, Employee of: The IRCCS Istituto Giannina Gaslini (IGG), where NR works as a full-time public employee, has received contributions from Bristol-Myers Squibb Company, Eli Lilly, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Novartis, Pfizer, Sobi. This funding has been reinvested for the research activities of the hospital in a fully independent manner, without any commitment with third parties. The registry is funded by Bristol-Myers Squibb Company, Speaker Bureau of: Ablynx, AbbVie, AstraZeneca-Medimmune, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb Company, Eli Lilly, EMD Serono, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, Pharma, Sanofi, Servier, Sinergie, Sobi, Takeda, D. Lovell Consultant for: consultant: AstraZeneca, Boehringer Ingelheim, F Hoffman-La Roche, GlaxoSmithKline, Novartis, UCB; principal/co-principal investigator: Bristol-Myers Squibb Company, F Hoffman-La Roche, Janssen, Pfizer, UCB; board member: Forest Research, N. Tzaribachev: None declared, E. Morgan: None declared, G. Simonini Consultant for: AbbVie, Novartis, Speaker Bureau of: AbbVie, Novartis, T. Griffin: None declared, E. Alexeeva Consultant for: grant/research support and consulting fees: AbbVie, Novartis, Pfizer, Roche, Speaker Bureau of: AbbVie, Novartis, Pfizer, Roche, J. Bohnsack: None declared, A. Zeft Shareholder of: Merck, Opko Health, Teva, G. Horneff Consultant for: AbbVie, Novartis, Pfizer, Sanofi, Speaker Bureau of: AbbVie, Novartis, Pfizer, Sanofi, R. Vehe: None declared, V. Stanevica: None declared, S. Tarvin: None declared, M. Trachana Consultant for: grant/research support: AbbVie, Bristol-Myers Squibb Company, Novartis Hellas, Speaker Bureau of: Novartis Hellas, F Hoffman-La Roche, Pfizer, A. Huber: None declared, I. Orban: None declared, J. Dare Consultant for: grant/research support: AbbVie, Bristol-Myers Squibb Company, F Hoffman-La Roche, Pfizer, UCB, Employee of: Centene Corporation, I. Foeldvari Consultant for: Amgen, Bristol-Myers Squibb Company, Eli Lilly, Novartis, Pfizer, Sanofi, P. Quartier Consultant for: consultant: AbbVie, Bristol-Myers Squibb Company, Chugai-Roche, Eli Lilly, Novartis, Novimmune, Swedish Orphan Biovitrum; board member: Sanofi, Speaker Bureau of: AbbVie, Bristol-Myers Squibb Company, Chugai-Roche, Eli Lilly, Novartis, Novimmune, Swedish Orphan Biovitrum, A. Dominique Shareholder of: Bristol-Myers Squibb Company, Employee of: Bristol-Myers Squibb Company, T. D. Kou Shareholder of: Bristol-Myers Squibb Company, Employee of: Bristol-Myers Squibb Company, R. Wong Shareholder of: Bristol-Myers Squibb Company, Employee of: Bristol-Myers Squibb Company, A. Martini Consultant for: Aurinia, Bristol-Myers Squibb Company, Eli Lilly, EMD Serono, Janssen, Pfizer, H. Brunner Consultant for: Abbott, Amgen, AstraZeneca, Boehringer Ingelheim, Celgene, GlaxoSmithKline, F Hoffman-La Roche, Novartis, Pfizer, Takeda, UCB, Wyeth (funds paid to employer), Speaker Bureau of: F Hoffman-La Roche, GlaxoSmithKline, Novartis

O053

DETERMINANTS OF DISCORDANCE BETWEEN CRITERIA FOR INACTIVE DISEASE AND LOW DISEASE ACTIVITY IN JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: It is currently agreed that disease remission should be an over-riding goal in the management of juvenile idiopathic arthritis (JIA), but the existence of multiple ways in which this target can be assessed in the clinical setting makes its definition more challenging.

Objectives: To assess concordance among criteria for inactive disease (ID) and low disease activity (LDA) in JIA, and to seek for factors driving discordance.

Methods: The frequency of fulfillment of existing ID and LDA definitions was evaluated in 10186 patients extracted from three cross-sectional datasets. Patients were divided in the "functional phenotypes" of oligoarthritis and polyarthritis. Concordance between criteria was examined through Venn diagrams. The role of each individual component in explaining discordance between criteria was assessed by calculating the absolute number and percentage of instances in which the component was responsible for discrepancy between definitions.

Results: ID criteria were met by 31.2 to 41% of patients with oligoarthritis and by 26.5 to 33% of patients with polyarthritis. LDA criteria were met by 44.8 to 62.4% of patients with oligoarthritis and by 44.6 to 50.4% of patients with polyarthritis. There was a 63.2 to 67.1% overlap between ID criteria and a 67.9 to 85% overlap between LDA criteria. The parent global assessment of child's well-being and the physician global assessment of disease activity were responsible for the majority of instances of discordance among ID criteria (9.2-17.5% and 9.6-12%, respectively).

Conclusion: We found fair concordance between definitions of ID and LDA in JIA, with the main drivers of discordance being the physician and parent global assessments. This observation highlights the need for further studies aimed to compare the relationship between physician- and parent-perceived remission and remission assessed by objective measures of inflammatory activity.

Disclosure of Interest: G. Giancane: None declared, C. Campone: None declared, M. F. Gicchino: None declared, A. Alongi: None declared, C. Bava: None declared, S. Rosina: None declared, Y. Boyko: None declared, N. Martin: None declared, Y. El Miedany: None declared, M. Harjacek: None declared, S. Hashad: None declared, M. Ioseliani: None declared, R. Burgos-Vargas: None declared, R. Joos: None declared, C. Scott: None declared, M. Hofer: None declared, Z. M. Ayala: None declared, M. Ekelund: None declared, S. Al-Abrawi: None declared, M.-F. Aiche: None declared, X. Norambuena: None declared, J. A. Melo-Gomes: None declared, N. Ruperto Employee of: BMS, Eli-Lilly, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Novartis, Pfizer, Sobi. This funding has been reinvested for the research activities of the hospital in a fully independent manner, without any commitment with third parties, Speaker Bureau of: Ablynx, Astrazeneca-Medimmune, Aurinia, Biogen, Boehringer, Bristol Myers and Squibb, Centrical Global, Domain Therapeutics, Eli-Lilly, EMD Serono, Glaxo Smith and Kline, Hoffmann-La Roche, Idorsia, Janssen, Merck, Novartis, Pfizer, R-Pharma, Sanofi, Servier, Sinergie, and Sobi, A. Consolaro: None declared, A. Ravelli Consultant for: AbbVie, BMS, Pfizer, Hoffman LaRoche, Novartis, Centocor, "Francesco Angelini" and Reckitt Benckiser

O054

CLINICAL OUTCOMES OF JUVENILE ARTHRITIS IN ADULTHOOD: A SYSTEMATIC REVIEW

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Introduction: Juvenile arthritis (JA) is the most common pediatric rheumatic disease, potentially having permanent functional impacts on patients long after initial diagnosis. There has not been a comprehensive review of these studies to collate and assess the quality of their information.

Objectives: The purpose of this systematic review is to summarize clinical outcomes in adults with JA (age >16) and assessing quality of current literature. We aim to identify areas of knowledge and methodological deficits that should be improved in future studies.

Methods: The systematic review was conducted in MEDLINE and EMBASE (2000-2017) by an academic librarian. Inclusion criteria included prognosis studies focused on quantitative outcomes related to JA, primary data, and adult outcomes.
The quality of publications was assessed using QUality In Prognosis Studies (QUIPS) risk-of-bias tool. QUIPS is classified into six domains of bias - study population, attrition, outcome, prognostic factor, confounding factor and statistical analysis. Papers were graded by trained reviewers who assigned a risk-of-bias grading (low/ moderate/ high) to the overall domain. We identified and extracted all statistically significant study outcomes and information related to studies. Statistical modelling was extracted to help determine the significance and validity of the results.

Results: 56 of 12 243 papers were included in this study for analysis. The majority (50.8%) of studies were cross-sectional, and the most common study queries were disease (34.9%), functional status/psychosocial (22.2%), temporomandibular joint (11.1%), and uveitis (9.5%) outcomes. 13 publications (21%) were repeat publications of non-unique cohorts, with the majority of these using the same cohort from Norway.
In terms of QUIPS, study confounding (95%), participation (81%) and attrition (82.1%) domains had the largest proportion of studies with moderate to high levels of bias.
In disease outcomes, the most common reported were remission (36%), and use of DMARDs (71%). HAQ functional status was reported with a median score of 0.49, signifying mild disability. VAS pain scale had a median score of 6.51 cm. DMARDs and NSAIDs usage ever were reported with 42.8% and 63.3% respectively. Uveitis was reported in 22.9% patients.
Out of 56 papers, 35 performed statistical multivariable modelling. Within each study topic there were no multivariable models of similar outcomes to allow for identification of consistent prognostic factors.
Conclusion: Only 2 (3.1%) truly longitudinal studies focused on the adult outcomes of JA patients. We therefore do not know the disease course information of adults with JA. The evidence in the studies had a high risk of bias in confounding factors, population and attrition, thus should be interpreted with caution. One theme that is not as prevalent is the effectiveness of medication and the complications with medication over time.
Limitations in our paper include being consistent in extracting the many categories of information. There are subjective biases in rating QUIPS as well. Another drawback exists in working with already presented results in published articles, which make come with biases in the information that is presented.
The majority of the studies have high levels of bias in study designs and outcomes. Future literature should describe the source of patients and report the differences between participants and non-participants. Our next step is to categorize outcomes by duration of disease and compare within the same subtype as well as make recommendations on formulating a standard reporting format for future JIA research.

Disclosure of Interest: None declared

O055

RELATIONSHIP BETWEEN PHYSICAL ACTIVITY AND CHARACTERISTICS OF ADOLESCENTS WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA): RESULTS FROM THE GERMAN PAEDIATRIC RHEUMATOLOGIC DATABASE

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Introduction: Adolescence is a challenging period of life involving profound physiological and psychological changes. Developed health-related habits such as regular physical activity (PA) often persist into adulthood, influencing health prognosis and risk of noncommunicable diseases in later life. Adolescents with JIA experience a number of symptoms, which might be aggravated by insufficient PA. Considering the lower levels of PA reported in children with JIA and the presumed tendency for a precipitous decline in subsequent years [1], adolescent patients can be at high risk of missing out on the general health benefits of PA.

Objectives: Since factors influencing the amount of PA can help in understanding and designing targeted interventions, we aimed to i) quantify the weekly frequency of PA and ii) identify its associated characteristics in adolescents with JIA.

Methods: Data from JIA patients recorded in the German Paediatric Rheumatologic Database in the year 2018 were considered for the analyses. In accordance with the WHO definition, early (10-14 years) and mid-late adolescence (15-19 years) were classified. The fulfillment of the WHO recommendations on PA for health was determined on the basis of self-reported outcomes corresponding to the methodology used in the general population survey [2]. Patients met the WHO criteria if they stated to be physically active for at least 60 minutes per day. Analyses of covariance were used to identify factors related to the number of weekdays spent with at least 60 minutes in PA.

Results: In 2018, data of 2.501 patients aged 10 to 14 years (mean age 12.1 ± 1.4 years, female 65%, disease duration 5.3 ± 3.6 years, persistent oligoarthritis 37%) and 2.394 patients aged 15 to 19 years (mean age 16.6 ± 1.2 years, female 67%, disease duration 6.7 ± 4.8 years, persistent oligoarthritis 26%) were analyzed. The proportion of patients who met the recommended level of PA was 27% (10-14-year-olds) and 16% (15-19-year-olds), respectively. According to JADAS-based criteria [3], 11% of mid-late adolescents with inactive oligoarthritis and 10% with inactive polyarthritis stated to achieve the minimum amount of PA on at most 2 days per week. In patients aged 10 to 14 years, cJADAS-10 ($p = 0.027$, $\eta^2 = 0.005$), CHAQ ($P = 0.001$, $\eta^2 = 0.011$) and BMI ($P < 0.001$, $\eta^2 = 0.008$) were significantly associated with PA. In comparison, in 15-19-year-olds were sex ($P = 0.000$, $\eta^2 = 0.015$), CHAQ ($P = 0.001$, $\eta^2 = 0.013$) and BMI ($P = 0.003$, $\eta^2 = 0.006$) significantly related to PA.

Conclusion: About 80% of adolescence with JIA fail to meet the global recommendations on PA, partly despite of an inactive disease state. In order to promote activities of daily life and to implement adequate interventions, JADAS and CHAQ should be controlled. To clarify both the safety of PA and the health risks associated with inactivity, efforts are needed to improve the quality of information provided for parents, health professionals, teachers and patients.

Acknowledgement: The National Paediatric Rheumatological Database has been funded by the German Children Arthritis Foundation (Deutsche Kinder-Rheumastiftung), AbbVie, Pfizer, Chugai and Novartis.

Disclosure of Interest: None declared

O056

INFLUENZA VACCINE UPTAKE AMONG JUVENILE IDIOPATHIC ARTHRITIS(JIA) PATIENTS: A MULTI-CENTRE CROSS-SECTIONAL STUDY

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Introduction: While most countries provide safe&effective influenza vaccines for patients at risk,coverage among target groups like children with rheumatic disease remains uncertain.
Objectives: To assess the influenza vaccination rate in children with JIA,to investigate knowledge,perceptions& practices about influenza vaccine uptake among caregivers of children with JIA and to identify barriers and facilitators that could be used to increase it.
Methods: A multi-center cross-sectional study was performed across 7 countries.Participants completed a questionnaire about influenza vaccination uptake history including the current year(2019-2020),knowledge& perceptions regarding influenza vaccination and demographics and clinical data regarding JIA.Chi-Square and logistic regression models were used;significance level was set at $p \leq 0.05$.
Results: A total of 287 JIA caregivers were surveyed;mean age is 41.6years(SD=7.27), 75.6% females. 7 countries participated in the study(Table).The majority of the participants was employed(72%),married(82.5%) and had tertiary education(50.9%). The commonest diagnosis was oligoarticular JIA(28.9%), while 28.6% of caregivers did not know the child's diagnosis.The mean age of children is 10.5years(SD=4.8) with a median disease duration of 4years(IQR:2-7). Most patients are currently treated systemically(71.4%), mainly with MTX(47%). 13.3% reported previous vaccine side effects;82.2% were fully vaccinated according to national vaccination schedules while 40.9% had received influenza vaccine in the past.
A total of 87 children(30.3%) were vaccinated against influenza for this season and 89.7% of them had a stable disease during the immunization.Most of the participants were informed of the recommendation by attending pediatric rheumatologist(33.4%) or pediatrician(28.2%).The highest vaccine uptake was recorded in Greece(70.8%),followed by Israel(41.9%),while none of the JIA patients from Croatia and Slovakia was vaccinated($p<0.05$).Compared to employed caregivers,unemployed ones were more likely to vaccinate their children(25.7%vs53.3%,$p<0.05$).Children with sJIA had the highest vaccine uptake(65.4%) while caregivers who did not know the child's diagnosis reported the lowest one(12.2%)($p<0.05$).Those who were informed of influenza vaccine recommendations by medical staff and had vaccinated their children in the past were more likely to vaccinate the current season(both $p<0.05$).However,children who had previously experienced adverse vaccine-related events reported the lowest vaccine uptake($p<0.05$).
Among non-vaccinators,59.5% did not have the opportunity to discuss their concerns with a specialist.Major reasons for non-vaccination included unawareness of the need(39.7%),fear of side effects(28.4%) and fear of disease flare(17.1%). The decision for non-vaccination was driven mainly by personal beliefs(41.5%),while 17.5% reported it was a doctor's advice.Among suggestions to improve influenza vaccine uptake,"informing families in advance" was the most commonly cited recommendation(59.6%),followed by "campaigns"(32.4%).

Country	**Participants N(%)**	**Vaccine uptake N(%)**
Israel	62(21.6)	26(41.9)
Greece	65(22.6)	46(70.8)
Slovenia	43(15)	7(16.3)
Slovakia	46(16)	0
Turkey	16(5.6)	5(31.3)
Croatia	33(11.5)	0
Cyprus	22(7.7)	3(13.6)
Total	287	87(30.3)

Conclusion: Despite the variations among European countries,influenza vaccine uptake remains low among JIA patients.Those previously vaccinated and those aware of the recommendations were more likely to be vaccinated.Informing families,discussing their concerns and organizing campaigns that will address the fears and highlight the importance of the influenza vaccine for this JIA population at risk may increase vaccination rates in children with rheumatic diseases.
Disclosure of Interest: None declared

O057

PREDICTING THE INDIVIDUAL RISK OF UVEITIS IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS: AN INTERNATIONAL MULTICENTER COHORT STUDY

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Introduction: Uveitis is the most common comorbidity in patients with juvenile idiopathic arthritis (JIA) and can lead to sight-threatening complications if not diagnosed and subsequently treated in an early stage. The estimated prevalence of JIA-U varies up to 30%, but the individual risk of acquiring uveitis is unknown.

Objectives: To build a clinical prediction model for JIA associated uveitis (JIA-U) providing individual risk estimates that could be used to inform patients/parents and aid physicians in determining screening frequencies.

Methods: Data from the international observational Pharmachild registry were used. For every patient with a follow-up period of at least 4 years, occurrence of JIA-U was determined from retrospective and prospective records since registration into Pharmachild. Multivariable logistic regression analysis was used to determine significant risk factors for JIA-U after correcting for confounding variables and to build a prediction model. Risk factors and confounders concerned were identified based on the existing literature and consensus of the authors, these included: age at JIA onset, gender, JIA subtype, ANA positivity, RF positivity and HLA-B27 positivity. The prediction model was selected based on Akaike information criterion and bootstrap resampling with replacement (n = 200) was used for internal validation and to adjust for model optimism.

Results: JIA-U was observed in 1,108 of 5,535 eligible JIA patients (20.0%). After correcting for confounding variables, independent risk factors for JIA-U were ANA positivity (OR: 1.89, 95% CI: 1.55 – 2.32), HLA-B27 positivity (OR: 1.47, 95% CI: 1.11 – 1.94), undifferentiated arthritis (OR: 1.70, 95% CI: 1.17 – 2.43), oligoarthritis (OR: 1.56, 95% CI: 1.27 – 1.91) and enthesitis-related arthritis (OR: 1.49, 95% CI: 1.02 – 2.14). Older age at JIA onset (continuous variable) was an independent protective factor (OR: 0.84, 0.81 – 0.87). Of all variables considered, the combination of age at JIA onset (in years), JIA subtype and ANA status (1 = positive, 0 = negative) performed best in predicting JIA-U (Table 1). Following the model, ANA positive patients with a young age at JIA onset and enthesitis-related arthritis run the highest risk of acquiring JIA-U. The prediction model had good discriminative power (AUC = 0.75, 95% CI: 074 – 0.77) and bootstrap resampling revealed little overfitting: optimism in the AUC estimate was 0.003. Based on this model, the individual risk of JIA-U can be calculated as: *p(uveitis) = 1/(1+EXP-(-0.55 + 0.68*ANA status – 0.17*age at JIA onset + JIA subtype coefficient))*

Table 1: Coefficients table of prediction model for JIA-U (n = 5,207, optimism-corrected AUC = 0.75). Reference JIA subtype is undifferentiated arthritis (β = 0).

Predictor	OR (95% CI)	β	Optimism-corrected β
(Intercept)	0.59 (0.43 – 0.79)	-0.54	-0.55
ANA positive	2.02 (1.73 – 2.36)	0.70	0.68
Age at JIA onset	0.84 (0.82 – 0.86)	-0.17	-0.17
Oligoarthritis	0.90 (0.68 – 1.20)	-0.10	-0.10
Polyarthritis (RF negative)	0.50 (0.37 – 0.67)	-0.70	-0.68
Polyarthritis (RF positive)	0.06 (0.01 – 0.18)	-2.88	-2.80
Psoriatic arthritis	0.76 (0.48 – 1.20)	-0.27	-0.26
Enthesitis-related arthritis	1.38 (0.95 – 2.01)	0.32	0.31
Systemic arthritis	0.07 (0.04 – 0.13)	-2.63	-2.56

Conclusion: Here, we present a clinical prediction model for JIA-U based on data from the largest (international) registry of JIA patients, that could be of use in current clinical practice.

Disclosure of Interest: None declared

O058

PROPOSAL FOR A DAMAGE AND RESPONSE INDEX FOR ANA-POSITIVE NONINFECTIOUS ANTERIOR UVEITIS FROM THE MULTINATIONAL INTERDISCIPLINARY WORKING GROUP FOR UVEITIS IN CHILDHOOD GROUP (MIWGUC)

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Introduction: Idiopathic chronic ANA-positive anterior non-infectious uveitis (CAU) has similar clinical characteristics as juvenile idiopathic arthritis related uveitis (JIAU), except for inflammatory arthritis. A damage and response index has already been developed by a European collaboration of pediatric rheumatologists and ophthalmologists for JIAU (MIWGUC)[1]. As innovative effective treatment options are emerging for pediatric uveitis, it is important to define a response and damage index to assess the effectivity of drugs in preventing ocular damage in children with idiopathic CAU.
Objectives: To develop a response and damage and response index to measure ocular damage in children with idiopathic CAU
Methods: MIWGUC already agreed on items to evaluate outcome [1] for JIAU. 6 paediatric rheumatologist and 6 uveitis specialized ophthalmologists were asked to score the items, which were derived from the JIAU response and damage index. Regarding relevance for response and damage in CAU (Table 1) the items were scored. Items with scores between 1-3 points were discarded, >7 were accepted, and 4-7 were further discussed in the group with nominal group technique. 80% agreement was required to keep the item.
Results: The MIWGUC group agreed in a consensus meeting in Barcelona, that idiopathic CAU and JIAU may be managed similarly. Tables one presents the result of the voting.

Accepted outcome items for response and damage form the MIWGUC group 2015 for JIA associated uveitis	Accepted outcome measures for chronic non-infectious ANA-positive anterior uveitis	Voting for acceptance for outcome measures for chronic non-infectious ANA-positive anterior uveitis n=12 (6 ophthalmologists and 6 paediatric rheumatologists) Yes/no votes
New Item Global disease score	 yes	 12/0
Flare	discarded	12/0
Posterior synechiae Cataract Maculopathy	Yes Yes Yes	12/0 12/0 12/0
Opticopathy	discarded	
Decreased visual acuity Ocular hypertony ≥21 mmHg Ocular hypotony ≤6 mmHg	Yes Yes Yes	12/0 12/0 12/0
Glaucomatous field loss and /or glaucomatous optic atrophy	yes	12/0
Band-keratopathy Epiretinal membrane formation Visual deterioration – less than 0.3 in any eye	Yes Yes Yes	12/0 12/0 12/0
Uveitis related disability VAS 0-100 by ophthalmologist Uveitis related disability VAS 0-100 by pediatric rheumatologist	Yes ?	12/0 ?

Conclusion: We propose items to assess response to treatment and ocular damage in children with CAU. Validation of these indices is required in clinical cohorts to assess effectivity of a given drug for treating activity and preventing eye damage. This proposal will be evaluated from the MIWGUC group in a prospective study.

1. Foeldvari I, Klotsche J, Simonini G, Edelsten C, Angeles-Han ST, Bangsgaard R, et al. Proposal for a definition for response to treatment, inactive disease and damage for JIA associated uveitis based on the validation of a uveitis related JIA outcome measures from the Multinational Interdisciplinary Working Group for Uveitis in Childhood (MIWGUC). Pediatr Rheumatol Online J. 2019 Oct 1;17(1):66.
Disclosure of Interest: None declared

LB004

THE EFFECTIVENESS OF POST-ISOMETRIC MUSCLE RELAXATION IN CHILDREN AND ADOLESCENTS WITH ANKYLOSING SPONDYLITIS

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Introduction: Ankylosing spondylitis (AS) is a chronic, gradually progressive inflammatory disease of the spine, which in a number of patients can occur simultaneously with lesions of entheses and peripheral joints.
Objectives: The aim of the study was to compare the effectiveness of treatment of juvenile forms of AS, with the use of post-isometric relaxation techniques in the treatment program, and without it.
The onset of the disease often occurs in childhood (juvenile AS). At the same time, in childhood, the manifestations of peripheral arthritis and enthesitis significantly prevail in patients over the symptoms of axial lesion, and in adolescence - the pathology of the hip joints (coxitis). Subsequently, the clinical picture of the disease becomes more typical for AS.
The aim of the study was to compare the effectiveness of treatment of juvenile forms of AS, with the use of post-isometric relaxation techniques in the treatment program, and without it.The aim of the study was to compare the effectiveness of treatment of juvenile forms of AS, with the use of post-isometric relaxation techniques in the treatment program, and without it.
Methods: Methods. A prospective clinical study was conducted with 98 children with a confirmed diagnosis of ankylosing spondylitis aged 10 to 14 years (68 girls, 30 boys). All patients had a period from the moment of diagnosis from 6 months to one and a half years. The exclusion criteria for patients were the presence of other diseases, joints and / or spine, which aggravated the course of the underlying disease.
All children were randomly divided into two groups: children (68) who received a combination treatment including massage, acupuncture and exercise and post-isometric muscle relaxation techniques and children (30) of the 2nd group (G2) who received the program, with the exception of post-isometric relaxation.
All children received treatment 5 times a week (from Monday to Friday, except Saturday and Sunday), the total duration of the rehabilitation course was 14 days. The therapeutic program included the following non-drug methods of exposure: for G1, 30 minutes - an acupuncture session, 20 minutes - a general massage session and at least 45 minutes of exercises in a gymnastics room with a physiotherapy instructor, as well as sessions of post-isometric muscle relaxation for the chest, back, upper and lower limbs. The visual analogue scale (VAS) was used as a method of assessing effectiveness, which was assessed at the beginning of the study, at the fifth, ninth and last clinic visits. Also, the BASDAI index was used.
Results: Results. 97 patients (99%) completed the protocol: 68 (100%) in G1 and 29 (97%) in G2. The average VAS score in G1 at the beginning of the study was 5.8 ± 0.6, and after the tenth session it dropped to 2.1 ± 0.3. A significant decrease in pain was also recorded in group G2 (from 5.8 ± 0.6 at the beginning of the study to 3.5 ± 0.2 after treatment), a statistically significant difference ($p < 0.05$) between different groups. To assess the period of time over which the treatment effect persists, all patients were asked to send a subjective VAS score to the treating physician after completing treatment on a monthly basis for 12 months. It was found that the inclusion of post-isometric muscle relaxation in the rehabilitation program allows the effects of pain reduction to be prolonged. Patients in the G1 group had lower VAS scores compared to patients in the G2 group by 4.3 months longer.
Conclusion: Conclusion. The results obtained indicate a high efficiency of the use of post-isometric muscle relaxation in the complex treatment of patients with established ankylosing spondylitis.
Disclosure of Interest: None declared

Lightening talks: Patient/Parent experience, e-health and psychosocial issues

O059

PROSPECTIVE OBSERVATIONAL STUDY ON VIDEO CONSULTATION (VC) IN PAEDIATRIC RHEUMATOLOGY - AN EXPERIENCE FROM MUMBAI, INDIA

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Introduction: VC, an offshoot of the communications technology boom has had a slow offtake in medical specialties in several countries due to legal, ethical and procedural concerns. An immense resource is thus spent to reach out to specialists. In the legitimized 'window of time' provided by lockdowns, we conducted a study on VC in pediatric rheumatology.

Objectives: To assess physician and care-giver (parent and referring doctor) satisfaction with VC in new and follow up patients across different age groups and diagnosis.

Methods: Following Indian Government Guidelines on Tele-medicine (25th March '20), we obtained ethics approval, informed referral network & patient database about VC. Bi-lingual instructions, disclaimers, consent for care, research and recording of VC were conveyed electronically. VC was carried out on subscribed platform observing security and privacy practices. Caregivers transmitted chronologic records, images (X-rays, rashes etc.) prior to VC. Referring physicians were encouraged to accompany new patients. After history, musculoskeletal examination was adapted with physician or parents eliciting signs under guidance. Three physicians attended each consult, graded their satisfaction on achievement of objective on a pre-defined 5-point Likert scale. Digital prescriptions were sent, explained telephonically. Referring physicians administered restricted-use drugs following written protocols. Counselling and educational inputs were offered to referring physicians & family members. Bi-lingual web-based feedback was obtained after VC.

Results: After excluding 10 poor quality VC, 186 VC were conducted over 41 days for patients world over but largely from a 700 km radius consulted. Age ranges (mean), physician-caregiver satisfaction with VC in differing age groups in new and old patients and their interobserver agreement is shown in Table 1. 6/7 new and 77/107 old patients and 9/9 physicians gave 5 star rating. 9/107 expressed dissatisfaction with physical examination on VC. Physicians expressed lacunae in the process, coordination and case presentation.

Table 1:

Patients (n=167)	**New (n=25)**	**Old (n=142)**
Mean age (y)	9.81	11.09
Inter Observer Agreement in all patients 1.Satisfaction with VC 0.765; CRONBACH'S ALPHA =0.772		
2. Across various age groups: (p value < 0.001 moderate to good)	< 5 y (n=29) O.778	
	5- 12 y (n=82) O.696	
	>12 y (n=75) 0.807	

3.Across diagnosis: (p value <0.0001)		Lupus 0.6860
	JIA	0.82

Conclusion: Benefits of VC as a resource saver is applicable to paediatric rheumatology, where perusal of records, meticulous history, and inspection stand crucial. Our study bears this out providing several highlights. However, lacunae like parents missing human connect, better elicitation of signs need to be addressed. VC provides excellent opportunity to partner with and educate referring physicians regarding diagnosis and management. Going forward VC can be proposed initially to selected follow-up patients >5years, alternating with in-person consultations. Educating caregivers on simple examination methods may make VC more conclusive. While structured in-person consultation remains the gold standard, VC can become viable alternative in difficult times or resource challenged situations. VC could plug the gaps in access to paediatric rheumatologists and open the concept of practice to a world without borders.

Disclosure of Interest: None declared

O060

INTERNET AND SMARTPHONE-BASED ECOLOGICAL MOMENTARY ASSESSMENT AND PERSONALIZED TREATMENT ADVICE (PROFEEL) IN ADOLESCENTS WITH CHRONIC CONDITIONS: A FEASIBILITY STUDY

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Introduction: Growing up with a chronic disease comes with challenges, such as coping with fatigue. Many adolescents are severely fatigued, thugh its associated factors exhibit considerable interpersonal and longitudinal variation.
Objectives: We assessed whether PROfeel, a combination of a smartphone-based ecological momentary assessment (EMA) method using the internet, followed by (face-to-face) patient-tailored treatment advice based on a dynamic network analysis report, was feasible and useful.
Methods: Feasibility study in fatigued outpatient adolescents 12-18 years of age with an autoimmune disease, post-cancer treatment, or with medically unexplained fatigue. Participants were assessed at baseline to personalize EMA questions. EMA was conducted via smartphone notifications five times per day for approximately six weeks. Hereby, data was collected and stored via the internet. The EMA results were translated into a personalized report, discussed with the participant, and subsequently translated into a personalized treatment advice. Afterwards, semi-structured interviews on feasibility and usefulness were held.
Results: Fifty-seven adolescents were assessed (mean age 16.2y±1.6, 16% male). Adolescents deemed the smartphone-based EMA feasible, with the app being used for an average of 49 days. Forty-two percent of the notifications were answered and 85% of the participants would recommend the app to other adolescents. The personalized report was deemed useful and comprehensible and 95% recognized themselves in the personalized report, with 64% rating improved insight in their symptoms and subsequent steps towards treatment as good or very good.
Conclusion: PROfeel was found to be highly feasible and useful for fatigued adolescents with a chronic condition. This innovative method has clinical relevance through bringing a patient's daily life into the clinical conversation. Personalized treatment advices to cope with fatigue can boost motivation and treatment adherence, and may lead to improved self-management of symptoms, thereby decreasing the need for additional treatment.
Disclosure of Interest: None declared

O061

EVALUATION OF EDUCATIONAL RESOURCES DESIGNED TO FACILITATE ACCESS TO CARE FOR CHILDREN WITH MUSCULOSKELETAL CONDITIONS

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Introduction: Electronic educational resources (e-resources) have the potential to promote awareness and knowledge about paediatric musculoskeletal (paed MSK) conditions, but if they are to achieve this goal, it is important to understand if and how they may lead to change in clinical practice. This is important and timely, given the current expansion of e-learning within clinical education. Our research group has developed a suite of e-resources with the overall goal of improving clinical skills and knowledge in healthcare professionals involved in paed MSK medicine.

Objectives: To develop an evaluative strategy, targeting healthcare professionals, focused on their use of our e-resources namely Paediatric Musculoskeletal Matters (PMM, www.pmmonline.org), paediatric Gait, Arms, Legs and Spine (pGALS) App (Google Play and Apple App Stores) and Newcastle University e-learning modules (ELM, https://cpd.ncl.ac.uk/courses).

Methods: Google Analytics and online survey with e-resource target audiences (PMM n=148, pGALS n=120, ELM n=111) to gather feedback on their design and usability; gain valuable insight into how they are used; and understand the drivers and barriers to their dissemination and uptake in order to bring about change. A random selection of PMM and ELM registered users were invited to complete the survey, in addition to purposive sampling using UK and international contacts within paediatrics, paed rheumatology and the global partners of PMM. Respondents were from 25 countries and comprised a range of roles within education and primary/community hospital care. Data was analysed using descriptive statistics and free-text comments using qualitative techniques. This study had ethical approval.
Results: To date the resources have wide international reach; (PMM: 627,275 hits, 246,515 users, 214 countries; pGALS App: 11,490 downloads; ELM: 152 users, 31 countries). Most survey respondents reported finding the e-resources useful or very useful (PMM 97%, pGALS App 98%, ELM 100%) and being able to use them for their required purpose quickly and easily (PMM 89% pGALS App 90%, ELM 90%). Most reported the e-resources have or could have an impact on the medical education of themselves or others (PMM 94%, pGALS App 90%, ELM 95%) and on their clinical or nursing practice (PMM 90%, pGALS App 83%, ELM 92%); reporting areas of impact that included: increased awareness and diagnostic capabilities, increased ease and capability in clinical examination, improved teaching, opportunity to view rare clinical cases, increased awareness in other healthcare providers, and the provision of resources and information to aid teaching and self review. Increased ratings of confidence in MSK medicine or examination were reported after use; 82% (PMM), 90% (pGALS App) and 87% (ELM) reported to be confident or very confident compared to 52%, 68% and 57% before. Suggestions to increase impact and use concerned increased awareness of resources, targeting a wider range of clinicians involved in the care of paed rheumatology patients, integration with local systems or curriculum, and linking in with professional organisations to increase visibility. Lack of awareness, time constraints, costs, potential language barriers and challenges in electronic access were reported as key barriers to use and impact.
Conclusion: E-resources have an increasingly key part to play in clinical education. Our findings suggest our e-resources are fulfilling their role in raising awareness and early recognition of MSK conditions in childhood. Future qualitative work will explore our findings in more depth in particular in relation to developing an evaluation strategy that may be applied to other e-resources.

Disclosure of Interest: None declared

O062

A REALIST APPROACH TO ELICITING THE INITIAL PROGRAMME THEORIES FOR THE SELF- AND SHARED-MANAGEMENT OF JUVENILE IDIOPATHIC ARTHRITIS BY CHILDREN, YOUNG PEOPLE, FAMILIES AND PROFESSIONALS INVOLVED IN THEIR CARE

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Introduction: Enabling children and young people (CYP) with juvenile idiopathic arthritis (JIA) to adopt self-management behaviours early on is likely to benefit their health and wellbeing through childhood and into adulthood. However, there is limited evidence of interventions focused on supporting the self-management of JIA by CYP, and the shared-management by families, and the most appropriate manner in which to deliver such support. Therefore, there was a need to develop a theoretical basis to underpin future self- and shared-management support, across public, private and voluntary sectors, to support CYP living with JIA and their families across the life-course.
Objectives: To elicit initial programme theories (IPTs) as the first stage of a realist evaluation pertaining to the self- and shared-management of JIA by CYP, their families and professionals involved in their care.
Methods: A realist evaluation approach guided the theory elicitation stage of this study. Firstly, information was obtained from an integrative review of self- and shared-management interventions targeted at CYP and families living with long-term conditions. Secondly, a document review of long-term condition self- and shared-management evidence was undertaken. A pragmatic search of JIA self- and shared-management support then followed. A realist evaluation heuristic (context-mechanism-outcome [CMO]) was used to synthesise information from sources into IPTs and CMO configurations, using retroduction to link theory and causality.
Results: Seven IPTs pertaining to the self- and shared-management of JIA by CYP, their families, and professionals involved in their care were identified. Four IPTs (1-4) were elicited at the individual and interpersonal level, while three IPTs (5-7) were elicited at the institutional and infrastructural level (Table). The elicitation process reiterated the argument that causality is located at the individual and interpersonal level – amongst the actions CYP and families take, individually and collaboratively, in response to the resources made available to them through self- and shared-management support interventions.

IPT number	IPT summary
1	Meaningful self-management support across the life course for CYP with JIA.
2	Meaningful shared-management support for families supporting CYP with JIA.
3	Individual healthcare plans as a shared management tool to aid other professionals in supporting the specific needs and preferences of CYP with JIA and their families.
4	Consistent recognition and approaches within the paediatric rheumatology multi-disciplinary team towards the value of self- and shared-management support for CYP with JIA and their families.
5	Self- and shared-management support services commissioned with statutory services as a component of routine care for CYP with JIA and their families.
6	Child, young person and family-centred holistic care across the lifecourse for those living with JIA.
7	Inclusive and proactive educational settings to enable CYP with JIA to secure equivalent educational attainment and social development to their peers.

Conclusion: The IPTs and the initial CMO configurations describe how and why JIA self- and shared-management support is expected to work. By qualitatively testing IPTs with key stakeholders using the realist evaluation approach, the IPTs can be refuted, refined, and consolidated into a refined theory of 'what works, for whom, in what circumstances and why' in the context of JIA self- and shared-management support.
Disclosure of Interest: None declared

O063

PATIENTS PERSPECTIVES ON LIVING WITH A SYSTEMIC AUTOINFLAMMATORY DISEASE: IMPACT ON QUALITY OF LIFE

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Introduction: Systemic autoinflammatory diseases (SAIDs) encompass clinical entities in which spontaneous inflammation occurs due to dysregulation of the innate immune response. The variability in presentation and rarity frequently lead to a diagnostic delay with potential damage from uncontrolled inflammation and negative impact on quality of life (QOL).
Objectives: We aimed to investigate the patient-reported factors underlying this negative impact.
Methods: A self-reported 25 question online survey on QOL of patients with SAIDs was developed by the non-profit organizations, the Autoinflammatory Alliance, KAISZ/VAISZ, ENCA and SJIA Foundation in English and Dutch. Respondents were recruited by convenience sampling through online social media posts. Data on triggers, medications, family history, and correlation of symptoms with labs were collected in addition to detailed information on QOL both during and in between flares.
Results: Between 2017 and 2019, there were 365 responses (342 in English and 23 in Dutch; Demographics are in the table). The most common diagnosis was undifferentiated SAID (uSAID). Seventy percent was diagnosed by a rheumatologist. Delay in diagnosis was common (5-20 years for 40% of patients). Almost half of the respondents saw 3-8 specialists before receiving their final diagnosis. In addition to the common features such as fever (79%), rash (60%), abdominal pain (70%), and oral ulcers (50%), SAID patients often experienced pain (80%) and fatigue (87%).
Fifty percent of patients rated being “severely limited” during flares and “somewhat limited” in between flares. 80% reported negative affect on their studies, job, and career.
We categorized open-ended responses into different impact domains of: 1.Physical: lack of understanding of the disease amongst both the medical and lay community, delays in diagnosis, unpredictable symptomatology, unknown long term side effects of medications, 2. Emotional: feelings of anxiety, hopelessness and frustration, feeling doubted about disease severity, constant worry about flares, 3. Social: inability to make plans for vacations/social events due to unpredictability of symptoms, leading to isolation, dependence on others, 4. Financial: insurance not covering specialists/medications, inability to work.

Demographics (n= 365)		**Age at Diagnosis (n=365)**		**Diagnosis (n=365)**	
Country of origin (n= 365)	n (%)	0-2 years old	30 (8%)	uSAID	92 (25%)
USA	236 (65%)	3-5 years old	65 (18%)	PFAPA	71 (19%)
UK	32 (9%)	5-10 years old	85 (23%)	CAPS	51 (14%)
Australia/ New Zealand/Oceania	27 (7%)	11-19 years old	47 (13%)	FMF	41 (11%)
Canada	23 (6%)	20-30 years old	33 (9%)	HIDS/all MKD	23 (6%)
Netherlands	19 (5%)	31-40 years old	33 (9%)	TRAPS	21 (6%)
Rest of EU, Northern & Eastern Europe	20 (6%)	41-50 years old	41 (11%)	CRMO/CNO/SAPHO	18 (5%)
Mexico, South America,	3 (1%)	51-60 years old	19 (5%)	Sweets	16 (4%)
Other, Asia, Middle East	5 (1%)	61+ years old	12 (3%)	Other	32 (9%)

Conclusion: Patient engagement in designing survey questions helps to capture the impact of a disease on all aspects of life. In addition to the well-known negative impact of chronic diseases on QOL, the unpredictable nature of the course of SAIDs magnifies the stress of daily living for patients and caretakers. More granular questionnaires paired with clinical and biomarker analyses are needed to identify specific vulnerabilities and risk factors so that preventive measures can be implemented to improve QOL of patients with SAIDs.

Disclosure of Interest: M. Marques: None declared, N. Tennermann: None declared, S. Angevare: None declared, R. Sinha: None declared, J. Tousseau: None declared, P. Readon: None declared, S. Lapidus: None declared, G. Schulert Consultant for: Novartis and SOBI, K. Durrant*: None declared, F. Dedeoglu* Consultant for: Novartis, UpToDate

O064

CLUSTER CONSORTIUM CHAMPIONS, AND THE IMPORTANCE OF PATIENT AND PARENT INVOLVEMENT AND ENGAGEMENT IN RESEARCH CONSORTIUMS

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Introduction: Juvenile Idiopathic Arthritis (JIA) is the umbrella term for a group of childhood, chronic rheumatic arthritides affecting approximately 1 in 1000 children and young people. It is defined as persistence of arthritis for more than 6 weeks of unknown origin, in patients aged under 16 years (1). Whilst much research has been conducted into understanding prognosis and treatment of JIA, there is still much unknown regarding tools to predict outcome, select treatment, or predict response. The Childhood arthritis and its associated uveitis: stratification through endotypes and mechanism to deliver benefit (CLUSTER) Consortium aims to address these research priorities. The role of patient and parent involvement has been key in the creation of the Consortium. To provide two-way fully-integrated involvement and engagement within the programme, we developed a patient and parent working group entitled the CLUSTER Consortium Champions.

Objectives: To develop a patient and parent working group that feeds into all aspects of research and management within the Consortium. The goal is for CLUSTER Champions to collate and express the thoughts, interest and ideas of patients, parents and the public. This provides an integrated two-way system of benefit.

Methods: A concept document was developed, providing background information on the potential role of CLUSTER Champions, along with expression of interest documents. The design was produced with local involvement and knowledge from NIHR INVOLVE standards (2). Building on previous success and the public launch of the CLUSTER Consortium (11th March 2019), a patient, parent and public day was developed and held on 21st June 2019. The concept of the CLUSTER Champions was presented at this event to acquire feedback and interest from those involved.

Results: The event hosted 22 family members (13 adults, 9 children aged <16 years old), 7 external volunteers and 5 charity representatives (excluding those also classified as parent/family members). Interest was overwhelmingly positive, with 16% of feedback focusing on methods of communication in the consortium and 32% of feedback around levels and degree of engagement for members. Upon launch of the scheme, six CLUSTER Champions have joined and are now fully integrated members.

Conclusion: Developing PPIE working groups within research allows for an exchange of ideas between researchers, families and the public. Our event showed that the public is generally enthusiastic and positive about involvement in research. PPIE working group provide an opportunity for researchers to understand public opinions and priorities and allows the public to gain insight into research methodology, governance and procedures. The Champions provide a link to the public for dissemination of papers, questionnaires, reports, as well as development and prioritisation of research ideas. Outside of the Consortium the CLUSTER Champions have provided expertise and dissemination of a COVID-19 risk algorithm developed at GOSH, and provided links to multiple families for dissemination of COVID-19 related information and help on research questionnaires and cohorts.

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Disclosure of Interest: F. Dekaj: None declared, L. Wedderburn Speaker Bureau of: Pfizer, Z. Wanstall: None declared, W. Thomson: None declared

O065

THE PERSPECTIVE OF PARENTS/CARERS ON VACCINATIONS IN CHILDREN AND YOUNG PEOPLE WITH RHEUMATIC AND AUTOINFLAMMATORY DISEASES: RESULTS OF AN INTERNATIONAL SURVEY

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Introduction: Vaccination coverage in children and young people (CYP) with rheumatic and auto-inflammatory diseases is reported to be lower than healthy CYP. However, the reasons why vaccinations are declined by parents/carers remain unclear.

In September and November 2019 a survey was posted online. Awareness for this survey was raised through social media and patient organisations.

Main objective of the survey was to get more insight into the knowledge and awareness of patients with specific diseases (autoimmune and auto inflammatory) and their potential use of certain vaccinations.

Objectives: To understand the views of parents/carers regarding vaccinations in CYP with rheumatic and autoinflammatory diseases.

Methods: An electronic survey of parents/carers of CYP with rheumatic and autoinflammatory diseases was distributed in English using the national organisations representing parents/carers and CYP. The survey consisted of 60 questions, and was accessible between September and November 2019. Aside from demographics, we asked respondents for their views on the value of vaccinations, risk/benefit balance, available information/commentary on vaccinations and shared decision-making opportunities with healthcare professionals (HCPs).

Results: A total of 463 responses were received (62% from Europe, 38% from non-European countries). We collected data on a variety of topics such as demographics, diseases, medications and vaccinations. While the majority of respondents recognised the importance of vaccinations (95%) and believed in the value of vaccination programmes (82%), 34% reported postponing vaccinations for personal reasons. Concerns were focussed more on short-term side effects (61%) than long-term side effects (48%); with 42% suggesting that they knew somebody else who had experienced a side effect. The most common vaccination concern was that a disease flare may be triggered. However, most were also concerned about vaccine-preventable diseases (62%). The top three reasons against vaccination were: risk of side effects, advice from HCPs (e.g. against live vaccines while on biologics) and poor information about vaccinations. The influence of media information about vaccinations was inconsistent. Most felt they were able to discuss vaccinations with HCPs (90%). Finally, several respondents called for an independent online resource about vaccinations for CYP with rheumatic and autoinflammatory diseases.

Conclusion: Parents/carers of CYP with rheumatic and autoinflammatory diseases generally recognise the importance and value of vaccinations. However, many are concerned about vaccinations triggering a disease flare, resulting in some parents/carers postponing vaccinations. It is clear that HCPs play an important role in discussing vaccinations with parents/carers as part of the shared decision-making process. An independent online resource about vaccinations, specifically for this population, may need to be developed to support evidence-informed decision-making.

Disclosure of Interest: None declared

O066

THE COVID-19 EUROPEAN PATIENT REGISTRY: DEVELOPMENT OF A PATIENT-LED RHEUMATOLOGY REGISTRY

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Introduction: On 11 March 2020, the World Health Organisation characterised COVID-19 (coronavirus) as a pandemic. It quickly infected hundreds of thousands of people worldwide. Whilst many people with COVID-19 infection appeared to have mild or no symptoms, a significant proportion of patients became seriously ill.
In late March 2020, little was known about how patients with rheumatic diseases or autoimmune conditions, many of whom use immunosuppressive medications and drugs, are affected by the virus.
Objectives: To develop a patient-led, longitudinal survey to identify the potential risk-factors associated with COVID-19 infection in people with rheumatic, autoimmune and autoinflammatory conditions; to compare outcomes among these patients; and to characterise and understand how they may be differentially affected by COVID-19.
Methods: The COVID-19 European Patient Registry (EPR) was developed by parents of children and young people (CYP) representing ENCA, with support and involvement from individuals and organisations across Europe, including adult patients and the Paediatric Rheumatology European Society (PReS). As partners of the Global Rheumatology Alliance, the EPR was specifically created as a longitudinal survey tool. Development was very rapid, allowing data to be collected within 3 days from the start of the project, maximising the potential for capturing vital information through the web-based survey tools at www.jarproject.org/covid.
The EPR has two parts: paediatric (to be completed by parent/caregiver) and adult. It comprises an online survey asking about rheumatic conditions, general health, medication and underlying comorbidities. Each participant is sent a short follow-up survey, weekly, asking about exposure to COVID-19, preventative steps taken to avoid infection, symptoms, diagnosis and outcomes.
The EPR was launched on 24 March 2020 and is available in 13 languages. Individuals can join it at any time, on a rolling basis. Each week, data from the initial and follow-up surveys are downloaded, anonymised and combined to generate the longitudinal registry. Consent is provided when enrolling, and confirmed at each follow-up survey.
Results: As of 24 May 2020, 3,740 people (603 CYP and 3,137 adults) had joined the EPR. Among the CYP, only 5 reported a COVID-19 infection (0.8%). The follow-up response rate at week 1 was 52%. Table 1 provides a summary of CYP participants to 24 May 2020.

Table 1. Summary of participants as of 24 May 2020 (N=3,740).

Data included in the European Patient Registry (EPR)	*Children / Young People*	*Adults*
Participants (% female)	603 (67%)	3,137 (89%)
Number of countries represented	30	52
Number (%) diagnosed with COVID-19	5 (0.8%)	40 (1.4%)
Number hospitalised due to COVID-19 (% of those with diagnosis)	0 (0.0%)	3 (7.5%)

Conclusion: The COVID-19 EPR provides an opportunity to develop an understanding of how COVID-19 infection affects paediatric and adult rheumatology patients, to identify risk-factors for infection and/or disease severity. Currently, COVID-19 in CYP has low prevalence and mild outcomes. Updated results will be presented at the PReS Congress.

Acknowledgments: We are grateful to the team of volunteers who helped translate the surveys, as well as ENCA , PReS and representatives from the rheumatology community for their expertise and support.
Disclosure of Interest: None declared

O067

PARENTING STRESS IN PARENTS OF CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Having a child with a chronic illness has been associated with increased levels of parenting stress across several health conditions. Parenting stress has not been examined in parents of children recently diagnosed with juvenile idiopathic arthritis (JIA). To help support parents, it is important to identify levels of parenting stress and to understand factors that may influence stress levels.

Objectives: To examine the relationship between the health status of children with JIA and illness-related parenting stress experienced by their parents.

Methods: Parents of children aged ≤12 years who had been recently diagnosed with JIA (≤6 months) were recruited during clinic appointments at tertiary paediatric rheumatology clinics in England. Participants were recruited to a multicentre randomised controlled trial of a website for parents of children with JIA. This abstract reports data collected prior to randomisation.

Parents completed the Pediatric Inventory for Parents (PIP) measure of childhood illness-related parenting stress. The PIP has two scales, measuring the frequency (PIP-F) and difficulty (PIP-D) of illness-related events that parents may face. Each scale provides a total score ranging from 42-210 with higher scores indicating greater stress. Child clinical data collected included: JIA subtype; time since diagnosis; medication; number of active and limited joints; erythrocyte sedimentation rate; Child Health Assessment Questionnaire; parent global rating; physician global rating; presence of co-morbid illness.

Multiple linear regressions were performed to analyse the relationship of child health status with PIP-F and PIP-D.

Results: Parents of 203 children participated; 166 mothers and 37 fathers are included in the analyses. Their mean age was 36.3 (6.5) years. Their children with JIA had an average age of 6.2 (3.4) years; most were female (n=136, 67%) and had oligoarticular (n=107, 52.7%) or polyarticular (n=65, 32.0%) JIA. Sixty-eight (33.5%) had been prescribed methotrexate. Mean (SD) scores on the PIP-F and PIP-D were 108.6 (32.1) and 103.1 (32.6) respectively. This is similar to stress levels reported by parents of children with other health conditions, including type 1 diabetes and sickle cell disease.

Regression analysis explained 24% of the variance in PIP-F. Significant independent predictors of higher scores on the PIP-F, representing greater frequency of difficult events were: Female parent gender (B=12.72, p=0.018), systemic JIA subtype (B=26.30, p=0.038) and presence of a co-morbid illness (B=11.05, p=0.041).

Regression analysis explained 20% of the variance in PIP-D. Significant independent predictors of higher scores on the PIP-D, representing greater difficulty experienced were: systemic JIA subtype (B=43.26, p<0.001) and a poorer parent global rating score (B=2.089, p=0.037).

Conclusion: This research identified levels of parenting stress among parents of children recently diagnosed with JIA that are similar to those of parents of children with other serious health conditions. Parents in this study who were at an increased risk of high stress levels were those whose children have systemic JIA or co-morbid conditions and those who rate their child's overall wellbeing more poorly. The study findings have helped to identify parents who may be at increased need for support to help reduce parenting stress.

Trial registration identifying number: This abstract presents independent research funded by the National Institute for Health Research (NIHR) under its Research for Patient Benefit (RfPB) Programme (Grant Reference Number PB-PG-1013-32005). The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

ISRCTN: 13159730

Disclosure of Interest: None declared

O068

SOME ASPECTS OF THE PSYCHOEMOTIONAL STATE OF PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS.

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Introduction: Juvenile idiopathic arthritis (JIA) - combines a diverse group of chronic joint diseases and is one of the most common and disabling rheumatic diseases of childhood. The course of the disease leaves its mark on both the lifestyle and the psychoemotional status of a sick child, which may determine the risk of various psychological changes and disorders of the emotional and motivational sphere. The study of the psychoemotional status of patients with JIA is an urgent problem of our time, requiring study to form a set of measures of psychological support for a sick child.

Objectives: Assess the psychoemotional status of patients with a verified diagnosis of JIA.
Methods: The study involved 70 patients aged 3.9 years to 16.11 years (mean age 9.6 ± 4.1 years) with an established diagnosis of JIA according to ILAR criteria, no later than 6 months from the start of the study. In the study group there was the following distribution of patients — 20 children with a systemic variant of the disease and 50 children with the articular form of JIA (30 patients with an oligoarticular and 20 with a polyarticular variant of the course of JIA). The comparison group consisted of relatively healthy children (n = 20). Assessment of the psychoemotional status in the main and control groups was carried out using a set of standardized methods: Sachs-Levy test “Method of incomplete sentences” (SSCT method), test M. Kovach “Questionnaire for childhood depression” (CDI) for patients older than 7 years, test L.S. Slavina "Three wishes."
Results: Analysis of the Sachs-Levy test “The method of unfinished sentences” showed that almost 75% of the children of the main group had certain fears and concerns associated with the course of the underlying disease, but positive attitudes prevailed in 30.8% of patients in all spheres of life, while while 17.7% of children in the study group had negative attitudes that were not related to the course of the disease, in the control group this indicator was 12%. When analyzing the method of M. Kovach's “Questionnaire for Child Depression,” the CDI score on the A scale showed that a general decrease in mood, a negative assessment of their own effectiveness, was generally observed in 45% of children in the study group and only 5% in the control group; on a scale B 19% of children in the main group identified themselves with the role of the bad, in the control group this indicator was 50%; on a scale of C, 27.5% of children showed a high level of conviction of inefficiency at school, in the control group, 2% of respondents; on a scale of D 35% of the respondents in the main group had a high level of exhaustion and a feeling of loneliness; on the E scale: a negative assessment of one's own inefficiency, the presence of suicidal thoughts was noted in 15% of the respondents in the main group and 1% of the control group. Evaluation of the results of the method L.S. Slavina's “Three Wishes” showed that in almost 90% of the children in the study group, at least one desire was associated with the course of the underlying disease, 15% had 2 wishes, and only one patient with a severe course of the systemic variant of JIA had all three wishes illnesses. An analysis of the data obtained indicated a narrowing of the motivational-consumer (MP) sphere in the study group.
Conclusion: A study of the psychoemotional status of patients suffering from JIA showed that, in general, more than half of the children showed changes in the emotional and motivational sphere of life compared with children from the control group. Thus, it is worth talking about the need for dynamic monitoring of the state of the psychoemotional sphere in rheumatological patients, and the need for psychological support, both at the stages of inpatient treatment and on an outpatient basis.
Disclosure of Interest: None declared

O069

DIAGNOSIS OF DEPRESSIVE DISORDERS IN CHILDREN WITH JUVENAL IDIOPATHIC ARTHRITIS

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Introduction: Depression is a common mental disorder, the leading cause of disability and makes a significant “contribution” to the global burden of diseases. Besides, depression is an associated condition in rheumatic diseases including arthritis even in childhood. The relevance of this problem is also due to the fact that in children, despite the presence of a chronic disease, high adaptive abilities of the psyche take place. Therefore, it is especially important to reliably determine the presence of the first signs of depressive conditions at earlier stages of the underlying disease.
Objectives: The aim of the study was to identify early signs of depressive states in children with juvenile idiopathic arthritis (JIA) and their relationship with the activity, duration and complex treatment.
Methods: This study included 16 children (8 girls and 8 boys) 6 - 17 years old (13.1±0.7) with JIA (poly- and oligoarticular variants according to ILAR classification, Edmonton, 2001), the average duration of the disease was 29.0±6.5 months. Disease activity according to the JADAS scale was 1 - 17 (4.4±1.1).
The main method of research was the Montgomery-Asberg scale (MADRS), which applies quickly assess the severity of depression. It contains 10 main subscales for assessing signs of depression on a 6-point scale. Interpretation of the results is carried out by arithmetic summation: from 0 to 6 points - no depressive episode; from 7 to 19 points - a small depressive episode; from 20 to 34 points - moderate depressive episode; more than 35 points - a major depressive episode. Results were analyzed using IBM SPSS Statistics for Windows with $p<0.05$ considered spastically significant.
Results: It was found that 9 children (56.25%; the MADRS indicator was 6.7±1.3) had no signs of emotional disturbances. 7 patients (43.75%) had manifestations of depressive states (the MADRS indicator was 22.5±3.4): 5 children had signs of a small depressive episode; 1 child - a moderate depressive episode, another child - a major depressive episode. Children with signs of depressive disorder had a longer duration of the disease (44.2±12.7 vs 20.6±6.2 mo., p=0.038), greater JADAS activity (7.7±2.4 vs 2.5±0.5, p=0.048) than children without positive MADRS scores. No reliable dependence of the scale indicators on the age (14.2±0.6 vs 12.4±1.0 years, p=0.054) and gender of patients (the MADRS indicator in girls 11.0±2.0 vs in boys 14.3±4.6, p=0.265), the inclusion of methotrexate in the treatment (the MADRS indicator with MTX 10.0±2.0 vs without MTX 14.2±3.7, p=0.169), was found. An analysis of the subscales used to assess the level of depression found that 68.0% of children had been depressed or in a bad mood for more than 3 days a week in the last month, looked depressed, but were quickly distracted from bad thoughts. 50.0% of children had problems falling asleep or short sleep, intermittent or restless sleep; 31.0% of patients noted difficulties with starting a new case; also 31.0% - difficulties in performing daily tasks that do not require much effort, 25.0% of children surveyed had sporadic thoughts about their own inferiority, failure in life and self-humiliation, and another 12.5% - thought it was better to die.
Conclusion: Mental health disorders are present in patients with JIA, starting in childhood. Their prevalence reaches almost half of teenage children, which requires additional diagnosis and rehabilitation measures.
Disclosure of Interest: None declared

O070

RHEUMATIC DISEASES IN MEXICAN CHILDREN AND THEIR PSYCHOSOCIAL AND ECONOMIC IMPACT ON CAREGIVERS

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Introduction: Pediatric rheumatic diseases (PRD) are a heterogeneous group of disorders. PRD patients and their caregivers face a number of challenges, these include the consequences of the PRD in patients and the impact on multiple dimensions of the caregiver's daily life. Our group developed and validated the CAREGIVERS questionnaire to measure the impact on caregivers of children with PRD.

Objectives: The objective of this study was to measure the economic, psychological and social impact that PRD has on the caregivers of Mexican children and the factors associated with these impacts.

Methods: This is a cross-sectional study in which primary caregivers were prospectively included between April and November 2019 in four public hospitals of specialized care. Descriptive statistics used used to the sociodemographic characteristics of the participants and the patients' clinics, a univariate analysis was performed with the interview responses of the CAREGIVERS questionnaire and the sociodemographic, clinical, and health system variables using the Chi square, Mann-Whitney U, and Kruskal-Wallis tests ($p < 0.05$).

Results: 200 participants were included, women (84.5%) with median age of 38 years; 54.5% cared for patients with JIA, 14% with JDM and 31.5% with JSLE. Most of the caregivers felt concern (42.5%) when learning about the diagnosis, which then was modified by tranquility (44%) when the current feeling was questioned; however, 40 expressed sadness when sharing the patient's PRD (20%) and 39 do not like to do so (19.5%).The main cause of concern is pain (41.5%), followed by difficulty in movement (28.5%) and covering the costs of treatment (25%). Social impact: In 99 caregivers (49.5%), the use of their time changed a lot upon learning the PRD. Social life varied according to the PRD, in JSLE it had a significant change (39.6%), but it did not change in JIA (44%) and it slightly changed in JDM (53.5%, $p < 0.01$).Financial impact: the family financial situation worsened upon diagnosis of the patient in most cases (JIA 63 [57.8%], JSLE 19 [69.8%] and JDM 44 [67.8%], $p = 0.27$). Almost two thirds had had to borrow money, more frequently in JSLE (48 [76.1%] vs JIA 62 [56.8%] and JDM 19 [67.8%], $p = 0.03$); 63 stopped buying medicines due to lack of money (31.5%) and 86 received additional financial support for the treatment (43%).The emotional impact increased in caregivers of male patients. Social dimension showed significant differences regarding PRD, healthcare system, time to reach the center, presence of disability, active disease, cutaneous and systemic manifestations and treatment.

Conclusion: This study highlights a series of lessons learned and the most important is the need to improve opportunities for support, especially regarding financial support, for caregivers of patients with PRD. The study has shown that social status can be devastating in the impact that PRD can have on families. We feel confident that, although all the participants are Mexican, the findings can be generalized to populations with similar characteristics in other regions.

Disclosure of Interest: None declared

O071

BARRIERS AND FACILITATORS TO PHYSICAL ACTIVITY IN JUVENILE IDIOPATHIC ARTHRITIS (JIA): A SCOPING REVIEW.

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Introduction: Physical activity is an important aspect in the management of JIA (Kuntze et al 2018). However physical activity levels are low in this population (Bos et al 2016). Limited research has been conducted to identify definitive barriers and facilitators to physical activity in children and adolescents who have JIA.

Objectives: The objective of this scoping review was to identify the common barriers and facilitators to physical activity in JIA.

Methods: Original studies, either quantitative or qualitative, including participants with a diagnosis of JIA, who were under 18 years of age were included. Two independent reviewers carried out a search of the literature and full text reviews of papers to determine eligibility for inclusion. The Critical Skills Appraisal Programme (CASP), Appraisal tool for Cross-Sectional Studies (AXIS) and Downs and Black critical appraisal tools were used to assess the quality of the included research articles.

Results:

Category	Quantitative studies (N)	Qualitative studies (N)
Barriers		
Physical barriers	N=13	N=4
Psychological barriers	N=7	N=5
Management barriers	N=5	N=3
Other barriers	N=7	N=0
Facilitators		
Physical facilitators	N=5	N=0
Psychological facilitators	N=6	N=6
Management facilitators	N=10	N=7
Other facilitators	N=4	N=0

Eighteen studies were included in the review. The included studies were of a variety of low, moderate and high quality. The synthesis of the data identified pain to be the most common barrier and the modification of physical activities to the need of the individual to be the most common facilitator to physical activity in JIA.

Conclusion: Identifying the most common barriers and facilitators to physical activity allows clinicians to apply better management strategies when treating an individual with JIA. Our findings demonstrate the need for further research in this area to assist increasing physical activity participation for children and adolescents who have JIA.

Disclosure of Interest: None declared

Lightening talks: Systemic lupus erythematosus and scleroderma

O072

UNDER DETECTION OF INTERSTITIAL LUNG DISEASE IN JUVENILE SYSTEMIC SCLEROSIS (JSSC) UTILIZING PULMONARY FUNCTION TESTS. RESULTS FROM THE JUVENILE SCLERODERMA INCEPTION COHORT.

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Introduction: Juvenile systemic sclerosis (jSSc) has a prevalence in around 3 in a million children. Pulmonary involvement occurs in approximately 40 % in the international juvenile systemic scleroderma cohort (JSScC). Traditionally in jSSc, pulmonary function testing (PFT) with FVC and DLCO are used for screening and computed tomography (HRCT) was more reserved for those with abnormal PFTs. More recently, it has become apparent that PFTs might not be sensitive enough for detecting interstitial lung disease (ILD) in children.

Objectives: To assess the sensitivity and specificity of FVC and DLCO assessment to detect ILD

Methods: The international juvenile systemic scleroderma cohort (JSScC) database was queried for available patients with recorded PFT parameters and HRCT performed to determine sensitivity of PFTs detecting disease process.

Results: Of 129 patients in the jSScC, 67 patients had both CT imaging and an FVC reading from PFTs for direct comparison. DLCO readings were also captured but not in as many patients with tandem HRCT (n =55 DCLO and HRCT scan). Therefore, initial analyses focused on the sensitivity, specificity and accuracy of the FVC value from the PFTs to capture the diagnosis of interstitial lung disease as determined by HRCT.

Overall, 49% of the patients had ILD determined by HRCT, with 60% of patients having normal FVC (>80%) with positive HRCT findings, and 24% of patients having normal DLCO (> 80%) with positive HRCT findings. Fourteen percent (n = 3/21) of patients with both FVC and DLCO values within the normal range had a positive HRCT finding.

Conclusion: The sensitivity of the FVC in the JSScC cohort in detecting ILD was only 39%. Relying on PFTs alone for screening for ILD in juvenile systemic sclerosis would have missed the detection of ILD in almost 2/3 of the sample cohort, supporting the use of HRCT for detection of ILD in children with SSc. In addition, the cut off utilized, of less than 80% of predicted FVC or DLCO could be too low for pediatric patients to exclude beginning ILD. This pilot data needs confirmation in a larger patient population.

Supported by the "Joachim Herz Stiftung"

Disclosure of Interest: None declared

O073

CROSS-CULTURAL ADAPTATION AND VALIDATION OF THE LOCALISED SCLERODERMA QUALITY OF LIFE INSTRUMENT (LOSQI) IN JLS: A MULTICENTRE STUDY OF THE PRES SCLERODERMA WORKING PARTY IN COLLABORATION WITH MEMBERS OF THE CARRA SCLERODERMA WORKING GROUP

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Introduction: ***Juvenile localised scleroderma (JLS)*** is characterised by chronic inflammation within the skin and tissues leading to fibrosis [1]. It is associated with significant complications including joint contractures, limb length discrepancy and facial atrophy that impact quality of life. Patient reported outcomes (PRO) are not well established within research settings and are not part of routine clinical care in many centres [2].

Several studies have measured health-related quality of life (HRQoL) in JLS, most commonly using the Children's Dermatology Life Quality Index[3-6]. This measure only captures impact of skin involvement and not HRQoL from extra-cutaneous manifestations. Psychometric analysis shows that it incompletely measures important concepts of HRQoL that are unique to JLS [7]. The Localised Scleroderma Quality of Life Instrument (LoSQI) has been developed in partnership with patients and families to capture aspects of disease which may not be well defined within generic HRQoL measures [8]. The initial development and validation process was iterative, patient-centred, and consistent with best practices in PRO development. Currently, the LoSQI is the only JLS-specific PRO, and the only PRO that includes both qualitative and quantitative validity evidence. It is currently being utilized within two large American scleroderma registries but will require cross-cultural adaptation for international use.

Objectives: to undertake cross-cultural adaptation and validation of the Localised Scleroderma Quality of Life Instrument (LoSQI) in juvenile localised scleroderma (JLS).

Methods: Workstream 1: cross-cultural adaptation of LoSQI via methods previously described by Guillemin et al, with pre-testing in selected study population. A single site in up to 35 PRINTO represented countries will take part.

Workstream 2: validation of the LoSQI via a multicentre prospective cohort study of 100 patients at 2 time points.

Results: This study was successful in obtaining funding from the **PReS 2025 / PRINTO Research Award** and is in study set up stage.

Conclusion: Collaboration between PRINTO centres, CARRA and PRES scleroderma working party members in partnership with patients and families will facilitate shared aims and this will be the first multi-national study of a disease-specific patient-reported outcome (PRO) in JLS. To allow further validation work of outcome measures, this important step will allow cohorts from multiple countries to combine datasets and results with an overarching aim to embed PRO in routine clinical practice. This is invaluable for a rare disease population, where research is continuously limited by small samples sizes, large geographical dispersion of subjects, and lack of consensus in selection and use of outcome measures.

Disclosure of Interest: None declared

O074

ISCHEMIC STROKE IN CHILDREN WITH SCLERODERMA EN COUPE DE SABRE.

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Introduction: Neurologic disturbances (ND) in children with localized scleroderma (LS) occur more frequent in linear scleroderma en coupe de sabre (ECDS). The frequency of Central nervous system involvement in pediatric craniofacial scleroderma is estimated to be 28–38%. Mostly epilepsy, headache, focal symptoms, neuropsychiatric disorders are described. Only several cases of stroke were recorded in adults with ECDS.

The origin of ND is still unclear. There is data for neurovasculitis hypothesis with endothelial cell injury, microthrombotic angiopathy. Other data suggests a prenatal malformation of one side of rostral neural tube resulting in hemiatrophy of facial tissue and underlying brain parenchyma.

Objectives: To analyze frequency of neurologic involvement ECDS in children, describe 3 cases ischemic stroke (IS).

Methods: Retrospective analysis of ND in ECDS childhood cases was done. All children carried out physical and neurologic examination, brain magnetic resonance imaging (MRI), electroencephalography (EEG), rheumatological observation (physical, instrumental and laboratory including homocystein serum level (Hcy), evaluation for genetic thrombophilia (GThr).

Results: We observed 115 children with ECDS, aged from 3 to 16 years, the mean age 12,4 years (M ±3,52), 63 girls and 52 boys (girls/boys = 1.2:1).

ND were found in 52 children (45%), among them: recent-onset headache in 25 patients (pts) (22%), seizures in 14 pts (12%), parasomnias in 5 pts (4,3%), IS in 3 pts (2,6%), cranial neuropathies in 3 pts (2,6%), hearing loss on the side of leisure in 2 pts (1,7%), paraplegic migraine in 1 pt. IS is a casuistic presentation of ECDS.

Clinical data on the IS patients is summarized in Table below.

2 of 3 presented cases (Pt.2 and 3) have neurologic signs, while typical skin scleroderma changes appeare in 8 and 12 months after IS. In another case (Pt.1) a patient suffered from LS for 2 years, before IS, received corticosteroids (CS) orally 0.5 mg/kg 10 weeks, methotrexate (MTX) 12 mg/b.sq. for 2 years with decrease of skin process activity. MRI showed local ischemic focus in the region of left middle cerebral artery. In cases of neurologic disease debut (Pt.2 and 3), focal neurologic deficit (hemiplegia, hemiparesis, aphasia, ataxia, and seizures) lasted for less than 24 hours. MRI showed ischemic foci in frontal and temporal brain regions. In both cases vascular brain anomalies were suspected. Pt.2 and 3 also had recurrent ischemic brain attacks. All pts showed mutations in MTHRF gene and elevated Hcy serum level. After the diagnosis of ECDS was clear in Pt.2 and 3, MTX 12 mg/b.sq. started, usage of CS was avoided. Pts received antithrombotic, neurotrophic and metabolic therapy, folic acid, and rehabilitation. Despite complex therapy, our pts have irrepressible changes of brain parenchyma revealed by MRI and serious neurologic sequelae in 2 -7 years follow up.

Pt Sex/age	LS onset (years)	IS onset (years)	Initial clinical display	Time span stroke – skin (months)	Facial atrophy side	MRI foci side	GThr	Follow up period (years)	Neurologic sequelae
1. M/13	7	9	skin	24	Left	Left	PAI-I, MTHRF	4	right hemiparesis
2. M/17	8	7	stroke	12	Left	Left	MTHRF	7	paresis n.facialis, anisoreflection

3 F / 9	6	5	stroke	8	Right	Right	MTHRF	2	Paresis left hand, left side deviation of the tongue

Conclusion: We speculate that IS in observed ECDS children was strongly associated with GThr and possible undiscovered brain vascular malformations, as addition to scleroderma vasculopathy. IS occurs in less than 3 % of ND in our cohort of ECDS children, but, it demands attention of rheumatologists due to life threatened consequences. Pts with ECDS have to be cheked for GThr, as a risk factor for stroke.

Disclosure of Interest: None declared

O075

RAYNAUD'S PHENOMENON IN CHILDREN: A SURVEY OF UK & IRELAND PRACTICE

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Introduction: Raynaud's Phenomenon (RP) is an episodic response to cold or emotional stress which causes colour change and symptoms including numbness and pain in the extremities. Primary Raynaud's, due to functional changes in blood vessels, does not cause tissue damage. Secondary Raynaud's, associated and often the first sign of a rheumatological condition e.g. scleroderma or SLE, can cause tissue loss, digital ulcers and gangrene. It is characterised by nailfold capillaroscopic (NFC) abnormalities and autoantibody formation, which appear to be risk factors for CTD progression. Repeat autoantibody profile and NFC is important as they can progress over time.
The PRES scleroderma working group developed recommendations for assessment, monitoring and treatment of Paediatric RP in 2016, including ANA testing in all and the recommendation to screen for SSc-specific antibodies, anti-dsDNA and ENA in ANA positive patients. NFC should be performed in all and classified as 'normal', 'non-specific changes' or 'SSc pattern'.
Objectives: To describe UK & Ireland assessment, management and monitoring of paediatric RP, considering PRES working party recommendations.

Methods: Electronic Survey sent to Paediatric Rheumatology networks.

Results: There were 64 respondents. 60% were unaware of PRES working party recommendations.
Definition of primary RP varied. Most defined it as RP in the absence of a definitive/evolving CTD (48%) .
Most tested for ANA 'always' (62%) or 'sometimes' (34%) in a new patient. Clinical suspicion of evolving CTD and family history influenced decision.
ANA, if positive, was mostly repeated 'sometimes' (50%), rather than 'always' (23%) or 'not repeated' (27%). Titre, clinical condition and symptom evolution influenced decision to repeat. This was mostly done at 6-months (37%) or 12-months (21%).
SSc-specific antibodies were mostly measured 'sometimes' (41%) - particularly if scleroderma features. 29% tested these only if ANA positive, 13% never did. Other ENA (93%), Scl70/topoisomerase I (82%) and centromere (71%) were most often included.
Most performed NFC at diagnosis: 'Yes always' (58%) or 'Sometimes' (28%). Only 14% did not. Ophthalmoscope was most often used (68%), followed by dermatoscope (28%). 3% used a USB microscope. 9% referred to another centre for formal video-capillaroscopy. Half could not access formal video capillaroscopy. The other half could directly or elsewhere.
Only 12% of respondents had received formal NFC training, with most receiving informal training (62%) or none (25%). Confidence levels were mixed. 43% of trainees were 'fairly confident' and 50% 'fairly unconfident'. 41% of consultants were fairly confident, 28% confident, 24% neutral and 7% fairly unconfident. 88% used descriptive free text to describe NFC changes. 14% classified as 'normal', 'non-specific' or 'scleroderma-type'.
FU of a patient with no risk factors for CTD varied with most choosing not to follow-up (37%) or to follow-up 'sometimes' (22%). Frequency of follow-up (FU) was 'It depends' (45%), 6-monthly (22%) or annually (24%). At subsequent visits, most would perform neither ANA nor NFC (33%).
The vast majority (94%) would FU a patient with clinical and laboratory risk factors for CTD (3-monthly 19%, 6-monthly 28%, annually 12%, 'It depends' 41%). Most would do both ANA and NFC at subsequent visits (41%)
The commonest first-line treatment for primary RP was calcium channel blocker (76%), for RP with tissue damage IV prostinoid (34%) and calcium channel blocker (34%).
Conclusion: Among UK & Ireland clinicians, there is variation in definition, diagnosis, monitoring and management of paediatric RP.
Access to imaging including NFC by video-capillaroscopy was poor. Our survey highlighted a NFC training need and un-warranted variation in practice from PRES working party recommendations.
Disclosure of Interest: None declared

O076

NO DISEASE PROGRESSION AFTER 36 MONTHS FOLLOW UP IN THE JUVENILE SYSTEMIC SCLERODERMA INCEPTION COHORT.

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Introduction: Juvenile systemic scleroderma (jSSc) is an orphan disease with a prevalence of 3 in 1 000 000 children. Longitudinal prospective follow up data of patients with jSSc is rare. In the international juvenile systemic scleroderma cohort (jSScC) patients are followed with a standardized assessment prospectively.
Objectives: To assess the progression of jSSc over 36 months in the jSScC
Methods: Patients diagnosed according the ACR 2013 criteria for systemic sclerosis were included, if they developed the first non-Raynaud symptom before the age of 16 and were under the age of 18 at the time of inclusion. Patients were followed prospectively every 6 months with a standardized assessment.
Results: 39 patients in the JSScC had 36 months follow up. 80% had a diffuse subtype. 95% of the patients were Caucasian origin. 31 of the patients were female (80%). Mean disease duration at time of inclusion was 3.5 years. Mean age onset of Raynaud's was 8.8 years and mean age of onset at the first non-Raynaud´s was 9.5 years. Around 30% of the patients were anti-Scl70 positive and none of them anti-centromere positive. The MRSS dropped from the time point of the inclusion into the cohort from 13.9 to 11.8 after 36 months. Pattern of organ involvement did not show any significant change, beside the increase of the nailfold capillary changes from 49% to 73% (p=0.037). No renal crisis occurred. No mortality was observed.
They were positive significant changes in the patient related outcomes. The physician global disease activity decreased from 40.0 to 22.1 assessed on a VAS scale of 0 to 100 ($p < 0.001$).
Patients global disease activity decreased from 43.3 to 20.4 and patients global disease damage from 45.0 to 21.7 both assessed on a VAS scale of 0 to 100 ($p<0.001$).
Conclusion: After 36 months follow up, we could observe a significant improvement of patient related outcomes and only one significant change in organ pattern involvement. In a mostly diffuse subset patient population this is a very promising result regarding outcome.
Supported by the "Joachim Herz Stiftung"
Disclosure of Interest: None declared

O077

LUPUS LOW DISEASE ACTIVITY STATE (LLDAS) IS ASSOCIATED WITH REDUCED FLARE FREQUENCY AND DAMAGE ACCRUAL IN CHILDREN WITH JUVENILE-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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Introduction: Treat to target (T2T), in which treatment is adjusted or escalated until a specific target is achieved, is now part of routine clinical care in many areas of medicine. It has been proposed as a strategy to improve management of juvenile-onset systemic lupus erythematosus (JSLE), using existing treatments in a more structured way. The TARGET LUPUS research programme: 'Targeting disease, Agreeing Recommendations and reducing Glucocorticoids through Effective Treatment, in LUPUS' has been established in order to develop a JSLE T2T study. In adult SLE, Lupus Low Disease Activity State (LLDAS) is considered one of the most achievable and realistic targets. LLDAS is based on the principle of "tolerated" or "acceptable" levels of disease activity in a patient with a stable treatment and low dose of corticosteroids, with a low likelihood of adverse outcome. The achievability and impact of achieving LLDAS has not been explored in children to date.
Objectives: To evaluate if and when JSLE patients achieve LLDAS and how this impacts on disease flare and damage.
Methods: Participants of the UK JSLE Cohort Study (2006-2019), <18 years at the time of diagnosis, with ³4 ACR criteria for SLE, were eligible for inclusion. At each study visit achievement of LLDAS was assessed for. LLDAS was defined as per the Asia-Pacific Lupus Collaboration: SLEDAI-2K ≤4, without involvement of major organs (renal, central nervous system, cardiopulmonary, vasculitis or fever) nor haemolytic anemia or gastrointestinal involvement, and no new features of JSLE compared with previous assessment, together with a physicians global assessment ≤1, allowing the patient to be on treatment with ≤7.5mg/day of prednisolone and/or well tolerated standard doses of immunosuppressive drugs.
Recurrent events analysis was undertaken using Prentice-Williams-Petersen GAP models, to determine the impact of recurrent episodes of LLDAS on severe disease flare (defined as a BILAG score of A/B in any organ domain). A Cox proportional hazards model with time-varying covariates was used to assess impact of LLDAS on new damage accrual (defined as ≥1 in the SLICC SDI index).
Results: 348/432 (81%) of JSLE patients achieved a state of LLDAS when followed-up for a median of 46 months (IQR 18-63). LLDAS was first achieved 10.6 months (IQR 4-20) after diagnosis, with patients achieving this state for 32% (IQR 11-51%) of their total follow-up time. Within a multivariate model, the risk of severe flare was reduced in those: achieving LLDAS (HR 0.19, 95% CI 0.16,0.23, p<0.001), with a disease duration of >1 year (HR 0.85, 95% CI 0.81,0.89, p<0.001) and of Asian (HR 0.82, 95% CI 0.69, 0.98, p=0.03) or white British ethnicity (HR 0.83, 95% CI 0.70, 0.97, p=0.02). The risk of new damage was also reduced in those achieving LLDAS, HR 0.73 (95% CI 0.58, 0.93, p=0.01).
Conclusion: To our knowledge this is the first paediatric study to evaluate the achievability and impact of LLDAS in JSLE in a national cohort. We have demonstrated that achieving a state of LLDAS is beneficial, reducing the risk of severe flare and damage. LLDAS should therefore be considered as a realistic treatment target for use within a future JSLE T2T study. Further studies evaluating alternative treatment targets (e.g. remission on/off treatment), comparing them also with LLDAS in children, are warranted.
Disclosure of Interest: None declared

O078

DEVELOPING A STANDARDIZED CORTICOSTEROID DOSING REGIMEN IN PEDIATRIC PROLIFERATIVE LUPUS NEPHRITIS

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Introduction: Corticosteroids (CS) remain the mainstay of therapy for childhood-onset systemic lupus erythematosus (cSLE). However, widely accepted strategies for oral (PO) or intravenous (IV) CS dosing are lacking.
Objectives: 1) Develop a standardized CS dosing regimen (SSR) and 2) achieve consensus for this SSR among pediatric rheumatology and nephrology physicians treating cSLE, including lupus nephritis (LN).
Methods: Step(S)1: A Delphi questionnaire helped select covariates influencing CS dosing in LN. S2: Data from 147 children with proliferative LN were used to generate Patient Profiles (PP) describing cSLE course at 2 subsequent visits. S3: PP were sent to 142 physicians experienced in cSLE to rate the course of LN, extrarenal disease (ER), and propose CS dosage for PP. S4: SSR was developed using PP data. S5: SSR was refined using a focus group of experienced physicians; and S6: validated using PP describing disease course for ≤6 months after kidney biopsy. Consensus was defined by majority of PP ratings.
Results: In Steps 1/3, 103 physicians rated 353 PP. In Step 6, 18 physicians were asked to review 33 PP each resulting in 564 PP ratings of which 437 (77.5%) and 460 (81.6%) yielded consensus on PO and IV CS dosages respectively. CS doses depend on courses of ER and LN. The latter is defined by 3 LN response variables (glomerular filtration rate, proteinuria, hematuria). PO CS ≥40mg are guided by LN course except in ER flares with organ damage. IV CS are used for disease courses that fail to respond to PO CS ≥40mg for up to 4 weeks (Table 1). Small decreases of PO CS occur with stable LN or ER. Complete renal remission (CRR) allows more pronounced reduction of PO CS. Six months after kidney biopsy CS dose is informed by partial renal remission (PRR) or CRR during induction therapy, the course of LN and ER (Table 1).

Table 1. Corticosteroid (CS) use provided by the standardized CS dosing regimen (SSR)

INITIAL 4 WEEKS OF INDUCTION THERAPY	
PO CS	**IV CS**
Patients≥50kg→Prednisone 60mg/day (or CS equivalent) Patients<50kg→Prednisone 1.5mg/kg/day Lowest dose at week 4→30mg/day for patients≥50kg	Up to 3 doses (30mg/kg; max 1 gram)
WEEKS 5–26 OF INDUCTION THERAPY*	
LN course	***Much worse:*** Increase PO CS to 50-60mg/day; After 1-3 weeks, if response is (a) *Satisfactory→ No IV CS; (b) Non-satisfactory→ IV pulses +PO CS* ***Mild–moderately worse****:* Increase PO CS by 30% (if dose<40mg; max 60mg) ***Active stable:*** Stable PO CS dose (if dose<40mg; else: slow decrease) ***Improved active or PRR[1]:*** Slow decrease; ***CRR[2]:*** More pronounced decrease of PO CS dose
Lowest PO CS dose at week 26	10mg/day
BEYOND 26 WEEKS POST KIDNEY BIOPSY*	

LN course	***Flare[3] after PRR/CRR:*** Prednisone≥40mg; After 1-3 weeks, if response is (a) *Satisfactory→ No IV CS; (b) Non-satisfactory→ IV pulses + PO CS* ***Worse after PRR/CRR:*** Increase PO CS dose FIRST ***PRR stable:*** Slow decrease; ***CRR or PRR improved:*** More pronounced decrease of CS dose	

[1] PRR: >50% improvement of ≥2 LN response variables (LN-RVs) +remaining LN-RV NOT worse; [2] CRR: LN-RVs are NORMAL; [3]LN flare: ≥1 of the LN-RV changes is persistently present on ≥2 subsequent time points ≥1week apart;
**(assumption stable ER)*

Conclusion: The proposed SSR for LN in cSLE may be useful for clinical care and to regulate background CS use in clinical trials of new medications for cSLE.

Disclosure of Interest: None declared

O079

RENAL ACTIVITY INDEX FOR LUPUS NEPHRITIS DISTINGUISHES ACTIVE RENAL DISEASE AMONG CHILDHOOD SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Introduction: Renal involvement in childhood-onset systemic lupus erythematosus (cSLE) is a major cause of morbidity and mortality. Conventional tools to identify lupus nephritis (LN) fall short compared to renal biopsy. The renal activity index in lupus (RAIL) was developed using 6 urinary biomarkers to reflect disease activity(1).

Objectives: To test the usefulness of the RAIL in the clinical setting to identify children with active LN.

Methods: Urine samples were collected cross-sectionally from cSLE patients at the time of active LN or routine clinic visit. Patients were classified into active LN, inactive LN or non-LN SLE based on results of a renal biopsy and/or absence of LN determined by routine urinalysis. The following urine biomarkers are included in the RAIL score (neutrophil gelatinase-associated lipocalin, ceruloplasmin, monocyte chemoattractant protein-1, adiponectin, hemopexin, kidney injury molecule-1, urinary protein and creatinine). Analysis was done by Enzyme-linked immunosorbent assay (ELISA) and nephelometry. RAIL scores were calculated per the defined algorithm for each urine sample. Other data was collected (Table 1). The accuracy of the RAIL score was compared between groups.

Results: Among 117 cSLE patients, 37 had active LN, 30 had inactive LN and 50 had no LN. Clinical characteristics and distribution of RAIL scores are outlined in Table 1. RAIL scores of inactive LN and no-LN group largely overlapped so they were combined in one group (Group 2) and compared to active LN (Group 1). The RAIL score was significantly higher in Group 1 vs Group 2 (median 0.7 vs -1.1 respectively, $p<0.0001$). The RAIL score diagnostic accuracy was assessed in a multivariable regression model. Adjusting for patient's age and extra-renal SLE activity index (SLEDAI) score, the RAIL score was associated with odds ratio of 2.16 (95%CI 1.4-3.3, $p=0.001$) for active LN vs. inactive LN and non-LN SLE. A receiver operating curve for a RAIL cut-off score of 0.35 produced an area under the curve of 0.9 (sensitivity 86%, specificity 84%) for active LN. A RAIL score <0.35 had a negative likelihood ratio of 0.17. Further adjustment for urinary protein and creatinine did not significantly influence the results.

Table 1. Clinical characteristics and distribution of RAIL scores among Group 1 (active LN) and Group 2 (inactive LN + non-LN SLE) patients.

	Group 1 Active LN N = 37	Group 2 Inactive LN + Non-LN SLE N = 80	*p*-value
Age (y)	15 (13-17)	18 (16-21)	<0.0001
NIH-AI¥	9 (4-13)	0 (0-0)	<0.0001
NIH-CI¥	1 (0-2.75)	0 (0-0)	0.12
Extra-renal SLEDAI	9 (6-13)	2 (0-4)	<.0001
GFR	91 (60-129)	108 (98-126)	0.05
Urinary creatinine	92 (61-191)	134 (73-183)	0.32
Urinary protein	254 (98-404)	21 (11-50)	<.0001
Urinary microalbumin	254 (189-316)	15 (9-43)	<.0001
RAIL Score	0.7 (-0.1-1.6)	-1.1 (-2.5-0.3)	<.0001

Values represent median (interquantile range).

¥ Includes active (N=24) and inactive LN (N=4) patients only. Only those who had renal biopsies within 30 days of urine collection are included.

Conclusion: The RAIL score is highly accurate in distinguishing active LN identified by renal biopsy, from inactive LN and non-LN SLE. A score of 0.35 identifies cSLE patients who very likely have active LN.

Disclosure of Interest: None declared

O080

NAILFOLD CAPILLARY ABNORMALITIES IN A CROSS-SECTIONAL STUDY IN CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS COMPARED WITH MATCHED HEALTHY CONTROLS

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Introduction: Nailfold capillaroscopy (NFC), a noninvasive magnification method, is used to visualize the capillaries of the fingertips. NFC is a diagnostic instrument, used in patients with Raynaud's phenomenon: a capillary scleroderma pattern is associated with systemic sclerosis (SSc). Systemic Lupus Erythematosus (SLE) patients also show capillary abnormalities in NFC. As concluded in a recent review, adults with SLE show significantly higher number of tortuous capillaries, abnormal capillary morphology and capillary hemorrhages, when compared to healthy controls. Additionally, the capillary abnormalities also seem to correlate with disease activity. Studies on nailfold capillary findings in children with SLE are scarce and inconclusive. For systemic sclerosis (SSc), multiple studies have shown that capillary abnormalities (by qualitative description) can also be of use as a prognostic biomarker. For selection of high-risk SLE-patients it is necessary to obtain more indicators of disease severity that predict disease damage. Nailfold capillary abnormalities could be such an indicator or biomarker in SLE.

Objectives: The primary objective of this cross-sectional study is to describe capillary abnormalities in cSLE patients and compare them with healthy controls, matched for skin pigmentation, age and gender. These demographic variables have been described as confounding factors in healthy controls in interpreting capillary characteristics, such as density. The secondary objective is to correlate the observed capillary abnormalities with demographical variables in both cohorts and with disease-specific variables in cSLE patients.

Methods: Healthy controls were matched for ethnic background, age and gender. Quantitative and qualitative assessments of nailfold capillaroscopy images were performed according to the definitions of the EULAR study group on microcirculation in Rheumatic Diseases.

Results: Both groups (n=41 cSLE-patients and n=41 healthy controls) were comparable for ethnic background (p=0.317). Counted per mm, cSLE-patients showed significantly more 'giants' (p=0.032), 'abnormal capillary shapes' (p=0.003), 'large capillary hemorrhages' (p<0.001) and 'pericapillary extravasations' (p<0.001). Combined 'abnormal capillary shapes and pericapillary extravasations' (in the same finger) were detected in 78% (32/41 patients). 'Microangiopathy' was detected in 68.3% (28/41) and a 'scleroderma pattern' in 17.1% (7/41) of the cSLE-patients. The number of abnormal capillary shapes per mm was significantly correlated with treatment-naivety (p=0.022). The number of large pathological hemorrhages per mm was significantly correlated with disease score (p=0.002) and presence of nephritis (p=0.012). Compared to healthy controls, pericapillary extravasations were found in significantly higher numbers per mm (p<0.001), as well as in percentage of patients (p<0.001). Pericapillary extravasations were also significantly positively correlated with darker skin pigmentation in both study cohorts.

Conclusion: As in adult SLE-patients, our nailfold capillaroscopy study confirms the presence of significantly more giants, abnormal capillary morphology and hemorrhages in cSLE, when compared to healthy controls. Significant correlations were found between these capillary abnormalities and disease activity. A high frequency and total amount of "pericapillary extravasations" was observed in cSLE patients, possibly revealing a new subtype of capillary hemorrhage.

Trial registration identifying number: Dutch trial register registration no. NL60885.018.17

Disclosure of Interest: None declared

O081

NEUROPSYCHIATRIC INVOLVEMENT IN JUVENILE-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS (JSLE): DATA FROM THE UK JSLE COHORT STUDY

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Introduction: Juvenile-onset systemic lupus erythematosus (JSLE) is a rare autoimmune/inflammatory disease, accounting for up to 20% of SLE cases. Though clinically similar to adult-onset disease, it frequently follows a more severe course. Neuropsychiatric (NP) involvement in JSLE can be aggressive and significantly affect patients' quality of life as well as disease outcomes.
Objectives: The aim of this study was to describe the demographic characteristics, clinical and laboratory features of NP involvement in JSLE.
Methods: We analyzed data from JSLE patients enrolled in the UK JSLE Cohort Study between August 2006 and June 2019. Demographic (age, gender, ethnicity, family history), clinical (1997 ACR classification criteria, disease activity BILAG, SLICC, and damage index SLICC-SDI) and laboratory (ESR, CRP, CBC with diff, ANA, anti-ENA, anti-dsDNA, aCL, lipid profile, renal function, C3, C4, Ig levels, thyroid function, UA) data collected at disease onset and at last visit were analyzed.
Results: A total of 428 JSLE patients were included, with a female:male ratio of 5.4:1. The median age at diagnosis was 12.2 years (range: 0-17). A majority of JSLE patients were Caucasian (51.4%), followed by patients of South Asian (23.3%), Black African/Caribbean (16.7%), and East Asian (6.5%) descent. Patients with headaches as the only NP symptom were excluded here, because of the low specificity of this feature.
Overall, one quarter of JSLE patients (107/428, 25%) showed NP features; in 48.5% of these cases, NP symptoms were the presenting manifestation. The median age at disease onset and ethnic composition did not differ between sub-cohorts with vs without NP involvement. Most frequently recorded NP manifestations recorded included cognitive impairment (n=45, 42%), seizures (n=21, 20%), psychotic features (n=11, 10%), peripheral nerve involvement (n=9, 8%), cerebral vasculitis (n=10, 9%), and ischaemic stroke (n=7, 6%). Headache was an accompanying manifestation in 74% of all NP SLE patients. While no differences were recorded in autoantibody patterns and immune cell counts, lower platelet counts (<100.000/mmc) were found in patients with NP involvement at disease onset (p=0.02). Children with NP involvement showed both a higher number of ACR criteria (mean 4.9 *vs* 4.6, p=0.07) and higher SLICC scores (0.3 *vs* 0.2, p=0.029) at disease onset.
Conclusion: Approximately 25% of JSLE patients enrolled in the UK JSLE Cohort Study have NP involvement. Patients with NP involvement exhibit more disease-associated damage at the time of diagnosis when compared to patients without NP involvement and therefore represent a high-risk group.
Disclosure of Interest: None declared

O082

UTILIZATION OF ANTI-NUCLEAR ANTIBODY ANALYSIS IN TERTIARY PEDIATRIC CLINIC

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Introduction: Anti-nuclear antibody (ANA) is a large group of autoantibodies that occurred predominantly against cellular antigens found in the cell nucleus. It uses as the diagnosticmarker for systemic lupus erythematosus (SLE) and the other autoimmune diseases. ANA positivity can be detected in malignancy,infection as well as healthy population.
Objectives: We aimed that evaluation of how the ANA test was used in the clinical practice of a tertiary center.
Methods: Patients performed ANA test under the 18 year old were collected in period of 2013-2017 years. Demographic and clinical features, diagnosis, ANA result, titer, and staining pattern were obtained from the medical records The sensitivity and specificity of ANA titer at ≥1/100 and ≥1/1000 were evaluated based on the features of the patients at the time of autoimmun disease diagnosis.
Results: Total number of patients performed ANA tests were 3812. Of these patients, we achieved 3320 patients' medical records.
Anti-nuclear antibody was positive in 909 (27,4%) and negative in 2411 (72,6%) of the patients. Positiveness was more in females than males (respectively n= 617 (18,6%), n=292 (8,8%), p<0,0001). The most frequent clinical reason of patients performed ANA test was musculoskeletal findings (n=1355 (40,8%)).
The most common autoimmune disease was juvenile idiopathic arthritis (n=174, 20,2%) in patients with ANA positivity. Patients with SLE (n:52, 6%) followed the JIA. In patients diagnosed autoimmune diseases, for ANA titer up to 1/100 , positive predictive value (PPV) was 37,9%, negative predictive value (NPV) was 78,6%, sensitivity was 40,1%, specificity was 77,1%. For the titer of ANA≥1/1000, positive predictive value (PPV) was 43,4%, negative predictive value (NPV) was 77%, sensitivity was 24,1%, specificity was 89%.

Table 1: The clinical findings and diagnosis of patients performed ANA test and ANA results in patients with and without autoimmune diseases

Clinical findings	**n (%)**	
Musculoskeletal	1355 (40,8%)	
Neurologic	417 (12,6%)	
Enterohepatic	363 (10,9%)	
Skin lesions	284 (8,6%)	
Hematologic	247 (7,4%)	
Other	654 (19,6%)	
	ANA negative n (%)	**ANA positive n (%)**
Rheumatic diseases		
Juvenile idiopathic arthritis	286 (33,2%)	174 (20,2%)
Systemic lupus erythematosus	0	52 (6%)
İdiopathic uveitis	37 (4,3%)	16 (1,9%)
Psoriasis	5 (0,6%)	4 (0,5%)
Systemic sclerosis	0	7 (0,8%)
Localize scleroderma	8 (0,9%)	1 (0,1%)
Mix connective tissue disease	2 (0,2)	4 (0,5%)
Juvenile dermatomyositis	4 (0,5%)	3 (0,3%)
Sjögren disease	0	3 (0,3%)
Non-rheumatic diseases		
Autoimmune hepatitis	11 (%1,3)	20 (2,3%)
Inflammatory bowel disease	4 (0,5%)	3 (0,3%)
Celiac disease	19 (2,2%)	10 (1,2%)
Immune thrombocytopenic purpura	44 (5,1 %)	12 (1,4%)
Autoimmune hemolytic anemia	9 (1%)	4 (0,5%)
Multiple sclerosis	17 (2%)	5 (0,6%)
Optic neuritis	8 (2%)	1 (0,1%)
Guillain Barre Syndrome	8 (0,9%)	2 (0,2%)

Acute disseminated encephalomyelitis Chronic autoimmune urticaria Type 1 diabetes mellitus Tubulointerstitial nephritis	4 (0,5%) 1 (0,1%) 6 (0,7%) 6 (0,7%)	2 (0,2%) 4 (0,5%) 2 (0,2%) 0	
Other	36 (4,2%)	16 (1,9%)	
Total	**515 (59,9)**	**345 (40,1%)**	
ANA ***≥1/100 titer***	**With autoimmune diseases n (%)**	**Without autoimmun diseases n (%)**	**Total (%)**
Positive Negative ***≥1/1000 titer***	345 (%10.4) 515 (%15.5)	564 (%17) 1896 (%57.1)	909 (%27.4) 2411 (%72.6)
Positive Negative	208 (6.3%) 652 (19.6%)	270 (8.1%) 2190 (66%)	478 (14.4%) 2842 (85.6%)

Conclusion: Our results showed that performances of ANA test have low specificity and sensitivity to diagnosis of autoimmune diseases in clinical practices. Therefore clinical findings should be carefully evaluated before ANA test performed.

Disclosure of Interest: None declared

O083

MEDICATION UTILIZATION AND RENAL BIOPSY PATTERNS IN CHILDHOOD-ONSET LUPUS NEPHRITIS IN THE CHILDHOOD ARTHRITIS AND RHEUMATOLOGY RESEARCH ALLIANCE REGISTRY

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Introduction: Little is known regarding variation in care patterns within early management of pediatric lupus nephritis, which may be contributing to documented disparities in long-term renal outcomes.

Objectives: Our objective was to characterize sociodemographics, disease characteristics, and care utilization patterns from a large, multi-center North American cohort of cSLE patients with nephritis.

Methods: A cross-sectional analysis of the longitudinal, observational Childhood Arthritis and Rheumatology Research Alliance (CARRA) cSLE Registry was conducted on data prospectively collected from March 2017 to December 2019. Registry enrollment is ongoing with data collection every 6 months. Lupus nephritis was defined in patients with at least one renal biopsy date recorded and positive histopathologic classification by either 1995 World Health Organization (WHO) or 2003 International Society of Nephrology (ISN)/Renal Pathology Society (RPS) criteria. We abstracted the following variables: sex, race/ethnicity, insurance status, reported household income, reported parent education level, age at diagnosis, date of cSLE diagnosis, date of initial renal biopsy, WHO or ISN/RPS classification of initial renal biopsy, Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) at enrollment, physician global assessment (PGA) of disease activity (0-10) at enrollment, and medications prescribed both prior to and following enrollment. Descriptive statistics were calculated using SAS v9.4.

Results: Out of 566 cSLE patients, we identified 220 with renal biopsy-positive lupus nephritis across 44 pediatric rheumatology centers. The cohort was 83% female, 31% Black, 25% White, and 24% Hispanic with a mean age of 13.6 years at cSLE diagnosis (Table 1). In 23% of patients, date of renal biopsy occurred > 90 days after date of cSLE diagnosis. On initial biopsy, 16% of patients had class I/II, 63% had class III/IV, 14% had class V, 6% had combined class III+V / IV+V, and 1 patient had class VI. Biopsies were classified using WHO criteria in 69% of patients, ISN/RPS in 43%, and both in 12%. Repeat biopsy was performed on 19 patients (9%) with a change in classification in 11 (58%). There was high ever-use of hydroxychloroquine (97%) and mycophenolate (84%) across the cohort, while cyclophosphamide (28%) and rituximab (25%) were more varied. In 15 centers with ≥ 5 patients with class III/IV proliferative disease, mycophenolate use ranged from 60-100%, cyclophosphamide use ranged from 0-100%, and rituximab use ranged from 0-100% of patients.

Table 1. Demographic and clinical characteristics of patients with renal biopsy-positive lupus nephritis.

	Total Cohort (n = 220)
Minority race/ethnicity, n (%)	166 (75)
Non-private insurance status, n (%)	128 (58)
Household income <$75,000, n (%)	87 (40)
Parent education of high school or less, n (%)	71 (32)
SLEDAI-2K at enrollment, median (IQR)	4 (2-10)
Physician global assessment of disease activity at enrollment (0-10), median (IQR)	2.5 (1-4)
Time between cSLE diagnosis and renal biopsy, mean (SD) months	4.9 (13.8)

Conclusion: This initial study of patients with pediatric lupus nephritis in the CARRA Registry demonstrates a diverse cohort of patients with predominantly proliferative lupus nephritis. There is substantial variation medication utilization for proliferative nephritis between centers, as well as biopsy reporting practices across the cohort. Further study and implementation of optimal management for cSLE nephritis is needed to improve long-term outcomes.

Disclosure of Interest: E. Smitherman: None declared, R. Chahine: None declared, T. Beukelman Consultant for: Novartis, UCB, L. Lewandowski: None declared, A. Rahman: None declared, S. Wenderfer: None declared, J. Curtis: None declared, A. Hersh: None declared

Lightening talks: MAS and COVID-19

O084

HOW THE COVID-19 PANDEMIC HAS INFLUENCED PEDIATRIC RHEUMATOLOGY PRACTICE: RESULTS OF A GLOBAL, CROSS-SECTIONAL, ONLINE SURVEY

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Introduction: The COVID-19 (coronavirus disease 2019) pandemic is a global health problem threatening millions of lives worldwide. As pediatric rheumatologists, we have a role in the multidisciplinary management of COVID-19. Our young patients with rheumatic diseases are a vulnerable population in this pandemic. Moreover, the drugs we use to treat rheumatic diseases are being tested for use against COVID-19.

Objectives: To analyze how the COVID-19 pandemic has affected pediatric rheumatology practice.

Methods: For this cross-sectional survey study, we developed an online, self-administered survey that included 18 questions regarding changes in pediatric rheumatology practice due to the COVID-19 pandemic. Results were analyzed using descriptive statistics.

Results: Worldwide, 271 pediatric rheumatologists (54% ≥45 years; 65.7% female) from 60 countries responded to the survey in May 2020. Almost 70% of the respondents were practicing in a university hospital. 221 (81.5%) had been in pediatric rheumatology practice for ≥5 years. Nearly two-thirds of the respondents disagreed that the COVID-19 pandemic had led to reduced prescription of nonsteroidal anti-inflammatory drugs, conventional synthetic disease-modifying anti-rheumatic drugs (DMARDs), and biologic DMARDs. 220 (81.8%) did not change the management of patients who are using biologic DMARDs. Around 10% of the respondents were more inclined to prescribe hydroxychloroquine, while 237 (87.5%) did not report any change in their attitude towards prescribing this drug. Interestingly, 117 (43.2%) were more likely to taper corticosteroids faster. Most respondents reported that during the pandemic they hesitated to initiate treatment with cyclophosphamide (36.2%), followed by rituximab (25%). About half of the respondents cancelled scheduled appointments with established patients and shifted towards smartphone applications for patient care, while 40% postponed clinic appointments with new patients and used video consultations instead.

Approximately one-third of respondents indicated that their patients had experienced a delay in the diagnosis of a rheumatic disease or in receiving an intraarticular steroid injection, while 56 (20.7%) stated that their patients experienced a flare due to delayed clinical appointments. 97 (35.8%) mentioned that their patients had difficulties in obtaining hydroxychloroquine due to shortages and 30 (11%) noted the same problem with tocilizumab. Almost half of the respondents (n=120; 44.3%) think that children on long-term corticosteroid treatment should avoid attending school, while 51 (18.9%) believe that children using biologic DMARDs should avoid school; especially those using rituximab (n=103; 38%).

The respondents indicated that they had seen increases in the numbers of patients with Kawasaki disease (25.5%), macrophage activation syndrome (13.3%), unusual vasculitic rashes (28%), and hyperinflammation (22.5%), since the beginning of the COVID-19 pandemic.

Conclusion: The COVID-19 pandemic has affected pediatric rheumatology practice extensively. Most changes arose from delays in clinic appointments, use of anti-rheumatic drugs in COVID-19 treatment/prophylaxis and concerns about the immunosuppressive effects of anti-rheumatic therapies. In addition, an increase in the use of virtual technologies for routine communication with patients was observed.

Disclosure of Interest: None declared

O085

PAEDIATRIC MULTI-SYSTEM INFLAMMATORY SYNDROME TEMPORALLY ASSOCIATED WITH SARS-COV-2 MIMICKING KAWASAKI DISEASE (KAWA-COVID-19): A MULTICENTRE COHORT

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Introduction:
Current data suggest that COVID-19 is less frequent in children, with a milder course. However, over the past weeks, an increase in the number of children presenting to hospitals in the greater Paris region with a phenotype resembling Kawasaki disease (KD) has led to an alert by the French national health authorities.

Objectives: To describe paediatric multi-system inflammatory syndrome temporally associated with SARS-CoV-2 mimicking Kawasaki disease ('Kawa-COVID-19') in Paris region since April 2020.
Methods: Multicentre compilation of patients with Kawa-COVID-19. A historical cohort of 'classical' KD served as comparator. Factors associated to a severe outcome were assessed.

Results: Sixteen patients were included (sex ratio=1, median age 10 years IQR [4·7-12.5]). SARS-CoV-2 was detected in 11 cases (69%), whilst a further 5 cases had documented recent contact with a q-PCR-positive individual (31%). Cardiac involvement included myocarditis in 44% (n=7). Factors prognostic for the development of severe disease (i.e. requiring intensive care, n=7) were age over 5 years and ferritinemia >1400µg/L. Only 5 patients (31%) were successfully treated with a single intravenous immunoglobulin infusion (IgIV), whilst 10 patients (62%) required a second line of treatment. The Kawa-COVID-19 cohort differed from a comparator group of 'classical' KD by older age at onset 10 vs 2 years ($p<0.0001$), lower platelet count [188, vs 383 G/L ($p< 0.0001$)], a higher rate of myocarditis 7/16 vs 3/220 ($p= 0.0001$) and resistance to first IgIV treatment 10/16 vs 45/220 ($p= 0.004$).
Conclusion: Kawa-COVID-19 likely represents a new systemic inflammatory syndrome temporally associated with SARS-CoV-2 infection in children. Further prospective international studies are necessary to confirm these findings and better understand the pathophysiology of Kawa-COVID-19.
Disclosure of Interest: None declared

O086

ABSENCE OF SEVERE COMPLICATIONS FROM SARS-COV-2 INFECTION IN CHILDREN WITH RHEUMATIC DISEASES TREATED WITH BIOLOGIC DRUGS

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Introduction: Children with SARS-COV-2 infection seem to develop a milder disease. A certain increasein infectious risk in children with autoimmune and autoinflammatory conditions is well known, and has beenattributed both to the intrinsic immune dysregulation, or to immunosuppressive therapy: this could begenerating reasonable concerns in pediatric rheumatologist and patients' families. Preliminary experience inadults treated with conventional disease-modifying antirheumatic drugs (cDMARDs) and biologic disease-modifying drugs (bDMARDs) seems to be reassuring

Objectives: To investigate the impact of SARS-COV-2 infection on pediatric patients with rheumaticdiseases treated with bDMARDs.

Methods: Survey evaluating patients' health conditions, direct exposure to subjects known to be affected byCOVID-19, modifications of ongoing DMARDs treatment and potential flares of underlying disease duringthe early weeks of Italian COVID-19 outbreak.

Results: Between February 25th and April 14th 2020, we collected data from 123 patient (83 F) treated with bDMARDs and followed in our unit. The survey was administered during outpatient clinic visits, or by telephone. Median age was 13 years (range 4-20), median disease duration ws 6 years. Diagnosis were: juvenile idiopathic arthritis (89), chronic uveitis (5), autoinflammatory disease (5), other (24). Therapy consisted in Anti-TNF (95), anakinra (7), tocilizumab (7), other (14); eighty-one patients were also on a cDMARD. None of them were confirmed cases of COVID-19 . Eight children presented mild respiratory symptoms; three of them were family members of adults with probable COVID-19 infection (i.e. with fever, cough, difficulty to breath but no confirmatory positive Sars-Cov-2 Real-Time PCR . No patient stopped ongoing therapy nor needed hospitalization. All patients adopted a preventive strategy against COVID-19 based on social distancing and use of personal protective equipment, but usually only after the beginning of the outbreak.

Conclusion: No definitive conclusions about the incidence of SARS-CoV-2 infection in children with rheumatic diseases, nor on the overall outcome of immunocompromised patients affected by COVID-19 can be drawn from our study. However, in agreement with observations on adult rheumatology patients , our preliminary experience supports the idea that patients with chronic diseases treated with bDMARDs do not seem to be at increased risk of severe or life- threatening complications from SARS-CoV-2 compared with the general population. A strict disease control may be of great importance since it is known that disease activity may be a risk factor for the development of infections.

Disclosure of Interest: None declared

O087

COVID-19 IN PEDIATRIC RHEUMATOLOGY PATIENTS TREATED WITH BIOLOGIC DRUGS: A CROSS-SECTIONAL, PATIENT SURVEY STUDY

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Introduction: COVID-19 pandemic is a global health problem. Children are affected less compared to adults. Children with rheumatic diseases especially if treated with biologic drugs could constitute a vulnerable group in this pandemic. We lack data on the COVID-19 infection rate and disease course in pediatric rheumatology patients treated with biologic drugs.
Objectives: We aimed to analyze the frequency/severity of COVID-19 in pediatric patients with rheumatic diseases, treated with biologic drugs.
Methods: This is a cross-sectional survey study. We collected data about direct exposure to COVID-19 patients, presence of COVID-19 or symptoms associated with flu, and difficulties in obtaining biologic drugs they were using; starting from March 1st, 2020 when the first COVID-19 case was announced in Turkey. The survey was administered by telephone to all patients. In May 2020, we tried to reach to a total of 189 children with rheumatic diseases treated with biologic drugs who were being followed up in the Pediatric Rheumatology Unit of Hacettepe University, Ankara, Turkey. Results were analyzed using descriptive statistics.
Results: The final study population included 162 patients (48% female; mean age 13.2 ± 4.7 years). The underlying rheumatic diseases were as follows: Familial Mediterranean Fever (n=66), juvenile idiopathic arthritis (n=52), enthesitis related arthritis (n=16), cryopyrin-associated periodic syndrome (CAPS) (n=9), chronic recurrent multifocal osteomyelitis (CRMO) (n=6), ADA2 deficiency (DADA2) (n=4), Sting-associated vasculopathy with onset in infancy (SAVI) (n=3), scleroderma (n=3), Takayasu arteritis (n=3), hyperimmunoglobulin D syndrome (HIDS) (n= 3), polyareritis nodosa (n=2), Behçet's disease (n=2). The patients were on these biologic drugs: canakinumab (n=59), etanarcept (n=30), anakinra (n=26), adalimumab (n=18), tocilizumab (n=13), tofatisitinib (n=6), infliximab (n=4), rituximab (n= 3), secukinumab (n=2), barisitinib (n=1). Thirty patients had flu-associated symptoms and 14 of these were tested with RT-PCR for COVID-19. The results were negative in all. Thirteen (8%) patients reported that they had difficulty accessing their prescribed drugs.
Conclusion: None of our patients with rheumatic diseases treated with biologic drugs were diagnosed with COVID-19 nor had severe flu-associated complications. In our cohort, the pediatric rheumatology patients treated with biologic drugs did not seem to be at increased risk for COVID-19-associated severe complications compared to general population.
Disclosure of Interest: None declared

O088

STUDY OF EMAPALUMAB, A FULLY HUMAN, ANTI-IFN GAMMA MONOCLONAL ANTIBODY, IN PATIENTS WITH MAS/SHLH ON A BACKGROUND OF SJIA AND WITH INADEQUATE RESPONSE TO HIGH-DOSE GLUCOCORTICOIDS

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Introduction: Macrophage activation syndrome (MAS) is a severe complication of rheumatic diseases and occurs most frequently in patients with systemic juvenile idiopathic arthritis (sJIA). Data from animal models and from observational studies in patients suggest that interferon gamma (IFNγ) is a driver of the hyperinflammation and hypercytokinemia observed in MAS/secondary hemophagocytic lymphohistiocytosis (sHLH).

Objectives: The purpose of this study is to assess the pharmacokinetics, efficacy, and safety of intravenous (IV) infusions of emapalumab, a fully human anti-IFNγ monoclonal antibody, in patients with MAS in the context of sJIA.

Methods: This ongoing, pilot, open-label, single-arm study (NCT03311854) includes patients with MAS (2016 ACR/EULAR criteria) on a background of confirmed, or high presumption of, sJIA, and with inadequate response to high-dose IV glucocorticoids. Twin study protocols are established in Europe and North America. Emapalumab is initiated at 6 mg/kg (1 dose) and continued at 3 mg/kg every 3 days for 2 weeks, and then twice weekly for a total of 4 weeks, or less upon achievement of complete response (CR). CR is defined as an absence of MAS clinical signs plus white blood cell and platelet counts above the lower limit of normal, LDH, AST and ALT <1.5 x upper limit of normal, fibrinogen >100 mg/dL, and ferritin decreased by ≥80% or to <2,000 ng/mL.

Results: We report preliminary data from the first 9 patients (median age [range] 11.6 [2.1-25.3] years) enrolled (7 in Europe and 2 in the USA). All patients had failed high-dose methylprednisolone, of which there were prior treatment failures from cyclosporin A (n=4) and from anakinra (n=4). Treatment with emapalumab resulted in rapid IFNγ neutralization, as demonstrated by a decrease in CXCL9 levels, and subsequent deactivation of T cells, as indicated by the decrease in sIL-2R levels (Table). CR was achieved in all patients after a median of 23 (12-56) days. A progressive improvement in all clinical and laboratory parameters of MAS was observed. Glucocorticoids were tapered in all patients (median tapering 92%; range 45% to 98% at Week 8). Emapalumab infusions were well tolerated by all patients, with no discontinuation. CMV reactivation was reported in 1 patient as a serious event possibly related to emapalumab and resolved with antiviral treatment.

Parameters	Median baseline value (range)	Median days of treatment (range)
D-dimers to <1000 mg/L	12,480 (550-89,552)	15 (1-49)
sIL-2R to <2000 ng/L	4,596 (1,664-20,954)	21 (6-37)
Ferritin <500 mg/L	29,240 (716-192,584)	21 (9-42)
Physician visual analog scale of MAS activity ≤1	9.0 (2-10)	19 (9-56)
All MAS laboratory parameters within range of complete response	NA	21 (15-55)
All MAS parameters within range of complete response	NA	23 (12-56)
Glucocorticoid tapering at ≤1 mg/kg prednisolone equivalent	NA	42 (16-53)

Conclusion: Emapalumab administration led to rapid neutralization of IFNγ (rapid decrease in CXCL9 levels) and was efficacious in controlling MAS (all patients achieved complete response) and had a favorable safety profile. These results support the pathogenic role of IFNγ in MAS/sJIA and the therapeutic value of IFNγ neutralization in MAS patients who have failed high-dose glucocorticoid treatment.

Trial registration identifying number: NCT03311854

Disclosure of Interest: F. De Benedetti: None declared, P. Brogan Consultant for: Sobi, Novartis, Roche, UCB, C. Bracaglia: None declared, M. Pardeo: None declared, G. Marucci: None declared, E. Sacco: None declared, D. Eleftheriou Speaker Bureau of: Sobi, C. Papadopoulou: None declared, A. Grom Consultant for: Novartis, NovImmune, AB2Bio, P.

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O089

RISK SCORE OF MACROPHAGE ACTIVATION SYNDROME IN PATIENTS WITH SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: MAS is a severe, life-threatening, complication of sJIA with a significant mortality. A score that identify sJIA patients with high risk to develop MAS would be useful in clinical practice.
Objectives: To evaluate whether routine laboratory parameters at disease onset may predict the development of MAS in patients with sJIA. To define a risk score of MAS using these parameters and to validate the score in a second population.
Methods: Laboratory parameters of disease activity and severity were retrospectively evaluated in 99 sJIA patients referred to Bambino Gesù Hospital in the last 10 years with at least 2 years of follow-up. Laboratory parameters were evaluated during active sJIA, without MAS, at disease onset or disease flare, immediately before treatment for sJIA was started or modified. Patients were divided in sJIA patients without MAS in the 2 years of follow-up and sJIA patients with at least one MAS episode. To create the MAS risk score, laboratory parameters with a statistically significant difference between the 2 groups were selected.
Results: Thirty patients, that fulfilled the 2016 classification criteria for MAS at time of sampling, were excluded from the analysis. Therefore, we analysed laboratory parameters of 69 sJIA patients, 41 without MAS in the follow-up and 28 with at least one episode of MAS. Levels of ferritin, AST, LDH and triglycerides were significantly higher in patients with MAS during follow-up compared to those without. Their respective cut-off were computed by means of ROC curve analysis. A regression coefficient-based scoring system was used to assign weights to the risk index and the optimal score cut-off was defined by ROC curve analysis (Table1). A MAS risk score $\geq$5 identified 27 out of 28 sJIA patients with MAS during the follow-up and 8 out of 41 sJIA patients without MAS. Sensitivity (Se), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV) of the score are detailed in table 1. In order to validate the MAS risk score on a different population, we applied the score on 132 sJIA patients from other paediatric Rheumatologic centres, 100 without history of MAS and 32 with at least one episode of MAS. Se, Sp, PPV and NPV of the score are reported in table 1.
Table 1. Laboratory parameters and cut-off used to create the MAS risk score in sJIA patients. Se, Sp, PPV and NPV in the construction and validation cohorts.

Laboratory parameters	**Cut-off**	**Score**
Ferritin (ng/ml)	>750	3.5
LDH (UI/L)	>540	2.5
AST (UI/l)	>30	2
Triglycerides (mg/dl)	>100	1.5
	Construction cohort	**Validation cohort**
Sensitivity (Se)	96.4	81.3
Specificity (Sp)	80.5	60.0
Positive predictive value (PPV)	77.1	39.4
Negative predictive value (NPV)	97.1	90.9

Conclusion: In conclusion we developed a MAS risk score based on routine laboratory parameters, available worldwide, that can help clinicians to identify early in the disease course sJIA patients with high risk to develop MAS.
Disclosure of Interest: S. Carbogno: None declared, D. Pires Marafon: None declared, G. Marucci: None declared, E. Sacco: None declared, M. Pardeo: None declared, H. Alsaleem: None declared, S. Fingerhutova: None declared, D. Ferhat: None declared, N. Čekada: None declared, M. Kostik: None declared, C. Kessel: None declared, O. Vougiouka: None declared, A. Gagro: None declared, J. Tibaldi: None declared, F. Minoia: None declared, I. Maccora: None declared, R. Schneider: None declared, P. Dolezalova: None declared, B. Sozeri: None declared, M. Jelusic: None declared, A. Insalaco: None declared, F. De Benedetti Consultant for: Grant Research Support from Novartis, Novimmune, Hoffmann- La Roche, SOBI, AbbVie, Pfizer, C. Bracaglia: None declared

O090

A PATIENT WITH IFNAR2 DEFICIENCY CAUSING DYSREGULATION OF NK CELL FUNCTIONS AND PRESENTING WITH HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS

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Introduction: Hemophagocityc lymphohistiocytosis (HLH) is a life-threatening syndrome characterized by a hyperinflammatory state. HLH is typically caused by biallelic mutations in genes encoding proteins involved in the cytotoxic activity of T lymphocytes and natural killer (NK) cells (primary HLH), but it can also occur, in the absence of known genetic causes, in the context of malignancies, infections and rheumatic diseases (secondary HLH). A constitutive or transient defect in NK cell cytotoxicity is typically occurring in patients with, respectively, primary and secondary HLH and is believed to play a key role in the pathogenesis of the disease.

Objectives: HLH has also been reported in patients with inherited primary immunodeficiencies, including those caused by inborn errors of type I IFN-mediated immune responses. Here, we describe a 2 years boy with two previously undescribed frameshift mutations in the interferon (IFN)α/β receptor 2 (*IFNAR2*) gene presenting with HLH following measles-mumps-rubella (MMR) vaccination. The relation between HLH and defective type I IFN-mediated responses is to date unclear.

Methods: Clinical Exome, using a custom panel including 6920 genes known as associated to genetic diseases, was sequenced on NovaSeq6000® platform. *In silico* analysis was performed on the basis of the patient's clinical phenotype. Peripheral blood mononuclear cells (PBMCs) were isolated from the patient and his family and stimulated with IFNα or IFNγ; phosphorylation of STAT1 and type I and type II IFN signatures were analyzed by flow cytometric and RT-PCR analyses. NK cell degranulation and IFNγ production were analysed by flow cytometry.

Results: Here we report the case of a 2 year old Caucasian boy presenting with high fever and lethargy five days after inoculation of live-attenuated MMR vaccine. Laboratory parameters were suggestive for secondary HLH, with progressive decrease in cell blood count, hyperferritinemia, elevation of liver enzymes and lactate dehydrogenase and hypofibrinogenemia. We identified two novel frameshift mutations c.234delT and c.555_559delAAAAG, in a compound heterozygous status, in *IFNAR2* gene (OMIM# 602376), resulting respectively in p.Leu79Ter and p.Ile185MetfsTer12 variants. Both mutations were predicted to be damaging by *in silico* tools, since they introduce premature stop codons leading to the putative complete lack of the protein. Functional analyses confirmed the absence of response to type I IFN in the patient's cells, as revealed by lack of phosphorylation of STAT1 and lack of induction of interferon-stimulated genes upon *ex vivo* stimulation with IFNα, and demonstrated that the response to IFNγ was not affected. In addition, consistent with data demonstrating that a direct action of type I IFN on NK cells is necessary for the innate immune defence against vaccinia viral infections, we showed that in patient's NK cells stimulated with IFNα the expected increase in degranulation and inhibition of IFNγ production were affected.

Conclusion: Our data support a role for NK cell function dysregulation and lack of inhibition of IFNγ production as contributors to the development of HLH in patients with impaired type I IFN signalling. Finally, from a clinical perspective, HLH episodes following administration of live-attenuated viral vaccine should be considered as suggestive of a defect in the type I IFN response.

Disclosure of Interest: None declared

O091

TRADITIONAL LABORATORY PARAMETERS AND NEW BIOMARKERS IN MACROPHAGE ACTIVATION SYNDROME (MAS) AND SECONDARY HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS (SHLH)

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Introduction: MAS, and sHLH are hyperinflammatory conditions caused by a cytokine storm, in which IFNγ plays a pivotal role.

Objectives: To evaluate clinical characteristics and laboratory parameters of sHLH, MAS and systemic Juvenile Idiopathic Arthritis (sJIA) patients at disease onset. To compare laboratory parameters of hyperinflammation (platelet count, ferritin, AST, triglycerides, fibrinogen) with IFNγ related biomarkers in samples collected in three different time points: active disease (T0), 7-10 days from starting therapy (T1) and in clinical inactive disease (from 1 to 3 months from onset) (T2).

Methods: Routine laboratory parameters of disease activity and severity were collected from a cohort of 82 patients with sHLH (38), MAS in the context of sJIA (26) and sJIA (18) at T0, T1 and T2. Serum levels of the IFNγ related biomarkers (CXCL9, CXCL10, neopterin and IL-18) were measured at each time points by ELISA.

Results: A total of 306 samples were collected; laboratory characteristics at T0 are detailed in table 1. Fever was present in the majority of patients (95%), while splenomegaly was more frequent in MAS (65%) and sHLH (63%) compared to sJIA (17%).

Using the 2016 classification criteria for MAS, we found that platelet count is a specific parameter, no patient with sJIA had a value <181x10^9/liter; ferritin is sensitive, 94% of patients with MAS had ferritin >684 mg/ml.

CXCL9, CXCL10 and neopterin levels in T0 were significantly higher in MAS and in sHLH compared to sJIA, while IL-18 was significantly higher only in MAS group.

In MAS, CXCL9 and neopterin were significantly correlated to laboratory parameters of hyperinflammation as well as IL-18, that did not correlate only with ferritin. In sHLH, only neopterin was significantly correlated to platelet count and triglycerides.

The ROC curves performed for each biomarker showed a statistically significant AUCs ($p<0.05$) in MAS. Instead, in sHLH the AUCs were significant for CXCL9, CXCL10 and neopterin ($p<0.0001$), but not for IL-18 ($p= 0.9$). CXCL9, CXCL10, neopterin and IL-18 levels decreased progressively at T1 and normalized in T2. CXCL9 decreased faster compared to neopterin, with a similar trend to laboratory parameters.

Table 1. Laboratory parameters and IFNg related biomarkers in T0. Data are reported as median (1st-3rd quartile).

N=number of samples (samples for IL-18)	**sJIA** N=22 (18)	**MAS** N=47 (35)	**sHLH** N= 45 (35)	**MAS vs sJIA** ***p***	**MAS vs sHLH** ***p***	**sJIA vs sHLH** ***p***
Platelet (x10^9/liter)	455 (349-540)	237 (168-455)	95 (42-178)	**0.0010**	**<0.0001**	**<0.0001**
Ferritin (ng/ml)	458 (323-738)	3143 (1473-5573)	5215 (2220-17271)	**<0.0001**	0.061	**<0.0001**
AST (U/L)	28 (19-43)	64 (39-114)	136 (51-324)	**<0.0001**	**0.003**	**<0.0001**
Triglycerides (mg/dl)	84 (67-104)	166 (136-216)	222 (159-367)	**<0.0001**	**0.037**	**<0.0001**
Fibrinogen (mg/dl)	641 (492-696)	392 (251-583)	236 (137-317)	**0.0001**	**<0.0001**	**<0.0001**
CXCL9 (pg/ml)	300 (300-838)	1258 (300-6063)	4180 (1836-10038)	**0.015**	**0.011**	**0.0001**
CXCL10 (pg/ml)	150 (150-269)	452 (150-1161)	717 (198-3048)	**0.0017**	0.30	**0.0001**
Neopterin (ng/ml)	3.9 (2.7-4.9)	8.7 (4.8-14.4)	23.1 (8.6-35.0)	**0.0001**	**0.0013**	**<0.0001**
IL-18 (pg/ml)	17924 (2171-36764)	150577 (60667-219466)	14429 (2635-103022)	**<0.0001**	**<0.0001**	0.75

Conclusion: Our results confirm that platelet counts and ferritin have high specificity and sensitivity, respectively, to diagnose MAS in the context of sJIA. Moreover, our results confirm that IFNγ related biomarkers are significantly high in

patients with MAS and sHLH compared to sJIA and could be useful for diagnosis in addition to traditional laboratory parameters. As already known, IL-18 seems to be a specific biomarker for MAS. Moreover, these biomarkers seem to be also useful to monitor clinical evolution and treatment response.
Disclosure of Interest: None declared

O092

MACROPHAGE ACTIVATION SYNDROME IN JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS: A SINGLE CENTER STUDY OF NINETEEN PATIENTS

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Introduction: Macrophage activation syndrome (MAS) is a severe complication of some pediatric rheumatic diseases (PRD), especially of systemic juvenile idiopathic arthritis (sJIA), which associated with high risks of the multiple organ failure and mortality. MAS can be observed in juvenile systemic lupus erythematosus (jSLE) with frequency about 0.9-4.6%, but compared to sJIA it is less studied and poorly recognized.
Objectives: To analyze the clinical and laboratory features of MAS as a complication of jSLE.
Methods: All patients (pts) with a history of MAS associated with jSLE from our whole database of 251 jSLE pts were included in retrospective study. Diagnosis of SLE was reviewed based on 2012 SLICC criteria. MAS was diagnosed according to preliminary diagnostic guidelines. SLEDAI 2K was used for disease activity assessment. Demographic data, clinical, hematological and immunological manifestations, SLEDAI-2K, and treatment were assessed.
Results: We studied 19 consecutive pts with jSLE who had the history of MAS, which was 7.6% of all pts with jSLE and 35.2% - with MAS cases (from total=54) observed in our center. 26.3% were boys, sex ratio F:M was 2.8:1, in compare to the group without episodes of MAS – 7.2:1. The median age at the onset was 11.8 y [8.6; 13.95], in the group without episodes of MAS – 13.7 y [11; 15.1]. The median disease duration at the time of jSLE verification was 5.5 months [3.5; 11.25]. Median disease activity by SLEDAI at the time of jSLE verification was 20.5 scores [15;25.5], in the group without episodes of MAS - 12 scores [8; 18]. In the group of pts with a history of MAS, statistically more often were observed: serositis ($p=0.0028$), mucosal ulcers ($p<0.0001$), neuropsychiatric disorders ($p=0.0024$), positive Coombs test ($p=0.026$). There was also a tendency towards a higher incidence of hypocomplementemia (52.5% and 33.2%, respectively, not statistically significant). A total of 20 episodes of MAS were recorded: 10 episodes of MAS developed at onset of jSLE, 8 – associated with flare of jSLE because of deviation of the treatment`s schedule. In 2 pts MAS developed just after infusion of rituximab (RTX). 1 patient had two episodes of MAS: at onset, on 6th years of disease (the 8th day after RTX - 1st infusion of 5th course,). First features of MAS were fever, sleepiness, lower platelet counts, increased transaminase level. Typical for MAS in sJIA bright rash with itching was not observed in jSLE. Lesions of the skin and mucous were mainly represented by point hemorrhages at an early stage. For the treatment of MAS all pts were received high dose of glucocorticoids (per os+iv), 5 pts (26.3%) - cyclophosphamide iv, 1 patient (5.2%) – cyclosporine per os, 6 pts (31.6%) - intravenous immunoglobulin, 2 pts (10.5%) - RTX. 5 pts (26.3%) died due to uncontrollable MAS (2 – at onset of jSLE).
Conclusion: In our study, it was found that pts with serositis, mucosal ulcers, neuropsychiatric disorders, and positive Coombs test are at higher risk to developing MAS. MAS may be more likely at the onset of jSLE, especially in pts an earlier age. MAS in jSLE should be suspected in pts with fever, CNS disorders, thrombocytopenia, and liver disorders. We observed a correlation between high jSLE activity at the onset of the disease, violation of the treatment protocol, and risk of MAS.
Disclosure of Interest: None declared

LB001

PEDIATRIC SYSTEMIC MULTI-INFLAMMATORY DISEASES IN ITALY DURING SARS-COV-2 EPIDEMIC: FROM KAWASAKI DISEASE TO KAWACOVID

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Introduction: Italy was affected by the SARS-CoV-2 epidemic after its outbreak in China. With a 4-weeks delay after the peak in adults, we observed an abnormal number of patients with characteristics of a multi-inflammatory disease and similarities with Kawasaki Disease (KD). Others reported similar cases, defined PIMS-TS or MIS-C.[1,2]

Objectives: To better characterize clinical features and treatment response of PIMS-TS and to explore its relationship with KD.

Methods: We conducted an observational, retrospective, multicenter study. On April 24th-2020 the Rheumatology Study Group of the Italian Pediatric Society launched a national online survey, to enroll patients diagnosed with KD or with a multisystem inflammatory disease between February 1st 2020 and May 31st. The population was then divided into two different groups: 1) Classical and incomplete KD, named Kawasaki Disease Group (KDG); 2) KD-like multi-inflammatory syndrome, named KawaCOVID (KCG). An expert panel of pediatric rheumatologists re-analyzed every single patient to ensure appropriate classification. Data were collected with an online database.

Results: 149 cases were studied, 96 with KDG and 53 with KCG. The two population significantly differed for clinical characteristics (see table 1). Lymphopenia, higher CRP levels, elevated Ferritin and Troponin-T characterized KCG such as lower WBC and platelets (all p values<0,05). KDG received more frequently immunoglobulins (IVIG) and acetylsalicylic acid (ASA) (81,3% vs 66%; p=0.04 and 71,9% vs 43,4%; p=0.001 respectively) as KCG more often received glucocorticoids (56,6% vs 14,6%; p<0.0001). SARS-CoV-2 assay more often resulted positive in KCG than in KDG (75,5% vs 20%; p<0.0001). Short-term follow data on KCG showed minor complications while on KDG a majority of patients had persistence of CAA. Comparing KDG with a KD-Historical Italian cohort (598 patients), no statistical difference was found in terms of clinical manifestations and laboratory data between the two groups

Table 1	**KCG**	**KDG**	**p value**
Age at onset	7 (y)	2 (y)	<0,0001
Maculo-papular rash	61,50%	39,60%	0,01
Diarrhea	52,80%	11,50%	<0,0001
Tachypnea	22,60%	4,20%	0,001
Myocarditis	60,40%	3,10%	<0,0001
ICU admission	23,10%	1,10%	<0,0001
HLH	18,40%	1,20%	0,001
Lenght hospitalization	12 days	10 days	0,02
SARS-CoV-2 assay positive	75,50%	20%	<0,0001

Conclusion: Our study would suggest that SARS-CoV-2 infection might determine two distinct inflammatory diseases in children: KD, possibly triggered by SARS-CoV-2, and PIMS-TS. Older age at onset and clinical peculiarities, like the

occurrence of myocarditis, characterize this multi-inflammatory syndrome. Our patients had an optimal response to treatments and a good outcome, with few complications and no deaths.
Consent: I have obtained written consent
Disclosure of Interest: None declared

LB002

IMMUNOPATHOGENESIS OF COVID-19-RELATED PEDIATRIC INFLAMMATORY MULTISYSTEM SYNDROME: CYTOKINE PROFILE AND SARS-COV-2 SPECIFIC IMMUNE COMPLEXES

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Introduction: A multisystem inflammatory syndrome (MIS-C) with temporary association with SARS-CoV-2 pandemics has been recently described in children. MIS-C shares some common features with Kawasaki disease (KD). We hypothesized that: 1) the immune cytokine profiles observed in MIS-C and pre-pandemic KD are different and might explain the different clinical patterns; 2) SARS-CoV-2 specific immune-complexes (IC) may explain the immunopathology of MIS-C.
Objectives: To compare the cytokine profile between MIS-C patients, children with SARS-CoV-2 infection without MIS-C, KD patients, and healthy controls (HC); and to explore the presence of circulating SARS-CoV-2 specific IC in MIS-C patients.
Methods: Patient's blood samples were drawn within day 1 to 8 of disease onset (prior to any treatment) for the quantification of 34 circulating cytokines (Cytokine & Chemokine 34-Plex Human ProcartaPlex, ThermoFisher) and evaluation of the presence of circulating SARS-CoV-2 IC (TaqPath™ COVID-19 CE-IVD RT-PCR Kit", ThermoFisher). Protocol was approved by the local ethics committee.
Results: Fifty-eight patients were included: 1) 14 with MIS-C (8 positive for SARS-CoV-2 by PCR or serology, mean age 4.58yo, 50% male); 2) 10 with positive PCR to SARS-CoV-2 without MIS-C (COVID; mean age 9.5, 50% male); 3) 14 with pre-pandemic KD (KD; mean age 2.6yo, 57% male) and 4) 20 pediatric healthy controls (HC; mean age 5.6yo, 94% male with negative SARS-CoV-2 IgG/IgM/IgA).
Compared to HC, MIS-C and KD groups displayed significant higher levels of most cytokines, ranging from 1-6 Log_2FC (Log_2 Fold Change). Of these, IFN-γ-related (IL-18, IFN-γ, IP-10) and inflammatory monocytes-related cytokines (MCP-1, MIP1-β, IL-1α, IL-1RA), were the main triggers of inflammation (based on PCA analysis using *ClustVis* tool). No significant differences were found between MIS-C and KD profiles; however, in a subgroup of patients with MIS-C Log_2FC was greater compared to KD for IFN-γ, IL-1RA and MCP-1, without reaching statistical significance. A gradation of inflammation is observed between COVID patients, with/without MIS-C.
There was no detection of circulating SARS-CoV-2 IC in MIS-C patients (with or without SARS-CoV-2 confirmation).
Conclusion: Our findings suggest a major role of IFN-γ and inflammatory monocytes through IL-1 in the pathogenesis of MIS-C, which can be of relevance for the therapeutic management of affected patients.
Funded by "Kids Corona" project by Hospital Sant Joan de Déu.
Consent: I have obtained written consent
Disclosure of Interest: None declared

LB003

COVID-19 PANDEMIC - RELATED CHILBLAINS: CLINICAL AND IMMUNOLOGICAL CHARACTERIZATION OF AN ITALIAN COHORT

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Introduction: During COVID-19 pandemic, acute acral chilblain-like lesions (ACBLL), reminiscent of lupus pernio, were initially observed among patients with highly suspected (but mostly unconfirmed) infection with SARS-CoV-2.The aetiology of this phenomenon has not been elucidated yet and pathogenetic mechanism remains unknown. Several studies have investigated cytokine and chemokine profile in patients with COVID-19 but a characterization of ACBLL patients is lacking.
Objectives: We aimed to describe the clinical, laboratory and immunological features of children presenting with ACBLL referred to our Institute during the COVID-19 pandemic spread.
Methods: We prospectively collected data of children referred to our Institute from April 1st to June 30th. We investigate the presence of SARS-CoV2 infection through RT-PCR from nasopharingeal swabs and two different serologic kit. Nine patients accepted to be studied prospectively. All patients underwent a laboratory work-up including coagulation, viral serology and autoantibodies panel. Finally, we analysed peripheral blood IFN signature and a panel of inflammatory biomarkers in serum/plasma by a flow cytometry bead array (CXCL10, CXCL9, IL-6, IL-1β,TNFα). Skin biopsy was not performed because of our Institute restriction measures adopted during the pandemic.
Results: We examined 31 children (F: 20; median age 12 y), at a median delay of 26 days after symptoms onset (2-73 days). Twelve patients (39%) presented non-specific systemic symptoms preceding ACBLL onset. Four patients (13%) reported a possible contagion from a close contact. All patients presented stereotypical features resembling classical chilblains with acral erythematous-edematous violaceous plaques and nodules localized on the toes (n=23, 74%), the fingers (n=4, 13%) or on both sites (n=4, 13%). SARS-CoV-2 RNA detection resulted negative except for 2 patients. Repeated SARS-CoV-2 specific IgG/IgA tests were negative for all patients except for the two cases with positive swabs who showed IgG positivity; one of them was also positive for IgA. Neither common virus serology nor coagulation studies revealed significative results. Two patients presented positive ANA and anti β2 glycoprotein,respectively. A positive IFN signature was detected only in 1/ 27 patients (4%).The cytokine array showed high levels of IP10 (n= 7, range 41-534 pg/ml, n.v. 0.0-0.2 pg/ml) and a mild increase of IL-6 (n=5, range 3.2-6.5 pg/ml, n.v. 0.5-2.2pg/ml), without alterations of CXCL9, IL-1β and TNFa.Nine patients agreed to further follow-up after a median of 32 days (22-61 days) from the first visit. No seroconversion was observed among them. In addition, 4/6 tested patients (66%) showed a reduction of IL-6 levels at follow-up.
Conclusion: Albeit the role of SARS-CoV-2 in the development of ACBLL remains to be elucidated, our preliminary results showed a significant increase in serum IP10 levels, not associated with a peripheral blood IFN signature, which is instead a characteristic of pernio-related chilblains. IP10 secretion is induced by type I and type II IFN and lack of type I IFN signature in peripheral blood opens at least two scenarios: a predominant role for type II IFN or a more local type I IFN activation, possibly triggered by the virus itself and not involving circulating blood cells, thus explaining lack of systemic symptoms in most of these patients.
Disclosure of Interest: None declared

Lightening talks: Juvenile dermatomyositis and vasculitis

O093

EFFICACY AND SAFETY OF JAK INHIBITORS IN JUVENILE DERMATOMYOSITIS: A RETROSPECTIVE MONOCENTRIC STUDY

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Introduction: Juvenile dermatomyositis (JDM) is a rare juvenile idiopathic inflammatory myopathy. Janus kinases inhibitors (JAKi) have recently shown to improve skin, articular and lung involvement in adult patients with dermatomyositis but little is known for JDM, with only four patients reported to date.
Objectives: To assess the efficacy and safety of Janus kinases inhibitors (JAKi) in juvenile dermatomyositis (JDM).
Methods: Monocentric retrospective study of children with JDM treated with JAKi for at least 4 months. Response to JAKi was assessed by PRINTO 20 levels of improvement and the skin Disease Activity Score (DAS). Clinically inactive disease was defined according to PRINTO criteria and the skin Disease Activity Score. Serum interferon (IFN)-α concentration was measured by SIMOA digital ELISA assay (Quanterix Homebrew).
Results: Seven patients (6 female) received ruxolitinib (n=5) or baricitinib (n=2). Myositis specific antibodies (MSA) were present in 6/7 patients, including anti-MDA5 (n=2), anti-NXP2 (n=3) et anti-TIF1-g (N=1) antibodies. All received corticosteroids in combination with JAKi. The main indications for JAKi were refractory JDM (n=6/7) (time elapsed from diagnosis: 4-22 months) or new onset JDM (n=1). Three months after JAKi introduction, five JDM patients achieved response without relapse, all had withdrawn immunosuppressive drugs other than corticosteroids and JAKi, with median daily corticosteroids dose decreased from 1.3 to 0.4 mg/Kg. At the last follow-up (median follow-up time, 11 months, range, 4-30), 6/7 achieved a JDM PRINTO 20 and skin DAS improvement , and 4/7 had a clinically inactive disease (CID) (median time to CID since JAKi initiation 3 months, range 1,7-5,3). The only patient without MSA did not respond. Serum IFN-α concentrations were elevated in all patients at JAKi introduction (median 333 fg/ml, range 31-31328) and normalized (<10 fg/ml) in all 4 patients in with CID (range, 0,3-10 months). A muscle biopsy repeated 22 months after the initiation of JAKi in one patient showed a complete regression of severe muscle vasculopathy. Herpes zoster occurred in 3 patients. Skin abscess developed in 3 patients with ulcerations, complicated by psoas abscess in two of them.
Conclusion: PRINTO 20 levels of improvement and CID occurred in 6/7 and 4/7 patients with refractory or new-onset JDM respectively. The frequency of herpes zoster was high. Prospective studies are required to identify the subset of patients who will require JAKi as a first line treatment.
Disclosure of Interest: None declared

O094

ALTERED METABOLISM IN JUVENILE DERMATOMYOSITIS (JDM) MONOCYTES: A NEW THERAPEUTIC FOCUS IN JUVENILE DERMATOMYOSITIS

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Introduction: JDM is a rare childhood autoimmune myositis that presents with proximal muscle weakness and associated skin changes. There is an unmet need to develop targeted treatments for JDM.
Objectives: This study aimed to identify dysregulated biological processes by RNA-sequencing in JDM and develop functional assays to confirm these pathways.
Methods: Peripheral blood samples were obtained from JDM patients and age/sex-matched child healthy controls (CHC). $CD4^+$, $CD8^+$, $CD14^+$ and $CD19^+$ cells were sorted by flow-cytometry from PBMC, and RNA was extracted and RNA-sequenced. Total PBMC were taken from JDM and CHC, sub-sets of the CD14+ cell population were analysed by flow cytometry. To measure cytokine expression; CD14+ monocytes were isolated by immunomagnetic positive selection from total PBMC populations from JDM and CHC samples. The monocytes were cultured overnight with and without LPS. Cytokine expression in the culture supernatant was measured by cytometric bead array (CBA). To investigate metabolic function, CD14+ monocytes were isolated by immunomagnetic positive selection from total PBMC populations from JDM and CHC samples. The monocytes were cultured in carbon-13 labeled glucose RPMI-media. Medium was sampled at hourly time points for 6hrs and then at 24hrs over a time course. The metabolism of the ^{13}C glucose into CO_2, lactate and ribulose-5-phosphate was measured by gas chromatography-mass spectrometry (GCMS).
Results: RNA-seq confirmed a strong IFN1 signature, and that genes involved in mitochondrial function were abnormally expressed in pre- and on-treatment CD14+ cells compared to CHC, indicating mitochondrial dysfunction not corrected by current treatment. A proportion of the JDM samples had a higher percentage of $CD14^{hi}CD16^{hi}$ intermediate monocytes (JDM median – 12.3 (25% percentile = 7.11, 75% percentile = 25.6); CHC median – 10.95 (25% percentile = 9.10, 75% percentile = 14.25), detected by flow cytometry. Linear regression showed a trend towards increased disease activity, reflected by a lower MMT8 score, with a higher percentage of intermediate monocytes, therefore, in samples from JDM patients naïve of treatment ($R = -0.57$, $p = 0.085$). Cytometric bead array (CBA) analysis showed that both pro-inflammatory and anti-inflammatory cytokines were down-regulated in monocytes from JDM compared to CHC (IL-6 ($p=0.0152$); IL-1β ($p=0.0152$); IL-10 ($p=0.0649$). Functionally, ^{13}C lactate concentration was significantly lower after monocytes had been cultured for 24hrs in ^{13}C glucose medium from JDM samples compared to CHC ($p=0.0063$). Ongoing work is being done to assess the expression of glucose transporters and uptake.
Conclusion: This study establishes that in JDM, monocyte metabolism and homeostasis is dysfunctional, identifying an exciting novel pathogenic mechanism. In the future a specific area to investigate is the mechanistic relationship between IFN1 driven inflammation and altered mitochondrial metabolism in monocytes, this has the potential to identify novel therapeutic targets.
Disclosure of Interest: None declared

O095

BIOMARKERS GALECTIN-9 AND CXCL10 ARE OF ADDITIONAL VALUE IN THE CLINICAL DECISION-MAKING IN JUVENILE DERMATOMYOSITIS

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Introduction: In patients with juvenile dermatomyositis (JDM) objective evaluation of disease activity is challenging but crucial for prevention of both over- and undertreatment. We recently validated galectin-9 and CXCL10 in a multi-center cohort study as sensitive and reliable biomarkers for disease activity in JDM, outperforming creatinine kinase (CK). Implementation of these biomarkers into clinical practice, as tools to monitor disease activity and guide treatment, might enable personalized treatment strategies for patients with JDM.

Objectives: We investigated the additional value of galectin-9 and CXCL10 in the clinical decision-making in JDM patients as assessed by pediatric rheumatologists.

Methods: Galectin-9 and CXCL10 serum levels as measured by multiplex immunoassay were implemented as routine tests in the diagnostic laboratory of a tertiary hospital in June 2017 and June 2018, respectively. Test results generally became available 1-2 weeks after sampling. Pediatric rheumatologists reported for all measurements performed in JDM patients between June 2017 and March 2020 whether, and if so, how the biomarker levels would have affected their clinical-decision making, had the results been available at time of consultation. In addition, they scored the additional value of the biomarker levels semi-quantitatively (*decisive, supportive, helpful, no added value (NAD), distracting* or *"other"*).

Results: Biomarker measurements from 184 consultations in a total of 39 JDM patients were included (175 galectin-9, 152 CXCL10). Median number of consultations per patient was 4 (range 1-17). In 154 consultations (84%) the galectin-9 and/or CXCL10 results were considered to be of additional value (8 *decisive*, 31 *helpful*, 115 *supportive*). Results were considered to be of *NAD*, *distracting* or "*other*" in 19, 7 and 4 consultations, respectively. Results were most often considered *decisive* or *helpful* when increased biomarker levels confirmed clinically active disease while CK remained low, when increased or rising levels indicated bad treatment response, or when low levels confirmed clinically inactive disease in cases with aspecific symptoms or increased CK. Results were most often considered *supportive* when low levels confirmed clinically inactive disease or when decreasing levels indicated good treatment response. Results were most often reported to be of *NAD* in patients in long-term drug-free clinical remission. Transient increases in biomarker levels during clinically inactive disease were considered *distracting*. Also, low levels in cases with evident clinical disease activity were scored as *distracting*. Interestingly, the latter was only reported in patients with skin but no muscle disease activity, indicating that the biomarkers do not reflect skin disease well. In 13% of consultations the galectin-9 and/or CXCL10 results would have led to changes in clinical decision making, mostly with regard to MRI requests and medication changes.

Conclusion: Galectin-9 and CXCL10 results were of additional value in the clinical decision-making in patients with JDM, as reported by pediatric rheumatologists. The biomarkers were particularly useful in monitoring treatment response and when CK was deemed unreliable. Also, their potential to guide personal treatment strategies and to reduce the use of expensive imaging modalities was shown. We are currently conducting a large prospective cohort study to further validate clinical implementation of these biomarkers, including their prognostic value and tissue specificity, and to develop recommendations for biomarker-guided treatment in JDM.

Disclosure of Interest: None declared

O096

SIGLEC-1 EXPRESSION REFLECTS THE INTERFERON SIGNATURE IN JUVENILE DERMATOMYOSITIS AND DEFINES SUBCLASSES OF PATIENTS WITH DISTINCT INFLAMMATORY AND CLINICAL PROFILES

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Introduction: Sialic acid-binding Ig-like lectin 1 (Siglec-1) is a strongly Interferon (IFN)-regulated marker expressed on CD14 positive monocytes in the blood. Since juvenile dermatomyositis (JDM) is a (partly) IFN-driven disease, Siglec-1 might be used as a surrogate marker in clinical practice.

Objectives: 1) To evaluate the relation between Siglec-1 expression, the IFN signature, inflammatory biomarkers and disease activity in JDM; 2) To demonstrate whether subgroups of JDM patients with different Siglec-1 expression and distinct inflammatory profiles at diagnosis can predict treatment response.

Methods: Forty-six JDM patients, 7 Duchenne muscular dystrophy (DMD) patients, and 15 healthy controls (6 children and 9 adults) were enrolled. Plasma samples (46 treatment-naïve JDM, 26 follow-up JDM during treatment ,and 7 DMD) were used to measure inflammatory biomarkers by Olink assay. PCR was used on PBMC to determine the expression levels of 5 type I IFN signature genes (MX-1, IFI44, IFI44L, Ly6E, and IFIT3) and Siglec-1 expression on CD14+ cells was assessed by flow cytometry. The IFN score was defined as the sum of relative expressions of the signature genes. JDM samples were classified into 3 groups based on clinical status; 1) onset (active disease before starting the treatment), 2) active on medication (active disease with medication), 3) remission on/off medication (clinically inactive with or without medication). The childhood myositis scale (CMAS; 0-52; 0-49 for age 4-5) was used to assess muscle disease activity and the physician's global assessment (PGA; 0-10) was used to determine overall disease activity, including skin.

Results: The Median fluorescent intensity (MFI) of Siglec-1 and the frequency of CD14+ Siglec-1+ cells were significantly higher in the onset group of JDM patients compared with DMD and healthy controls, and significantly decreased over time in longitudinal follow-up. The IFN score showed a similar pattern. Both Siglec-1 and the IFN score were significantly correlated with CMAS (r_s=-0.67, p<0.0001 and r_s=-0.60, p<0.0001) and PGA (r_s=0.71, p<0.0001 and r_s=0.75, p<0.0001). JDM patients with high levels of Siglec-1 MFI at diagnosis had more severe muscle involvement and required more intense treatment within 3 months after diagnosis. Unsupervised clustering of inflammatory biomarkers at the onset of JDM patients revealed two distinct clusters: the larger cluster with high levels of CXCL-10, CX3CL1, MCP-1, MCP-2, MCP-3, and PD-L1 had significantly lower CMAS and higher PGA than the smaller cluster. In a Kaplan-Meier analysis, the larger cluster needed a longer time to achieve clinically inactive disease than the smaller cluster with statistical significance. Importantly, JDM patients in the larger cluster had a significantly higher Siglec-1 expression on CD14+ cells when compared to the other cluster, whereas no significant difference in IFN score between these 2 clusters was found.

Conclusion: Siglec-1 could be used as a surrogate biomarker reflecting IFN activity and monitoring disease activity in JDM. Siglec-1 expression at the onset of JDM patients might be a useful tool to define subgroups of JDM patients and identify patients at risk who may benefit from more aggressive treatment.

Disclosure of Interest: None declared

O097

VALIDATION OF THE EULAR/ACR 2017 IDIOPATHIC INFLAMMATORY MYOPATHY CLASSIFICATION CRITERIA IN JDM PATIENTS

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Introduction: Juvenile dermatomyositis (JDM) is the most common inflammatory myopathy of childhood. In 2017, a new set of criteria has been proposed by EULAR/ACR.
Objectives: We aimed to validate EULAR/ACR 2017 classification criteria[1]in JDM patients.
Methods: This study was held at Hacettepe University Department of Pediatrics, Divisions of Rheumatology, Neurology and Pediatric Pathology Unit. Control patients included inborn errors of metabolism presenting with myopathy and/or rhabdomyolysis (glutaric aciduria type 2 (n=8), carnitine-palmitoyl transferase II deficiency (n=2), LCHAD (n=1)), idiopathic rhabdomyolysis (n=3), dystrophinopathies (Duchenne/Becker muscular dystrophy (n=10)), neuromyotonia (n=1) and systemic rheumatological disorders (SLE (n=5), MCTD (n=4), interferonopathies (n=4), PAN (n=2)).
Results: 58 JDM patients (61.3% female) and 40 controls (32.5% female) were included in this study. Mean age at disease onset (JDM 8.1±4.3 vs control 8.7±5.4) and diagnosis (JDM 8.7±4.4 vs control 9.9±5.3) were comparable.
When the probability cut-off was set at 55% as recommended, the sensitivity/specificity of the new criteria to diagnose JDM were 96.5%/85% in the total cohort, 95.8%/84.6% without muscle biopsy data and 97%/85.7% with biopsy data (Table 1.) With the ROC curve analysis, the optimal probability cut-off for sensitivity and specificity was found >62% in our cohort; providing a sensitivity and specificity of 96.6% (95% CI: 88.1% to 99.6) and 90% (95% CI: 76.3% to 97.2%) respectively.
The new EULAR/ACR criteria[1] was the most sensitive however, the least specific compared to the Tanimoto[2] (sensitivity/specificity 64%/97.5%) and Bohan-Peter criteria[3,4] (sensitivity/ specificity 74.1%/92.5%). The specific skin rash as a mandatory criterion increased the specificity of Tanimoto and Bohan-Peter criteria which was not mandatory in the new EULAR/ACR criteria. Six control patients were misclassified as JDM with the new criteria. Muscle weakness parameters lowered the specificity and led to misclassification for three patients with inborn errors of metabolism; two patients with interferonopathy and one with mixed connective tissue disorder who presented with skin features. Although 75.5%(34/45) of our JDM patients who were checked for antibodies had at least one myositis-specific antibody, none of them had anti-Jo1 which causes a major drawback for the new criteria. Four out of 34 muscle biopsies did not met the new EULAR/ACR criteria, however, they had other features which were included in the previously validated muscle biopsy score tool[5,6] such as, overexpression of MHC-I, capillary drop-out and neonatal myosin positivity.

Table 1. Sensitivity and Specificity of Different Criteria for Classification of JDM

	Sensitivity (n=58)	**Specificity (n=40)**	**Positive predictive value**	**Negative predictive value**
EULAR/ACR criteria	96.5%	85%	90.1%	94.4%
- **Without biopsy**	- 95.8%	- 84.6%	- 85.1%	- 95.6%
- **With biopsy**	- 97%	- 85.7%	- 94.3%	- 92.3%
Bohan-Peter criteria	74.1%	92.5%	93.4%	71.1%
Tanimoto criteria	64%	97.5%	97.3%	65%

Conclusion: The new EULAR/ACR criteria performed favourably well in our JDM cohort especially with the probability cut-off of >62%. The yield of the criteria in childhood presentations may be improved by including the recently identified myositis-specific antibodies, validated muscle biopsy score tool parameters, and muscle magnetic resonance imaging data.
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Disclosure of Interest: None declared

O098

COMPARISION OF IVIG RESISTANCE PREDICTIVE MODELS IN KAWASAKI DISEASE

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Introduction: Intravenous immunoglobulin (IVIG) resistance may be observed in 10% to 20% of patients diagnosed with Kawasaki disease (KD). It is fundamental to define this group in early stages of the disease for improving prognosis and determining the need for additional treatment.

Objectives: We aimed to compare nine different prediction models (Kobayashi, Egami, Harada, Formosa, Sano, Piram et al, Wu et al, Yang et al, and Tan et al) and evaluate risk factors for IVIG resistance in Turkish children.

Methods: Patients who diagnosed with Kawasaki disease at the Hacettepe University between June 2007 and September 2019 were evaluated retrospectively. Complete or incomplete KD patients were included in the study.

Results: A total of 129 patients, 79 boys (61.2%), with a median age 36 (IQR 19.5-57.0) months were enrolled. Sixteen patients (12.4%) had IVIG resistance. The specificity of all scoring systems predicting IVIG resistance was higher than their sensitivity. Tan, Sano, and Egami predictive models had the highest specificity (97.3%, 89.4%, 86.7%, respectively). Almost all scoring systems distinguished the group of patients with low-risk for IVIG resistance but could not differentiate IVIG-resistant patients. High serum levels of total bilirubin, ALT, AST, GGT, and platelet count less than $300´10^9$/L were associated with IVIG resistance in univariate analysis. Five risk factors were re-evaluated with multivariate analysis; platelet count less than $300´10^9$/L and GGT serum levels were independent risk factors for IVIG resistance (OR: 3.896; 95%CI: 1.054-14.404; p=0.042 and OR: 1.008; 95%CI: 1.001-1.015; p=0.050).

Coronary artery involvement was detected in 44 of 129 patients (34.1%) which was more frequently observed in patients under the age of 1 year and in boys (p=0.01, p=0.02, respectively). The multivariate analysis identified male gender and young age (<1 year of age) as independent risk factors for coronary involvement (OR: 0.399; 95%CI: 0.175-0.908; p=0.029 and OR: 3.802; 95%CI: 1.248-11.582; p=0.019, respectively).

Conclusion: The adaptation of the current scoring systems is limited due to lack of sensitivity in our study population. Increased serum GGT levels and low platelet count were risk factors for predicting IVIG resistance.

Disclosure of Interest: None declared

O099

KAWANET-SCORE FOR PREDICTING RESISTANCE TO FIRST IMMUNOGLOBULINS IN KAWASAKI DISEASE: CONFIRMATION OF ITS GOOD SENSITIVITY AND PROPOSAL TO IMPROVE SPECIFICITY.

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Introduction: Kawasaki disease (KD) is the leading cause of acquired heart disease in childhood in developed countries. Early identification of these high-risk patients is critical to initiate aggressive therapies, but available scoring systems lack sensitivity in non-Asian populations. In their recent publication in Science Reports, Piram et al. proposed a new scoring system to predict the need for secondary treatment in non-Asian populations, the Kawanet score(sensitivity 77%, specificity 60%).

Objectives: To validate the Kawanet score in an independent cohort.

Methods: We retrospectively analyzed clinical and epidemiological data from a registry including all successive KD patients followed in our French tertiary center from 2006 to 2019. After exclusion of patients who had participatedin the Kawanetstudy (n=20), 186 children were included in our study. Cardiac abnormalities at the first echocardiography were defined as presence of at least one abnormal echocardiography finding including coronary artery dilatation, aneurysm, zMax ≥2.0, perivascular coronary artery brightness, pericardial effusion, valvular dysfunction.

Results: In our cohort the Kawanet score had a sensitivity of 81,4% but a specificity of only 32,7%. Given the low specificity, we tried to implement other parameters to improve the Kawanet score performances. Abnormal findings at the initial echocardiography were observed in 61/186 (32.8%) patients. In multivariate regression analysis adjusted on the Kawanet score, initial cardiac abnormalities at the initial echocardiogram was significantly associated with a need of secondary treatment (OR 3.2, 95% CI [1.4; 7.6], p=0.0060). We built a "modified Kawanet score", including the Kawanet score variables plus cardiac abnormalities (one point per variable). The modified Kawanet score, with a cutoff at >=3, was associated with need for secondary treatment (OR of 3.4, 95% CI [1.4; 8.3], p=0.0069). Combining the Kawanet score with information on abnormalities observed at the initial echocardiogram allowed to obtain a sensitivity of 71.4% and a specificity of 59.5%.

Conclusion: In conclusion, our observations confirm the good sensitivity of the Kawanet score to predict need for secondary treatments in European populations but point out a poor specificity. The specificity of this score can be substantially improved by adding initial echocardiography findings as an additional parameter.

Disclosure of Interest: None declared

O100

DIFFERENT HISTOLOGICAL CLASSIFICATIONS FOR HENOCH-SCHÖNLEIN PURPURA NEPHRITIS - WHICH ONE IS THE BEST PREDICTOR OF DISEASE OUTCOME? PILOT STUDY OF THE PRES VASCULITIS WORKING PARTY

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Introduction: Henoch-Schönlein purpura nephritis (HSPN) is the main and almost the only cause of morbidity and mortality among children suffering from this most common vasculitis in childhood. Several histological classifications are used in the analysis of renal biopsy findings in HSPN, but it remains unknown which one has the strongest association with the severity and outcome.

Objectives: The aim was to compare the four most commonly used histologic classifications for HSPN to determinate which one is the best predictor of disease outcome and to establish which variables of each histological classification have the strongest association with unfavorable outcomes.

Methods: The cross-sectional study included 69 patients with HSPN (diagnosed by EULAR/PRES/PRINTO criteria) and available renal biopsy specimens for analysis using the four histological classifications for HSPN (the International Study of Kidney Disease in Children (ISKDC) classification, the Oxford classification, the Haas histologic classification of IgA nephropathy and the modified semi-quantitative classification (SQC), developed by Koskela *et al.*). The clinical outcome was defined through four categories, graded according to the modified classification of Counahan (physical examination, hematuria, proteinuria, urine albumin-to-creatinine ratio, hypertension and eGFR). The linear relationships between outcome and histological classifications were analysed using ordinal regressions using the first-order of polynomial orthogonal contrasts.

Results: The SQC classification proved to be the best, reducing the deviation (of the model-predicted outcome value from the observed value) by 9.5% (X^2_1=13,89, $p < 0,001$), followed by the Oxford classification with a deviation reduction of 8.0% (X^2_1=11,76, $p = 0,001$), then the ISKDC classification with a decrease in deviation of 3.3% (X^2_1=4,89, $p = 0,027$), and the worst was the Haas classification with a decrease in deviation of 2.1% (X^2_1=3,06, $p = 0,080$). Analysis of individual variables of Oxford and SQC classifications showed that with increasing values in the variables of interstitial fibrosis ($t_{66} = 3,23$, $p = 0,002$), tubular atrophy ($t_{66} = 2,94$, $p = 0,005$) and tubular dilatation ($t_{66} = 2,40$, $p = 0,019$) in the SQC classification, and endocapillary hypercellularity ($t_{66} = 3,14$, $p = 0,003$) and crescents ($t_{66} = 2,07$, $p = 0,043$) in the Oxford classification the outcome worsens.

Conclusion: The pilot study showed that the SQC classification, developed by Koskela *et al.*, has the strongest association with the severity and outcome of HSPN, followed by the Oxford classification, while other classifications are less related to the outcome of the disease. Although crescents on renal biopsy were considered the most important outcome indicators, this pilot study suggests that tubulointerstitial changes could be even more important as predictors of poor outcome. Histological changes in the interstitium and renal tubules of HSPN patients should be further explored in order to have an even better predictive value in terms of disease outcomes and to be incorporated into existing or new classifications, on the basis of which guidelines for the treatment of patients would be developed.

SUPPORT: Croatian Science Foundation project IP-2019-04-8822.

Disclosure of Interest: None declared

O101

A PILOT PROTEOMIC ANALYSIS OF PLASMA BIOMARKERS IN IGA VASCULITIS

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Introduction: IgA vasculitis/ Henoch Schönlein Purpura (IgAV/HSP) is the most common vasculitis of childhood, characterized by the IgA1 immune deposits in the small vessels. Although it is very common, the understanding of its molecular pathogenesis is still very limited.

Objectives: We aimed to analyse plasma proteomes of IgAV/HSP patients using nano liquid chromatography – tandem mass spectrometry (nLC-MS/MS) to investigate the disease pathogenesis.

Methods: IgAV/HSP was diagnosed according to the Ankara criteria in 2008 (1). Five active IgAV/HSP patients and two age and gender-matched health controls were enrolled in this pilot study. Serum samples from subjects were collected on the same day of IgAV/HSP diagnosis and before steroid or other immunosuppressive treatment initiated. Sample preparation was carried out using PreOmics İST Kit. We investigated the alteration of serum proteome using the nano LC-MS/MS approach. Bruker raw files were analyzed using the proteomics software Max Quant (1.6.7.0). The human reference proteome set from UniProt was used to identify proteins. Proteomic data were analyzed with Perseus 1.6.7.0.

Results: The data file includes peptide and protein identification, accession numbers, protein and gene names, sequence coverage and label free quantification (LFQ) values of each sample. 345 proteins were reported per sample. Identifications from the reverse decoy database, identified by site only and known contaminants were excluded. Data were log transformed. Two sample T-test was performed between groups. We identified 23 significantly different expressed proteins. Mainly the differentially expressed proteins were in the innate immune system, Ig and complement pathway. The levels of Complement C3, Apolipoprotein E, Glyceraldehyde-3-phosphate dehydrogenase, Filamin-A, Alpha-1B-glycoprotein, Tubulin beta-1 chain, Lipopolysaccharide-binding protein, Ig mu chain C region were significantly higher in IgAV patients.

Conclusion: This pilot proteomic study may provide us a perspective in the pathogenesis of IgAV (HSP).

Grant Support: This work was supported by Hacettepe University Scientific Research Coordination Unit
Disclosure of Interest: None declared

e-Poster viewing: Autoinflammatory diseases

P001

A FEVER LASTING FOR FOUR GENERATIONS

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Introduction: Autoinflammatory diseases are clinical conditions characterized by recurrent episodes of fever, associated with symptoms such as skin rash, abdominal pain, chest pain, lymphadenopathy, arthritis and elevation of inflammatory markers. Cryopyrin-associated periodic syndromes (CAPS) are autoinflammatory disorders caused by mutations of the gene NLRP3 (NOD-like receptor 3), with autosomal dominant transmission. It encodes a protein called cryopyrin, connected to the activation of proinflammatory interleukin-1 (IL-1). Different point mutations in this gene promote an inappropriate, excessive IL-1 production, responsible for the clinical features of different CAPS. These are: familial cold autoinflammatory syndrome (FCAS), Muckle-Wells syndrome and chronic infantile neurological cutaneous articular syndrome (CINCA) also called neonatal-onset multisystem inflammatory disease (NOMID). FCAS is the mildest form. Symptoms usually appear during the first year of life and include urticarial rash, arthralgias, conjunctival injection and fever spikes of short duration (usually 24 hours), induced by the exposure to generalized cold.
Objectives: To present the peculiar characteristics of FCAS, through a case report that includes four generations of the same family. To stress the importance of familial history, that together with clinical features, can lead to the hypothesis formulation and to the request of a genetic assessment that will confirm the diagnosis.

Methods: We describe a case of FCAS in a 2-years-old child, who came for the first time to our rheumatology clinic because of a history of recurrent fever episodes, associated with urticarial rash and elevations in acute phase reactants, beginning at 6-7 months of life.
Both father and paternal grandmother were in follow up for hives rash and arthritis since childhood, diagnosed as seronegative polyarthritis. In addition, father presented conjunctivitis. The episodes of urticarial eruption and fever appeared to be induced by cold exposition. Paternal great-grandmother was reported to have the same clinical situation. The medical and familial history were suggestive for an autoinflammatory disease, therefore genetic analysis was performed and the family was referred to the Autoinflammatory Diseases Centre of the IRCCS Gaslini in Genova. Written informed consent to publication of the case report was obtained by parents.

Results: The genetic analysis found a point mutation on the gene NLRP3 (Ala439Val), thus confirming the diagnosis of FCAS. The same mutation was found on blood samples of father and paternal grandmother, while great-grandmother is still being analyzed. Treatment with Anakinra was promptly initiated in both child and relatives.

Conclusion: Cryopyrin-associated periodic syndromes are rare disorders with relatively aspecific manifestations. An infant presenting with recurrent episodes of fever and urticarial rash exacerbated by generalized cold exposure, should be investigated for FCAS. Early diagnosis and rapid initiation of IL-1 inhibition control the inflammation and prevent organ damage with rapid resolution of clinical symptoms. Anti-interleukin-1 treatment with anakinra, rilonacept or canakinumab induces in most cases complete remission and normalization of inflammatory markers.
Disclosure of Interest: None declared

P002

ATTENTION AND THINKING FUNCTIONS IN CHILDREN WITH MONOGENIC AUTO-INFLAMMATORY DISEASES

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Introduction: Monogenic auto-inflammatory diseases (mAID) are a group of severe chronic multisystemic diseases with recurring episodes of fever and other manifestations that significantly affect the patients' life quality. Moreover, the hyper expression of pro-inflammatory cytokines (IL1β, etc.) observed in these patients may have a negative effect on the central nervous system.
Objectives: to study the state of the functions of attention and thinkingin children suffering from monogenic auto-inflammatory diseases.
Methods: there were examined 22 children at the age of 7 to 17 years old diagnosed with CAPS-9, TRAPS-8, FMF-5. Among them there were 12 boys and 10 girls. The diagnosis in all the patients was confirmed through detection of pathogenic mutations in the NLRP3, TNFRSF1A and MEFV genes. The following methods were used: a clinical conversation; attention diagnostics (Schulte tables); thinking diagnostics (establishing a sequence of events, "four is a crwod", simple analogies, interpretation of proverbs).
Results: Tabl. №1
The functions of attention of children suffering from monogenic auto-inflammatory diseases.
Tabl. №1
The functions of attention of children suffering from monogenic auto-inflammatory diseases.

Attention processes	TRAPS N=8		CAPS N=9		FMF N=5	
	Normal	Disturbance	Normal	Disturbance	Normal	Disturbance
Concentration	3(37,5%)	5(62,5%)	4(44,4%)	5(55,5%)	3(60%)	2(40%)
Distribution of attention	0	8(100%)	2(22,2%)	7(77,8%)	2(40%)	3(60%)
Exhaustion	2(25%)	6(75%)	6(66,7)%	3(33,3%)	3(60%)	2(40%)
Efficiency	2(25%)	6(75%)	4(44,4%)	5(55,5%)	3(60%)	2(40%)
Degree of workability	3(37,5%)	5(62,5%)	4(44,4%)	5(55,5%)	3(60%)	2(40%)
Sustainability	3(37,5%)	62,5%	8(88,9%)	1(11,1%)	1(20%)	4(80%)

In the majority of patients with TRAPS and CAPS, indicators of the operational side of thinking were normal (87.5% and 55.5%, respectively).The majority of the examined patients with FMF (80%) had a non-severe violation of establishing causal relationships. Inertia of thinking was more often registered in patients with TRAPS (37.5%). Violations in the motivational sphere of thinking were not detected in any group.
Conclusion: Impaired attention functions were observed in the majority of patients with TRAPS and were expressed in them to the maximum extent. Most patients with CAPS and FMF had impaired attention distribution, and all other attention functions were not impaired in most of these patients. Non-rough thinking disorders were registered in the majority of patients with FMF. In the majority of patients with CAPS and TRAPS, indicators of thinking function were within the normal range . In patients with TRAPS, more often than in patients with CAPS and FMF, inertia of thinking was observed.
Disclosure of Interest: None declared

P003

IMMUNOLOGICAL EVALUATION OF THE PATIENTS WITH CAPS

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Introduction: Cryopyrin-associated periodic syndrome is a group of rare, heterogeneous autoinflammatory disease characterized by interleukin 1β-mediated systemic inflammation and clinical symptoms involving skin, joints, central nervous system, and eyes. There are three clinical subtypes; familial cold autoinflammatory syndrome (FCAS), Muckle-Wells Syndrome (MWS) and, neonatal-onset multisystem inflammatory disease (NOMID)/ chronic infantile neurological cutaneous and articular syndrome (CINCA), which share several overlapping clinical features.
Objectives: In this study, we aimed to evaluate the status of the adaptive immune system in our patients with CAPS.
Methods: Nine patients who were diagnosed with CAPS were included in the study. The data were obtained retrospectively from the hospital records.
Results:

	Median	Minimum	Maximum
Absolute lymphocyte count (/mm^3)	2280	1190	3530
CD3 /mm^3), (%)	1740.33, (77.3)	952, (68.5)	2534.54, (84.4)
CD4 /mm^3, (%)	1120.22, (51.5)	685.45, (37.6)	1736.76, (63.2)
CD8 /mm^3, (%)	523.75, (23.7	215.4, (14)	893.34, (31.5)
CD19 /mm^3, (%)	289.56, (11.6)	138.04, (8.2)	528.8, (18.6)
CD3-CD16/56 /mm^3, (%)	154.65, (7.1)	57.12, (4)	582.45, (17.9)
Ig G (mg/dl)	1060	931	1870
Ig M (mg/dl)	131	84	223
Ig A (mg/dl)	296	110	393

Conclusion: CAPS is classified as a subgroup of innate immune deficiencies by the International Union of Immunological Societies in 2017. In this study, we disclosed that there was no adaptive immune system deficiency in CAPS patients.
Disclosure of Interest: None declared

P004

PYRIN ASSOCIATED AUTOINFLAMMATION WITH NEUTROPHILIC DERMATOSIS: A RARE CAUSE OF LEUCOCYTOCLASTIC VASCULITIS.

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Introduction: We describe a case of a six year old girl who presented with episodes of recurrent abdominal pain and petechial and purpuric rashes affecting the lower limbs. The clinical picture resembled Henoch Schonlein Purpura but following her third episode, we requested additional investigations including genetic analysis and found a homozygous mutation in an exon 2 of gene MEFV, which is associated with a recently reported disease of Pyrin associated autoinflammation with neutrophilic dermatosis (PAAND).
Objectives: To describe the clinical presentation of a child who was found to be homozygous for the MEFV variant c.623G>C.
Methods: A six year old girl presented with recurring stereotyped episodes of abdominal pain, joint pain and petechial and purpuric rashes to the lower limbs resembling Henoch-Schonlein purpura. The typical episode lasted for six-eight weeks and resolved spontaneously. She remained systemically well on each occasion with normal urinalysis and vital signs. On the third presentation she was noted to have a petechial rash to the extensor surfaces of her lower limbs and a swollen left ankle. The physical examination was otherwise unremarkable with no organomegaly or lymphadenopathy. She had no history of fever, weight loss or fatigue. She was of Pakistani ethnicity and her parents were consanguineous. There was no family history of note. She attended a mainstream school, there were no developmental concerns. Abdominal ultrasound was normal. Her blood tests showed a mild normocytic anaemia and a mild eosinophilia with maximum 0.82. The rest of the full blood count was unremarkable. She had normal renal and liver function. Her inflammatory markers were mildly elevated with maximum erythrocyte sedimentation rate (ESR) 87 mm/h, CRP 59 mg/L, serum amyloid 13.0 mg/L. Complement factors C3 and C4 were normal. Antinuclear antibody (ANA) and anti C1q antibodies were negative. Atypical p-ANCA antibodies were detected with negative specific ANCA PR3 and MPO antibodies. Skin biopsy showed small vessel leucocytoclastic vasculitis. She was kept under follow up and following her fifth presentation with similar picture, we requested genetic testing focusing on autoinflammatory diseases and she was found to be homozygous for the MEFV mutation c623G>C.

Results: MEFV is a gene associated with recessive Familial Mediterranean Fever (FMF). This specific mutation is known to be associated with a phenotype of Pyrin associated autoinflammatory disease. Another three patients of Pakistani consanguineous background carrying the same mutation have already been described. All patients share a remitting–relapsing course of disease, characterized by raised inflammatory markers, eosinophilia, oral ulceration, intestinal inflammation and lymphadenopathy [1]. Following her fourth flare of rash and joint pain, our patient commenced a short course of oral prednisolone with good response. She remains under regular follow up with a plan to trial colchicine in case of further flare
Conclusion: FMF is the most frequent autoinflammatory disease caused by mutations in MEFV gene. Pyrin associated autoinflammation with neutrophilic dermatosis is a recently described condition associated with mutations in exon 2 of the MEFV gene [2, 3].

Disclosure of Interest: None declared

P005

THE DIAGNOSTIC CHALLENGE OF PAMI SYNDROME: A CASE REPORT

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Introduction: Mutations in PSTPIP1 gene, encoding for proline–serine–threonine phosphatase-interactive protein 1, are associated to an autosomal dominant autoinflammatory syndrome called PAPA (sterile pyogenic arthritis, pyoderma gangrenous and cystic acne) and to pyoderma gangrenous, acne and suppurative hydrosadenitis with or without pyogenic arthritis syndromes (PASH and PAPASH). Recently, two PSTPIP1 mutations (p.E250K and p.E257K) have been described in a disease characterized by pancytopenia, hepatosplenomegaly, acne and gangrenous pyoderma, known as PSTPIP1-associated myeloid-related protein inflammatory (PAMI) syndrome, a distinct autoinflammatory disorder with its own clinical and biochemicals features.
Objectives: To describe the clinical course of PAMI syndrome in a 15-year-old girl.
Methods: Case report.
Results: The patient, a 15-year-old girl, suffered from migrant and recurrent arthralgias, hepatosplenomegaly and elevation of inflammatory markers since the first year of life. She firstly came to our attention at the age of 20 months for upper and lower limb pain episodes, mostly nocturnal and associated with functional impotence. At past medical history, left shoulder arthralgia appeared 10 days after a Roseola Infantum infection was reported at the age of 14 months, in association with anemia, neutropenia and inflammatory markers and lactate dehydrogenase (LDH) increase.
At admission, clinical examination showed hepatosplenomegaly and enlarged neck and submandibular lymph nodes, but joint assessment was normal. At laboratory investigation, anemia and neutropenia were confirmed and LDH was persistently high. Immunological and autoimmune screening were normal, including the neutrophilic degranulation test. Bone marrow aspiration was negative too. A total-body X-ray was negative while abdomen ultrasound confirmed hepatosplenomegaly.
During the following years, the patient presented arthralgias in several districts, responsive to short courses of nonsteroidal anti-inflammatory therapy. Joint symptomatology progressively improved during the growth until complete remission after puberty. Since the age of 6 years, she had presented recurrent blepharitis and chalazion episodes, treated first with antibiotic therapy and then with surgery, and a mild form of psoriasis. A relapsing abscess of median cyst of the neck was treated with oral antibiotic therapy. Periodic blood exams showed neutropenia and raised LDH, c-reactive protein and erythrocyte sedimentation rate.
Suspecting an autoinflammatory syndrome, in 2008 and 2016 she underwent genetic investigations (Sanger technique) resulted normal. In August 2018, a new genetic study performed with Next Generation Sequencing highlighted the *de novo* genomic variant p.E250K (c.748G>A) in heterozygosity of the PSTPIP1 gene, described as a pathogenetic variant associated to PAMI syndrome. The diagnosis was confirmed after the evaluation of serum zinc levels resulted elevated (538 ug/dl).
Conclusion: PAMI syndrome is a rare auto-inflammatory disease, genetically determined, with early onset, incomplete penetrance and variable expression. Our patient presented a mild phenotype of PAMI syndrome, since some typical features of the disease, such as poor growth, skin inflammation, thrombocytopenia and arthritis, were absent. PAMI syndrome should be considered in the differential diagnosis of patients with neutropenia and undefined systemic inflammation, even if other clinical manifestations are absent; the dosage of serum zinc may be a useful tool in the differential diagnosis in these cases because high serum zinc values can lead the clinician towards an early diagnosis.
Disclosure of Interest: None declared

P006

THE PECULIARITIES OF THE COURSE OF FAMILIAL MEDITERRANEAN FEVER AMONG PATIENTS OF THE CRIMEAN TATAR NATIONALITY: PRELIMINARY RESULTS OF A RETROSPECTIVE STUDY.

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Introduction: Familial Mediterranean fever (FMF) is the most common monogenic auto-inflammatory disease with peculiar ethnic predisposition. The disease occurs frequently among Mediterranean populations like Turks, Jews, Armenians, and Arabs. It was not until 2016, the Crimean Tatars, people of Turk origin, became first considered as the population with prominent incidence of FMF.
Objectives: the study examines the clinical and genetic features of FMF among children of Crimean Tatar nationality and studied the distribution of exon 10 MEFV alleles in healthy adults.
Methods: the retrospective study included data from case histories of 16 children aged 5 to 18 years. Diagnosis of FMF was based on Eurofever/PRINTO 2019 criteria. In each patient clinical characteristics including administered colchicine dose, tolerance, side effects, and biologics therapy were evaluated. All patients underwent direct Sanger sequencing of exon 10 of the MEFV gene. For population study we included 127 healthy unrelated adults without FMF and any periodic fever, whome exon 10 of the MEFV gene were analyzed.
Results: The mean age of FMF diagnosis was 9.5 (4.0; 14.2), the mean time from the first symptoms to the diagnosis was 5.5 (2.0; 9.3) years. The main clinical manifestations were fever (100%), arthritis (100%), peritonitis (50%), pleuritis (7%), and erysipeloid rash (57%). Most commonly involved joints were knee (100%) and hip (25%); in 13% of patients both joints were affected during the attack. Patients were at first diagnosed as having acute respiratory infection (n=14) or juvenile idiopathic arthritis (n=2). Genetic analysis revealed well-known pathogenic alleles of MEFV, p.M694V (88%), p.M680I (6%) and p.V726A (6%). The most common p.M694M mutation was found in heterozygous/homozygous state in 81% and 19%, respectively. Parents of 8 patients (50%) were consanguineous. Colchicine intolerance was observed in 13%, and colchicine resistance in 25% of the patients. 6 patients (38%) received biologic treatment: canakinumab - 4 (25%), and tocilizumab - 2 (13%). Colchicine treatment and biologics were effective in 100% of patients. In healthy adults from Crimean Tatar origin 13/127 (10.2%) had pathogenic exon 10 mutations: V726A (n=2, 1.6%), M694V (n=9, 7.1%), M680I (n=2, 1.6%)
Conclusion: MEFV mutations are frequent in Crimean Tatars probably due to founder effect. The main clinical features observed in the FMF patients were fever and arthritis. A high proportion of patients receives biologic therapy. Further investigations required to evaluate the characteristics of FMF in the Crimean Tatars population.
Trial registration identifying number: This work was supported by the Russian Foundation for Basic Research (grant № 18-515-57001).
Disclosure of Interest: None declared

P007

MULTIPLEX LONG-RANGE PCR FOR ROUTINE GENOTYPING OF UP TO NINE AUTOINFLAMMATORY GENE IN A SINGLE ANALYTICAL RUN BY NEXT GENERATION SEQUENCING

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Introduction: During the last decade, remarkable progress with massive sequencing has been made in the identification of disease-associated genes for AIDs using the next generation sequencing technologies (NGS). International group of experts described the ideal genetic screening method which should give information about SNVs, InDels, Copy Number Variations (CNVs), GC rich regions.
Objectives: Our aim was to develop and validate molecular diagnostic method in conjunction with NGS platform as an inexpensive, extended and uniform coverage and fast screening tool which consist of nine genes known to be associated with various AIDs.
Methods: To validation of four and nine gene containing panels, long range multiplex models were setup on 9 healthy sample without any known variations for MEFV, MVK, TNFRSF1A, NLRP3, PSTPIP1, IL1RN, NOD2, NLRP12 and LPIN2 genes. Ten patients with AIDs who had already known causative genes were sequenced for analytical validation. As a last step, multiplex models validated on 46 patients with pre-diagnosis of AIDs. All sequencing steps were performed on Illumina NGS platform. Validity steps included the selection of related candidate genes, primer design, development of screening methods, validation and verification of the product. GDPE (Gentera) bioinformatics pipeline was followed.
Results: Although there was no non-synonymous variation in 9 healthy samples, 127 synonymous variant alleles and some intronic and UTR variants were detected. In 10 patients who underwent analytical validation, beside the 11 known non-synonymous variant alleles, 9 additional non-synonymous variant alleles and a total of 110 exonic variant alleles were found. In clinical validation phase, 46 patients sequenced with multiplex panels, genetic and clinical findings were combined for diagnosis.
Conclusion: In this study, we described the development and validation of NGS-based multiplex array enables the “long-amplicon” approach for targeted sequencing of nine AIDs genes. This screening tool is less expensive and more comprehensive compared to other methods and more informative than traditional sequencing. Our panels have a great advantage compared to WES or hybridization probe equivalents in terms of CNV analysis, high sensitivity and uniformity, GC-rich region sequencing, InDel detection and intron covering.
Disclosure of Interest: None declared

P008

ADHERENCE TO COLCHICINE TREATMENT AND COLCHICINE RESISTANCE IN A MULTICENTRIC FMF NATIONAL COHORT

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Introduction: Colchicine is the standard treatment for Familiar Mediterranean Fever (FMF), however about 5% of patients (pts) experience colchicine resistance. There is no standard definition of colchicine resistance. Recently a panel of experts elaborated a new definition based on a Delphi consensus approach.
Objectives: We aim to describe main features of the disease and clinical outcome of a cohort of FMF pts with particular interest on the colchicine resistance and tolerability according to the definitions proposed by the recent consensus.
Methods: Since November 2009, 425 Italian pediatric and adult FMF pts from 13 centers were enrolled in a national longitudinal cohort study, using the EUROFEVER registry. Demographic, genetic and clinical data, including response to treatment, were analyzed. Supplementary information on quality of life and treatment adherence was also collected by a specific questionnaire.
Results: Complete information were available in 341 pts (M/F 189/152, 211 children and 120 adults). The median age at disease onset was 5.0 years (range 0.1-59); the median diagnostic delay was 8.7 years (0-61). The median age at enrollment was 12.1 years (0.4-82). The MEFV genotype was the following: 103 (30.2%) pts carried biallelic pathogenic (P) variants; 59 (17.3%) one P variants and one variants of unknown significance (VOUS)/likely benign (LB) variant; 27 (7.9%) had biallelic VOUS/LB variants; 97 (28.45%) were heterozygous for P variants; 30 (8.8%) were heterozygous for VOUS/LB, 25 (7.33%) were genetically negative.
Colchicine treatment was used in 280 patients; during treatment, biologic treatment (anti-IL1) in 22 patients. 61 patients received NSAID or steroid on demand.
We analyzed the behavior of the pts treated with colchicine according to the statements on resistance/intolerance defined by Ozen (1) (Table 1).

Table 1.

Adherence	62% displayed a total adherence (> 90% of prescription); 10.8% a good adherence (50-89% of prescriptions); 1.9% poor adherence (< 50% of prescriptions); 0.9% no adherence
Dose adjustment criteria/ Recommended maximum colchicine dose	Mean colchicine dose: Pts <5 years: 0.57mg/de (std. dev. 0.18) 5-10 year: 0.77mg/die (std. dev. 0.23) 10-18 years: 1.1mg/die (std. dev. 0.39) Adults : 1.16 mg/die (std. dev. 0.37) Pts with a dose equal or lower to the recommended starting dose: 5-10 years: 35.3% 10-18 years: 58.9% Adults: 67.6%
Resistance to Colchicine	Resistance was be defined as persistence of fever attacks, despite optimal treatment. 54% pts had a complete disease control 46% pts had some disease activity: - 30.4% pts had < 1 episode/month for 3 months - 7.8 % had ≥1 episode/month for 3 months - 7,3% frequency not known
Inclusion of secondary amyloidosis in the definition of colchicine resistance	5 adult pts (1.5%) displayed amyloidosis
Colchicine intolerance	11 pts (3.2%) withdraw colchicine because of drug intolerance
Patient quality of life and patient-	20.7% of pts experience fatigue or chronic pain, 16.9% limitations in daily activities, and 16.9% have lost school/work days.

reported outcomes	

Conclusion: Almost 46% of FMF pts display some disease activity despite colchicine treatment. The treatment is generally under-dosed, especially in children. The adherence and the compliance to the treatment is generally good.

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Aknowlegments This research was financially supported by Novartis AG

Disclosure of Interest: R. Gallizzi: None declared, M. Bustaffa: None declared, F. Mazza: None declared, D. Sutera: None declared, G. Fabio: None declared, L. Obici: None declared, M. Alessio: None declared, D. Rigante: None declared, L. Cantarini: None declared, A. Insalaco: None declared, M. Cattalini: None declared, M. C. Maggio: None declared, G. Simonini: None declared, A. Olivieri: None declared, S. Pastori: None declared, M. Lancieri: None declared, F. Calzantini: None declared, N. Ruperto: None declared, M. Gattorno Consultant for: Novartis, Sobi, Speaker Bureau of: Novartis, Sobi

P009

EFFICACY OF ANAKINRA TREATMENT IN PEDIATRIC RHEUMATIC DISEASES; A SINGLE-CENTER EXPERIENCE

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Introduction: Anakinra, a recombinant IL-1 receptorantagonist, is a treatment option that acts byblocking the biological activity of IL-1 in autoinflammatory conditions. The diseases that the IL-1 was over expressed are the potential conditions for this treatment. Such as familial Mediterranean fever (FMF), cryopyrin-associated periodic syndrome (CAPS), and hyperimmunglobulin D syndrome (HIDS) with monogenic inheritance, and systemic juvenile idiopathic arthritis (SoJIA) or idiopathic recurrent pericarditis as non-Mendelian polygenic diseases, can be listed as examples of these diseases.
Objectives: We aim to report our experiences of pediatric rheumatic diseases treated with anakinra.
Methods: The study group consisted of children with pediatric rheumatic diseases followed up in the Pediatric Rheumatology Department of University of Health Sciences and treated with anakinra (anti-IL 1) for at least one month, between 1 July 2016 and 1 January 2020. The data of these patients were collected retrospectively. The disease activity of the patients at 3rd month and 12th month after the treatment were assessed.
Results: There were 28 patients treated with anakinra for the different pediatric rheumatic diseases. The diagnoses of these patients were as follows; eight were macrophage activation syndrome (MAS) complicating SoJIA, six were HIDS, four were CAPS, four were FMF, four were idiopathic recurrent pericarditis, one was deficiency of interleukin-36 receptor antagonist (DITRA), and one was undefined systemic autoinflammatory disease. 46.4% of the patients were male and 53.6% were female. The median age of diagnosis of the patients was 6.5 ((interquartile range (IQR): 4-12.7) years. The median follow-up duration of the patients was 14 (IQR: 3.7-28) months. The patients median anakinra treatment duration was 3 (IQR: 1-4) months. Fever reduced and C-reactive protein normalized within median 2 (IQR: 1-3) and 5 (IQR: 5-7) days, respectively. In the 3rd month after treatment; It was observed that 53.6% of patients achieved a complete remission (no attack was seen or MAS was improved). The frequency of attacks were decreased more than 50% in 35.7% of patients and less than 50% in 7.1%. 3.6% of patients were unresponsive to treatment. In the 12th month assessment after the initiation of treatment, it was observed that 28.6% of patients were still under anakinra treatment and in remission, 10.7% of them were in remission without anakinra treatment. In 60.7% of patients, anakinra was switch to other biological treatments for different reasons (35.7% partial response or unresponsiveness, 17.8% injection site reactions and 7.1% daily-injection difficulty). Biologic drug switch to canakinumab and tocilizumab was observed in 88.2% and 11.8% of patients , respectively. One patient developed recurrent MAS episodes when the anakinra dose was tapered, and one another patient was unresponsive to the anakinra and dead due to secondary to MAS.
Conclusion: Anakinra seems to be a successful treatment to achieve inactive disease in a significant portion of patients in the early period. The recurrence of disease attacks while drug tapering and injection site reactions were appears the main causes of treatment switch or discontinuation.
Trial registration identifying number: None
Disclosure of Interest: None declared

P010

MAJEED SYNDROME AND FMF IN A LEBANESE PATIENT: A CASE REPORT

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Introduction: Familial Mediterranean Fever (FMF) and Majeed syndrome are both rare autosomal recessive periodic fever syndromes that are most prevalent in the Eastern Mediterranean population(1). Majeed syndrome is extremely rare and caused by mutations in the LPIN2 gene which encodes phosphatidate phosphatase LPIN2 (Lipin-2), that controls excessive production of pro-Interleukin-1 beta(pro–IL-1β) during inflamasome priming(2). This syndrome associates recurrent fever, congenital dyserythropoetic anemia, chronic recurrent multifocal osteomyelitis (CRMO) and neutrophilic dermatosis and it has a poor long-term outcome(2).
Objectives: We report the association of these 2 rare auto-inflammatory diseases in a Lebanese child and the dramatic clinical and biological improvement with IL-1 blockade.
Methods: A now 8-year-old girl born to consanguineous parents, presented with severe anemia since the age of 3 months (Hb=4g/dL). Intermittent high LDH and low neutrophils counts were seen. Repeated Bone Marrow Aspiration (BMA) and bone marrow biopsy came in favor of myelofibrosis with signs of dysmyelopoiesis. The child was successfully treated with long duration oral steroids.
She came to our attention at the age of 3 years for intermittent fever and mild arthritis in both ankles with no other abnormality. Her family history was notable for JIA in a paternal cousin. Biology showed normal CRP, WBC, platelets with Hb at 10g/dL. ANA, antiDNA, antiENA, RF and anti-CCP were negative. C3, C4, C1q inhib and C1q were normal. X-rays of ankles showed bilateral unspecific diaphysal and metaphysal osteocendensation.
She received NSAID with Methotrexate; ankles normalized but anemia worsened motivating re-use of glucocorticoids.
History was then marked with repeated episodes of fever for 3 days with abdominal pain. Genetic testing for FMF showed compound heterozygous mutations (M694I/E148V). Methotrexate was stopped and colchicine was started.
The patient was then lost to follow-up and took colchicine inconsistently due to digestive intolerance. Fever recurred daily and ankle pain was intermittent. Seen again at the age of 7 years, we noted growth delay with normal physical exam. Biology showed anemia(Hb=8.3g/dL) with increased inflammatory markers (CRP=125mg/L, SAA 877mg/L). X-ray of ankles was normal.
Results: Given the atypical association of FMF to probable auto-inflammatory myelofibrosis and the atypical osteoarticular findings, genetic testing was performed and revealed a homozygous mutation in LPIN2(c.362delC) confirming the diagnosis of Majeed syndrome. Anakinra treatment was then started. Fever and arthralgia resolved. After 9 months of biotherapy, the patient was still asymptomatic with normal biology and catch-up growth.
Conclusion: Majeed syndrome is an extremely rare disease with only few recent reports in literature(3). This is the first report of a Lebanese patient. To the best of our knowledge, there was no previous association of Majeed syndrome and FMF.
Based on this clinical presentation, other genetic inflammatory diseases should be considered in case of atypical symptoms or resistant FMF.
In this patient who received steroid therapy for years, IL-1 blockade with Anakinra was attempted and showed sustained control of inflammation with correction of anemia and complete resolution of symptoms.
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Disclosure of Interest: None declared

P011

MUSCULOSKELETAL SYMPTOMS AND THEIR IMPACT ON HEALTH-RELATED QUALITY OF LIFE IN CHRONIC NONBACTERIAL OSTEOMYELITIS PATIENTS

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Introduction: Chronic nonbacterial osteomyelitis (CNO) is a rare, non-infection-related inflammatory disorder that affects children and teens (1). Clinical manifestations of CNO range widely from moderate, time-limited, monofocal inflammation of the bone to extreme multifocal or chronically active inflammation of the bone (2). Patients are increasingly complaining of bone and joint pain, sometimes very crippling (3).
Objectives: The main aim of this study was to explore the correlation between musculoskeletal (MSK) symptoms and health-related quality of life (HRQoL) in patients with CNO.
Methods: Children and adults with CNO and their parents were asked to answer a web-based survey .The survey consisted of multiple questions centered around demographic, clinical and therapeutic data , MSK discomfort form based on the Nordic MSK Questionnaire and HRQoL based on Pediatric Quality of Life Inventory-4 (PedsQL-4) and PedsQL rheumatology module. The inclusion criteria included diagnosis of CNO before the age of 18. Patients who had malignancies or any chronic rheumatic, MSK, neurological disease were excluded.
Results: There were a total of 68 participants, mostly females (66.2 %), with median age 14 years and median disease duration 4.75 years. The median number of bones affected by CNO was 5 and ranged from 1 to 24 bones. Among the studied patients, 45 patients (66.2%) had musculoskeletal manifestations at the last month. The most commonly affected part was ankle and feet (26.5%). Regarding HRQoL, patients with MSK manifestations had lower scores than did patients without in PedsQL-4 (p<.001) including domains of physical functioning (p<.001), emotional functioning (p=.033), social functioning (p<.001) and school functioning (p=.007) in addition to lower scores in PedsQL rheumatology module (p<.001) including domains of pain and hurt (p<.001), daily activities (p<.001), treatment (p=.035), worry (p=.001) and communication (p<.001).
Conclusion: MSK manifestations have a negative impact on HRQoL in CNO patients. So, early identification and treatment are highly recommended.

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Disclosure of Interest: None declared

P012

NLRP1-ASSOCIATED AUTOINFLAMMATION WITH ARTHRITIS AND DYSKERATOSIS (NAIAD SYNDROME) IN A 3-YEAR-OLD BOY

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Introduction: NLRP1-associated auto-inflammation with arthritis and dyskeratosis (NAIAD) is a rare, genetic auto-inflammatory and autoimmune disease in childhood. It was first reported in 2016 in three patients from two families with dyskeratosis, arthritis, recurrent fever and increased inflammatory markers.
Objectives: To report a case of a 3-years-old Turkish boy who presented with some clinical features of NAIAD syndrome.
Methods: Presentation of clinical and genetic finding of a patient with NAIAD.
Results: A 3-years-old boy attended our clinic with progressive joint swelling and limping lasted for six months. In the physical examination; generalized polyarticular joint involvement, mild dyskeratotic lesions of the limbs and trunk, and nail dystrophy on his foot were detected. The level of acute phase reactants was high. He received pulse steroid and IVIG treatment due to severe autoimmune hemolytic anemia (hemoglobin=3.9 g/dl, direct coombs=4+, reticulocytes=11%) when he was two years old. The family reported that he had dyskeratotic lesions on his limbs and trunk, and nail dystrophy on his foot since he was two months old and these lesions regressed following the steroid treatment. The patient was scanned in terms of metabolic diseases due to skeletal dysplasia and polyarthralgia. Skeletal radiographs revealed abnormal features such as overgrowth and osteopenia in the epiphysis and metaphysis of distal femoral and proximal tibias. Ultrasonography detected intraarticular effusion and synovitis in hands, feet, knees, ankle and wrists, and these findings were confirmed with magnetic resonance imaging. ANA and rheumatoid factor were negative. C3 and C4 were normal. No signs of uveitis were detected. Subcutaneous methotrexate and oral steroid (2mg/kg/day) were administered due to an initial diagnosis of polyarticular juvenile idiopathic arthritis. Despite the improvements, steroid could not been tapered. Recurrent episodes of unprovoked fever and systemic inflammation associated with elevated levels of CRP and ESR occurred. Persistent arthritis, presence of skin lesions, history of autoimmune hemolytic anemia, and abnormal features in the skeletal radiographs suggested autoinflammatory diseases. Anti-TNF inhibitor (etanercept) was added to treatment. However, no clinical response was achieved at 6 months. A heterozygous mutation in NLRP1 c.1887 C>A, p. Phe629Leu was detected in the patient. Anti-TNF treatment was ceased and IL-1B inhibitor (canakinumab) and steroid (2mg/kg/day) were administered. The arthritis dramatically improved. However, steroid treatment could not be reduced below 1mg/kg/day. Eventually, IL-1 inhibitor was ceased and IL-6 inhibitor was started. The patient is currently well under the tocilizumab treatment once in a two week for 6 months.
Conclusion: Only four patients with NAIAD were reported worldwide so far. The NLRP1 mutation of the present patient (c.1887 C>A, p. Phe629Leu) was predicted as “probably damaging” according to PolyPhen-2 database. To the best of our knowledge, this patient is the first NAIAD case presenting this mutation.
Disclosure of Interest: None declared

P013

ASSESSMENT OF BLOOD FERRITIN LEVELS IN PATIENTS WITH MONOGENIC AUTO-INFLAMMATORY DISEASES AND SYSTEMIC JUVENILE ARTHRITIS.

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Introduction: Auto-inflammatory diseases (AIDs) are a group of monogenic and polygenic diseases caused by violations of the functioning of the innate immune system. The development of such a life-threatening complication as macrophage activation syndrome, which is significantly less common in monogenic AIDs, is characteristic of systemic juvenile arthritis(sJA). The main laboratory marker of macrophage activation syndrome is an increase in ferritin.
Objectives: to evaluate serum ferritin levels in children and adults with various monogenic AIDs and sJA.
Methods: ferritin was detected in 85 samples of blood serum of 74 patients(pts): in 30 children with sJA (female 16, male 14). 17 samples from 13 FMF pts (children -10, adults - 3, male -6, female-7). In 4 pts, the study was performed in dynamics before and past the appointment of therapy(in 2 colchicine, in 2 colchicine with biologic (and etanercept). 25 samples of serums were from 22 pts with CAPS pts(children -11, adults - 11, male -9, female-13); in 4 pts, the study was performed in dynamics before and past the appointment of canakinumab therapy. 13 serums from 10 pts with TNF-receptor-associated periodic syndrome (TRAPS): (children -9, adults - 1, male -5, female-5, including 3 pts in dynamics on the background of canakinumab therapy. Ferritin was determined by enzyme immunoassay with a set of reagents ORGENTEC. The normal value for ferritin varies between 20 and 150 µg/L. Diagnoses of monogenic AIDs (FMF, CAPS, TRAPS) were confirmed by the detection of pathogenic mutations of causal genes. The diagnosis of sJA was based on ILAR criteria. Statistical analysis was performed using standard indicators: median, 25th and 75th quartiles, and the difference between the groups according to the Mann-Whitney criterion. In all patients the same sera values of CRP and SAA were determined using the nephelometric method.
Results: Tabl.1
Ferritin levels in serum of patients with monogenic AIDs and systemic juvenile arthritis.

	Median µg/L	Min µg/L	Max µg/L	Lower quartile µg/L	Upper quartile µg/L
sJA	61.09	0.73	1 500	22.03	385.76
FMF	57.22	3.36	174.22	21.36	133,52
CAPS	28.88	0.98	183.57	8.13	118
TRAPS	16.52	2.42	930.1	5.42	67.27

In patients with sJA the normal ferritin values were found in 12 (41%) pts; in FMF the normal values were found in 100% of pts; in pts with CAPS normal values in 8 (32%) sera semples; in pts with TRAPS normal values were found in 9 (90%) pts, and only 1 pt showed an increase in ferritin despite treatment with canakinumab. A statistically significant difference was obtained between the groups of sJA and CAPS ($p<0.001$), sJA and TRAPS ($p=0.03$). The correlation between the level of CRP and ferritin was maximal for pts with CAPS: $r=0.64$($p<0.001$) and with sJA: $r=0.6$ ($p<0.001$). There was no significant correlation between the level of CRP and ferritin in patients with FMF. The correlation of SAA and ferritin levels was maximal in pts with TRAPS: $r=0.7$($p=0.0072$) and CAPS: $r=0.54$ ($p=0.0051$). There was no significant correlation between SAA and ferritin levels in patients with FMF.
Conclusion: the maximum sera values of ferritin were observed in pts with sJA, their value was statistically significantly higher than in the CAPS and TRAPS groups. Among pts with mAIDs, the most frequent increase in ferritin was observed in patients with CAPS. In patients with FMF, no elevated ferritin levels were detected; in a patient with TRAPS, a persistent increase in ferritin in dynamics was observed in 1 patient whose phenotype had the similarity to sJA. Ferritin may be used as an additional laboratory differential diagnostic sign between patients with sJA and mAIDs.
Disclosure of Interest: None declared

P014

GENETICS OF CHRONIC NONBACTERIAL OSTEOMYELITIS IN THE IRISH POPULATION: NO EVIDENCE OF A ROLE FOR FBLIM1 VARIANTS

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Introduction: Chronic nonbacterial osteomyelitis (CNO) is a rare inflammatory disease affecting bone predominantly affecting the paediatric population. CNO is frequently associated with other inflammatory conditions including psoriasis, synovitis and pustulosis, and the typically adult-onset disease SAPHO syndrome is considered to be part of the same disease spectrum. The *FBLIM1* gene has been implicated in the pathogenesis of CNO with rare variants identified in 2 patients of South East Asian descent, enrichment of a nonsynonymous variant rs114077715 in European population and also in an Italian cohort. However, there was no association of *FBLIM1* variants in a European SAPHO population. The Irish paediatric CNO population has a high frequency of extraosseous involvement, particularly cutaneous involvement.
Objectives: To ascertain the frequency of variants in *FBLIM1* in an Irish cohort of patients with CNO and compared to the gnomAD non-Finnish European (gnomAD NFE) population.
Methods: 43 Irish children and adolescents currently attending paediatric rheumatology services with CNO were recruited; all met the Bristol criteria for diagnosis of CNO. Whole exome sequencing was performed using Agilent SureSelect XT Human All Exon V6 kits and Illumina HiSeq 3000 with 150bp paired-end reads. Reads were aligned to the hg19 reference genome using BWA software, duplicates removed using Picard tools and GATK software used to realign indels and call variants. The resulting VCF files were annotated using wAnnovar. Rarer variants (gnomAD NFE </= 0.05) were hard filtered for mapping quality (MQ > 40) and depth of coverage (QD > 2)[GW1] . A MAF of <0.05 was selected in order to include previously published candidate variants. Statistical analysis was performed in RStudio (version 1.1.456).
Results: Five individuals had variants in FBLIM1 with MAF <0.05, all were heterozygous. Four carried the nonsynonymous minor allele rs114077715 indicating a MAF in this population of 0.0465 with no significant enrichment (gnomAD NFE MAF=0.0264, OR 1.79, p=0.29). One carried the synonymous minor allele rs140170023 indicating a similar MAF to that reported in gnomAD (NFE MAF=0.017). No variants were present with a MAF between 0.03 and 0.05.
Conclusion: Variants in *FBLIM1* do not occur at a significantly higher frequency than expected in the Irish paediatric population with CNO compared to gnomAD non-Finnish European allele frequencies. This may be a reflection the clinical heterogeneity of CNO in different populations.
Disclosure of Interest: None declared

P015

TOWARDS A COMBINED PEDIATRIC RHEUMATOLOGY-DERMATOLOGY CLINIC: ONE-YEAR EXPERIENCES

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Introduction: Dermatological findings may be the sole complaints of diseases in pediatric rheumatology practice. It is well-known that evaluating patients with a multi-disciplinary approach may facilitate access to an accurate diagnosis.

Objectives: Herein, we reported our one-year experiences of collaborative pediatric rheumatology-dermatology.

Methods: Patients were initially evaluated separately in pediatric rheumatology-dermatology outpatient clinics. Subsequently, once a week, final diagnoses of patients with suspected skin rash were colloboratively discussed by two pediatric rheumatologists and a dermatologist.

Results: A hundred and one patients were included to the study. Of these patients, 65 attended initially to dermatology outpatient clinic while the remaining 36 applied to pediatric rheumatology outpatient clinic. The most common mucocutaneous finding was squamous lesions in 30 patients, followed by erythematous lesions in 28 and mucosal ulcers in 14. Finally, 69 patients were diagnosed with a rheumatic disease while 32 had differential diagnoses apart from rheumatic diseases.

Table 1. Demographic and clinical characteristics of the patients

	Psoriasis (n=30)	BH (n=14)	SLE (n=13)	Scleroderma (n=7)	JDM (n=2)	DADA2 (n=3)	Non-rheumatologic conditions (n=32)
Gender (F/M)	20/10	10/4	10/3	6/1	0/2	2/1	20/12
Age, median (min-max)	10.7 (1.8-16.9)	15.1 (10.2-17.8)	13.6 (8.1-16.7)	9.8 (3.-17.5)	11.1/11.5	15.2 (8.2-15.6	11.5 (3.1-17.5)
Type of skin lesion	Papulosquamous lesions	Oral aphthous	Malar rash (n=12) and lupus pernio (n=1)	Sclerotic lesion	Gottron papule	Livedoid rash	Erythematous lesions, hyper-pigmented lesion, xerosis
Arthralgia, n	22	8	4	2	0	3	31
Arthritis, n	13	2	8	1	0	1	7

BH, Behçet's disease; DADA2, deficiency of adenosine deaminase 2; F, female; M, male; max, maximum; min, minimum; n, number of patients; SLE, systemic lupus erythematosus

Conclusion: Patients with rheumatologic diseases frequently present with only mucocutaneous findings. So a detailed examination of the mucosa, skin and its attachments is of paramount importance in rheumatology practice. We suggest that a close interaction between pediatric rheumatology-dermatology and formation of consensus clinics are going to assist clinicians to make easier and accurate diagnoses.

Disclosure of Interest: None declared

P016

THE MUSCULOSKELETAL SYSTEM MANIFESTATIONS IN CHILDREN WITH FAMILIAL MEDITERRANEAN FEVER

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Introduction: Familial Mediterranean fever (FMF) is a monogenic inherited periodic fever syndrome presenting with episodes of self-limiting fever and inflammation of serosal membranes. The attacks emerge with arthritis were defined as one of the major diagnostic criteria besides involvement of serosal membranes. Non-specific musculoskeletal findings such as myalgia, arthralgia, transient synovitis, and more rare manifestations like protracted febrile myalgia can also be seen in FMF patients attacks

Objectives: We aim to reveal the frequency and genotype association of musculoskeletal manifestations in children with FMF.

Methods: The patients diagnosed with FMF between January 1, 2017 and June 1, 2019, and followed for at least 6 months in our pediatric rheumatology clinic were included in the study. Musculoskeletal manifestations of patients were enrolled. The patients were grouped according to the “Mediterranean Fever” (MEFV) gene variants. Musculoskeletal manifestations of the patients were compared between the groups

Results: The study group included 634 children with FMF (336 female and 298 male, F/M: 1.13/1). The clinical manifestations of patients in attack period were as follows: 99% of the patients had fever, 87.3% had abdominal pain, 20.7% had chest pain, 11.3% had vomiting, 10.7% had erysipelas like erythema, and 9.3% had headache. The musculoskeletal symptoms were accompanied by 58.6% (n: 372) of the patients during the attack period. The most common musculoskeletal manifestation was found as arthralgia (32.6%, n: 206). Also, the other musculosceletal manifestations were found as follows during attacks; arthritis in 23.7% (n: 150), myalgia in 20.5% (n: 130), exertional calf pain in 6.5% (n: 41), and protracted febrile myalgia in 1% (n: 7) of the patients. It was observed that the musculoskeletal manifestations were significantly higher in patients with homozygous M694V variant in exon-10 (p=0.017). Also, it was found that the musculoskeletal manifestations are more common in the attack periods of patients carrying the M694V variant in at least one allele (p = 0.019).

Conclusion: We found that the musculoskeletal manifestations were accompanied in more than half of FMF patients. M694V variant found as a risk factor for emerge of musculoskeletal manifestations.

Trial registration identifying number: (Approval No/Date: B.10.1.TKH.4.34.H.GP.0.01/233 / 18.12.2019)

Disclosure of Interest: None declared

P017

AN ITALIAN COHORT OF PATIENTS WITH CHRONIC RECURRENT MULTIFOCAL OSTEOMYELITIS

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Introduction: Chronic Recurrent Multifocal Osteomyelitis (CRMO) is a rare disease characterized by sterile bone inflammation with many unclear aspects in terms of diagnosis, treatment and follow-up.
Objectives: To evaluate demographic, clinical, laboratory, imaging, histopathological characteristics, and treatment responses of pediatric CRMO patients.
Methods: The clinical records of patients with CRMO diagnosed between 2006 and 2019 at three tertiary centers in Italy were reviewed. The diagnosis was based on clinical findings, radiological images and histopathological studies.
Results: We identified 50 patients (62% female) with a median age at onset of 10.00 yrs. Median follow up time was 27 months (range 5-156) and median delay in diagnosis was 7 months (range 1-62). Bone pain was the most common presenting symptom (98%) followed by functional impairment (76.6%). Swelling and fever occurred in 40.4% and 24% of the cases respectively. Median number of affected sites was 3 (range 1-17). Multifocal bone lesions were described in 86% of the patients. Long bones (66%) and vertebrae (52%) were the most commonly affected sites. Increased inflammatory markers (ESR or CRP) at presentation were detected in 32 (64%) patients. Biopsy from bone lesions was performed in 66% of patients. All of the biopsy samples showed evidence of mixed inflammatory infiltration and sclerosis and no infectious agents were found. Whole-body magnetic resonance imaging (MRI) was used as a diagnostic tool in 68% of patients and always was abnormal revealing marrow edema (97.8%), soft tissue edema (85.1%), osteolytic lesions (76.1%), asymptomatic lesions (59.1%), sclerosis (39.1%), joint involvement (23.4%), hyperostosis (15.2%). Other autoimmune diagnosis were associated with 30% of patients (SAPHO n=2, Crohn's disease n=2, autoimmune thyroiditis n=2, JIA n=1, pulmonary fibrosis n=1, coeliac disease=1) although no association with psoriasis. The medications and treatment response are summarized in Table 1. At the last visit, disease status was considered to be in remission in 31 of 50 patients, of whom 43.5% (n=20) without medication and 32.6% (n=15) still on therapy.

Table 1. Medications and treatment response according to physician assessment

	Full response	**Partial response**	**No response**
NSAIDs (n=39)	12 (30.8%)	7 (17.9%)	20 (51.3%)
Corticosteroid (n=10)	5 (50.0%)	3 (30.0%)	2 (20%)
Methotrexate (n=17)	9 (52.9%)	4 (23.5%)	4 (23.5%)
Infliximab (n=11)	5 (45.5%)	4 (36.4%)	2 (18.2%)
Neridronate (n=15)	8 (53.3%)	4 (26.7%)	3 (20%)
Pamidronate (n=11)	5 (45.5%)	4 (36.4%)	2 (18.2%)

Conclusion: MRI is a very sensitive technique for detecting bone lesions in CRMO and can be used for monitoring the disease course. Methotrexate, bisphosphonates, corticosteroid and anti-TNF seem more effective than NSAIDs in treating CRMO, but there is no consensus yet about the management of this rare condition. Rarity and unclear pathophysiology leads to challenges in conducting randomized controlled trials with sufficient power to provide a definitive outcome.
Disclosure of Interest: None declared

P018

PRESENCE OF R202Q MUTATION OF THE MEFV GENE DEFINES AN ATYPICAL SUBTYPE OF PFAPA WHICH BENEFITS FROM COLCHICINE TREATMENT

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Introduction: PFAPA syndrome (periodic fevers, aphthous stomatitis, pharyngitis and cervical adenitis) is the most common autoinflammatory disorder in childhood but its pathophysiology is still unknown. In patients with PFAPA, variants of the MEFV gene including R202Q alteration, have been reported. Furthermore, the role of R202Q is still unclear. The first studies described R202Q as a benign polymorphism. However, further studies suggest that R202Q may play a role as a disease-causing mutation associated with a mild phenotype of Familial Mediterranean Fever (FMF).
Objectives: To compare the clinical features of patients with clinical diagnosis of PFAPA and R202Q alteration of the MEFV gene in both heterozygosity and homozygosity (atypical PFAPA, aPFAPA) to patients affected by typical PFAPA (tPFAPA). The second objective was to compare the clinical phenotype of patients with heterozygous R202Q to patients with homozygous R202Q alteration and to evaluate the efficacy of colchicine treatment in both groups.
Methods: We reviewed the demographic and the clinical characteristics of consecutive patients with clinical diagnosis of PFAPA. Data were analyzed using SPSS version 18.0 Chi-square and Mann-Whitney tests.
Results: 91 patients, 41 with aPFAPA and 50 with tPFAPA, entered the study. The average age at disease onset was higher in aPFAPA than in tPFAPA (4.5 vs 2.1 years; *p = 0.004*). aPFAPA had significantly higher rates of irregular interval between febrile attacks (19.5% vs 2.0%, *p=0.010*), abdominal pain (56.1% vs 30.0%, *p=0.012*), vomiting (22.0% vs 2.0%, *p=0.004*), diarrhea (19.5% vs 4.0%, *p=0.039*) and arthralgias (53.7% vs 30.0%, *p=0.022*). Conversely, pharyngitis and apthous stomatitis were significantly less frequent in aPFAPA than in tPFAPA (75.6% vs 100%, *p<0,005*, and 36.6% vs 58.0%, *p=0,042,* respectively). There were no significant statistical differences between the two groups based on family history for recurrent fevers, presence of cervical adenitis, chest pain, arthritis or skin lesions during febrile attacks.
As for the second objective, we found no significant differences in the phenotype of patients with heterozygous and homozygous R202Q mutation. Colchicine was administered to 48.1% of patients with heterozygous and 63.6% of patients with homozygous R202Q. Both groups had a notable clinical improvement with colchicine treatment although it was significantly higher in patients with homozygous R202Q mutation (100% vs 46.2%; *p = 0.049*). 63.6% of the patients with homozygous R202Q mutation had a complete resolution of the symptoms whereas 36.4% had a partial clinical improvement. Colchicine-related side effects lead to a withdrawal of the therapy in 30.8% of the patients, all from heterozygous R202Q group.
Conclusion: R202Q alteration of the MEFV gene is associated with atypical PFAPA, overlapping some clinical features of FMF, characterized by older age at onset, less regular interval between febrile attacks and more frequent abdominal pain, vomiting, diarrhea and arthralgias, as compared to typical PFAPA phenotype. We have demontrated that patients with R202Q mutation, particularly in homozygosity, may benefit from colchicine treatment.
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Disclosure of Interest: None declared

P019

OCULAR INFLAMMATORY DISEASES IN CHILDREN WITH FAMILIAL MEDITERRANEAN FEVER: A TRUE ASSOCIATION OR A COINCIDENCE?

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Introduction: Familial Mediterranean fever (FMF) is typically described as an autoinflammatory disease that can involve joints, skin, muscles, and kidneys. A variety of different clinical entities have been associated with FMF over time [1]. Ocular inflammatory diseases (OIDs) are one of the uncommon entities reported with FMF [2].
Objectives: We aimed to describe the characteristics of OIDs observed in children with FMF and to criticize possible relations between these two inflammatory entities.
Methods: Demographic and clinical data were extracted from the electronic medical records of FMF patients followed in the Department of Pediatric Rheumatology of Ankara University School of Medicine. The diagnosis of FMF was based on Yalcinkaya criteria [3]. OIDs were diagnosed and treated in collaboration with the Department of Ophthalmology.
Results: Among 512 pediatric patients with FMF, five patients were found to have OIDs: chronic bilateral panuveitis in two patients, one patient for each of recurrent orbital myositis (ROM), recurrent optic neuritis (RON), and acquired Brown's syndrome. All patients had at least one M694V mutation and received a diagnosis of OIDs during the follow-up while on colchicine. None had any other concomitant disease. Serum biochemistry, urinalysis, an infectious screen, autoantibodies, HLA testing, serum angiotensin-converting enzyme level, a chest X-ray, and in addition to these, in patients with ROM, RON, and Brown's syndrome cranial and orbital magnetic resonance imaging were carried out to exclude other secondary causes of OIDs. All these investigations were within normal limits for all patients. Colchicine and steroids were used in all patients and methotrexate and biologics were added according to the course of OID. The demographic and clinical characteristics of patients are presented in Table 1.

Table 1. Demographic and Clinical Characteristics of Patients

	Patient 1	**Patient 2**	**Patient 3**	**Patient 4**	**Patient 5**
Gender	Female	Male	Female	Male	Male
Age at FMF onset	6 months	Neonatal	4 years	18 months	18 months
Age at FMF diagnosis	1 year	6 years	5 years	3 years	6 years
Clinical findings of FMF	Recurrent fever, abdominal pain, joint pain	Recurrent fever, abdominal pain, joint pain	Recurrent fever, chest pain, abdominal pain	Recurrent fever, chest pain, joint pain, abdominal pain	Recurrent fever, chest pain, joint pain, arthritis, abdominal pain
MEFV gene mutation	M694V/M680I	M694V/M694V	M694V/M680I	M694V/M694V	M694V/M694V
A family history of FMF	+	+	+	+	+
Age at OID onset	6 years	8 years	12 years	5.5 years	8 years
Type of OID	Bilateral panuveitis	Bilateral panuveitis	Recurrent bilateral orbital myositis	Recurrent bilateral orbital neuritis	Unilateral acquired Brown's syndrome
Treatment	Colchicine, topical and systemic steroids, methotrexate, cyclosporine A, adalimumab, infliximab	Colchicine, topical steroids, methotrexate, adalimumab	Colchicine, systemic steroid	Colchicine (dose increased), systemic steroid, anakinra	Colchicine (dose increased), systemic steroid, anakinra

FMF: Familial Mediterranean Fever, MEFV: MEditerranean FeVer, OID: Ocular Inflammatory Disease
Conclusion: Although uveitis and optic neuritis have been reported in patients with FMF before, to the best of our knowledge, the first cases of ROM and acquired Brown's syndrome have been introduced. As the presence of M694V

mutations creates a pro-inflammatory state, FMF may be a susceptibility factor for various inflammatory diseases like OIDs. Identification of pathogenic pathways linking FMF to OIDs warrants further investigations.
Ethics approval: Parental informed consent and institutional ethical approval were obtained.
Disclosure of Interest: None declared

P020

MOLECULAR AND CLINICAL FINDINGS IN CHILDREN WITH UNDIFFERENTIATED PERIODIC FEVER SYNDROMES

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Introduction: Periodic fever syndromes (PFS) are genetically determined disorders which appear with episodes of unprovoked inflammation. It should be noted that a range of conditions including autoinflammatory disorders (AID), primary immune deficiency syndromes (PIDS), rheumatic diseases, infections and malignancy may manifest themselves by periodic fevers. The main diagnostic difficulties are related to differentiation between AID and PIDS due to similar clinical signs and inflammatory profile. Some PFS such as familial mediterranean fever (FMF) or cryopyrin-associated periodic fever syndromes can be reliably diagnosed on clinical grounds while others may be revealed only by genetic testing. Finding causative genes may drastically improve patient's quality of life allowing earlier diagnosis and proper treatment.

Objectives:

To evaluate the role of next generation sequence in the diagnosis of PFS.

Methods:

41 unrelated patients with PFS and clinical suspicion of AID were included in the study. Clinical and laboratory findings of these patients were evaluated. DNA samples were subjected to targeted next-generation sequencing (MiSeq, Illumina) with enrichment for coding sequences of 344 PID-associated genes including 27 of those associated with autoinflammatory diseases.

Results: The following clinical symptoms were presented: periodic fever (n=17, 42%), persistent fever (n=17, 42%), peripheral lymphadenopathy (n=18; 44%), rash of different types (n=22; 54%), arthritis (n=27; 66%), vasculitis (n=13; 32%), and serositis (n=13; 32%).

Laboratory findings included high ESR, CRP and WBCs and were presented in all patients. Genetic testing allowed us to divide patients into 3 groups:

I - patients with mutations in the typical AID genes: TNFRSF1A (n=5), TNFAIP3 (n=2), NLRP12 (n=4.), MEFV (n=5), MVK (n=1). Mutations in these genes are associated with tumor necrosis factor receptor-associated periodic syndrome (TRAPS), Bechet-like syndrome, Muckle–Wells syndrome, FMF, and HIDS.

II - patients with mutations in PIDS - associated genes (n=4), such as WAS, CTLA4, NFKB2 and MBL2. Mutations in these are associated with Wiscott-Alrdrich syndrome, autoimmune proliferative syndrome, common variable immunodeficiency with adrenal insufficiency and insufficiency of complement activation.

III - patients (n=20) in which we failed to find variants in known periodic-fever associated genes.

We have not found any significant difference between patients with AID (group I) and without AID (groups II+III) in terms of onset age, clinical and laboratory findings, except ESR: 58 (40; 68) vs 28 (18; 53) mm/h ($p = 0.005$) and hepatomegaly 73% vs 36% ($p = 0.002$).

Conclusion: Targeted sequencing is a helpful tool for obtaining genetic diagnosis in patients with PFS. Considering somewhat similar clinical presentation of autoinflammatory diseases and primary immunodeficiencies, genetic testing is sometimes the only way to distinguish one from the other.

Trial registration identifying number: This work was supported by the Rssian Foundation for Basic Research (grant № 18-515-57001).

Disclosure of Interest: None declared

P021

BROADENING THE GENETIC AND CLINICAL SPECTRUM OF A20 HAPLOINSUFFICIENCY

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Introduction: Heterozygous mutations in TNFAIP3 gene werefound to cause a systemic autoinflammatory disease known as A20 haploinsufficiency (HA20) that resembles Behcet's disease. The protein A20 encoded by TNFAIP3 is structurally divided into two types of domains, OTU domain and C-terminal domain. It is involved in the negative regulation of nuclear factor-kB (NF-Kb). Dysregulation of A20, due to mutations in both domains, leads to constitutive NF-kB activation and development of inflammation. Patients with HA20 can also show an autoimmune phenotype

Objectives: To describe a novel mutation in TNFAIP3 gene leading to a novel phenotype in four patients from an Italian family

Methods: Clinical data of the patients were reviewed. Clinical Exome was sequenced on Illumina NovaSeq6000® platform. *In silico* analysis was performed on the basis of the patient's clinical phenotype. We took into account only variants with an allelic frequency in global population lower than 1%, according with GnomAD database. Production of pro-inflammatory cytokines following *ex vivo* stimulation of PBMCs with lipopolysaccharides (LPS) was analysed by ELISA. B and T cell phenotyping were performed. Moreover, B and T cells stimulation were done to follow the ability of the cells to respond to stimuli and the ability to proliferate

Results: Patient (Pt) 1 was referred to our hospital because of a severe relapsing remitting form of haemolytic anaemia that was treated with immunoglobulin, glucocorticoids and a course of rituximab. From the age of 5 she suffered from autoimmune thyroiditis. In addition, at 9 years she developed an antinuclear-antibody (ANA) negative polyarthritis, treated with intra-articular glucocorticoids and methotrexate. Her mother (Pt2) presented with autoimmune thyroiditis and oral aphtosis. Her elder sister (Pt 3) suffered from type I diabetes and autoimmune thyroiditis; at 20 years, she presented with wrist arthritis and tenosynovitis that required subcutaneous treatment with methotrexate and etanercept. Her younger sister (Pt4) suffered from recurrent febrile episodes associated with cervical lymphoadenopathy not related to infections until the age of 7. All of them were evaluated for short stature; Pt 2 was treated for one year with growth hormone therapy that was dismissed due to inefficacy. Sequencing analysis revealed the heterozygous c.1723_1724insC variant, not described previously in human genetic database. This variant leads to a premature stop codon causing a putative truncation of the protein and segregates with phenotype in the family. Western blot analysis, that could demonstrate the truncation of the protein, is still ongoing. PBMCs obtained from Pt1-4 were stimulated ex vivo with several concentration of LPS releasing significantly higher levels of the pro-inflammatory cytokines Il-1b and IL-6 compared to healthy subjects. Pt1 immunological assay revealed a marked reduction of memory and transitional B cells. The few switched memory B cells present did not express IgG and IgA on the surface. Table 1 shows the clinical features of patients

Conclusion: We identified, in four patients of an Italian family, a novel mutation of TNFAIP3 gene that, based on our functional data, seems to be pathogenic. The majority of the patients (3/4) showed autoimmune rather than autoinflammatory features. This study confirms that HA20 is characterized by different phenotypes even among members of the same family carrying the same mutation. Our results expand the phenotype and genotype spectrum of A20 haploinsufficiency.

Disclosure of Interest: None declared

P022

PERICARDIAL EFFUSION AFTER CARDIAC SURGERY: RETROSPECTIVE STUDY IN A PEDIATRIC COHORT.

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Introduction: Post pericardiotomy syndrome (PPS) is an inflammatory process involving the pericardium, pleura or both. PPS is a common complication of any cardiac surgery with an incidence ranging from 1 to 40%. Atrial septal defect (ASD) surgical correction is associated with the highest incidence of PPS.

Objectives: To evaluate the incidence and predictive risk factor for PPS after surgical ASD closure.

Methods: We collected patients followed at Bambino Gesù Hospital (Rome) between January 2015 and September 2019 who underwent cardiac surgery for ASD closure. Statistical analysis: chi-square (or Fisher's exact test as appropriate) and Mann-Whitney U test.

Results: A total of 203 patients (124 female) with different ASD type (secundum-type ASD, primum-type ASD [partial atrioventricular canal defects], sinus venosus-type ASD and coronary sinus-type ASD) were included. Median age at cardiac surgery was 4.4 years (IQR 2.7-7.3). Patients were divided in two groups: group 1 including 38/203 patients (18.7%) who developed pericardial effusion (PE) and group 2 including 165/203 (81.3%) patients without PE. The incidence of PPS after surgical ASD closure in our cohort was consistent with that reported in the literature No significative differences were noted between the two groups with regards to gender or age at the surgery, Moreover there were no significant differences between the two groups regarding duration of surgery and/or presence of comorbidities. The median time for the development of pericardial effusion in group 1 was 15 days after surgical correction (IQR 6–20). Incidence of fever after surgey was significantly higher in group 1 as compared to group 2 (23.7% vs 2.4%; $p<0.0001$). Furthermore, the eletcrocardiogram performed routinely at the time of hospital discharge showed significantly ST segment elevation in children who subsequently developed PPS (24.3% vs 1.8%; $p<0.0001$). We further subdivided patients with PPS in two subgroups on the basis of the severity of PE: 1) slight PE (<7mm; n=33) and 2) moderate/severe PE (≥7 mm; n=5). Patients with moderate/severe PE underwent surgery at an older age than the others and, they tend to have an higher body mass index (BMI) values (median 18 [IQR 17.4-21.1] vs 15.6 [13.5-16.5]; $p=0.013$). BMI percentile (72 [71-84] vs 23 [1-57]; $p=0.017$) confirmed this trend. Among the 38 patients with PE, only three patients did not required any therapy, 27 were treated only with ibuprofen and 8 with a combination of ibuprofen and colchicine.

Conclusion: In this study we evaluated the incidence of PPS in a large pediatric cohort of 203 cases and the presence of predictive risk factors associated to the development of PPS. Analyzing the two groups (with or without PPS) no differences were noted in terms of gender, duration of intervention or presence of comorbidities. An older age at the moment of surgery and an higher BMI seem to be associated to an higher risk of development of clinically significant pericardial effusion. The presence of fever and ST segment elevation at ECG following surgery can be predictive for a later development of PPS requiring a closer follow-up of these patients after discharge.

Disclosure of Interest: None declared

P023

LONG-TERM EFFICACY AND SAFETY OF CANAKINUMAB IN PATIENTS WITH AUTOINFLAMMATORY PERIODIC FEVER SYNDROMES – FIRST INTERIM ANALYSIS OF THE FMF/TRAPS/HIDS SUBGROUP

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Introduction: Autoinflammatory periodic fever syndromes characterized by excessive interleukin(IL)-1ß release and severe systemic and organ inflammation have been successfully treated with the anti-IL-1ß inhibitor canakinumab (CAN). In clinical trial situations and real life, rapid remission of symptoms and normalization of laboratory parameters were observed in most patients.

Objectives: The present study explores long-term effectiveness and safety of CAN under routine clinical practice conditions in pediatric and adult patients with CAPS (cryopyrin-associated periodic syndromes), FMF (familial Mediterranean fever), TRAPS (tumor necrosis factor receptor-associated periodic syndrome) and HIDS/MKD (hyperimmunoglobulinemia D syndrome/mevalonate kinase deficiency).

Methods: RELIANCE is a prospective, non-interventional, multi-center, observational study based in Germany with a 3-year follow-up period. Pediatric (age ≥2 years) and adult patients with clinically confirmed diagnoses of CAPS, FMF, TRAPS and HIDS/MKD that routinely receive CAN are enrolled in order to evaluate effectiveness and safety of CAN under standard clinical practice conditions. Evaluation of disease activity and fatigue by patients' assessment, days absent from school/work due to study indication, inflammatory markers and physician global assessment (PGA) was performed at baseline and will be further assessed at 6-monthly intervals within the 3-year observation period of the study.

Results: This first interim analysis of a patient subset diagnosed with FMF, HIDS and TRAPS includes baseline data of 41 patients (29 FMF, 10 TRAPS, 2 HIDS) as well as preliminary 6-month data of the FMF subset (N=16).

Preliminary results of a first subset of N=16 patients diagnosed with FMF indicate stable remission and disease control upon long-term CAN treatment. Within the first study interval, no major changes were observed regarding the analyzed parameters (table 1). Physician Global assessments of disease activity (% none-mild/moderate-severe) were for FMF patients at baseline 35-28-7 and 38-44-0 at month 6, for TRAPS patients at baseline 11-67-0 and for HIDS/MKD patients at baseline 100-0-0. Serious adverse events were reported for 2 patients including tonsillectomy and arthritis.

	FMF			**TRAPS**	**HIDS**
	Baseline	Baseline*	6 Months	Baseline	Baseline
Number of patients, N	29	16	16	10	2
Mean age, years (SD)	26 (5; 56)	16 (5; 47)	16 (5; 47)	22 (4; 43)	11 (5; 18)
Mean duration of prior CAN treatment, years (min; max)	2.2 (0; 6)	2.2 (0; 6)	2.2 (0; 6)	1 (0; 2)	3 (2; 4)
Patient's assessment of disease activity 0-10, mean (min; max)	3 (0; 10)	2.8 (0; 8)	2.2 (0; 7)	2.1 (0; 5)	0 (0; 0)
Patient's assessment of fatigue 0-10	4.4 (0; 9)	4.6 (0; 9)	3.9 (0; 8)	3.4 (0; 8)	0 (0; 0)
Number (%) of patients with days absent from school/work due to study indication during last 6 months	5 (17)	2 (13)	5 (31)	4 (44)	2 (100)
CRP, mean (mg/dL)	0.9	0.5	0.6	2.0	0.1
SAA, mean (mg/dL)	5.3	2.4	2.4	7.9	0.6

Conclusion: Baseline characteristics of the FMF/TRAPS/HIDS-subgroup and first interim data of FMF patients are available from the RELIANCE study, the longest running real-life CAN registry. Further interval data will be analysed to assess efficacy and safety of long-term CAN-treatment in patients with autoinflammatory periodic fever syndromes.

Disclosure of Interest: K. Tilmann Speaker Bureau of: SOBI, Roche, CSL, Novartis, N. Blank Speaker Bureau of: Novartis and SOBI, M. Borte: None declared, I. Foeldvari Consultant for: Novartis, J. Henes Speaker Bureau of: Novartis, Roche-Chugai, G. Horneff Speaker Bureau of: Abbvie, Chugai, Roche, Novartis, Pfizer, MSD, Bayer, M. Hufnagel: None declared, B. Kortus-Götze Speaker Bureau of: Novartis, C. Schuetz: None declared, F. Weller-Heinemann: None declared, J. Weber-Arden Employee of: Novartis, J. Kuemmerle-Deschner Speaker Bureau of: Novartis, AbbVie, SOBI

P024

A PEDIATRIC CASE OF FAMILIAL CHILBLAIN LUPUS WITH R152H HOMOZYGOUS MUTATION IN TREX-1 GENE

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Introduction: Familial chilblain lupus (FCL) is a rare form of monogenic systemic SLE that typically develops in early childhood with chilblain-like skin involvement. It presents with autosomal dominant inheritance (1). Typical clinical findings are painful and ulcerated erythematous plaques that occur after cold contact on the acral faces (2).
Objectives: Here, we present a case of FCL who was followed with the diagnosis of lupus pernio since infancy and diagnosed with FCL after show up homozygous mutation in the TREX1 gene.
Methods: Written consent form was taken from our patient and his family.
Results: A 13 year-old male patient presented with the complaint of painful wounds on his ears, cheeks and toes. It was reported that similar complaints developed in the ears and cheeks, since nine-year-old. There was no additional rheumatologic complaint in the history. Skin biopsy of erythematous lesions on the soles of the feet performed in infancy was found consistent with lupus pernio. Physical examination of the patient shown painful and in places ulcerated erythematous plaque lesions on the both ears helix, on both cheeks and dorsal faces of bilateral toes. All laboratory parameters were found in normal range. Brain MRI and echocardiography were performed and found normal. FCL was considered as a preliminary diagnosis in the patient with chilblain-like lesions onset at an early age and triggered by cold. Genetic panel analysis was performed. Homozygous R152H mutation was shown in TREX-1 gene. The patient was diagnosed as FCL due to the presence of just chilblain lesions. Hydroxychloroquine, prednisolone and tofacitinib treatment were started, respectively. All chilblain lesions healed, leaving hyperpigmentation. During the follow-up, prednisolone was tapered and discontinued. The 23-year-old sister of the index patient, who had arthritis and chilblain lesions, had also the same TREX-1 mutation and was diagnosed with FCL.
Conclusion: Familial chilblain lupus should consider in differential diagnosis in patients with chilblain lesions beginning at early age and with a similar family history.
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Acknowledgments: We thank our patient and his family
Disclosure of interest: None declared
Trial registration identifying number: According to the legal status in our country, ethics committee approval is not required for case reports. It is adequate to obtain informed patient consent.
Disclosure of Interest: None declared

P025

FROM SMART WORKING TO SMART CO-WORKING IN THE COVID-19 ERA: A PILOT PROGRAM OF COOPERATION AROUND AUTOINFLAMMATORY DISEASES

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Introduction: The last time was signed by the pandemic diffusion of COVID-19, with an emergency area COVID-19 dedicated and the need to minimize the inflow of children and adolescents affected by chronic diseases into the hospitals. Otherwise, paediatricians had to limit visits and to consider a new setting for febrile children.
Objectives: Patients affected by autoinflammatory diseases were assisted by telephonic consultations guaranteed by the paediatricians of free choice and by the paediatric rheumatologists.
However, the patients frequently needed a direct clinical approach and a specialistic evaluation in the case of flares and/or abnormal laboratory parameters and adverse reactions to drugs.
Another frequent question was the differential diagnosis of febrile episodes, to distinguish a recurrent fever, linked to autoinflammation, from an infectious disease.
Methods: we proposed to paediatricians of free choice in west-Sicily a questionnaire about difficulties met in the follow-up of children with autoinflammatory syndromes; needs of scientific or bibliographic support, number of patients with these diseases and treated with biological drugs.
Results: 55 questionnaires were collected: the most frequent recorded conditions were PFAPA and Familial Mediterranean Fever (FMF); a lower percentage followed CAPS; MVK, TRAPS.
The most frequent treatment in PFAPA was steroids on demand; in FMF was colchicine. A low percentage (10%) was treated with anti-IL-1 drugs, needing the access to the hospital to receive the therapy.
All the paediatricians needed specialistic support to adequately control flares, especially in FMF, CAPS, TRAPS and MVK. PFAPA patients were almost individually controlled by paediatricians.
Conclusion: Patients and paediatricians needed a specialistic help to organize the follow-up of these patients and to guarantee a good compliance to treatment.
This period characterized by smart working, telemedicine, strategies to monitor remotely the patients, can find the winning strategy in the approach of the “Co-working”, a new cooperation between hospital and paediatricians of free choice, in the global follow-up of autoinflammatory diseases.
Disclosure of Interest: None declared

P026

JUVENILE IDIOPATHIC ARTHRITIS WITH NOD2/CARD5 GENE MUTATION OR BLAU SYNDROME WITH ARTHRITIS AND UVEITIS: LESSONS FROM FAMILIAL CASE REPORT

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Introduction: Blau syndrome (BS) is systemic autoinflammatory disease characterized by an early onset granulomatous arthritis, uveitis and skin rash, caused by a mutation in the NOD2/CARD5 gene. In real practice an extremely rare monogenic disease like BS is difficult to recognize and it's initially diagnosed as Juvenile idiopathic arthritis (JIA) due to phenotypically similar symptoms.
Objectives: To analyze the diagnosis pathway and results of biologics therapy in a family case of two siblings with BS.
Methods: Case report of 2 brothers with BS genetically confirmed by NOD2/CARD5 gene mutation.
Results: Two brothers of 15 and 3 years old were examined in our clinic. The elder brother presented arthritis of both wrist joints at the age of 2 years. The appearance of a scaly erythematous maculopapular rash on the trunk and extremities preceded the development of onset of arthritis. 3 years later he developed polyarthritis involved knees, ankles and three PIF joints of the left hand. There was no significant improvement after treatment with NSAID, methotrexate (MTX) and cyclosporine A in regional hospital, so etanercept was added since 2012 with variable result. Despite of biologic and MTX therapy the disease has not been gone into remission. Intra-articular glucocorticosteroids injections were required from 4 to 10 times a year. On admission in our clinic in November 2019 he had high degree of activity polyarthritis. Also, during the examination uveitis de novo as a well-known "paradoxical effects" after 7 years of using etanercept was detected. At the same time the second patient (his younger brother 3 y.o.) was admitted to our clinic with recently appeared polyarthritis with «boggy-like» synovitis and tenosynovitis of wrists, ankles and knees. Anterior uveitis of both eyes was identified. In previous months he developed a small-spotted rash with desquamation that was preceded the onset of arthritis. Blood examination didn't show increased inflammatory activity in both sibs throughout the disease. Because of clinical picture in younger brother we revised the initial diagnosis (JIA) and suggested the Blau syndrome. Molecular genetic testing of the NOD2/CARD15 gene in both brothers showed the same mutation of c.1001G>A (p. Arg334Gln). Because of inefficacy of etanercept therapy and active uveitis in older brother we decided to switch etanercept to golimumab with success. Younger brother showed an excellent initial response to methotrexate and adalimumab for arthritis and uveitis. This history seems to be usual for a lot JIA pts without any other conditions. So we have two pts from one family with typical for BS gene mutation and clinical picture of arthritis and uveitis which responded to TNF-monoclonal antibodies and MTX. It should be noted that the eldest brother (20 years old) has been suffering from arthritis of large joints since his early childhood and inflammatory back pain at present time. We are also going to perform a molecular genetic test for him and extended study for the whole family.
Conclusion: our case report shown that there are now certain answer for the question: Is BS the separate disease or NOD2/CARD15 gene mutation just determines clinical features of JIA. One of the most fascinating aspects of this clinical case is the presence of BS in two (or 3?) children of the family. The further study is needed.
Disclosure of Interest: None declared

P027

SYSTEMIC AUTOINFLAMMATORY DISEASE RESEMBLING VERY EARLY ONSET INFLAMMATORY BOWEL DISEASE: A FAMILIAL CASE REPORT

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Introduction: Systemic autoinflammatory diseases (SAIDs) are characterized by the presence of chronic or recurrent inflammation secondary to an abnormal activation of innate immunity, generally due to mutation of genes encoding proteins with a key role in regulating inflammatory response.
Objectives: To report a familial case of an autoinflammatory disorder in order to improve our knowledge of genetic patterns associated to SAIDs.
Methods: Case reports.
Results: P1 was an 8-month-old male child. Since five months of life, he presented recurrent episodes of fever, perianal abscess and bloody diarrhea associated to raised inflammatory markers, elevated calprotectin level and anemia. Family history revealed death of older brother at the age of 2 years, suffering from an undefined syndrome characterized by persistent fever, diarrhea, perianal abscesses, anemia, arthritis and severe growth retardation. An older sister (9 years old) (P2) presented recurrent episodes of fever associated to exudative pharyngotonsillitis, enlarged neck lymph nodes and elevation of inflammation indexes, with good response to steroids, since the 6 months of life. Skin rash, diarrhea, arthritis and abdominal pain were not reported during the first years of illness. Suspecting PFAPA, she underwent tonsillectomy, without benefit. Over time, abdominal pain appeared during fever episodes.
At laboratory investigation, P1 presented C-reactive protein (167.2 mg/L) and serum amyloid A (215 mg/L) elevation, calprotectin increase (405 mg/kg), neutrophilic leukocytosis, non-hemolytic anemia (Hb 7.8 g/dl). No signs of infection were detected. Immunological and autoimmune profiles were normal. Bone marrow aspiration was normal. Suspecting very early-onset inflammatory bowel disease (VEO-IBD), ileocolonoscopy was performed. Macroscopic findings resulted normal but a chronic inflammatory infiltrate of the lamina propria was found. Next Generation Sequencing for VEO-IBD, including Mevalonate kinase gene (MVK), was performed. The presence of two heterozygous variants, c.803T> C and c.1129G> A in the MVK gene in exon 9 and 11, causing the variants p.Ile268Thr and p.Val377Ile, was detected. Both these mutations are described as rare and pathogenetic. Due to the family and personal history, clinical and laboratory findings, a SAID was suspected, and genetic investigation was also performed in P2, revealing the same two heterozygous MVK mutations. The variant of uncertain significance c.586G> A in the MEFV gene in heterozygosity was also detected in P1. Although MVK mutations were present in heterozygosity, given the highly suggestive clinical picture and the death of a brother with similar clinical characteristics, Canakinumab was started, with clinical resolution and laboratory normalization in both patients. Parents genetic analysis is ongoing.
Conclusion: Even though MKV deficiency is inherited in an autosomal recessive pattern, both these siblings presented an autoinflammatory phenotype, responsive to anti-IL1 therapy. Allegedly, also the other brother died from an unidentified SAID. These SAID familial cases show how clinical features of autoinflammatory disorders can vary even among relatives who share common mutations: while milder clinical features resembling PFAPA were described in P2, P1 presented a phenotype compatible with a VEO-IBD. Indeed, since chronic intestinal inflammatory disease has been described in association of SAIDs, it is important to consider SAIDs in the differential diagnosis of VEO-IBD.
Disclosure of Interest: None declared

P028

THE LONG AND WINDING ROAD TO THE DIAGNOSIS IN A PATIENT WITH EARLY-ONSET SARCOIDOSIS AND MULTIPLE ORGAN INVOLVEMENT

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Introduction: Early-onset sarcoidosis (EOS) is a sporadic form of a rare granulomatous autoinflammatory disease associated with mutations in the NOD2 gene. It usually presents in infancy and is characterized by the triad of rash, arthritis and uveitis. However, anterior uveitis and arthritis in the absence of typical skin lesions in a patient with EOS may be misdiagnosed as juvenile idiopathic arthritis (JIA). Therefore, proper diagnosis may be delayed, depending on other EOS-related conditions, e.g. panuveitis, fever, hypercalcaemia (HC), or involvement of spleen, liver, lymph nodes, lung, kidneys, and nervous system. In addition, other causes of such symptoms should always be considered. Regarding the therapy, basic principles are fortunately similar for JIA and EOS.
Objectives: To demonstrate the sequential development of EOS multiple symptoms in association with changes in medication strategy in a boy initially diagnosed with JIA.
Methods: A case report of a patient diagnosed and treated at a paediatric rheumatology centre.
Results: A 23-month-old boy with no familial history of rheumatic diseases, presented with polyarthritis, accompanied by bilateral chronic anterior uveitis with multiple posterior synechiae of iris. At that time, he had no systemic symptoms, not even a rash. The laboratory tests showed elevated CRP, ESR, mild anaemia and negative autoantibodies (AB). Due to the initial diagnosis of JIA with uveitis, the patient was treated with local corticosteroids (CS), methotrexate (MTX), along with systemic CS; after 3 months, CS were changed to adalimumab (ADA). Several mild relapses during a 30-month treatment period were followed by a significant arthritis and uveitis flare, leading to increase in ADA dose of 20 mg from q2w to qw. Six weeks later, full neurological examination was performed because of 2 brief, mild episodes of dysarthria, qualitative consciousness alteration and slight motor deficit. Brain MRI revealed multiple demyelinating lesions and CSF analysis detected pleocytosis, elevated protein and positive oligoclonal bands. No infection was found, AB were negative. MTX and ADA were withdrawn owing to their potential association with the condition, particularly ADA-induced demyelination was suspected. Instead, high-dose systemic CS were introduced with a positive effect on overall status. Unfortunately, decreasing the CS dose resulted in relapse of eye and joint disease; moreover, a transient macular rash (not indicated for biopsy) occurred, followed by fevers, unilateral peripheral facial nerve palsy, HC and nephropathy with elevated serum 1,25-dihydroxy vitamin D and chitotriosidase (ChT) activity, while ACE level was normal. The kidney biopsy revealed granulomatous interstitial nephritis and the EOS diagnosis was confirmed by genetic testing showing heterozygous R334Q mutation in NOD2 gene. CS were escalated and tocilizumab plus MTX were added. The skin, ocular, neurological, and kidney symptoms seem to be well controlled at present. Nevertheless, in correlation with serum ChT levels, especially arthritis control still requires higher CS doses.
Conclusion: High-dose (off-label) ADA was administered to our patient with putative JIA and uveitis resistant to conventional ADA and MTX doses. Subsequently, the change to single CS therapy due to the neurological complications may have contributed to manifestation of new symptoms including HC and nephritis leading to final diagnosis on the histological and genetic basis. Serum ChT unlike ACE was useful for the diagnosis and activity assessment in our case, as also reported by other authors.
Disclosure of Interest: None declared

P029

BARICITINIB-INDUCED REMISSION IN PRAAS/CANDLE SYNDROME: A CASE REPORT

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Introduction: PRAAS/CANDLE is a rare genetically defined autoinflammatory interferonopathy caused by mutations in genes that code for proteasome components[1]. At present, less than 100 cases have been reported worldwide.
Objectives: To describe the therapeutic effect of the JAK1/2- inhibitor, baricitinib, on the inhibition of the type I interferon (IFN) inflammatory pathway in a patient with PRAAS/CANDLE.
Methods: n.a.
Results: A one-year-old girl presented with an erythematous and nodular rash on the upper and lower extremities, mostly pretibial. At first, an erythema nodosum was suspected. Two weeks later, she developed pyrexia, hand and feet swelling, arthralgia in her ankles and myalgia. Her echocardiography revealed pericardial and bilateral pleural effusions. She was treated with steroids and non-steroidal anti-inflammatory drugs (NSAIDs), upon which she became afebrile and her symptoms partially improved. Steroid tapering was followed by fever reappearance and deteriorating of the patient´s conditions with abdominal pain, loss of appetite, weight loss and muscle atrophy. Laboratory investigations revealed ongoing severe systemic acute phase responses and hypochromic anemia. Her abdominal MRI revealed a mesenteric panniculitis. Escalation of treatment with etanercept only achieved a ten-day sustained defervescence. She developed progressive lipodystrophy, hypertriglyceridemia and increased liver function tests. A combination therapy with anakinra, steroids and NSAIDs led temporarily to milder symptoms, but did not influence disease progression. She developed lipoatrophy (mostly in the face), finger swelling, prominent abdomen, growth arrest, hypertrichosis, lymphadenopathy and hepatosplenomegaly, which led to the clinical diagnosis of PRAAS/CANDLE. RNA-sequencing revealed a type I IFN signature with evident up-regulation of IFN-inducible genes, which confirmed the diagnosis. No mutation was found in *PSMB8*, the results of the Whole Exome sequencing (WES) are pending. The patient was treated *off-label* with baricitinib 4 mg daily. Within days, she was fever-free and CRP-, ESR-, CK- and transaminase levels dropped. Anemia improved, the weight normalized, lymphadenopathy and mesenteric panniculitis were not further seen, and myalgia and arthralgia subsided, allowing her to walk again and attend preschool.
Conclusion: PRAAS/CANDLE is considered a type I interferonopathy. The genetic background is heterogeneous. Besides mutations in *PSMB8*, mutations in a number of other proteasome-associated genes are described[1]. Interferon signature and Whole Exome sequencing serve as key diagnostic tools in autoinflammatory disorders. Therapeutically, JAK1/2 blockage through baricitinib proved to be very effective in down-regulating type I IFN pathway sustained activation
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Disclosure of Interest: None declared

P030

CONTRIBUTION OF THE NEXT GENERATION SEQUENCING TECHNIQUE IN THE MANAGEMENT OF FAMILIAL MEDITERRANEAN FEVER PATIENTS

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Introduction: Familial Mediterranean Fever (FMF), the autoinflammatory inherited prototype with a autosomal recessive mode, is mainly diagnosed by clinical criteria and supported by genotyping, especially in atypical phenotypes. Genotyping however is not covered by public insurance in many countries.
Objectives: Primary objective: To depict the FMF genotype of Greek pts (patients) and investigate the contribution of Next Generation Sequencing technique (NGS) beyond the contemporary technique (PCR& hybridization) Secondary objective: To unravel any associations between the mutated genes with the disease course and response to treatment.
Methods: This is a single center, retrospective study including young and adult pts with an established clinical diagnosis according to Tel-Hashomer or Livneh diagnostic criteria. FMF pts with non-confirmative genetic analysis based on PCR & hybridization technique underwent NGS testing during the 15-mo period March 2015 to July 2017.
Results: Overall 31 pts, 12 male and 19 female with a mean age of 18.69 ± 10.14 years participated in the study.
PCR and hybridization technique detected ≥1 mutation in 25/31 pts (80.7%), most frequently p.Met694Val (29%), p.Met680Ile (16.1%), p. Arg202Gln (12.9%). The majority of the pts were heterozygous (20/25, 64.5%), 2/25 (6.5%) homozygous and 3/25 (9.7%) compound heterozygous, respectively. None of the pts had a complex genotype.
NGS analysis detected mutations in 26/31 (83.9%), most frequently, p. Arg202Gln (61.3%), p.Met694Val (48.4%), p.Met680Ile (19.4%). 9 pts (34.6%) were compound heterozygous, 5 (19.2%) heterozygous, 1 (3.8%) homozygous and 11 (42.3%) had a complex genotype.
Noteworthy, the application of NGS revealed that 4 genotypes among 8 pts remained unchanged and 17/25 pts were carriers of other mutations. Two siblings with a former negative PCR genotype but a classical phenotype turned out to have a complex genotype (M694V/R761H/R202Q).
Among the 17 pts who were characterized as heterozygous by PCR, 7 were found to have a complex genotype, 9 a compound one and the remaining 1 without any mutation. The latter had a mild early-onset phenotype and had been on medication for 15 years, but discontinued colchicine after the NGS analysis. This FMF-like pts is in clinical remission 7 years off medication (Table 1). The frequency of p. Arg202Gln was higher by NGS 61.3% than by PCR 12.9% (p=0.09) and correlated with FMF phenotype.
Rare mutations were detected by NGS in 5/26 pts (19.2%), namely p.Arg761His, p.Glu148Val, p.Glu167Asp, p.Phe479Leu, p.Arg408Gln and p.Pro369Ser. NGS genetically confirmed the clinical diagnosis (heterozygosity to compound or complex genotype) in 19 pts. The above findings highlight the mutational heterogeneity in our FMF pts.
Table 1. Genotype update by NGS among 19 FMF pts

PCR & Hybridization	NGS	
Negative (2)	M694V/R761H/R202Q	
M694V/0 (8)	M694V/R202Q (3)·M694V/M680I/R202Q (2)·M694V/E148V/R202Q·M694V/R202Q/R202Q·M694V/M694V/R202Q/R202Q	
M680I/0 (5)	M694V/M680I/R202Q·M680I/R202Q·M680I/V726A·(-)·M680I/M680I	
M694I/0	M694V/R202Q	
K695R/0	K695R/R202Q	
P369S/0	P369S/ R408Q	

V726A/0	V726A/E167D/F479L

Conclusion: Although sequencing by PCR & hybridization is the standard technique in clinical practice, NGS can be judiciously applied in selected cases. Since PCR sequencing analyzes a rather limited number of genomic regions, uncommon mutations might be missed, as in 19.2% of our studied pts. NGS screens though the whole MEFV exome. Thus, it clarifies genetic profile in pts with atypical phenotypes and supports management decisions, regarding the treatment.

Funding

Roche Hellas, Novartis Hellas and Friends' Association of Children with Chronic Rheumatic Diseases supported the reagents supply.

Disclosure of Interest: None declared

P031

FOSTERING PATIENT REGISTRIES AS PLATFORMS FOR FUTURE EPIDEMIOLOGICAL, CLINICAL AND TRANSLATIONAL RESEARCH

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Introduction: Autoinflammatory diseases (AID) are characterized by recurrent, self-limiting, systemic inflammatory reactions and are associated with a dysregulation of the innate immune system. AID are characterized by their symptoms (fever, serositis, joint, abdominal and skin involvement, etc.) raised inflammatory markers and, in hereditary diseases, by a positive mutation analysis. Since the discovery of the various auto-inflammatory diseases, a number of national and international patient registries have been set up: for instance EUROFEVER started in 2008 on an European basis, AIDnet took place in 2009 in Germany and the JIRcohort was founded in 2013.
Objectives: To develop a collaborative research project on different existing patient registries within the PReS working party on AID.
Methods: A kick-off meeting was held on 9th June 2020 with the main persons in charge of the 3 databases collaborating in this project (EUROFEVER, AIDnet and JIRcohort). Common research questions will be defined by the project managers and analyzed separately in every registry. Results of the research questions will then be shared between the different project partners and comparative analyses will be carried out centrally. Results including the patients of all 3 databases will be presented jointly.
Results: The EUROFEVER database, the AIDnet registry and the JIRcohort represent a unique collection of information on patients with HPFs with only a minimal overlap of individual patients. Conducting joint epidemiological or clinical studies on patients from different databases remains a real challenge, mainly for reasons of IT interoperability and regulatory issues. Yet success in conducting such studies will also be a real advance in our knowledge of these diseases. Several initiatives to harmonize the different databases and develop common strategies for such studies have been launched. An example of this type of initiative is the MERITA project led by the European Rare Disease Network RITA which main objectives are to promote the interoperability of the different ERN registers and to develop a new registry for sharing essential clinical data provided by different European registries. In parallel of this initiative, we propose here an additional research strategy that will be complementary to the MERITA initiative and that could also be applied to registries that are not harmonized a priori.
Conclusion: If the experience shows to be feasible in these 3 different registries managed by 3 different teams, the methodology could be extended to other existing cohorts or registries and open the way for collaborative registry studies regardless of IT operability. Furthermore some common data elements identified during this study protocol could be shared prospectively in the MERITA project and thus participate to a wider European initiative.
Disclosure of Interest: None declared

P032

MRI AS A DIAGNOSTIC TOOL IN PROTRACTED FEBRILE MYALGIA

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Introduction: Protracted febrile myalgia syndrome (PFMS) is a rare complication of familial Mediterranean fever (FMF). The diagnosis is based on clinical symptoms and is often challenging especially when PFMS is the first ever manifestation of FMF.
Objectives: The aim of this report was to present the magnetic resonance imaging (MRI) findings in pediatric patients with PFMS.
Methods: Four children with PFMS attending 3 different medical centers are described. Clinical data were collected from the medical files, and all MRI scans were revised by an experienced radiologist. All patients were genetically tested by Sanger sequencing for the 9 most common MEFV mutations.
Results: There were three girls and one boy aged 6 months to 12 years. All had Mediterranean ancestry. PFMS was the first manifestation of FMF in all patients. One patient had familial history of FMF and two patients had clinical background supporting the diagnosis. Two of the patients had more than one episode of PFMS. All patients had extreme asymmetric myalgia, 3 of them had high-grade fever, and all had elevated inflammatory markers. A long comprehensive work-up was performed during hospitalization, including multiple CT and CT-angiography scans, bone marrow aspirations, and skin and muscle biopsies. MRI of the extremities as part of the workup yielded findings suggesting myositis with normal CPK levels. After diagnosis, all patients were referred for Sanger sequencing for the 9 most common MEFV mutations (M694V, M694I, M680I, K695R, R761H, A744S, P369S, V726A, E148Q). One was homozygous for M694V mutation, two were heterozygous for M694V mutation, and one was hemizygous for the M694V and V726A mutations.
Conclusion: MRI is a noninvasive no radiation method that may serve as an auxiliary diagnostic tool in the challenging diagnosis of PFMS.
Disclosure of Interest: None declared

P033

TRISOMY 8 – A GENETIC MIMIC OF EARLY-ONSET BEHÇET-LIKE DISEASE?

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Introduction: Behçet disease (BD) is a systemic vasculitis presenting with bipolar ulcers, uveitis, skin lesions and organ inflammation. Etiology is considered multifactorial with participation of genetic susceptibility and environmental triggers. More recently, monogenic mimics of early-onset BD have been reported.
Objectives: To present a case of early-onset Behçet-like disease associated with trisomy 8 in order to further expand the spectrum of genetic mimics of early-onset BD.
Methods: Retrospective chart review from initial presentation to last follow-up. Informed parental consent was obtained for genetic analysis and for publication.
Results: The patient, a 15-year-old Caucasian adolescent, developed recurrent fevers at age 6 months. Subsequently, oral and genital ulcers, cutaneous manifestations (severe acneiform lesions, folliculitis) and asymptomatic anterior uveitis occurred. At age 7, progressive peripheral neuropathy of the right foot was noted, evolution was eventually favorable after two surgical interventions and intensive physiotherapy. She had important biologic inflammation during disease flares, but normal inflammatory markers in between flares. Trisomy 8 mosaicism was suspected on next-generation sequencing and confirmed by FISH. Treatment with colchicine, prednisone, methotrexate and golimumab was partially efficient, symptoms finally improved on azathioprine and adalimumab.
Discussion. Behçet-like disease has previously been reported in adults with myelodysplastic syndromes and acquired somatic trisomy 8. More recently, a BD-like disease has been described in a few patients with constitutional trisomy 8 with and without mosaicism (1). Characteristic symptoms included early-onset recurrent fever episodes, mucocutaneous ulcers and bleeding diatheses. These patients were found to have increased monocyte activation and upregulated IL-1, TLR- and NFkB-related genes; they responded to TNFα or IL-1 blockade. We reported lately a 17-year-old Caucasian woman with developmental delay and multiple malformations resulting from a *de novo* complex partial 8p23.1 trisomy associated with a monosomy 7p (2). She had recurrent episodes of fever since infancy, and subsequently developed bipolar aphthosis, abdominal pain, polyarthritis and non-thrombocytopenic purpura. Topical and systemic corticosteroids as well as colchicine were partially efficient; eventually anakinra was started with excellent response and complete resolution of inflammatory symptoms.
Conclusion: Trisomy 8 with or without mosaicism may mimic early-onset BD. Recognition of genetic mimics of BD may help to understand the underlying pathology and guide treatment.
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Disclosure of Interest: None declared

P034

COVID-19 INFECTION IN PEDIATRIC AND ADULT PATIENTS WITH AUTOINFLAMMATORY DISEASES AND IMMUNOSUPPRESSIVE THERAPY: A CASE SERIES

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Introduction: Poor outcome in coronavirus (COVID-19) infection correlates with clinical and laboratory features of cytokine storm syndrome (CSS) [1]. The macrophage activation syndrome (MAS) is a special form of CSS [1]. Cytokine targeting therapies particularly started early in disease course may achieve cytokine neutralization. Increased IL-1β release has been reported in COVID-19 patients [2]. Several ongoing clinical trials investigate the role of anti-IL-1, anti-IL-6 and anti-INFɣ therapies in COVID-19. Risk factors for poor outcome in COVID-19 are old age, male sex and comorbidities, whereas pediatric patients with immunosuppressive therapy seem not to be at increased risk for severe disease course [3]. So far, there is scarce data on COVID-19 in patients with autoinflammatory diseases (AID).
Objectives: To assess disease course of COVID-19 in AID patients treated with immunosuppressive therapy.
Methods: Case series. Patient 1 is a 34 year-old women with rheumatoid arthritis and unclassified AID treated with methotrexate (MTX) 20 mg/weekly. She developed rhinitis, fever, headache, fatigue, cough and was tested positive for *SARS-CoV-2* eleven days after symptom onset. On day 10 she reported loss of taste and an episode of gastrointestinal symptoms. On day 14 she developed respiratory insufficiency with need for oxygen. On day 21 computed tomography showed typical signs of COVID-19 pneumonia. On day 40 she still suffered from dyspnea, fatigue, loss of taste and muscle pain. **Patient 2** is a 14 year-old girl with Cyropyrin-Associated Periodic Syndrome (CAPS; variant *Q703K*) on anti-IL-1 maintenance therapy since 5 years (Canakinumab 150 mg/month). Last administration was 25 days before diseases onset. **Patient 3** is a 13 year-old boy with CAPS (variant *Q703K*) treated like patient 2. Patients 2 and 3 developed fever, cough, fatigue and rhinitis 10 days after patient 1. Loss of taste was reported from day 4 to 13. On day 6 both had gastrointestinal complaints. After 14 days they recovered and anti-IL-1 maintenance therapy was administered. On day 28 a painful rash appeared on both arms of patient 3. As all patients live in the same household, patients 2 and 3 were not tested but clinically diagnosed for COVID-19.
Results: Patient 2 and 3 displayed typical COVID-19 disease symptoms but had a mild disease course without complications while on anti-IL-1 maintenance therapy, which was held back in the acute episode, and restarted after recovery. Patient 1 experienced a disease course more severe and ≥ 2 times longer than patients 2 and 3. Maintenance MTX treatment was paused since onset of COVID-19 symptoms.
Conclusion: As excessive IL-1 seems to be involved in COVID-19 immunopathology, IL-1 inhibition may prevent a severe disease course in COVID-19 infected AID patients. Both juvenile CAPS patients on anti-IL-1 maintenance therapy showed a milder disease course compared to the adult patient on MTX. This might be due to their younger age but also due to type of immunosuppressive therapy. This is one of the first reports about patients with AID on anti-IL-1 maintenance therapy with COVID-19. Data collection and merge of reports about these rare cases is needed to compile reliable insights on the effects of immunosuppression for AID on COVID-19 disease course.

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Disclosure of Interest: T. Welzel: None declared, S. Samba: None declared, J. Kuemmerle-Deschner Consultant for: Novartis, SOBI

P035

A MULTI-CENTRE SERVICE EVALUATION OF ACCESS TO CARE FOR CHILDREN DIAGNOSED WITH CHRONIC RECURRENT MULTIFOCAL OSTEOMYELITIS IN THE UK

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Introduction: Chronic Recurrent Multifocal Osteomyelitis (CRMO) is an autoinflammatory bone condition causing bone pain, swelling and disruption to musculoskeletal function in children(1). Although CRMO is uncommon, significant disease burden has been described from patient and family perspectives, one such example being delay to diagnosis (2).

Objectives: To describe the clinical pathways leading to CRMO diagnosis within three tertiary paediatric rheumatology centres, thereby identifying and addressing delays to diagnosis.

Methods: A retrospective review of medical records was undertaken for patients presenting over a 5 year period who ultimately received a diagnosis of CRMO. A standardised spreadsheet was used to capture demographics, clinical presentation, investigations and management, and referral pathway details.

Results: A total of 45 patients were included for whom details of symptom course, referral and diagnosis were known (68.9% female, 95.3% Caucasian ethnicity, median age at symptom onset 10 years 3 months). The median time from symptom onset to diagnosis was 7 months; most (median 5 months) was within secondary care between first appointment and diagnosis. Patients saw a median of 2 specialties (range 1-5). 14 children (32.5%, n=43) waited > 12 months to receive a diagnosis; median time 17 months (IQR 15-22). In patients presenting with pain exclusively in the lower limbs (n=15) the median time from symptom onset to diagnosis was 11 months compared with 5 months for patients presenting with clavicle pain (n=9). Median time from symptom onset to first rheumatology consultation in the whole group was 6 months (IQR 2-14, n=42). Table 1 shows the times from symptom onset to diagnosis according to specialties patients were first referred to and ultimately diagnosed by.

Table 1 - Timings of symptom onset to diagnosis pathways for children diagnosed with CRMO, subdivided by specialty

		By specialty first referred to				By specialty making diagnosis		
	Specialty first referred to, n=42 (%)	Median time (months) from onset of symptoms to first secondary care appointment, n=35	Median time (months) from first secondary care appointment to diagnosis, n=33	Median total time (months) from symptom onset to diagnosis n=39	Specialty making diagnosis, n=45 (%)	Median time (months) from onset of symptoms to first secondary care appointment, n=38	Median time (months) from first secondary care appointment to diagnosis, n=35	Median total time (months) from symptom onset to diagnosis, n=43
Rheumatology	5 (11.9)	2 (n=5)	10 (n=5)	14 (n=5)	30 (66.7)	1 (n=27)	5 (n=25)	6 (n=29)
Orthopaedics	25 (59.5)	2 (n=19)	5 (n=19)	9 (n=23)	10 (22.2)	6 (n=7)	3 (n=6)	11 (n=9)
Other	12* (28.6)	1 (n=11)	3 (n=9)	5 (n=11)	5† (11.1)	1 (n=4)	5 (n=4)	5 (n=5)

* General paediatrics (9), Oncology (2) Maxillofacial surgery (1)
† Oncology (2), Infectious diseases (2), Infectious diseases/rheumatology joint service (1)

Conclusion: Pattern of bone involvement which is more specific to CRMO (i.e. clavicular) appeared to be associated with quicker diagnosis. Identifying and addressing potential delays to diagnosis could help to reduce investigations and worry for patients and begin treatments sooner.

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Disclosure of Interest: None declared

P036

CLINICAL FEATURES, GENOTYPE AND TREATMENT IN CHILDREN WITH DEFICIENCY OF ADENOSINE DEAMINASE 2 IN COHORT OF ONE RUSSIAN CENTER

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Introduction: Deficiency of adenosine deaminase 2 (DADA2) require studying in different populations because of this polyarteritis nodosa (PAN)-like disease disables patients and leads to the dramatic presentations like stroke, bowel perforation and fatal outcome.

Objectives: To describe patients with manifestations of PAN and mutations in Cat Eye Syndrome Chromosome Region 1 (CECR1) gene from National Medical Research Center for Children's Health (Russian Federation).

Methods: The retrospectively analysis of the clinical course and treatment of 7 children with CECR1 mutations and PAN features. Next generation sequencing (NGS) used to screen CECR1 gene, Sanger sequencing used to verify NGS data.

Results: Two girls died. Onset of disease at ages 2.8 and 3.1, duration of disease 4,5 and 2.7 years, respectively. Both had the recurrent febrile fever, livedo racemosa, high acute markers in the blood serum, strokes, intestinal ulcers with perforations. Glucocorticoids, mycophenolate mofetil, cyclophosphamide, intravenous immunoglobulin, rituximab, tocilizumab were used in both cases with partial effect. In terminal stages infliximab was used in one case, adalimumab – in other case. There were homozygosis mutations in CECR1: c.1309G>A, p.Val437Met and c.139G>C, Gly47Arg, respectively.

In two siblings one girl had onset of disease at 6 months old by macrophage activation syndrome, isolated. She received tocilizumab with good effect during 1.5 years. Then she developed livedo racemose and ischemic stroke with hemorrhagic impregnation. The glucocorticoids, mycophenolate mofetil and etanercept were admitted. After that the sister of girl had onset of disease at 4,4 years old (y.o.) by livedo racemose and high C-reactive protein (CRP) in blood serum. She started treatment with glucocorticoids and etanercept. Girls have the same heterozygosis mutations in CECR1: c.1078A>G, p.Thr360Ala. After initiation etanercept girls had not clinical features of DADA2 10 months and 1 year, respectively.

In other two siblings one boy had onset of disease at 6.1 y.o. by recurrent febrile fever, livedo, colitis, ulnar nerve mononeuropathy, elevation of acute phase reactants. We followed the patient until 18 y.o., during this time he received glucocorticoids, mycophenolate mofetil, cyclophosphamide, plasmapheresis, rituximab, azathioprine with good effects. The brother of boy developed DADA2 in 7,2 y.o.. He had livedo, fever and high level of CRP. He started therapy with glucocorticoids and azathioprine with good effects, after genetic confirmation DADA2 the etanercept was initiated to prevent stroke. Boys have the same homozygosis mutations in CECR1: c.1358A>G, p.(Tyr453Cys).

7.3 years old girl developed disease by livedo, fever, arthralgia and elevation of CRP and erythrocyte sedimentation rate. She started glucocorticoids and mycophenolate mofetil with partial effect. There were detected two heterozygosis mutations in CECR1: c.1358A>G, p.(Tyr453Cys) and c.140G>C, Gly47Ala and she started etanercept. She haven`t had disease features during 4 months.

Conclusion: All patients with suspicion for PAN require the identification of CECR1 mutations to prevent serious outcomes. It is unpredictable what course of DADA2 will be developed in patients with the same mutations, like in siblings. Further identification of mutations in different populations with PAN will help in understanding disease management.

Disclosure of Interest: A. Mamutova Speaker Bureau of: Novartis, E. Alexeeva Speaker Bureau of: Novartis, Pfizer, Sanofi, MSD and Roche, T. Dvoryakovskaya Speaker Bureau of: Novartis, Pfizer, MSD and Roche, R. Denisova Speaker Bureau of: Novartis, MSD and Roche, K. Isayeva: None declared, A. Chomahidze: None declared, A. Fetisova: None declared, O. Lomakina: None declared, K. Chibisova: None declared, M. Gautier: None declared, D. Vankova: None declared, I. Kriulin: None declared, E. Krekhova: None declared, M. Shingarova: None declared, A. Pushkov: None declared, K. Savostyanov: None declared

P037

NUMBER OF EPISODES CAN BE USED TO MONITOR DISEASE ACTIVITY IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER

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Introduction: Monitoring disease activity in FMF is essential to define disease effects on the general health and quality of life (QoL) of patients, to determine treatment response, optimize disease follow-up and prevent complications. The importance of monitoring disease activity and doing regularly are highlighted in the international recommendations for the management of autoinflammatory diseases. It is necessary to assess disease activity easily in research and clinical practice.
Objectives: The aim of this study is to compare Pediatric Quality Life Inventory (PedsQL), Childhood Health Assessment Questionnaire (CHAQ), the four-item Morisky Medication Adherence Scale (MMAS-4), Wong-Baker FACES pain rating scale (FACES), Children's Depression Inventory (CDI) among the patients with FMF grouped according to the number of episodes in a year to define if it is the key element to detect the disease activity in FMF.
Methods: In this cross-sectional study, patients were recruited from the pediatric rheumatology outpatient clinics of tertiary hospitals in Turkey. Patients with FMF were evaluated face to face interviews to complete outcome measures such a PedsQL, CHAQ, MMAS-4, FACES, and CDI. We also recorded demographic data, main clinical symptoms of the episodes, treatment modalities, genetic mutations, possible triggers of episodes.
Results: A total of 239 patients (male 44.4%, female 55.6%) were grouped according to the number of episodes in a year: first group consist of 74 patients (31%) without any attacks in a year (Group 1), 99 patients (41.4%) have 1-4 episodes in a year (Group 2), 66 patients (27.6%) have more than 4 episodes in a year (Group 3). Age at diagnosis, gender, consanguinity, family history and history of amyloidosis were not different among the groups ($p>0.05$). The main clinical symptoms were similar among the groups ($p>0.05$). The comparison of fatigue, stress, sadness among the groups were significantly different, respectively $p=0.008$, $p=0.002$, $p=0.002$. All of these symptoms were more common in the last group than others. Most of the patients (232 of 239 patients, 97.1%) were treated with colchicine. Groups were similar in terms of M694V, and V726A allele frequency ($p=0.843$, $p=0.46$).
For parent and child PedsQL scale scores, patients in no episode group (Group 1) had higher scores that means better HRQoL than Group 2, and Group 2 had higher scores (better HRQoL) than Group 3. CHAQ scores of patients in Group 1 were significantly lower than Group 2 ($p=0.006$). Patients in Group 2 had lower CHAQ scores than patients in Group 3 ($p=0.004$). Both parent and child MMAS scores were not different among the groups. In Group 3, patients have higher parent CDI scores than no episode (Group 1) group ($p<0.001$). Child CDI scores were significantly lower in Group 1 than Group 2 ($p=0.01$), and in Group 2 than Group 3 ($p=0.03$). Both parent and child FACES scores were significantly lower in no episode group than Group 2, and patients in Group 2 lower than Group 3.
Conclusion: In a homogeneous patient population in terms of demographic features, mutation types, clinical symptoms, and treatment, PedsQL, CHAQ, CDI, and FACES have significantly different among the groups according to number of episodes in a year. We speculate that number of episodes is the key element of disease activity in patients with FMF and can be used to assess disease activity by alone
Disclosure of Interest: None declared

P038

KAWASAKI DISEASE AND AUTO INFLAMMATION, A RETROSPECTIVE STUDY ON 80 CHILDREN IN MONTPELLIER UNIVERSITY HOSPITAL CENTER

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Introduction: The physiopathology of Kawasaki disease (KD) remains unknown even if Pediatric Multi System Inflammatory Syndrom (PMIS) consecutive to COVID 19 infection have been largely studied. Autoinflammatory pathway have been evoked as a major component of KD, unexpectedly clinical studies about overlap between KD and autoinflammatory diseases are rare.
Objectives: The aim of this study is to evaluate the occurence of an autoinflammatory disease among KD patients.
Methods: This is a monocentric retrospective study that include all chidren under 15 years old diagnosed as KD in the Montpellier University Hospital Center between may 2012 and may 2019. Clinical and biological data were collected (sex, age, type of Kawasaki disease, inflammatory biomarkers, hepatic cytolysis) as well as the results of echocardiographies and treatments received. Follow up consultations have been analyzed to assess the onset of relapsing fever.

Results: 80 patients were included between 2012 et 2019. There was 57 boys and 23 girls.The average age was 30.2 months. Fifty percent of the patients had an anormal echocardiography. Height patients presented relapsing fever. Among these 8 patients, 3 patients met the criteria of PFAPA syndrome (Periodic Fever Adenitis, Pharyngitis Aphtous), which is more than expected in the general population ($p<0.05$).
Conclusion: This study shows a significant increase of PFAPA syndrome frequency in children that have presented KD. A genetic popensity to auto inflammatory syndroms and altered immune response can be discussed. This association suggests an auto inflammatory origin to the KD.
Disclosure of Interest: None declared

P039

THE UTILITY OF A NEXT GENERATION SEQUENCING PANEL IN DIAGNOSING SYSTEMIC AUTOINFLAMMATORY DISEASES IN INDIA - A SINGLE CENTRE EXPERIENCE

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Introduction: Systemic Autoinflammatory Diseases (SAIDs) are a diverse group of genetic diseases caused by dysregulation in the innate immunity and often presenting with overlapping phenotypes. Advances in genetic testing over the past 20 years have led to the discovery of more than 50 monogenic AIDs but they remain largely under-recognised, undiagnosed and consequently underreported in India largely due to poor awareness in doctors and reliance on foreign collaboration for costly genetic testing.
Objectives: 1. To make available a genetic testing facility for SAID in India and to test a shortlisted high-risk population of patients with the above panel.
2. To study the yield of this panel and to identify novel mutations, if any, in our population.
Methods: We suspected 38 children from our clinic to have SAID based on multisystem inflammatory disease (fever, rashes, arthritis, mucocutaneous manifestations, serositis and organ specific symptoms) occurring recurrently or with prototypic features, onset early in life, consanguinity or a positive family history and elevated acute phase reactants during episodes. A 53 gene panel was curated and a local laboratory performed next generation sequencing (NGS) under our instruction. In addition to multilingual consent for genetic testing and research / publication, ethics clearance for data collection and publication was obtained. Patient contributions were supplemented by funds from donors for testing.
Results: 11 of 38 patients (28.9%) received a closure in their diagnosis. Thus, in addition to the 27 patients who were previously diagnosed (largely by personal request to international centres), the total count of patients molecularly confirmed to have monogenic SAID in our centre rose to 38 (*Table 1*).
Table 1: Number of patients with SAIDs in our clinic and total number reported in India

SAID	**Using NGS Panel To date (38 patients tested)**	**Diagnosed outside of this initiative**	**Total in our centre today / total reported in India survey (until Aug. 2019)**
Blau Syndrome	2	3	5 / 26
CINCA/NOMID	-	3	3 / 15
Majeed Syndrome	3*	2	5 / 3
DADA2	1	6	7 / 13
MVK/HIDS	2	0	2 / 17
DIRA	1	0	1 / 2
LACC-1	2	0	2 / 0
Others	0	13**	13 / 32***
Total	11 / 38 (28.91%)	27	38 / 108

*Novel mutations identified

**13 from our center include SPENCD (2), Hereditary C1Q deficiency (7), H syndrome (4)
*** 32 from other centres in India include TRAPS (10), DITRA (1), HA20 (2), APLAID (5), AGS (4), FMF (2), FCAS (1), MWS (3), NLRP12 (1), IBD (3)

Conclusion: Our centre reports the first experience in India, to use a gene panel and test locally in a shortlisted group to arrive at a diagnosis in SAID. This study will hopefully provide impetus to other Indian studies, thereby identifying the commoner SAIDs in India, resulting in the use of abbreviated and cheaper panels. With consanguinity and endogamy prevalent in our country (reaching as high as 38% in some states), and a population of 1.2 billion, in a backdrop of colonisation by various European nations where these diseases are regularly recognised, this study opens our eyes to the tip of this looming iceberg.
Disclosure of Interest: None declared

P040

CHARACTERIZATION OF A GROUP OF PATIENTS WITH MEVALONATE KINASE DEFICIENCY

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Introduction: Mevalonate kinase deficiency (MKD) is a very rare, autosomal recessive autoinflammatory disease with multiple organ involvement. MKD is caused by mutations in the gene encoding mevalonate kinase (MVK) that lead to its reduced or deficient activity. However, not all patients have typical symptoms at the time of onset. MKD treatment remains an unsolved problem, since none of the modalities previously used for MKD treatment are fully effective in the disease control.
Objectives: To analyze clinical features, laboratory, molecular genetic data and response to therapy of a group of patients with MKD.
Methods: We characterize 26 patients (15 males, 11 females, median age 4.9 years (range 0.2–17 years), including four familial cases, with MKD diagnosis confirmed by detection of the *MVK* gene biallelic mutations via Sanger sequencing or targeted NGS panels. Mevalonic acid in urine was determined by gas chromatography-mass spectrometry in 14 patients.
Results: Median age at disease onset was 1.5 months (range birth–30 months). Clinical characteristics were very diverse: all patients had periodic fever, 25/26 - peripheral lymphadenopathy, 23/26 - abdominal pain, 20/26 – nausea/vomiting, 19/26 – diarrhea, 9/26 – hepatomegaly, 11/26 – splenomegaly, 6/26 – hepatosplenomegaly, 10/26 - respiratory failure. Rash was seen in 12/26 patients and one patient had periorbital edema and hyperemia during attacks. Myalgia, arthralgia were observed in 14/26. Oral ulcers were noted in 15/26 children. 8/26 patients had neurological involvement including two patients who suffered from epilepsy, one - from ataxia and cerebellar cortical atrophy and one from paraparesis with myopathic syndrome. All patients had increased laboratory inflammatory markers (C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR). Also most patients had a variety of hematologic abnormalities: neutropenia was present in 2/26 patients, thrombocytopenia – in 4/26, macrophage activation syndrome –in 1/26. In 3/14 patients tested increased level of mevalonic acid, and in 5/14 - of mevalonate lactone in urine were noted. In our cohort the p.Val377Ile mutation was the most common *MVK* gene mutation. However, we have identified 10 novel *MVK* mutations and four of them occurred twice in our cohort. 23/26 patients are currentlyy receiving anti-IL-1 therapy, with complete remission in 17/23 and partial in 3/23.
Conclusion: MKD symptoms can be variable and sometimes atypical, which requires physician’s awareness. In our cohort of MKD patients anti IL-1 therapy was highly effective.
Disclosure of Interest: None declared

P041

A RARE RHEUMATOLOGICAL CAUSE OF DEATH SECONDARY TO AORTIC CALCIFICATION: A CASE REPORT OF SINGLETON-MERTEN SYNDROME

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Introduction: Singleton-Merten syndrome (SMS) is a Type 1 Interferonopathy characterised by skeletal, dental and cardiac abnormalities classically caused by a gain-of-function mutation in the interferon-induced helicase C domain-containing protein 1 (IFIH1) gene.
Objectives: We describe a case of SMS leading to death at 13 years secondary to rapidly progressive aortic calcification.
Methods: Case report
Results: A white-British girl of non-consanguineous parentage presented at 5 years of age with calcaneovalgus and hallux valgus deformities, proximal muscle weakness and stiffness of the joints without synovitis or swelling. A heliotrope rash was present with prominent nail fold capillaries and ichthyoses vulgaris but no Gottron's. Dentition was abnormal with dentine hypoplasia, unformed roots of permanent teeth and crowns of abnormal morphology. Routine echocardiogram showed asymptomatic pericarditis and screening of her eyes revealed severe glaucoma causing unilateral amblyopia. Autoantibodies were abnormal with positive anti-nuclear (hep2, Elisa 4.4), anti-double stranded DNA (88iu/ML), rheumatoid factor (97 IU/l) and anti-cardiolipin IgG (73 U/ml) antibodies.
A tentative diagnosis of a connective tissue disease overlap with juvenile Systemic Lupus Erythematosus was given with glaucoma likely secondary to previous untreated uveitis. Treatment was commenced with prednisolone, methotrexate, hydroxychloroquine and low-dose aspirin. She responded well and surgery for glaucoma was also successful. Two years on, she developed anterior uveitis and worsening skin rashes with livedo reticularis, chilblains and vasculitic lesions. She was commenced on infliximab and remained clinically well for the following three years with CRP, ESR, autoantibodies and complement factors repeatedly within normal limits.
Aged 11 years, a diagnosis of SMS was confirmed via Deciphering Developmental Disorders with trio whole exome sequencing identifying a de novo mutation of the IFIH1 gene (c.2465 G>A). Around this time, she was noted to have an ejection systolic murmur. Echocardiogram and cardiac magnetic resonance imaging confirmed aortic stenosis with mild-moderate left ventricular outflow tract narrowing.
Over the following two years, she continued on infliximab with no evidence of an ongoing inflammatory process. Regular echocardiograms were stable and she remained asymptomatic. However, during a six-month interval, the aortic stenosis worsened significantly. Imaging showed unexpected and severe calcification of the aortic annulus, aortic cusps and the aortic wall up to the level of the descending aorta. Our case was discussed at length but the extent and severity of calcification was not amenable to cardiac intervention and the decision was made for palliative care. It was agreed to continue her disease-modifying medications to avoid a flare of inflammation and for symptomatic control. Sadly, three months after the aortic calcification was first noted, our patient collapsed suddenly and died later that day.
Conclusion: SMS is a rare condition with fewer than twenty affected families reported. Twelve cases are reported to have succumbed to aortic calcification at variable ages from 6 to 60 years. Early treatment with aortic valve replacement has been reported. There is little known about the mechanism of arterial calcification in the context of SMS, and control of inflammation does not appear to influence progression.
We report this case to highlight consideration of SMS in a child with features of an inflammatory disorder, glaucoma, abnormal dentition, lower limb deformities and cardiac disease. Our case highlights that aortic calcification in SMS can progress unexpectedly rapidly and lead to early death, despite regular cardiac monitoring and good inflammatory control of disease.
Disclosure of Interest: None declared

P042

CORRELATION OF A WHOLE-BODY MRI DERIVED RADIOLOGICAL ACTIVITY INDEX WITH DISEASE ACTIVITY IN CHRONIC NONBACTERIAL OSTEOMYELITIS

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Introduction: Due to the lack of validated diagnostic criteria, chronic nonbacterial osteomyelitis (CNO) remains a diagnosis of exclusion. Whole-body MRI (WB-MRI) has become one of the mainstays in supporting the diagnosis of CNO.
Objectives: Based on the recently developed ChRonic nonbacterial Osteomyelitis MRI scoring tool (CROMRIS), in order to quantify the bone involvement at multiple sites in CNO patients, we developed a Radiological Activity Index (RAI-CROMRIS).
Methods: WB-MRI images were assessed using the CROMRIS. Parameters included in our RAI-CROMRIS were: bone marrow hyperintensity, signal extension, soft tissue/periosteal hyperintensity, bony expansion, vertebral collapse. These parameters were evaluated for each bone unit yielding a score from 0 to 7. A total score was obtained adding up the scores of all bone units. We analyzed 76 treatment-naïve patients with CNO collecting clinical and radiological findings at baseline. Clinical disease activity was evaluated using a physician's global assessment (PGA). Fourty-six of 76 patients were evaluated at 6 and 12 months after baseline.
Results: A significant correlation of the RAI-CROMRIS with the PGA (r_s=0.32; p=0.0055), in particular with presence of functional impairment and increased inflammatory markers was found at baseline. During the follow-up, the RAI-CROMRIS decreased significantly (p=0.0039) from a median of 17 (IQR 12-26) at baseline to a median of 12 (IQR 6-20) at 6 months and remained stable at a median of 11 (IQR 4-20; T12 vs baseline p=0.0030 and T12 vs T6 p=0.52) at 12 months. A significant correlation between the RAI-CROMRIS and the PGA was observed at baseline and during follow up with a moderate correlation at T0 (p=0.0044; r_s=0.41) and a weak correlation at T6 (p=0.025; r_s=0.33) and T12 (p=0.010; r_s=0.38). Patients who subsequently received bisphosphonates had higher baseline RAI-CROMRIS (median 20, IQR 13-42) compared to that of patients who received other treatments (median 12, IQR 8-18; p=0.0078). In patients who received bisphosphonates, a decrease of the RAI-CROMRIS was observed from a median of 20 at baseline (IQR 13-42) to a median of 15 at T6 (IQR 4-25) (p=0.0032).
Conclusion: The RAI-CROMRIS provides a measure of the overall radiological burden of disease in individual CNO patients. It is well correlated with clinical and laboratory measures of disease activity and it shows significant short-term changes following treatment with bisphosphonates. This tool can be used in clinical practice and clinical trials after validation.
Disclosure of Interest: None declared

P043

OBSERVATION AND TREATMENT EXPERIENCE IN CHILDREN WITH MULTISYSTEM INFLAMMATORY SYNDROME, ASSOCIATED WITH COVID-19 IN MOROZOV CHILDREN'S CITY CLINICAL HOSPITAL OF THE MOSCOW CITY HEALTHCARE DEPARTMENT

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Introduction: COVID – 19 infection in children is commonly evaluated as mild or asymptotic.

However, from the start of May 2020, there was published some reports from Europe and North America describing children and teenagers, with multisystemic inflammatory syndrome characterized as Kawasaki-like syndrome. These patients required ICU hospitalization.

Hypothesis about connection this syndrome with COVID-19 was based on mostly positive serology tests.

Objectives: Boys to girl's ratio was 2:1, median age = 5 (± 4,5). All patients met Kawasaki-like symptoms (fever more than 5 days, rash, scleritis, cheilitis, lymphadenopathy, edema of palms and feet), also 6/9 children had meningeal symptoms, 2/9 had acute renal injure. All patients had myocarditis.

Methods: We observed 9 children with: multisystem inflammatory syndrome diagnosis, which were stated in may 2020. Our evaluation covers clinical symptoms, general blood test, CRB, PCT, ferritin, Il-6, CT, ultrasound.

Results: According to laboratory tests most symptoms was similar to systemic inflammatory diseases. All patients had increase of CRP in 9 times or more than normal, PCT was positive in 7/9 cases, increased ferritin from 62,7 to 1175 µg/l. Hypoalbuminemia was common symptom in all cases (18-24.8 g/l). Leukocytosis in 5/9 children (55,5%), thrombocytopenia in 4/9 cases (64-108*10^9/l), anemia in 4/9 cases (44.4%). In 8/9 (88.8%) children detected increased troponin (36 pg/ml - 899 pg/ml).

5/9 patients were undergoing through lumbar puncture, 3 out of this 5 had aseptic meningitis.

COVID IgM – positive -1/9; COVID IgG – positive 9/9 children.

Results of diagnostic interventions: pericarditis – 5/9, 1/9 – coronary alterations (ectasia LCA and RCA), pleuritis – 7/9, ascites – 4/9.

Treatment – all patients received antibacterial therapy, IVIG, steroids – 4/9, 1 patient was on hemodialysis. 1/9 patient required pleural puncture.

Conclusion: Multisystemic inflammatory syndrome patients require complex treat with help of various specialists (rheumatologists, cardiologists, surgeon, neurologists, resuscitationist).

No described strategy of management of such patients is available. Our experience declares that it's rational to administrate antimicrobial treatment (ceftriaxone, vancomycin, linezolid, sulperazone, cefepime, amikacin, meropenem), IVIG with steroids.

Disclosure of Interest: None declared

P044

NOVEL MUTATION IN PSME4 INVOLVED IN PROTEASOME-ASSOCIATED-AUTOINFLAMMATORY-SYNDROME

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Introduction: Proteasome-associated-autoinflammatory-syndrome (PRAAS) is an extremely rare congenital interferonopathy with high morbidity and mortality. In this disease, autoinflammation is caused by dysfunction of the ubiquitin-proteasome-system. So far, PRAAS-causing mutations have been restricted to genes encoding components of the proteasomal core complex and assembly helpers. These mutations may be both monogenetic (homozygous or compound heterozygous) as well as digenic.

Objectives: The aim of this study is to identify further components of the ubiquitin-proteasome-system involved in autoinflammation.

Methods: Experiments were conducted using whole blood and primary fibroblasts from a clinical index patient, the patient's mother and unrelated disease and healthy controls.

Results: In this work, we could detect a significantly increased expression of interferon-stimulated-genes in a clinically confirmed PRAAS patient who was devoid of genomic alterations in any of the previously published PRAAS-associated genes. Remarkably, patient's fibroblasts recapitulate diseases hallmarks including perturbed protein homeostasis, as evidenced by reduced proteasome activity and concomitant accumulation of ubiquitin-protein conjugates. Trio exome sequencing allowed us to identify in this subject a paternally inherited variant affecting the proteasome activator PSME4- as well as two maternally inherited variants within the ubiquitin-E3-Ligase HECW2 and the amino acid sensor kinase EIF2AK4 (also referred to as GCN2). *In silico* predictions classify these variants as disease-causing.

Interestingly, cells carrying these heterozygous variants failed to express the corresponding unaffected alleles at protein level, suggesting a dominant negative mode of action. Finally, and similarly to other PRAAS patients, proteasome impairment in our subject was associated with an exhausted unfolded protein response in the IRE1α-, ATF6- and PERK-pathways.

Conclusion: Thus, we propose that mutations in genes encoding proteasome activators and/ protein ubiquitination can also cause multigenic PRAAS.

Disclosure of Interest: None declared

P045

REAL-LIFE EVALUATION OF RECOMMENDATIONS REGARDING RESISTANT FMF BY PERA RESEARCH GROUP-A DELPHI CONSENSUS SURVEY

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Introduction: Familial Mediterranean fever (FMF) is a serious condition with no clear diagnosis and management protocols.
Objectives: To review the current landscape of FMF diagnosis, quality measures for follow-up, decision making for management and settling a protocol for prolongation of biologic treatment intervals and take advantage of an expert panel consensus
Methods: A total of 14 pediatric rheumatologists (PR) across Turkey expertised in the management of FMF participated to the study. A detailed literature search was performed by a fellow and systematic review of the literature was executed. A shortlist of 15 key points were selected by 3 PRs. Key-points were converted to 78 statements with a 9-point Likert scale and a 3-round modified Delphi panel was assessed. A sum of 75% or above agreement was accepted as consensus.
Results: Consensus was reached on 46 statements. Panelists agreed that the screening periods of patients with FMF should not be longer than 6 months of duration, SAA test at each visit was accepted as mandatory in patients resistant to colchicine, had subclinical inflammation and had family history of amyloidosis. There was no consensus regarding to routine SAA, protein/creatinine in spot urine, sedimentation testing at each visit. 64 % of the panellists found scoring systems as applicable at each visit. There was unity among panellists regarding commencing colchicine at the time of diagnosis and starting the drug to the patients with subclinical inflammation, ordering genetic analysis when clinical findings support FMF, starting colchicine when pathogenic mutations plus nonspecific findings and family history of amyloidosis are present. Response to colchicine treatment was defined as decrease in duration and number of attacks and was accepted in consensus. Defining colchicine resistance as presence of 6 or more attacks/year or ≥3 attacks in 4-6 month period or elevation of 2 of the acute phase reactants in incomplete attacks were confirmed with consensus of the panellists. All participants confessed starting biological agents to resistant FMF patients and patients with amyloidosis. Presence of adverse reactions to colchicine was not accepted as a reason for initiating biologics in consensus. Except cost of the biologic agents; efficiency, ease of use, treatment adherence, accessibility and presence of adverse events were accepted in consensus as factors choosing biologic agents. Decrease in duration and number of attacks and ceasing of subclinical inflammation was accepted as response to biologics, but scoring systems applicable at each visit for evaluating response were not accepted in harmony. In patients whose attacks went in to remission with biologics, prolongation of the duration of application of biologics were considered and asked to the panellists, they collectively welcomed this statement. All participants voted in favour of curtailing the frequency of injections in patients who are in remission both clinically and in laboratory means during last six months of biologic treatment.
Conclusion: Even though recommendations are present for diagnosis, screening and treatment of patients with FMF, use of these issues in real life is not so clear. Herein, data concerning applicability and relevance of these points and prolongation of biologic intervals were evaluated with PRs who are dealing with large number of FMF patients
Disclosure of Interest: None declared

e-Poster viewing: Bone in rheumatic diseases

P046

OSTEOPOROSIS IN ENTHESITIS RELATED ARTHRITIS

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Introduction: Osteoporosis is seen in all subtypes of juvenile idiopathic arthritis (JIA). The loss of bone mass and microarchitectural abnormalities lead to an increased risk of fractures with associated morbidity.
Objectives: Our objective is to describe the bone involvement observed in our patient population of JIA in its Enthesitis-related arthritis form (ERA) and to determine the relative effects of the activity of the disease, corticosteroids and physical activity on the development of osteoporosis in JIA.
Methods: This is a retrospective monocentric study that collected patients with ERA according to ILAR criteria, in whom a bone densitometry was performed by dual-energy x-ray absorptiometry (DEXA, in order to determine their bone status. An assessment of the factors linked to the disease and to the environment which could influence the modification of the bone architecture was also carried out.
Results: We enrolled 22 patients (sex ratio M / F 10); average age of onset of the disease 13.1 years. The clinical presentation was purely axial in 4 patients, peripheral in 12 patients and enthesitic in 4 patients. The average BASDAI score was 55.3 / 100, the average MASES score was 2.7. Seven patients were on general corticosteroid therapy and only 9 of our patients participated in regular sports activities. The results of the bone densitometry measured concluded that normal bone mineral status was found in 13.3%, osteopenia was objectified in 20% of patients and osteoporosis in 36.7%.
An agreement was assessed between the absence of sports activity and osteoporosis ($p = 0.01$) as well as osteopenia ($p = 0.03$). A high BASDAI is strongly associated with osteoporosis ($p = 0.04$). No association was observed between BASDAI and osteopenia ($p = 0.3$). No correlation was observed between the MASES score and osteoporosis ($p = 1.2$). No link was observed between taking corticosteroid therapy and bone architecture abnormalities ($p = 0.8$).
Conclusion: Osteoporosis is frequent in ERA. Like the adult onset of spondylarthritis, low bone mass is influenced by disease activity and sedentarity.
Disclosure of Interest: None declared

P047

THE CYTOKINE PROFILE IN THE PATIENTS WITH CHRONIC NON-BACTERIAL OSTEOMYELITIS, JUVENILE IDIOPATHIC ARTHRITIS, INSULIN-DEPENDENT DIABETES MELITUS AND HEALTHY CONTROLS: THE DATA OF PROSPECTIVE COHORT STUDY

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Introduction: Chronic non-bacterial osteomyelitis (CNO) is an autoinflammatory disorder of bone, which primarily affects children and adolescents. Dysfunction of the immune system as well as cytokine dysbalance is a key point for CNO pathogenesis.

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well as cytokine dysbalance is a key point for CNO pathogenesisChronic non-bacterial osteomyelitis (CNO) is an autoinflammatory disorder ofbone, which primarily affects children and adolescents. Dysfunction of the immune system aswell as cytokine dysbalance is a key point for CNO pathogenesis.
Objectives: The aim of our study was to evaluate the cytokine levels in the pediatric CNO patients and compare to other immune-mediated diseases and healthy controls.

Methods: In the prospective study 42 children with CNO were included. For comparison plasma of non-systemic juvenile idiopathic arthritis (JIA) patients (n=28), insulin-dependent diabetes mellitus (IDDM) patients (n=17) and healthy controls (HC, n=30) with similar age were collected. In each CNO patients and comparison groups the levels of 14-3-3-η protein, S100A8/A9 protein, interleukine - 4 (IL - 4), interleukine - 17 (IL - 17), interleukine - 18 (IL - 18), interleukine - 1β (IL - 1β), tumor necrosis factor-α (TNF-α) were measured by ELISA assay. We used the chi-squared test or the Fisher's exact test, Kruskall-Wallis test, Spearman's correlation analysis and univariate and multivariate linear regression and discriminant analysis.
Results: All studied cytokines in the CNO patients were higher compare to controls and IDDM, 14—3-3 protein, IL-18, IL-4, IL-17, IL-1β and TNF-α were less than in JIA patients (table 1). In discriminant analysis ESR, 14-3-3 protein, S100A8/A9, IL-18, IL-4 and TNF-α can discriminate CNO from JIA and 14-3-3 protein, S100A8/A9, IL-18, IL-17, IL-4 and TNF-α can discriminate CNO from other diseases and HC. Table 1. Cytokine levels in immunocompromised patients and healty controls

Parameters	CNO (n=42)	JIA (n=28)	IDDM (n=17)	HC (n=30)	p	p1	p2	p3
14-3-3η, pg/ml	20.2 (18.4; 27.1)	53.1 (39.7; 60.7)	-	15.2 (10.2; 17.9)	0.00001	0.0000001	-	0.000006
Calprotectin, pg/ml	5.9 (5.2; 6.7)	3.6 (3.1; 15.0)	-	0.54 (0.3; 0.8)	0.00001	0.115	-	0.0000001
IL-6, pg/ml	126.3 (112.9; 137.5)	132.5 (117.4; 142.9)	16.3 (10.4; 20.0)	4.1 (2.1; 5.4)	0.00001	0.160	0.0000001	0.0000001
IL-18, pg/ml	270.1 (201.1; 316.1)	388.4 (373.9; 405.1)	49.7 (39.4; 70.9)	119.4 (115.6; 128.4)	0.00001	0.000003	0.0000001	0.0000001
IL-4, pg/ml	15.3 (11.5; 18.2)	18.7 (16.2; 20.2)	0.004 (0.0; 0.1)	0.0002 (0.0; 0.02)	0.00001	0.003	0.0000001	0.0000001
IL-17, pg/ml	83.2 (71.1; 97.3)	99.1 (87.4; 115.8)	1.5 (1.0; 2.4)	0.33 (0.2; 0.4)	0.00001	0.004	0.0000001	0.0000001
IL-1β, pg/ml	47.4 (42.0; 51.3)	70.8 (65.3; 73.7)	3.3 (2.5; 7.7)	0.95 (0.7; 1.3)	0.00001	0.0000001	0.0000001	0.0000001

TNF-α, pg/ml	19.4 (17.9; 21.3)	23.1 (20.2; 25.9)	2.1 (1.5; 5.1)	0.9 (0.6; 1.3)	0.00001	0.0008	0.0000001	0.0000001

Conclusion: our data indicate the role of cytokine imbalance in the pathogenesis of CNO. The increased level of pro-inflammatory cytokines confirms the role of monocyte-driven inflammation in CNO patients. More research is needed to validate the role of cytokines as biomarkers and potential therapeutic targets for CNO.

Trial registration identifying number: This work supported by the Russian Foundation for Basic Research (grant № 18-515-57001)
Disclosure of Interest: None declared

P048

OSTEOCALCIN: ASSESSING BONE MINERAL DENSITY IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: A principal manifestation of juvenile idiopathic arthritis (JIA) is the skeletal system alteration. One of the disease complications is a decrease in bone mineral density (BMD) with the possible osteoporosis (OP) formation. The latter can lead to a life quality deterioration and possible disability in adulthood. In rheumatic diseases, BMD impairment contributes to osteoblast function inhibition, especially in patients taking steroids. Therefore, an essential addition to dual-energy X-ray absorptiometry (DXA) in children with JIA is the assessment of biochemical markers of osteosynthesis, which include osteocalcin (OC).
Objectives: We aimed to establish the specificity and sensitivity of OC levels in relation to the DXA data of JIA patients to make an intermediate assessment of BMD without the use of X-ray absorptiometry.
Methods: The BMD data and serum OC levels were estimated in 134 JIA patients (88 girls, 46 boys) aged 5 to 17 years. 24 patients had the systemic form of the disease, 46 of them had oligoarticular form, and 64 had polyarticular form. The mean age was 11.5 ± 0.4 years, and the mean disease duration was 5.2 ± 0.4 years. 64 children (48%) took methotrexate, 70 (52%) took immunobiological drugs (tocilizumab (24), adalimumab (44) and etanercept (2)). Specificity and sensitivity were calculated according to generally accepted formulas.
Results: The reference values of serum OC were 2-22 ng/ml, which were significantly lower than the levels of JIA patients with whom we were dealing. Thus, it was decided to determine the median [5^{th}; 95^{th} procentile] for the OC levels of our JIA patients, in which DXA indices were within the normal range, and establish the sensitivity and specificity of this value. Sensitivity was measured according the formula: Sensitivity = TP / (TP + FN) × 100%, where TP is the number of true positive results in the patient group, FN is the number of false negative results. Specificity was calculated according the formula: Specificity = TN / (TN + FP) × 100%, where TN is the number of true negative results in the patient group, FP is the number of false positive results. The median OC value of JIA patients, in which BMD results were correlated to chronological age, was 26.9 [19.4; 36.9] ng/ml (83 children out of total 134 patients). There were 13 patients with the DXA Z-score ≤ -2 SD and 80 patients with the DXA Z-score > 2 SD among the 93 patients with OC values within the 5^{th} and 95^{th} procentile (19.4-36.9 ng/ml). Based on this, the sensitivity of these OC values was 86%. There were 36 children with negative DXA results and 5 children with positive DXA results (the OC level values exceeded the 95^{th} procentile in more than 3 of them) among 41 children, whose OC values were not in the 5^{th}-95^{th} procentile range (< 19.4 or > 36.9 ng/ml). The specificity of the calculated OC values was 87.8%.
Conclusion: Osteocalcin levels within the 19.4-36.9 ng/ml with a sensitivity of 86% and a specificity of 87.8% correspond to the chronological age-related bone mineral density assessed by the dual-energy X-ray absorptiometry. The obtained data can be useful for the intermediate assessment of BMD without the use of DXA in JIA patients.
Disclosure of Interest: None declared

e-Poster viewing: COVID-19 (Coronavirus)

P049

AN ETHICAL DILEMMA IN THE TIME OF SARS-COV2: A CASE REPORT OF DELAYED INVESTIGATION AND MANAGEMENT OF KIKUCHI SYNDROME WITH SECONDARY HAEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS (HLH)

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Introduction: Kikuchi syndrome, histiocytic necrotising lymphadenitis, is a rare and idiopathic disorder of the lymph node. Prompt investigation is required to rule out malignancy and to reduce complications including life-threatening secondary HLH[1].
Objectives: Case report of a 14 year old girl with Kikuchi syndrome and features of secondary HLH presenting during the 2020 SARS-CoV2 pandemic
Methods: A 14 year old girl presented with a 5 week history of cervical lymphadenopathy and febrile neutropenia. She had no features of systemic disease including arthritis, serositis and vasculitis. Initial blood tests revealed a pancytopenia. Bone marrow aspirate was negative for leukaemia and HLH but on-going blood monitoring showed an increasing inflammatory process. Infection screening including CMV, EBV, hepatitis, HIV and blood cultures were negative as was an auto-antibody screen. CT chest was unremarkable. MRI whole body showed significant right sided cervical lymphadenopathy. She was treated with tazocin, vancomycin and amphotericin but the inflammatory markers continued to rise.
An urgent lymph node biopsy was required for diagnosis, which led to concerns about her SARS-CoV2 status. She had a negative SARS-CoV2 PCR at her referring centre and a normal CT making the diagnosis of SARS-CoV2 unlikely. It was felt by the anaesthetic and surgical teams that repeat SARS-CoV2 testing was required and that it was unsafe to take her to theatre prior to the results being available. Her excisional biopsy was postponed pending results. During this time her ferritin increased to 16000. She developed an oxygen requirement and an ECHO showed a pericardial effusion. She met HLH HScore 196 and required urgent treatment with steroids. With the underlying pathology unknown this could have led to delayed treatment of a malignancy. She received intravenous immunoglobulin on 2 consecutive days. This afforded some improvement but she continued to have pyrexia, a spreading follicular rash and a ferritin of >10000. She was eventually taken to theatre for lymph node extraction on day 7 of admission and was successfully treated.
Results: The current pandemic has caused unprecedented disruption to healthcare provision worldwide.
Ethical dilemmas have included resource allocation with routine clinical care being postponed to accommodate high volumes of emergency work and the balance of providing care for patients while limiting risk to healthcare professionals. In this case emergency surgery was delayed to limit risk to medical staff which led to acute and potentially life threatening deterioration in this patient. One negative SARS-CoV2 swab and a normal CT chest had to be balanced against the perceived risk of SARS-CoV2 spread to multiple members of staff. This case puts the beneficence for the patient in direct conflict with the management of risk to professionals and makes us ask: how far does the ethical principle of non-maleficence apply to all those involved?
Conclusion: This case illustrates one of numerous patients whose inpatient management was delayed during the SARS-CoV2 pandemic; in addition to cancellations of elective surgeries, deferred preventative measures and outpatient appointments. This patient made a full recovery; she expressed understanding for the delay in management and gratitude to her medical team. The question still remains: was this a risk worth taking?
Disclosure of Interest: None declared

P050
MANAGEMENT STRATEGIES FOR CHILDREN WITH RHEUMATIC DISEASES DURING THE COVID-19 PANDEMIC

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Introduction: The SARS-CoV-2 infection (COVID-19), which causes severe acute respiratory syndrome, was accepted as a pandemic by the World Health Organization on March 11, 2020, resulting in 4.258.666 confirmed cases of COVID-19 (World Health Organization. Coronavirus disease 2019 Situation reports. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports, last access 14 May 2020).
Patients with rheumatic diseases are known to have increased infectious risks due to a general disorder of the immune system specific to the disease itself and it is also associated with the use of immunosuppressive drugs.
Since immunosuppression is WHO-defined risk factor for a more severe course of COVID-19, the patients with pre-existing rheumatic diseases who used immunosuppressive and biological therapies assume to have heightened vulnerability to develop COVID-19. The prevalence of COVID-19 in children with rheumatic diseases is lacking in literature. Moreover, we do not clearly know the effect of pre-existing rheumatic disease, immunosuppressive and biological therapies on COVID-19 course in children. Here, it is aimed to determine the frequency and course of COVID 19 of patients who use biological agents for childhood rheumatic diseases and to detect of risky patients who need to withdrawal of their treatment.
Objectives: To determines the frequency and course of COVID 19 of patients who use biological agents for childhood rheumatic diseases.
Methods: A telephone-based survey was administered in Turkey to 52 patients who received biological therapies for rheumatic diseases from the 11th of March to 13th of May 2020. The survey included demographics, clinical information of patients about rheumatic disease, the incidence of COVID-19, the presence of definite or possible COVID-19 in the household, the frequency of respiratory symptoms of suspected viral infections and the course of rheumatic disease.
Results: All patients were treated with biological therapies (26 etanercept, 17 canakinumab, 6 adalimumab, 2 rituximab, 1 infliximab), about 80% of patients were receiving conventional disease-modifying drugs. None of the patients using biological therapies had any possible or definitive COVID-19. Fifty have maintained stable disease activity without experiencing flare-ups.
Conclusion: Our preliminary outcomes are hopeful for potentially more susceptible patients to COVID-19. Children with rheumatic diseases receiving biological therapies should be monitored for the risk of COVID-19, but it is reasonable not to withdrawal of their treatment to avoid flare-ups of rheumatic diseases.
Disclosure of Interest: None declared

P051

MULTISYSTEM INFLAMMATORY SYNDROME WITH FEATURES OF ATYPICAL KAWASAKI DISEASE: A CASE REPORT FROM IRAN DURING THE COVID-19 PANDEMIC

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Introduction: Although Kawasaki disease (KD) is the most common self-limited systemic vasculitis in pediatrics, the exact etiology of the disease and its association with other diseases and pathogens is still unknown. In order to achieve a better understanding and management of the disease, documentation and reporting of atypical cases is justified, particularly with the growing number of children with inflammatory syndrome with clinical features simulating KD during the ongoing COVID-19 pandemic.
Objectives: Based on similar reports of KD from numerous countries with temporal relation to COVID-19 infection in the community, it is essential for general pediatricians to be on alert for such atypical presentations and early referral to tertiary care should be considered as appropriate.
Methods: Here we present a case of an atypical case of KD presenting as Multisystem Inflammatory Syndrome (MIS) during the COVID-19 pandemic.
Results: The patient is a 7-year-old girl who developed fever (39°C) and erythematous multiform rash on the abdomen and along with erythema and edema on the extremities. Laboratory evaluation revealed neutrophilia and lymphopenia along with elevated C-reactive protein, erythrocyte sedimentation rate, troponin, lactate dehydrogenase, ferritin, and D-dimer. Although the patient didn't fore fill the KD criteria, based on approved guidelines and approaches regarding atypical KD and Multisystem Inflammatory Syndrome in Children (MIS_ C) during the COVID-19 pandemic, intravenous immunoglobulin along with aspirin was administered for the patient. The patient's symptoms resolved with an uneventful post-discharge course.
Conclusion: Early diagnosis and treatment of patients meeting full or partial criteria for KD are critical to preventing end-organ damage and other long-term complications, such as myocarditis and coronary involvemt, especially during times of public crisis and global health emergencies, such as the novel coronavirus pandemic.
Disclosure of Interest: None declared

P052

THE IMPACT OF COVID-19 PANDEMIC ON PEDIATRIC RHEUMATOLOGY PATIENTS UNDER IMMUNOSUPPRESSIVE THERAPY: A SINGLE-CENTER EXPERIENCE

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Introduction: During severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) disease 2019 (COVID-19) pandemic, several drugs already with essential roles in rheumatology practice emerged as promising treatment alternatives with encouraging results. On the other hand, dysregulation of innate immunity and virus-host interactions in the etiopathogenesis serve a major concern for patients in an immunosuppressive state or under immunosuppressive treatment**.**

Objectives: This study set out to determine whether COVID-19 showing a milder course in children entails a risk for patients with rheumatic diseases in terms of immunosuppressive therapy either disease-modifying anti-rheumatic drugs (DMARDs) or biologic disease-modifying anti-rheumatic drugs (bDMARDs).

Methods: Telephone-survey was administered by conducting interviews with the parents and inviting them to participate. A message containing a link to the questionnaire was sent to their phones simultaneously. The medical records of the patients were reviewed for gathering information about demographic data and clinical follow-up.

Results: Patients who were followed up with immunosuppressive treatment (n=439) were attempted to be contacted between 1 May 2020 and 15 May 2020. The diagnostic distribution of patients who were accessible and eligible for the study was as follows: juvenile idiopathic arthritis (JIA) (n = 243, 58.7%), autoinflammatory diseases (n = 109, 26.3%), autoimmune connective tissue diseases (n = 51, 12.3%) and vasculitis (n = 11, 2.7%). In the entire cohort, mean age (at the study) was 12 ± 4.7 years and 54.1% (n=224) of the patients were female. We identified that one patient with seronegative polyarticular JIA, receiving methotrexate and leflunomide has been diagnosed with COVID-19. Table 1 details the survey results.

TABLE 1. Telephone Survey Results

Analyzing Survey Data	**Results, n(%)**
Symptoms	
Fever	20 (4.8)
Non-productive cough	8 (1.9)
Sputum production	-
Sore throat	9 (2.2)
Rhinorrhea	3 (0.7)
Fatigue	8 (1.9)
Arthralgia,	49 (11.8)
Myalgia	15 (3.6)
Anosmia/dysgeusia	3 (0.7)
Dyspnea	1 (0.2)
Headache	-
Nausea/vomiting	2 (0.5)
Diarrhea	8 (1.9)
Rash	4 (1)
Confirmed diagnosis in the family (household contact)	17 (4.1)
History of contact with confirmed or suspected cases	18 (4.3)
Attendance at a hospital emergency department for suspicion of COVID-19	9 (2.1)
History of contact (n)	6
Computed tomography for COVID-19	4 (0.9)
History of contact	3
Consistent with COVID-19	-

Pharyngeal swab test History of contact Positive for COVID-19	9 (2.1) 6 1
Treatment interruption during the outbreak Concern about an increased risk Trouble in medicine supply Inability to reach the healthcare provider or health institution	59 (14.3) 16 (27.1%) 14 (23.7%) 29 (49.2%)

Conclusion: In our cohort consisting of patients who received DMARDs and bDMARDs for various rheumatological diseases, we identified that one patient has been diagnosed with COVID-19. None of the patients, including the patient diagnosed with COVID-19, had any severe symptoms. More than half of the household contacts have not been required to attend a hospital because they were asymptomatic. Since similar complaints were encountered in the course of rheumatic diseases, the hospital attendance rate was low among patients who had complaints such as arthralgia, myalgia, and fever during the pandemic process and no history of contact. The findings of this study support the idea that COVID-19 rarely causes serious disease in children and the use of immunosuppressive therapy does not pose an additional risk in patients with rheumatic diseases.
Disclosure of Interest: None declared

P053

A META-ANALYSIS OF SEX BIAS IN COVID-19

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Introduction: A striking anecdotal feature of the Coronavirus disease 2019 (COVID-19) outbreak, caused by the novel severe acute respiratory syndrome coronavirus SARS-CoV-2 is the difference in morbidity and mortality between the sexes. In contrast to the female preponderance seen in many autoimmune diseases, there appears to be a male sex bias in COVID-19 deaths and intensive treatment unit (ITU) admissions.

Objectives: We present a meta-analysis of 206,128 globally reported cases, in order to determine whether males are statistically more susceptible to severe disease outcome from COVID-19 than females.

Methods: A search of government websites and published literature was performed for reports on COVID-19 cases that included sex as a variable in data describing case number, ITU admission or mortality. Covariates such as lifestyle and comorbidities could not be controlled for as data were available at the level of country summary, but not at the level of covariates for all individuals.

Meta-analysis was performed to estimate an overall proportion of male infected cases with 95% confidence intervals (CI) and to estimate odds ratios (ORs) with 95% CI associated with male sex for ITU admission and death, based on pooled average effect measures that were weighted according to the size and precision of each report. Fixed and random effects models were estimated and are reported. Meta-analyses were performed using R and the "meta" package.

Results: 42 reports were found from across the world, from 01.01.2020 - 30.03.2020. Reports were excluded if they did not report total infections by sex, if they were thought to overlap in reported cases or for containing less than five cases. This left a total of 29 reports from 27 different countries (two included for analysis of ITU admissions only and excluded from case and mortality analysis). For the analysis of case numbers by sex, the 27 reports described 206,128 infections. Five reports included ITU admission by sex, describing 43,075 cases with 1,758 ITU admissions. 12 reports included data on mortality by sex, describing 170,983 cases and 6,961 deaths.

The proportion of male cases with COVID-19 in these reports was only slightly over half at 0.52 (95% CI=0.52,0.53, p=2.3e-97 for fixed effects model; 95% CI=0.50,0.53, p=0.12 for random effects model) demonstrating that males and females have similar number of infections. Male sex associated with an increased risk of ITU admission (OR=2.50; 95% CI=2.25, 2.78; p=3.8e-64 and 7.3e-64 for fixed and random effects models, respectively). Male sex also associated with an increased risk of mortality (OR=1.62, 95% CI=1.54, 1.71, p=5.5e-77 for fixed effect model; OR=1.60, 95% CI=1.41, 1.82, p=7.4e-13 for random effects model). Funnel plots and sensitivity analyses indicated these results were unlikely to be influenced by reporting bias.

Conclusion: We report that although differences do not exist in the rates of infection between sexes, males are more likely to require ITU admission and more likely to die from COVID-19 than females. Important differences in the immune response to infection exist between sexes, which are likely to contribute to the male bias in infectious diseases and the female bias in autoimmunity. An appreciation of how sex is influencing COVID-19 outcomes will have important implications for clinical management and mitigation strategies for this disease and highlights the importance of sex as a variable in all biological research.

Disclosure of Interest: None declared

P054

KAWASAKI DISEASE DURING COVID-19 EPIDEMIC

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Introduction: At the peak of the pandemic, clinicians across Europe have identified clusters of Kawasaki-like disease. Italy was one of the most involved country by COVID-19, mainly in northern regions as Lombardia (37.8% of Italian cases). Verdoni *et al.* reported an outbreak of severe Kawasaki-like disease in Bergamo, a city of Lombardia.
Objectives: To compare incidence and features of patients affected by Kawasaki disease (KD) in the last two years in Naples.
Methods: Retrospective analysis of patients diagnosed by KD in two main pediatric centres in Naples during the first four-month period (January-April) of the years 2019 (group 1) and 2020 (group 2). Diagnosis of KD was defined according to the 2017 criteria of the American Heart Association, including both the classic and incomplete types.
Results: The number of cases is similar in the two groups: 12 patients in group 1 (10 males, 2 females) and 13 patients in group 2 (7 males, 6 females). It is evident a different ratio of males to females, respectively 5:1 and 1,1:1. Average age at onset was 20.5 months in groups 1 (range 3-68 months) and 23 months in group 2 (range 4-65 months). Typical form is most represented in both group: 10/12 (83%) in group 1, 10/13 (77%) in group 2. Mean value of the inflammatory indexes ferritin and CRP resulted higher in group 2 ($p \leq 0.05$): ferritin 317 ng/ml and CRP 134 mg/l versus ferritin 200 ng/ml and CRP 73 mg/l. MAS was not diagnosed in any of the patients. According to Italian Health Ministry guidelines, only two patients qualified investigations for SARS-CoV-2, resulted negative (qualitative serology and nasopharyngeal swab). However, no signs of pneumonia were evidenced by chest X-Ray in group 2. An abnormal echocardiogram (coronary ectasia) was recorded in 4/13 patients (31%) of group 2 versus 1/12 patients (8%) of group 1. Concerning treatment, 3/12 patients (25%) presented IGIV resistance in group 1, 4/13 (31%) in group 2. In Table 1 we reported the main features of these two different cohorts. Not even case of hyperinflammatory syndrome in patients infected by SARS-CoV-2 was evidenced.

	Group 1	**Group 2**	p value
Number of patients	12	13	NA
Mean age at onset, months (range)	20.5 (3-68)	23 (4-65)	ns
Male	10/12	7/13	$p \leq 0.05$ *
Incomplete or atypical Kawasaki disease (%)	2/12	3/13	ns
Mean CRP, mg/dl (+ SD)	73 ($\pm$ 47)	134 ($\pm$ 98)	$p \leq 0.05$ *
Mean ferritin, ng/ml (+ SD)	200 ($\pm$ 110)	318 ($\pm$ 371)	$p \leq 0.05$ *
Coronaritis	1/12	4/13	$p \leq 0.05$ *
Immunoglobulin resistance	3/12	4/13	ns
Steroid treatment	1/12	1/13	ns

Conclusion: At the end of May, Campania (region of southern Italy) recorded 2% of Italian cases of SARS-CoV-2, with a cumulative incidence of 78.29 by 100000 individuals, versus 867.33 by 100000 individuals recorded in Lombardia. In our region incidence of KD seems not increased. Patients diagnosed with KD during first four months of 2020, including SARS-CoV2 time, presented substantially similar features than observed in the previous year. Considering the lower incidence of SARS-CoV-2 infection in southern part of Italy, our experience supports the hypothesis that the emerging disease recently described might represent post-infectious inflammatory syndrome different from classic KD.
Disclosure of Interest: None declared

P055

A SURVEY TO UNDERSTAND THE FEELINGS TOWARDS AND IMPACT OF COVID-19 ON THE HOUSEHOLDS OF JUVENILE DERMATOMYOSITIS (JDM) PATIENTS FROM A PARENT OR CARER PERSPECTIVE

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Introduction: The COVID-19 pandemic and 'lock down' in the world is potentially a worrying time for everyone. The opinions of families that are caring for a child/children/young person with chronic disease need to be heard and addressed appropriately.

Objectives: The aim of this study was to gain a better understanding of how they feel about the effects and impact of the COVID-19 lock down on them and their child/children/young person with JDM. We asked parents/carers of JDM patients to complete a questionnaire and add any comments.

Methods: We have approached 139 participants from the Juvenile Dermatomyositis Cohort Biomarker Study (JDCBS)database, with specific consent to approach electronically for research studies. A questionnaire with study summary was sent to participants for their parents/carers to complete by email. The questionnaire wasdesigned and managed through a secure University Software System compliant with data protection. On completion of the questionnaire data were submitted electronically. Parents/carers were informed that we were sending them the questionnaire as their child/children/young person is part of the UK wide JDM study consent was already present to approach by email for such studies.

The data recorded from the questionnaire will be analysed in relation to demographics. Demographics of the whole cohort of JDCBS participants will be compared between those sent the questionnaire and those who were not. Descriptive analysis will be carried out on the data collected from the completed questionnaires. Median and inter-quartile-range (IQR) of the scores from the cohort will be used. Free text will be analysed using thematic analysis.

Results: Table 1 - Comparative data between those sent the questionnaire and those who were not

	JDM cohort	
	Questionnaire sent (n = 136)	**Questionnaire not sent (n = 454)**
Age at diagnosis (years), median (IQR)	7.57 (4.63 – 10.53)	7.46 (4.80 – 10.91)
Current age (years), median (IQR)	18 (12.39 – 22.92)	20.52 (14.60 – 26.35)
Time since diagnosis (years), median (IQR)	9.18 (5.20 – 13.59)	12.05 (6.97 – 17.55)
Female sex, No. (%)	90 (66.18%)	323 (71.15%)
Ethnicity:		
White	106(77.94%)	348 (76.65%)
Black-Caribbean	6 (4.41%)	14 (3.08%)
Black-African	6 (4.41%)	20(4.40%)
Black other	1 (0.74%)	8 (1.76%)
Indian	3 (2.21%)	11 (2.42%)
Pakistani	4 (2.94%)	14 (3.08%)
Bangladeshi	0 (0.00%)	6 (1.32%)
Chinese	0 (0.00%)	1 (0.22%)
Other Ethnic group	10 (7.35%)	32 (7.05%)

Conclusion: This study will provide important additional insights to the Juvenile Dermatomyositis Cohort Biomarker Study during the current time of COVID-19 lock down in the United Kingdom. The answers from the questionnaire will enable us to assess how to support the participants and their families further now and in the future.

Disclosure of Interest: None declared

P056

A COHORT OF 20 CASES OF PAEDIATRIC INFLAMMATORY MULTISYSTEM SYNDROME TEMPORALLY ASSOCIATED WITH SARS-COV-2 MANAGED BY A UK TERTIARY PAEDIATRIC CENTRE.

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Introduction: In April 2020 in the midst of the COVID-19 pandemic, a UK alert reported seriously ill children presenting with hyper-inflammation and shock with evidence of present or recent SARS-CoV2 infection in a proportion of these. The Royal College of Paediatrics and Child Health then proposed a case definition for these named Paediatric Inflammatory Multi-system Syndrome Temporally Associated with SARS-CoV2 (PIMS-TS). Presenting features are a spectrum of manifestations of hyper-inflammation mainly overlapping those of Kawasaki Disease and/or Toxic Shock Syndrome.
Objectives: To describe the clinical features and outcomes of cases seen at Leeds Children Hospital.
Methods: We reviewed 20 patients with suspected PIMS-TS between 01/05/20 & 05/06/20. All were managed by a PMIS-TS multidisciplinary team including rheumatology, cardiology, infectious diseases, haematology, intensive care and general paediatrics.
Results: 15 (75%) were male, mean age was 7 years (3 months - 15 years), 6 (30%) were from Black and Asian ethnic groups. All patients were tested for SARS-CoV-2 infection by polymerase chain reaction (PCR) on nasopharyngeal swab, stool and endo-tracheal secretions if intubated. Serology samples were taken for all patients and testing is in progress. 2 (10%) patients tested positive for COVID-19 on PCR. All patients except one had no pre-existent conditions. The length of stay was 6.3 days. 6 patients (30%) required short paediatric intensive care admission for inotropes administration; one required intubation. Clinical features were fever (100%), skin rash (65%) -mainly maculo-papular-rash resembling Kawasaki disease and less frequently Henoch-Schonlein Purpura , gastrointestinal symptoms (55%), circulatory shock or hypotension requiring fluid resuscitation (45%), conjunctivitis (40%), lips and oromucosal changes (30%), extremities changes -mainly hyperaemia and oedema- (25%), and lymphadenitis (20%). CRP was significantly raised in all cases with the highest CRP value being 0-100mg/L in 30%, 100-150mg/L in 20%, 150-200mg/L in 20%, and >200 in 30%. Other laboratory features included liver dysfunction (84%), raised d-dimer (80%>range 466 - 41758ng/ml), lymphopenia (75%, with 30% <1), hypoalbuminaemia (70%), anaemia (55%), coagulopathy (50%), thrombocytopenia (45%, range 51 - 14710^9/L) and raised ferritin (45%, range 324 - 1104ug/L).
Most had abnormal echocardiograms, showing impaired function and peri-cardial effusions with prominent left coronary artery a common early finding (55%). Troponin and pro-BNP were abnormal in 35% and 80% respectively. 16 (80%) received immunoglobulin therapy at 2g/kg (a single infusion in 75% and twice in 25%), 9 (45%) required IV methylprednisolone pulses (10 mg/kg, usually repeated for three consecutive days), and 6 (30%) patients received both. 19 received aspirin initially at high dose then low dose until follow-up. There have been no deaths and all patients have been discharged home with plan for cardiology and rheumatology follow-up. Preliminary follow-up data are reassuring.
Conclusion: Our cases of PIMS-TS showed a range of hyper-inflammation features overlapping with typical or atypical Kawasaki Disease and/or Toxic Shock in a large proportion of cases. Distinct clinical features included the high prevalence of early cardiologic involvement (mainly myocarditis and pericardial effusions) which responded well to immune-modulatory treatment. Distinct laboratory features included very raised CRP, d-dimer and cardiac enzymes. Treatment rapidly resolved the hyper inflammation in all cases. Short term outcomes were excellent and follow-up for a minimum of 6 weeks is planned for all patients as longer-term cardiac outcomes of the condition remain uncertain.
Disclosure of Interest: None declared

P057

ACRAL ERYTHEMATOUS/CYANOTIC LESIONS ASSOCIATED WITH VESSELS ARCHITECTURE DISTORTION DEFINE A NEW CLINICAL ENTITY DURING COVID19 PANDEMIC

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Introduction: Skin manifestations, in particular acral lesions, commonly identified as “Covid Toes” have been observed during the Covid-19 pandemic. Inflammation of the microcirculation of the extremities has been implicated in the pathogenesis. Whether it is the result of a viral-induced immune response remains to be address
Objectives: Our prospective longitudinal study aims at (1) describing the clinical features of these skin lesions in children, (2) assessing their association with SarsCoV2 infection, (3) performing a throughout investigation of the immune-mediated events and metabolic changes occurring during the disease course
Methods: 15 children referred for erythema pernio-like lesions in April-May 2020 were enrolled at admission (T1) and reassessed 4 weeks later (T2). Evaluation of the lesions was performed combining serial pictures, physical examination, capillaroscopy, dermatoscopy and skin biopsy (in selected cases). SarsCoV2 molecular (nasal and fecal) and serological tests were carried out. Samples were collected to perform immunological (blood) and metabolomic (serum, saliva, urine and stools) studies
Results: All patients (9M:7F, median age 13.2yrs IQR:12.58-14.23) presented with erythematous/cyanotic lesions at the periungual area of the toes. Lesions were bilaterally distributed in 14 (93.3%), heels were involved in 5 (33.3%). Ulceration complicated 1 case, while desquamation developed in 3 (20%) cases during follow-up. A concurrent bilateral involvement of the fingers was observed in 1 subject. Commonly associated signs/symptoms were pain (8, 53.3%), swelling (7, 46.6%), erythema (6, 40%), pruritus (5, 33.3%) and burning sensation (3, 6.6%) of the involved areas. Concomitant sore throat (2), cough (1), diarrhea (1), dysgeusia (1) were rarely reported. Upper respiratory symptoms preceded (~20days) the onset in 3 (20%) subjects. One patient had a past history of acrocyanosis and 5 (33.3%), including 2 siblings, had a family history of autoimmunity.
Three patients had uncertain contact with Covid19 cases. Nasal swab was negative for SarsCoV2 in all patients. Rapid test showed negative IgM/IgG in 7 tested cases. Quantitative serology and molecular analysis for SarsCoV2 in the stools are ongoing. Labs were within normal ranges in all patients at T1, except for a mild elevation of the complement C3 fraction (ave.1.24±0.20, unl=0.95 g/l), notably found in all patients. Dermatoscopy revealed active inflammation in 8 (53.3%) cases and a skin biopsy (obtained in 4) revealed lymphocyte infiltration. Capillaroscopy showed dilated capillaries in 7 (46.6%) and winding organization of vessels in 2 (13.3%) patients. Clinical improvement was observed in all 4 children who received the T2 clinical assessment. Immunological and metabolomic analysis are ongoing
Conclusion: A novel clinical entity characterized by bilateral erythematous/cyanotic lesions of the periungual area of the toes is emerging in children. Microscopic signs of lymphocyte infiltration, evidence of vessels architecture distortion, associated with an increase of the complement C3 fraction suggest an inflammatory process of the micro-vascular compartment in the derma. While our preliminary data do not support an association with SarsCoV2, we cannot exclude that a delayed immune activation in response to a viral infection might play a role in the genesis of these lesions. Our ongoing immunological and metabolomic studies will contribute to clarify the events leading this clinical emerging picture
Disclosure of Interest: None declared

P058

PSYCHOSOCIAL IMPACT OF SARS COV-2 OUTBREAK ON PATIENTS WITH PEDIATRIC ONSET SYSTEMIC LUPUS ERYTHEMATOSUS AND THEIR CAREGIVERS

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Introduction: An aggravation of psychological and psychiatric illnesses is expected in patients with pediatric onset SLE (pSLE)and their caregivers during the SARS-CoV-2 outbreak.

Objectives: To assess peritraumatic distress, sleep disturbances, abnormalities of affect and psychosocial impact of SARS CoV-2 outbreak on patients with pSLE and their caregivers.

Methods: Patients with pSLE (diagnosed at an age of < 16 years)under follow-up in Pediatric Rheumatology clinic of Advanced Pediatrics Center, PGIMER, Chandigarh and their caregivers were recruited in the study. We conducted telephonic interviews and sent the questionnaires through email or WhatsApp® services to the eligible patients and their caregivers.Participants who had difficulty in understanding the questions were excluded. The study was approved by the Institute's ethics committee. The demographic and clinical data were extracted from the clinic files. We used four different questionnaires:

1. Peritraumatic Distress Inventory (PDI)
2. Insomnia Severity Index (ISI)
3. Positive and Negative Affect Schedule short form (PANAS-SF)
4. SLE-COVID-19 stress questionnaire: 23 questions for qualitative assessment of different components of psychosocial well-being during the COVID-19 pandemic. Stress was evaluated under 4 domains: COVID-19 related stress, SLE related stress, hydroxychloroquine (HCQ) related stress, family and social relations related stress.

The data were recorded through telephonic interviews and Google forms® and transferred onto a MS Excel® database and analyzed using the SPSS software

Results: Telephonic contacts were made with 80 patients with pSLE, 2 patients were excluded, 61(78.2%) patients and 55(70.5%) caregivers answered the questionnaire. Two patients experienced a disease relapse during the period of lockdown, telephonic consultations were sought by 10 (12.8%) patients for disease related queries and 3 (3.8%) required hospitalization during the lockdown period. Assessment of PDI revealed that 20 (32.8%) patients and 18 (32.7%) caregivers experienced significant peritraumatic distress. Maximum distress was experienced in the factor domain of life threat (mean score: 9.04±3.3 in patients and 9.2±2.256 in caregivers). Sleep disturbances were noted in almost all patients with SLE and their caregivers as per the ISI. Significant insomnia was noted in 50 (82%) patients and 39 (70.9%) caregivers. Caregivers of patients with minor organ involvement faced significantly more insomnia related problems than caregivers of patients with major organ involvement ($p = 0.013$). High positive affect scores were seen in 65.5% patients and 78.2% caregivers, low positive affect scores were noted in 34.5% patients and 21.8% caregivers.

Higher risk of COVID-19 was perceived by 23% patients, 98.3% participants practiced social distancing, 86.6% patients showed good compliance to therapy, 38% faced difficulties in procurement of medications/HCQ, 78.7% patients and 80% caregivers were aware of HCQ use for treatment of COVID-19, 52.5% patients and 43.6% caregivers knew about side effects of HCQ, 23% patients felt that their regular use of HCQ will protect them from COVID-19, 12% patients thought about giving HCQ to other family members. Female patients with pSLE reported significantly higher HCQ related stress than males (0.313, $p=0.014$). Male caregivers reported significantly higher COVID-19 related stress ($p= 0.001$). Patients with major organ involvement showed higher HCQ related stress ($p= 0.033$).

Conclusion: Patients with pSLE and their caregivers are at risk of psychosocial abnormalities during the COVID-19 pandemic. These patients and their caregivers may benefit from early psychological interventions.

Disclosure of Interest: None declared

P059

WHAT HAPPENED IN THE PEDIATRIC RHEUMATOLOGY CLINIC DURING COVID19 PANDEMIA

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Introduction: Since the first reports of cases from Wuhan, COVID-19 was recognized as a pandemic by the WorldHealth Organization (WHO) on March 11th, 2020. Although children tend to experience only mild symptoms, younger previously healthy adults have also succumbed to Covid-19.In Turkey as well as in other countries, the disease was less in children..Patients with any rheumatic disease (eg. juvenile idiopathic arthritis, lupus) are considered at-risk for serious infections due to their immunocompromised state resulting from their underlying immune conditions and use of targeted immune-modulating therapies such as biologics.
Objectives: We aim to share our experience in pediatric patients during pandemia.
Methods: We admitted the patients observed during the pandemic time, from March 2020 to May in the study.The COVID 19 suspected patients was accepted as follow: -The patients admitted to hospital with complaints of fever and acute respiratory infection symptoms (cough and/or respiratory distress) that were not explained for any other reason and who needed hospitalization. -The patients who have at least one of the symptoms of fever, cough or respiratory distress, and have also a history of contact with a patient with COVID-19 infection.The patients diagnosed the cytokine storm syndrome, hyperinflammation were defined as follow: 1) A child presenting with persistent fever and systemic inflammation, with or without evidence of single or multi-organ involvement with additional features. This may include children fulfilling full or partial criteria for Kawasaki disease; 2) Exclusion of any other microbial cause and of flare of a chronic underline inflammatory disease.
Results: We evaluated 1024 patients who applied to our outpatients clinic between 11 March and 15 may were included in the study. Except those patients, 847 appointments were postponed, and the schedule of treatments in 50 patients was adjusted via telemedicine.COVID-19 outbreak caused exacerbation of 25 patients due to lack of medication or delayed drug change.145 (14%) of the all patients admitted to the outpatient clinic were hospitalized, 28 (19.3%) of them were covid suspects.34 patients were hospitalized with suspicion of COVID related situation. While 21 (62%) patients were diagnosed before the pandemic, 13 (38%) patients were diagnosed during the pandemic period.The demographic findings of these 21 pre-diagnosed patients were as follows: 11 females, 52.3%, median age 8.5 years,; median disease duration 2.5 years (range 1–4). Among them, 4.8 % of all patients were on hydroxychloroquine (HCQ), 14.2% on prednisone (≤7.5mg/day), 33% on methotrexate, and 28.5 on any biologic drugs (etanercept, tosilizumab and canakinumab). Eight patients (38%) with familial Mediterranean fever were on colchicine.The sixteen patients (57% of the total population) had swab and or thorax CTconfirmed COVID-19**.** While 25(89.3%) patients had clinical-COVID-19 findings, 3 were asymptomatic. 7 patients (25%) established contact with a COVID-19 patient.The cytokine storm syndrome, hyperinflammation were observed in 13 patients, 1.3 % of all admitted patients. The general characteristic of them were as follows: 4 female, median age 5,5 years who were younger than others ($p<0,01$). All cases treated with medium-low dose steroid , 5 was treated IVIG, 5 was cyclosporine and Anakinra or Tocilizumab.
Conclusion: The COVID-19 epidemic is now a pandemic and mayaffect millions of people worldwide. The patients with chronic diseases, in particularimmunosuppressed subjects, should be aware of the possible risks linked to the drugs used to treat rheumatologic disorders.Use of social isolation and hygienic measure arefundamental in order to decrease viral spread.
Disclosure of Interest: None declared

P060

THE IMPACT OF COVID 19 ON A SPANISH PEDIATRIC RHEUMATOLOGY UNIT: PATIENT-REPORTED OUTCOMES (PRO) UTILITY

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Introduction: COVID-19 outcomes remain poorly understood in children with rheumatic diseases.
Objectives: To describe the impact of COVID-19 in a cohort of pediatric patients with rheumatic diseases attended in a Spanish tertiary hospital; assessing the possible effects on the clinical course, functional ability using Juvenile Arthritis Functionality Scale (JAFS) and health-related quality of life (HRQoL), through patient-reported outcomes (PRO).
Methods: A cross-sectional study was conducted. We performed an e-health record review and an e-survey. We collected:Juvenil Arthritis Multidimensional Assessment Report (JAMAR)1, questions related to activity from other autoimmune or autoinflammatory diseases (AIDs), JAFS, HRQoL tests and COVID-19 aspects. We also included questions about medical visits and the ease of contacting with the rheumatologist during the lockdown.
Results: 146 patients received the survey, of which 94 answered, 50 of them did not answer back in time, and 2 refused to participate. Mean age was 14 years. Of the 94 patients who answered the survey, the diagnoses were: 45 (47.9%) non-systemic JIA; 10 (10.6%) childhood-onset Systemic Eritematous Lupus (cSLE); 10 (10.6%) AIDs, including HIDS and OCMR; 8 (8.5%) systemic JIA (sJIA); 4 (4.3%) Behçet disease; 4 (4.3%) vasculitis; 2 (2.5%) Juvenile Dermatomyositis; and 1 (1%) Juvenile Scleroderma.
45.7% of them received biological disease modifying anti-rheumatic drugs (bDMARDs): Adalimumab (ADA) 16%, Tocilizumab (TCZ) 9.6%, Etanercept 7.4% and Belimumab 3.2%, among others. 36.26% of patients were treated with methotrexate and 10,5% with hidroxychloroquine.
Related to SARS-CoV2 infection, 12 patients (12.8%) reported being under COVID-19 suspicion. 5 patients underwent PCR, of which 2 of them were positive. Both patients also suffered from pneumonia. One of the children, treated with Canakinumab due to sJIA, was admitted to the Intensive Care Unit and the other one, diagnosed with cSLE, did not required hospitalization. No deaths were registered.
Regarding bDMARDs, 3/12 children (25%) of infection confirmed or suspected group (ICSG) were on treatment (ADA, TCZ and Canakinumab) compared with 39/82 (47.56%) of healthy group. 3 bDMARDs were interrupted by medical judgment, none reported by patient's choice.
Concerning COVID-19 related symptoms, headache was the most frequent (26, 27.7%), followed by cough (19, 20.2%) and fever (14, 14.8%). Only 2 (2.1%) patients reported dysgeusia or anosmia. 49 (52.1%) children were asymptomatic.
16/94 patients (17%) had at least one COVID19- confirmed contact, and 14.9% of the group had at least one COVID19-confirmed closed relative.
The mean physical function test result was 0.79 (12-0), being ICSG results slightly higher (1.08 vs 0.76). In relation to HRQoL assessment, mean score for total group was 3.15 (0-18). The ICSG showed, as well, subtly worse results (4.17) compared to non-infected group (3.04). Mean rating of patient's pain intensity and level of disease activity on a visual analogue scale was 0.97 and 1.33, respectively. 8 patients (8,5%) reported physical impairment and psychological balance due to COVID-19 pandemic, 15 (16%) only physical impairment and 8 (8,5%) only psychological balance.
Conclusion: PRO could be a good option for patient assessment during a lockdown period when the outpatient visit was limited. Some important aspects such as disease activity, functional ability, HRQoL and risk of COVID- 19 could be evaluated.Worse results at physical function and HRQoL tests were detected on ICSG.
Around 50% of children were symptomatic during the pandemic period, so COVID-19 may be underdiagnosed in pediatric patients with rheumatic diseases. However, only 2 of them had a confirmed diagnosis. Therefore, further investigations may be necessary.

Disclosure of Interest: None declared

P061

KAWASAKI DISEASE AND COVID-19 ANALYSIS AND REVIEW

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Introduction: The coronavirus disease 2019 (COVID-19) has been an emerging, rapidly evolving situation in China since 2019 then became world pandemic. The first case of severe childhood novel coronavirus pneumonia in China was reported in March 2020, nearly five months after the onset of this disease in Wuhan city, China.
Objectives: The severity differs between adults and children, with a lower death rate and lower severity as age decreases to less than 20 years old. Increased cased of Kawasaki disease (KD) was reported from New York city and some area of Italy and U.K. with almost 6-10 times increased when compared with previous years.
Methods: We conducted this article to compare the clinical characters and laboratory data between KD and COVID-19 in children. A total of 24 COVID-19 children were collected from the literature review and 234 KD cases were from our hospital via retrospective chart review.
Results: We found that patients with KD had higher white blood cell (WBC), platelet, neutrophil percentage, C-reactive protein, procalcitonin, AST and body temperature while COVID-19 had higher age, hemoglobin and lymphocyte percentage. After multiple logistic regression analysis, age, WBC, platelet, procalcitonin and AST provide identical markers for distinguish COVID-19 from KD.
Conclusion: In this pandemic period of COVID-19, clinician should pay attention to COVID-19 children when higher WBC, Platelet, procalcitonin and AST to provide precision treatment with intravenous immunoglobulin for Kawasaki-like disease .
Disclosure of Interest: None declared

P062

THE COV-ASAKI SURVEY FROM THE PEDIATRIC TUSCANY NETWORK DURING COVID-19 ERA

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Introduction: At the end of April 2020, national and international Pediatrics scientific societies diffused an alert about a rise in the number of pediatric severe, inflammatory syndrome, coronavirus 2 (SARS-CoV-2) related, resembling Kawasaki disease (KD).

Objectives: The Pediatric Rheumatology Tuscany Network worked out the COV-ASAKI survey to track children who received a KD diagnosis in during COVID-19 pandemic in a region hosting 593.606 people aged less than 18 years.

Methods: We retrospectively collected demographics, clinical findings, treatment and outcome of KD children between February 1st to April 30th,2020 comparing the cases in the 2020 index trimester with the same trimesters of the previous 5 years and with the total number in the last 5 years.

Results: Eight children were diagnosed as KD, with an incidence rate of 2.6 per month. Only 1/8 children could be classified as an incomplete KD. Seven were Caucasian and 1 Asiatic, without any underlying disease. Six out eight recovered after one course of intravenous immunoglobulins (IVIG), no specific intensive support was required. One patient needed two IVIG courses and a young girl developed an incipient macrophage activation syndrome (MAS) responsive to a single steroid pulse. The SARS-CoV-2 on nasopharyngeal swab, available in 6/8 children, was always negative. Four KD children were sampled for antibodies after recovery and resulted negative. No coronary involvement was reported. From February 1st and April 30th, 1992 nasopharyngeal swabs have been performed to the Tuscan children admitted to the hospitals: 85/1992 (4.3%) resulted positive for SARS CoV-2. Fifty serological tests have been performed with 7 children positive results. Considering the previous 5 years, 165 children were diagnosed with KD (incidence 2.7 per month). Fifty-nine were incomplete forms; 3 developed MAS and 1 experienced Kawasaki disease shock syndrome (KDSS). Thirty-eight showed coronary involvement during the acute phase, 11 received steroid pulses and additional 3 biologic therapy. No statistically significant difference regarding the incidence/month was found (RR 1.09, 95% CI 0.52-2.04, p=0.76), neither limiting the analysis to the 45 KD children diagnosed during the same corresponding 3-months of the last 5 years: 3 vs 2.6 (RR 1, 95% CI 0.46-1.98, p=0.96). Chi square analysis with Fisher's exact test correction failed to detect significant differences among the principal outcomes of KD children observed during the COVID-19 time and in the last 5 years: incomplete KD 59 *vs* 1, c^2=1.82; KDSS 1 *vs* 0, c^2=0.04; MAS: 3 *vs* 1, c^2=3.85; coronary involvement 38 *vs* 0, c^2=2.36. The same results have been detected adjusting the analysis for the 45 cases during the corresponding trimesters of the last 5 years (p=n.s, Fisher's exact test).

Conclusion: In Tuscany, during the COVID-19 pandemic, almost all KD patients, showed a mild disease course and completely recovered without complications. Our data underline the important role of our pediatric network during COVID-19 pandemic. The long-lasting collaboration and the well-structured communication provided a prompt intervention in new KD cases and allowed a comparison between 2020 KD cluster and the previous ones, referring to the Tuscany KD register. A comparison between our data and the results seen worldwide will be helpful to define the multifaceted nature of the pediatric COVID-19 disease and its potential relationship with the KD.

Disclosure of Interest: None declared

P063

EMERGENCE OF KAWASAKI DISEASE RELATED TO SARS-COV-2 INFECTION IN CHILDREN, A TIME-SERIES ANALYSIS

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Introduction: Kawasaki disease (KD) is an acute febrile systemic childhood vasculitis which has been known to be triggered by respiratory viral infections.
Objectives: Here, we examined whether the ongoing COVID-19 epidemic is associated with an increase of Kawasaki disease.
Methods: We conducted a quasi-experimental interrupted time series analysis over the last 15 years in a tertiary center in a French epicenter of COVID-19.The main outcome was the number of KD cases over time, estimated by quasi-Poisson regression. In the same center, we described the evolution (2005-2020) of hospital admissions from the emergency department and the evolution of the respiratory pathogens identified by nasopharyngeal multiplex PCR (2017-2020). These data were compared with the evolution of daily admissions due to confirmed COVID-19 in the same region, recorded by Public Health France.
Results:
We included 230 patients with KD. On April 2020, we identified a rapid emergence of KD related to SARS-CoV-2 (+497% increase, 95% CI [+72; +1082], p=0.0011), starting two weeks after the peak of the COVID-19 epidemic. SARS-CoV-2 was the only virus circulating at high levels during this period, and was found in 80% (8/10, SARS-CoV-2 positive PCR or serology) of KD patients since April 15th. Among these patients, five had a complete KD and 5 patients had fever with only 3 other KD criteria. The age of KD patients ranged from 18 months to 15.8 years. Six children (60%) had cardiac abnormalities, including one major coronary aneurysm (Z score: 12) and five myocarditis. Six patients (60%) required intensive care and five had inotrop treatment (50%). None required mechanical ventilation, and no fatal outcome was observed. A second peak of KD hospitalizations was detected by the model in December 2009 (+365% increase, 95% CI [+31; +719], p=0.0053), concomitant with the influenza A (H1N1) pandemic.

Conclusion: Health care providers should be prepared to manage an increased surge of patients with severe KD, particularly in countries where the peak of COVID-19 has just been reached.
Disclosure of Interest: None declared

P064

ACRAL LESIONS IN A PEDIATRIC COHORT DURING COVID-19 EPIDEMIC

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Introduction: From the end of March, during COVID-19 epidemic, pictures of chilblain-like lesions with similar characteristics were diffused by social networking among pediatricians and dermatologists in Italy.
Objectives: Describe features of a pediatric cohort affected by acral lesions during COVID-19 epidemic.
Methods: Patients ≤ 14 years old with acral lesions were recruited from Paediatric Department of Santobono-Pausilipon Hospital during the month of April 2020. In addition, information from outpatients was obtained by Italian Federations of General Pediatricians Doctors (F.I.M.P.) through a questionnaire sent to family paediatricians of Campania to collect clinical details of patients with similar lesions managed by territorial primary pediatric care during the same period.
Results: Clinical information was obtained for 25 patients (14 males, 11 females), 18 by FIMP questionnaire and 7 evaluated in Santobono-Pausilipon Hospital. Age range from 2 to 17 years (median 11 years). No one referred contact with COVID-19 individuals, previous history of perniosis or drug intake. Lesions involved acral regions: foot (toes and heels) was mostly involved (92%) with symmetrical involvement in 80% of patients, hands in 2 patients (8%). Lesions presented as erythrocyanotic discoloration of the fingers or toe, erythemato-violaceous papules or macules of foot and hand. Associated symptoms were: erythema in 11 patients (44%), swelling in 10 patients (40%), pain in 6 patients (24%), itching in 6 patients (24%). Among hospitalized patients, all of them performed laboratory assessment: no alteration was found in blood count, inflammatory indexes, hepatic and kidney function, coagulation parameters including D-dimer, LAC, antiphospholipid antibodies, S protein, C protein, homocysteine, autoimmunity. Level of vitamin D resulted insufficient (median value 19,2 ng/ml). No infection was found. Qualitative serological test for COVID was performed resulted negative for IgM in all patients, IgG positive in one patient. 5 patients performed nasal and pharyngeal swab for SARS-CoV-2 resulted negative. 2 patients underwent biopsy with similar result: lymphocytic vasculitis with edema and thickening of vessel wall associated to mural and perivascular infiltrate of lymphocytes. Concerning treatment, all patients applied topical emollient. Topic steroid was used in 12 cases outpatient, 1 case inpatient. Heparin cream was mainly used in patients with worsening of lesions after the first week. Improvement of lesions started mostly after one week, in certain cases lesions blistered and ulcerated. Resolution occurred in variable time, up to 4 four weeks from the onset, sometimes with desquamation.
Conclusion: Italy was one of the most involved country by COVID-19 pandemic, extraordinary restricted measures were performed all over the national territory. Up to the May 4, at the end of the first phase, 211.938 cases were assessed, 1.9% of patients in the age 0-18 years. There has been an outbreak of chilblain-like lesions observed mainly in young patients during COVID-19 epidemic, unreported in the previous years. The direct connection with COVID-19 is not demonstrated yet, however a role has been assumed. In most patients of our cohort there was not evidenced a defined correlation with clinical or laboratory findings of COVID-19. Improvement of lesions started mostly after one week spontaneously or with topical treatment. The new life habit due to the lockdown (physical inactivity, barefoot) could play a role mimicking a similar pathway of cold exposition. Further studies are necessary to better understand mechanism underlying COVID-19 in children.
Disclosure of Interest: None declared

e-Poster viewing: Disease outcome and transition

P065

PATTERNS AND RATE OF NON-REFERRAL TO ADULT CARE OF PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA) AT A TERTIARY PAEDIATRIC RHEUMATOLOGY CENTRE.

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Introduction: In cohort studies and transition research there has been little focus on the rate of non-referral of patients with Juvenile Idiopathic Arthritis (JIA) for ongoing adult care and the reasons why this occurs.
Objectives: To determine the characteristics of JIA patients at a tertiary paediatric rheumatology centre not referred for adult care and the frequency of and reasons for non-referral.
Methods: JIA patients in the Royal Children's Hospital (RCH) rheumatology database who turned 18 y.o. between 2012-18 were identified. The medical record of each patient was examined and those who had not been referred for adult care were entered into the study. Data regarding diagnosis, treating clinician and date of first and last RCH visit was collected. Note was made of any documented plan where the last RCH visit was intentionally the final visit for formal rheumatologic care and of subsequent events where it was unintentional.
Results: 177 patients were identified. 63 (~35%) were not referred for adult care. Of these, 24 (38.1%) had been in long term remission and were discharged back to the GP. The commonest JIA subtypes in this group were persistent oligoarticular (45.8%) and systemic JIA (25%). The remaining 39 (61.9%) patients were not referred as they had been lost to clinic follow-up at a mean age of 15.1yr. Of this group, 21 (53.8%) had been in long-term remission. 16 (41%) were lost to follow-up despite having recently active disease or being on clinic-prescribed medication, most frequently in the context of multiple missed and cancelled clinic appointments.
Conclusion: At our centre a significant minority of patients with JIA are not referred for adult care. In many cases this is due to patients being in long-term remission and occurs as either a deliberate decision by the treating rheumatologist or their failure to attend clinic appointments and eventual loss to follow-up. A substantial number of patients are lost to follow-up despite having active disease and/or being on clinic-prescribed medications. The outcome of these patients is unknown.
Disclosure of Interest: None declared

P066

PATTERNS AND RATE OF CONFIRMED TRANSITION TO ADULT CARE OF PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA) AT A TERTIARY PAEDIATRIC RHEUMATOLOGY CENTRE.

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Introduction: Juvenile Idiopathic Arthritis (JIA) commonly persists with clinically active disease into adult life. The transfer of these patients into adult healthcare services can be a challenging process, with previous studies showing successful transfer being as low as 50% in spite of a coordinated transfer effort.
Objectives: To determine the number, characteristics and referral pattern of JIA patients being transitioned from a public tertiary paediatric rheumatology centre to adult care and the rate of confirmed transition.
Methods: JIA patients in the Royal Children's Hospital (RCH) rheumatology database who turned 18 y.o. between 2012-18 were identified. The medical record of each patient was examined and those referred for adult care entered into the study. Data regarding diagnosis, treating clinician, date of first and last RCH visits, date of referral for ongoing adult care and confirmation of transition, defined as proof of establishment of follow-up with the referred service, was collected.
Results: 178 patients were identified. 64% were referred for adult care. Mean follow-up prior to transition was 7.4 years. The commonest subtypes referred were seronegative polyarticular (30.7%) and oligoarticular JIA (19.3%). 65.8% were referred to public hospital rheumatology services with the remainder referred to private rheumatologists. Confirmation of transition occurred in 62.3% with correspondence received from adult services in 49.1%. There was no difference in rate of return correspondence from public versus private providers (47.9 vs. 53.8%, p=0.69). 37.7% had an unknown outcome after referral to adult care as a result of no correspondence from the adult service and no follow-up at the RCH. The use of 'backstop' appointments – final review at RCH several months after the estimated date of adult review – was more likely in those with confirmed transition (66% vs. 30%, p=0.0002).
Conclusion: Lack of confirmation of transition for JIA patients moving to adult care is common and has the potential for suboptimal outcomes in substantial numbers of patients during this critical period. Strategies to improve communication with the referring centre following initial assessments with adult services and vigilance regarding potential loss to follow-up during this time by paediatric centres would minimise this risk.
Disclosure of Interest: None declared

P067

STATE OF IODINE SUPPLY OF CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS OF NORTH - EAST REGION OF UKRAINE

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Introduction: The problem of combined organ damage (organ-specific autoimmune syndromes) is relevant in systemic processes, which include juvenile idiopathic arthritis (JIA). Such lesions in rheumatoid arthritis in adults include autoimmune diseases of the thyroid gland, primarily chronic autoimmune thyroiditis. On the other hand, the basis for the development of thyroid pathology is endemic iodine deficiency. In accordance with the results of studies conducted in 2002 in 22 regions of Ukraine (with the participation of the Ministry of Health, NAMS of Ukraine, Goskomstat, specialized scientific research centers and UN Children's Fund (UNICEF), iodine deficiency detected in all studied territories. Ubiquitous iodine supplementation can lead to its excessive consumption, which is a problem in individuals who already have thyroid disorders, such as nodules, hyperthyroidism and autoimmune thyroid disease.
Objectives: To evaluate the current state of iodine supply in children with JIA living in the North-Eastern region of Ukraine.
Methods: Target group included 52 schoolchildren (29 girls and 23 boys) with JIA (according to ILAR classification, Edmonton, 2001) aged from 7 to 16 years (11.8±2.71). Control group included 11 children (5 girls and 6 boys), residents of the same region, of comparable gender and age (13,6±3,12). Methods: dietary iodine intake evaluation by urinary iodine concentration (Sandell-Kolthoff reaction), followed by calculation of the median. The average concentration of iodine in urine (median of urinary iodine concentration) can be used to assess iodine supply of the population. A cohort of schoolchildren is the most reflect average consumption iodine in a given territory in the general population. According to the WHO recommendation, iodine intake is considered sufficient with a median of 100–299 mcg/l in school-age children.
Results: Median urinary iodine excretion in children with JIA was at the lower normal range and amounted to Me=101.7µg/l; [QR 56.5; 169.9]. Moreover, the median iodine in urine was significantly lower than in the group of healthy peers (Me=101.7 µg/l vs Me=183.7 µg/l, p=0,003).The survey revealed that only 50,1±6,9% of children had adequate iodine supply (Me=144.8 µg/l; [QR 119.1; 215.1]). Mild iodine deficiency was diagnosed in 28,8±6,2% patients (Me=33.5 µg/l; [QR 20.4; 36.2]). Moderate iodine deficiency (Me=87.7µg/l; [QR 70.7; 97.1]) has been identified in 17.3±5.2% children with JIA. Severe iodine deficiency was diagnosed in 3.8±2,6% patients (Me=14.1 µg/l; [QR 12.43; 15.7]). JIA girls had worse results (in girls: Me= 97.7 µg/l; [QR 77.8; 130.2] vs in boys: Me=109.6 µg/l, [QR 48.4; 154.1] p=0,051). Indicators of iodine excretion did not depend on the variant, activity and duration of the JIA.
Conclusion: The risk of developing pathological changes in the thyroid gland in children with JIA is caused not only by systemic immune disorders, but also by a deficiency of iodine intake. The obtained results can serve as the base for screening testing of thyroid function in JIA and for resolving the issue of prescribing iodine-containing drugs. This should be taken into account to improve the overall prognosis of the disease and the quality of life in adulthood.
Disclosure of Interest: None declared

P068

THE 15-YEAR EVOLUTION OF JIA BIOLOGIC THERAPY PATTERNS IN THE CZECH REPUBLIC

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Introduction: Collection of structured clinical information in the form of disease and/or pharmacovigilance registries have become a standard for many rare diseases including juvenile idiopathic arthritis (JIA). Although the total JIA paediatric population is not known in the Czech Republic participation to the Rheumatic Diseases Biologics Registry (ATTRA) has been required in order to secure drug reimbursement by insurance companies. Patient data including demography, disease activity and damage scores, comorbidities and concomitant therapies have been prospectively collected in the ATTRA registry since 2002 for the spectrum of rheumatic diseases under the auspices of the Czech Rheumatological Society. Paediatric patients have been entered since biologic therapies became available for children with JIA in late 2004.
Objectives: To present country-specific policies and practice in JIA biologic therapy and analyse major trends in their use over the past 15 years.
Methods: Description of the biologic therapy organisation within the Czech healthcare system. Analysis of the main demographic and disease characteristics from the JIA part of the ATTRA registry from 2005 up to January 2020.
Results: JIA biologic therapy is concentrated in paediatric rheumatology units satisfying the predefined criteria agreed by the Czech Rheumatological Society. These include personnel qualifications as well as unit equipment and availability of specialised paediatric services. When used in approved indications majority of common biologics including etanercept, adalimumab, golimumab and tocilizumab are fully reimbursed via the special budget-limited contracts among approved healthcare providers and insurance companies. Reimbursement of IL-1 blockers, abatacept and rituximab requires formal application which is time consuming, but usually successful. Over the past 2 years number of units prescribing biologics has expanded from 3 towards currently 7 approved centres in the country of over 10 million population. Nevertheless, the 3 "oldest" units care for 94% (701/743) of registered patients who were further analysed. The number of registered (=ever biologic-treated) patients has been steadily increasing from the total of 50 individuals in 2005 by the 5-year annual mean of 77 patients (calculated from years 2015-20). When data from 2005 were compared with 2015-20, interval from the diagnosis to the introduction of the first biologic as well as the JADAS-71 (range 0-101) at therapy onset have been steadily decreasing from the median (5-95th centile) of 4.8 (4-12.7) years and 21.2 (8.9-59.5) respectively to 1.1 (0.2-8.8) years and 14.3 (1.4-34.7), respectively. From the total of 1186 patients currently followed by the 3 largest units 30% (356) of patients are receiving following biologics: TNF inhibitors (85%), tocilizumab (10%), IL-1 inhibitors (5%). Data on patient demography, JIA subtype distribution and disease complications (mainly uveitis), treatment efficacy, relapse and switch to different agent rates as well as adverse events are further presented in detail.
Conclusion: Biologic therapy has been well established in the Czech Republic and is currently being received by one third of JIA paediatric patients. Its accessibility is somewhat limited by reimbursement rules and by the budget, but TNF and IL-6 inhibitors are readily available without delay when used in approved indications. Decreasing interval from disease onset to the start of therapy as well as generally milder disease (as reflected by JADAS) required for treatment initiation illustrate their expanding use over the past years in line with available treatment recommendations and similar to other JIA series.
Disclosure of Interest: None declared

P069

CHANGE IN DAMAGE INDEX VALUES IN CHILDREN WITH SYSTEMIC LUPUS ERYTHEMATOSUS DURATION OF TWO AND MORE YEARS

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Introduction: High disease activity, the presence of prognostically unfavorable syndromes of systemic lupus erythematosus in children much more often requires the appointment of a more aggressive than in adults complex of immunosuppressive therapy (hormones, cytostatics, immunobiological drugs). The development of endothelial dysfunction, immaturity of the regulatory systems (central nervous and endocrine) further create the conditions for the formation of irreversible damage in many organs with the development of their insufficiency. The nature of these injuries in childhood and the period of their formation remain unclear.
Objectives: The purpose of the study was to determine the frequency and nature of irreversible changes (damage index) in children with systemic lupus erythematosus (SLE), depending on the duration of the disease, the nature of the course, and activity of the process.
Methods: 53 patients with SLE at the age of 7-18 years old and suffering from more than one year were examined in dynamics twice at intervals of 12 months. The average duration of disease was 37,92±7,90 years at the time of the first examination. Changes in the cardiovascular system were determined (using an ECG in 12 main leads, an echo test, a 6-minute walk test), kidneys (according to glomerular filtration rate, serum creatinine concentration, proteinuria level and the range of changes in the specific gravity of urine during days), pulmonary system (according to X-ray examination and spirometry). The presence of pathology of the organ of vision, the nervous system (assessment of neurological status, conductivity, sensitivity of the cranial and peripheral nerves, EEG, MRI of the brain, the use of the Montgomery and Åsberg Depression Rating Scale), changes in the musculoskeletal system (by X-ray, ultrasound, MRI of the joints , bone densitometry) were studied. The blood lipid spectrum of patients (total cholesterol, triglycerides, HDL, LDL, VLDL-cholesterol, atherogenic coefficient) was investigated.
Results: In half of children and adolescents with SLE (52.83%), potentially irreversible organ injuries were revealed. During the initial examination lesions of the nervous system dominate (20.75%), lung injuries were next (13.21% of patients), which were represented mainly by pleural fibrosis. Visual organ damage (11.32%) in the form of cataracts was registered with a slightly lower frequency. On repeated examination the frequency of irreversible changes has increased (68,92%), wherein eyes lesions (18,87%), stunted growth (18,87 %), lungs changes (16,98 %) are added, that is a feature characteristic of juvenile debut SLE. Growth retardation (9,43%)was characteristic of the age of SLE onset up to 8 years. Menstrual disorders were observed in 13.04%, mainly at the onset of SLE at 8-12 years. Presence of atherogenic dyslipoproteinemia (22.64%), insulin resistance (13.21%), osteopenia (22.64%) can be considered as precursors of damage (atherosclerosis, diabetes mellitus, osteoporosis) in the further course of the disease. The accumulation of irreversible organ damage occurs with an increase in the duration of the disease ($r = 0,355$; $p < 0,001$) and is associated with persistent activity of the lupus process ($r = 0,515$; $p < 0,001$) and long-term cytostatic therapy ($r = 0,3$; $p < 0,01$).
Conclusion: The results of study indicate the need for prospective monitoring of the state of organs and systems for the formation of persistent damage in order to timely correction of therapy.
Disclosure of Interest: None declared

P070

A SYSTEMATIC REVIEW EXPLORING THE BIDIRECTIONAL RELATIONSHIP BETWEEN PUBERTY AND AUTOIMMUNE RHEUMATIC DISEASES

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Introduction: Adolescence and puberty are associated with significant changes which are initiated and mediated by sex hormones. There is evidence that sex hormones also influence the development and regulation of the immune system, and with it auto-immune rheumatic diseases (ARDs).

A clear sex bias exists in the incidence of ARDs, with females being at significantly higher risk. However, there is a limited understanding of the physiological mechanisms for sex-specific immune modulation.

Previous research has observed a relationship between puberty and ARD onset, suggesting that sex hormone changes at puberty play an immunomodulatory role in triggering ARD onset and development. In addition to triggering autoimmunity, sex hormones can influence various outcomes of ARDs, and testosterone is thought to exert a protective effect.

No previous systematic reviews have addressed the impact of puberty on disease outcome measures in ARDs, or the impact of ARDs on puberty-related outcomes. Understanding the interplay between the neuroendocrine and immune systems can provide valuable insights into the immune-pathogenesis of the peri-pubertal onset of ARDs, and help to improve the clinical approach to treatment of these patients in the long term.

Objectives: To elucidate the bidirectional relationship between puberty and autoimmune rheumatic diseases (ARDs).

Methods: Studies published in English until October 2019 were identified using a systematic search on bibliographic databases and manual checking of reference lists. Information was extracted on study design, sample size, demographics, puberty outcome measures, and main findings. The methodological quality of the studies included was analysed using the Newcastle-Ottawa Scale (NOS) for non-randomised trials.

Results: 14 non-randomised studies reporting on the impact of puberty on ARD outcomes (*n*=7), ARD impact on puberty-related outcomes (*n*=6), or both (*n*=1) have been identified. One study focused on patients with juvenile idiopathic arthritis (JIA)-associated uveitis, all others investigated patients with juvenile systemic lupus erythematosus (JSLE) or healthy controls who developed adult-onset SLE. Quality assessment of studies showed a small to moderate risk of bias overall (NOS 4-9/9). Due to large heterogeneity of the studies it was not possible to perform a meta-analysis. Multiple studies reported on delayed puberty in patients with JIA/JSLE, menstrual and hormonal abnormalities, and lower height and weight than controls. Earlier (pre-pubertal) onset of JSLE was correlated with more severe disease and more need for systemic treatment.

Conclusion: It is clear that a bidirectional relationship exists between puberty and ARDs. More and better research is required to elucidate this relationship. Therefore, we propose a comprehensive set of clinical assessments of patients with ARDs, to be recorded at hospital visits.

Increased awareness of the relationship between puberty and ARDs, and subsequent monitoring of the impact of disease and treatment on the normal development of young people with ARDs, can benefit clinicians, patients and their families. Moreover, it will facilitate future research into new strategies of minimising the negative impact of ARD on pubertal development as well as managing ARD flares from a broader perspective, which should take into account puberty-related outcome measures, ultimately shedding light on this complex but important relationship.

Disclosure of Interest: None declared

P071

LONG-TERM OUTCOME OF JUVENILE IDIOPATHIC ARTHRITIS IN ADULT PATIENTS UNDER BIOLOGICAL THERAPY

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Introduction: As available treatment options for juvenile idiopathic arthritis (JIA) have expanded over the last decades, there is a need for studies to characterize its long-term outcome, especially in patients treated with biological therapy.
Objectives: To study clinical and patient related outcomes of adults with JIA on biological treatment after transition to adult care.
Methods: In this cross-sectional study, adult JIA patients under treatment with biologicals and followed in the University Hospital of Leuven were included. Patient-administered questionnaires were used to examine social and professional participation, overall well-being(VAS), physical disability(HAQ), health-related quality of life(SF-36), fatigue(MFI-20), perception of illness(IPQ-R), coping(UCL) and self-efficacy(ASES). We registered disease and treatment characteristics, disease activity(DAS28-CRP), joint damage(JADI-A), systemic sequelae and side effects of biologicals from the patient's medical record.
Results: Twenty-five patients with a mean age of 32.6 years were included. All JIA subgroups were represented, but the polyarticular JIA was the most common. At their last hospital visit, 7/25 patients used low-dose steroids, 12/25 were treated with cDMARDs and 24/25 were on biological therapy. After a mean follow-up time of 23.6 years, 4/25 participants had active disease defined as DAS28≥ 2.6. The mean JADI-A and HAQ score were 6.5 and 0.8 resp. 3/25 patients developed serious infections, 4/25 developed MAS during their disease course. None developed malignancies. Arterial hypertension was present in 8/25, pulmonary hypertension occurred in 2/25. Two patients had osteoporosis, while 6 had osteopenia. Growth failure was identified in 4/25. 5/25 developed discrepancy in leg length. 2/25 underwent surgery for excessive varus or valgus deformity of the limbs. Patients scored their health-related quality of life with a mean of 71.6/100±18.3 on the VAS. The SF-36 physical and mental component score (PCS and MCS) were calculated, resulting in a mean (± SD) of 40.9±11.7 for PCS and 52.0±12.2 for MCS. A mean (± SD) of 13.2±4.4 was found for the MFI-20 subscale "general fatigue". The mean (± SD) for the ASES subscale "pain" was 3.3±0.8, and for "other symptoms" 3.8±0.7. Almost 3/4 of participants practiced sports. 18/25 participants were employed, 15/25 were in a relationship and 6/25 had a child.
Conclusion: In this cross-sectional study, we examined clinical and psychosocial outcomes of JIA patients under treatment with biological therapy after transition to adult care. Although the population was biased to a more severe subtype due to our inclusion criteria (use of biological therapy), disease activity at the last hospital visit was lower in our cohort compared to previous studies. The proportion of patients using steroids and cDMARDs remained stable during follow-up but the steroid dose declined over time. The presence of side effects of biological therapy was in line with data from previous studies. Despite lower disease activity and joint damage scores, our patients experienced more physical disability and pain compared to the general population and recent studies in adult JIA patients. Their fatigue, illness perception and coping levels were however comparable to those of patients with other rheumatic conditions. Compared to the general population, our cohort had a similar health-related quality of life, employment rate and social participation. Participation in sports was surprisingly high. Overall, we may conclude that the access to biological therapies for JIA patients seems to improve disease control, resulting in an overall good physical functioning as well as psychological well-being.
Disclosure of Interest: None declared

P072

MULTIDISCIPLINARY AND SYSTEMATIC CARE MODEL OF A TRANSITIONAL RHEUMATIC CLINIC IN MEXICO

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Introduction: The caregiver is the most active in caring for a child with a rheumatic disease, once the patient grow, the responsibility of care need to be passed to the adolescent. Transition programs in rheumatology have shown improving quality of life and disease activity.The best transitional care model in rheumatology is still uncertain.

Objectives: The aim of this study was to describe the process of design a program that provide an uninterrupted, multidisciplinary and coordinated attention to adolescents during transition from pediatric to adult services in Mexico

Methods: Between January and June 2017 we created the care model protocol according to three steps: **1. Creation a Multidisciplinary team.** A group of specialists were invited to participate. **2. Evaluation of transition skills of patients and caregivers**.The Spanish version of the Got Transition questionnaire was applied to youth and parents/caregivers, includes: “Transition Importance and Confidence”, “My Health” and “Using the Health Care System”. Analyzed using SPSSv.24, concordance were compared using Spearman’s test. **3. Establish a model of care**.We appraise variables which includes chronological age, maturity, medical status, adherence, independence, transitional issues, adolescent readiness, and availability of an adult physician.

Results: Step 1.Creation a Multidisciplinary team. The team was made up of three pediatric rheumatologists, two adult rheumatologists, two physical medicine and rehabilitation specialists, one child psychiatrist, two nutritionists, one clinical psychologist, one nurse and one social worker.**Step 2. Evaluation of transition skills of patients and caregivers.** 38 questionnaires were applied to 19 patients and their caregivers. Most of the youth were female (79%), with median age of 18 years. Juvenile Idiopathic Arthritis and Systemic Lupus Erythematosus were the most frequent.We observed that parents/caregivers reported less confidence about their child´s ability to change to an adults’ doctor. We also observed a low correlation (rho coefficient < 0.7) between the reported skills (in “My Health” and “Using the Health Care System” items) by youth and the parent/caregiver perception. **Step 3. Establish the model of care.** We established a three steps model: pre-transition, transition clinic and pos-transition, divided in eight phases. Each phase includes different administrative activities and abilities which must be met in order to continue with the next phase. (Figure 1)

Conclusion: The transition clinic that we presented represents the first step to establish a program to get selfcare capabilities in patients from a low-resource setting. Approaching in a multi-assessment manner, allowing personalized interventions.The transition model proposed is a possible intervention in developing countries.

Disclosure of Interest: None declared

P073

LIPID SPECTRUM IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS IN A PROSPECTIVE STUDY

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Introduction: It is known that in adult patients with rheumatoid arthritis (RA) the risk of cardiovascular disease associated with atherosclerosis increases by almost 50% compared to the general population. Atherosclerotic process usually begins long before its clinical manifestation. Similar studies are also conducted in the pediatric population of patients with JIA. However, how persistent these changes are in childhood is not fully understood.
Objectives: The aim of the study was to determine the state of the blood lipid spectrum in dynamics under the conditions of treatment of the disease.
Methods: 65 children (8-18 years) with JIA (oligoarthritis 61.5% and polyarthritis 38.5%) were examined twice in the dynamics with an interval of 1 year. Among patients females predominated (66.2% (43 girls) vs males 33.8% (22 boys)). The average duration of the disease was (74.1 ± 6.3) months. All patients received methotrexate (MTX), including in combination with TNF-α blocker -adalimumab 8 people (12.3%).The physical development of children was within the age population norms. Children with signs of chronic rheumatoid cachexia or overweight and obesity were not included in the development. Control group included 19 children, residents of the same region, of comparable gender and age.
General clinical assessment, disease activity and drugs were rated. Total cholesterol (TCh), triglycerides (TG), high density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL),very low-density lipoprotein cholesterol (VLDL)apolipoprotein B, ApoA-I and lipoprotein-α, atherogenic coefficient were evaluated. Results were analyzed using IBM SPSS Statistics for Windows with $p<0.05$ considered spastically significant.
Results: Analysis of the lipid profile in children with JIA showed that patients had significantly higher rates of TCh (5.0 ±0,1 vs 3.8 ±0.2 mmol/l in control group; $p <0.05$), TG(1.0 ±0,1 vs 0.7±0.1 mmol/l; $p <0.05$), LDLP cholesterol (3.0 ±0,1 vs 2.3±0.1 mmol/l) and cholesterol VLDL (0.5 ±0,0 vs 0.1±0.1 mmol/l, $p <0.05$), that led an increase in the level of atherogenic coefficient (2.4 ±0.2 vs 1.9±0.2 mmol/l, $p <0.05$) and the atherogenic dyslipoproteinemia's formation.
The study of the lipid spectrum of the blood in a year showed a reduction of the level of TCh in compare with first results (4.6±0,11 vs 5.0±0,11 mmol/l; $p <0.05$), TG(0.8 ±0,1 vs 1.0±0.1 mmol/l), LDLP cholesterol (2.7 ±0,1 vs 3.0±0.1 mmol/l) and uptrend of cholesterol VLDL (0.4±0.1vs 0.5±0.0 mmol/l), downward trend of the level of atherogenic coefficient (2.4 ±0.2 vs 2.0±0.2 mmol/l, $p <0.05$) that indicates positive changes of lipid's spectrum. The dynamics of lipid profile indices did not differ depending on the applied complex of therapy except from the atherogenic coefficient, which was significantly reduced during treatment with methotrexate and adalimumab (2.9 ±0.3 vs 1.6±0.1 mmol/l, $p <0.05$) and did not change with monotherapy by methotrexate (2.1 ±0.2 vs 2.0±0.1 mmol/l).
Conclusion: In children with JIA on the background of active inflammatory process revealed a traditional model of formation of atherogenic lipid spectrum of blood. Appointment complexes of basic therapy with methotrexate in combination with immune biological drugs leads tonot only reduce inflammation but and normalization blood lipid spectrum.
Disclosure of Interest: None declared

P074

PREGNANCY OUTCOME AND IMPACT ON DISEASE ACTIVITY IN YOUNG WOMEN AFFECTED BY JUVENIL IDIOPATHIC ARTHRITIS (JIA): A MONOCENTRIC EXPERIENCE IN A TERTIARY CENTRE IN MILAN.

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Introduction: Juvenile Idiopathic Arthritis (JIA) is a chronic inflammatory disease affecting children and adolescents, but many refractory forms continue into adulthood. In the era of biologic therapy we experienced an increasing willing for childbearing in many patients due to outcome improvement. Currently data regarding pregnancies in JIA patients are scarce.
Objectives: The aim of this study was to describe a monocentric case series of pregnant women affected by JIA and therefore to evaluate pregnancy outcome, the presence of major complication in newborns and the impact of gestation on disease activity.
Methods: All pregnant women affected by JIA referring to the Transition Clinic, Division of Rheumatology, G. Pini Institute of Milan, in a period of twenty years were enrolled in this study. Data regarding pregnancy outcome, drug exposure and disease activity were recorded. Gestational age, birth weight, APGAR score and newborn conditions were also collected.
Results: We collected data from 28 women affected by JIA and 35 pregnancies. All patients presented long standing refractory JIA. All patients were treated with DMARDs close to conception, of whom 85,7 % with bDMARDs.Exposure to biologic treatments included mostly anti-TNF agents (17 etanercept, 3 adalimumab, 5 golimumab and 2 certolizumab), but also other agents (3 rituximab,1 sarilumab). bMARD were used in monotherapy (28/30) or in association with csDMARDs (1 leflunomide, 1 methotrexate), hydroxycloroquine (3), or both (1 cyclosporine and hydroxycloroquine). All patients discontinued therapy at gravindex positive test or during first trimester. Pregnancies outcomes and data regarding drugs exposure are reported in table 1. One case of cleft palate was observed. We did not observe any major early or late complications in infants. Eight patients underwent intra-articular glucocorticoid injections during pregnancy, while 23 patients resumed therapy shortly after childbirth. One patient needed to start a biologic treatment after delivery.

Table 1 Summary of results

Total sample (n)	28
Pregnancies (n)	35
Age at conception, mean (S.D.), years	30,5 (4,8)
Duration of disease at conception, mean (S.D.), years	23,26 (6,4)
Time of discontinuation of therapy, mean (S.D.), week	7,48 (5,7)
Time of exposure to bDMARDs, mean (S.D.), days	51,58 (41)
Pregnancy outcome	3 voluntary interruption, 4 early miscarriage
Mean time at delivery (week)	37,47
Maternal complications	1 gestosis, 1 placental detachement
Neonatal complications	1 cleft palate, 2 premature births, 1 phenylketonuria

Conclusion: Despite a large amount of studies demonstrating the safety of anti-TNF during pregnancy, data in young women affected by JIA who become pregnant are still limited. In our monocentric experience, no greater number of unexpected complications were observed during pregnancy and also in children, compared to other autoimmune disease. Discontinuation of therapy increased the risk of flares confirming that EULAR recommendations for the use of biologics during pregnancy may be applied also in JIA patients.[1,2]

1-Bazzani C et al. Prospectively-followed pregnancies in patients with inflammatory arthritis taking biological drugs: an Italian multicentre study. Clin Exp Rheumatol. 2015 Sep-Oct;33(5):688-93.
2-Götestam Skorpen C, et al.The EULAR points to consider for use of antirheumatic drugs before pregnancy, and during pregnancy and lactation. Ann Rheum Dis. 2016 May;75(5):795-810.

Disclosure of Interest: None declared

P075

A SCOPING REVIEW TO SUPPORT THE DEVELOPMENT OF PGALSPLUS: A MULTI-PROFESSIONAL TOOL AND RESOURCE

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Introduction: Musculoskeletal (MSK) problems in children and young people (CYP) are common. The majority will present to healthcare professionals in the community but it can be challenging to identify those with serious disease requiring onward referral. pGALS (paediatric Gait, Arms, Legs and Spine) was developed as a simple, quick MSK clinical assessment to discern abnormal joints. Anecdotally, pGALS can detect joint and functional problems in CYP with other serious conditions but alone is unlikely to be specific enough.
Objectives: Our aim was to scope the literature about MSK assessments applicable to CYP used in clinical practice, focusing on evidence of validity in the context of diagnosis and assessment of Juvenile Idiopathic Arthritis (JIA), Mucopolysaccharidoses (MPS), Muscular Dystrophy (MD) and Developmental Coordination Disorder (DCD) to develop an extended pGALS (to be called pGALSplus).
Methods: Scoping review using the Newcastle University Library search tool and Google Scholar, and consulting NICE guidance and pathways. Search terms included dyspraxia, paediatric MSK assessment, screening tools, balance, rheumatology, assessment tools for MD, MPS, JIA. Studies cited within relevant articles uncovered through searches were also checked. The search was conducted between 1st October and 1st December 2018, publication date limited to post 1998, and all languages included unless translation was unavailable.
Results: 32 journal articles were deemed appropriate, describing specific assessment or screening tools in the context of diagnosis of our target conditions. Within DCD, motor co-ordination test batteries are part of specialist assessment, but are regarded as too lengthy for the purpose of screening; a questionnaire may be useful as a first-step diagnostic tool, along with an assessment of static balance (found to be significantly worse in children with DCD). In paediatric rheumatology, pGALS is the only validated screening tool to discern normal from abnormal joints. Other tools to assess health and wellbeing, disability and function are validated in the context of established disease only. For neuromuscular conditions the North Star Ambulatory Assessment is valid, reliable and practical as a functional assessment, and includes activities that are necessary to remain functionally ambulant. With regards to MPS, searches did not reveal specific MSK tests, but evidence suggests that skeletal malformations and joint problems were the most frequently presenting signs. pGALS performs well to identify abnormal joints with restriction within an MPS group.
Conclusion: This review supports the development of 'pGALSplus' to facilitate identification and assessment of CYP with potentially serious MSK disease. pGALSplus will be targeted at community-based clinicians and likely include physical examination, questionnaire(s) and appropriate adjuncts. Our group is currently developing pGALSplus, aimed at multi-professionals to describe feasibility and acceptability with educational and training resources.
Disclosure of Interest: None declared

P076

EXPLAINING JUVENILE IDIOPATHIC ARTHRITIS (JIA) AND ITS TREATMENT TO PAEDIATRIC PATIENTS USING PICTORIAL EDUCATION MATERIALS AND EASY-TO-READ TEXTS

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Introduction: In order to reach adherence to therapy, understanding of the disease and the treatment options are of utmost importance. Standardised validated pictorial education materials and texts in an easy-to- read language are an important tool to improve patients' knowledge of JIA.
Objectives: To develop specially designed graphic depictions complemented by standardised, easy-to-read textual information materials supporting a comprehensible informative medical dialogue with paediatric patients starting from school-age. The information material was tested in order to validate its comprehensibility.
Methods: The graphic depictions were designed by a graphic artist after detailed introduction to the topic by pediatric rheumatologists. Informative texts were written by pediatric rheumatologists and consecutively transformed to easy-to-read language to improve comprehensibility.
The materials are designed as a modular system allowing physicians to select individually the information needed for each specific patient.
The materials were tested for comprehensibility in healthy children and adolescents (controls) and in children and adolescents affected by JIA (patients). A standardised presentation to the probands was given by a student of psychology. Gain of knowledge about the illustrated items was quantified using a short questionnaire before and after the training session.
Results: 38 patients and 45 unaffected healthy individuals were tested in a standardised setting. In both groups gain of knowledge was significant (patients: $M = 2.58$, $SD = 2.13$, $t(37) = 7.48$, $p<0.001$, controls: $M = 3.53$, $SD = 2.14$, $t(44) = 11.08$, $p <0.001$).
Conclusion: Explanation of rheumatic diseases and therapeutic strategies is a time- consuming part of our daily practise. To avoid incomprehensible explanations in medical jargon, graphics with accompanied easy-to-read texts were created. Standardised presentation of the newly created materials resulted in a highly significant improvement of disease knowledge in patients and controls.
Our created graphics allow a fast instruction to the disease and its management that can also be performed by trained medical staff.
Disclosure of Interest: None declared

P077

TRANSITIONAL CARE IN RHEUMATOLOGY: CURRENT PRACTICE IN SWITZERLAND

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Introduction: About half of the children with rheumatic diseases need ongoing medical care during adolescence and adulthood. A good transition into adult rheumatology is essential. A structured transition process has therefore been recommended by the European League Against Rheumatism (EULAR) and the Pediatric Rheumatology European Society (PReS). However, these recommendations are not yet widely implemented.

Objectives: To assess the current practice of transitional care (TC) in Switzerland in relation to EULAR/PReS standards and to describe gaps and challenges in following the recommendations.

Methods: All ten pediatric Swiss rheumatology clinics offering transition service to adult care agreed to participate. In each clinic the responsible pediatric (n= 10) and adult (n= 10) rheumatologist were separately interviewed using a structured manual addressing EULAR/PReS transitional care standards.

Results: The median number of patients in follow-up in pediatric centers ranged from 50 to 363 (median 140). Fifteen of twenty rheumatologists reported to have a written procedure for TC. Three pediatric and two adult rheumatologists used a checklist. The start of TC varied between the ages of eleven and twenty. Adherence to medication and appointments followed by disease activity and age were rated as important for initiating TC. Topics discussed most often by rheumatologists during consultations were vocational issues (n= 17), effects of alcohol, smoking on disease/treatment (n= 16) medication (n= 16) and the impact of disease/treatment on daily life, sexuality, fertility and pregnancy (n= 15). All pediatric teams performed consultations with the patients alone whereas only two performed consultations with the parents alone. Median clinical experience of all rheumatologists in TC was ten (range 3 to 40) years. Only two centers had a transition coordinator. Slightly more pediatric (70%) than adult (60%) rheumatologists rated their TC process as good or very good. Only half of the adult rheumatologists, but all pediatric colleagues evaluated support provided for self-management skills of the young patients as good or very good. None of the physicians carried out formal evaluations of their TC, including patient satisfaction. The main barriers identified for further development of local TC included lack of funding and staff.

Conclusion: The current practice of TC in Swiss rheumatology centers is heterogeneous. About half of the rheumatologists were satisfied with their current practice, although no structured evaluation was conducted. To ensure that patients' needs are sufficiently addressed during transition further evaluation within the network of pediatric and adult rheumatologists is needed.

Disclosure of Interest: None declared

e-Poster viewing: e-health and digital health applications

P078

PEDIATRIC RHEUMATOLOGY RESEARCH IN SWEDEN; AVAILABLE PREREQUISITES, ONGOING PROJECTS, AND INTEREST FOR FUTURE REGISTRY STUDIES

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Introduction: The Swedish Pediatric Rheumatology Registry is a national quality register containing diverse clinical data of children with rheumatologic diseases. Despite this, incoming requests for its use in registry-based research are few.
Objectives: To survey ongoing pediatric rheumatology research in Sweden and to evaluate prerequisites and common interest for future registry studies.
Methods: An electronic questionnaire was sent by e-mail to practicing physicians in all 32 pediatric rheumatology units in Sweden.
Results: Thirty-three physicians from all pediatric rheumatology units in Sweden replied. Thirteen units (41%) reported 25 ongoing research projects in pediatric rheumatology, 20 (80%) of these were reported by physicans from university hospital units. The study designs included basic, pre-clinical and clinical studies performed locally or in national or international collaboration. Eight (25%) of the pediatric rheumatology units had local access to a biobank for sample storage. Most projects were JIA related, other approached Kawasaki disease, autoinflammatory diseases, Juvenile scleroderma, SLE and EDS. Only 5 (20%) of the studies used data from The Swedish Pediatric Rheumatology Registry. In order to improve the interest for registry-based research in Sweden, measures to improve registration habits, better information about research possibilities and guided research support were proposed. Suggested topics for future registry studies were validation of registry data, population based descriptive studies and national or international comparisons of patient reported outcomes, clinical care and treatment effects. The need of a better understanding on how to individualize treatment regimens was acknowledged. Likewise, a better feedback to enable evaluation of local activity and coherence to national recommendations was requested. Twenty-five physicians (76%) were interested to participate in a national research meeting in order to collaborate in planning for future registry studies.
Conclusion: The current activity of pediatric rheumatology research in Sweden was considerable, relatively widespread throughout the country and a subject for diverse study topics. Although a minority of ongoing studies included data from The Swedish Pediatric Rheumatology Registry, the interest in future national collaboration in registry-based studies was high.
Disclosure of Interest: None declared

P079

PRELIMINARY EVALUATION OF OUR NEWLY LAUNCHED SUB-SPECIALTY PEDIATRICS E CASE SERIES (SPECS) TO INCREASE PEDIATRICIANS' WATCHFULNESS REGARDING UNTOUCHED DISEASES IN CHILDREN IN AN INDIAN STATE OF GUJARAT

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Introduction:
There is very limited information and awareness about pediatric rheumatic and immunodeficiency diseases amongst primary physicians in Gujarat and to make this matter even worse, we are not having a single exclusive pediatric rheumatology and immunology center for a population of around 60 million.[1-3]

Objectives:
To measure an effectiveness of Subspecialty Pediatrics e-Case Series (SPeCS) in spreading awareness and alertness amongst pediatricians about rheumatic and immunodeficiency diseases in children.

Methods:
On 28th may 2020, I and my endocrinologist colleague decided to deliver weekly one e-class consisting of three real life case discussions from a single or two pediatric subspecialties .Duration of e-class was kept limited to 45 minutes. We propagated this idea for the next two days through various social media platforms to reach to a maximum numbers of pediatricians. Pre e-class evaluation forms were sent to the registered participants. First preliminary e-class was completed on 31st may 2020 which was a fusion of one endocrinology and three rheumatology cases. Post e-class feedback forms were sent to the registered participants. Second e-class was completed on 5th June 2020 which was again a fusion of endocrinology and rheumatology cases.

Results:
Table 1 showed overall response of first two SPeCS webinars

Parameter	1st e-class	2nd e-class
Invited Pediatricians	250	20
Registered Participants	89	14
Attendees	35	11
Feedback Form Responses 1. How would you rate an idea of SPeCS overall? 1. Do you agree that SPeCS would be relevant and useful in your day-to-day practice? 1. Do you wish to continue onward journey with us every Sunday? 1. Do you prefer to present your cases under SPeCS?	16 5 stars (87.5%) 4 star (12.5%) Agree (100%) Yes (100%) Yes (81.3%) No (18.7%)	Was not sent
Most common advice or comment	All the attendees were satisfied with the way of learning and presentation.	

Though the numbers of participants were less during first e-class but the feedbacks from the attendees were outstanding. Subsequently in a second e-class there was a wonderful response and social media feedbacks from all the participants. On 7th June 2020, SPeCS was officially launched with some innovative modifications under the aegis of Rajkot academy of pediatricians (AOP) in view of outstanding feedbacks given by the attendees. The next e-class would be planned under a

new name SPeCS-AOP Rajkot in a couple of weeks with more fascinating talks and cases from practicing pediatricians under a guidance of senior expert pediatricians and subspecialists from our region.

Conclusion:

SPeCS is proven to be successful in terms of spreading awareness and alertness amongst pediatricians about untouched diseases which are used to be missed easily in day to day practice. A new model would be definitely more beneficial for presenters, attendees, residents and ultimately our little patients.

Trial registration identifying number:

1.Review.Indian J Pediatr2010 Sep;77(9):993-6.doi: 10.1007/s12098-010-0134-x. Epub 2010 Sep 3.
The Place of Pediatric Rheumatology in India
Sujata Sawhney 1, Prudence Manners

2.Journal of Natural science,Biology & Medicine-2018
Clinico-epidemiological profile of pediatric rheumatology disorders in Eastern India
PratapKumarPatra, ManishKumar
Department of Pediatrics, All Institute of Medical Sciences, Patna, Bihar, India

3.International Journal of Advanced Medical Health & Research (JIPMER)
Pediatric rheumatology: An under-recognized subspecialty in India
Year : 2017 | Volume : 4 | Issue : 2 | Page : 47-53
AkhilaKavirayani1, SumaBalan2
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Disclosure of Interest: None declared

P080

DEVELOPMENT OF AN APP FOR THE MANAGEMENT OF AUTOINFLAMMATORY DISEASES USING AN INNOVATIVE PATIENTS-CLINICIANS CODESIGN APPROACH

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Introduction: Autoinflammatory diseases are rare conditions characterized by recurrent episodes of inflammation with fever associated to elevation of acute phase reactants and symptoms affecting mainly the mucocutaneous, musculoskeletal or gastrointestinal system. These diseases affect negatively the quality of life of patients and their families
Objectives: Aim of this project is to develop a tool able to ameliorate patients' management of the disease and to enhance patient-physician communication
Methods: In order to develop a tool based on real-life needs, we involved patients and caregivers since the initial phase of the project. A first workshop designed to capture their needs and desires was organized. Innovative co-design activities were performed through "Lego Serious Play™" (LSP) methodology. During a first phase of "divergence" 13 patients (from teen-agers to adults) affected by different AIDs (FMF, TRAP, CAPS, MKD) and 2 physicians where involved in the LSP activities. Participants were asked to describe, through LEGO and metaphors: 1) The disease, 2) Themselves in comparison with the disease, 3) Solutions and supports which could help them in managing the disease. After each step the participants presented their LEGO model and everyone was engaged in the discussion. The ideas collected during the three phases allowed to have, at the end of the workshop, a list of functionalities identified as necessary for the app to be developed, the so-called "Killer-Features". Due to the actual Sars-CoV-2 sanitary emergency the second phase of the project, aimed at presenting the participants the results of the first meeting and procede with the App finalization was performed through following web-based meeting and surveys in which the patients and caregivers actively participated
Results: In the first phase patients and caregivers participated actively expressing various needs, that we subsequently summarized in 4 main areas (table 1). In the second phase (still ongoing) they were further involved and their opinion taken into consideration for the User Experience and User Interface definition for the development of the Mobile App including the required functionalities (after a further activity of prioritization).

Area	Main request	N°
Patient's clinical information-diary	Fever attacks and symptoms registration Repository of health information	12 5
Community	Online chat, blog and forum patient to patient Direct connection with the physician	14 11
Personal agenda	Calendar for therapy, visits, exam scheduling Alerts (appointments, deadlines, reminders)	13 4
Clinical and practical information	Disease information (in medical and simple language) Legal information-patients' rights	20 7

Conclusion: our project shows that active involvement of patients and caregivers in the design of a mobile-App can be achieved through innovative approaches. The objective is to obtain an App tailor-made on the real patients' needs and a consequent high satisfaction and long-term adoption of the tool.

AKNOWLEDGMENT: Project promoted and funded by Novartis
Special thanks to the patients and parents of patients who participated in the project with enthusiasm, contributing to the definition of the App

Disclosure of Interest: None declared

e-Poster viewing: Genetics and environment

P081

ANALYSING SYMPTOMATIC FEMALE PATIENTS WITH LESCH-NYHAN SYNDROME

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Introduction: Lesch-Nyhan Syndrome (LNS) is an X-linked recessive disorder caused by a deficiency of the enzyme hypoxanthine-guanine phosphoribosyl transferase (HGPRT). This occurs due to mutations on the HPRT1 gene found on the X-chromosome. HGPRT deficiency causes a body wide build-up of uric acid leading to hyperuricaemia and hyperuricosuria. Symptoms of LNS include severe gout, kidney problems and neurological problems. One of the most striking features of LNS is self-mutilation (e.g. lip and finger biting). Since LNS is an X-linked recessive it is almost exclusively symptomatic only in males. Females which are heterozygous for LNS are usually asymptomatic, but they can experience increased levels of uric acid excretion and therefore may develop symptoms of hyperuricaemia (e.g. gout in later years). Few reported cases of LNS in females have been reported.
Objectives: The primary purpose of this paper was to summarise the phenotypic characteristics of symptomatic, female Lesch-Nyhan patients. A secondary objective was to identify the genetic causes of LNS in these patients.
Methods: To identify articles and case reports involving symptomatic female LNS patients, a search was carried out across 3 scientific databases. These were: Pubmed, Web of Science and the Library of Congress.
Results: 18 papers were identified where a female sufferer of LNS was present. A consistent theme emerged that if a female patient suffered from LNS they suffered a classical, complete LNS. All the patients described had decreased HPRT levels causing gout, neurological problems, and intellectual disabilities. The severity of LNS was generally consistent but we noticed one singular case where the symptoms were more severe. This patient presented with acute renal failure at 2 months. As expected, there was a strong genetic component in families of symptomatic female LNS sufferers. 13 papers mentioned more than one family member being affected by LNS. Most papers however showed that female sufferers of LNS had asymptomatic mothers or siblings. These unaffected family members all expressed the causative mutant alleles for LNS at similar frequencies to the affected family members in peripheral blood cells. All female LNS patients had a mutation on the gene where HGPRT is expressed as well as x-inactivation of the other normal HGPRT expressing allele. Finally, A minor link between being a twin and suffering from LNS also emerged.
Conclusion: In conclusion, our results show that female patients who develop LNS are fully symptomatic in a manner similar to their male peers. Furthermore, this review shows that for LNS to develop in a female two concurrent genetic events are required: a mutation at the specific disease gene and an inactivation of the corresponding normal allele. Finally, since there appeared to be a small link between twins and x-linked diseases then it could potentially be said that (as with many other reported cases of x-linked diseases), that the process responsible for monozygotic twinning may play a part to the emergence of LNS in females (potentially by triggering skewed X-inactivation).

Disclosure of Interest: None declared

P082

SLCO1B1 RS4149056 VARIANT AS THE PREDICTOR OF METHOTREXATE – RELATED GASTROINTESTINAL TOXICITY IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Methotrexate (MTX) administered at the dose 10-15mg/m^2 is currently recommended as the first-line therapy in most of juvenile idiopathic arthritis (JIA) subtypes. Gastrointestinal side effects are the most prevalent clinical demonstration of MTX toxicity, frequently leading to the discontinuation of otherwise effective treatment. Genetic variability within *SLCO1B1* gene has been associated with MTX efficacy and toxicity in paediatric patients with acute lymphoblastic leukaemia.
Objectives: The aim of our study was to determine the association between single nucleotide polymorphisms (SNPs) in *SLCO1B1* gene (rs4149056, rs2306283) on the disease activity and presence of MTX therapy side effects in patients with JIA.
Methods: One hundred children with JIA of all subtypes treated with MTX were recruited to the study. Demographic and clinical parameters were collected at the baseline of MTX therapy and on a control visit 4-6 months after starting MTX. SNP genotyping was performed using genomic DNA isolated from peripheral blood samples.
Results: *SLCO1B1* rs4149056 CT/CC variant was significantly associated with 4.5 times higher odds ratio of MTX gastrointestinal side effects occurrence (OR=4.55, 95%CI 1.37-15.13; p=0.0135) in comparison to wild-type allele.
Conclusion: *SLCO1B1* rs4149056 may become the determinant of MTX gastrointestinal toxicity in children with JIA.
Disclosure of Interest: None declared

P083

THE RELATIONSHIP OF EBV INFECTION WITH PAEDIATRIC AUTOIMMUNE DISEASES.

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Introduction: The Epstein–Barr virus (EBV) is a virus which can cause severe infections in patients with immunodeficiency due to its high incidence in the population, the possibility of latency and reactivation. For many years a connection with the triggering of autoimmunity has been postulated as well. The aetiology of autoimmune disease is multifactorial: including genetic, hormonal, immunological, environmental, and infectious factors. There are studies confirming the existence of an association of EBV infection with some autoimmune diseases but other studies fail to confirm the existence of any such relations. The presented study concerns children. Primary EBV infection in the majority of the population occurs in this group. In children, the time between primary EBV infection and the onset of autoimmune disease is the shortest.
Objectives: The purpose of this work is to examine the following two questions: 1. Is the history of EBV infection (measured as the presence of anti-EBV antibodies in the IgG class, in a titer considered positive) related to the frequency of selected autoimmune diseases in children (ICD10: E10.9, M08, N04.9, L52, M30.3, D69.3, D69.0, M35.0, M35.9, M35.8) 2. Is there a difference in the immune response among children with and without autoimmune disease?
Methods: Retrospective analysis of EBV VCA IgM, EBV VCA IgG ELISA serum test results of 939 patients hospitalized in a children's clinical hospital in Lublin in the years 2012-2017.
Results: As a result of the statistical analysis of the collected data, there was no relationship between the history of EBV infection and the onset of selected autoimmune disease. There is no statistical difference between EBV VCA IgG and IgM antibody levels in healthy children and in children with a diagnosis of autoimmune disease. No statistical differences were revealed between the groups when dividing them into younger and older children. Statistically significant lower levels of IgG antibodies were found in male subjects with autoimmune diseases compared to female subjects with autoimmune diseases ($Z (N = 227) = -2.08$; $p < 0.05$).
Conclusion: Our study did not confirm the relationship between EBV infection and the onset of autoimmune diseases in childhood. Studies focusing on infectious agents (especially in the paediatric population) are subject to many difficulties, including abnormalities in the production of post-infectious antibodies in young children, or the rare occurrence of autoimmune diseases in children. The issue of the EBV infection and the phenomenon of autoimmunity requires further study.
Disclosure of Interest: None declared

P084

CLINICAL AND MOLECULAR CHARACTERISTIC OF 13 PATIENTS WITH CACP SYNDROME

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Introduction: CACP syndrome (Camptodactyly, Arthropathy, Coxa vara, Pericarditis) is a rare autosomal recessive disease characterized by congenital or early onset camptodactyly, non-inflammatory arthropathy, pericarditis and progressive deformity of the proximal femur
Objectives: to describe clinical and genetic features of Russian patients with CACP syndrome
Methods: we evaluated clinical and radiological features and performed Sanger sequencing of PRG4 gene in 13 patients with CACP syndrome from 10 unrelated families.
Results: the disease most commonly starts with camptodactyly manifesting as the first symptom in 99% of cases (12 out of 13 patients) at the age of 1-2 years. In all the patients large joints were affected with symmetrical non-inflammatory arthropathy, joint swelling, restricted mobility and flexion contractures. Knee, elbow, and wrist joints were affected in 100% of cases, less often hip (61%), ankle joints and feet (69%) were involved. According to radiographic examination, deformity of the proximal femur occurred in 70% of cases; in 26% of patients intraosseous cysts of the ischial bone connecting to the hip join had been noted. Osteoporosis and pain were reported in 53.8% and 7.6% of cases, respectively.
All patients were initially treated as juvenile idiopathic arthritis. An average time from the disease onset to the diagnosis of CACP syndrome was 7.6 years.
CACP mutations were detected in 11 patients (85%); of those 6 patients had homozygous and another 5 – compound heterozygous deleterious PRG4 variants (Table 1). The most commonly found recurrent pathogenic alleles were c.1910_1911del (p.P637fs) and c.3462_3465del (p.T1155Lfs)

Table 1. Patients with PRG4 mutations

Patient ID	PRG4 mutation	Clinical manifestations
716	c.5_6insAT (p.A2fs); c.1910_1911del (p.P637fs)	Pericarditis,varus deformity of the femoral head
959,960	c.1910_1911del (p.P637fs); c.1910_1911del (p.P637fs)	intraosseous cysts of the ischial bone
965,966	c.2754_2758delGACAA (p.K918fs*10); c.3481delA (p.T1161Hfs*2)	Varus deformity of the femoral head
995,996	c.3684C>A (p.Y1228*); c.3684C>A (p.Y1228*)	Pericarditis
1010	c.1934_1935del (p.P645fs) c.3462_3465del (T1155Lfs)	Pericarditis,varus deformity of the femoral head
1078	c.2164C>A (p.P722T); c.2248G>A (p.A750T)	varus deformity of the femoral head
1393	c.3462_3465del (p.T1155Lfs); c.3462_3465del (p.T1155Lfs)	Pericarditis
1529	c.3462_3465del (p.T1155Lfs); c.3462_3465del (p.T1155Lfs)	varus deformity of the femoral head

Conclusion: the results complement the existing data on spectrum of clinical presentation and molecular defects associated with CACP syndrome
Trial registration identifying number: This work supported by the Russian Foundation for Basic Research (grant № 18-515-57001)
Disclosure of Interest: None declared

P085

ASSESSMENT OF THE RELATIONSHIP BETWEEN EPSTEIN-BARR VIRUS INFECTION AND THE ONSET OF JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic childhood disease of still unknown etiology. It is widely recognized that apart from the genetic factors, also environmental factors play a significant role in the disease pathogenesis. One of the potential factors which may influence the development of the disease is the Epstein-Barr virus (EBV) infection.
Objectives: The objective of the study was to define the relationship between the EBV infection and the onset of JIA.
Methods: The study estimated EBV infection markers: the number of EBV DNA copies in the peripheral blood mononuclear cells (PBMC) and the serum concentration of specific immunoglobulin (Ig) A, IgG and IgM against EBV antigens: viral capsid antigen (VCA), EBV early antigen (EA), and nuclear antigen 1 (EBNA-1) in 44 patients with JIA during the disease diagnosis, before initiating treatment, 23 children with different types of arthritis also during the disease diagnosis, before starting treatment, and in the control group of 44 children. Statistical methods were employed to estimate both the dependencies between the EBV infection and the development of JIA and other types of arthritis.
Results: In JIA group, a positive concentration of IgM anti-EA antibodies (Ab) (>1.2 U/ml) was confirmed in 11.4% of patients and a positive level of IgG and IgA anti-VCA Ab (>1.1 U/mL) was found in 43.1% and 2.3%, respectively. The presence of EBV DNA copies has been revealed in 25% of JIA patients, in 25.1% of patients with other types of arthritis, and in 36.4% of healthy children. The highest number of EBV DNA copies in 1 µg DNA in the JIA group amounted to 23.06, in the group with other arthritis types - 268.2, whereas in the control group – 23.3. The analysis of correlation between the EBV infection markers (both the antibodies against EBV antigens and viral load) and JIA activity, has not revealed any statistically significant dependency.
Conclusion: The relationship between EBV infection and the development of JIA has not been confirmed. The obtained results do not indicate a need for routine estimation of EBV infection markers among patients with JIA.
Disclosure of Interest: None declared

e-Poster viewing: Imaging

P086

COMPARISON OF CLINICAL AND ULTRASONOGRAPHIC EVALUATIONS IN JUVENILE IDIOPATHIC ARTHRITIS.

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Introduction: Juvenile idiopathic arthritis (JIA) is the most common chronic childhood rheumatic disease affecting 1 of 1000 children worldwide (0,07 - 4.01/1000). In paediatric rheumatology, ultrasound plays an important role in narrowing the differential diagnosis and can be useful for treatment monitoring. It is superior to clinical examination in diagnosing disease activity and in detecting subclinical disease.
Objectives: The aim of this study was to determine the frequency, localization and radiological characteristics of ultrasonographic findings in patients with juvenile idiopathic arthritis and to find and characterize the relationship with clinical data.
Methods: In a prospective study were analyzed 55 Children's Clinical University Hospital patients from Department of Rheumatology with proven or suspected juvenile idiopathic arthritis, between February 2019 and March 2020. Clinical data were collected – vitamin D level, CHAQ (Childhood Health Assessment Quietionnaire), physicinan, parent and/or patient visual analogue scale (VAS) assesment, JIA type and disease duration. Each patient underwent ultrasonography of 68 joints. Ultrasonography findings were evaluated in connection with the patient's current clinical condition, physician's assessment and the course of the disease.
Results: From 55 patients 41 (74.5%) were girls, 14 (25.5%) were boys. The youngest was 2 years old, the oldest was 17 years old. Mean age 11.82, median 13 (SD ± 4.66) years. RF- polyarthritis was 24 (43.6%), RF + polyarthritis 1 (1.8%), oligoarthritis 14 (25.5%), arthritis with enthesitis 10 (18.2%), psoriatic 2 (3.6%) and undifferentiated type 4 (7.3%). The mean age of onset was 9.7 years (SD ± 5.11). Compared to JIA type, there was a statistically significant relationship between JIA type and age at onset of the disease - early onset of oligoarthritis (Fisher's test, $p < 0.001$). Analyzing the association of JIA type with gender, a statistically significant (Fisher's test, $p < 0.001$) relationship was found between the higher incidence of RF-polyarthritis and female gender - 53.7% (boys 14.3%) and the incidence of enthesitis-related arthritis and male gender - 64.3% (2.4% for girls). Each patient underwent ultrasonography of 68 joints, for a total of 3,740, of whom 342 (9.1%) had symptoms in the patient, 277 (7.4%) were assessed by a physician, and 108 (2.9%) were diagnosed with ultrasonography (38.9% of those referred by a rheumatologist). Ultrasonographic changes were recorded in 42 (76.4%) study patients. It was found that changes were most often found in knee joints - 43 (39.8%), feet - 24 (22.2%) and wrists - 15 (13.9%), no changes were found in shoulder joints. The relationship between the finding of a VAS physician, the US, and the reason for the physician's referral was assessed in knee joints. Changes were found in all patients with swelling, patients with marked pain are more likely to experience synovitis and / or tendon changes in the US, no change was found in stress pain in the US. If the physician's VAS (visual analogue scale) > 3, there is a tendency for changes in the US. US changes were found in all patients with wrist pain and / or mobility impairment in combination with physician's VAS > 3. In ankle physician's VAS> 3, in combination with pain and / or swelling, increases the incidence of US changes.
Conclusion: The most affected joints by ultrasound were knee, wrist and feet, where also found correlations with a physician's assessment, which could improve the assessment of the need for US. The study looked at how to deal with unclassified US changes – effusion up to 2 mm thick, concluding that these changes are not significant and can't be interpreted - this aspect should be considered so that communication between the ultrasonographer and the rheumatologist where understandable and clear.
Disclosure of Interest: None declared

P087

USEFULNESS OF WHOLE-BODY MAGNETIC RESONANCE IMAGING IN PEDIATRIC RHEUMATOLOGY

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Introduction: Whole Body Magnetic Resonance Imaging (WBMRI) is a multiregional imaging technique able to study the entire body, suitable to investigate the extent of multisystem diseases without exposure to radiation, and offers a large coverage of the skeleton with a high sensitivity to bone alterations.
Objectives: The **aim** of our study is to evaluate the role of WBMRI in the work-up of children with non specific musculoskeletal features, and non indicative laboratory and instrumental data, suspected to have a rheumatologic disease.
Methods: We retrospectively analyzed medical records, including laboratory tests and radiological data, of 34 children who have been evaluated in our Pediatric Rheumatology Department from 2014 to 2019, due to non-specific musculoskeletal manifestations, and for which a WBMRI was prescribed.
Results: We included 34 children, 19 females and 15 males, median age 10 years (range 2-17 years), with the following clinical features: diffuse arthralgia (12 children), persistent fever (2 children), persistent fever and diffuse arthralgia (20 children). Serologic inflammatory markers resulted increased in 29 patients out of 34. Twenty-five children underwent a radiological examination (X-Ray and/or ultrasound) before WBMRI, all with a negative/uninformative result. WBMRI was performed 3-6 weeks (median, 3.5 weeks) after the initial presentation of symptoms.
In 21 children out of 34 (61.7%) WBMRI revealed abnormalities that supported the final diagnosis: 12 chronic recurrent multifocal osteomyelitis (CRMO), 2 polyarticular JIA, 2 infectious osteomyelitis, and primary bone lymphoma, scurvy, hypophosphatasia, Jaffe-Campanacci syndrome, eosinophilic granuloma (one each).
WBMI resulted silent or uninformative in the rest of the patients, in whom the final diagnosis was pain amplification syndrome (2 cases), malaria (1 case). Five children spontaneously recovered without a specific diagnosis was made, while in 4 cases fever persisted and were labeled as FUO.
Conclusion: The experience in our paediatric rheumatology clinic suggests that WBMRI is a helpful tool in situations characterized by non specific constitutional and musculoskeletal manifestations, in which the conventional work-up findings are negative or uninformative. WBMRI has proven to be useful both in the definition of some specific diagnosis, and in their differential diagnosis. In our experience, CRMO resulted the disease that mostly benefits from its use, allowing the early detection of lesions and defining their exact number and distribution.
Disclosure of Interest: None declared

P088

A NEED TO TRAIN PAEDIATRIC RHEUMATOLOGISTS IN MUSCULOSKELETAL ULTRASOUND SCANNING. HOW DO WE MOVE FORWARD?

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Introduction: Only a few paediatric rheumatologists in the UK use musculoskeletal ultrasound scan (MSK-USS) in their daily practice.
Objectives: To explore the demand for a musculoskeletal ultrasound (MSK-USS) training module for paediatric rheumatology consultants and trainees.
Methods: A questionnaire was sent to paediatric rheumatologist consultants in the UK and paediatric rheumatology trainees. The questionnaire explored; current use of MSK-USS, opinion about benefits of MSK-USS done by clinicians, and interest and needs for training.
Results: 40 out of 45 paediatric rheumatologists replied (response rate of 89%) and 7 out of 14 specialist trainees responded (response rate of 50%).
All of the respondents used MSK-USS performed by radiologists. MSK-USS and MRI scans were requested equally frequent, median 4-7/month. 80% (n=32) consultants and all paediatric rheumatology trainees felt that MSK-USS performed by a clinician in clinic would benefit their patients. Majority stated that for urgent cases, it could take up to 2 weeks in their centre for a departmental USS to be done and reported. Only 32.5% (n=13) could arrange MSK- USS on the same day for urgent scans. 70% (n=28) of the clinicians and trainees have access to an ultrasound scanner. Majority of clinicians expressed their enthusiasm (median of 80%) for an interactive paediatric rheumatology musculoskeletal ultrasound online module combined with a platform in which images and clips can be uploaded and discussed. 100% (n=7) of trainees were keen to learn MSK-USS as part of their training and majority felt that they could dedicate regular time for it alongside their other clinical duties.
Conclusion: In summary, MSK-USS is a tool commonly used in paediatric rheumatology. MSK-USS performed by the clinician is seen as beneficial for the patient by the majority, but a small group reports reservations which need to be addressed. There seems to be a demand in the UK for a training module in MSK-USS in paediatric rheumatology.
Disclosure of Interest: None declared

e-Poster viewing: Immunodeficiency and infection related arthritis

P089

INSIGHT INTO CLINICAL CROSS TALK BETWEEN RHEUMATIC AND IMMUNODEFICIENCY DISEASES IN CHILDREN

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Introduction:
There are many primary immunodeficiency diseases which present with either musculoskeletal or autoimmune features. It is vital to detect subtle clinical clues in such cases for a complete management.

Objectives:
To unveil features which indicate primary immunodeficiency in paediatric rheumatic conditions.

Methods:
I included eight paediatric patients with suspected primary immunodeficiency diseases (PIDs) according to 2019 update of the IUIS Phenotypical Classification[1] who were seen at Dev Children's Hospital between January 2019 and December 2019. My collected data included demographics, clinical presentation and laboratory results.

Results: Average age of children (6 boys and 2 girls) in our group was 5.3 years.
Table 1 showed characteristics of eight paediatric patients with suspected PIDs in rheumatic conditions in children
(Number of '+' indicate number of patients in respective group)

PID groups (N=number of patients)	Immunodysregulation- syndromes (1)	Phenocopies of PID (1)	Immunodysregulation HLH (2)	Cryopyrinopathy (3)	Auto inflammatory syndromes (1)
Joint involvement	+			+++	+ (CRMO)
Cutaneous Lupus		+	++		
MAS/ HLH	+				
Enteropathy					
Type 1 diabetes	+				
Hypoparathyroidism	+	+			
Rash			++	+++	+
Serositis			++	+	
CMC		+			
Recurrent skin , ear & sinus	+		+		
Syndromic face	+				
Severe dental caries	+	+			

Recurrent mouth ulcers Recurrent and/or predictable episodes			+ 	 ++	+ +
Significant family history	+	+	++	++	+
Suspected PID/s	IPEX[1,2] LRBA[1,3] CTLA4[1,3] STAT1 GOF[1,4]	CMC[1] APECED[1]	pHLH[1,5]	MWS[1]	Majeed sydrome[1]
Systemic inflammation Ig levels Flow Cytometry	 Wnl High CD45 Very high CD25	 wnl nd	++ wnl nd	+++ nd nd	 wnl nd
Genetic screen Complement levels EBV PCR	Pending nd nd	Pending wnl nd	Pending (one patient died) wnl Negative	Negative in two patients nd nd	Negative nd nd

(Abbreviations: MAS = Macrophage Activation Syndrome,CRMO=Chronic Recurrent Multifocal Osteomyelitis, IPEX= Immunodysregulation PolyEndocrinopathy X-linked, LRBA= Lipopolysaccharide Responsive Beige-like Anchor protein, CTLA4= Cytotoxic T-cells Associated protein,CMC=Chronic Mucocutaneous Candidiasis, HLH= Hemophagocytosis Lymphohistiocytosis,, APECED= Autoimmune–polyendocrinopathy-candidiasis-ectodermal dystrophy,wnl=within normal limits, nd= not done, EBV= ebstein barr virus, MWS= Muckle Wells Syndrome)
There are some financial and laboratory limitations to evaluate such patients completely at our place.

Conclusion:
All above cases reemphasize the need for an extremely detailed history, family history, pattern recognition and high index of suspicion in paediatric rheumatology.. In our cohort, the features like arthritis pattern different than JIA, early age of onset for autoimmune features, endocrine manifestations, significant family history, recurrent inflammatory episodes and recurrent and/or severe and/or unusual infections at unusual site were some of the important clues which inspired me to suspect PIDs in these patients.
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Disclosure of Interest: None declared

e-Poster viewing: Immunoregulation and basic science

P090

EARLY DIAGNOSIS OF THE AUTOIMMUNE LYMPHOPROLIFERATIVE SYNDROME (ALPS)/ALPS-LIKE SYNDROME IN PATIENTS WITH UNDEFINED AUTOINFLAMMATORY OR AUTOIMMUNE DISORDERS: A MULTIVARIATE ANALYSIS APPROACH IN A PEDIATRIC RHEUMATOLOGY TERTIARY CENTER

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Introduction: ALPS is a rare disorder due to a defective apoptotic mechanism leading to abnormal lymphoproliferation and autoimmunity. It is characterized by lymphoadenopathy and hepatosplenomegaly with autoimmune haemolytic anemia, neutropenia or thrombocytopenia. The disease is difficult to identify in the early phase when it may be misdiagnosed. Elevated TCR alpha-beta CD4-CD8- lymphocytes (double negative T lymphocytes DNT) together with hypergammaglobulinemia, high levels of IL10, Il18, vitamin B12 and soluble Fas ligand have been suggested as the main ALPS hallmarks (1). Therefore, a specific flow cytometry panel (number of DNT cells, the ratio of CD25+CD3+ to HLA−DR+CD3+ cells, increased B220+ T-cells, and decreased CD27+ memory B cells) has been proposed to serve as a diagnostic screen for ALPS (2).
Objectives: to test the usefulness of Oliveira's diagnostic criteria and of a specific panel of lymphocyte subsets (LS) for the identification of ALPS in children referred for a suspected autoinflammatory or autoimmune disorder
Methods: The clinical data of patients referred to the pediatric Rheumatology Unit of the Istituto Giannina Gaslini Hospital for a suspicion of autoimmune or autoinflammatory condition from October 2015 to April 2018, were retrospectively analyzed. Data on clinical manifestations, laboratory workup, genetic analysis and treatments were collected. Flow cytometry including CD4-CD8-TCR αβ+ T lymphocytes (DNT), CD25+CD3+, HLA−DR+CD3+ cells, B220+ T-cells, and CD27+ memory B cells, was included among the screening panel. Data were analyzed with an univariate logistic regression analysis, followed by a multivariate analysis
Results: 475 patients were retrospectively analized. 211 patients not fulfilling the inclusion criteria were excluded. All remaining patients were classified as follows: i)Autoimmune diseases and vasculitis 26 pts ii) JIA 35 pts iii) Monogenic systemic autoinflammatory disease 27 pts; iv)PFAPA 100 pts; v) Systemic Undefined Recurrent Fever 45 pts; vi) Undetermined-SAID:15 pts; vii)ALPS 16 pts. The flow cytometry panel showed elevated DNT in all ALPS patients, even if a slight positivity was found also in other patients. The ratio CD3CD25+/CD3HLADR+ and TCRαβ+B220+ lymphocytes, were significatively altered in ALPS, but when compared to other diseases only TCRαβ+B220+ lymphocytes showed statistical significance ($p<0.0005$). The multivariate analysis revealed 5 clinical/laboratory parameters positively and significantly associated to ALPS: splenomegaly, female gender, arthralgia, elevated DNT and TCRαβ+B220+lymphocytes
Conclusion: The use of specific LS in patients with undefined autoinflammatory or autoimmune disorders may identify a subgroup of patients with ALPS. Oliveira's criteria where useful in the identification of patients, but the cut-off identified for DNT is not probably strong enough to identify real ALPS patients when used in a pediatric population affected with different immune-mediated conditions.

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CMC and LOM equally contributed to this work
Disclosure of Interest: None declared

e-Poster viewing: JIA (oligo, poly, psoriatic)

P091

COEXISTENCE OF AUTOIMMUNE DISEASES IN DIFFERENT SUBTYPES OF JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in children. With the exception of the systemic JIA it is considered an autoimmune disease.
Objectives: To evaluate whether there are differences in the prevalence of coexisting autoimmune diseases in children according to the different subtypes of juvenile idiopathic arthritis.
Methods: A retrospective, single small center study was performed. All patients diagnosed with JIA who were examined at our pediatric clinic in the last 10 years were enrolled. JIA was classified according to the International League Against Rheumatism (ILAR) criteria. Data was collected from patients' medical records.
Results: A total of 111 patients were included. The results are presented in Table 1.
Table1

Autoimmune disease	Oligoarthritis N=55 (49.5%)	Polyarthritis N=15 (13.5%)	Enthesitis related arthritis N=22 (19.8%)	Psoriatic arthritis N=11 (10%)	Systemic arthritis N=5 (4.5%)
Uveitis	8 (14.5%)	1 (6.7%)	3 (13.6%)	1 (9%)	0
Autoimmune thyroid disease	2 (3.6%)	0	0	0	0
Celiac disease	2 (3.6%)	1 (6.7%)	0	0	0
Henoch-Schonlein vasculitis	1 (1.8%)	0	0	0	0
Idiopathic thrombocytopenic purpura	1 (1.8%)	0	0	0	0
Psoriasis	0	0	0	3 (27.3%)	0
Inflammatory bowel disease	1 (1.8%)	0	0	0	0

The mean age was 8.1 years. 71 patients (64%) were female. 3 patients (2.7%) were diagnosed with undifferentiated arthritis. In our cohort none of the patients had rheumatoid factor positive polyarthritis. 1 patient with systemic JIA developed macrophage activation syndrome (MAS). 28 patients (26.1%) presented with a family history of autoimmune disease.
The most common coexistent autoimmune disease was uveitis, which was most commonly present in patients with oligoarthritis and enthesitis related arthritis. Associated autoimmune diseases were most frequent in patients with oligoarthritis whereas patients with systemic and undifferentiated arthritis had none of them. This confirms the hypothesis that systemic JIA is an autoinflammatory and not an autoimmune disease.
Conclusion: Our study demonstrated that autoimmune diseases are frequently coexistent in children with JIA, especially in patients with oligoarthritis. Therefore, all patients with JIA and especially those with oligoarthritis should be regularly screened for associated autoimmune diseases.

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Disclosure of Interest: None declared

P092

COVERAGE AND FACILITATORS OF INFLUENZA VACCINE UPTAKE AMONG JIA PATIENTS IN GREECE

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Introduction: Children with rheumatic diseases are considered as a population at risk of severe influenza disease and are therefore targeted for vaccination.Nonetheless, influenza vaccine coverage among JIA patients is still unclear.
Objectives: We investigated knowledge,attitudes& practices about influenza vaccine uptake among caregivers of children with JIA in Greece,aiming to depict the current situation and identify barriers and determinants to improve influenza vaccination rate.
Methods: This was a dual-centre cross-sectional study that took place across Pediatric Rheumatology Units in Athens,Greece.A detailed questionnaire about knowledge,practices and attitudes regarding influenza vaccination was disseminated among JIA caregivers.Chi-Square was used to explore factors associated with vaccine uptake& the significance level was set at $p \leq 0.05$.
Results: A total of 65 caregivers(72% females) with a mean age of 42.1years(SD=7.6) participated.Country of origin was Greece(75%),followed by Albania(19%). The majority of the participants were employed(67.7%),married(87.7%) and held a secondary education degree(42%).Principal diagnosis was polyarticular JIA(29%),followed by oligoarticular JIA(26%),while 14% of caregivers were unaware of the child's diagnosis.JIA patients' mean age was 9.8 years(SD=3.8) with a mean disease duration of 4.7years(SD=3.3). Most of them were on systemic treatment(88%). Of note,74% were fully vaccinated according to national vaccination schedule and 80% had received influenza vaccine in the past (median:4 times),while only a patient had previously experienced vaccine-related adverse event.
A total of 46 children(71%) were vaccinated against influenza during the current season(2019-20) and in 96% the disease status was stable.Most participants were informed by their pediatric rheumatologist(65%) and/or their pediatrician(51%).The highest vaccine uptake was recorded among Greek participants(83%),while only 33% of Albanian caregivers vaccinated their children($p<0.05$).Caregivers of secondary or tertiary education were more likely to vaccinate their children(81.5% & 80.8% respectively) compared to those with elementary education(25%)($p<0.05$).All children with psoriatic JIA were vaccinated,while children whose caregivers did not know the diagnosis reported the lowest vaccine uptake(11.1%)($p<0.05$).Disease duration was not related to vaccination rate.Among vaccinators,93.5% were under systemic treatment,81% were fully vaccinated according to national vaccination schedule and 96% of them had been vaccinated during the previous years($p<0.05$). Caregivers who were informed of influenza vaccine recommendation by medical staff were more likely to vaccinate their children against influenza in the current season(78.5%,$p<0.05$).
Among non-vaccinators,78.9% did not have the chance to discuss their concerns with a specialist.Being uninformed of the need to immunize against influenza(52.6%) was the major reason for non-vaccination,while few caregivers reported fear of disease flare and not being aware of requiring flu immunization on an annual basis(10.5% respectively).Caregivers suggested that informing in advance(71%) and organizing national campaigns(63%) may improve vaccine uptake in the future,while most of them(71%) disapproved reminder calls/sms.
Conclusion: Influenza vaccine uptake in JIA patients in Greece is moderately high.Those previously vaccinated and those fully vaccinated according to national vaccination schedule were more likely to be vaccinated during the current season.Higher education, thorough informative discussion and notifying families in advance may address fears and lead to universal vaccine coverage in children with JIA and other rheumatic diseases.
Disclosure of Interest: None declared

P093

EFFECTIVENESS AND SAFETY EVALUATION OF ETANERCEPT IN CHILDREN WITH JUVENILE PSORIATIC ARTHRITIS

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Introduction: Juvenile Psoriatic Arthritis (JPsA) is presented in 4 - 9% of children with juvenile arthritis (1,2). Biologic therapy, particularly etanercept, is proved to be effective and safe in the treatment of Psoriatic Arthritis in adults (3). However, little evidence exists in pediatric patients.
Objectives: to study the effectiveness and safety of etanercept in patients with JPsA.
Methods: open-label, single-center, prospective, observational (2012-2019) cohort clinical study included 18 patients (2-13.0 y/o) who met Vancouver and I/E criteria and received etanercept SC (0.8 mg/kg QW, max 50 mg per week) in combination with methotrexate (10-15 mg/m^2 QW).
Effectiveness evaluation was performed at months 6, 12, and 18 after treatment initiation with results reported on an intention-to-treat group. To assess articular manifestations of JPsA, we applied ACRpedi criteria, and BSA and PASI scores to estimate the surface area of involved skin and severity of psoriasis.
Results: We observed 18 patients with JPsA aged from 2 to 13 years, who were initiated by etanercept.
The clinical and demographic characteristics are presented in Table 1.

Table 1. The clinical and demographic characteristics of patients with JPsA before etanercept therapy (n=18)

clinical and demographic indicators	**M ± σ / Me (Q1-Q3)**
Girl/Boy Ratio	12:6 (2:1)
Average age, years Duration of the disease, years	7,58 ± 3,7 3,0 (1,4-6,6)
No. active joints No. joints with LOM	8,0 (5-16,5) 9 (5,75-18,25)
PGA of disease activity, mm	70 ± 15
Parent's global assessment of the child's pain, VAS	71,5 (65-90)
CHAQ	1,34 (1,1-1,68)
Psoriasis BSA, % PASI score	7,0 (4-13) 5,7 (3-8,2)
ESR, mm/h	28,0 (20,75-40)
LOM - limitation of motion, PGA - physician's global assessment; VAS - visual analog scale, CHAQ - Childhood Health Assessment Questionnaire; BSA - body surface area; PASI - Psoriasis Area Severity Index, ESR - erythrocyte sedimentation rate; CRP - C-reactive protein.	

In patients with JPsA who received a combination of etanercept with methotrexate, at month 6 ACRpedi NoResp/30/50/70 was 5.56/94.4/55.56/5.56%. ACRpedi 90 and ACRpedi 100 at month 6 were not achieved.
At month 12 - ACRpedi 30/50/70 was 94.4/88.9/61.1%. ACRpedi 90 and ACRpedi 100 were 11.1% and 5.56%, respectively. Drug-induced remission at month 18 was 11.1%.
At month 18 - ACRpedi 30/50/70 was 77.8/77.8/72.2%. ACRpedi 90 and ACRpedi 100 were 33.3% and 11.1%, respectively. Drug-induced remission at month 18 was 33,3%.
The BSA at months 6, 12, and 18 was 4.9 (1.0-7.0)%, 1.5 (0.75-3.15)%, 0.7 (0.5-1.0)%, respectively. The PASI 75, PASI 90 and PASI 100 at months 6 were 38.5/13.4/7.7%, at month 12 – 76.9/53.8/15.4%, and at month 18 – 69.2/61.5/23.1%, respectively. Drug-induced remission of psoriasis at month 18 was 23.1%.
No serious adverse events occurred during the study.
Conclusion: our clinical study showed the effectiveness and safety of etanercept in JPsA patients with active articular manifestations and psoriatic lesions.
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Disclosure of Interest: K. Aleksanyan: None declared, E. Zholobova Speaker Bureau of: Pfizer, AbbVie, Novartis, Roche., S. Chebysheva: None declared

P094

GROWTH PATTERN IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Growth patterns may be impaired in patients with juvenile idiopathic arthritis (JIA).
Objectives: To evaluate the growth parameters of patients with JIA depending on various treatment regimens in identifying the causal factors of growth disorder.
Methods: 142 JIA patients (91 girls and 51 boys) aged 3 to 17 years were examined. All patients were divided into 2 groups depending on the therapy type. I group consisted of 70 children treated with methotrexate (MTX) (7 of them had systemic form, 29 – oligoarticular and 34 – polyarticular). II group included children treated with biological DMARDs (bDMARDs) (n=72, 17 patients with systemic form, 26 – oligoarticular, 29 – polyarticular). 23 patients were treated with tocilizumab, 47 patients with adalimumab and 2 patients with etanercept. Mean age in I group was 10.4 ± 0.5 years, in II group – 11.4 ± 0.4 years; mean disease duration in I group – 4.2 ± 0.4 years, in II group – 5.1 ± 0.4 years respectively. 34 patients from II group achieved clinical pharmacologic remission in contrast to only 9 patients from I group. To assess the impact of disease activity on patient's growth, we used a total activity index (TAI) – cJADAS-27 (4 components of the Juvenile Arthritis Disease Activity Score for 27 joints) for the last 12 months. We evaluated the growth velocity (GV) expressed in % for the previous year regarding the appropriate age- and gender values and body mass index (BMI). Some patients underwent hand X-ray to assess bone age. Insulin-like growth factor-1 (IGF-1) in blood serum were measured in children with growth delay. Quantitative indicators distribution is given as a median [5th; 95th procentile], the calculations were carried out using the Mann-Whitney U test, and the correlation was studied by multiple regression analysis.
Results: Our results demonstrated that there was no growth delay in patients with an oligoarticular form of JIA. 12 patients (8.5 %) of both groups were diagnosed with growth delay (height < -1 SD), in 6 patients with systemic form and 6 patients with a polyarticular form of JIA. GV in I group -10 [-91; 133] in case of polyarticular form, 10 [-41; 32] in case of oligoarticular form. GV in II group – 20 [-23; 240] and 12 [-10; 62] respectively. The relative growth velocity for the previous year was significantly higher in patients with both oligoarticular ($U = 225.5$, $p = 0.009$) and polyarticular ($U = 222.5$, $p = 0.0001$) forms of disease when used bDMARDs. In a group of patients on bDMARDs, the relative growth velocity is 2% higher in patients with oligoarticular form and 30% higher in patients with polyarticular form, compared with the use of MTX alone. 19 patients (13.4%) had an underweight, 8 patients (5.6%) were overweight, and 7 patients (4.9%) had obesity. Most overweight or obese children did not have a history of long-term use of corticosteroids (CS). 4 patients with height delay < 2-3 SD and 1 patient with height delay > 3 SD were ahead of the bone age by 4 years. In 17 children (10 of whom had height delay), IGF-1 in blood serum was age-appropriate. The TAI has a significant inverse correlation between the growth index expressed in SD ($\beta = -0.4$, $p = 0.005$) and GV ($\beta = -0.62$, $p = 0.000009$). Thus, the higher is the total disease activity index, the greater is the growth velocity delay. There was no detected correlation between these indicators and the disease duration, the age of onset, the total dose of CS and cJADAS-27 at the moment of the study.
Conclusion: The disease activity affects growth pattern. The relative growth velocity for the previous year was significantly higher in patients when used bDMARDs.
Disclosure of Interest: None declared

P095

DYNAMICS OF VITAMIN D STATUS IN CHILDREN WITH JIA

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Introduction: There is well known the role of vitamin D as an immune and inflammatory mediator in autoimmune diseases, including chronic arthritis, its low serum concentration is associated with an increase of the synthesis of anti-inflammatory mediators and, accordingly, the activity of autoimmune diseases.

Objectives: The purpose of this study was to determine the status of vitamin D in children with juvenile idiopathic arthritis (JIA) depending on the age of the patients, the clinical variant of the disease and therapy in the dynamics of observation during the basic therapy and additional intake of vitamin D.

Methods: The main group included 39 patients with JIA corresponded to the ILAR criteria. Female patients predominated (74.36%, p <0.05). The average age of patients was 10.8±4.6 years. The results were analyzed depending on patient's age (up to 6 years, from 6 to 10 years, from 10 to 14 years and older than 14 years), variant of the disease (oligoarthritis, polyarthritis, undifferentiated arthritis) and basic therapy (the presence of methotrexate or his absence). The study was conducted twice: the first - in the absence of additional intake of vitamin D, the second - after 6 months of supplementation of 2000 IU of vitamin D. The control group consisted of 20 peers who did not take vitamin D. Serum 25-hydroxyvitamin D [25 (OH) D] levels were measured using chemiluminescent method (Cobas 6000, Roche Diagnostics, Switzerland).

Results: The average serum vitamin D level was 22.26±2.53 ng/ml, that was significantly lower than in children in the control group (28.67±2.38 ng/ml; p<0.05). No gender dependence was found. A correlation was established between the age of patients and the level of vitamin D. Children under 6 years of age had a significantly higher vitamin D status compared than older children (p<0.05). The dependence of the concentration of vitamin D in serum on the variant of the disease in children during the initial study was not found.

An analysis of the vitamin D content in a re-examination showed that male patients had a positive trend compared with female patients; in young children compared with older patients than 14 years; an oligoarthritis compared with other variants; in the presence of basic therapy with methotrexate compared to therapy without it (table).

Table. Dynamics of vitamin D levels in children with JIA, M±m, ng/ml

Sings	vitamin D level		Significance of differences
	in the absence of additional intake of vitamin D	after taking of vitamin D	
girls, n=29	22,46±3,13	26,30±4,27	p>0,05
boys, n=10	21,69±4,83	28,89±8,80	**p<0,05**
before 6y,n=15	24,51±2,01	31,13±2,87	**p<0,05**
6-10 y., n=10	22,46±2,47	26,25±3,52	p>0,05
10-14 y., n=9	20,27±2,61	25,39±3,71	p>0,05
older 14y.,n=5	18,68±3,50	19,45±4,98	p>0,05
oligo, n=17	24,27±1,89	34,47±2,30	**p<0,05**
poly, n=12	21,11±2,25	20,59±2,74	p>0,05
undifferentiated arthritis, n=10	20,22±2,46	22,23±3,01	p>0,05
MTX +	21,53±7,16	30,32±9,99	**p<0,05**
MTX -	22,42±2,86	26,37±3,42	p>0,05

Conclusion: In patients with JIA there was an insufficient level of vitamin D which increased after an additional intake of 2000 preparations of vitamin D for 6 months. Girls, children over 14 years old, patients with non-deferred arthritis and polyarthritis as well as patients who did not receive basic methotrexate therapy, had insufficient level recovery of vitamin D, that requires a review of the regimen of additional vitamin D intake and basic therapy in these categories of patients.

Disclosure of Interest: None declared

P096

CORRELATION BETWEEN SERUM CALPROTECTIN (S100A8/A9) LEVELS AND DISEASE ACTIVITY STATUS IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: S100A8/A9 (calprotectin) has been widely studied as candidate biomarker for predicting disease activity and treatment response in rheumatic diseases. Its high levels may also predict disease flares in systemic juvenile idiopathic arthritis (JIA). In clinical practice, ultrasound (US) could be a useful tool to define the disease activity status. To our knowledge there are no published articles to examine simultaneously the correlation between S100A8/A9 levels, clinical and US assessment in JIA.

Objectives: To explore the association between S100A8/A9, clinical and US assessment in JIA patients.

Methods: Patients with JIA were blinded assessed by clinical examination and ultrasound and serum levels of S100A8/A9 were measured by chemiluminescence solid phase assay. Ultrasonographic B-mode and Power Doppler assessment of 44 joints for each patients were performed. Clinical disease activity was evaluated using Wallace criteria.

Results: Thirty (18 F) consecutive patients with diagnosed non-systemic JIA were prospectively included in our study (Table 1). S100A8/A9 levels were also measured in age matched healthy controls. Median age at disease onset was 10.6 yrs (mean 10.8, range 2–16) and mean disease duration was 5.4 yrs (range 0.1–15.9). Clinically active disease according to the Wallace criteria was present in 14 patients and 16 patients were active according to US evaluation. US and physical examination agreed in 80% of cases. The concordance between US and physical examination to define synovitis in all joints was moderate (kappa=0.602). The median calprotectin levels was 31.2 (8.1-203.8) ng/ml in healthy control, 29.75 (5.4-198.1) ng/ml in clinically active disease and 24.8 (14.1-204.3) ng/ml in clinically inactive disease group. We found no differences in the S100A8/A9 levels in clinically active and inactive disease group (p=0.73). There were also no difference in calprotectin levels between US active disease [29.75 ng/ml (5.4-204.3)] and US inactive disease [24.8 (12.1-197.1)] (p=0.83). S100A8/A9 levels correlated moderately with CRP (Spearman r=0.4380; p=0.01) but no correlations were found with ESR (Spearman r 0.193; p=0.325). Only 6 pts (4 out of 6 with polyarticular course) showed calprotectin levels higher than normal.

Table1. Demographic and laboratory findings of patients with JIA

	Wallace Active (14)	Wallace Inactive (16)	Total (30)
Female Sex	10 (71.4%)	8 (50.0%)	18 (60%)
Mean Age yrs (range)	10.40 (2.41-17.46)	11.23 (5.18-17.22)	10.8 (2-18)
Mean Age of disease onset, yrs (range)	7.44 (1.20-16.00)	3.68 (1.60-8.20)	4.2 (1.19-16.00)
Mean Disease duration yrs (range)	2.9 (0.12-8.84)	7.54 (1.96-15.90)	5.4 (0.1-15.9)
Extra-articular involvement (uveitis)	2 (14.28)	4 (25.0%)	6 (20%)
ANA positivity, n (%)	10 (71.42%)	12 (75.0%)	22 (73.3%)
WBC median, (range)	7.15 (4.0-10.7)	6.15 (3.3-10.70)	6.7 (4-10.7)
ESR mm/h, median, (range)	18.5 (3-67)	9.5 (2-20)	12 (2-67)
CRP mg/dl, median, (range)	0.275 (0.1-4.6)	0.16 (0.1-0.98)	0.20 (0.1-4.6)

Conclusion: S100A8/A9 levels were moderately correlated with CRP while no correlation were found with JIA categories. High serum calprotectin levels could be related with a polyarticular disease either in clinical activity or in subclinical remission. Our preliminary study need to be extended with large number of patients and designed prospectively.

Disclosure of Interest: None declared

P097

METHOTREXATE EFFECT ON MONOCYTES IN JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Monocytic cells with production of proinflammatory chemokines are attributed a significant role in local and systemic inflammation of juvenile idiopathic arthritis (JIA) (1).
Objectives: The aim of this study was to analyze monocyte (MON) response to methotrexate (MTX) and other treatment methods for the juvenile idiopathic arthritis (JIA) patients.
Methods: We performed a retrospective single-center study. All children diagnosed with JIA were included into the study, excluding systemic JIA. Complete blood count (CBC) before (at the time of diagnosis) and during the treatment (in disease exacerbation and remission) was analyzed. All patients were divided into MTX monotherapy group (T1), MTX and biological disease modifying antirheumatic drug (bDMARD) group (T2), and other (bDMARDs only, low doses prednisolone, NSAIDS, sulfasalazine) (T3). Data were analyzed using SPSS 20. P value <0.05 was considered significant.
Results: 30 patients were included into the study, 60% of whom were female. Mean age of first diagnosis was 9.06±4.08 years. We found 77 documented exacerbations for all these patients from the first diagnosis till the retrospective analysis start. A meadian of 2.57 exacerbations per patient (min 0, max 15). 23 of them were during MTX monotherapy, T2 – 31, and T3 – 23, In all groups, higher counts of leucocytes, neutrophils and platelets (PLT) at the time of diagnosis compared to remission were observed but it was not significant. The difference in monocyte counts in T1 vs other groups at first diagnosis and exacerbation did not differ showing that during exacerbation cells are stimulated in the same way like at the start of the disease. However, the MON during clinical remission were significantly lower in T1 compared to other groups (0.46±0.15 vs 0.64±0.2, p=0.0154). Besides, monocytes were significantly lower in MTX monotherapy group in remission vs exacerbation (0.46±0.15 vs 0.73±0.31, p=0.0104). Moreover, we combined all groups and investigated possible prediction of disease exacerbation or remission regarding monocyte count in CBC. MON below 0.3 predicted JIA remission with likelihood ratio (LR) of 2.76 (AUC 0.64, p=0.014).
Conclusion: Findings of the study could be useful to predict the course of the disease according to the changes in the MON seen in the complete blood count. Further studies are required to determinate changes of the blood cells in different stages of JIA, as this would help to define full remission in the patients of this chronic disease in cellular level.
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Disclosure of Interest: None declared

P098

PREDICTION OF DISEASE REMISSION AND EXACERBATION IN JUVENILE IDIOPATHIC ARTHRITIS FROM COMPLETE BLOOD COUNT PARAMETERS

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Introduction: In recent years more attention has been paid for the complex parameters seen in the complete blood count (CBC) that could help to evaluate the course of chronic diseases (1). Defining the exact stage (remission or exacerbation) of the juvenile idiopathic arthritis (JIA) could influence the long term immunosuppressive treatment strategy in these patients.
Objectives: The aim of this study was to analyze changes of complete blood count (CBC) parameters during different stages of the disease in the juvenile idiopathic arthritis (JIA) patients.
Methods: We performed a retrospective single-center study. All children diagnosed with JIA in the last 7 years were included into the study, excluding systemic JIA. CBC before (at the time of diagnosis) and during the treatment (in disease exacerbation and remission) was analyzed. We compared a CBC results in different stages of the disease and evaluated the predictive ability of different parameters, such as leucocyte (LEU), lymphocyte (LYM), neutrophil (NEU) and platelet (PLT) counts, mean platelet volume (MPV), platelet distribution width (PDW), platelet larger cell ratio (P-LCR), platelet neutrophil lymphocyte ratio (PNLR) and neutrophil lymphocyte ratio (NLR). Data were analyzed using SPSS 20. P value <0.05 was considered significant.
Results: 30 patients were included into the study, 60% of whom were female. Mean age at first diagnosis was 9.06±4.08 years (min-13 months, max-17 years). We found 77 documented exacerbations for all these patients from the first diagnosis till the retrospective analysis start. An average of 2.57 exacerbations per patient (min-0, max-15) and 6.4 per year for all patients were found. Higher count of PLT in JIA exacerbation compared to remission was observed (348.12±92.6 vs 310.5±68.9), but it was not significant (p=0.0976). Also, there were no differences in LEU, LYM, NEU, MPV, PDW or P-LCR levels between remission and exacerbation. However, we found significantly higher PNLR (604±412.8 vs 482±339.8, p=0.027) and NLR (1.74±1.99 vs 1.6±1.2, p=0.049) during exacerbation. Besides this, we looked at possible prediction of disease exacerbation or remission. PNLR below 143.9 predicted JIA remission with likelihood ratio (LR) of 5.55 (AUC 0.63, p=0.027) and NLR below 0.46 predicted remission with LR 5.55 (AUC 0.61, p=0.049). Also, we found that P-LCR more than 27.2 predicted JIA exacerbation with LR 2.42 (AUC 0.66, p=0.039). When comparing first CBC (treatment naïve, on time of JIA diagnosis) with clinical remission CBC, we found that NEU below 3.15 predicted JIA remission with LR of 5.85 (AUC 0.67, p=0.016).
Conclusion: Findings of the study could be useful to predict the course of the disease according to the changes seen in the complete blood count parameters such as NEU, PNLR, NLR and P-LCR. Further prospective studies are required to estimate changes of the blood cells and their ratios in different stages of JIA and possible influence of different treatment strategies. This would help to define full remission in the patients of this chronic disease in cellular level.
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Disclosure of Interest: None declared

P099

VALIDATION OF THE PSORIASIS EPIDEMIOLOGY SCREENING TOOL (PEST) AND THE NEW EARLY ARTHRITIS FOR PSORIATIC PATIENTS (EARP) IN PEDIATRIC POPULATION- PILOT STUDY

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Introduction: Juvenile Psoriatic Arthritis (JPsA) is an inflammatory arthritis associated with irreversible joint damage among pediatric population and is associated with psoriasis in most cases.
There are few validated screening tools for diagnosis of arthritis for adults patients with psoriasis those screening tools were never evaluated in children.

Objectives: The aim of this study was to evaluate two screening tools among pediatric patients with psoriasis.
Methods: Thirty nine patients with the diagnosis of psoriasis were administered two screening questionnaire: the new Early ARthritis for Psoriatic patients (EARP) questionnaire and the Psoriatic Arthritis Screening and Evaluation (PASE) questionnaire.
All patients were evaluated by rheumatologist for the diagnosis of JPsA and the diagnostic accuracy of the two questionnaires for the diagnosis of JPsA was compared.
Results: four patients were diagnosed with JPsA (10.2%). Four patients of 39 patients had a PEST questionnaire score of ≥ 3 all were with the diagnosis of JPsA. Thus, the sensitivity and specificity of the PEST in diagnosing JPsA were 100% and 100%,respectively, the median PEST score of the patients without the diagnosis of JPsA was 0 (0-2).
For the EARP questionnaire, 7 patients of 39 had a screening questionnaire score of ≥ 3 suggestive of JPsA, 4 were true positive and 3 were false positive. Thus, the sensitivity and specificity of EARP in diagnosing JPsA were 100% and 92%, respectively.
Conclusion: Both PEST and EARP questionnaire were easy to use and with high sensitivity for pediatric population with psoriasis, PEST questionnaire had higher specificity than EARP.

Disclosure of Interest: None declared

P100

WHEN RHEUMATOLOGY AND GENETICS MEET: A CASE OF JUVENILE IDIOPATHIC ARTHRITIS IN A PATIENT CARRYING 18Q DELETION.

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Introduction: Deletions of the long arm of the chromosome 18 (18q-) occur in 1/40.000 live-born infants. Common clinical features are facial dysmorphism, short stature, foot deformities, congenital aural atresia, variable intellectual disability, microcephaly, cerebral white matter abnormalities. Kidney malformations, bone dysplasia, growth hormone deficiency, congenital heart disease, IgA deficiency are less commonly reported. Autoimmune diseases such as juvenile idiopathic arthritis (JIA), thyroiditis, type 1 diabetes mellitus (DM1)have been described.
Objectives: We report a case of a 10-years-girl suffering from JIA associated to dysmorphic features who was diagnosed to carry a distal 18q deletion.
Methods: A 10 years old girl came to our department because of pain in her left knee and ankles for the past 5 weeks. Her parents were consanguineous, her 2 sisters were healthy. She was born at term with normal weight and length. After birth inter-ventricular septum defect and pulmonic stenosis were diagnosed, and the latter was corrected through cardiac catheterisation at 12 months. At 2 years ataxic gait was noted.The musculoskeletal examination showed arthritis of the both ankles, left knee .At neurological examination horizontal nistagmus, dysmetria of finger nose test, hyporeflexia, unstable gait were present. Romberg test was negative. Her height and her weight were normal.The genetic evaluation revealed facial dysmorphism, hypertelorism, thickened ears with prominent antitragus, squared tip of the nose, smooth and long nasolabial filter, prominent chin, thin lips, dental crowding and narrow palate. Proximal implant of the first finger of both hands with hypoplastic last phalanx, and both fifth fingers clinodactyly were noted; at the feet medially deviated large first toes with short I metatarsus and short Vth finger with nail hypoplasia were detected. The geneticist requested an Array CGH and a brain MRI.

Results: Blood test revealed increase in CRP (5,52 mg/dL)and ERS (68 mm/h). ANA was positive with a titer of 1:640. Patient presented IgA deficiency (< 5mg/dL) and increase in thyroglobulin antibody (305UI/mL), with normal levels of thyroid hormones. The left knee and ankles ultrasound showed moderate joint effusion. Thyroid gland ultrasound showed a dishomogeneous echoic pattern in line with a thyroiditis. An eye examination was normal.Brain MRI showed dysmelination of white matter, segmental stenosis of the third distal part of the aqueduct of Sylvius with enlarged lateral ventricles. The Array CGH revealed a *de novo* heterozygous 18q22—>qter deletion, a syndrome which explain all features of our child. The patient underwent to steroids intraarticular injection in the left knee, then methotrexate and folic acid were prescribed. After a clinical response, one year later she presented arthritis of both ankles, so etanercept was started. A control brain MRI showed progression of ventriculomegaly and subependimal trasudation, thus she underwent endoscopic ventriculocisternotomy. At last rheumatologic evaluation the patient was in good general condition, and did not present signs of active arthritis, biologic treatment was confirmed.
Conclusion: Our report provides an example of how autoimmune diseases can associated to genetic diseases. The association of 18q deletion to several autoimmune diseases offers chances to identify one or more genes implicated in regulation of immunity and predisposition to autoimmunity. This is the first report of acqueductsl stenosis linked to the distal 18q deletion syndrome.
Disclosure of Interest: None declared

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RESPONSE TO ABATACEPT IN JIA CATEGORIES: RESULTS FROM THE PRCSG/PRINTO JIA ABATACEPT PHASE IV REGISTRY

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Introduction: Abatacept (ABA), a selective T-cell co-stimulation modulator, has been demonstrated to be safe and effective in two Phase III studies.[1,2] The ongoing Phase IV Pediatric Rheumatology Collaborative Study Group and Paediatric Rheumatology International Trial Organization (PRINTO-PRCSG) registry aims to provide monitoring data from a real-world setting regarding longitudinal effectiveness of ABA in JIA.
Objectives: To assess effectiveness of ABA in JIA categories in patients (pts) who enrolled ≤1 month after starting treatment.
Methods: Using a standardised protocol and data collection process, clinical sites enroll pts with JIA currently receiving/starting IV/SC ABA and follow for up to 10 years. Pts are assessed at baseline (BL) and at 3, 6, 9, 12 and 24 months. JIA-ACR70 response rate was determined using a validated definition based on 5/6 JIA core set measures (CRP/ESR not included).[3] The clinical 10-joint Juvenile Arthritis Disease Activity Score (cJADAS10) used validated cut-offs for inactive disease (ID).[4] As-observed analysis is presented.
Results: As of 31 March 2018, 115 pts were included. Of these, 93 (80.9%) were female; BL mean (median) age at enrollment was 12.8 (13.1) yrs, age at JIA onset 4.9 (3.4) yrs and disease duration 2.4 (2.2) yrs. The JIA categories identified were: polyarticular RF–, 52 (45.2%); oligoarticular, 36 (31.3%); polyarticular RF+, 11 (9.6%); enthesitis-related arthritis (ERA), 9 (7.8%); psoriatic and undifferentiated, 3 (2.6%) each; systemic, 1 (<1%). The proportions of pts achieving JIA-ACR70 response and cJADAS10 ID are shown in Table 1 (pt with systemic JIA excluded).

Table 1. Proportion of patients achieving JIA-ACR responses and cJADAS ID

	Baseline	**3 months**	**6 months**	**9 months**	**12 months**	**24 months**
Overall population	115	83	82	49	41	23
JIA-ACR70 response	0 (0)	17 (15.5)	22 (20.6)	15 (14.9)	23 (23.0)	14 (15.2)
cJADAS10 ID	0 (0)	8 (11.4)	9 (14.3)	9 (22.0)	13 (28.9)	7 (35.0)
Polyarticular RF-	52	40	36	26	28	14
JIA-ACR70 response	0 (0)	8 (16.3)	9 (18.8)	6 (13.0)	9 (19.6)	6 (13.6)
cJADAS10 ID	0 (0)	3 (8.6)	2 (6.7)	3 (15.8)	2 (10.5)	1 (10.0)
Oligoarticular JIA	36	29	30	21	19	13
JIA-ACR70 response	0 (0)	6 (16.7)	7 (19.4)	6 (18.2)	7 (21.9)	5 (16.7)
cJADAS10 ID	0 (0)	2 (8.7)	4 (19.1)	4 (30.8)	6 (35.3)	3 (50.0)
Polyarticular RF+	11	6	7	6	5	2
JIA-ACR70 response	0 (0)	1 (10.0)	1 (11.1)	1 (11.1)	2 (22.2)	0 (0)
cJADAS10 ID	0 (0)	1 (33.3)	1 (20.0)	0 (0)	2 (50.0)	0 (0)
Enthesitis-related arthritis	9	5	7	4	4	1
JIA-ACR70 response	0 (0)	2 (25.0)	5 (62.5)	1 (14.3)	3 (42.9)	1 (20.0)
cJADAS10 ID	0 (0)	1 (20.0)	1 (16.7)	1 (25.0)	2 (66.7)	1 (100.0)
Psoriatic JIA	3	2	2	2	2	2
JIA-ACR70 response	0 (0)	0 (0)	0 (0)	1 (33.3)	0 (0)	1 (33.3)
cJADAS10 ID	0 (0)	1 (100.0)	1 (100.0)	1 (50.0)	1 (50.0)	2 (100.0)

Data are n (%).
cJADAS10=clinical 10-joint Juvenile Arthritis Disease Activity Score; ID= inactive disease; RF=rheumatoid factor.
Conclusion: Abatacept treatment resulted in rapid, clinically important and sustained JIA-ACR70 response in all JIA categories with polyarticular or oligoarticular disease course and few achieved cJADAS10 ID. Limitations of the study include a low number of pts with ERA, psoriatic, undifferentiated and systemic JIA.

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Trial registration identifying number: NCT01357668
Disclosure of Interest: D. Lovell Consultant for: consultant: AstraZeneca, Boehringer Ingelheim, F Hoffman-La Roche, GlaxoSmithKline, Novartis, UCB; principal/co-principal investigator: Bristol-Myers Squibb Company, F Hoffman-La Roche, Janssen, Pfizer, UCB; board member: Forest Research, N. Ruperto Consultant for: Ablynx, AbbVie, AstraZeneca-Medimmune, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb Company, Eli Lilly, EMD Serono, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, Pharma, Sanofi, Servier, Sinergie, Sobi, Takeda, Employee of: The IRCCS Istituto Giannina Gaslini (IGG), where NR works as a full-time public employee, has received contributions from Bristol-Myers Squibb Company, Eli Lilly, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Novartis, Pfizer, Sobi. This funding has been reinvested for the research activities of the hospital in a fully independent manner, without any commitment with third parties. The registry is funded by Bristol-Myers Squibb Company, Speaker Bureau of: Ablynx, AbbVie, AstraZeneca-Medimmune, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb Company, Eli Lilly, EMD Serono, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, Pharma, Sanofi, Servier, Sinergie, Sobi, Takeda, N. Tzaribachev: None declared, E. Morgan: None declared, G. Simonini Consultant for: AbbVie, Novartis, Speaker Bureau of: AbbVie, Novartis, T. Griffin: None declared, E. Alexeeva Consultant for: grant/research support and consulting fees: AbbVie, Novartis, Pfizer, Roche, Speaker Bureau of: AbbVie, Novartis, Pfizer, Roche, J. Bohnsack: None declared, A. Zeft Shareholder of: Merck, Opko Health, Teva, G. Horneff Consultant for: AbbVie, Novartis, Pfizer, Sanofi, Speaker Bureau of: AbbVie, Novartis, Pfizer, Sanofi, R. Vehe: None declared, V. Stanevica: None declared, S. Tarvin: None declared, M. Trachana Consultant for: grant/research support: AbbVie, Bristol-Myers Squibb Company, Novartis Hellas, Speaker Bureau of: Novartis Hellas, F Hoffman-La Roche, Pfizer, A. Huber: None declared, I. Orban: None declared, J. Dare Consultant for: grant/research support: AbbVie, Bristol-Myers Squibb Company, F Hoffman-La Roche, Pfizer, UCB, Employee of: Centene Corporation, I. Foeldvari Consultant for: Amgen, Bristol-Myers Squibb Company, Eli Lilly, Novartis, Pfizer, Sanofi, P. Quartier Consultant for: consultant: AbbVie, Bristol-Myers Squibb Company, Chugai-Roche, Eli Lilly, Novartis, Novimmune, Swedish Orphan Biovitrum; board member: Sanofi, Speaker Bureau of: AbbVie, Bristol-Myers Squibb Company, Chugai-Roche, Eli Lilly, Novartis, Novimmune, Swedish Orphan Biovitrum, A. Dominique Shareholder of: Bristol-Myers Squibb Company, Employee of: Bristol-Myers Squibb Company, T. Kou Shareholder of: Bristol-Myers Squibb Company, Employee of: Bristol-Myers Squibb Company, R. Wong Shareholder of: Bristol-Myers Squibb Company, Employee of: Bristol-Myers Squibb Company, A. Martini Consultant for: Aurinia, Bristol-Myers Squibb Company, Eli Lilly, EMD Serono, Janssen, Pfizer, H. Brunner Consultant for: Abbott, Amgen, AstraZeneca, Boehringer Ingelheim, Celgene, GlaxoSmithKline, F Hoffman-La Roche, Novartis, Pfizer, Takeda, UCB, Wyeth (funds paid to employer), Speaker Bureau of: F Hoffman-La Roche, GlaxoSmithKline, Novartis

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ARTICULAR AND EXTRA-ARTICULAR DAMAGE IN UKRAINIAN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS TREATED ACCORDING STRATEGY "TREAT 2 TARGET"

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Introduction: Targeted treatment of patients with Juvenile idiopathic arthritis (JIA) is recommended. The frequency of damage in children and adolescents with JIA has hardly been investigated in Ukraine.
Objectives: To assess the prevalence and accrual of damage in patients with JIA treated according modern strategy "Treat to Target" (T2T).
Methods: Study included 76 children aged 5 to 17 years with JIA treated using strategy "T2T" minimum during 6 months. The Juvenile Arthritis Damage Index Articular (JADI-A) score and the Juvenile Arthritis Damage Index Extraarticular score (JADI-E) were used for determination of irreversible changes in patient.
Results: 30.26 % of children performed JADI-A above 1 point ranged from 1 to 5 points. JADI-E was below 1 point only in 3.95 % of patients. 25.00 % of children had JADI-E equaled 1 point, 40.79 % - 2 points and 30.26 % - 3 or more points. Growth retardation, significant disproportion of leg length, severe muscular atrophy and uveitis were the most commonly reported among the JADI-E criteria. The mean values of JADI-A and JADI-E showed the absence of their dependence on sex, inflammatory activity, RF-positivity and ANA-positivity. Depending on the duration of the JIA, there was no significant difference in the mean JADI-A score. Mean JADI-E score showed a clear tendency to its gaining with increasing of the disease duration ($p < 0.05$). It was found that the mean score JADI-E was independent on the type of baseline therapy and was not significantly different in patients receiving only methotrexate compared to those, who treated with methotrexate in combination with IBT. Mean JADI-A score was significantly higher in patients treated with methotrexate alone than in children treated with combination therapy ($p < 0.05$).
Conclusion: The accumulation of irreversible persistent changes in patients with JIA does not depend on sex, disease activity, positivity in RF and ANA. With the increase in the duration of the disease, progressive accumulation of joint lesions does not occur. Therapy with methotrexate in combination with IBT significantly improves the average JADI-A score. Extra-articular changes accumulation has a clear dependence on the duration of the disease, regardless of the type of baseline therapy.

Disclosure of Interest: None declared

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RF-POSITIVE JUVENILE IDIOPATHIC ARTHRITIS: A STUDY OF 69 CASES IN SINGLE CENTER

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Introduction: Approximately 5-10% of children with juvenile idiopathic arthritis have rheumatoid factor-positive (RF+) arthritis (RF+ JIA), which requires earlier administration of more aggressive therapy due to rapid progression.
Objectives: To analyze epidemiological, clinical characteristics and treatment of patients (pts) with RF+ JIA in the single center.
Methods: Retrospective study of all consequently pts of single-center last 10 years in pediatric department by results of fulfilled examination to diagnose RF+ JIA.
Results: The diagnose RF+ JIA was verified in 69 pts (11,6% were boys) – 6.5% from all pts with JIA. The median age of JIA at onset was 12.2 y.o. (7.0; 14.0). The median of disease duration at the time of JIA verification was 6 mo (4; 12). The median of the number of active joints at the time of JIA verification was 16.5 [10.75; 23.25], 11.2% of pts had oligoarthritis at onset. RF+ were detected in 94.2% of pts, ACCP+ - in 78.2% of pts. 72.5% of pts had combination RF+ and ACCP+, 5.8% of pts had only ACCP+. The median of ESR was 29 [19.75;44.5] mm/h, CRP was 15.0 [6.9;34.4] mg/l at onset. Extra-articular manifestations observed in 26% of pts: 7.2% - fever at onset, 24.6% - lymphadenopathy, 4.3% - rheumatoid lung disease, 2.9% - rheumatoid nodules, 1.4% - pericarditis. Secondary Sjögren's syndrome was diagnosed in 15.5% of pts, autoimmune thyroiditis – in 8.5%. 19.7% of pts had family history of autoimmune disorders. The therapy included NSAIDs (97.1%), steroids (49.2%), DMARDs (methotrexate (MTX) alone – 78.3%, 2 DMARDs – 14.5%, 3 DMARDs consecutive – 7.2%), biologics (B) – 94.2% of pts. B was started during the 1st year of disease in 78.2% of pts due to the rapid progression of the erosive process. 63.8% of pts received only 1 B, 18.8% - 2 B, 7.2% - 3 B. As the 1st B used: infliximab (INF) – 5.6%, tocilizumab (TCZ) – 4.3%, etanercept (ETA) – 17.4%, adalimumab (ADA) – 10.1%, abatacept (ABA) – 44.9%, rituximab (RTM) – 7.2%, golimumab (GLM) – 2.9%, sarilumab – 1.8%. As the 2nd B used: 9.5% - TCZ, 14.3% - ETA, 23.8% - ADA, 19% - ABA, 28.6% - RTM, 4.8% - GLM. As the 3d B used: 25% - TCZ, 25% - PTM, 37.5% - ADA, 12.5% - ETA. 4.3% of pts received successively 4 B (ABA-ETA-ADA-TCZ, ABA-ETA-ADA-RTM, TCZ-ABA-ADA-RTM). The reasons for substitution therapy were serious adverse effects, subsequent loss of effect. The frequency of ACCP+ was not statistically different in groups with the effective use of only 1 B and, if necessary, replacement. In the presence of systemic manifestations, preference was given to TCZ or RTM, with secondary Sjogren's syndrome - RTM or ABA.
Conclusion: RF+ JIA is rare subtype of JIA, which characterized by high activity at onset. Most pts required the early appointment of aggressive therapy in connection with the rapid progression of the erosive process. The presence of systemic manifestations/secondary Sjogren's syndrome influence on choice of therapy. An analysis of the prescribed therapy did not reveal the effect of ACCP+ on preferred choice B or frequency of replacement B.
Disclosure of Interest: None declared

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THE MAIN CHALLENGES IN THE TRANSITION OF PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS TO ADULT SERVICE IN UKRAINE

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Introduction: The organization of the transition of a patient with a chronic disease from the pediatric to the adult service is a global problem. Different countries have adopted different approaches to this process, while most of the difficulties encountered are similar. Maintaining continuity between services during the transition of a patient with juvenile idiopathic arthritis (JIA), treated with biologics, is fundamentally important.
Objectives: To evaluate the procedure for transferring patients to adult service in Ukraine: its characteristics, difficulties and expectations of specialists.
Methods: A survey of 49 pediatric specialist services was conducted
Results: It was determined that the transition to adult service occurs simultaneously after the patient reaches 18 years. 45(91.8%) of respondents consider it mandatory to preserve the initial diagnosis of JIA upon transition process; 4(8.2%) believe that it is possible to transform the diagnosis of JIA into one used in adult service. To assess arthritis activity, 30(61.2%) specialists at the transition stage consider it appropriate to use JADAS27 with the subsequent transition to the corresponding integral activity indices used in adult practice; 15(30.6%) consider it possible to use JADAS27 throughout the entire period of patient monitoring; 4(8.2)% suggested the simultaneous implementation of the integral index DAS28 at the stage of patient transition to adult service. 29(59.1%) pediatric rheumatologists begin preparing patients with JIA for the transition immediately when biological therapy is initiated, regardless of the patient's age; 20(40.8%) respondents prepare the patient 1-2 years before reaching 18 years of age. Differences are identified in therapeutic tactics. 39(79.5%) specialists prefer not to change the treatment of the disease on the eve of the transition. At the same time, 25(51.0%) respondents believe that the decision to reduce/cancel biologics is advisable after the patient with JIA has been in a state of stable remission for 2 years, 2(4.1%) prefer to continue biologics until 5 years of remission. 12(24.5%) responders consider it possible to stop biologics >5 years before reaching the age of 18; 27(55.1%) think that it possible to stop them 1 year before the transfer, at the same time 10(20.4%) specialists prefer to follow therapeutic strategy without any changes. In case of combined DMADRs therapy, 37(75.5%) pediatric rheumatologists initially taper methotrexate or other synthetic DMARDS, which also differs from approaches at the adult service. Regarding the patient’s readiness for transition, 26(53.1%) of responders chose the need for a comprehensive procedure taking into account the opinions of specialists from both services, parents, a psychologist and the results of a patient survey; 18(36.7%) specialists believed that a pediatric rheumatologist can independently determine the patient’s readiness for transition, while 4(8.1%) believed that the results of one survey are enough. The main problem of the transfer to the adult service of 19(38.8%) pediatric rheumatologists noted the lack of a collaboration between pediatric and adult rheumatological services and 19(38.8%) noted the complication of access to the rheumatologist in the adult service.
Conclusion: In Ukraine, there is no unified approach to the procedure for transition of patients with from pediatric to adult rheumatology service. Among the main difficulties pediatric rheumatologists determined: the lack of a standardized approach for diagnosis formulation, assessing the disease activity, therapeutic tactics of a patient, including biological therapy. The issue of creating structures to coordinate the patient’s transition for maintaining their access to treatment, rehabilitation programs and psychological support in Ukraine is extremely relevant.
Disclosure of Interest: None declared

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COMORBID INFECTIONS IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Infectious complications are one of the leading causes of adverse outcomes in rheumatic diseases. The early administration of immunosuppressive and biotechnological drugs has significantly changed the course and outcome of diseases, but at the same time, it causes the risk of activation of latently ongoing comorbid infections. In this regard, it is urgent to prevent both the onset and exacerbation of chronic infections, primarily bronchopulmonary and urinary systems, which complicate the course of the underlying disease and require additional treatment costs.
Objectives: The goal of the study is to determine the frequency and role of comorbid infections in children with juvenile idiopathic arthritis (JIA).
Methods: Material and methods. A total of 147 children with JIA were examined in the rheumatology department of the 4th City Children's Clinical Hospital in Minsk. Enthesitis-associated arthritis was diagnosed in 8 children (5.4%). Systemic onset JIA was detected in 20 children (13.6%). Polyarticular JIA was detected in 48 children (32.7%). Oligoarticular JIA was observed in 71 children (48.3%). The determination of antigen in the biological environments of the body (blood, saliva, urine) was carried out by PCR. A bacteriological study of nasal and pharynx was carried out for the presence of pathogenic flora.
Results: Infection was named as the cause of the disease by 1/3 of the patients: the acute respiratory infection suffered the previous day was noted in 27 (38.1%) children with oligoarticular JIA, in 15 (31.3 %) children with polyarticular JIA, in 8 (40%) children with systemic onset JIA, in 3 (37.5%) children with enthesitis-associated arthritis. The presence of a nasopharyngeal infection (sinusitis, pharyngitis or tonsillitis) was noted in 18 (25.3%) children with oligoarticular JIA, in 10 (20.8%) children with polyarticular JIA, in 6 (30%) children with systemic onset JIA. About 1/3 of the patients answered positively to the question about the relationship of the exacerbation of the disease with an acute respiratory viral infection (35.2% of children with oligoarthricular JIA, 37.5% of children with polyarticular JIA, 35% of children with systemic onset JIA and 25% of children with enthesitis-related arthritis).
Due to the persistence of a high degree of disease activity, 18 patients with JIA were prescribed adalimumab in combination with methotrexate, and 22 patients received tocilizumab. Among children with JIA treated with methotrexate and adalimumab, a respiratory tract infection developed in 22.2%, including severe infection in 5.5% of patients. Among children treated with tocilizumab, a respiratory tract infection developed in 27.3% of patients. Herpetic rashes on the lips, wings of the nose and other parts of the face in most children appeared 2-3 times a year, in some cases up to 7-8 times a year. The most prone to relapse of this viral infection were patients with systemic onset JIA. Urinary tract infection was observed in 13 (18.3%) children with oligoarticular JIA, in 10 (20.8%) children with polyarticular JIA, and in 5 (25%) children with systemic JIA. The incidence of urinary tract infections in children with JIA treated with methotrexate and adalimumab was 5.5% when using methotrexate, 11.1% when using adalimumab. Among children receiving tocilizumab, urinary tract infection was noted in 13.6%.

Conclusion: Conclusion The data obtained indicate first of all the importance of infection in the initiation of a number of JIAs and the need for a thorough history taking in children with JIA, which will allow them to identify comorbid infectious diseases that complicate the course of the underlying disease and choose the optimal treatment regimen.
Disclosure of Interest: None declared

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EVALUATION OF HEPATITIS B VACCINE RESPONSE IN PATIENTS WITH JIA

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Introduction: Juvenile Idiopathic Arthritis (JIA) is a heterogeneous, idiopathic, chronic inflammatory disease of unknown cause which begin before 16 years of age. Vaccination is the most effective way to prevent infectious diseases. In the literature, there is limited data regarding Hepatitis B vaccine response in patients with the recent diagnosis of JIA.
Objectives: With this study; we aimed to evaluate and compare the presence of antibodies against hepatitis B vaccine at the time of diagosis of JIA with the healthy peers.
Methods: Between January 2015 and January 2020, patients referred to three pediatric rheumatology outpatient clinic with the recent diagnosis of JIA were evaluated for the presence of antibody titers against Hepatitis B vaccine. A response to the HBV vaccine was accepted as the production of an anti-HBs antibody level ≥ 10 IU/L. The results were compared with the age and sex matched control group consisting of patients without any chronic disease but prepared for surgery, their blood tests anti-HBs ab levels were obtained before surgical operations.
Results: The study included 262 patients with JIA and 275 healthy controls. The most common JIA subtypes were 98 (37.4%) oligoarticular followed by 49 (18.7%) enthesitis related arthritis, 33 (12.5%) polyarticular, 11 (4.1%) systemic, 6 (2.2%) psoriatic arthritis and 4 (1.5%)unclassified. Of the cohort, 262 patients diagnosed with JIA 135 were boys and 127 were girls, 147 of the control group were boys, 128 were girls. There was no difference between the patient and control groups in terms of age and gender ($p > 0.03$, $p > 0.028$) The mean age at diagnosis of patients was 10.9 ± 4.6 years and the mean follow-up duration was 16.1 ± 5.8 months. While anti-HBs ab positivity was present in 59.1% (n = 155) of JIA patients, it was positive in 73% (n = 201) of the control group ($p < 0.002$). HbsAg positivity was not detected in neither in any of the patients nor the controls. Thirty-seven patients of the JIA cohort had antinuclear antibody (ANA) positivity. Of those with ANA positivity, 28 (75.6%) had anti-HBs ab positivity, while in ANA negative (n = 78) patients this rate was 53.8% (n = 42) ($p < 0.02$).
Conclusion: This study had shown that hepatitis B vaccine response was lower in patients with recent diagnosis of JIA even before starting medications. At the time of diagnosis with JIA, hepatitis B vaccine response assessment should be routinely performed and booster dosing should be considered in cases without any response.
Disclosure of Interest: None declared

P107

OBESITY IMPAIRS ACHIEVEMENT OF CLINICAL INACTIVE DISEASE (CID) IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA) TREATED WITH TNF INHIBITORS

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Introduction: Obesity has been associated with more severe disease activity and reduced response to TNF-inhibitors (TNFi) in obese patients with rheumatoid arthritis (RA) or with psoriatic arthritis (PsA).

Objectives: to assess prevalence and disease features associated with obesity in juvenile idiopathic arthritis (JIA) and to evaluate the impact of obesity on the achievement of clinical inactive disease (CID) at six months from the start of treatment with TNFi.

Methods: retrospective analysis of demographic, clinical and laboratory features and body mass index (BMI) collected at the start of TNFi treatment in patients with oligoarticular and rheumatoid factor (RF)-negative polyarticular JIA. Patients were divided into obese and non-obese; demographic, clinical and disease features were compared in the two groups. The distribution of obese, overweight, healthy-weight and underweight patients according to the achievement of CID at 6 months was investigated.

Results: 234 patients with JIA (39% RF-negative polyarthritis, 25% extended oligoarthritis, 36% persistent oligoarthritis) were enrolled in the study. Obesity (BMI ≥95th percentile for age and gender) was present in 31 patients (13.2%). Obese patients compared to non-obese patients, had an older age at disease onset (p=0.020), lower frequency of antinuclear-antibody positivity (p=0.043), a higher number of active joints at baseline (p=0.0048) and higher C-reactive protein at baseline (p=0.043). Obese JIA patients achieved clinical inactive disease (CID) at 6 months with a lower frequency compared to non-obese patients (p=0.005). In multivariate regression analysis obesity at baseline was confirmed as an independent risk factor for non-achievement of CID at 6 months from starting TNFi (OR 2.42 [95% CI 1.04-5.61]; p=0.040).

Conclusion: obesity negatively affects response to TNFi in oligo- and RF-negative polyarticular JIA, independently from other disease-associated variables.

Disclosure of Interest: None declared

P108

USE OF TELEMEDICINE IN PEDIATRIC RHEUMATOLOGY IN ONE RUSSIAN CENTER

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Introduction: The pediatric rheumatology workforce is committed to a mission of providing children with access to care and superior clinical outcomes. With a limited number and distribution of pediatric rheumatologists, telemedicine has been proposed as one way to meet this mission, yet the adoption of this modality has been slower than expected.
Objectives: The main goal of the department of Telemedicine is to organize and conduct effective assistance with the remote interaction of doctors in the regions of Russia with the Center's consultants to assess the patient's health status, clarify the diagnosis, determine the prognosis and tactics of the diagnostics and optimal treatment, correct the previously prescribed treatment, and in difficult cases to transfer the patient to Federal Center. Provide an overview of the use of telemedicine consultations in rheumatology department at the Federal Center.
Methods: The telemedicine consultations department was established on the basis of the Federal Center on 7th of September in 2018. It is equipped with all the necessary equipment for organizing telemedicine consultations in real time, as well as holding deferred consultations on documents and selecting for hospitalization.
Results: In 2018 43 applications were received (8 - emergency, 13 - urgent, 22 - planned), rheumatic diseases were excluded in 4 patients, 39 patients were hospitalized (4 of them in the ICU). In 2019 268 requests were received (75 - emergency, 48 - emergency, 145 - planned), rheumatic diseases were excluded in 43 patients, 92 patients received the recommendations of diagnostics and correction of therapy, 133 patients were hospitalized (11 of them in the ICU). In 2020 (3 months) - 85 applications (16- emergency, 27 - emergency, 42- planned), rheumatic diseases were excluded in 5 patients, 33 patients were hospitalized in the rheumatology department (2 of them in the ICU). In 2020 (from January to March) the number of applications increased 3.5 times in comparison with 2019.
Conclusion: Telemedicine increased acceptability of providing children professional care. Outreach clinics were acceptable to a majority. In telemedicine setting, physicians face various difficulties and challenges, requiring special expertise, qualities and skills. Special measures are needed to obtain proper diagnosis and decisions and decrease the number of hospitalizations.
Disclosure of Interest: E. Alexeeva Speaker Bureau of: Novartis, Pfizer, Sanofi, MSD and Roche, T. Dvoryakovskaya Speaker Bureau of: Novartis, Pfizer, MSD and Roche, A. Fetisova: None declared, R. Denisova Speaker Bureau of: Novartis, MSD and Roche, A. Babayan: None declared, A. Mirzaeva: None declared

P109

CLINICAL SPECTRUM OF CHILDHOOD ARTHRITIS: EXPERIENCE FROM A SINGLE CENTRE IN SUB- HIMALAYAN REGION IN NORTH WEST INDIA

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Introduction: Arthritis is one of the commonest presentations of rheumatological illnesses in children.It is often accompanied by fever,rash,uveitis,hepatosplenomegaly,lymphadenopathy and serositis.Growing up with arthritis is often challenging. With optimal care and treatment,most children with arthritis live life to full potential.

Objectives: To present clinical,laboratory characterstics and treatment in patients with Childhood -Arthritis followed up in Pediatric -Rheumatology- Clinic(PRC) at DR .Rajendra Prasad Government Medical College ,Tanda, Himachal Pradesh ,India

Methods: A Retrospective Chart Review was conducted for all patients who attended PRC with a musculoskeletal complaint.International-League-of-Associations-for-Rheumatology(ILAR)criteria were used to diagnose Childhood-Arthritis. Data collected included:gender,age at onset of symptoms,initial manifestations,clinical and laboratory-parameters, final diagnosis,treatment,follow-up and duration before attending PRC.

Results: Total of 44 children with arthritis were included.There was male predominance(male:female=1.3:1),mean age at onset of symptoms was 10.14±3.89years.Median-interval between onset of symptoms and diagnosis was 2 months. Various subtypes of arthritis identified are shown in figure 1.Commonest joint involved is Knee followed by Hip and elbow joints.Fever at time of presentation was present in 6(13.63%) patients.One child with Systemic-JIA had splenomegaly.One with Camptodactyly-Arthropathy-Coxavara-Pericarditis-Syndrome(CACP) had panserositis.Mean hemoglobin was 11.33±1.60 g/dl.ANA which was done by Indirect-Immunofluorescence on Hep-2 cell line was positive in 10(22.72%), of which 5 had Oligoarthriitis.HLA-B27 which was done by PCR was positive in 7(15.90%) patients. Uveitis was observed in 4(9.09%) patients and all had oligoarthritis.11(25.00%)patients were treated by NSAIDS only and 12(27.27%),7(15.90%),3(6.81%) patients were given Methotrexate,Intra-Articular-Corticosteroid-Injection and Sulfasalazine respectively. Cyclophosphamide was started in 1 patient with SLE arthritis and 1 patient with systemic-JIA is on Tocilizumab.16(36.36%) patients are on regular follow-up with mean duration of 93.92 person-months.

Conclusion: We highlighted various clinical and labortary characterstics in children with arthritis.Oligoarthritis-JIA is the commonest subtype in our study.Unusual causes like CACP and SLE arthritis were seen among study population.Childhood musculoskeltal pain is still a dilemma among pediatricians.Knowledge of clinical spectrum will increase the awareness for early referral,diagnosis and treatment .

Disclosure of Interest: None declared

P110

DERMATOLOGIC ADVERSE EVENTS ASSOCIATED WITH JUVENILE IDIOPATHIC ARTHRITIS TREATMENT

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Introduction: Steroids and disease-modifying anti-rheumatic drugs (DMARDs) are widely used in the treatment of juvenile idiopathic arthritis (JIA). Dermatologic adverse events including psoriasis have been reported in treatment of various inflammatory diseases (1-3). However, data regarding the occurrence of dermatologic adverse events in JIA patients are scarce (4-6).
Objectives: To determine the prevalence of dermatologic adverse events in JIA patients treated with systemic steroids and DMARDs. To investigate an association between drugs and dermatologic adverse events and the association between anti-TNF treatment and psoriasiform lesions.
Methods: Data from the international, observational registry Pharmachild were used. It includes patients with JIA who were treated with NSAIDs, steroids and/or synthetic and biological DMARDs. Pharmachild started in 2011 and data on adverse events were collected. Treatment of patients with and without a dermatologic adverse event was compared. The start date of the drug had to be at least one day before the adverse event date and the end date needed to be similar or later than the adverse event date.
Results: Among 8841 patients, 439 (5.0%) patients had at least one dermatologic adverse event and in total 492 dermatologic adverse events were reported. Median follow-up time was 3.9 years. Erythema, rash and pruritus occurred in 65 of 492 (13.2%) dermatologic adverse events, other dermatologic adverse events in 46 (9.3%), eczema in 34 (6.9%), hair disorders in 33 (6.7%), and psoriasisform lesions in 30 (6.1%). Several drugs were used more often in patients with such an event than patients without. In five of eight patients with psoriasiform lesions during anti-TNF treatment the lesions disappeared with the discontinuation, reduction or interruption of the dose.
Conclusion: A wide range of dermatologic adverse events was reported in this cohort underlining the importance to be aware of such adverse events.

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Trial registration identifying number: ClinicalTrials.gov Identifier: NCT01399281
Disclosure of Interest: None declared

P111

ESTIMATION OF THE VITAMIN D STATUS AND ITS CORRELATION WITH CLINICAL ACTIVITY IN CHILDREN WITH JIA

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Introduction: JIA is the most common rheumatologic disease and these patients suffer from the condition with difficult pathogenesis and as well other underestimate conditions - microelement and vitamin deficiency. Vitamin D deficiency in pediatric population plays a leading role according to WHO reports.
Objectives: The aim of our study was to evaluate status of vitamin D and its correlation with clinical activity of the disease in patients with JIA.
Methods: We did complete clinical and laboratory investigation of 83 children with JIA, at the age range from 3 to 16 years and middle duration of the disease 14 months. Estimation of the vitamin D status was done with classification approved by experts of International endocrine society, concentration of the serum hydroxyvitamin D was done without connection with child's age, osteocalcin level was measured. For characteristic of the clinical activity we took into account amount of the active joints, results of CHAQ, VAS, CRP, IL-1β, IL-6 in serum by using of the ELISA method.
Results: Laboratory activity of the inflammatory response was presented by enlarged concentration of CRP (6,9±2,7g/l), IL-1β (5,8±4,2 pg/ml; N ranges <5 pg/ml), IL-6 (10,2±2,4pg/ml; N ranges <9 pg/ml). Concentration of CRP, IL-1β was slightly increased through all patients in different subtypes of JIA, IL-6 was significantly higher in patients with polyJIA. Patients with anamnesis of the JIA in more than 18 months had slightly lower laboratory activity ($p < 0,05$). We figured out that half of the patients were detected with vitamin D deficiency (40 cases (48,19 ± 5,17) %), that exceeded frequency of vitamin D insufficiency (31 cases (37,35 ± 4,68) %, $p> 0,05$) and observed more often than number of them with normal amount (12 cases (14,45 ± 4,21) %, $p< 0,01$). Children with JIA had concentration of 25(OH)D in serum ((21,13 ± 2,64) ng/ml, 95% CI: 16,02 – 27,44 ng/ml). Vitamin D deficiency was more often found in kids with high disease activity (23 children (57,5 ± 9,05) %, $p<0,05$; OR = 0,51, S = 0,56, 95% CI: 0,17 – 1,58), than in kids with mild or moderate process. As well, we found that increasing of the inflammatory activity in patients influence on decreasing of 25(OH)D in serum ($r = – 0,43$, $p < 0,01$). Rising of the vitamin D deficiency followed by significant decrease of the osteocalcin in serum ($p < 0,05$). We estimated correlation between osteocalcin amount and hydroxyvitamin D in serum of the children with mild and moderate activity ($r = 0,51$, $p < 0,01$), and high disease score ($r = 0,6$, $p < 0,01$).
Conclusion: So, patients with high activity of the JIA have lowest concentration of 25(OH)D in serum ((19,33 ± 2,17) ng/ml, 95% CI: 14,55 – 23,84 ng/ml) and low intensity of bone metabolism accoding to serum osteocalcin ((52,27 ± 3,74) ng/ml; 95% CI: 46,19 – 61,36 ng/ml).

Disclosure of Interest: None declared

P112

INAUGURAL HIP INVOLVEMENT IN JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Juvenile idiopathic arthritis (JIA) is the most common chronic arthritis of childhood. Hip involvement often represents a turning point in the course of the disease.
Objectives: The aim is to study the epidemiological, clinical, radiological and therapeutic characteristics of hip involvement during JIA.
Methods: Retrospective study over 13 years (2006-2019) enrolling patients followed for JIA meeting the criteria of the International League of Associations for Rheumatology (ILAR) and presenting a hip involvement.
Results: Among the 25 cases of JIA collected, 14 patients had hip involvement with a sex ratio of 1. The average age at the onset of the disease was 11 years. The average time to diagnosis of JIA was 25 months. Subtypes of JIA according to The ILAR were: enthesitis-related arthritis in 7 cases, seropositive polyarticular JIA in 2 cases, seronegative polyarticular JIA in 2 cases, oligoarticular JIA in 2 cases and juvenile psoriatic arthritis in one case.
Hip involvement was bilateral in 12 cases. Examination revealed lower limb inequality in 5 cases, limited hip mobility in all planes in 12 cases and irreducible hip flessum in 4 cases. Lequesne algofunctional index averaged 8.5.
Standard radiographs showed minimal to moderate pinching in 9 cases and destructive hip disease in 5 cases.
All patients were initially treated with a combination of non-steroidal anti-inflammatory drugs (NSAIDs) and rehabilitation. Disease modifying anti-rheumatic drugs were initiated in 11 patients (salazopyrine in 2 cases and methotrexate in 9 cases). Hip joint injection of steroid has been indicated in 11 cases with improvement in clinical symptoms in 9 cases.
Total hip replacement (THR) was necessary in 2 cases. The average duration of progression of JIA at the time of THR was 9 years and 6 months. No patient had any post-surgical complications.
Conclusion: Hip involvement is common and estimated to occur in approximately 35–63% of children with JIA. It is a predictor of disease severity because of the disability it can cause. Hence the need for early diagnosis and management to delay the progression of the disease and the use of THR.
Disclosure of Interest: None declared

P113

JUVENILE IDIOPATHIC ARTHRITIS AND GROWTH PATTERN IN EGYPTIAN PATIENTS.

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Introduction: Juvenile idiopathic arthritis (JIA) is one of the most common rheumatic diseases in childhood and is frequently associated with growth retardation. Along, Vitamin D is critical to the growth and development of the skeleton as well as to bone mineral metabolism.
Objectives: We aimed to evaluate growth pattern and Vitamin D level in patients with JIA and its different subtypes.
Methods: 80 JIA patients and 80 healthy controls were included. For all patients and controls we assessed body weight, standing height, body mass index (BMI), Serum 25(OH) D3. Thyroid function tests were assessed to exclude patients with hypothyroidism or autoimmune thyroiditis, liver and renal function tests, calcium, phosphorus, alkaline phosphatase, fasting blood sugar were done to evaluate other causes of short stature.
Results: JIA patients' mean height, weight, and BMI were significantly lower compared to controls (135.4±22.1 vs. 145.7±21.8, p=0.042 for height), (34.6±13.6 vs. 39.8±11.4, p=0.039 for weight) and (18.52±3.96 vs. 21.73±5.43, p= 0.041 for BMI). Mean serum 25(OH) D3 level was significantly lower in JIA patients than controls (15.69±6.6 ng/ml vs. 31.62±4.9 ng/ml, p<0.0001), patients with systemic onset and seropositive polyarthritis (RF positive) have the lowest 25(OH) D3 level compared with other JIA subtypes. There was significant negative correlation between steroid dose, duration and JIA patients' height (r= -0.456, p=0.017 and r=-0.776, p=0.001 respectively). Serum 25 (OH) D3 level was significantly correlated with patients' height and BMI (r=0.33, p=0.029 and r=0.32, p=0.043).
Conclusion: the nutritional status of JIA patients is multi-factorial. Onset subtype and low level of vitamin D were found to have an effect on growth parameters as height and body mass index in patients with JIA.
Disclosure of Interest: None declared

P114

MUSCULOSKELETAL COMPLAINTS OF CHILDREN WITH PSORIASIS AND ULTRASONOGRAPHIC EVALUATION OF SUBCLINICAL ACHILLES ENTHESOPATHY

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Introduction: Psoriasis (Pso) is an immune-mediated inflammatory skin disease displaying several presentations such as plaque, nail, guttate, inverse, pustular and erythrodermic . Pso may be complicated with systemic features including arthritis, uveitis and metabolic syndrome. Various musculoskeletal manifestations, such as peripheral arthritis, enthesitis, dactylitis and spondylitis may accompany Pso. According to adult studies, the prevalence of Pso is approximately 2% to 3% of general population, whereas psoriatic arthritis (PsA) is present in 30% of patients with Pso. However, there are no studies evaluating the subclinical musculoskeletal findings of juvenile Psos patients.

Objectives: To evaluate the presence of articular/extra-articular inflammatory conditions and enthesis thickness by ultrasonographic imaging in pediatric Pso patients.

Methods: Pso patients without known musculoskeletal features and healthy peers were evaluated with standardized forms and physical examination by pediatric rheumatologist. Both patients and controls underwent ultrasonographic evaluation for Achilles tendon thickness in order to define subclinical enthesopathy.

Results: A total of 55 pediatric Pso and 46 age and gender matched selected healthy children were included in the study. Of patients with Pso 56.4% had arthralgia, 25.5% had lower back pain, 18.2% had heel pain, 12.7% had hip pain, and 10.9% described morning stiffness. Arthritis of knee was detected in 7.3%, sacroiliac tenderness in 12.7% and enthesitis in 9.1% of the patients. Arthralgia, lower back pain and heel pain were significantly frequent in Pso group than healthy children (p=<0.001, p=0.02 and p=0.03 respectively). None of the healthy children had inflammatory lower back pain, arthritis, morning stiffness, sacroiliac tenderness and enthesitis. Median left and right Achilles tendon thicknesses of Pso patients were significantly greater than that of healthy controls (p=0.03 and p=<0.001). Prevalence of psoriatic arthritis (PsA) among Pso patients was 7.3 %.

Conclusion: Evaluation of a child with Pso regularly for the musculoscelatal complaints is critical for early recognition of PsA. Collaboration between dermatologists and pediatric rheumatologists should be provided for preventing diagnostic delay in PsA. Ultrasonography is a useful technique for screening Pso patients in order to detect subclinical enthesopaty early.

Disclosure of Interest: None declared

P115

SCREENING FOR DEPRESSION IN A SINGLE PEDIATRIC RHEUMATOLOGY CENTRE USING THE BDI-FAST SCREEN

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Introduction: Depression is a known comorbidity in juvenile idiopathic arthritis (JIA) and has an impact on quality of life and therapy outcome. In clinical routine, depression is probably under-detected.
Objectives: Prevalence of depressive symptoms, manifest depression and suicidal ideation was evaluated and associations with patient characteristics, disease activity and treatment were analysed in a cross sectional study.
Methods: Patients aged 10-18 years from a pediatric rheumatology centre were screened with the BDI-FS. An abnormal score of ≥4 points (out of 21) led to psychologically evaluation.
Results: 148 JIA patients (72% female) were evaluated. 19 (13%) had an abnormal BDI-FS score.. Frequent statements were sadness (n=31, 21%), lack of joy (n=43, 29%), hopelessness (n=23, 16%) and self-blame (n= 26, 18%). Suicidal ideation was present in 9 (6%). 4 (3%) patients had a previously diagnosed depression, 10 (7%) were newly diagnosed with depression. Patients with an increased BDI FS score more frequently presented with a diagnosis in JIA subcategories RF-negative and -positive polyarthritis and psoriatic arthritis but rarely with extended oligoarthritis or enthesitis related arthritis. There was an association between an increased BDI FS score and pain experienced by patients in both the patient reported pain visual analogue scale (VAS) (p=0.002) and in the number of painful joints (p=0.017). Patients with a BDI-FS ≥4 also had significantly higher scores concerning disease activity as measured by physician and patient global assessment of disease activity and by the JADAS 10. A significantly higher percentage of patients with a normal BDI FS were in remission and had minimal disease activity. Patients with an abnormal BDI-FS score also had a significantly higher disability index as measured by the CHAQ (p=0). More patients with a BDI-FS ≥4 were taking NSAR, steroids, biologicals or a combination of biologicals and DMARDs as well as an overall higher number of different drugs.

	Total n= 148	Score <4 n= 129 (87%)	Score ≥4 n=19 (13%)	p
Age, median (1./3. quartile)	14,7 (13/16,2)	14,6 (12,8/16,1)	15,5 (14,2/16,6)	n.s.
Disease duration [y], median (1./3. quartile)	4 (2/7)	4 (2/7)	2,5 (1,75/6,25)	n.s.
Sex female, n (%)	106 (71,6%)	89 (69%)	17 (89,5%)	n.s.
Diagnose				
JIA, n (%)	148 (100%)	129 (87%)	19 (13%)	n.s.
RF - polyarthritis	44 (29,7%)	34 (26,4%)	10 (52,6%)	**0.019**
RF + polyarthritis	3 (2%)	1 (0,8%)	2 (10,5%)	**0.005**
Oligoarthritis	29 (19,6%)	28 (21,7%)	1 (5,3%)	n.s.
Extended Oligoarthritis	25 (16,9%)	24 (18,6%)	1 (5,3%)	n.s.
ERA	24 (16,2%)	22 (17,1%)	2 (10,5%)	n.s.
Psoriatic arthritis	16 (10,8%)	13 (10,1%)	3 (15,8%)	n.s.
Active Joints, median (1./3. quartil)	0 (0/1)	0 (0/1)	0,5 (0/2,5)	n.s.
Tender joints	1 (0/2)	1 (0/2)	2 (0,5/4)	**0.017**
Pat. Global Asessment	1 (0/3)	0,7 (0/2,5)	3,5 (1/6)	**0.002**
Physician Global Assessment	0 (0/1,5)	0 (0/1)	1 (0/3)	**0.026**
CHAQ-DI	0 (0/0,4)	0 (0/0,4)	0,4 (0/1)	**0.00**
JADAS 10, med. (1./3. quartil)	2 (0/6)	2 (0/5)	5 (2/10)	**0.008**
JADAS ADA, n (%)	101 (73,2%)	92 (76%)	9 (52,9%)	**0.044**
JADAS MDA, n (%)	76 (55,1%)	71 (58,7%)	5 (29,4%)	**0.023**
JADAS-remission, n (%)	56 (40,6%)	53 (43,8%)	3 (17,6%)	**0.04**

Conclusion: The BDI-FS is a convenient tool for detecting depression during routine checkups as it is simple in execution and evaluation. A high percentage of the patients showed signs of depression and suicidal ideation was detected. Patients with JIA especially with polyarthritis (RF negative and positive) and psoriatic arthritis have an increased risk for depressive symptoms. Increased scores were associated with pain, disability and higher disease activity especially if present despite intensified drug therapy. Only 26% of patients with an abnormal BDI-FS were already receiving psychological treatment. Screening for depressive symptoms in clinical practice is highly recommended to ensure adequate psychological support
Disclosure of Interest: None declared

P116

SWITCHING PATTERNS OF BIOLOGIC DRUGS AMONG CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS: A SINGLE CENTER EXPERIENCES

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Introduction: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease of childhood with an estimated incidence of 10–20 per 100,000 children. The conventional treatment of JIA includes non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and disease modifying anti-rheumatic drugs (DMARDs) . However, some patients do not experience complete response to conventional first-line options and require second-line therapy with biologic agents(BA). Though the BA provide JIA patients a better disease control, knowledge concerning switching patterns of BA in JIA is scarce.
Objectives: To evaluate the clinical responses and safety profiles of patients who required switching from one biological therapy to another for any reason
Methods: Children with JIA who received at least one biologic drug were included to the study. Disease activity was evaluated by juvenile arthritis disease activity score 71 (JADAS71). Demographic, clinical and laboratory findings, switching patterns and etiology of switching were recorded.
Results: A total of 191 (91 girls, 100 boys) JIA patients receiving BA were included into study. The mean ± SD age of diagnosis was 9.1±4.9. Biologic drugs were prescribed with a median of 14 (2-66) months after diagnosis. Among 191 patients, 37 (19.3%) patients required to switch BA with a median of 10.5 (1-38) months after first biologic initiation. Tocilizumab (n=19) was the most commonly switched drug. The main reason of switching was inadequate response (n=32). The frequency of biologic switch was higher in patients with extended oJIA and pJIA and also in patients with uveitis. Biologic drugs were switched twice in nine and three times in three patients. When compared the 1st switchers to 2nd and 3rd switchers, there were not any differences in terms of JIA subgroups whereas, 2nd and 3rd switchers had higher active joint number and JADAS71 scores at the 6th month of first biologic drug initiation.
Conclusion: Some JIA patients could not achieve remission despite to the first prescribed biologic. Therefore, the biological drug has to be replaced by a second BA in these patients. We demonstrated both patterns and etiologies for switching that may facilitate the management approach of those dealing with JIA.
Disclosure of Interest: None declared

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EARLY REGISTRATION OF MYOCARDIAL DISORDERS IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS USING THE 4TH GENERATION ELECTROCARDIOGRAPHY

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Introduction: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in children and often leads to disabilities due to joint and non-joint lesions, especially cardiovascular (CV) ones. New diagnostic methods may be useful to find these lesions before clinical manifestations or even predict them.
Objectives: To evaluate the results of electrocardiography (ECG) of the 4th generation (signal-averaged ECG obtained by processing several electrocardiographic complexes except atypical) in children with JIA in early diagnosis.
Methods: 46 patients with JIA (60.9% f, 9.69±0.93 y.o., duration of the disease 1.45±0.51 y.) were examined using 4th generation hardware-software complex ECG "Cardio plus P". Disease course and activity (JADAS27) were rated. In addition to standard laboratory&instrumental markers the level of immunoglobulins (IG), IL6, TNFα in the serum of patients was determined by ELISA, a correlation analysis of clinical and laboratory parameters was made.
Results: There were no instrumental (by standard ECG and cardiac ultrasound (US)) and laboratory signs of CVS injury among observed group, 50% JIA patients had unfavorable course of the disease (UCD), 10.5% had hepatosplenomegalia, JADAS27 9.7±2.04. Serum level of IL6 was 5.19±2.21 pg/ml, ALT, AST, LDG, cholesterol were normal. Using the 4th generation ECG showed the presence of significant changes in the myocardium in the majority of patients. Following indicators of heart rhythm variability and myocardium state evaluation in patients with JIA were deviated most often: stress index was 245.96±44.33s^{-2} (69.56% cases), condition of regulation reserves 61.65±2.77 (86.96%), overall heart rate variability 2279.74±406.36 (65.21%), immediate control of condition of myocardium 51.56±3.91 (95.65%), its reserve 61.04±1.82 (95.65%), T-wave/R-wave ratio lead I was 0.67±0.11 (80%), amplitude-areas index lead I-III from 48.65±2.64 to 61,17±4,33 (up to 95.65%), Macruz index 1.39±0.76 (94%), complex indicator of condition of myocardium 56.30±2.57 (95.65%) complex indicator of functional state 66.13±2.41 (65.2%). Previously, the best combination of ECG indicators to evaluate activity was found using CART algorithm: integral indicator of form ST-T lead II (55.41±5.09), T wave symmetry based on derivatives ratio and on areas of triangles (1.78±0.71, deviation in 100%) & T amplitude lead II (112.23±71.96 uV, in 86.36%), heart ratio, alpha QRS angle in the frontal plane. Some correlations between these parameters and other data were found: immediate control of the regulation with serum IL6 ($r=-0.73$, $p<0.05$), and with UCD ($r=-0.53$, $p<0.05$); heart ratio with ESR ($r=0.53$, $p<0.05$), hepatosplenomegalia ($r=0.57$, $p<0.05$), cholesterol serum level ($r=0.58$, $p<0.05$); integral indicator of form ST-T with serum IgG ($r=-0.55$), IgA ($r=-0.55$); T wave symmetry based on derivatives ratio had correlations with metabolic myocardial changes ($r=-0.68$, $p>0.1$), IgA ($r=0.85$, $p>0.1$), DMARD replacement ($r=0.51$, $p>0.1$); T wave symmetry based on areas of triangles with hepatosplenomegalia ($r=0.67$, $p<0.05$), US reactive changes of parenchymal organs ($r=-0.96$, $p>0.1$), IgM, IgA ($r=0.74$ and 0.98), serum TNFα ($r=-0.59$, $p>0.1$); T amplitude, lead II with IgG total ($r=-0.72$, $p>0.1$), TNFα ($r=0.99$, $p>0.1$); alphaQRS angle with ALT ($r=-0.72$, $p<0.05$), cholesterol ($r=0.49$, $p<0.05$), NSAIDs ($r=0.82$, $p<0.05$); complex indicator of condition of myocardium with cholesterol ($r=-0.62$, $p<0.05$).
Conclusion: With the help of "Cardio-Plus P" the changes in CVS and latent heart rhythm disorders in children with JIA can be found more frequently by evaluating complex indicators than using standard 12channel ECG. Most of registered changes had no other clinical, laboratory or instrumental signs, in accordance with the obtained correlations they may be due to immune inflammation.
Disclosure of Interest: None declared

P118

A FAMILY HISTORY OF AUTOIMMUNITY IS A RISK FACTOR FOR CELIAC DISEASE AND JUVENILE IDIOPATHIC ARTHRITIS CO-OCCURRENCE

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Introduction: Autoimmune disorders share common predisposing factors and immune pathogenic mechanisms. The prevalence of celiac disease (CD) has been reported to be consistently higher in patients with juvenile idiopathic arthritis (JIA) in comparison to the general population, however not negligible variations in the prevalence have been observed in distinct geographic locations.
Objectives: To investigate the co-occurrence of JIA and CD in southern Italy and to identify potential predisposing factors.
Methods: A single-center retrospective study was conducted. Patients diagnosed with JIA according to International League of Associations for Rheumatology criteria, admitted to the Pediatric Rheumatology Unit of the University of Naples Federico II from January 2001 to December 2019, who underwent CD serological screening at least once, were included. For each patient, demographic, clinical and laboratory data were extracted from clinical charts. Differences between patients affected by JIA with or without CD were analyzed.
Results: Three hundred twenty-nine JIA patients (246 females, 83 males; median age 12.5 years, IQR 9.1-16.1) were included in our study. Median age at JIA onset was 4 years (IQR: 2.2-7.8). Eight patients (2.4%) received a diagnosis of CD. Five were diagnosed according to the ESPGHAN guidelines. Two were diagnosed solely based on positive serology that normalized after the beginning of the gluten-free diet (GFD). One patient received a diagnosis of Potential CD (positive serology in the absence of villous atrophy). All of them started a GFD. Only in one patient CD onset preceded JIA, that occurred despite the GFD. The remaining seven developed JIA first. Most of those (5/7, 71,4%) were asymptomatic and diagnosis followed the screening for CD that all JIA patients undergo in our clinic. In our cohort the prevalence of CD was higher than that reported in the general population (2.4% vs 1%, $p<0.05$). No differences were observed in regard to JIA subtype and ongoing treatment for JIA ($p=0.59$) between patients with or without CD. Notably, 87.5% patients with JIA and CD had at least one family relative with an autoimmune disorder compared to 45.8% of those without CD ($p<0.05$). In none of those patients GFD promoted clinical improvement, nor prevented JIA relapse. Indeed, five patients required a new disease modifying antirheumatic drug (DMARD). Finally, 87.5% patients with JIA and CD required both a conventional DMARD and a biological DMARD (bDMARD) over time compared to 36.8% (118/321) of those without CD ($p=0.006$).
Conclusion: A higher prevalence of CD in patients with JIA was found in our wide southern Italian cohort in comparison to the general population. Notably, a positive family history of autoimmunity was found to be associated with a higher co-occurrence of JIA and CD, suggesting that common predisposing factors shared across autoimmune disorders may contribute to both diseases. Furthermore, our patients with JIA and CD more frequently required a bDMARD than patients without CD, suggesting that JIA course can be more aggressive in children with CD. Our findings support the need for an active screening for CD in patients with JIA, especially in those with a positive family history of autoimmunity. This is clinically relevant since the clinical course seems to be more aggressive in these patients and require a step-up therapy.
Disclosure of Interest: None declared

P119

A LARGE PROPORTION OF PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS UNDERGO ANTIBIOTIC TREATMENT AND ARTHROTOMY AT THE ONSET OF DISEASE.

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Introduction: Acute arthritis is a common cause of consultation in pediatric emergency wards. It can be caused by septic (SA), juvenile idiopathic arthritis (JIA), or undetermined arthritis (UA). An early accurate diagnosis is essential to provide appropriate treatment and follow-up.

Objectives: To compare clinical and biological characteristics, exposure to antibiotics and invasive orthopedic management and lengths of hospital stays according to the final diagnosis of patients with JIA, SA and UA.

Methods: We retrospectively analyzed data from <16-year-old children, hospitalized between 2008–2009 or 2015–2018 at a French tertiary center for acute arthritis, who underwent a joint aspiration. Non-parametric tests were performed to compare children with JIA and children with SA or UA, respectively (Bonferonni-adjusted statistical threshold = 0.025).

Results: Among the 251 included patients, 123 (49%) had SA, 32 (13%) had JIA and 96 (38%) had undetermined arthritis (UA). Patients with JIA were older when compared to SA (2.9 years [1.9-5.3] versus 1.5 [1.1-2.7], p<0.01). Presence of fever and fibrinogen were not different between JIA and SA or UA. White blood cells in serum and synovial fluid were lower in patients with JIA (11.2x109/l [9.6-12.7] and 42.05x103cells/mm3 [10.5-100.0]) when compared to SA (13.2x109/l[11.0-16.6] and 105.5x103cells/mm3 [44.0-210.0], p<0.01 and p<0.01). Intravenous antibiotics were administered to 87.5% of children with JIA, 100% of patients with SA, and 91,5% of UA. Arthrotomy was performed in 43.3% of patients with JIA, 69.7% of patients with SA, and 54.1% of patients with UA.

Conclusion: At onset of acute arthritis currently used clinical and biological parameters do not allow to reliably differentiate between JIA, SA and UA. A large proportion of patients with JIA undergo antibiotic treatment and invasive surgical treatments. There is a need for the identification of new diagnosis biomarkers that allow early identification of JIA.

Disclosure of Interest: None declared

P120

EXTRA_ARTICULAR MANIFESTATIONS OF JUVENILE IDIOPATHIC ARTHRITIS AND THEIR IMPACT ON HEALTH RELATED QUALITY OF LIFE

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Introduction: Juvenile idiopathic arthritis (JIA) is the commonest rheumatic disease in children (1).It is associated with a range of extra-articular manifestations (EAM) (2).These EAM may have a negative impact on health related quality of life (HRQoL) in these patients .However ,this issue is not deeply studied .
Objectives: This study aimed to investigate EAM in patients with JIA and assess their impact on HRQoL among these patients.
Methods: This cross-sectional analytic study was carried out on 117 patients with JIA. EAM were identified clinically by history and examination. Sicca symptoms, peripheral neuropathy, enthesitis and skin lesions were picked up during clinical examination .Pulmonary involvement was evaluated by high resolution CT .Patients were assessed by abdominal ultrasonography to assess the size of liver and spleen. Atlantoaxial sublaxation was evaluated by cervical spine x-rays. Patients were evaluated by Pediatric Quality of Life Inventory-4 (PedsQL-4) and PedsQL arthritis module.
Results: The median age of patients was 14 years with a median disease duration 4 years ,82.9% were females .Of the studied 117 JIA patients , 85 patients (72.6%) had EAM in the form of persistent fatigue (70.6%), significant weight loss (14.1%),recurrent attacks of fever (18.8%), enthesitis (21.2%),lung disease (8.2%), rheumatoid nodules (2.4%),peripheral neuropathy (4.7%),uveitis (16.5),lymphadenopathy (80.2%),hepatomegaly (3.5%),splenomegaly (5.9%),sicca symptoms (2.4%), atlantoaxial sublaxation (2.4%),psoriasis (2.4%) and inflammatory bowel diseases (2.4%). Patients with EAM scored significantly lower in physical functioning (p=.001), emotional functioning (p <.001), social functioning (p=.005), and school functioning (p=.001).Regarding PedsQL arthritis module, patients with EAM had also significantly lower scores than did patients without EAM on the domains of pain and hurt (p<.001), daily activities (p=.008) and worry (p= .001).
Conclusion: Conclusion
EAM are prevalent among JIA patients and have a negative impact on their HRQoL. So, early identification and treatment are highly recommended.
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Disclosure of Interest: None declared

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JOINT DISTRIBUTION AT PRESENTATION OF JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Juvenile idiopathic arthritis (JIA) is the most common chronic inflammatory rheumatic disease in childhood and includes a heterogeneous group of different forms of arthritis of unknown etiology and pathophysiology. The major clinical manifestation of JIA is persistent joint swelling that results from the combination of synovial fluid accumulation and synovial thickening. Such swelling may cause deformities of affected joints due to stretching of periarticular ligaments and tendons, with inflammation of enthesis. Any joint can be affected, although the large ones are more frequently involved.
Objectives: The aim of this study is to assess the first joint involved in patients diagnosed with JIA in a Pediatric Rheumatology Unit
Methods: We retrospectively studied patients observed between January 1st of 1987and December 31st of 2019. The diagnosis of JIA was defined by ILAR criteria.
Results: A total of 563 patients were identified: 336 (60%) girls and 227 (40%) boys (female/ male ratio 1,5:1). Mean age was 6,2 ± 4,2 years. Most of the patients had oligoarthritis by the time of the diagnosis (*n* = 299, 53%), 17% (*n* = 107) had poliarthritis (9% with positive rheumatoid factor) and 9% (*n* = 51) had systemic arthritis. A total of 404 (72%) patients had only one joint affected at the presentation of JIA. Lower limbs joints were more frequently involved (*n* = 334, 83%), followed by upper limbs joints (*n* = 42, 10%) and axial joints (*n* = 28, 7%). Among upper limbs, metacarpophalangeal and interphalangeal joints were mainly affected (*n* = 17, 40%), followed by elbow (*n* = 12, 29%), wrists (*n* = 9, 21%) and shoulder (*n* = 4, 10%). Among lower limbs, knee was the first joint more frequently involved (*n* = 236, 71%), followed by ankle (*n* = 55, 16%), metatarsophalangeal and interphalangeal (*n* = 22, 7%) and hip (*n* = 21, 6%). Cervical spine was the most affected axial joint (*n* = 14, 50%), followed by sacroiliac joint (*n* = 10, 36%), temporomandibular joint (*n* = 3, 11%) and costochondral/sternocostal/sternoclavicular joints (*n* = 1, 3%).
Among the 404 patients, the knee was involved in 58%, ankle in 14%, metatarsophalangeal and interphalangealin 5,4% and hip in 5,2%. Proximal joints (shoulder and hip) were the first affected joints in 6% of the cases (*n* = 25). Hip was the first joint affected in 4 cases of oligoarthritis (1,3%), 3 cases of polyarthritis (3%) and 2 cases of systemic arthritis (4%).
Conclusion: This study emphasizes the frequency of the first joint involvement in different JIA subtypes with only one joint affected at presentation. Lower limb's joints are the most affected ones, specially knee and ankle. However any joint can be the first one involved in JIA. Hip's involvement is common in pediatric rheumatology, although among rheumatological disorders, JIA is a less probable diagnosis if hip is the first joint affected. Cervical spine's prolonged involvement should raise the diagnosis of JIA *ab initio.*
Disclosure of Interest: None declared

P122

METABOLIC DISORDERS IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS ON BIOLOGICAL THERAPY

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Introduction: Juvenile idiopathic arthritis (JIA) is a chronic immuno-inflammatory joint disease with a high degree of disability and an unfavorable prognosis. In recent decades, drugs aimed at pro-inflammatory cytokines, such as tumor necrosis factor (TNF), have been used very often for the treatment of JIA. The effect of these drugs on metabolic processes is not well understood.
Objectives: The aim of the study was to study metabolic disorders in children with JIA receiving biological therapy.
Methods: 36 children with polyarticular JIA and 20 healthy children were examined in the rheumatology department of the 4th city children's clinical hospital in Minsk. All children with JIA have long received methotrexate, non-steroidal anti-inflammatory drugs and, if necessary, glucocorticoids. In connection with the preservation of a high degree of disease activity during therapy, patients were prescribed adalimumab.
All children were determined by the main indicators of the lipid spectrum of the blood. Proteins that make up lipoproteins (apoproteins ApoA, ApoB, ApoE) were determined by the immunoturbidimetric method in the research laboratory of the Belarusian Medical Academy of Postgraduate Education. Statistical data processing was carried out by traditional methods of variation statistics on a personal computer using the program Statsoft Statistica 6.0.
Results: In children with JIA, the use of adalimumab showed a significant ($p < 0.05$) decrease in the concentration of ApoA (92.3 [69.7; 99.1] mg / dl) compared with the control group (127.2 [122.1; 132.3] mg / dl) and an increase in ApoB (60.9 [48.9; 73.4] mg / dl) compared with the control group (32.1 [19.9; 50.8] mg / dl).
The determination of ApoA and ApoB is used to calculate the ApoB / ApoA coefficient, which is a more reliable tool for assessing cardiovascular risk. With the ApoB / ApoA index <1, atherogenicity is regarded as low, with the ApoB / ApoA> 1, atherogenicity increases. ApoB / ApoA> 1 was established in 10 (27.8%) children with JIA.
Apolipoprotein E (ApoE) plays an important role in the regulation of lipid metabolism, has a strong antiatherosclerotic effect. There is an assumption that apoE has allele-specific antioxidant abilities. The study found a reduced level of ApoE in the blood serum of children with JIA compared with the control group.
During adalimumab treatment, a remission of the disease was achieved. According to the results of a second study of the indicators ApoA, ApoB and ApoE, 6 months after the start of biological therapy, an improvement in these indicators was found. Thus, the content of ApoA increased to 118.9 [113.2; 129.4] mg / dL, and the ApoB content decreased to 33.6 [20.8; 49.4] mg / dl. An increase in ApoE to reference values was also noted.
Conclusion: The results of the study indicate the likelihood of a reduction in cardiovascular risk in children with JIA in the treatment of adalimumab.
Disclosure of Interest: None declared

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VACCINATION COVERAGE IN A COHORT OF PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS: A SINGLE-CENTRE EXPERIENCE

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Introduction: Juvenile idiopathic arthritis (JIA) represents the most common pediatric chronic rheumatic disease. Children with JIA present an increased risk of infections, due to the immune-regulatory effects of disease modifying antirheumatic drugs (DMARDs); many of these infections are vaccine-preventable. Nevertheless, suboptimal vaccinations rates are reported in children with JIA.
Objectives: To evaluate vaccination coverage in a population of children with JIA and to describe the prevalence of the adverse events following immunization (AEFIs) in our cohort.
Methods: A single-centre retrospective study was conducted by reviewing medical records of all JIA patients, diagnosed according to ILAR criteria, admitted to the Pediatric Rheumatology Unit of University of Naples Federico II from January to December 2019. Parents were asked to provide the vaccinations records in form of the vaccination booklet. The occurrence of AEFIs was explored by telephone interviews.
Results: Data were obtained by 121 out of the 212 (57.1%) invited patients (90 females; median age: 12.2 years, interquartile range 9.25-15). The most frequent diagnosis was oligoarticular JIA (69.4%), followed by polyarticular (21.5%), systemic (8.3%), and psoriatic (0.8%) subtypes. Vaccination status was complete in 65 out of 121 of patients (53.7%): anti-diphtheria-tetanus-pertussis (DTP) and anti-poliomyelitis was complete in 76% and 72% of eligible cases, respectively; anti-hepatitis B virus in 99.2%; anti-haemophilus influenzae b in 97.5%; anti-measles-mumps-rubella (MMR) 69.4%. The most frequently omitted vaccine is MMR. There was no association between vaccination coverage and age of onset of JIA (p=0.524), gender (p=0.885) or JIA subtype (p=0.298).
The vaccination status differed in a statistically significant manner with respect to JIA treatment: vaccination coverage was complete in 75% (21/28) of patients who underwent solely nonsteroidal anti-inflammatory drugs and/or intra-articular injections of steroids compared to in 68.4% (26/38) of patients treated with methotrexate (MTX) and in 32.7% (18/55) of patients who underwent a biological DMARDs (bDMARDs) treatment (p<0.001). In particular, in the group of patients treated with bDMARDs, coverages for DTP and MMR were 67.3% and 49.1%, respectively.
In regard to non-mandatory vaccinations, 67 patients (55.4%) received the pneumococcal vaccine, 56 meningococcal C (46.3%), 14 meningococcal conjugate (ACW135Y) (11.6%), 6 meningococcal B vaccine (5%). The 15.7% of our population received at least one dose of influenza vaccine. 47.2% of eligible female patients did not receive any human papillomavirus (HPV) vaccine dose, 3.8% 1 dose, 32.1% 2 doses, and 17% 3 doses.
37 AEFIs were reported (30.6%): 11 were local reactions (9.1%), 11 fever episodes (9.1%), 2 sleepiness (1.7%). In 3 cases (2.5%), the onset of JIA occurred approximately one month after the vaccine administration and was classified as a “coincidental event", according to WHO AEFI classification.
Conclusion: In our cohort, 46.3% of patients presented an incomplete vaccination status and a low coverage for non-mandatory, though recommended, vaccinations was observed. No serious AEFI was reported. Patients treated with bDMARDs showed the lowest vaccination coverage for live-attenuated vaccines, as expected, but also for non-live vaccines, resulting in a major risk for serious diseases preventable by vaccines. Further communication strategies are therefore needed.
Disclosure of Interest: None declared

P124

MINIMAL SEDATION/ANXIOLYSIS IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS UNDERGOING INTRARTICULAR INJECTION OF CORTICOSTEROIDS

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Introduction: Intrarticular corticosteroid injections (IACI) are widely used in the management of patients with juvenile idiopathic arthritis (JIA). General anesthesia can be avoided in case of a small number of joints to inject or in older children. However, pain and anxiety may reduce the patient compliance to IACI, and may compromise the accuracy of the procedure. In order to overcame such problems, the use of appropriate methods of pain and anxiety control is advisable.
Objectives: To assess the effectiveness and satisfaction of patients undergoing IACI with the use of topical numbing agent or under minimal sedation.
Methods: Patients with JIA who underwent an IACI of up to 3 joints were recruited. Depending on age and number of joints to treat, a group of patients (group A) were injected with the application 30 minutes prior the procedure of a topical numbing agent (prilocaine+lidocaine) to the skin over the injection site. Another group of patients (group B) were treated under minimal sedation (Ketorolac/Tramadol or Morphine + Midazolam). The physician was asked to record the degree of motion and pain of the patient during the procedure and the patient (or parents for patients aged less than 4 years) was asked to report the degree of pain and satisfaction on a Visual Analogue Scale (VAS) from 0 to 10.
Results: Twenty-seven patients were enrolled for a total of 30 procedures, 17 and 13 of them in group A and B, respectively. The median age at the procedure was 10 years for group A and 11 years for group B. For group A median pain scores for patients, parents and physicians were 2, 2 and 1.5, respectively. In patients of group B who underwent the IACI under Ketorolac/Tramadol the median pain scores for patients, parents and physicians were 3, 5.25 and 2.5, whereas in patients treated with Morphine median pain scores were 6, 6 and 2, respectively. Overall, we found that pain as reported by the patient/parent were higher with increase in the number of sites injected (and, consequently, duration of procedure) and age of patient. Amount of motion during procedures was overall negligible. The majority of patients/parents was satisfied for the procedures. Only 2 patients treated with Midazolam had psychomotor agitation during the IACI.
Conclusion: IACI in a small number of sites without the use of general anesthesia is well tolerated by patients. The level of pain perceived from patients is irrespective of the power of the painkiller used, but seems to correlate with the duration of the procedures. It is possible that, in the paediatric age, the psychoemotional component seems to be decisive, with a progressive loss of tolerance with the increase in the number of injected joints.
Disclosure of Interest: None declared

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THE EFFECT OF ANTI-TNF ON ADRENAL STEROID METABOLISM IN JUVENILE IDIOPATHIC ARTHRITIS; A STEROID METABOLOMICS APPROACH

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Introduction: Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in children and is a major cause of functional disability. The chronic inflammatory synovitis and systemic features of JIA are mediated by cytokine products of an activated immune system. Decreased production of adrenal androgens and cortisol production has been observed in RA. Recent studies showed that urinary free cortisol levels in active JIA patients are significantly lower than in remission periods and control groups.

Among the cytokines that are involved in the acute phase of the disease,-TNFα has a major role.

Objectives: The aim of our study was to evaluate the impact of anti TNFα on adrenal activity by evaluating urinary adrenal steroid hormone metabolites by using GC-MS analysis before and after Etanercept treatment.

Methods: Eleven JIA patients were enrolled into the study, eight female and three male, average age was 12±6.2 years (range 3 to 21 years). The average disease duration was 6.3 ±5.2 years (range1.6-18 years) and the duration of Etanercept treatment was 3 ±2.8 years (range 6 months to 10 years). The patients were treated once weekly with Etanercept injection (0.8 mg/kg). Urine was collected 3 times (just before and +1,+3 days following Etanercept injection) for GC-MS analysis of the steroid hormone metabolites age and sex-matched healthy controls were matched to each patient. Patients were excluded if they were treated with corticosteroids in the preceding 3 months.

Results: Of the 35 metabolites measured, 23 were significantly lower in JIA patients before the Etanercept treatment compared to the healthy control group. One day after the injection only 5 metabolites were still significantly lower in the JIA patients and all the other 30 metabolites normalized and were similar to the control group. Urine metabolite ratios reflecting CYP21 and 11β-HSD2 enzymatic activity indicate that these two enzyme activities were lower in JIA patients. The slowest recoveries noted were for metabolites of DHEAS and 17 OH pregnenolone.

Conclusion: Prior to Etanercept treatment almost all urine adrenal metabolites were significantly lower mainly due to the active inflammatory process. Immediately after the treatment many metabolites raised to normal values as in the control group. The two adrenal enzymes that were found to be affected in JIR are CYP21 and 11β-HSD2. Blocking TN alpha immediately restore adrenal function in JIA.

Disclosure of Interest: None declared

P126

TRANSLATION AND VALIDATION OF THE MTX INTOLERANCE SEVERITY SCORE QUESTIONNAIRE FOR PORTUGUESE VERSION IN BRAZIL IN JUVENILE IDIOPATHIC ARTRITHIS

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Introduction: Methotrexate Intolerance Severity Score Questionnaire, MISS, is the tool in patients with juvenile idiophatic arthritis (JIA). During therapy, there are frequent reports of discontinuation of MTX, a drug classified as an the first choice for the treatment of JIA, either by physicians or patient's own conduct.
Objectives: Translate and validate the MTX Intolerance Severity Score questionnaire (MISS) to Portuguese of Brazil in patients with JIA.
Methods: The MISS was translated into Portuguese following the "Guidelines for the process of cross-cultural adaptation of self-report measures". The MISS consists of 4 domains: stomachache, nausea, vomiting, and behavioral complaints. The new version was tested on patients with JIA and relatives, both on the same day. The psychometric properties were analyzed according to the Consensus based Standards for the Selection of Health Measurement Instruments (COSMIN), analyzing acceptability for each item; internal consistency using Cronbach's alpha coefficient and reproducibility assessed by Kappa. We plot the ROC curve to evaluate the discriminant validity of the MISS compared to gold standard (clinical interview).
Results: We included 246 subjects to answer the MISS questionnaire, of these, 138 with JIA in use for least 3 months of MTX (oral/parenteral) and 108 relatives of children. All the subjects answered the MISS with less than 5 minutes and with no difficult of understanding it. The internal consistency of MISS had a Cronbach's considered good, with coefficient 0.88 (patients) and 0.79 (relatives). The reproducibility between the test (40 patients) and the retest done after 15 days (36 patients - less than 1% of missing data) was almost perfect (kappa >0.8), except item restless (kappa = 0.54). We didn't use test and retest in relative group. Reliability between patients and families was almost perfect (kappa> 0.8), except stomachache by anticipatory (weak kappa = 0.30), stomachache by association (kappa = 0.54) and restless (kappa = 0.45) when taking MTX; both values considered with moderate kappa. We plot the ROC curve and result was 0.90 (95% CI 0.85 – 0.94) for the JIA patients. We found a cutoff score of 6 denoted the best sensitivity (84% ICC 72.9-89.9) and specificity (80% ICC 70.6-91.4) for the MISS. If we considered total sample (JIA and relative), the result was 0.89 (95% CI 0.80 – 0.95) with score of 6 points denoted sensitivity 82% and specificity 79%. The original MISS version found cutoff MISS score 5 and 6 during the validation, we found a good concordance between both points, with a kappa 0.73 and 0.79, respectively; but the score 5 obtained a sensitivity 77% and specificity with 79% in the ROC curve. Finally, we considered MISS with a score 6 points through of these statistic data and comparing with other studies that used the MISS to measure the MTX intolerance in the literature. We found 96 intolerant patients (69.6%) and 42 tolerant patients (30.4%) of MTX. In intolerant, the median score MISS was 12.82 points SD±5.47, whereas tolerant were 2.42 points SD±1.75. The median score MISS for these both groups were 6.0 points SD±6.5 in 246 subjects.
Conclusion: MISS is a viable and practical tool for the routine clinical, showing a good detection between intolerant and tolerant in MTX treatment in JIA. Children or relatives can complete the questionnaire with no discrepancy.
Disclosure of Interest: None declared

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ANTI-ADALIMUMAB ANTIBODIES IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS: PREVALENCE RATE AND CLINICAL RELEVANCE

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Introduction: Patients with juvenile idiopathic arthritis (JIA) receive adalimumab treatment. Adalimumab is a monoclonal antibody that blocks TNF-α and is structurally and functionally similar to human IgG_1. Nevertheless, there are reports of the development of anti-drug antibodies. The production of these antibodies may be associated with treatment failures (a decrease in the effectiveness of therapy or drug inefficiency that developed over time) and hypersensitivity reactions. To our knowledge, there is currently limited information on the availability of adalimumab antibodies (AAA) in patients with JIA.
Objectives: to evaluate the prevalence rate and the clinical significance of AAA in patients with JIA on adalimumab treatment.
Methods: 26 patients with JIA were examined, 17 of whom had the oligoarticular form of the disease, 7 of them with uveitis, and 9 patients had the polyarticular form of the disease, 3 of them with uveitis. Among them, there were 13 (50%) girls and 13 (50%) boys. The mean age was 11.0 ± 3.4 years; the mean disease duration was 4.1 ± 2.2 years. Patients received adalimumab (at least 1 year before the study) with concomitant administration of methotrexate (MTX) or adalimumab only – 13 children who did not receive MTX for at least 3 months prior to the study as a result of either adverse events of MTX administration (5 patients) or permanent drug remission (8 patients). Before starting adalimumab therapy, all participants were treated with MTX. The mean duration of adalimumab treatment for these patients was 1.8 ± 1.0 years. The serum AAA level of antibodies was determined using the enzyme immunoassay (EIA) method. This method determines both free and bound antibodies to adalimumab at reference values less than 10 AU/ml. a and was used every 2 weeks for 3 months. The values were presented as mean ± standard deviation. Data processing and analysis were carried out using Pearson's chi-squared test and Spearman's correlation test.
Results: 8 (31%) of the 26 patients enrolled in the study had AAA-positive results. The mean AAA level in positive patients was 40.8 ± 20.1 AU/ml. Further disease relapses tended to occur significantly more often in AAA-positive patients than in AAA-negative ones ($\chi 2 = 5.46$, $p = 0.019$). Thus, 5 of 8 (62.5%) AAA-positive children had at least 1 exacerbation of the disease within 3 months, compared with 3 of 18 (16.7%) in AAA-negative ones. 7 out of 8 (87.5%) AAA-positives did not take MTX for at least 3 months compared to 6 out of 18 (33.3%) in AAA-negative ones. Thus, AAAs are found to be significantly more frequent without concomitant administration of MTX in the treatment of JIA ($\chi 2 = 6.5$, $p = 0.01$). There were no observed adverse events or side effects during adalimumab therapy. No significant correlation was found between the presence of AAA and sex, JIA form, uveitis presence, antinuclear antibodies high titer, rheumatoid factor, or disease duration.
Conclusion: We assume it would be appropriate to evaluate the AAA level in patients with JIA on adalimumab therapy, especially in the case of MTX withdrawal and the disease exacerbation. This gives a valuable advantage for further therapy enhancement.
Disclosure of Interest: None declared

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ESTABLISHMENT OF A REGISTRY FOR JUVENILE IDIOPATHIC ARTHRITIS PATIENTS IN SOUTH AUSTRALIA: FOCUS ON PATIENT-REPORTED OUTCOME AND EXPERIENCE MEASURES (PROMS/PREMS)

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Introduction: Patient outcomes and experiences are key components in the measurement of overall health outcomes in Juvenile Idiopathic Arthritis (JIA) and can be measured by validated patient-reported outcome and experience measures (PROMs and PREMs) questionnaires. There is little information in the published literature regarding the relationship between PROMs and PREMs and clinical disease activity in JIA.
Objectives: The objective was to establish a registry for JIA patients in South Australia (SA) and to understand the relationship between PROMs and PREMs and clinical disease activity.
Methods: JIA patients attending the Paediatric Rheumatology outpatient clinic at Women's and Children's Hospital were invited to participate. After obtaining written informed consent, data regarding demographics, JIA subtype, disease onset, investigation results, medications used and the clinical JIA Disease Activity Score (cJADAS) were documented. Patients/carers completed questionnaires at each clinic visit, namely the Childhood Health Assessment Questionnaire (CHAQ), the Quality of My Life (QoML) and the British Society for Paediatric and Adolescent Rheumatology (BSPAR) PROMs and PREMs Questionnaire. Disease activity states were defined based on cJADAS. Descriptive statistics, Spearman correlations and Kruskal-Wallis tests were used to analyse the data as appropriate.
Results: A hundred and twelve patients were recruited (mean age 11.7 ± SD 4.4 years) in this registry, including *n*=11 newly diagnosed JIA (9.8%) and *n*=75 female (67%). The median disease duration was 3.6 years [interquartile range (IQR) 1.2-7.7]. *N*=40, 35.7% patients had oligoarticular onset (oligo) and *n*=72, 64.3% had polyarticular onset (poly) disease.
At the time of recruitment, the median cJADAS for oligo JIA was 0.5 (IQR 0.0-4.7) and for poly JIA was 1.9 (IQR 0.1-5.0). The median quality of life (QoL) was 7.9 (IQR 6.9-9.3) for oligo and 7.6 (IQR 6.4-8.9) for poly JIA. Functional ability was excellent, with a median CHAQ score of 0.1 (IQR 0-0.6) for oligo and 0.1 (IQR 0-0.7) for poly JIA. Among those patients with established disease (*n*=101/112, 90.2%), *n*=20/33, 60.6% of oligo JIA had clinically inactive disease (cJADAS≤1), whilst only *n*=28/68, 41.2% of poly JIA had cJADAS≤1.
Patients with higher cJADAS reported lower QoL ($p<0.001$) and lower health-related QoL (HRQoL, QoL affected by health or illness) ($p<0.001$). In subgroup analysis, these associations remained significant for oligo and poly JIA. There was a statistically significant positive correlation between CHAQ score and cJADAS ($p=0.018$ for oligo, $p<0.001$ for poly), visual analogue pain score and cJADAS ($p<0.001$ for oligo, $p<0.001$ for poly).
Preliminary analysis of PROMs suggested a positive correlation ($p<0.001$ for all) between disease activity and fatigue ($R=0.39$), pain ($R=0.58$), poor sleep ($R=0.40$) and medication side effects ($R=0.33$). Also, there was a negative correlation between disease activity and social wellbeing ($R=0.59$, $p<0.001$), disease activity and emotional wellbeing ($R=0.47$, $p<0.001$).
Most participants were satisfied with the clinic environment during their hospital visits (Fully 89.9%, Mostly 9.2%), whereas relatively fewer participants felt well supported in between hospital visits (Fully 75.2%, Mostly 15.6%). Twenty-nine out of 111 (26.1%) participants experienced a delay in being seen during a clinic visit, and *n*=5/29, 17.2% of these patients felt the waiting time was unacceptable.
Conclusion: We have successfully commenced the development of a JIA registry in SA and have shown a direct relationship between clinical disease activity and PROMs, such as QoL, HRQoL, CHAQ score and PROM items for our JIA patients.
Disclosure of Interest: None declared

P129

POSSIBLE ROLE OF EARLY-LIFE EXPOSURES AND ENVIRONMENTAL RISK FACTORS IN JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Advances on molecular medicine, illumination of the cytokine network and the immune pathways shed light on the etiopathogenesis for a better understanding of Juvenile idiopathic arthritis (JIA). However, the fact that the course of the disease differs individually strongly suggests the effect of external factors.
Objectives: The current study was undertaken to evaluate sociodemographic and sociocultural features, parent behavior, the gestation and breastfeeding period, nutritional status of early childhood in our patients with JIA, and to determine their relationship with disease activity, damage index, remission time, and relapse rate.
Methods: The study was conducted with a face-to-face questionnaire method with the parents of 171 patients with JIA and 183 healthy children. The medical patient records were reviewed. Juvenile Arthritis Disease Activity Score (JADAS) 27, Wallace clinical inactive disease criteria, Juvenile Arthritis Damage Index (JADI), and relapse rates were used to assess the general medical condition of each patient.
Results: The median age of JIA patients (n = 171) was 13(3-20), with a female ratio of 59,1%. Age at disease onset was 7(1-16) years. The first remission time was 5(1-17) months. The patients were evaluated according to disease subtypes and treatment modalities. There was no difference in the duration of breastfeeding according to the distribution of the subtypes (p = 0,97). When the breastfed and formula-fed patients were compared, there was a marginally significant difference in terms of first remission time (p = 0,05), whereas there was a significant difference in relapse rate in patients who introduced to cow milk early (<12 months) (p = 0,019). The early risk factors and their relationship with the disease are presented in Table 1. Both breastfeeding durations and maternal literacy levels showed a significant difference in terms of relapse rates (p = 0,01; p=0,03, respectively). There was no significant difference in breastfeeding durations and gestational risks between the patients and the healthy group (p = 0,1; p= 0,65), respectively. However, the smoking rate among family members was significantly higher in the patient group (p = 0,03).

Table 1. Early Risk Factors and The Course Of Juvenile Idiopathic Arthritis

Closed-ended Questions	Positive answers, n (%)	JADAS, *(p)*	JADI, *(p)*	Remission, *(p)*	Relapse Rate, *(p)*
Have you ever used a cigarette during pregnancy?	41 (24)	0,20	0,72	0,13	0,63
Have you had a major illness during pregnancy?	14 (8,2)	0,2	0,4	0,97	0,92
Did you take any medication during pregnancy?	8 (4,7)	0,14	0,41	0,95	0,54
Has the child ever breastfed?	165 (96,5)	0,76	0,43	**0,05**	0,94
Has the child fed with cow's milk before 12 months of age?	21 (12,3)	0,50	0,36	0,54	**0,01**
Has the child ever been fed with formula?	85 (49,7)	0,11	0,22	0,59	0,86
Is the child's immunization in line with the vaccination schedule?	155 (90,6)	0,63	0,92	0,10	0,24
Has the child gone to preschool?	84 (49,1)	0,77	0,42	**0,008**	**0,005**
Is there any smoking indoors near the child?	107 (62,6)	0,11	0,71	0,80	0,93

Conclusion: In patients with juvenile idiopathic arthritis, breastfeeding rate and duration did not differ when compared to healthy controls. However, breastfeeding duration, cow's milk commence age, and maternal literacy appeared to be relevant to the relapse rates. Going to preschool both influence the remission time and relapse rate. These findings suggest a role for parental attitude and nutritional status during early childhood in the course of JIA.
Disclosure of Interest: None declared

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ARTICULAR AND EXTRA ARTICULAR MANIFESTATIONS IN JIA PATIENTS DURING TRANSITION

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Introduction: Juvenile idiopathic arthritis (JIA) constitutes the most common rheumatic disease in childhood. Few studies have evaluated the prevalence of activity in patients with JIA when they reach adulthood and how the presence of activity influences a transition.
Objectives: To evaluate the frequency of patients with JIA who reach 18 years of age with joint and extra articular activity.
Methods: A cross-sectional, descriptive study was conducted, including patients with JIA, aged 18 years or older. The variables studied were current age, sex, subtype of the disease and presence of articular and extra articular activity at 18 years old.Disease activity was evaluated by JDAS 78 and remission by preliminary criteria by Wallace.
Results: One hundered and thirty JIA patients were included, 77 (59.24%) of the female sex. Of these, 19 (14.62%) had the systemic form, 25 (19.3%) Oligoarticular form, 19 (14.62%) RF + polyarthritis, 42 (32.3%) FR-Polyarthritis, 5 (3.85%) Psoriatic arthritis, 17 (13.15%) Enthesitis-Associated Arthritis and 3 (2.35%) Undifferentiated arthritis. Of the 130 patients, 89 (68.4%) were inactive at the age of 18. 41 (31.6%) had joint activity and 26 (20%) active uveitis at age 18. No association between subtype of the disease, age of disease-onset, treatment and immunological features were associated with remission at age of 18.
Conclusion: Juvenile rheumatologic diseases frequently continue in adulthood requiring complex regimens of drug treatment, psychological support and complementary therapies. Our data showed that 32% of patients with JIA reached adulthood with disease activity and 20% of the patients had active uveitis, which warns of the vulnerability of young adults with JIA and the importance of a Coordinated Interdisciplinary Transition Program, focusing on orientation and education, patient satisfaction, quality of life and outcomes of the disease.

Disclosure of Interest: None declared

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ADALIMUMAB TROUGH CONCENTRATIONS ARE ASSOCIATED WITH TREATMENT RESPONSE IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Immunogenicity and low trough concentrations have been associated with adalimumab treatment failure in several studies of paediatric inflammatory diseases, indicating the possible value of therapeutic drug monitoring (TDM). Adalimumab efficacy may be improved by changing dose or treatment intervals based on drug concentrations. However, lack of standardization, assay heterogeneity, and paucity of research hinder the implementation of TDM in clinical practice.
Objectives: To assess the relationship of trough concentrations, immunogenicity and adalimumab response in paediatric patients with JIA.
Methods: Monocentric cohort study of patients ≤18 years with JIA treated with adalimumab due to active arthritis. Clinical data and plasma samples were collected during routine follow-up. Adalimumab trough concentrations were measured by liquid chromatography-tandem mass spectrometry (LC-MS/MS). Anti-adalimumab antibodies were measured in samples with trough concentrations <5mg/l. Disease activity was evaluated using the clinical Juvenile Arthritis Disease Activity Score with 71 joint count (cJADAS71). Response to adalimumab was defined as at least 50% reduction of disease activity within 3 months of therapy followed by clinical inactive disease or minimal disease activity after 6 months. The latter was defined as cJADAS71 ≤1.5 and ≤2.5, for oligoarthritis and polyarthritis, respectively, or an active joint count equal to zero when cJADAS71 was unavailable.
Results: 36 adalimumab trough samples were available from 35 JIA patients. Although there was no significant difference in median adalimumab dose, trough concentrations were significantly lower in patients with secondary failure compared to primary failure or an adequate adalimumab response (p-values <0.01). In addition, there were 11 samples with trough concentrations <5mg/l, 9 in the group with secondary failure and 2 in the group with adequate adalimumab response (Table 1).

Table 1. Characteristics of included JIA patients.

	Responders	**Primary failure**	**Secondary failure**
Patients, n	16	8	12
MTX, n (%)	12 (75)	7 (88)	5 (42)
MTX dosage (mg/m^2/week)	6.7 (5.3-12.3)	12.1 (7.7-12.8)	7.3 (5.3-8.4)
ADA duration (days)*	218 (98-398)	160 (132-264)	728 (387-1021)
ADA dosage (mg/kg/week)	0.34 (0.31-0.45)	0.35 (0.31-0.4)	0.38 (0.27-0.53)
ADA concentration (mg/l)*	14.94 (10.31-16.19)	13.37 (10.85-15.99)	1 (1-5.3)
ADAb-positive	1/2	0/0	7/9
AJC*	0 (0-0)	2 (2-5)	1 (1-3)
cJADAS71*†	0.2 (0-0.4)	5.5 (3.9-9.2)	6.5 (4-9.2)

*Significant difference, p-values <0.01. **†** cJADAS71 was available for 10/16 patients with adequate response, 7/8 with primary failure, and 11/12 with secondary failure; Continuous data are presented as median (interquartile range); ADA: adalimumab; ADAb: anti-drug antibody; AJC: active joint count.
Conclusion: Adalimumab trough concentrations were significantly lower in JIA patients with secondary failure compared to primary failure or an adequate response to adalimumab. Anti-adalimumab antibodies were present in 8 out of 11 samples with trough concentrations <5mg/l. Adalimumab trough concentration measurements may identify JIA patients that would benefit from increased doses or shorter treatment intervals. In addition, JIA patients with primary failure and adequate adalimumab trough concentrations may respond better to biologic agents with other therapeutic targets. Although biologic agents have improved disease outcome of patients with JIA, concentration measurements using reliable and cost-effective methods, such as LC-MS/MS, could further improve efficacy of biologic agents and guide treat-to-target strategies.
Disclosure of Interest: None declared

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COMORBIDITIES IN JUVENILE IDIOPATHIC ARTHRITIS - IMPORTANT TO EVALUATE PATIENT MENTAL HEALTH

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Introduction: The role of comorbid disease among children with juvenile idiopathic arthritis (JIA) differ, and while the evidence for malignancy is inconclusive (1-5), there seems to be an increased prevalence of comorbid depressive and/or anxiety disorders (6) as well as an increased risk for other autoimmune diseases i.e. type 1 diabetes mellitus (DM1), hypothyroidism and coeliac disease (CD) (7-9).

Objectives: To study the long-term occurrence of comorbid malignancy, psychiatric and autoimmune disease in JIA in a population-based cohort of children with a validated diagnosis of JIA collected over nine years.

Methods: The study cohort comprised of 252 validated cases of JIA diagnosed 2002-2010 in Skåne (10), the southernmost region of Sweden (population 1.24 million; 17.6% aged < 16 years, year 2010). ICD-codes registered 1998-2019 for malignant tumours including hematologic malignancies (C00-C97), depression and anxiety disorders (F32, F33, F34.1, F41) and the autoimmune conditions DM1 (E10), hypothyroidism (E03) and CD (K90.0) were collected from the Skåne Health-care Register. Data is descriptively presented as percentage of comorbid disease in the cohort.

Results: No cases of malignant disease were found. Depression or anxiety occurred in 19.8% of the cohort. DM1 was present in 2.8% of the cohort. 5.6% of the patients had comorbid hypothyroidism; no case was due to exogenous substances or complication after infection. CD occurred in 5.2% of the cohort. (Table 1).

Table 1. Comorbidities in JIA (n=252)

	Total (%)
Malignancy	0
Depression/Anxiety	19.8
Diabetes mellitus, type 1	2.8
Hypothyroidism	5.6
Coeliac disease	5.2

Conclusion: In all, 1/5 of the individuals with JIA in this validated population-based cohort were diagnosed with either depression and/or anxiety disorder over a period of 22 years. The presence of a comorbid autoimmune disease in this cohort was, except for a lower proportion of hypothyroidism, in line with previously published results. However, the results need to be compared with the age-matched general population. Knowledge of high-risk comorbidities will contribute to better care for JIA patients, with potential development of new screening routines and our results highlight that it is important to continuously evaluate the patient's mental health to early detect symptoms of mental illness.

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Disclosure of Interest: None declared

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ECHOCARDIOGRAPHIC FINDINGS OF CHILDREN WITH JUVENILE SPONDYLOARTHROPATHIES

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Introduction: Juvenile spondyloarthropathies (jSpA) is an umbrella definition of a group of inflammatory diseases characterized by asymmetric peripheral arthritis (especially in lower extremities), axial skeleton involvement and enthesitis. Although, cardiovascular findings of inflammatory diseases such as juvenile systemic lupus erythematosus, juvenile scleroderma, juvenile dermatomyositis well-documented, it has not been extensively studied in children with JSpA, and there are only few studies in the literature.

Objectives: This cross-sectional study had conducted for evaluating the cardiac functions of the children and adolescents with JSpA.

Methods: Forty patients with JSpA and twenty healthy control were included into the study. Healthy children or adolescents who attended the outpatient clinic for routine control were enrolled in the control group after the informed consent was taken. Patients with history/evidence of congenital heart disease, any rhythm abnormalities, other chronic systemic diseases (including renal, pulmonary diseases, diabetes, etc.), and those taking medications other than JSpA therapy were excluded. Cardiac functions of the patients and healthy controls were evaluated by conventional echocardiography and pulsed-wave tissue Doppler.

Results: Female/male ratio in patient and control groups were 0.6 and 0.81 respectively. The mean ages were 15 ± 3 years in patients with JSpA and 11.9 ± 3.6 years in control group. The mean age at diagnosis was 12.6 ± 2.9 years and the median follow-up duration was 23 (1-129) months. Tricuspid lateral annulus TDI-PW velocities E'/A' ratio was significantly lower in patients with JSpA than in healthy controls [1.5 (0.72-4) versus 1.7 (1.2-2.2), $p<0.05$]. Ejection fraction, right ventricle FAC and TAPSE were similar in both groups. Cardiac function parameters of patients were compared according to presence of enthesis, HLA-B27 positivity, morning stiffness, hypertension, medications they were on and erosion/sclerosis on X-ray of pelvis. There were no significant differences between the patients with and without enthesis, HLA-B27 positivity, morning stiffness and erosion/sclerosis on X-ray of pelvis. When cardiac function parameters were compared for magnetic resonance imaging (MRI) findings like bone marrow edema, enthesis, erosion, sclerosis, synovitis; there were no significant differences between groups except for enthesis. Patients with enthesis that is detected on MRI had lower ejection fraction ($p<0.05$). The correlation analysis that was made for comparing the effect of the disease activity on the cardiac functions; showed significant, moderate correlation between BASDAI score and PW-trans mitral A velocity ($r=-0.352$, $p=0.03$) and moderate negative correlation between BASDAI score and TAPSE ($r= -0.407$, $p=0.03$). There was significant, moderate negative correlation between follow-up duration and shortening fraction ($r=-0.41$, $p=0.009$).

Conclusion: In this cross-sectional study, we are reporting disturbed RV diastolic function with preserved RV systolic function and possible association between MRI confirmed enthesis and lower LV systolic functions. Early identification of cardiac dysfunctions in these patients can help to prevent long-term cardiovascular complications in JSpA before irreversible changes take place.

Disclosure of Interest: None declared

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GENDER DIFFERENCES IN PHYSICAL FITNESS RELATED TO SELECTION IN CLUB-SPORT ACTIVITIES IN JIA

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Introduction: Most studies of physical fitness (PF) in juvenile idiopathic arthritis (JIA) have shown decreased levels of maximal oxygen consumption (VO_2max) compared to healthy peers. In JIA, boys have higher PF-levels than girls and younger children have higher levels than adolescents, congruently with data of healthy peers. Previously, we have shown that more than half of JIA-patients had below normative average of VO_2max. However, monitoring physical activity (PA) using accelerometry, 68% of boys and 39% of girls with JIA fulfilled the recommendations of WHO of ≥1 hour of PA per day, which was comparable to normative values (61%/39%). Moreover, patients reporting engagement more than 7 hours per week in club-sports exceeded accelerometry values of healthy peers.
Objectives: To explore the association between PF and specific sport habits in 10 to 16-year-old JIA-patients, related to gender, BMI, disease activity, and pain, and comparing the most fit quartile (Q4) of patients (respectively boys and girls) to the least fit quartile (Q1).
Methods: Sixty patients with JIA performed an indirect ergometer-test of VO_2max (Watt max test) and answered the Physical Activity and Sport Questionnaire (PASQ). Objective PA-monitoring for one week was conducted using the GT1M accelerometer. Cut-offs for moderate-high and high intensity PA were set to >1000 and >2500 counts per minute, respectively. Disease activity was assessed with the JADAS-27, current pain and worst pain last week were measured on visual analogue scales (VAS) and in a one-week pain diary using the Faces Pain Scale-Revised (FPS-R).
Results: Girls with JIA (n=36) had lower mean PF than the boys (n=24) (36.5±8.2/43.4±6.73 ml/kg/min), being below normative values, respectively. In both genders the most fit boys and girls (Q4; 49.3-57/40.9-54) had average to well-above normative average PF. The least fit boys (Q1; 33.5-37.4) all had PF-levels well-below normative average. In girls Q1-levels (18.7-30.9) were well-below to below normative average.
We found significant differences between most fit (Q4) and least fit (Q1) patients regarding patient´s global wellbeing (p=0.040) and pain diary (p=0.026). These differences were not significant when separating genders, though differences were more pronounced in girls. The least fit girls (Q1) had significantly higher disease activity (JADAS-27) than the most fit girls (Q4)(p=0.019).
The most fit boys and girls (Q4) engaged equally in high intensity sports (soccer: 3/24; 2/36, handball: 0/24; 2/36, gymnastics: 2/24; 4/36, rowing: 1/24; 0/36). However, more boys than girls played soccer (11/24; 3/36), whereas more girls preferred sports of lower intensity (riding: 8/36; 0/24). Eight of 11 boys in soccer and 2 boys in gymnastics or rowing had below average to well-above normative average of PF (Q3+Q4: 41.6-57). Three girls in gymnastics, 2 girls in soccer, and 2 girls in handball were in Q4 (40.9-54) with levels of average to well-above average PF. The third girl in soccer was in Q2 (31-36.3) with levels of well-below to below normative average. None of the riding girls were in Q4 and only 1 was in Q3 (36.3-40.8) (Below to average normative PF). Comparing accelerometer-monitored values of PA-intensity in girls with low (Q1) and high (Q4) PF, PA-values of Q1 were significantly lower than in Q4. The same tendency was observed in boys, but not to significance.
Conclusion: Our results are in accordance with most other studies of PF in JIA, adding to the knowledge of gender-specific differences in PF and type and behavior in sport activities. It emphasizes the need of regular PF-testing and guidance in high intensity PA and sport in order to improve PF and avoid the risks of inactivity and lifestyle diseases in JIA.
Disclosure of Interest: None declared

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THE RATIO OF SOME CYTOKINES LIKE A MARKER OPTIONS AND COURSE OF JUVENILE ARTHRITIS

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Introduction: The leading role in the implementation of inflammation in the human body belongs to cytokines. The study of the role of each of them and their cooperation continues with autoimmune diseases. New data on the importance of chronic inflammation of interleukin 17 (IL-17) have found. The effect of their ratio on the activity of inflammation is not well understood.

Objectives: To study the ratio of some initiating and blocking cytokines of IL-17 in children with juvenile idiopathic arthritis (JIA).

Methods: 40 children with JIA (12 oJIA, 17 pJIA, 1 with positive RF, 6 eJIA, 5 sJIA were examined during the period of exacerbation of the disease with an assessment of the activity and course of the disease. All cases were additionally studied IL-1β, receptor (IL-17R), IFN-γ in blood serum using linked immunosorbent assay sandwich option.

Results: The data obtained showed IL-1β was significantly increased only in sJIA (30.15±17.09 pg/ml), significantly ($p<0.05$) higher than in other JIA (6.71±0.91 pg/ml in oJIA, 8.61±1.11 pg/ml in sJIA). This was detected in 2/3 of the patients, higher ($p<0.05$) in adolescents (16.69±8.32 pg/ml) compared with children 4-12 y.old (6.69±0.86 pg/ml). IFN-γ was increased above normal values (up to 50 pg/ml in healthy children) in all cases of JIA, it could be possible its role in the initiation of outbreak. Maximum values were noted in oJIA, especially in cases with uveitis (7029.2±4750 pg/ml) and were higher ($p<0.1$) in children 1-3 years old versus adolescents. IL-17R was maximum in pJIA patients (2058936±35.21 pg/ml) and eJIA (22723.65±16022.54 pg/ml), which also showed the highest the frequency of detection of its increase. It was absent in sJIA (7.52±4.74 pg/ml). The highest values of IL-17R (1849836.4±176751 pg/ml) were in the middle age group. The data obtained suggest the compensatory value of increasing IL-17R and the simultaneous initiation of inflammatory and anti-inflammatory processes during exacerbation of JIA. Assessment of the ratios of stimulating and inhibiting cytokines showed in patients with uveitis, the ratio of IFN-γ/IL-1β (4379.29 ±476.83) was higher than with other JIA (from 60.84 ± 14.92 in oJIA to 105.20±66.01 in pJIA) and IFN-γ/IL-17R (4474.01 ±3899.19 versus from 20.14±11.48 in oJIA to 934.55±931.37 in sJIA). An increase of IL-1β/IL-17R ratio was characteristic only for sJIA (34.12±26.17). All of these ratios increased with disease activity ($r=0.22$-0.37) & they did not reflect the unpleasant course of the disease.

Conclusion: The balance of cytokines determines the direction of the inflammatory process in JIA. The most unfavorable presence of an increase IL-1β/IL-17R. The ratios IFN-γ/IL-1β and IFN-γ/IL-17R could be considered as potential markers of uveitis & IL-1β/IL-17R - sJIA.

Disclosure of Interest: None declared

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TREATMENT WITH METHOTREXATE AND ETANERCEPT DOES NOT ALTER THE FECAL MICROBIOTA COMPOSITION IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: The first-line treatment for juvenile idiopathic arthritis (JIA) is usually methotrexate (MTX), followed by treatment with an anti-tumour necrosis factor alpha (anti-TNF-α) drug, such as etanercept (ETN). The effects of MTX and anti-TNF-α drugs on the fecal microbiota in children with JIA have not been studied previously.
Objectives: To study the effects of MTX and ETN treatments on the fecal microbiota composition in children with JIA.
Methods: In this multicenter, case-control study, 113 fecal samples were collected from 91 children with JIA, with 72 of these samples collected from untreated children (67 of whom were treatment-naïve children). Samples from 28 children with JIA were collected during treatment with MTX as single treatment and samples from 13 children during treatment with ETN. Of those 13 children, four were treated with ETN as single treatment and nine had a combination of ETN and MTX.
We compared 28 children on single treatment with MTX with 57 untreated children (52 treatment-naïve), and 13 children on treatment with ETN (nine in combination with MTX) with 62 untreated children (57 treatment-naïve). We also did pairwise comparisons of samples taken before any medication was given (n = 22) and samples taken during ongoing treatment with MTX (n = 14) or ETN (n = 8, four in combination with MTX).
The microbiota was characterized by sequencing amplicons from the V3 and V4 regions of the 16S rRNA gene.
Alpha diversity of the fecal samples was measured using the Chao-1 index and the Shannon diversity index. To compare these indices between treated children and untreated children, we used a logistic regression model with age at sampling as a covariate. For pairwise analyses, we used the Wilcoxon signed-rank test.
To analyze the community composition of the microbiota, principal coordinate analysis (PCoA) plots based on Bray-Curtis distances were generated for visual comparisons, and analysis of similarity (ANOSIM) was used to test for differences.
Analyses for relative abundances of taxa were performed at three taxonomic levels (phyla, families, and genera), and logistic regression with age as a covariate was used for calculations of differences between treated and untreated children, while the Wilcoxon signed-rank test was used for pairwise comparisons. Significance was set to $p < 0.05$ and corrections for multiple comparisons were made using the Benjamini-Hochberg method.
Results: Analyses showed no significant differences in α-diversity between children treated with MTX or ETN and untreated children, and pairwise comparisons of samples before and during treatment with MTX or ETN also showed no differences.
PCoA plots for children treated with MTX or ETN, in comparison with untreated children, did not show any clustering. ANOSIM showed no significant differences between treated and untreated children.
PCoA plots were also made for the pairwise comparisons of children sampled before and during treatment, and according to that analysis the community compositions of microbiota did not change in any uniform way during treatment with either MTX or ETN.
Furthermor, analyses of relative abundances of specific taxa did not reveal any significant results in any of the comparisons, after adjustment for multiple analyses.
Conclusion: Treatment with MTX or ETN did not alter the composition of fecal microbiota in children with JIA.
Disclosure of Interest: None declared

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SYNOVIAL FLUID NEUTROPHILS FROM PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS DISPLAY A HYPERACTIVATED PHENOTYPE

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Introduction: Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in childhood and an important cause of short-term and long-term disability if patients are not treated appropriately. By definition, JIA clinically presents with peripheral joint inflammation of unknown origin, persisting for at least six consecutive weeks and starting before the age of 16 years. The predominant subtypes, *i.e.* oligoarticular (oligo) and polyarticular (poly) JIA, have long been assumed autoimmune diseases caused by dysregulation of the adaptive immune system, with a central role for autoreactive T cells belonging to the Th1 and Th17 lineages and autoantigens that may include aggrecan, fibrillin, matrix metalloproteinase (MMP)-3 and heat shock proteins. Nevertheless, the original T cell-centered hypothesis has been challenged since it does not cover nor completely explain the full spectrum of immune-pathological phenomena observed in patients.
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Objectives: Emerging evidence suggests a potentially important role for neutrophils in JIA pathogenesis. Here, we investigated extensively the phenotypical features of neutrophils present in the peripheral blood and inflamed joints of JIA patients.
Methods: Synovial fluids and parallel blood samples from patients with oligo- or polyJIA and blood samples from healthy children were collected. Multicolor flow cytometry panels allowed for in-depth phenotypical analysis of neutrophils, focusing on the surface expression of adhesion molecules, activation and maturation markers, chemoattractant- and Toll-like receptors. Multiplex technology was exploited to quantify pro- and anti-inflammatory cytokines in plasma and synovial fluids.
Results: The vast majority of synovial fluid neutrophils displayed a strongly activated, hypersegmented phenotype with decreased L-selectin (CD62L) expression and increased numbers of nuclear lobes, upregulation of adhesion molecules CD66b, CD11b and CD15 and downregulation of chemokine receptors CXCR1/2. An elevated percentage of CXCR4-expressing aged neutrophils was detected in synovial fluids from patients. Strikingly, significant percentages of synovial fluid neutrophils showed a profound upregulation of atypical neutrophil markers, including CXCR3, ICAM-1 and HLA-DR.
Conclusion: Our data indicate that neutrophils present in inflamed joints of JIA patients are strongly activated cells with elevated pro-inflammatory and antigen presenting potential. This detailed molecular analysis supports the notion that a complex intertwining between these innate immune cells and adaptive immune events drives JIA.
Disclosure of Interest: None declared

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THE MAIN FACTORS, ASSOCIATED WITH INCOMPLETE VACCINATION AGAINTS MEASELS, PAROTITIS, RUBELLA AND DIPHTHERIA IN 170 JUVENILE IDIOPATHIC ARTHRITIS PATIENTS.

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Introduction: Patients with juvenile idiopathic arthritis (JIA)may have incomplete vaccination againts different vaccines leads to lower protective levels of anti-vaccine antibodies.
Objectives: The aim of our study was to evaluate the rate and the main factors of incomplete vaccination against measels,parotitis, rubella (MMR) and diphtheria in JIA patients.
Methods: In the present study were included data 170 JIA(55 boys and 115 girls)aged from 2 to 17 years,who received scheduled vaccination before the age of 2 years and before JIA onset against measles,parotitis,diphtheria and rubella.Incomplete vaccination means the reduced number of vaccine to age.In all patients the Ig G anti-vaccine antibodies levels were detected with ELISA.JIA categories were:oligoarthritis - 73,polyarthritis - 61,systemic-16 and enthesitis-related arthritis-20.Data presented with median and 25%>75%
Results: Incomplete vaccination against MMR was in 50 (42%)diphtheria in 85 (50%) of the JIA patients. The main differences in the studied groups are in the table.There were no differences in sex,JIA categories and treatment, except biologics compare to complete and complete vaccination in all vaccines.No differences in antimeasels(p=0.18),antiparotitis (p=0.1) and anti-rubella(p=0.17)vaccination between complete and incomplete vaccination group.Number of patients with protective level of anti-vaccine antibodies was similar, except parotitis(70% vs 84.2%, p=0.035).The anti-diphtheria antibodies IgG level was lower in the patients with incomplete vaccination group (0.07 IU/ml [95%CI:0.03; 0.22] vs 0.2 [95%CI:0.06; 0.4], p=0.001)as well as number of patients with protective level(34% vs 54%, p=0.002). In the multiple regression model only JIA onset age(p=0.00001)and methotrexate treatment duration(p=0.003) were predictors of incomplete vaccination against MMR and methotrexate treatment duration(p=0.005) and biologic treatment(p=0.05) for diphtheria incomplete vaccination.Incomplete MMR vaccination influence on the maintenance of the protective anti-parotitis level(p=0.036)in regression model.In correlation analysis the number of vaccination influences on anti-diphtheria antibodies level(p=0.017)and number of patients with protective level of anti-diphtheria antibodies(p=0.017). The main predictors in logistic regression for incomplete vaccination for MMR were:onset age<6 years(OR=7.8 [95%CI:3.2;18.7], Se=0.6, Sp=0.86, p=0.000001),JIA duration>3.1years (OR=4.4 [95%CI:2.0;9.9], Se=0.5, Sp=0.81, p=0.0002), methotrexate duration>3.1 years (OR=5.7 [95%CI:2.7;12.0], Se=0.74, Sp=0.67, p=0.0000012); biologic treatment(OR=2.5 [95%CI:1.3;4.9],Se=0.64, Sp=0.58) and treatment>1 biologic (OR=3.3 [95%CI:1.1;10.4], Se=0.63, Sp=0.67); for diphtheria were:JIA duration>3.1years (OR=3.4 [95%CI:1.8;6.5],Se=0.55,Sp=0.73,p=0.0002), methotrexate duration>2.8 years (OR=4.1 [95%CI:2.1;8.1], Se=0.73,Sp=0.61, p=0.00004),biologic treatment (OR=2.4 [95%CI:1.3;4.4], Se=0.59, Sp=0.62).

Parameter	MMR, incomplete		p	Diphtheria, incomplete		p
	yes	no		yes	no	
Onset age, y	4.0 (3.0; 5.9)	7.0 (4.9; 11.0)	0.000001	5.0 (3.0; 8.0)	6.6 (4.4; 10.1)	0.016
JIA duration, y	5.5 (3.2; 8.6)	3.1 (1.5; 5.4)	0.0005	4.5 (2.8; 8.7)	2.9 (1.3; 5.5)	0.0006
Biologics, n (%)	32 (64)	50 (42)	0.008	50 (59)	32 (38)	0.006
More than one biologics, n (%)	10 (20)	6 (5)	0.002	10 (12)	6 (7)	0.022
Methotrexate duration, y	5.0 (2.1; 7.5)	1.8 (0.9; 3.2)	0.000006	3.3 (1.7; 7.3)	1.7 (0.9; 2.9)	0.00002

Conclusion: Younger onset of JIA age, longer duration of JIA and methotrexate treatment, biologics and more than 1 biologics are the main predictors of incomplete vaccination againt MMR and diphtheria.
Disclosure of Interest: None declared

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BIOMARKERS PREDICTING THE FURTHER DISEASE COURSE IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA): RESULTS FROM THE INCEPTION COHORT OF NEWLY DIAGNOSED PATIENTS WITH JIA (ICON-JIA)

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Introduction: Biomarkers have shown potential as diagnostic and prognostic tools in juvenile idiopathic arthritis (JIA).
Objectives: To describe the association of baseline serum biomarkers in patients with newly diagnosed JIA and their 1-year outcomes.
Methods: Serum samples of JIA patients enrolled in the German Inception Cohort of Newly diagnosed patients with JIA (ICON-JIA) at ≤ 1 year of JIA diagnosis were collected at study enrolment and after 3 months. Standard laboratory markers of inflammation (CRP, ESR), as well as novel biomarkers - CXCL-9, CXCL-10, CXCL-11, G-CSF, IL-6, IL-17A, IL-18, MCP-1, MIP-1a, MMP-3, S100A8/A9, S100A12, TNFa, and TWEAK were analyzed for their potential to predict the 1-year outcome. Demographic and clinical parameters were also recorded. Disease activity was assessed with the clinical Juvenile Arthritis Disease Activity Score (cJADAS)10.
Results: Two-hundred-sixty-six JIA patients had active disease at baseline, with oligoarthritis and rheumatoid factor-negative polyarthritis representing the largest proportion (72.9%). CRP, ESR, IL-18, S100A8/A9 and S100A12 levels were higher in patients with systemic JIA compared to other JIA categories. Baseline levels of G-CSF, IL-18 and TWEAK were lower in oligoarthritic JIA patients with disease extension within one year. Higher baseline ESR, G-CSF, IL-6, and TNF levels indicated the risk of increased disease activity at 12 months. Additionally, higher levels of ESR, CRP, S100A8/A9, and S100A12 at baseline were associated with the necessity to escalate therapy during the first 12 month of follow-up and subsequent addition of biologic disease-modifying antirheumatic drugs.
Conclusion: Our data demonstrate that increased disease activity at baseline, defined through both clinical parameters and biomarker levels is associated with the risk of continued disease activity after 12 months.
Disclosure of Interest: None declared

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SCREENING FOR ANTITHYROID ANTIBODIES IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS: A SINGLE-CENTRE EXPERIENCE FROM SOUTHERN ITALY

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Introduction: The prevalence of autoimmune thyroid disorders (AITD) has been reported to be higher in patients with juvenile idiopathic arthritis (JIA) in comparison to the general population. Nevertheless, there is a lack of studies investigating risk factors for AITD development in children with JIA.
Objectives: To investigate the co-occurrence of JIA and autoimmune thyroiditis in southern Italy and to identify potential predisposing factors to anti-thyroid antibodies (ATA) positivity in a JIA population.
Methods: A single-centre retrospective study was conducted. All JIA patients admitted to the Pediatric Rheumatology Unit of the University of Naples Federico II, from January 2001 to December 2019, tested for ATA at least once and with a minimum of 6-months follow-up, were included. For each patient, demographic, clinical and laboratory data were extracted from clinical charts. Differences between patients affected by JIA with or without ATA were analyzed.
Results: Three hundred thirty JIA patients (247 females; median age 12.5 years, IQR 9.1-16.1) were included in study. Median age at JIA onset was 4 years (IQR: 2.2-7.8). Twenty-three patients [7% (95% CI 4.5-10.3)] presented ATA positivity. Twenty-one of them (91.3%) were females. Anti-thyroperoxidase was positive in 18/23 patients (78.2%) while 12 patients presented anti-thyroglobulin positivity (52.1%). Both antibodies were present in 8/23 (34.8%). 19 patients showed the typical ultrasound findings of autoimmune thyroiditis, resulting in a prevalence of Hashimoto's thyroiditis of 5.7% (95% CI 3.5-8.8) in our cohort. Three female patients developed subclinical hypothyroidism, whereas one male patient presented subclinical hyperthyroidism. The remaining 19 patients were euthyroid. No statistically significant difference was observed in regard to age of JIA onset, follow-up duration and JIA subtype between the patients with or without ATA. The proportion of females was marginally significantly higher (p=0.059) in the group with ATA positivity compared to children without thyroid antibodies (91.3% vs 73.6%, respectively). 56.5% of patients with ATA showed ANA positivity compared to 37.5% of patients without ATA (p=0.07). Family history for AITD was significantly higher in children with thyroid antibodies positivity (p=0.01). Anti-TNF-alpha inhibitors were administered in only 3 children (13%) with thyroid antibodies before their detection compared to 35.5% of patients without thyroid antibodies (p=0.028). Multivariate regression analysis showed that patients with a family history for AITD were about four times more likely to develop ATA (OR 3.75, 95% CI 1.401-10.017, p=0.008) and confirmed that ATA positivity is less likely to occur in patients undergone anti-TNF-alpha therapy (OR 0.127, 95% CI 0.031-0.518, p=0.004).
Conclusion: A high prevalence of ATA positivity and Hashimoto's thyroiditis in patients with JIA was found in our wide southern Italian cohort. As expected, a positive family history of AITD was found to be associated with a higher risk to ATA development during the follow-up. This finding supports the usefulness of an active screening for AITD in JIA children, in particular in patients with relatives affected by thyroid disorders. Notably, patients treated with TNF-alpha inhibitors resulted less likely to develop thyroid antibodies. Further studies are needed to investigate the effect of anti-TNF-alpha therapy on thyroid autoimmunity in JIA.
Disclosure of Interest: None declared

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WHICH MUSCULOSKELETAL SITES INVOLVED CAN WE EXPECT AT JUVENILE IDIOPATHIC ARTHRITIS (JIA) ONSET?

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Introduction: The knee is considered by far the joint most frequently affected at JIA onset. Nonetheless, JIA onset may present with unusual musculoskeletal involvement, eventually leading to a delay in the diagnosis and treatment.
Objectives: To identify the type and number of musculoskeletal sites affected at JIA onset in consecutive patients seen at the study center in an 8 years period.
Methods: Records of patients with new diagnosis of JIA from June 2012 to May 2020 available information in the medical history and standardized joint assessment at diagnosis, were retrospectively reviewed. Systemic JIA subtype according to ILAR classification criteria were excluded. Demographic and clinical features, including the type and number of joints at disease onset and diagnosis, were registered. Data were analyzed through descriptive statistics.
Results: Of a total of 333 Caucasian patients included in the study (75.7% females), 241 patients (72.4%) had oligoarthritis, 79 (23.7%) RF-negative polyarthritis, 7 (2.1%) RF-positive polyarthritis, 1 (0.3%) psoriatic arthritis, 5 (1.5%) enthesitis-related arthritis (ERA). Antinuclear antibody (ANA) were positive in 188 patients (56.5%). The median age at onset was 4.8 years (IQR 2.3-9.3). At diagnosis 103 (30.9%) patients had only 1 active joint, 143 (43.0%) had 2-4 active joints, 87 (26.1%) had ≥ 5. As expected the knee, the tibiotalar and the wrist were the most frequently affected joints (77.2%, 41.1%, 21.0%, respectively); cervical spine was involved only in patients with polyarthritis (n=13). Notably, of 103 patients with monoarthritis at diagnosis 98 presented with large joints involvement, among which n=2 isolated elbow and n=2 isolated wrist, and 5 with small joints involvement (Table 1). No sufficient data were available regarding the involvement of tendons and bursae, since the standard joint assessment form did not include them. Nonetheless, additional 4 patients, not included in the sample analysis, had isolated tenosynovitis involvement at diagnosis (n=1 both-sided ulnar extensor tendons; n=2 isolated tenosynovitis of the flexor digiti proprius; n=1 tenosynovitis of 2 flexors digiti proprii).

Table 1. **Number of patients with mono- or oligo-arthritis at disease diagnosis according to specific joint involvement.**

	NAJ=1 (N=103)	**NAJ=2-4** (N=143)
Temporomandibular joint	0	2
Shoulder	0	1
Hip	1	1
Metacarpophalangeal joint	0	20
Proximal interphalangeal joint	2	31
Distal interphalangeal joint	2	5
Metatarsophalangeal joint	0	6
Toe	1	22

Conclusion: Our study confirms the knee, the tibiotalar and the wrist as the most frequently affected joints at JIA diagnosis. On the other hand, musculoskeletal sites, such as small joints of hands and feet, the hip and the shoulder, usually involved in polyarticular JIA, can be the site of disease presentation in oligo- and also mono-articular JIA. Further, JIA may present with isolated tendon involvement. Our results foster not to delay JIA diagnosis in persistent synovitis occurring in infrequent joints and to include musculoskeletal sites, other than joints, in the standard articular evaluation. This could be realized by merging clinical and imaging (i.e. ultrasound) musculoskeletal examinations in the same assessment.
Disclosure of Interest: None declared

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COMBINING AGE AT JIA ONSET, FEMALE GENDER, ANA POSITIVITY AND FAMILY HISTORY OF AUTOIMMUNE DISEASE TO PREDICT AUTOIMMUNE THYROID DISEASE IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Comorbidities occur more often in patients with juvenile idiopathic arthritis (JIA) than in the general population. In adults, the association between rheumatoid arthritis (RA) and other autoimmune diseases, such as autoimmune thyroid disease (AITD) is reported. Little is known about the association between JIA and other autoimmune diseases, like AITD.
Objectives: The purpose of this study is to evaluate the prevalence of symptomatic AITD in JIA patients and to investigate whether there are any factors associated with a higher risk of developing AITD.
Methods: Data of 8,971 patients, classified by the International League of Associations for Rheumatology (ILAR) criteria, were analyzed in a dataset from the worldwide PharmaChild registry. Patients with diagnosed Hashimoto's thyroiditis, Graves' disease and non-specified autoimmune thyroiditis were labeled as suffering from AITD. Logistic regression analyses were used and a prediction model was developed.
Results: In this study, the prevalence of symptomatic AITD was 1.1% of all JIA patients. In multivariate analyses, being older at JIA onset (OR= 1.12; 95% CI= 1.05-1.19) , female gender (OR= 2.33; 95% CI= 1.32-4.11), ANA positivity (OR= 3.27; 95% CI= 1.78-6.00) and family history of autoimmune disease (OR= 3.07; 95% CI= 1.76-5.37) were significantly associated with developing AITD ever. The final prediction model of developing AITD ever (AUC =0.702; 95% CI= 0.64-0.77) included the predictors age at JIA onset ($p<0.001$), gender ($p= 0.058$), ANA positivity ($p= 0.001$) and family history ($p<0.001$).
Conclusion: The best predictors for the development of AITD in JIA patients ever were shown to be age at JIA onset, female gender, ANA positivity and family history of autoimmune diseases.
Disclosure of Interest: None declared

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METHOTREXATE RESPONSE SUBGROUPS IDENTIFIED IN TWO UK JUVENILE IDIOPATHIC ARTHRITIS COHORTS

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Introduction: Treatment response in JIA is currently viewed as a binary outcome: response or non-response. However, JIA is a heterogeneous disease and it is likely that different, identifiable subgroups of children and young people (CYP) may demonstrate different patterns of disease following treatment. Identifying these response subgroups can assist the tailoring of stratified treatment approaches in JIA.

Objectives: To identify subgroups of CYP defined by different trajectories of juvenile arthritis disease activity score (JADAS) components following methotrexate (MTX) initiation for JIA.

Methods: MTX-naïve CYP with JIA were selected if enrolled prior to January 2018 in the BSPAR Etanercept Cohort Register or the Biologics for Children with Rheumatic Diseases Study at point of starting MTX. JADAS components (active joint count, physician's global assessment (PGA, 0-10cm), parental global evaluation (PGE, 0-10cm) and standardised ESR (0-10) were calculated based on data collected in the year following MTX initiation.

Multivariate group-based trajectory models were used to explore MTX response clusters across the different JADAS components, which were log1p transformed for analysis. Optimal models were selected based on a combination of model fit (BIC, relative entropy, average posterior probabilities), parsimony and clinical plausibility. Clinical and demographic characteristics and achievement of ACR Pedi 30/90 by six months were compared across identified groups.

Results: Of 658 CYP selected, the majority were female (68%) and of white ethnicity (86%), with RF-negative JIA the most common disease category (35%).

Six subgroups of CYP were identified with differing patterns of disease activity following MTX initiation. Two groups improved across all JADAS components: Fast improvers (11%), and Slow improvers (16%). Persistent PGA (8%), and Persistent PGE (13%) groups maintained one persistent disease feature but otherwise improved. One group relapsed (7%) and a final group had persistent disease overall (44%).

There were no differences in active joint counts at MTX initiation between subgroups and all ILAR categories were represented across each subgroup. However, CYP in persistent disease and slow improver groups had higher CHAQ, PGA and PGE scores at MTX initiation. Those with persistent disease were also older at MTX initiation.

The majority of CYP fulfilled ACR Pedi 30 response (>60% across every group). ACR Pedi 90 achievement was low at 6 months for slow improvers (30%) and high in the relapse group (68%). Between 41% and 73% achieved ACR Pedi 90 response in groups with persistent disease in one JADAS component.

Conclusion: We identify different patterns of disease activity within CYP initiating MTX, suggesting a simple responder/non-responder analysis at a set point may be over-simplistic. Commonly used response measures did not adequately describe these heterogeneous response patterns. Understanding both clinical factors associated with, and biological mechanisms underpinning, these subgroups would aid stratified medicine in JIA.

Disclosure of Interest: S. Shoop-Worrall: None declared, K. Hyrich Speaker Bureau of: Abbvie, L. Wedderburn Speaker Bureau of: Pfizer, W. Thomson: None declared, N. Geifman: None declared

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PRESSURE PAIN THRESHOLDS IN YOUNG ADULTS WITH JUVENILE IDIOPATHIC

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Introduction: Despite modern treatment and improved disease control, pain is the most common complaint in juvenile idiopathic arthritis (JIA). Knowledge about pain thresholds and pain sensitivity among young adults with JIA is sparse.
Objectives: To study pressure pain thresholds (PPTs) in young adults with JIA, 16 years after disease onset compared with controls.
Methods: Consecutive newly diagnosed children with JIA and a disease onset between 1997-2004 from Central Norway, were included in this prospective population-based long-term follow-up study. Children with onset 1997-2000 were part of the Nordic JIA cohort[1,2]. Age- and sex-matched controls were drawn from the National Population Register of Norway. Inactive disease and remission were defined according to Wallace[3,4]. At the follow-up between 2015-17, data from a clinical examination and blood tests were included in addition to an investigator-blinded quantification of PPTs. A digital algometer was used to manually apply pressure three times with an even rate at the upper and lower limb. PPTs from JIA and controls, and from subgroups of JIA defined by disease status, were compared with multilevel models in STATA.
Results: Among the 96 participants with JIA, 71% were female, median age was 22.7 (IQR 18.7-26.2) years, median disease duration was 16.1 (IQR 14.2-17.1) years, 47% had an oligoarticular disease (persistent or extended), and 45% were in remission off medication. In the control group, 71% were female and median age was 23.5 (IQR 20.2-26.7) years. Results from the multilevel regression model showed significantly lower PPTs among participants with JIA compared to controls (Table 1). In the JIA group, participants with inactive disease had lower PPTs than both JIA in remission off medication and JIA with active disease (Table 1). The results were consistent for both upper and lower limb.

Table 1. Pressure pain thresholds in young adults with JIA compared to controls

		Pressure pain threshold	
	n	Upper Limb kPa (95% CI)	Lower Limb kPa (95% CI)
Control	109	1029 (999, 1059)	760 (726, 794)
JIA (total group)	96	888 (846, 930)	702 (670, 734)
Remission off medication[a]	43	893 (824, 963)	732 (675, 789)
Inactive disease[a]	20	836 (762, 911)	626 (575, 678)
Active disease[a]	33	910 (842, 979)	707 (662, 752)

n = number; kPa = kilopascal; CI = confidence interval
[a]According to Wallace[3,4]

Conclusion: In this long-term follow-up study of young adults with JIA, we found significantly lower PPTs compared to controls. This may indicate that young adults with JIA have altered pain sensitivity possibly due to accumulated earlier pain experiences.

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Disclosure of Interest: None declared

P145

RENAL OUTCOMES OF A COHORT OF PAEDIATRIC PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Juvenile Idiopathic Arthritis (JIA) represents the most common chronic rheumatic disease in childhood. Non-steroidal anti-inflammatory drugs (NSAIDs) and intra-articular steroids are the first line treatment for JIA. Systemic steroids, disease modifying anti-rheumatic drugs (DMARDs) and biologic drugs are used in children with severe disease. It is not possible at onset of disease to predict when a child can suspend pharmacological treatment, so children affected from JIA have to continue pharmacological treatment for several months or years. Anecdotal reports showed that rarely JIA could present renal involvement due to uncontrolled inflammation or to long exposure to drugs.
Objectives: Because no cohort studies investigating renal injury in children with JIA are available, we designed this kind of study in our population.
Methods: We retrospectively evaluated 110 patients suffering from JIA. JIA diagnosis was made according to ILAR criteria, treatment was assigned with ACR recommendations. For each patient we recorded the type and the duration of pharmacological treatment and the presence of renal injury. Renal injury was defined by the presence of hypertension (systolic and/or diastolic blood pressure >95th percentile for age, sex and height), proteinuria (persistent –confirmation within 3 months– urinary protein/creatinine ratio>0.5 mg/mg for children <2 years old and >0.2 mg/mg for patients >2 years old) or reduced estimated glomerular filtration rate (<90mL/min/1.73m2). Development of renal injury was determined by survival analysis according to Kaplan-Meier method.
Results: All the patients underwent NSAIDs administration for a mean time of 44.3±42.6 months. 63 patients (57.3%) underwent also MTX administration for a mean time of 47.1±46.2 months. 34 patients (30.9%) underwent biologic agents with a mean duration of the treatment of 37.8±30.1 months. Among these 34 patients, 30 patients underwent biological agents after administration of NSAIDs and MTX, while only 4 underwent biological agent administration without ever undergoing MTX administration. Mean age at the last follow-up was 13.3±5.6 years. The mean duration of JIA was of 84.0±65.4 months. 9 of 110 patients (8.1%) showed renal injury (8 with hypertension and 1 with proteinuria). Patients with renal injury presented longer duration of the disease (152.8±58.2 Vs 77.9±62.7 months; p=0.001), shorter intervals free from JIA relapses (0 (0/1) Vs 12 (6/40); p<0.001), longer duration NSAIDs treatment (80.2±40.9 Vs 41.13±40.5 months; p=0.008)but with similar cumulative NSAIDs dose (270 Vs 252 grams; p=0.83) and higher rate of MTX prescription (100% Vs 53%; p =0.007), longer time of MTX administration (86.0±50.5 Vs 40.5±38.86 months; p=0.005) and higher cumulative MTX dose (4.8Vs 1.72 grams p= 0.005)compared with the patients without renal injury.

Conclusion: 8% of the children with JIA develop renal injury. The principal risk factor was longer exposure to NSAIDs and MTX for a more severe disease. Probably, the renal damage could be “time dependent” for NSAIDs exposure and “both time and dose dependent” for MTX exposure. Rheumatologists taking care of children with JIA should pay attention also to kidney health, avoiding long-time treatments with NSAIDs and/or MTX possibly preferring biological treatments in case of poor control of the disease. Moreover, in these patients, periodic evaluation of renal function, blood pressure and proteinuria should be warranted.
Disclosure of Interest: None declared

P146

SYNOVIAL NEUTROPHILS HAVE AN ALTERED PHENOTYPE AND IMPAIRED EFFECTOR FUNCTIONS COMPARED TO CIRCULATING NEUTROPHILS IN OLIGOARTICULAR JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Juvenile idiopathic arthritis (JIA) is a pediatric rheumatic disease with partially unknown etiology and pathogenesis. Neutrophils are the most common immune cell present in synovial fluid from inflamed joints in oligoarticular JIA, but the role of neutrophils in the immunopathogenesis of oligoarticular JIA has not been investigated.
Objectives: To characterize neutrophil phenotypes and effector functions in the circulation and in the inflamed joint during active arthritis in children with oligoarticular JIA.
Methods: Paired samples of blood and synovial fluid from 17 children with oligoarticular JIA were investigated regarding surface markers, phagocytic ability and oxidative burst. Healthy blood neutrophils exposed to cell-free JIA synovial fluid and healthy oral cavity neutrophils were studied as controls for synovial fluid exposure and transmigration respectively.
Results: Synovial neutrophils had a shifted phenotype, characterized by high surface levels of neutrophil activation markers CD11b and CD66b, and mannose receptor CD206 and decreased levels of adhesion molecule CD62L compared to circulating neutrophils. In comparison to oral cavity neutrophils, synovial neutrophils had higher levels of CD11b and a different overall phenotype, suggesting that the phenotype shift in synovial compared to circulating neutrophils is not dependent on transmigration alone. JIA synovial fluid in itself induced activation of healthy blood neutrophils, measured as increased CD11b levels. Synovial fluid neutrophils had impaired ability to phagocytose opsonized *E. coli* and to produce oxygen radicals upon neutrophil activation with phorbol-myristate-acetate (PMA) compared to circulating neutrophils. The impaired effector functions in synovial neutrophils was not dependent on the synovial fluid alone, as addition of cell-free synovial fluid to blood neutrophils did not alter phagocytosis and oxidative burst.
Conclusion: JIA synovial fluid neutrophils are activated, have a “polarized” phenotype and impaired effector functions compared to neutrophils in the circulation. This study will help bridge the current knowledge-gap regarding the role of neutrophils in the immunopathogenesis in oligoarticular JIA.
Disclosure of Interest: None declared

P148

JIA-ACR50 RESPONSE AS A PREDICTOR OF MINIMAL DISEASE ACTIVITY IN PATIENTS AGED 2–17 YEARS WITH POLYARTICULAR-COURSE JIA TREATED WITH SC ABATACEPT

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Introduction: Effectiveness of SC abatacept (ABA) in patients (pts) with polyarticular-course JIA (pJIA) was shown in a 2-year (yr), open-label Phase III international study (NCT01844518).

Objectives: To assess potential predictors of Juvenile Arthritis Disease Activity Score 27-CRP (JADAS27-CRP) minimal disease activity (MDA), inactive disease (ID) and remission.

Methods: Pts with pJIA aged 2–17 yrs received weight-tiered SC ABA (10–<25 kg: 50 mg; 25–<50 kg: 87.5 mg; ≥50 kg: 125 mg) weekly for 4 months (mos).[1] JIA-ACR30 responders at Mo 4 could receive SC ABA for another 20 mos.[1] Potential predictors of response over 11 time points to Mo 21 were determined with a multivariate logistic regression (MVR) analysis; Mo 4, 13 and 21 data are presented. MVR variables were baseline (BL) age, sex, race, weight, geographic region, CRP, MTX use, prior biologic use, number of active joints and joints with limitation of motion, physician's global assessment of disease activity, Childhood HAQ-DI (CHAQ-DI), parental assessment of well-being (PaGA) and JIA-ACR50 or JIA-ACR70 responses at Mo 3. Variables were deemed significant if corresponding p values were <0.05 at ≥6 time points. Missing values were imputed as non-responders. BL continuous variable cut-offs (high/low) were determined with receiver-operator curve analysis. Outcomes analysed included JADAS27-CRP MDA (≤3.8), ID (≤1) and remission (JADAS27-CRP ID for ≥6 months) rates. Odds ratios and 95% CIs were computed.

Results: In all treated pts (N=219), median (range) BL characteristics were: age 11.0 (2.0–17.0) years, CRP 0.2 (0.1–21.1) mg/dL, CHAQ-DI 1.0 (0.0–2.9) and PaGA 47.2 (0.0–95.8). Variables with the highest number of significant p values (≤0.05) were BL CRP, CHAQ-DI, PaGA and Mo 3 JIA-ACR50 and JIA-ACR70. BL CRP, PaGA and CHAQ-DI were predictive of JADAS27-CRP MDA, ID and/or remission at multiple time points (Mo 13; Table 1). JIA-ACR50 response at Mo 3 significantly predicted achievement of JADAS27-CRP MDA at Mo 13 (Table 1) and Mo 21.

Table 1. ORs (95% CI) for variables potentially predictive of JADAS27-CRP MDA, ID or remission at Mo 13

	MDA		ID		Remission	
	Cut-off	OR (95% CI)	Cut-off	OR (95% CI)	Cut-off	OR (95% CI)
CRP	>1 vs ≤1	0.58 (0.23, 1.42)	>0.6 vs ≤0.6	0.33 (0.13, 0.83)[a]	>0.7 vs ≤0.7	0.08 (0.01, 0.78)[a]
CHAQ-DI	>0.75 vs ≤0.75	0.38 (0.15, 0.94)[a]	>0.75 vs ≤0.75	0.53 (0.23, 1.18)	>0.5 vs ≤0.5	0.39 (0.13, 1.24)
PaGA	>43.16 vs ≤43.16	0.48 (0.21, 1.10)[b]	>39 vs ≤39	0.41 (0.18, 0.91)[a]	>27.37 vs ≤27.37	0.24 (0.08, 0.75)[a]
JIA-ACR	Yes	6.93 (2.20, 21.89)[a]	Yes	1.65 (0.47, 5.73)	Yes	1.15 (0.12, 11.08)

50 at Mo 3	vs no		vs No		vs No	
JIA-ACR 70 at Mo 3	Yes vs no	1.53 (0.58, 4.00)	Yes vs No	3.01 (1.09, 8.29)[a]	Yes vs No	4.14 (0.72, 23.82)

[a]Statistically significant (p<0.05).
[b]Showing trend (p=0.05–0.1).
ID=inactive disease; MDA=minimal disease activity; OR=odds ratio.
Conclusion: Clinically important JIA-ACR50 response at Mo 3 was predictive of the attainment of JADAS27-CRP MDA status at Mo 13 and Mo 21 in pts aged 2–17 yrs with pJIA treated with SC abatacept.
Reference:

1. Brunner HI, et al. *Arthritis Rheumatol* 2018;70:1144–1154.

Trial registration identifying number: NCT01844518
Disclosure of Interest: N. Ruperto Consultant for: Ablynx, AbbVie, AstraZeneca-Medimmune, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb Company, Eli Lilly, EMD Serono, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, Pharma, Sanofi, Servier, Sinergie, Sobi, Takeda, Employee of: The IRCCS Istituto Giannina Gaslini (IGG), where NR works as a full-time public employee, has received contributions from Bristol-Myers Squibb Company, Eli Lilly, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Novartis, Pfizer, Sobi. This funding has been reinvested for the research activities of the hospital in a fully independent manner, without any commitment with third parties. The registry is funded by Bristol-Myers Squibb Company, Speaker Bureau of: Ablynx, AbbVie, AstraZeneca-Medimmune, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb Company, Eli Lilly, EMD Serono, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, Pharma, Sanofi, Servier, Sinergie, Sobi, Takeda, H. Brunner Consultant for: Abbott, Amgen, AstraZeneca, Boehringer Ingelheim, Celgene, GlaxoSmithKline, F Hoffman-La Roche, Novartis, Pfizer, Takeda, UCB, Wyeth (funds paid to employer), Speaker Bureau of: F Hoffman-La Roche, GlaxoSmithKline, Novartis, A. Berman: None declared, F. Ávila-Zapata: None declared, G. Horneff Consultant for: AbbVie, Novartis, Pfizer, Sanofi, Speaker Bureau of: AbbVie, Novartis, Pfizer, Sanofi, M. Alessio: None declared, M. Becker: None declared, A. Belot: None declared, R. Burgos-Vargas: None declared, A. Boteanu: None declared, C. Goldenstein-Schainberg: None declared, I. Scheibel: None declared, M. T. Terreri: None declared, L. Zemel: None declared, R. Wong Shareholder of: Bristol-Myers Squibb Company, Employee of: Bristol-Myers Squibb Company, M. Nys Shareholder of: Bristol-Myers Squibb Company, Employee of: Bristol-Myers Squibb Company, M. Askelson Employee of: Bristol-Myers Squibb Company, A. Martini Consultant for: Aurinia, Bristol-Myers Squibb Company, Eli Lilly, EMD Serono, Janssen, Pfizer, D. Lovell Consultant for: consultant: AstraZeneca, Boehringer Ingleheim, F Hoffman-La Roche, GlaxoSmithKline, Novartis, UCB; principal/co-principal investigator: Bristol-Myers Squibb Company, F Hoffman-La Roche, Janssen, Pfizer, UCB; board member: Forest Research

e-Poster viewing: Juvenile dermatomyositis

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JUVENILE DERMATOMYOSITIS (JDM) WORKING PARTY UPDATE

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Introduction: The JDM working party has 140 active members. Since June 2019, they have been represented by a core group of 7 elected members (Chair: Liza McCann, UK; Secretary: Meredyth Wilkinson, UK; Past Chair: Helga Sanner, Norway; Representative for basic science: Judith Wienke, Netherlands; Representative for clinical care / clinical science: Charris Papadopoulou, UK; Representative for education/training (& EMERGE): Raquel Campanilho-Marques, Portugal) and 3 co-opted members (Allied Health Professional Representatives: Sara Röstlund, Sweden and Mette Nørgaard, Denmark; Parent representative, Joanne Swan, Scotland).
Objectives: Our aim is to frame our work in line with the PReS pillars – clinical / research, basic science and education / training. We think that part of our role within the PReS Working Group is to help standardise care, facilitate multi-centre research projects and enhance educational opportunities.
Methods: The core group meet via teleconference every 2 months with a set agenda incorporating each of the PReS pillars. An update was distributed to all working party members in February 2020, encouraging submission of ideas and/or collaboration on proposed projects.
Results: The core group to date has:

- Established and completed a survey to define opinion / use in practice of the SHARE JDM consensus guidelines (Enders FB et al, Ann Rheum Dis 2017). Results of this (n=46) submitted in abstract to PReS 2020; manuscript in preparation.
- Clarified the role of databases / data sharing in JDM across Europe; PReS JDM Working Party and Euromyositis Position Statement available on PReS website.
- Informed members of the EMERGE group of training opportunities / fellowships relating to JDM.
- Produced a summary of research projects and educational resources, available on PReS website.
- Collaborated with the International Myositis Assessment & Clinical Studies Group (IMACS), promoting shared working.

Work currently in progress includes:

- Collaborating in the extension of the JDM SHARE consensus for management of JDM in North America (IMACS project).
- Research proposal on sleep in JDM - in development.
- Training package / educational resource on myositis specific antibodies near completion; will be available in PReS website.
- Proposal for a Policy Statement on management of JDM during Covid-19 with a particular focus on transition to adult services.
- Survey of practice in JDM proposed; in early stages of development.

Conclusion: The JDM PReS working party provides a platform for collaboration in JDM, incorporating clinical and research issues, basic science and education / training. Ideas and collaborations are welcomed and encouraged within an open membership structure. To join the group, e-mail: meredyth.wilkinson.14@ucl.ac.uk.
Disclosure of Interest: None declared

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VITAMIN D SUPPLEMENTATION OF CHILDREN WITH RHEUMATIC DISEASES

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Introduction: VITAMIN D SUPPLEMENTATION OF CHILDREN WITH RHEUMATIC DISEASES
Objectives: To determine supplementation level of vitamin D in children with Juvenile idiopathic arthritis (JIA) and Juvenile dermatomyositis (JDM)
Methods: 52 children (35 girls and 17 boys), aged from 5 to 17 years were observed. 29 children had JDM, JIA was in 23 children.The level of 25(OH)D in plasma was measured by chemiluminescent immunoassay method. All patients with JDM and 16 (69.5%) JIA patients were taking vitamin D drugs (cholecalciferol 200 IU/day and/or alfacalcidol 0,25 μg). Concentration level 21-30ng/ml was determined as insufficiency, less than 20 ng/ml as deficiency.
Results: Vitamin D insufficiency was in 50 (94.3%) children of our cohort, including 100% cases in patients with JIA (21 (91.3%) children had a deficit, 4 of them (17.4%) with extra deficit). 25(OH)D <30 ng/ml was observed in 90% cases in JDM patients, 70% of them with deficit. The average 25(OH)D level in JDM group was significantly higher than in JIA group (21,51±11,87 vs 14,98±0,91 ng/ml)
Conclusion: The overwhelming majority of children with JIA and JDM have an insufficiency or deficiency of vitamin D in comparison with Russian population. Traditional therapy with complex calcium salts drugs and cholecalciferol in low doses is insufficient to achieve the optimal level of vitamin D.
At the same time, vitamin D supplementation in children with JDM is higher than in JIA patients. Perhaps this is partly due to more intensive vitamin D therapy.
Disclosure of Interest: None declared

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FAVORABLE CLINICAL RESPONSE OF REFRACTORY JUVENILE DERMATOMYOSITIS TO RUXOLITINIB

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Introduction: Juvenile dermatomyositis (JDM) is a rare systemic inflammatory disorder of childhood associated with vasculopathies and a constitutive type I interferon (IFN) activation. Standard immunosuppression does not always control disease activity and may have serious side effects.

Objectives: JAK1/2 inhibitors were recently shown to be therapeutically effective in patients with monogenic type I interferonopathies. We applied this rationale in a JDM patient with therapy-refractory course and elevated IFN signature.
Methods: A 14-year-old boy with NXP2-positive JDM presented with a relapse almost 10 years into remission. He failed to improve on first-line treatment and was transferred to our center with dysphagia due to severe myositis. His initial Childhood Myositis Assessment Scale (CMAS) score was 6/52. Besides elevation of CK and von-Willebrand antigen, he had a strong IFN signature consistent with the diagnosis of relapsed JDM.
Results: In view of insufficient disease control and the persistent high IFN signature, cyclophosphamide, rituximab and steroid pulses were stopped, and the patient was started on ruxolitinib. During the first three months of ruxolitinib therapy (30 mg/d), the patient experienced increasing muscle strength and significant clinical improvement. He was able to walk short distances and to climb one flight of stairs. At seven months, he is able to ride his bicycle for 10 minutes. His CMAS score improved from 18/52 to 40/52. This was accompanied by a sustained reduction the IFN signature.
Conclusion: The observation of a sustained reduction of the IFN signature under ruxolitinib supports a primary role of constitutive type I IFN activation in JDM pathogenesis. Thus, ruxolitinib should be considered early in the treatment of refractory JDM, not necessarily as second-line therapy.
Disclosure of Interest: None declared

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OVERLAP SYNDROME OF IDIOPATHIC INFLAMMATORY MYOPATHY WITH JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS PRESENTING WITH MACROPHAGE ACTIVATION SYNDROME

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Introduction: Some patients with connective tissue diseases cannot be assigned to a single disease category, presenting characteristics from two or more immune mediated conditions, the so-called overlap syndromes (OS). OS are infrequent in children and their description in literature is limited to some case series.
Objectives: Our aim is to present a rare case of an OS of idiopathic inflammatory myopathy (IIM) with juvenile systemic lupus erythematosus (jSLE) in a child that initially presented with macrophage activation syndrome (MAS).
Methods: A case report is described. Data was extracted from the medical chart of the patient and a literature review was undertaken.
Results: A 7-year-old girl was transferred to our tertiary center after being admitted for prolonged intermittent fevers, abdominal pain, fatigue and polyarthralgias. On examination, there was symmetrical proximal muscle weakness, a vasculitic lower limb rash, facial erythema with eyelid edema (Fig. 1) and oral mucositis. Initial laboratory exams revealed pancytopenia, high muscle enzymes, increased erythrocyte sedimentation rate with moderately elevated reactive C-protein, and hypocomplementemia. She also had non-nephrotic proteinuria, without hematuria.Further investigations showed a positive direct antiglobulin test, antinuclear antibodies, anti-double-stranded DNA, anti-Mi 2 and anti-Ku. Serositis (pericardial and pleural effusions, ascitis) and hepatosplenomegaly were present. Lower limb MRI documented diffuse muscle edema. The diagnosis of an overlap syndrome of jSLE and IIM was established. While being treated for concomitant bacteremia, the patient became ill-appearing, with persistent fevers, worsened cytopenias, low fibrinogen and high ferritin and triglycerides, and a Macrophage Activation Syndrome (MAS) diagnosis was assumed. The patient received antibiotics and intravenous immunoglobulin, followed by methylprednisolone pulses, IV cyclosporine (CYC), hydroxychloroquine and supportive therapy with progressive improvement.
Due to hypertension (possibly related to CYC) and persistent proteinuria a renal biopsy was performed showing class IV lupus nephritis. After achieving clinical stability, CYC was switched to mycophenolate mofetil as an induction treatment, which is ongoing.
Conclusion: IMM with SLE OS is uncommon, and has seldom been described in children. In addition to fulfilling SLE criteria, our patient had clinical, laboratory and imagiologic evidence of IMM. The presence of myositis specific antibodies (especially anti-Mi 2) further supports the diagnosis of an OS rather than an atypical presentation of a lupus myopathy. Juvenile dermatomyositis appears to be the IMM subtype - it is associated with anti-Mi 2, and mild heliotrope and eyelid edema are compatible. Facial rash sparing the nasolabial folds is more suggestive of SLE.
MAS is a rare but life-threatening condition that should be suspected in rheumatologic conditions and might be triggered by infections or disease flares. Its identification may be particularly challenging at presentation, especially in SLE where cytopenias are common. The reported prevalence in adult SLE ranges from 0.9% to 4.6%; disease-specific criteria have been proposed. MAS has occasionally been described in IIM.
In a patient with a predisposing condition, persistent fevers and ill-appearance must always prompt a MAS workup, since early diagnosis and treatment are paramount.
Due to an early referral to a pediatric rheumatology center, the patient received a prompt diagnosis and treatment, which probably improved her prognosis.
Trial registration identifying number:

Disclosure of Interest: None declared

P153

BILATERAL KNEE AVASCULAR NECROSIS IN JUVENILE DERMATOMYOSITIS: THE PITFALLS OF DIAGNOSIS

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Introduction: Skeletal complications seem to be particularly frequent in JDM: bone mineral density loss before treatment initiation seems more frequent than in other inflammatory diseases and vertebral fractures may occur during the first months of CS therapy. Avascular osteonecrosis (AVN) is a rare complication of corticosteroid (CS) use.Rare cases of multifocal AVN in sometimes unusual locations have previously been described in JDM patients[1,2], but information about associated myositis-specific autoantibodies was not available in these cases.
Objectives: To report the occurrence and characteristics of knee AVN in juvenile dermatomyositis (JDM) patients
Methods: Retrospective single-center study of JDM patients with knee AVN followed at the national paediatric rheumatology reference center of Necker hospital between January 2013 and December 2019
Results: Three female patients out of the 55 patients of our JDM cohort (5.5%) developed knee AVN over a period of 6 years**.** Patient A, a 11-year old girl, was treated with the successive association of CS and mycophenolate mofetil (MMF), methotrexate (MTX) and eventually ruxolitinib due to persistent severe cutaneous ulcerations. Six months after diagnosis, she presented with bilateral knee swelling and pain of both inflammatory and mechanical character. An articular relapse was suspected, but MRI of the knees, revealed multiple bilateral epiphyseal, metaphyseal and diaphyseal bone infarction sites of the femur and tibia (fig. 1A). Patient B, a 14-year old adolescent, was treated with CS, MTX, and the subsequent addition of MMF and RTX. She presented 6 months after diagnosis with bilateral knee and ankle pain of mechanical character, with minimal knee effusion and normal range of motion. Whole-body MRI showed giant femorotibial (fig. 1B) and ankle bone infarction sites. Patient C, a 6-year old girl, was treated with CS, MTX and RTX. Nine months after diagnosis she started complaining of mechanical left-knee pain. There was no swelling and range of motion was normal. MRI showed a focal epiphyseal lesion of the tibia compatible with bone infarction. The three patients were positive for anti-MDA5 antibody (3/11 MDA5 positive JDM patients (27%)), while none of the 44 MDA-negative patients had a diagnosis of AVN.
Conclusion: Knee AVN occurred in 5.5 % (3/55) patients of our cohort. All of them had severe anti-MDA5-positive JDM, and AVN was diagnosed within the year following the diaagnosis.AVN should be considered as a differential diagnosis in JDM patients presenting with joint pain. Larger studies are warranted to assess the possible link between its occurrence and the presence of anti-MDA5 autoantibodies

Disclosure of Interest: None declared

P154

SUCCESSFUL USE OF CYCLOPHOSPHAMIDE IN CALCINOSIS IN JUVENILE DERMATOMYOSITIS

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Introduction: Juvenile Dermatomyositis (JDM) is the commonest inflammatory myopathy of childhood. One of the important causes of morbidity in JDM is calcinosis – dystrophic calcification affecting skin, soft tissue and muscles – seen in approximately one-third of patients. The longer duration of active disease, cardiac involvement and presence of certain myosotis specific antibodies have been suggested to increase the risk. The complications include secondary infection, panniculitis, and ulceration, in addition to pain and tenderness. The treatment strategies include anti-inflammatory medications, medications affecting calcium and phosphorus metabolism and surgical options, although the results are mixed with limited evidence. Intravenous Immunoglobulin (IVIG), anti-Tumour Necrosis Factor (TNF) agents, Abatacept and Rituximab have all been tried with varying success, in addition to corticosteroids.
Objectives: To describe the clinical and laboratory characteristics of five patients with JDM with calcinosis, who were treated successfully with Cyclophosphamide.
Methods: Retrospective analysis of digital health records.
Results: Four of the five patients were female (80%) and all aged between 6 and 10 years. Four of them had calcinosis at the time of diagnosis, although they may have had symptoms for 12 to 18 months prior to diagnosis. Skin involvement was severe requiring multiple systemic and topical therapeutic agents in four out of the five patients - significantly more affected than the muscles. One patient had amyopathic subtype with normal Childhood Myositis Assessment Score (CMAS) throughout. None of them had cardiac involvement. All had weakly positive Anti-Nuclear Antibodies (ANA); but were negative for myositis antibodies except the patient with most severe skin involvement and calcinosis (patient 2), who was positive for Anti-TIF1gamma antibodies.
Two of the three patients with calcinosis at onset had Cyclophosphamide as the second line agent (chosen due to calcinosis) following systemic corticosteroids with complete resolution of the lesions after six cycles at 500mg/m2. One patient responded to Infliximab, which failed to work after 20 months, following which Cyclophosphamide was tried with good response. The other two patients were given Cyclophosphamide after they failed to respond to Rituximab, which did work for muscle disease. One patient had recurrent episodes of calcinosis needing surgical curettage despite initial response to Cyclophosphamide and later IVIG.

Gender	Female	Female	Female	Female	Male
Age	6y 9m	7y 4m	8y 3m	8y (rash – 6m)	9y 2m (12 – 18m history)
Age at calcification	At presentation	13y 6m	At presentation	At presentation	At presentation
Site	Upper arms, elbows	Upper arms, elbows, thighs, knees, occipital area	Elbows	Forearm, thigh	Elbows, knees
Skin disease	Severe	Severe	Severe	Moderate	Mild
Muscle	Affected – CMAS 28/52	Affected – CMAS 23/52	Amyopathic	Mild – CMAS 44/52	Affected – CMAS 28/52
Other interventions		Surgical curettage	Surgical excision		
Response	Complete resolution	Stopped new lesions – later flared	Stopped new lesions	Complete resolution	Complete resolution
Other agents tried	MTX Rituximab (muscles responded) HCQ Dapsone	IVIG – worked for skin & calcinosis Rituximab (muscles responded) MTX	Infliximab (worked for 20 months) MMF MTX Dapsone	MTX MMF	MTX
Abbreviations MTX–Methotrexate MMF–Mycophenolate Mofetil					

IVIG–Intravenous Immunoglobulin
HCQ–Hydroxychloroquine

Conclusion: Although Cyclophosphamide does not feature prominently in literature in the management of calcinosis associated with JDM, it has proven to be useful in this cohort of patients, especially when tried early on for calcinosis. Based on our experience, although the numbers are small, Cyclophosphamide is worth trying in patients with calcinosis, after careful discussion with the patient and family about the risks against benefits.

Disclosure of Interest: None declared

P155

USE OF MYCOPHENOLATE MOFETIL IN INFLAMMATORY MYOPATHIES OF CHILDHOOD

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Introduction: The juvenile idiopathic inflammatory myopathies (JIIM) consist of heterogeneous inflammatory diseases that primarily affect the skeletal muscles, but can potentially also affect the skin and visceral organs. To date, there is still limited evidence regarding the treatment of these rare disorders.

Objectives: To evaluate the efficacy of mycophenolate mofetil (MMF) in the JIIM.

Methods: Patients diagnosed with JIIM and treated with MMF enrolled in the Juvenile Dermatomyositis Research Group (JDRG) in the United Kingdom and under the care of the G. Gaslini Institute (IGG) in Genoa, Italy were included in this study. Data collected included: sex, onset year, onset age, onset type, clinical manifestations, disease duration, disease course and activity, laboratory data and treatment received. Outcomes were muscle strength/endurance, cutaneous and global disease activity, cumulative damage and physical function. Data were retrospectively analysed at time of starting MMF, after 3, 6, 12 months and last clinical follow up.

Results: 29 children were included in this study, 25 were from the UK cohort and 4 were followed at IGG in Italy. Of these 29 patients, 79.3% were diagnosed with juvenile dermatomyositis and the remaining 20.7% were overlap myositis. We observed a significant improvement in the muscle-related outcome measures (Manual Muscle 8=80 from 50% to 83.3%; Childhood Myositis Activity Score=52 from 53.5% to 88.9%; Disease Activity Score-Muscle from 55.2% to 84.2%) and overall disease activity (Global Visual analogue scale (VAS)=0 from 7.1% to 42.1%), and also an improvement of the skin-related outcome measures (Disease activity score-Skin=0 from 31% to 42.1%; skin visual analogue scale=0 from 25% to 47.4%). The number of patients with inactive disease significantly improved from 10.3% at baseline, to 68.5% at last study visit.

The corticosteroid dose was significantly reduced from 0.3 to 0.1 mg/Kg/day. No significant side effects were reported.

Conclusion: The use of MMF has shown to be efficacious and safe in children with IIM, especially in patients with refractory muscle disease.

Disclosure of Interest: None declared

P156

EVALUATION OF DISEASE ACTIVITY IN CHILDREN WITH JUVENILE DERMATOMYOSITIS: A COMPARISON BETWEEN ELECTROMYOGRAPHY AND WHOLE BODY-MAGNETIC RESONANCE IMAGING

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Introduction: Juvenile Dermatomyositis (JDM) is the most common pediatric inflammatory myopathy. The Juvenile Dermatomyositis Activity Index (JDMAI) is composed of four clinical items and has been proposed for use in both clinical and research settings. Needle electromyography (EMG) examination is the most informative part of the electro diagnostic study in myopathic disorders. Whole body-magnetic resonance imaging (WB-MRI) allows to reliably visualize the extent of the inflammatory process and to estimate the total disease burden. To date, the role of EMG and WB-MRI in assessing disease activity in JDM is still not fully defined.
Objectives: To perform a comparison between EMG testing and WB-MRI with disease activity score in a group of JDM patients.
Methods: All patients diagnosed with JDM and referred to our Centre between January 2018 and January 2019 were enrolled. Clinical, laboratory and radiological data were collected. A standardized clinical evaluation through manual muscle test (MMT)-8, hybrid MMT/CMAS (hMC) and JDMAI was performed at each visit; laboratory test included muscle enzymes levels; WB-MRI and EMG were performed within one month of the clinic visit. WB-MRI signal intensity was scored using a 0-2 point scale in 42 muscular groups; myofascial and subcutaneous tissue inflammation were assessed on the upper and lower extremities using a 0-1 point scale. The EMG evaluated the presence of fibrillation potentials on four muscles (deltoid and extensor digitorum communism for the upper limb, and vests medals and tibias anterior for the lower limb). The degree of fibrillation potentials in every muscle was scored using a 0-2 point scale (0 = no fibrillation potentials; 1 = presence of fibrillation potentials in < 50% of the sites analyzed; 2 = presence of fibrillation potentials in > 50% of the sites analyzed).
Based on JDMAI, visits were grouped as follows: visits of patients in clinically active disease vs visits of patients in clinically inactive disease.
Mann-Whitney U test, Chi-square/Fisher test and Spearman's rank correlation coefficient were used for statistical analysis.
Results: Thirteen patients were included in the study for a total of 18 visits. WB-MRI score resulted significantly higher for visits of patients with active disease then in those of patients with clinically inactive disease (p 0.011 and 0.007 respectively). No difference was found in EMG scores for both visits of patients with active and inactive disease (p 0.274 and 0.310, respectively). WB-MRI score had a moderate to high correlation with all clinical evaluation tools of muscle strength or disease activity (Spearman's rank coefficient = 0.61, 0.58, and 0.86 with MMT-8, hMC and JDMAI respectively), while EMG score had a moderate correlation (0.48, 0.42, and 0.62 with MMT-8, hMC and JDMAI respectively).
Conclusion: In this pilot study, WB-MRI seems to better discriminate between active and inactive disease compared to EMG in patients with JDM. Further studies on larger populations of children with JDM could contribute to define the role of EMG and WB-MRI in the assessment of disease activity.
Disclosure of Interest: None declared

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PULMONARY FINDINGS ON HIGH RESOLUTION COMPUTED TOMOGRAPHY IN PATIENTS WITH JUVENILE DERMATOMYOSITIS: RETROSPECTIVE STUDY

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Introduction: Juvenile Dermatomyositis (JDM), are complex, heterogeneous, autoimmune diseases that affect skeletal muscles and the skin. The interstitial lung disease (ILD) is a complication that has been observed in 20-78% of patients and can be a determining prognosis, causing greater morbidity and mortality.
Objectives: To evaluate the finds pulmonary by high-resolution Computerized Tomography (HRCT) in accompanying patients in outpatient pediatric rheumatology unit.
Methods: Retrospective study of 62 patients diagnosed with JDM, which are submitted to the examination of image for clinical monitoring of the disease. TCAR tests were observed in approximately 10 years, including repeated CT scans assessed: interstitial pneumopatia; pneumomediastium; the presence of nodules; opacity in ground glass; fibros elastic stretch marks; septal thickening; bronquica wall thickening. Two patients were excluded because they had overlap with systemic lupus erythematosus.
Results: HRCT was retrieved for analysis in 62 of patients. We observed interstitial pneumopatia in 9 (14.51%), showed; nodules/micronodules in 20 (32.25%), opacity in ground glass in 21 (33.87%), fibroatelectasias in 13 (20.96%), septal thickening in 7 (11.29%), bronchial wall thickening in 10 (16.12%) and pneumomediastium in 1 (1.61%). Findings were observed during the first 2 years of disease In 62 patients.
Conclusion: We conclude that pulmonary involvement in the diseases devolps more frequently during the first two years of the disease. Carefull follow-up with HRCT is essential for early diagnosis and adequate treatment.
Disclosure of Interest: None declared

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SURVEY OF THE USE OF SHARE JDM RECOMMENDATIONS IN CLINICAL PRACTISE: REPORT OF THE PRES JDM WORKING GROUP

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Introduction: The *S*ingle *H*ub and *A*ccess point for paediatric *R*heumatology in *E*urope (SHARE) guideline for Juvenile Dermatomyositis (JDM)[Enders FB et al, Ann Rheum Dis 2017], directed towards healthcare professionals, aims to provide uniform, optimal access to care via evidence-informed consensus on diagnosis/treatment.

Objectives: Audit impact of SHARE guidance, ascertain opinion of Working Group regarding usefulness and if recommendations need to be revised/updated.

Methods: An online survey was written (CH,LM) using Survey Monkey®, ratified/piloted by the Working Party core group, then distributed to membership of the JDM working party (n=140) and EMERGE (PReS trainee/young scientist) group (n=150) November 2019-February 2020. Reminders were sent to encourage participation. Results were collated and descriptive analysis performed. Responses were anonymous, but questions were asked regarding clinical role, time of practice and number of JDM cases treated/year.

Results: 46(16%) responses were received from 39 paediatric rheumatologists, 3 adult rheumatologists, 2 physicians with rheumatology interest, 1 internist, 1 parent representative. 31 (67.4%) had ≥10 years' experience. Number of cases treated/year varied from <5(17.4%) to >30(23.9%). The majority of respondents reported SHARE guidance as important to their practice; 43.5% stated important/incorporated into hospital/national guidelines and 6.5% stated very important/critical for decision-making. Only 5(10.9%) reported not using SHARE guidance. Overall opinion/experience was positive (Table). 33(73.3%) thought the SHARE guidance was relevant to practice as it is, although 21(46.7%) suggested revision/update. Suggestions for revision included biomarkers, myositis antibodies, novel treatments (biologics/JAK inhibitors), managing resistant disease/calcinosis and addressing mental health. For effect of guidance on clinical practise, 60% reported no change, with only 20% giving a positive answer.

SHARE SURVEY	Question	Yes N (%)	No N (%)	Unsure N (%)	Total N (%)	Comments (abbreviated)
Opinion	Clear & easy to use	**41 (89.1)**	1 (2.2)	4 (8.7)	46 (100)	- 'More on treatment resistant disease' - 'NHSE restricts treatment options for biologics' - 'Guidelines for treatment should be written more accurately' - 'No mention for professionals to check mental health in the flow charts; (very important in a chronic illness)'
	Useful for education & training	**41 (89.1)**	1 (2.2)	4 (8.7)	46 (100)	
	Helps get investigations	**28 (60.9)**	10 (21.7)	9 (19.6)	46 (100)	
	Helps get treatment	**31 (67.4)**	10 (21.7)	5 (10.9)	46 (100)	
Experience	Contains investigations that cannot access in my hospital	8 (17.4)	**35 (76.1)**	3 (6.5)	46 (100)	- 'Cannot access TNF blockers' - 'Do not go far enough to help specialists' - 'Revision should be done on a regular basis (2-5 yearly) as for all other recommendations/guidelines. JDM does not need it yet.'
	Contains treatments that cannot get in my hospital	4 (8.9%)	**36 (80)**	5 (11.1)	45 (97.8)	
	Needs to be revised & updated	**21 (46.7)**	16 (35.56)	8 (17.8)	45 (97.8)	
	Relevant to my practice as it is	**33 (73.3)**	5 (11.11)	7 (5.6)	45 (97.8)	

Conclusion: According to this survey, SHARE JDM guideline has been implemented widely. Despite not necessarily changing practice, the majority of respondents rate it as important, clear/easy to use and helpful for investigations/treatment. A small number of respondents cannot access investigations/treatments within the guidance, determined by local/national factors. Almost half of all respondents thought the guideline should be updated to include biomarkers, myositis antibodies, new treatments, resistant disease and mental health.
Disclosure of Interest: None declared

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CLINICAL FEATURES, MUSCLE BIOPSY SCORES, MYOSITIS SPECIFIC ANTIBODY PROFILES AND OUTCOME OF JDM PATIENTS

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Introduction: Juvenile dermatomyositis (JDM) is the most common inflammatory myopathy of childhood.

Objectives: We aimed to analyse the clinical features, clinical implications of muscle biopsy scores and myositis specific antibodies (MSA), treatment responses and long-term outcomes of our JDM patients.
Methods: JDM patients followed at Hacettepe University, Department of Pediatric Rheumatology between 2000-2020 were included. Patients data were collected retrospectively from patient files.
Results: Fifty-eight (60.3% F) JDM patients were included with a mean age of onset 8.1±4.3 years. The mean follow-up period was 5.66±3.59 years. The classical rash (91%; heliotrope rash and/or Gottron's papules) and muscle weakness (76%) were the most common presenting features. Electromyography was positive in 23/25 patients and muscle MRI revealed myositis in 12/15 patients. 35 patients had muscle biopsy and 16 of them were scored according to the score tool[1, 2] with a mean total biopsy score of 18.5±5.7 (max 27). Overexpression of MHC-I (94%) was the most prominent feature followed by inflammatory cell infiltration (78%) and perifascicular atrophy (72%). Elevated creatine kinase levels were seen in 86% of the patients, ANA and ENA were positive in 77% and 13% of them respectively. 76% (34/46) patients had MSA/MAA. The most common MSA was NXP2 (21.7%) followed by TIF1-g (17.4%), MDA-5 (8.7%) and Mi-2 (8.7%). Muscle involvement was less prominent in MDA-5 positive patients. TIF-1g and NXP2 positive patients had a severe course similar to previous cohorts; MDA-5 positive patients had a milder disease course with only 25% of them having pulmonary involvement and Ku positive patients had a remarkably more severe course in contrast to previous studies.[3-5] Remission rates did not differ but 43.9% of NXP2 positive and 33.3% of TIF-1g positive patients had a relapse. Corticosteroids (100%) combined with methotrexate (93%) was the initial treatment, hydroxychloroquine (47%), cyclosporin-A (40%), IVIG (34%), azathioprine (14%), cyclophosphamide (14%) and pamidronate (10%) were also used. Biological DMARDs (anti-TNFs, rituximab and abatacept) were used in 22% of the patients. Remission was achieved in 65.5% of the patients in a median 24 (IQR 11.8-42.5) months however 26.3% had a relapse. Overall disease course was monophasic in 31%, polyphasic in 17.2% and chronic in 51.8% of the patients.
Calcinosis (36%) was the most common long-term complication. The factors associated with the development of calcinosis were disease onset ≤6 years, higher muscle biopsy scores, MDA-5, TIF-1g and NXP2 positivity. In a multivariate analysis, the disease onset ≤6 years of age [5.3 (1.16-24.33) p=0.031] and MDA-5 positivity [42.4 (1.51-1190) p=0.028] were the predictive factors for the development of calcinosis during the disease course.
Conclusion: Recent advances on muscle biopsy scores, muscle imaging with MRI and myositis specific antibodies may provide us valuable informations for the diagnosis, disease course and prognosis of JDM.
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Disclosure of Interest: None declared

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CORRELATION OF SERUM NEOPTERIN LEVELS WITH DISEASE ACTIVITY AND TREATMENT IN JUVENILE DERMATOMYOSITIS (JDM).

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Introduction: Activation of the type 1 and type 2 interferon (IFN) pathways seems to play a prominent role in the pathogenesis of dermatomyositis. Neopterin is a marker of immune activation induced by IFNγ stimulation. Previous studies showed that serum neopterin levels are elevated in JDM at diagnosis and correlate strongly with muscle strength impairment.

Objectives: In this study we aimed to investigate neopterin levels in peripheral blood of JDM patients and assess their correlation with clinical and laboratory findings during follow-up.

Methods: We collected 276 blood samples from 55 JDM patients at different time points during follow-up. In 16 patients the first blood sample was obtained at diagnosis before starting treatment. Serum neopterin levels were analyzed by ELISA. We used sera from 19 healthy subjects as controls (HC). At each visit, the following data were recorded: physician's global assessment (PGA) of disease activity VAS (Visual Analogue Scale); cutaneous VAS, Cutaneous Assessment Tool (CAT) activity score; Childhood Myositis Assessment Score (CMAS); serum levels of creatine kinase (CK), AST, ALT and LDH; presence of myositis specific or myositis associated antibodies (MSA/MAA); prednisone (or equivalent) dose (mg/kg/daily); ongoing immunosuppressive medications. Disease remission was defined according to modified Paediatric Rheumatology International Trials Organisation (PRINTO) criteria for clinically inactive disease. According to their disease status and treatment, patients were divided into 4 groups: patients with active disease not receiving medication (A), patients with active disease receiving medication (AM), patients in remission receiving medication (RM) and patients in remission not receiving medication (R).

Results: Serum neopterin levels are significantly higher in JDM patients with active disease (both A and AM group) when compared to HC ($P < 0.0001$, $P < 0.0001$, respectively), with active patients not receiving medication showing the highest levels ($P < 0.0001$ when compared to the AM group). Patients of the RM group have neopterin levels that are comparable to HC, whereas patients in in the R group tend to have higher levels than HC ($P < 0.01$). Neopterin levels are highest in patients at time of diagnosis and decrease under treatment. Serum neopterin levels are significantly correlated with PGA, cutaneous VAS and CAT activity score (Spearman's rank coefficient (r): 0.5, 0.36 and 0.39 respectively, $P < 0.0001$, $P < 0.0001$ and $P < 0.0001$ respectively) and inversely correlated with CMAS (r: -0.35, $P < 0.0001$).

Conclusion: Neopterin levels are significantly correlated with global, cutaneous and muscular disease activity in JDM patients and are influenced by treatment. Our data support the role of neopterin as a biomarker for disease activity in JDM.

Disclosure of Interest: R. Nicolai: None declared, I. Caiello: None declared, D. Pires Marafon: None declared, S. Rosina: None declared, L. Bracci Laudiero: None declared, F. Licciardi: None declared, A. Ravelli: None declared, F. De Benedetti Consultant for: Dr. De Benedetti's Institution received unrestricted research grants from BMS, Pfizer, Abbvie, Novartis, Novimmune, Roche, SOBI, Sanofi, UBC and travel support from Roche, Novartis, Novimmune, SOBI., G. M. Moneta: None declared

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INVESTIGATING NOVEL MECHANISMS OF T CELLS IN THE PATHOGENESIS OF JUVENILE DERMATOMYOSITIS

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Introduction: Juvenile Dermatomyositis (JDM) is a rare autoimmune disease causing skin and muscle inflammation with an average onset of 7 years old. At present, JDM aetiology is poorly understood and current treatment options are not evidence based. This highlights the need for research investigating underlying disease pathogenesis. A skewed T helper (Th)17 phenotype in CD4+ T cells resulting in a Th1/17 imbalance has been observed in both child and adult-onset immune-mediated diseases including rheumatoid arthritis, and multiple sclerosis.

Objectives: The aim of this project is to investigate whether a Th1/17 imbalance can be observed in patients with JDM compared to age/sex-matched child healthy controls (CHC).

Methods: Expression of IL-17 and IFN-γ in CD4+ T cells within peripheral blood mononuclear cells (PBMC) from JDM pre-treatment (n=7), JDM on-treatment (n=28) and CHC (n=22) was assessed by flow cytometry after stimulation with PMA/Ionomycin/Brefeldin A (P/I/B) for 4 hours. For secreted cytokine production, isolated CD4+ T cells were isolated by magnetic separation and stimulated with anti-CD3 or anti-CD3/anti-CD28 for 36 hours in the presence of IL-2. Supernatants were analysed for secreted IL-17 and IFN-γ and measured by cytokine bead array. In parallel, extracellular Th1 (CD3+CD4+CXCR3+CCR6-), Th17 (CD3+CD4+CXCR3-CCR6+) and Treg (CD3+CD4+CD127-CD25hi) subsetting was carried out using flow cytometry and proliferative capacity of T cells was assessed following stimulation by intra-nuclear staining for Ki67 protein. Finally, fluorescence co-staining of JDM muscle biopsies (n=4) to identify Th1 cells (CD3+CD4+IFNγ+) was performed to assess possible Th1 migration to the primary disease site.

Results: Both intracellular cytokine staining and stimulation experiments to assess secreted cytokine revealed a decreased trend of IFN-γproduction in JDM compared to CHC within CD4+ T cells, regardless of treatment status. The JDM CD4+ T cell phenotype was significantly skewed towards a Th17 phenotype (p= <0.0016) compared to controls after ratio analysis of CD4+IFN-γ+ to CD4+IL-17+ cells within peripheral blood after PMA/Ionomycin stimulation. A Th17 skew was confirmed when analysing surface markers for Th1 (CXCR3) and Th17 (CCR6) on JDM pre-treatment-treatment CD4+ T cells compared to controls (p=0.0001). Central and Effector Memory compartments within CD4+ T cells were reduced in JDM pre-treatment patients compared to controls (p=0.02, p=<0.001 respectively). Co-staining of CD3+CD4+IFN-γ+ cells in JDM muscle were observed however a higher proportion of CD3-CD4+IFN-γ+ in JDM pre-treatment patients were also identified.

Conclusion: These novel findings show a Th1/17 imbalance in JDM CD4+ T cells compared to CHC. Whilst results show promising avenues for further investigation there are no definitive explanations for this low Th1 response at present. Future work aims to investigate memory and naive compartments within JDM pre-treatment CD4+ T cells in addition to further testing of cell markers within the muscle. Additionally, other immune and metabolic pathways that may explain this Th17 skew could be targeted to restore IFN-γ loss in JDM patients.

Disclosure of Interest: None declared

e-Poster viewing: Macrophage activation syndrome

P163

AN UNUSUAL CASE OF MACROPHAGE ACTIVATION SYNDROME, COMPLICATED BY THROMBOTIC MICROANGIOPATHY, WITH CLINICAL RESPONSE TO IL-1 BLOCKADE

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Introduction: Macrophage activation syndrome(MAS) with associated thrombotic microangiopathy(TMA) is rare, but has been reported[1]. We present an adolescent with features of MAS and renal impairment with TMA on renal biopsy. Despite partial steroid response, he remained steroid-dependent until addition of an IL-1 blocker with rapid clinical and biochemical improvement.
Objectives: To report this case of an adolescent with MAS and TMA and describe use of IL-1 blockade in his management.
Methods: Retrospective case review
Results: This previously well 14 year old boy presented with 5 weeks malaise, lethargy, poor appetite and 2 weeks dyspnoea and productive cough. There was no history of fever or rash. Similar to other family members, he had a vomiting illness 5 weeks earlier.
He was tachycardic and tachypnoeic, with pleural effusions and hepatosplenomegaly. He had significant renal impairment (urea 18mmol/L, creatinine 124µmol/L), anaemia (Hb 10.7g/dL), thrombocytopenia (platelets $75x10^9$/L), raised inflammatory markers (CRP 99mg/L, ESR 80mm/hr, ferritin 1653ng/mL), albumin 19g/L. He received IV co-amoxiclav and albumin/frusemide infusions.
He continued to deteriorate; remaining febrile, hypertensive and oliguric, with worsening peripheral oedema, ascites and pleural effusions, requiring oxygen. Echocardiogram and MRI showed pericardial effusion, with thickened pericardium. Non-specific dural thickening identified on MRI brain. Extensive bacterial and viral investigations were negative. Bone marrow identified increased myeloid series with no haemophagocytosis. ANA, ANCA, ADAMTS13 and complement levels (CH100/AP100/terminal complement complex) were normal. Perforin and SAP(XLP1) expression were normal. XIAP(XLP2) expression was reduced, but with no pathogenic variant on sequence analysis XLP type 2 was excluded. No autoinflammatory diagnosis found on genetic testing. VIP3 panel[2] identified class 3 variants of unknown significance in IFIH1, LACC1, NLRP6, HTR1A, SCN9A,TGFBR2 and NOTCH3.
On day 9 he was given 600mg/m^2 methylprednisolone followed by oral steroids. High dose steroids resulted in transient biochemical improvements, but this was not sustained, requiring further IV doses. Chest drains removed high volume inflammatory exudate. Renal biopsy on day 20 showed TMA; abnormal glomeruli, increased mesangial and endocapillary cellularity, fragmented red blood cells within the mesangium, with mesangiolysis and fibrin thrombus. Full body MRI and PET excluded malignancy. MMF, introduced on day 48, was stopped due to worsening cytopenia. IVIG had no apparent effect. Anakinra, started on day 60, had dramatic benefit clinically and biochemically. He reported rapid subjective improvement, renal function and ferritin levels improved and diuretics were stopped.
He was subsequently managed as an outpatient; anti-hypertensives and oral steroids slowly weaned and stopped. 18 months later he had a mild recurrence with an intercurrent infection (ferritin 780ng/mL), which responded to IV methylprednisolone and twice daily anakinra. He responded clinically and biochemically and has remained well since.
Conclusion: The association between MAS and TMA has recently been recognised[1]. Our case showed clear response to high-dose steroids and achieved sustained remission with IL-1 blockade. This could be a useful therapeutic option for future patients presenting with features of both MAS and TMA.

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Disclosure of Interest: None declared

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MACROPHAGE ACTIVATION SYNDROME IS A PREVENTABLE LIFE-THREATENING END POINT SYNDROME

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Introduction:

Macrophage activation syndrome(MAS) is still underrecognized perplexed syndrome and usually results in delayed in diagnosis, which leads to high morbidity and mortality. [1]

Objectives:

To highlight frequent clinical and laboratory clues in MAS irrespective of its etiology for an early diagnosis

Methods:

I gathered a data of nine patients who were presented to Dev Children's Hospital as MAS or impending MAS between August 2018 and March 2020. I compared all available clinical and laboratory data of these nine patients in context of HLH-2004 protocol[2] , Modified 2009 HLH criteria[3],2014 H score for reactive HLH[4], 2016 sJIA-MAS diagnostic criteria[5] and 2019 Ferritin:ESR Ratio[6].

Results: Table 1 showed detailed analysis of clinical and laboratory data of our cohort in context of parameters taken from above mentioned criterias.

Parameter	N (%) – Number of Patients
Fever	9 (100%)
Rash	6 (66.6)%)
Bleeding manifestations	2 (22.2%)
Hepatomegaly	6 (66.6%)
Splenomegaly	2 (22.2%)
Lymphadenopathy	3 (33.3%)
CNS dysfunction	4 (44.4%)
HB (<9gm%)	6 (66.6%)
Neutrophils < 1 * 10^9 / L	2 (22.2%)
Platelets </=181* 10^9 /L	6 (66.6%)
Platelets </= 100* 10^9 / L	1 (11.1%)
Number of Cytopenias	
1 lineage	6 (66.6%)
2 lineage	2 (22.2%)
3 lineage	1 (11.1%)
SGPT > 48 u/L	6 (66.6%)
SGPT >30	7 (77.7%)
Triglycerides (mg/dl)	
>156mg/dl	6 (66.6%)
>132 mg/dl	7 (77.7%)
>265 mg/dl -	2 (22.2%)
Fibrinogen (mg/dl)	
</= 360	7 (77.7%)
</=250	5 (55.5%)
</=150	2 (22.2%)
Ferritin level (ng/ml)	
> 684 -	9 (100%)
> 500	9 (100%)
< 2000	2 (22.2%)
2000-6000	2 (22.2%)

< 6000 **Increased Ferritin** : **ESR Ratio**	5 (55.5%) 9 (100%)
Bone Marrow Hemophagocytosis[$] **LDH (>500IU/L)** Low Sodium level Abnormal PT,aPTT Elevated bilirubin Decreased albumin CRP >40mg/L	1 (11.1%) 7 (77.7%) 3 (33.3%) 3 (33.3%) 1 (11.1%)3 3 (33.3%) 6 (66.6%)
Subtle progressive changes in laboratory parameters rather than actual value	9 (100%)
Responded to Oral /IV steroids	9 (100%)

$= Bone marrow examination was performed only in five patients.
NK cell function test and CD25 level was not done for any of these patients.

Conclusion:

Most frequent early clinical findings in MAS are high grade fever , rash, hepatosplenomegaly and subtle CNS features irrespective of its etiology. More common changes in laboratory results are decreasing trend in CBC, increasing trend in ferritin:ESR ratio, triglycerides, LDH and SGPT rather than an actual value. We can use these findings in a very large cohort to progress towards a new universal weightage based specific classification criteria for MAS irrespective of its etiology. It is very important to note that just because of an early diagnosis, all these patients responded to oral or IV steroids dramatically without any further requirement for more toxic immunosuppressive agents.

Trial registration identifying number:

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Ferritin to erythrocyte sedimentation rate ratio: simple measure to identify macrophage activation syndrome in systemic juvenile idiopathic arthriti**s.** Esraa m. A. Eloseily md, mrcpch **,**francesca minoia md **,**courtney b. Crayne md, msph timothy beukelman md, msce **,**angelo ravelli md randy q. Cron md, phd

Disclosure of Interest: None declared

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MAS/SJIA WORKING PARTY ACTIVITIES

F. Minoia[1], S. Vastert[2], C. Kessel[3], C. Bracaglia[4,*] on behalf of on behalf of the MAS/sJIA Working Party
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Introduction: Systemic Juvenile Idiopathic Arthritis (sJIA) is a unique form of childhood arthritis. According to current understanding sJIA is primarily driven by innate immune mechanisms at disease onset, but can progress towards chronic destructive arthritis, which can involve T cellular immunity. For yet incompletely understood reasons, sJIA can be complicated by Macrophage Activation Syndrome (MAS), a severe hyperinflammatory condition characterized by a catastrophic cytokine storm resulting in multiple organ failure and high mortality.

Objectives: The sJIA/MAS Working Party (WP) aims to promote knowledge and international multidisciplinary collaboration among experts in the field of MAS and sJIA and to foster translational research in order to improve the care and outcome of these patients
Methods: Currently 60 PReS members participate to the MAS/sJIA WP. The WP arranges an annual meeting during the PReS Congress, open to all members activities. The MAS/sJIA WP core team frequently report about ongoing activities by email.
Results: Several studies are currently ongoing. A project aimed to **establish and validate a risk score for MAS in sJIA patients** using routine laboratory parameters of disease activity and severity has already completed the construction phase. Recently, building of a validation cohort comprising data form 182 patients from 10 paediatric rheumatologic centers has been accomplished and is awaiting analysis (Claudia Bracaglia). A second project focused on **MAS patients with systemic thrombotic microangiopathy (TMA)** has just completed the collection of 27 patients with MAS and TMA from 18 centers in 9 countries and results will soon be published (Francesca Minoia). Furthermore, the MAS/sJIA WP participated in the data collection phase of a project on the **development of new criteria for primary HLH** (Jan-Inge Henter and AnnaCarin Horne).
A main goal of the WP is to improve clinical care. Within the project **Current treatment in sJIA and MAS/secondary hemophagocytic lymphohistiocytosis (sHLH): a PReS/PRINTO survey** (Francesca Minoia and Sebastiaan Vastert) the initiators aim to better understand the real-life experience in sJIA and MAS/sHLH treatment in pediatric rheumatology centers. To foster the achievement of a uniform approach, pediatric hemato-oncologists and Intensive Care Unit physicians will be involved, to capture all the different settings in which MAS/sHLH patients may be treated. The project was proposed for the first PReS/PRINTO grant and was ranked second.
Among translational science activities, MAS/sJIA WP members (Sebastiaan Vastert and Claudia Bracaglia) aim to collect biosamples and clinical data from patients with treatment refractory/resistant sJIA, connecting existing large national sJIA cohorts and open for new patients from paediatric rheumatology centers throughout Europe/world (**ReSyst study**).
A second translational project focuses on the role of viral triggers of MAS and proposes to **analyze type I IFN score and IL-18 expression in MAS and MAS risk patients** to deepen understanding on type 1 interferons as critical regulators of IL-18 expression (Christoph Kessel).
Finally, the MAS/sJIA WP aims to organize a **focused PReS academic course** on sJIA and MAS in 2021.
Conclusion: At present, the MAS/sJIA WP is coordinating several clinical and translational research activities. Any proposal for new collaborative projects is highly appreciated.
Claudia Bracaglia, Chair
Francesca Minoia, Secretary and Lead of Clinical Care Pillar
Sebastiaan Vastert, Lead of Training&Education Pillar
Christoph Kessel, Lead of Science&Research Pillar
Disclosure of Interest: None declared

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HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS IN INFANCY: A CASE SERIES

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Introduction: Hemophagocytic lymphohistiocytosis (HLH) is an immunological disorder characterized by clinical signs and symptoms of severe uncontrolled inflammation, due to massive release of inflammatory cytokines. A delay in diagnosis is common, and is one of the factors that determine the poor outcome. HLH is classified into primary (pHLH) and secondary (sHLH). It is important to differentiate between the two as management differs.

Objectives: To describe the clinical and laboratory profile of HLH in infancy.

Methods: The electronic case files of children (age<1 year) diagnosed with HLH at the AIMS, Kochi, Kerala, between January 2012 and December 2019, was retrospectively reviewed and described.

Results: Eight infants, with age range 1.5 months to 7 months, were clinically diagnosed with HLH. All were immunised and had normal development for age. None had a family history suggestive of HLH. Third degree consanguinity was present in parents of patient no.5 and second degree for patient no.7. Duration of symptoms before presentation ranged from 2 days to 68 days. Duration of follow up with us ranged from 12 days to 192 days, for those who expired.
All, eight of them, had fever, anemia, thrombocytopenia, hyperferritinemia, transaminitis, raised LDH and CRP. Lymphadenopathy was present only in patient no.4. Before starting specific treatment patient no. 7 had Pseudomonas sepsis, patient no.5 had Roseomonas gilardii infection; patient no.3 and 4 were IgM CMV positive but their PCR was negative. Both of them had received prior blood transfusion.
Before making a definitive diagnosis of HLH patients were treated for PUO, sepsis ? cause and acute liver failure. There was a delay in diagnosis for all patients except patient no.7.
All of them were treated with HLH 2004 protocol with modification according to clinical status of the patient. Later, broad spectrum antibiotics, antifungals and antivirals were used for all. Anakinra was tried for patient no.5.
Five patients (pHLH) succumbed to sepsis and MODS and three (one pHLH and two sHLH) are continuing follow up. HSCT was not done in any of them. Other clinical features are shown in Table 1.

Table 1: Clinical and lab characteristics in infantile HLH

No	rash	jaundice	Splenomegaly	Hepatomegaly	Neutropenia <1000/mm^3	Triglyceride >265mg/dl	Fibrinogen <150g/dl	Hemophagocyte	Mutated gene
1*#	1	1	1	1	0	1	1	1	Neg
2*	1	1	0	1	1	1	1	0	Neg
3*#	0	1	0	1	0	1	1	1	Nd
4*	0	0	1	1	1	0	0	1	PRF1
5*#	1	1	1	1	1	1	0	0	PRF1
6	1	0	1	1	1	1	0	1	UNC13D
7#	1	0	0	1	0	0	0	0	Nd
8	1	0	0	0	0	1	1	0	Neg

Foot note: patients no. 1 to 6- pHLH, no.7- sHLH due to pseudomonas infection, no. 8-SJIA with MAS. *- expired, #- female patients f-female, m-male, Neg-negative, Nd-not done, Expd-expired

Conclusion: Making a timely diagnosis of HLH is difficult. Differentiating pHLH from sHLH is very important as the management differs. Genetic testing should be done for all infants with HLH. Negative genetic study doesn't rule out pHLH. The only curative treatment for pHLH is HSCT. sHLH infants, once their primary condition is treated, can have normal survival. Hyperbilirubinemia, splenomegaly, neutropenia, hepatomegaly, tissue hemophagocytes and hypertriglyceridemia were more common in pHLH.

Disclosure of Interest: None declared

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MACROPHAGE ACTIVATION SYNDROME : 12 YEARS DATA FROM AN INDIAN CENTER

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Introduction: Macrophage Activation Syndrome (MAS) is a dreaded complication of systemic inflammatory diseases and is most commonly seen in systemic onset juvenile idiopathic arthritis (SJIA). Data of patients admitted in the Department of Pediatric Rheumatology, Institute of Child Health, Kolkata diagnosed as having MAS, admitted between July 2008 and April 2020 was tabulated and retrospectively analyzed .
Objectives: To evaluate the clinical features, laboratory findings and outcomes in pediatric MAS, assess the response to different pharmacological therapies, and finally to identify possible factors associated with an unfavourable outcome.
Methods: The data of patients diagnosed with MAS over the study period was analyzed for the clinical and laboratory features, treatment details, response to therapy and outcome.
Results: 35 patients were diagnosed as having MAS. Primary illness was SJIA in 29 (82%), SLE in 5 (14%) and Kawasaki Disease (KD) in 1(4%). All had fever with varying degrees of multi systemic involvement. Hyperferritinemia was universally present. In the absence of Anakinra in India, pulse methylprednisolone with Cyclosporine was used for treating the majority.10 patients (28.5%) expired. Patients on biologics and steroids can present with a silent MAS which may be difficult to diagnose.

Conclusion: MAS is a near fatal complication with protean manifestations and multi organ dysfunction. Hyperferritinemia is characteristic, higher values being associated with increased mortality. Patients resistant to steroids and cyclosporine had a poor prognosis. Early recognition with aggresive management forms the backbone of a successful outcome as reflected by improved prognosis over successive years. Late presentations with multiorgan dysfunction are associated with the poorest outcomes.
Disclosure of Interest: None declared

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LIFE-THREATENING MACROPHAGE ACTIVATION SYNDROME WITH FULMINANT MYOCARDITIS SUCCESSFULLY RESCUED BY HIGH DOSE INTRAVENOUS ANAKINRA

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Introduction: Macrophage activation syndrome (MAS) is a rare, potentially life-threatening complication of some rheumatologic diseases[1].
Objectives: We report the case of a child with systemic onset Juvenile Idiopathic Arthritis (sJIA) complicated by severe MAS and acute myocarditis, needing veno-arterial Extracorporeal Membrane Oxygenation (VA-ECMO), successfully rescued by high dose intravenous Anakinra (HDIV-ANA).
Methods: Case report's description
Results: A two-year-old boy presented with one month history of fever associated with limping gait, cervical lymphadenopathy and skin rash. Laboratory tests showed elevation of inflammatory markers and ferritin. By exclusion criteria, sJIA was diagnosed and steroid therapy started. After a soft tissue bacterial infection, fever relapsed and laboratory tests were consistent with MAS (day 1): Hb 8.5 g/dL, PLT 44000/mm3; FDP 1522 ug/L, CRP 100 mg/L, ferritin 2200 ug/L. High doses intravenous metilprednisolone and oral Cyclosporin A (CSA) were started. On day 2 he presented a Systemic Capillary Leak Syndrome and acute myocarditis. He was admitted into the pediatric intensive care unit (PICU) where intravenous immunoglobulin and subcutaneous Anakinra (ANA) were added. On day 4, due to an episode of cardiac arrest, VA-ECMO was started and we tried high dose intravenous ANA (HDIV-ANA, 8 mg/Kg/day q6h). This treatment brought immediate benefit: echocardiography showed progressive resolution of myocarditis so that VA-ECMO was definitely weaned off in six days. Laboratory test showed isolated neutropenia (PMNs 0-100/mm^3). Suspecting a iatrogenic cause, HDIV-ANA was gradually reduced to the maintenance dose without benefit. On day 22, ANA was stopped and neutropenia resolved. Analysis of PRF1 gene revealed a mutation (c.[272C>T] p.[Ala91Val]) in heterozygosis. 49 days after admission he was discharged on oral prednisone and CSA. Neither neurological nor other organ consequences related to MAS were reported. A few months later, on tapering down of therapy, he relapsed. ANA was restarted with rapid improvement and no side effects, including neutropenia. Currently, after 12 months, the disease is in clinical remission on medication.
Conclusion: MAS is a rare life-threatening complication of sJIA, triggered by infections in up to one-third of the patients [2]. It is the result of a cytokine storm that lead to a dysregulated inflammatory activation of the immune system, with rapid progression to multiorgan failure. Treatment usually includes high dose corticosteroids and immunosuppressive agents. Recently, the use of selective cytokine inhibitors has been suggested. No standardized guidelines are available to date, but the use of ANA has been already reported , pointing out the need for a higher doses regimen in refractory cases. MAS in our patient appeared after a soft tissue infection which could have act as triggering factor in a patient with sJIA and genetic predisposing pattern. The choice of intravenous administration of ANA was partly due to the generalized edema and partly to the severe discoaugulopathy. Considering the higher doses needed for rapidly suppressing the cytokine storm and ANA pharmacokinetics, we split the daily dose into four administrations. No major adverse events were reported, except for a transient neutropenia, already reported [6].

Based on our experience, HDIV-ANA is a safe and effective treatment for refractory life-threatening sJIA-related MAS. This therapeutic approach may be also considered in the current pandemic COVID-19 emergency where recent evidence showed IL1-driven MAS-like complication triggered by SARS-CoV-2 virus as predictor of bad outcome[7].

Disclosure of Interest: None declared

e-Poster viewing: Miscellaneous rheumatic diseases

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PULMONARY INVOLVEMENT AS INITIAL MANIFESTATION OF PEDIATRIC SJOGREN

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Introduction: Sjögren's syndrome is a systemic autoimmune disease characterized by dry syndrome and lymphocytic infiltration of the exocrine and extraglandular glands. Pulmonary involvement in primary Sjögren's syndrome occurs in 9-20% of patients, with very heterogeneous manifestations, and occasionally as an initial manifestation[1]. Diffuse interstitial lung involvement is one of the most characteristic pulmonary manifestations and the most frequent subtypes in lung biopsy are interstitial lymphocytic pneumonia and nonspecific interstitial pneumonia[2].
Objectives: 14-year-old girl presented to our hospital because of bilateral interstitial involvement with ground glass areas in lower lobes of both lungs on thorax and abdominal CT scan after for kidney stones follow-up. The patient had grade 1 mMRC dyspnoea and dry cough but denied having symptoms of arthralgia or arthritis, photosensitivity, oral and genital ulcers, Raynaud's phenomenon or episodes of dry mucosa. She had no history of autoimmune disease nor family antecedents of any autoimmune disease. A physical examination disclosed no finger clubbing or swollen superficial lymph nodes but indicated crackles on pulmonary auscultation. Laboratory work showed elevated acute phase reactants, positive rheumatoid factor, positive antinuclear antibodies (1/40), positive cytoplasmic antineutrophil antibodies (1/320) and IgG and IgA hypergammaglobulinemia. An examination for autoantibodies were negative for anti-SS-A, anti-SS-B, anti Jo-1, anticentromere and anti-scl-70 antibodies. Iontophoresis with pilocarpine and 6-minute walk test was also normal. Pulmonary function tests demonstrated a mild restrictive impairment and a reduced percent diffusion capacity for carbon monoxide of 55%. Fibreoptic bronchoscopy showed acute inflammation in bronchial mucosa. Flow cytometry of bronchoalveolar lavage and cytology showed lymphocytosis with a 15% of CD4 and 85% of CD8 lymphocytes in bronchoalveolar lavage fluid. Finally, a transbronchial lung biopsy lead to a definitive diagnosis, showing mixed interstitial inflammation and lymphocytic follicular hyperplasia with formation of germinal centers, suggestive of a lymphoid interstitial pneumonia of unreleased autoimmune etiology. Throughout time, the patient reported progression of her symptoms with increasing dyspnoea, persistent dry cough, xerostomia and arthralgia. Schirmer and Rose Bengal dye test were negative, and a salivary gland biopsy showed interstitial plasmacytosis and no IgG4 plasma cells expression which suggested Sjogren's disease. A high resolution computerized axial tomography was requested, suggesting organizing pneumonia in the context of Sjogren's disease.
Methods: Several studies indicate that lung involvement in Sjögren is more frequent in advanced stages of the disease and rarely as an initial manifestation. Sjögren's syndrome in paediatric age is rare and the subtype of secondary Sjogren's is the most common. The course is longer, and the symptoms are more heterogeneous than in adulthood[5] . The diagnosis in children is delayed, because children less frequently report dryness and frequently present with extra-glandular clinical features suggestive of other autoimmune diseases. A systematic review on primary Sjögren's syndrome in male and paediatric population reported a 2.4% of pulmonary involvement in paediatric patients. [6] Pulmonary involvement is associated with an increase in the mortality of patients with Sjögren's, therefore, it is essential to periodically monitor patients with respiratory symptoms, making an early diagnosis and treatment of the disease.
Results: -
Conclusion: We present a case of a patient with childhood Sjögren's disease with atypical onset of disease with lung involvement.
Disclosure of Interest: None declared

P170

A FRONTAL BONE OSSEOUS LESION: AN UNUSUAL PRESENTATION OF CHILDHOOD SARCOIDOSIS

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Introduction: Sarcoidosis is a multi-system disorder. Little is known about its pathogenesis. In children, the early onset sarcoidosis phenotype including Blau syndrome is more often seen.[1,2] The diagnosis of sarcoidosis is confirmed by demonstrating a typical non-caseating granuloma on a biopsy specimen. Other granulomatous diseases should be excluded, in particular mycobacterial infections, Crohn's disease and immunodeficiencies. The clinical presentation may vary depending on the organs involved and the age of the patient.[3,4]
Objectives: We are reporting the case of a boy with a presentation of bone sarcoidosis at a young age. This is a rare phenotype in children.
Methods: Clinical details were retrospectively collated using routine clinical records. Confirmation of diagnosis was confirmed with bone biopsy.
Results: A 5 year old non-identical twin boy of Ghanaian descent born in the UK had a slowly growing, painless frontal bone mass which started to develop from 7 months of age. He was developmentally normal, with no history of fever, rashes or joint pains.
Examination findings revealed frontal bossing while the remainder of the musculoskeletal examination was normal. There was no evidence of rashes, hepatosplenomegaly and ocular examination was normal.
The patient was initially referred for neurosurgical review with suspected fibrous dysplasia, after an initial MRI scan of the head revealed abnormal marrow signal and expansion of the frontal bone, with no soft tissue swelling. However, the CT scan of the calvarium was not suggestive of fibrous dysplasia. Consequently, bone biopsy was performed demonstrating inflammation with granuloma formation.
He was referred to Infectious Diseases and Rheumatology.
There was no travel history and no TB contact. QuantiFERON TB was negative. Infectious work-up was negative especially for mycobacterial infections.
Rheumatology work-up identified on skeletal survey another bone location: a well-defined lytic lesion in the right distal fibula that was biopsied. Infection cultures and PCR were negative. Histopathology identified fibrous tissue and poorly formed granulomas. Laboratory investigations revealed a mild microcytic anaemia with iron deficiency and eosinophilia. He had normal serum calcium and vitamin D and his ESR was 25 mm/hr. ANA, ANCA and rheumatoid factor were negative, and complement C3 and C4 were normal. His serum Angiotensin Converting Enzyme (ACE) level was raised at 125 nmol/ml/min (normal <40 nmol/ml/min). Investigations revealed mild renal impairment with normal urinary tests including normal calcium, protein and tubular proteins. Ultrasound of the kidneys was normal. Chest X-ray was normal. Lung function was performed and was normal. DLCO couldn't be performed due to low lung volume.
Vascular and inflammation genetic panel identified a variant in the NEMO gene. Functional studies excluded NEMO deficiency and patient did not display any of the clinical features.
However, a pattern of dysregulated T cells response was identified.
He was treated with oral steroids and methotrexate. The oral steroids were successfully weaned off. He has been successfully treated with Methotrexate 10mg s/c to initially stabilise disease with no bone growth, and had no significant side effects.

Repeat MRI 2 years later showed increased burden of disease with other newly affected sites however, including the right femoral diaphysis and signal changes in the left tibial metaphysis.

Based on the MRI and increasing musculoskeletal pain, decision was made to escalate to anti-TNF (adalimumab) with good clinical response.
Conclusion: Bone sarcoidoisis is rare in children but this should be considered in the differential diagnoses when granulomatous inflammation is identified on histopathology. Response to steroids and methotrexate is usually good but some patients will need escalation to anti-TNF.
Disclosure of Interest: None declared

P171

NIGHT PAINS IN CHILDREN CAN BECOME A NIGHTMARE FOR RHEUMATOLOGIST

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Introduction:

The most worrisome non-rheumatic condition causing persistent night pain in children which closely mimics arthritis is malignancy[1,4]. It is vital to pick up subtle clues at an early stage especially in absence of hematological manifestations , organomegaly and lymphadenopathy.

Objectives:

To reveal early clinical clues in pediatric patients with predominant musculoskeletal (MSK) night pains who were initially diagnosed as suffering from some form of chronic arthritis but ultimately turned out to be affected by malignancy.

Methods:

I gathered a data of five pediatric patients fulfilling above mentioned criteria who were seen at Dev Children's Hospital between January 2019 and March 2020. It included demographics, clinical presentation and laboratory results.

Results:

TABLE 1 showed characteristics of five children with persistent MSK night pains

Age (years)/ Sex	7/M	4/F	5/F	2.5/M	2.5/F
Joint involvement	*Hip*	*Hip* *Elbow*	*Elbow* Knee Ankle	*Hip* *Elbow*	--
MSK pain	*Thigh* Back	*Thigh* Calf	--	--	?Calf *?Thigh*
Fever	+	+	+	--	+
Persistent Limp	+	+	+	+	--
Organomegaly	+	--	--	--	+
Lymphadenopathy	+	--	--	--	+
HB (gm%) TLC(/cumm) Platelet (/ul)	9 7560 *1,52,000*	*6.7* 9300 1,90,000	8 9800 3,21,000	8 6500 *1,65,000*	*6* 30,300 7,22,000
ESR(mm/hr) CRP(mg/L) LDH(IU/L)	42 56 *708*	46 35 300	81 65 321	45 34 456	53 125 461
Final Diagnosis	NHL	ALL	ALL	ALL	Multisystem LCH

(Abbreviations: MSK=musculoskeletal, NHL= non-hodgkin lymphoma , ALL= acute lymphoblastic leukemia, LCH = langerhans cell histiocytosis, LDH=lactate dehydrogenase)

Conclusion:

All above cases reemphasize the need for an extremely detailed history pertaining to characteristics of pain & pattern recognition in pediatric rheumatology. Prolonged fever , persistent MSK night pain, persistent limp, upper limb and hip joint involvement which is unlikely for JIA at onset are proven to be the earliest subtle clues which should not be missed.[1, 2, 3, 4] LDH has served as a reliable screening tool here. Most of these patients have been diagnosed without organomegaly, lymphadenopathy and major changes in CBC at this stage.

Trial registration identifying number:

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Chronic musculoskeletal pain in children

Ioanna Fragkandrea, Md, Phd, The Royal Marsden Hospital, Sutton, London, United Kingdom. John Alexander Nixon, Md, Epsom And St. Helier Nhs University Hospital, Sutton, London, United KingdomParaskevi Panagopoulou, Md, Mph, Phd, Panagiotis And Aglaia Kyriakou Children's Hospital, Athens, Greece
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Jennifer l. Junnila, m.d., m.p.h., army medical department center and school, san antonio, texas
Victoria w. Cartwright, m.d., m.s., madigan army medical center, tacoma, washington
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Chronic musculoskeletal pain in children: part ii. Rheumatic causes
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Disclosure of Interest: None declared

P172

COMPLETE REMISSION OF AURICULAR RELAPSING POLYCHONDRITIS BY TREATMENT WITH ADALIMUMAB AND METHOTREXATE

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Introduction: Relapsing polychondritis (RP) is a rare disease with wide spectrum, ranging from isolated auricular chondritis, to life threatening cardiopulmonary manifestations. Even isolated auricular inflammation may result in significant morbidity due to collapse of the external ear cannal leading to conductive deafness and to significant deformity. On the other hand auricular chondritis may represent the inaugural symptom of a more aggressive, systemic disease. In children RP is rarer than in adults and often has a more severe course and more frequent involvement of the respiratory tract. Heart valve damage may develop silently with significant morbidity and mortality. Isolated auricular involvement may be complicated with sensorineural or conductive deafness and significant structural damage. First line treatment is corticosteroids. There are conflicting reports on the efficacy of DMARDs and TNFα inhibitors
Objectives: To report the clinical picture of isolated auricular relapsing polychondritis and the response to anti-TNFa treatment with adalimumab
Methods: Case presentation
Results: A 9-year-old girl was reported to the pediatric rheumatology unit by the ENT department due to 4 recurrent episodes of bilateral ear (more severe left) inflammation, with painful violaceous edema confined to the cartilaginous part of the ear, sparing the lobe during the past year. Nonspecific back pain was the only other symptom. Other constitutional symptoms, respiratory, cardiovascular, ophthalmologic or osteoarticular involvement were absent. Growth was unaffected. Auditory tests were normal. Systemic antibiotic treatment and local steroids were ineffective. Laboratory findings were unremarkable, with only mild elevation of ESR (28mm/1st hr). ANA and ANCA were absent in repeat meausrements (3 months intervals). Cardiovascular disease was excluded. Abdominal US was normal. On the basis of relapsing bilateral auricular chondritis and confirmatory histological findings revealing inflamed cartilage from the pinna of the ear with chondrocyte degeneration, perichondrial infiltrates of lymphocytes, plasma and polymorphonuclear cells and replacement of cartilage with fibrous tissue perivascular infiltrates of polymorphonuclear cells and lymphocytes, relapsing polychondritis was diagnosed. One month NSAIDS trial, pending histology results was ineffective. Methotrexate SC and steroids 1mg/kg/d gradually tapered over a 3-month period were given with significant improvement of auricular inflammation and normalization of markers of inflammation. Auricular chondritis worsened after steroid withdrawal and adalimumab was added to treatment with significant improvement of auricular inflammation in 2 months. In the following 8 months auricular chondritis relapsed during URIs with mild elevation of ESR (25mm 1st hr) and CRP (13 mg/l). After 15 months of treatment, in an effort to prolong the intervals of adalimumab administration, bilateral auricular chondritis relapsed. After 24 months of MTX and 21 months of adalimumab administration inflammation was put in complete remission. The following year no flares or involvement of other systems were observed, under methotrexate and adalimumab treatment.
Conclusion: In this patient isolated auricular relapsing polychondritis was unresponsive to NSAIDs. Steroids and methotrexate greatly improved inflammation but did not induce complete remission. Complete remission was achieved by addition of adalimumab to methotrexate treatment, which also allowed for steroids discontinuation.

Disclosure of Interest: None declared

P173

FIRST EVER SINGLE CENTER STUDY REVEALING SPECTRUM OF RHEUMATIC DISEASES IN 114 CHILDREN FROM AN INDIAN STATE OF GUJARAT

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Introduction:

There is very limited information and awareness about pediatric rheumatic and immunodeficiency diseases amongst primary physicians[1,2,3] in Gujarat and to make this matter even worse, we are not having a single exclusive pediatric rheumatology and immunology centre for a population of around 60 million.

Objectives:

To guesstimate a status of children with rheumatic and immunodeficiency diseases in Gujarat and spectrum of these diseases at Dev Children's Hospital.

Methods:

I gathered a retrospective data of 174 patients who attended Dev Children's Hospital between January 2019 and January 2020. Out of these, 114 children with confirmed diagnosis of inflammatory rheumatic diseases and suspected primary immunodeficiencies were included. Patients with non-inflammatory musculoskeletal(MSK) pains and non-rheumatic diseases causing MSK pains were excluded. My collected data included referral details, demographics, clinical presentation, laboratory results and diagnosis.

Results:

Majority of the cases were referred by pediatricians, orthopedicians, hemato-oncologist and general physicians. Main reasons for referral were joint involvement , undiagnosed fever , multisystem disease and elevated inflammatory markers. Many physicians had put a diagnosis like rheumatoid/rheumatic arthritis, autoimmune disease or connective tissue disease. Almost 80% of patients had been evaluated with RF, ASO titer, ANA and joint imaging irrespective of clinical pattern by their primary physicians before referral. Fever , MSK involvement, extreme fatigue, constitutional symptoms, skin and mucosal involvement were prominent complaints noted by me. Family history of rheumatic, primary immunodeficiency (PID) or consanguinity was found in 1/3 of patients. Anemia of chronic disease, elevated ESR and thrombocytosis were almost universal laboratory findings in our cohort.

Table 1 showed demographics and spectrum of pediatric rheumatic diseases in our cohort.

Demographics N(%)	Age <5 years 48(42%)	Age 5-10 years 39(34%)	Age >10 years 27(24%)	Sex F:61(53.5%) M:53(46.5%)
Group of Conditions N(%)	**Vasculitis 27 (24%)** Kawasaki Disease > IgA-Vasculitis **Infections 29 (25%)** Brucella > PSRA > MRSA >ARF > TB arthritis = ReA	**Juvenile Idiopathic Arthritis (JIA) 27 (24%)** RF +ve JIA > sJIA > Early onset ANA+ve JIA > ESRA JIA>Other > Unclassified (as per preliminary PRINTO JIA Criteria)[4]	**Connective-tissue diseases (CTDs) 20(17.5%)** SLE > Overlap syndromes > MCTD > JDM > systemic sclerosis >Inherited CTDs	**Suspected Primary Immunodeficencies (PID) & Auto inflammatory syndromes 11 (9.5%)** Immune dysregulation (IPEX,APECED,HLH) > Cryopyrinopathy > CRMO > Bone marrow failure > cyclic neutropenia

Macrophage activation syndrome was seen to be associated with sJIA in 4 patients, SLE in 2 patients, PID in 1 patient and brucellosis in 2 patients.

(Abbreviations: PSRA=Post Streptococcal Reactive Arthritis,ARF=Acure Rheumatic Fever, ReA=Reactive Arthritis , ESRA= enthesitis-spondylitis related arthritis,APECED=Autoimmune–polyendocrinopathy-candidiasis-ectodermal dystrophy, IPEX=Immunodysregulation-polyendocrinopathy-enteropathy-x linked)

Conclusion:

Rheumatic diseases in children are not anymore rare but due to lack of expertise and awareness , these children are not getting diagnosed. Many cases were advised unnecessary rheumatological investigations even before referral. Prolonged fever, MSK involvement, skin manifestations, fatigue, constitutional symptoms and unexplained multisystem features with systemic inflammation mainly elevated ESR are found to be very sensitive features to suspect rheumatological problems. The frequency of various rheumatic conditions can be depicted as Infections > Vasculitis = JIA > CTDs > PID in our cohort.

Trial registration identifying number:

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AkhilaKavirayani[1], SumaBalan[2]
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[2] Department of Paediatric Rheumatology, Amrita Institute of Medical Sciences, Kochi, Kerala, India

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Disclosure of Interest: None declared

P174

PARASITES AND ARTHRITIS: AN UNHEARD DUO AMONG CHILDREN

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Introduction: Based on literature reports, arthritis is a rare manifestation of parasitic infestation and it occurs more frequently in adults with Giardia lamblia, Strongyloides stercoralis, Schistosoma mansoni and Toxocaridae infestations. Reports of this symptom in children are extremely rare. Enterobius vermicularis is the most common helmintic parasite in the Italian general population. It is usually asymptomatic or associated with mild and heterogeneous manifestations, including diffuse or perianal itching, restless sleeping, discomfort, gastrointestinal symptoms and arthralgia, with frequent evidence of peripheral eosinophilia.
Objectives: A cohort of pediatric patients evaluated in the Pediatric Rheumatology Medical Clinic of Verona from 2010 to 2020, affected by mono- and polyarthritis during parasitic infestation was described in this study with the aim of reporting clinical, instrumental and laboratory data, including research of parasites in order to raise awareness of this clinical entity in children and promote its systematic description.
Methods: Patients who presented joint pain or clinical signs of arthritis and evidence of parasitic infestation by scotch tape test or stool examination were selected among Pediatric Rheumatology patients of Verona Day Hospital from 2010 to 2020. The following indicators were considered: articular manifestations at onset, presence of eventual systemic symptoms associated, laboratory test abnormalities, elapsed time between onset and diagnosis, response to treatment and eventual relapse. Patients presenting signs of joint inflammation underwent an ultrasound examination.
Results: We selected 14 patients of prevalent age at onset of 7,71 years (2-14 years), male-to-female ratio 8:6. The majority of patients (86%) presented a symmetric polyarthritis, exclusively involving the lower extremities in 54% of the cases. At onset of the articular manifestation, 78% of the patients presented one or more associated symptoms, such as diffuse or anal itching (30%), gastrointestinal symptoms (abdominal pain 43%) and a less specific symptomatic including headache (21%), fatigue (14%) and dermatitis or skin rash (21%). The laboratory tests, performed by nearly all patients (93%), showed eosinophilia in 92% of the cases, presence of antinuclear antibodies (ANA) (38%) and elevated inflammation markers (0,08%). Ultrasound was performed in 64% of the patients and showed synovial thickening and synovitis in all cases and joint effusion in 44% of the cases. Stool examination and scotch tape test repeated on 3 consecutive samples resulted positive for E. vermicularis in 93% of the cases and for Dientamoeba fragilis in one patient. After eradication therapy with repeated doses of mebendazole and pyrantel pamoate every 2-4 week for all cohabitants and pets, all the patients showed a significant reduction of symptoms and subsequent normalisation of test results. In 2 cases re-infestation occurred with recurrence of articular symptoms and treatment was restarted with benefit, as long as needed until complete eradication.
Conclusion: The study suggests that intestinal parasitic infestations are an under-reported cause of joint pain and arthritis in children. Indeed, parasites should be considered in the differential diagnosis in patients that present joint pain or signs of arthritis with clinical and laboratory findings suggestive of parasitic infestation. A re-infestation should also be excluded in case of recurrence of articular symptoms. A concomitant parasitic infestation should furthermore be excluded in chronic polyarthritis requiring immunosuppressant therapy, due to risk of disseminate infestation.
Disclosure of Interest: None declared

P175

OUTCOMES OF MOTHERS WITH RHEUMATIC DISEASES AND FOLLOW-UP OF WITH A FOCUS ON AUTOIMMUNITY AND NEURODEVELOPMENT.

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Introduction: Autoimmune rheumatic diseases (ARD) predominantly affect women of childbearing age, including systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) being the most prevalent. Maternal ARD have been associated with early and late abortions, premature births, and low birth weight babies, which will subsequently have repercussions on their neurological development.

Objectives: The aim of this study is to describe the birth outcomes of newborns born to woman with rheumatic disease, and the impact of their neurological development.

Methods: A prospective study from July 2017 to April 2020, from children born to women with ARD treated at our center. Sociodemographic and clinical characteristics of newborns and their mothers were evaluated; medication used during pregnancy, perinatal complications and prospective neurological evaluations were performed.

Results: 42 children born to 39 women were included,one twin and one triplet pregnancy.RA in 35%.Median gestational age were 36 weeks (26-41), 38% children were preterm,4.7% extremely premature. Median weight 2509 grs (700-3920), 23% low birth weight. The mortality was 9.5%. 2.3%was prenatally diagnosed with neonatal Lupus and complete AVB, treated with parenteral steroids prenatally and a pacemaker at birth. Neurological evaluations were abnormal in 4.7% in the first month and in 19% at 3 months, 7.1% patients had axial hypotonia,4.7% a higher head circumference, 2.3% presented fists and no cephalic support.

ARD	**n= 42**	**Abnormal**	**Newborn**
RA	14	1 (2.3 %)	Polycythemia
SLE	5	0	Normal
SJOGREN	3	1 (2.3 %)	Patent ductus arteriosus
APS	9	1 (2.3 %)	Cyanogenic heart disease
Asymptomatic	2	1 (2.3 %)	Neonatal lupus AV block
SLE + APS	1	0	Normal
Dermatomyositis	1	0	Normal
Others	7	7 (16.6%)	Normal

Table 1. RA=Rheumatoid Arthritis, APS=Antiphospholipid Syndrome, SLE=Systemic Lupus Erythematosus, AIJ=Juvenile Idiopathic Arthritis, AV=Atrioventricular

Conclusion: Data collected during follow-up of this cohort of children born to women with rheumatic diseases show alterations in gestational age, antropometrical measures, neurological development and ARD features, at this moment to follow-up only 2.3% of children had an autoinmune disease. A more extensive follow-up is required to obtain noteworthy data on the impact of this deviations during children development.

Disclosure of Interest: None declared

P176

ANKLE TENOSYNOVITIS IN PONCET'S DISEASE

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Introduction: Musculoskeletal manifestations of TB account for 10–19% of the cases of extrapulmonary form(1,2). Poncet's disease is a reactive arthritis associated with active TB, with no evidence of TB in the joints, bones or tendons(3). The typical manifestation is symmetric polyarthritis(4).
Objectives: Report a rare case of ankle tenosynovitis in Poncet's disease.

Methods: Case report and literature review.
Results: A 10-year-old female patient was referred to the rheumatology clinic at our hospital with a previous history of fever of 39°C (102.2ºC), loss of appetite, and acute polyarthritis of wrist, knees, and ankles. At that time, laboratory exams revealed a hemoglobin of 11.1 g/dL, C reactive protein 78.6 mg/L, and antistreptolysin O titers of 400 UI/mL (normal range <200UI/ml. Clinical symptoms were relieved only after using NSAIDs. After 6 months, the patient returned to our hospital with a 7-month history of weight loss and claudication related to pain and daily morning stiffness (15 minutes) on her right ankle. New laboratory findings demonstrated positive antinuclear antibodies 1:320, negative rheumatoid factor, and alpha-1-acid glycoprotein of 171 mg/dL (normal range: 44-113mg/dL). Clinical signs suggestive of chronic arthritis with exuberant swelling of the ankles were observed on physical examination (figure A). She was screened for tuberculosis (TB) and had a positive (18mm) tuberculin skin test (figure B). Chest CT revealed infiltrative soft tissue mass in the posterior mediastinum, with homogeneous contrast enhancement (figure C). Magnetic resonance imaging of both ankles was performed and demonstrated bilateral and symmetrical tibiotalar arthritis and prominent tenosynovitis of extensors, flexors, and fibularis tendons (figure D). Right ankle synovial biopsy revealed no granulomas and joint fluid culture was negative for *Mycobacterium tuberculosis*, confirming reactive arthritis (Poncet's) and tenosynovitis, that may follow mycobacterial infection with no infective agent in the joints.
Conclusion: To our knowledge, there is no report of Poncet's disease associated with inflammatory tenosynovitis, showing the particularity of this case. The patient's symptoms resolved after two months of anti-TB therapy.
Disclosure of Interest: None declared

P177

CAMPTODACTYLY-ARTHROPATHY-COXA VARA-PERICARDITIS SYNDROME: A RARE AND MISDIAGNOSED CONDITION

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Introduction: CACP is characterized by congenital or early-onset camptodactyly (usually bilateral); non-inflammatory arthropathy (more frequently in the wrists, knees, ankles, elbows, and hips); coxa vara (reduction of the angle between the neck and shaft of the femur); and non-inflammatory pericardial effusion (a late manifestation, less frequently reported). Recognizing the radiological aspects of this syndrome and differentiating it from JIA is crucial since CACP has no effective treatment and JIA is usually treated with NSAIDs and methotrexate (2, 3).

Objectives: To report a rare case of CACP syndrome mimicking JIA.
Methods: Case report and literature review.
Results: A 5-year-old male patient presented with arthropathy characterized by painless progressive swelling and restricted movement of the hands, hips, knees, and ankles since the first year of life. He had a family history of camptodactyly from his paternal grandfather. On physical examination, symmetric camptodactyly of the hands and feet was observed (A). He had no history of rash or weight loss and inflammatory markers were unremarkable. The echocardiogram was normal. The pelvic radiograph showed a widening of the joint space and bilateral coxa vara. Magnetic resonance imaging (MRI) of the hips (B) and knees (C) was performed and depicted large joint effusions (arrows, B and C) with normal synovial thickness and mild synovial enhancement in all joints, without bone marrow edema-like signal. A synovial biopsy of the knee was performed and revealed mild synovial hyperplasia without inflammatory cells. The patient was diagnosed with camptodactyly-arthropathy-coxa vara-pericarditis syndrome (CACP – OMIM 208250), a recently described genetic disorder with no gender predominance identified to date (1).
Conclusion: An important differential diagnosis of CACP is juvenile idiopathic arthritis (JIA), a painful inflammatory chronic arthritis that can cause not only joint effusions due to synovial inflammation, but also contractures resembling camptodactyly when not effectively treated.
Disclosure of Interest: None declared

P178

FEATURES OF CHILDHOOD SJOGREN'S SYNDROME: A LITERATURE REVIEW BASED COHORT.

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Introduction: Sjogren's syndrome (SS) is an autoimmune chronic disease characterized by inflammation of exocrine glands, but it can affect other organs as well.
Objectives: To describe childhood SS (cSS) features by reviewing pediatric published cases with individual data.
Methods: We conducted a literature review of cSS (age < 18 years). Eligible papers were identified through a Medline search of English language articles published in the PubMed database until February 2020. Statistical analysis was performed in order to detect associations between clinical/laboratory features.
Results: Two-hundred-forty patients were identified (191 female); the median age at disease onset was 10 years (range 3 months-17 years). Main clinical features are shown in Table 1. The most frequently reported clinical SS-specific feature was parotitis (134/198 patients; bilateral:unilateral=2.5:1); fewer patients had sicca symptoms (89/159 with dry eyes; 85/144 with dry mouth). Arthritis was the most frequent extraglandular manifestation. Renal tubular acidosis represented the typical expression of renal involvement (19 cases). Neuromyelitis optica and aseptic meningoencephalitis (6 and 9 cases, respectively) were the most typical neurologic manifestations. Two cases of interstitial lung disease and one of pulmonary hypertension were reported. Almost all patients had autoantibodies, mostly ANA (200/224 patients) and anti-SSA/Ro (170/208 patients). The Schirmer test was performed in less than half of the patients, of whom 62% tested positive. A positive result of minor salivary biopsy was reported in 129/140 cases with available data. Juvenile idiopathic arthritis was the most frequently associated disease, followed by systemic lupus erythematosus (16 and 8 cases, respectively). No significant differences between patients with or without parotitis were found except that patients with parotitis showed increased levels of CRP more frequently than those without it (p= 0.00). Patients with anti-SSA/Ro had more frequently a positive Schirmer test (p= 0.04). The presence of RF was significantly associated with dry mouth (p= 0.00), arthritis (p= 0.00), and rash (p= 0.04). A positive minor salivary biopsy was more common in children with dry eyes than in those without this clinical feature (p= 0.02). Arthritis was more frequent in patients with other diseases than in those with primary SS (p= 0.00). We further investigated SS features according to the age groups (≤ 6 years, 7-11 years, ≥ 12 years). Parotid involvement was inversely proportional to the age and occurred more frequently in younger patients (79% of those ≤ 6 years; p= 0.03). Interestingly, the rate of anti-SSA/Ro positivity increased with age (97% of those ≥ 12 years; p= 0.00).

Table 1. Clinical features of cSS cohort.

SS features	Positive pts	Percentage (% of available data)
Parotitis	134	67.7
Dry eyes	89	56.0
Dry mouth	85	59.0
Arthritis	59	72.8
Fever	52	70.3
Rash	42	64.6
CNS involvement	40	85
Renal involvement	31	59
Raynaud phenomenon	14	58.3

Conclusion: Even though parotitis was the most frequently reported feature, a wide range of clinical manifestations in children with SS has been reported so far. A better knowledge of cSS features will help to pave the way for the development of cSS specific diagnostic criteria.
Disclosure of Interest: None declared

P179

PACHYDERMODACTYLY: A MIMICKER IN THE PAEDIATRIC RHEUMATOLOGY OUTDOOR CLINICAL PRACTICE

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Introduction: Pachydermodactyly (PDD) is a rare benign fibromatosis, characterized by progressive painless swelling of soft tissue of proximal interphalangeal (PIP) joints without inflammation signs. Generally PDD affects PIP joints of the fingers, rarely of the thumb. The involvement is typically symmetrical, in few cases unilateral. It usually occurs more frequently in young males. Etiology is unknown, but it arises from mechanical stimulation of periarticular skin (i.e repetitive rubbing, interlacing, and cracking of fingers). PDD has to be considered in the differential diagnosis of arthritis (i.e. juvenile idiopathic arthritis, JIA) and many syndromes (i.e. progressive pseudorheumatoid dysplasia). Prognosis is good with cessation of mechanical stimulation[1].
Objectives: The aim of this study, is to improve our knowledge about this problem leading to a correct diagnosis. We describe a cohort of outdoor pediatric patients attending the Rheumathology Pediatric Medical Clinic in Verona.
Methods: A retrospective analysis was conducted in the Pediatric Rheumatology Day Hospital of Verona from January 2014 to April 2020. We selected six patients with painless swelling of soft tissue of PIP joints. Male-to female ratio was 1:1. Prevalent age at diagnosis was 11 years. Among all cases, only one practiced sport (16%), in particular canoeing. All cases had painless swelling of soft tissue of PIP joints of fingers, bilateral in 66% of the cases. Associated symptoms were paresthesia and functional limitation (33%), tic (16%), anxiety disorders (16%) and repetitive mechanical movements (i.e rubbing and interlacing of fingers) (33%). None of our patients had findings of articular inflammation. Laboratory tests were completely normal objective and strumental for all reported cases,in particular all inflammatory markers were normal.
Results: Half of the evaluted patients had previously consulted a medical specialist (16% orthopaedist, 33% rhumatologist). Ultrasonography was performed in 33% of patients and it was negative for joint damage in all cases. The hand MRI, performed in 66% of cases, excluded the presence of arthropathic or osteopathic lesions with exclusively swelling of the periarticular soft tissue. For 50% of the patients a genetic test for Progressive pseudorheumatoid dysplasia (gene WISP3) was conducted and it resulted negative in all cases. In one patient the exclusion of the diagnosis of JIA was complicated by concomitant knee pain and suprapatellar effusion on ultrasound; both findings successively regressed and were probably due to previous trauma.
Conclusion: Pachydermodactyly is a rare pathology that should be suspected in a patient who presents with swelling of PIP hand joints without clinical and laboratory findings of inflammation and related to the exclusive involvement of the soft tissue component on imaging. PDD resolves spontaneusly after behavioural therapy. PDD shares with JIA clinical appearance of joint swelling and its time of onset (months). However, a complete anamnesis, which should pay attention in particular to the habit behaviours and involuntary movements of the patient, and an accurate physical examination can help distinguish PDD from JIA, therefore prevent unnecessary immunosuppressant therapy; Refer child tot he neuropsychiatrist is indicated for the proper follow up.

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Disclosure of Interest: None declared

P180

TREATING TWO FIBRODYSPLASIA OSSIFICANS PROGRESSIVA PATIENTS WITH INTERLEUKIN-1 INHIBITORS

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Introduction: Fibrodysplasia ossificans progressiva (FOP) is the most catastrophic form of heterotopic ossification (HO), due to activating mutations in the ACVR1/ALK2 gene, and ongoing intracellular signaling through the bone morphogenic protein (BMP) pathway. Painful soft tissue swellings usually appear by the age of 3-4 years, but the typical bilateral greater toe deformity can be noted at birth. Average life expectancy is 45 years. Currently, there is no proven effective treatment.
The recurrent paroxysmal appearance of inflammatory lumps (local erythematous tender swellings, which partially respond to anti-inflammatory agents), accompanied by elevated inflammatory markers during flares, suggest that FOP may be an auto-inflammatory disease. The episodic formation of bone, often following a trivial injury, suggests that innate immune-related triggers induce tissue transformation through the BMP pathway. Moreover, interleukin-1β (IL-1β), a well-known mediator of the innate immune system, has been linked to HO and mineralization in mesenchymal stem cell cultures derived from human bone marrow. We hypothesized that treating FOP patients with anti-IL-1 agents could help ameliorate the progression of this devastating disease. We report our experience treating two FOP patients with anakinra and canakinumab.
Objectives: To decrease the frequency of FOP paroxysms, and/or limit the symptoms and extent of residual lesions, by using anti-IL-1 agents.
Methods: Patients' data and blood IL-1 levels were analyzed to characterize the efficacy of anti-IL-1 treatments in ameliorating the natural progression of FOP.
Results: A 13.5 year old boy and a 5 year old girl were diagnosed with FOP, both clinically and genetically (the typical R206H mutation was found). Various treatments, including high-dose corticosteroids, pamidronate infusions, celecoxib, monteleukast and sirolimus, did not change the course of the disease.
Both patients are receiving canakinumab (the male patient was initially treated with anakinra). The male patient has been treated for over 2 years. Flare rate was markedly reduced from one new lump every 8 days to approximately one every 25 days (Figure 1). The lumps involved in almost all of these flares are the same: at the left scapular base and within the sternocleidomastoid muscle. The female patient has been treated for a year, and has not experienced any HO flares during canakinumab treatment.
Temporarily withholding canakinumab in both patients, led to serious flares 8 weeks after the last dose. Notably, while undetectable levels of IL-1β (<0.125 pg/ml) were found in the three plasma samples obtained from the male patient during treatment with anakinra or canakinumab, high levels (up to 21.52 pg/ml, about 90-fold higher compared to average levels measured in healthy controls) were found in his plasma samples collected during the flare (Figure 2). In contrast, IL-18 and IL-6 plasma levels, measured before, during and after withholding treatment, were comparable or slightly higher than those observed in healthy controls (Figure 3A, B).
Conclusion: We report here, for the first time, that anti-IL-1 agents were found efficacious in treating two FOP patients. We also found markedly increased IL-1β levels during flares, which normalized following the treatment. We suggest a role for IL-1β in the pathogenesis of this disease. Although it is too soon to conclude whether FOP may be included under the umbrella of auto-inflammatory syndromes, anti-IL-1 agents can be effective in ameliorating the natural progression of FOP.
Disclosure of Interest: None declared

P181

GENETIC SYNDROMES MIMICKING RHEUMATOLOGIC DISEASES

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Introduction: Musculoskeletal symptoms are one of the common reasons for applying to rheumatology departments in general practice[1]. Although inflammatory causes are generally considered in the foreground, it is known that non-inflammatory causes including genetic diseases may also be responsible. The absence of signs of inflammation (morning stiffness, redness, tenderness) and normal inflammatory markers in laboratory findings may support non-rheumatologic diseases[2].

Objectives: To present genetic disorders that can mimic rheumatologic symptoms and to answer when genetic diseases should be considered in the differential diagnosis in patients presenting with rheumatological complaints.

Methods: We retrospectively evaluated 60 patients who applied to Hacettepe University pediatric rheumatology department with musculoskeletal compliants between January 2015 and December 2019 and had been consulted to genetics departmant. The rate and degree of consanguinity, clinical diagnosis, indication for consultation, accompanying musculoskeletal and other findings had been recorded. The diagnosis of genetic diseases were based on physical examination, radiological evaluations and genetic analysis.

Results: A total of 60 patients, 19 boys (31.6%), with a mean age 12.46 ± 1.41 years were included in the study. The rate of consanguinity was 25.0%. The most frequent referral to the genetic department was the presence of skeletal anomalies (n:12) such as camptodactyly, clinodactyly, and bone shortness accompanying joint findings. Other causes include short stature (n:4), joint deformity (n:5), joint hyperlaxicity (n:10), dysmorphic findings such as atypic facial appearance (n:9), accompanying diseases that may be part of a syndrome (n:11), genetic diagnosis suspicion according to the results of radiological examination (n:4) and joint findings without clinical and laboratory signs of inflammation (n:5). Distribution of joint involvement in 20 patients with genetic disease were hands, knees, and hips respectively. In the laboratory evaluation of patients presenting with joint swelling and arthralgia, acute phase reactants (erythrocyte sedimentation rate and C-reactive protein concentrations) were within normal reference values. One third of the patients (33.3%) had a final diagnosis of a genetic disease. The diagnoses of these patients were as follows; CACP (camptodactyly, arthropathy, coxa vara deformity and pericarditis) syndrome (n:3), trichorhinophalangeal syndrome (n:1), progressive pseudoromatoid dysplasia (n:2), LIG4 syndrome (n:1), 3M syndrome (n:1), H syndrome (n:1), SPENCD (spondyloenchondrodysplasia, n:3), and nonspecific connective tissue disease (n:8).

Conclusion: Genetic syndromes with musculoskeletal findings are often unrecognized and misdiagnosed as rheumatologic diseases leading to unnecessary procedures and treatments. Summarizing the genetic diagnosis spectrum that can be detected in these patients will increase the awareness of physicians.

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Disclosure of Interest: None declared

P182

INFECTIOUS TRIGGERS OF ERYTHEMA NODOSUM IN CHILDREN.

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Introduction: The aim of the study was to study the role of etiological triggers on the clinical course and severity of erythema nodosum in children.
Objectives: 65 children with nodular erythema aged from 3 years to 15 years
Methods: 65 children with nodular erythema aged from 3 years to 15 years were monitored. The examination included General clinical research, C-reactive protein (CPR) , antistreptolysin, rheumatoid factor, antinuclear factor (ANF) with method of immunofluorescence. To determine the etiological factor, bacteriological studies of nasopharyngeal smears, Epstein-Barr virus, fecal studies for intestinal diseases, diagnoses for Listeriosis, Yersiniosis, Chlamydia were conducted.
Results: According to the results of observation, the disease was more common in the age group of 7-11 years (65%), to a lesser extent among children in the group of 12-15 years (35%), less often in the group of 3-7 years (5%). When examining infectious agents, zoonotic infection was detected in 41% (Listeria monozytogenes, Yersinia enterocolitica). Clinical course of nodular erythema in this group was characterized by an expressed activity of the inflammatory process with multiple elements in the lower and upper extremities, joint syndrome, increased ESR to 45± 3.8 mm per hour, CRP 28± 2.5 mg\l. The disease was preceded by an episode of acute infection with an increase in body temperature, intoxication, in some cases with short-term intestinal syndrome, pharyngitis. The rashes were persistent and recurrent, with a slow regression of laboratory activity. Streptococcal etiology of nodular erythema was detected in 37% of cases. There was an increase in ESR to 25±3.8 mm per hour, CRP 15±2.7 mg/l, a significant increase in antistreptolysin on average 480±34% IU / ml. with an increase in individual cases to 870 IU/ml. In 13% of cases, erythema nodosum developed after an intestinal infection. Among the pathogens were identified Sh. disenteria, E. coli, Yersinia enterocolitica, enterovirus. The disease was characterized by moderate activity, a good response to etiological therapy and a short course of NSAIDs . An interesting fact was the development of nodular erythema in 4% of cases caused by the Epstein-Barr virus in groups of children from 3 to 7 years and 7-9 years. They had clinic picture with normothermia, no symptoms of intoxication, periodically occurring elements of nodular erythema on the shins, no blood changes. Therapy aimed at eliminating the virus gave a positive result and did not require specific anti-rheumatic therapy. In 5% of cases, the etiology of nodular erythema was not defined.
Conclusion: The clinical course of nodular erythema in children depends on the infectious agent that was the trigger of the pathological process. The higher activity and duration of the disease is caused by zoonotic infection, which requires more active anti-inflammatory therapy with corticosteroids, which may be associated with the activation of autoimmunity. This group of children was taken for further observation as a group at risk of developing systemic connective tissue disease. Changes in the etiological structure of nodular erythema and treatment tactics require further study.
Disclosure of Interest: None declared

P183

PEDIATRIC SJÖGREN SYNDROME: AN ITALIAN CASE SERIES

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Introduction: Sjögren syndrome (SS) is a chronic autoimmune disorder characterized by inflammation of the lacrimal and salivary glands leading to oral and ocular dryness. Childhood SS is rare and poorly defined and underdiagnosed owing to the lack of child-specific diagnostic or classification criteria.

Objectives: The purpose of this study is to describe 12 cases with pediatric SS in order to better clarify the characteristics of the disease in the pediatric age.

Methods: We retrospectively reviewed medical records of patients (pts) with pediatric SS referring to three Italian pediatric rheumatology centers. Due to lack of childhood validated SS-specific criteria, physician diagnosis was the only inclusion criteria.

Results: We collected data on 12 pts (9 females). The mean age of disease onset is 10.0 yrs (median 10.2, range 4-17). The mean age of diagnosis is 11.83 (median 11.45, range 6-18). The follow up period varied from 0.1 to 9.3 yrs (mean 3.95, median 5.0). The most common manifestations were articular involvement (mainly with arthralgia) (9/12 pts) and parotid/salivary glands swelling (8/12 pts). Xerostomia and xerophthalmia were found in 6/12 pts and in 4/12 respectively. Vaginal dryness was reported only by one pt. Fever and fatigue occurred in 3/12 and 7/12 pts respectively. We also recorded 3 cases of circulating immune complexes manifestations in 3 pts, purpura (n=2) and glomerulonephritis (n=1). We observed an endocrine involvement in 3 pts (1 metabolic syndrome, 2 autoimmune thyroiditis). Abdominal pain was found in 4/12 pts. All pts were positive for autoantibodies (positivity for ANA or anti-SSA or anti-SSB or FR) at presentation. RF test results were available in 8 pts, all positive. Positive ANA (titer>1/320) and anti-SSA were present in 10/12 pts and in 9/12 respectively. Hypergammaglobulinemia (range 1,6-8.04 g/dl) was found in 8/11 pts (1 NA).

Abnormal Schirmer test was observed in the half of cases (6/12). Minor salivary gland biopsy was performed in 10 pts resulting in histological evidence of focal lymphocytic sialadenitis in 9/10. Sonographic evaluation of salivary glands was abnormal in all of the patients (10/10).

With regard to treatment, 6/12 pts received corticosteroids and eight were also treated with one or more DMARDs such a hydroxychloroquine (n=8), methotrexate (n=3), azathioprine (n=1), leflunomide (n=1). Biological therapy was used in 3 patients for systemic involvement: 1 received belimumab and then rituximab, while the other patients received rituximab.

Conclusion: Xerostomia and keratoconjunctivitis sicca were not common in our series while recurrent parotid swellings were more frequent than what reported in adults. Pediatric recurrent parotitis should increase the suspicion for Sjögren syndrome. Current diagnostic criteria for SS do not include parotitis and therefore, the incidence of SS may be under-recognized in childhood. The disease is not always benign and patients with severe course may need second line treatment including immunosuppressant and biologics.

Disclosure of Interest: None declared

P185

RHEUMATOLOGICAL DISORDERS PRESENTING IN THE FIRST YEAR OF LIFE

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Introduction: Improving our understanding of pediatric rheumatological (PR) patient population is crucial for pediatric rheumatologists to know rheumatic disease epidemiology and to raise awareness leading to early detection. We didn't find studies of PR disorders presenting in the first year of life.
Objectives: The aim of this study is to assess the prevalence of PR disorders with onset in the first year of life.
Methods: We retrospectively studied patients observed in our Pediatric Rheumatology Unit between January 1st of 1987 and December 31st of 2019. We defined acute (<2 weeks), subacute (≥2 and <6 weeks) and chronic (≥6 weeks).
Results: A total of 3751 patients were observed in 32 years. Diseases' onset occurred in the first decade of life in 2290 patients (61%) and in the first year of life in 158 (4,2%). Among the latest group, chronic inflammation was the most frequent group of diagnosis (30%), followed by recurrent inflammation (23%), acute inflammation (11%), infection (9%), infiltrative/ degenerative disorders (8%) and subacute inflammation (3%). The remaining patients (16%) were diagnosed with other disorders classified as miscellaneous. Among chronic inflammation group, 14 patients were diagnosed with juvenile idiopathic arthritis (4 systemic); 14 had neonatal lupus and one patient had polyarteritis nodosa. Among recurrent inflammation group, 13 patients were later diagnosed with PFAPA (periodic fever, aphthous stomatitis, pharyngitis and adenitis), 8 were diagnosed with Behçet disease and 6 had an autoinflammatory disorder. Acute vasculitis was diagnosed in 13 patients (9 Kawasaki disease and 4 acute hemorrhagic edema of infancy). Among infectious diseases group, there were two cases of congenital syphilis with arthritis and two cases of osteomyelitis secondary to BCG vaccination.
Conclusion: Rheumatological diseases presenting in the first year of life are not exceptional. Although many patients didn't have a definitive diagnosis at the beginning of the symptoms, many of them were later diagnosed with rheumatic disorders, mostly chronic inflammation (30%), which requires early diagnosis, specific treatment and long-term follow-up. Rheumatic diseases must be considered as differential diagnosis in the first year of life in order to avoid delayed intervention and long term disabilities and sequelae.
Disclosure of Interest: None declared

P186

SYSTEMIC JIA, KAWASAKI SYNDROME AND MACROPHAGE ACTIVATION, WHAT ELSE? NOT ONLY COVID-19.

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Introduction: Macrophage Activation Syndrome (MAS) is a well-known complication of Systemic Juvenile Idiopathic Arthritis (sJIA) and a rare consequence of Kawasaki Disease (KD). The diagnosis of MAS, in patients with KD, could be very challenging especially when Measles infection is the primary trigger. If from one side, Measles and KD have very similar clinical features and can easily mask each other (1), on the other side measles-induced MAS has rarely been reported (2).
Objectives: We present the case of a child known to have sJIA in remission, who presented a Measles primary infection and a secondary KD complicated by MAS.
Methods: A 5 years old girl, not fully vaccinated and known to have sJIA in remission under Methotrexate, presented for frequent high grade fever of 3 days duration associated with flat flash red spots on the face and trunk as well as the palms and soles. A Koplik's spot was identified. Conjunctivitis and coryza were also present. Initial viral serology, including measles, returned negative. Fever persisted and on day 7, edema of both hands and feet appeared with bilateral cervical adenopathy, erythematous tonsils, gingivitis, cracked lips and hepatomegaly was noted. All cultures were negative and chest X-ray was normal. Inflammatory markers rose up. Viral serology was repeated and measles IgM came back positive. Cardiac ultrasound ruled out coronary aneurism and the ophthalmic exam showed no uveitis. KD criteria were met and 2g/kg of intravenous immunoglobulins (IVIG) were administered. After 48 hours of clinical improvement, fever reappeared and the patient returned to be ill looking although the rash regressed. We noted high ferritine(2016 ng/ml) together with low C3, decrease in platelets(170 $x10^3$/ml) and elevation of hepatic enzymes, LDH and CPK, without increase in the inflammatory biomarkers. MAS was suspected and a bone marrow aspirate showed the presence of mild macrophage hemophagocytosis. Antibodies for Lupus and auto-immune myositis were all negative. Steroids were given, fever disappeared, and spectacular clinical and biological improvements were objected. 2 weeks later, desquamation of all extremities was noted. SARS-CoV-2 was not investigated because historically this case presented 1 year earlier than the pandemic.
Results: We hereby report, for the first time, KD and MAS triggered by Measles infection in a child with sJIA in remission. The exact mechanism involved in KD-induced MAS and Measles-induced MAS has not yet been defined but a defective immune response is suspected (3).
Conclusion: Significant similarities and overlap between measles, KD, sJIA and MAS make an early diagnosis very challenging (1)(3). The recent COVID19 pandemic emphasizes how a viral illness can be responsible of KD and sometimes degenerating in MAS. We report this clinical case as an example of a Systemic Inflammatory Syndrome (SIS) taking place after a viral infection to Measles. In the era of COVID19 pandemic and secondary SIS in children, an additional challenge is present in regions lacking Measles vaccine coverage.
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Disclosure of Interest: None declared

P187

THE MUSCULOSKELETAL MANIFESTATIONS OF SCURVY: A DIAGNOSTIC CHALLENGE FOR THE RHEUMATOLOGIST

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Introduction: An increasing trend in the incidence of scurvy has been reported in the last years, especially in children with food selectivity associated to autism. Still, a diagnostic delay in the identification of scurvy is common, due to non-specific clinical features mimicking rheumatological, hematologic or infectious conditions.
Objectives: To describe clinical features of 5 patients with scurvy, referred to two pediatric Rheumatology Units in Southern Italy, from July 2018 to December 2019.
Methods: Case reports
Results: P1 was a 4-year-old boy presenting limp and bilateral hyperemic tibial swellings for a week. He suffered from autism spectrum disorder and, since the third year of life, he developed marked food selectivity. Joint assessment was normal. Laboratory tests showed elevated erythrocyte sedimentation rate (ESR) level (70 mm/h). Main causes of erythema nodosum were excluded. Vitamin C level resulted greatly reduced: 1.5 µmol /l (26.1-84.69). Supplemental therapy was started with clinical resolution.
P2 was a 5-year-old boy, with autism spectrum disorder, malnutrition and severe food selectivity, admitted to our Unit for refusal to bear weight and bruises in lower limbs. The auxological evaluation showed a strongly dystrophic aspect. Coagulation profile and main organ function markers were normal. At nutritional biochemical parameters evaluation, iron and Vitamin C deficiencies were detected (vitamin C: 2 µmol/l). Oral vitamin C therapy was started, with prompt clinical response.
P3 was a 7-year-old boy with autism spectrum disorder, admitted to our Unit for lameness and difficulty in walking for a month. At clinical examination, a mottled skin at lower limbs was noted. Joint examination was normal. Auxological parameters and main blood tests were adequate for age. Given the presence of food selectivity, he underwent serum vitamin C dosage (11 µmol/L); hence he started oral vitamin C therapy, with rapid clinical improvement.
P4 was a 2 years old boy who was referred for coxalgia and fever. At clinical examination, pale skin, gingival hyperemia, and pain in mobilization of the left hip were present. Microcytic anemia was detected, but main organ and inflammatory markers were normal. No evidence of infection was present. X-ray of femur and knee showed morpho-structural alteration of the distal metaphysis bilaterally. A low intake of fruit and vegetables was reported; hence, dosage of vitamin C was performed, resulting reduced (2.5 µmol/L). He started Vitamin C oral therapy with clinical response.
P5 was a 13-year-old girl with behavioral disorder and intellectual disability, admitted for fever and right knee swelling which appeared two days after a right leg burning. C-reactive protein and ESR were elevated and ultrasound exam confirmed intra-articular knee effusion. Suspecting a septic arthritis, antibiotic therapy was started with laboratory normalization and partial clinical improvement. Considering the persistence of knee swelling after nine days of intravenous antibiotic therapy, the presence of gingival hyperemia and history of food selectivity, vitamin C dosage was practiced (12 µmol/l). Oral vitamin C was administered with complete clinical resolution.
Conclusion: Although scurvy is considered a disease of the past, it still occurs nowadays. Food selectivity associated to autism is a major risk factor for vitamin C deficiency in childhood. Rheumatologists should take into account the diagnosis of scurvy in the diagnostic approach of musculoskeletal disorders in children, especially when development disorders are present.
Disclosure of Interest: None declared

P188

INTERSTITIAL LUNG DISEASE IN PATIENTS WITH RHEUMATIC DISEASES

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Introduction: Pulmonary involvement of systemic autoimmune and autoinflammatory diseases mostly occurs as pleural involvement and rarely as interstitial lung disease.
Objectives: The aim of this study is to retrospectively examine the demographic, clinical, laboratory findings, and clinical follow-up of patients diagnosed with interstitial lung disease during the course of rheumatic diseases.
Methods: Patients diagnosed with interstitial lung disease based on clinical and radiological findings or lung biopsy at Departments of Pediatric Rheumatology and Pulmonology in Hacettepe University, between 2005-2020 were included in the study. Data were recorded retrospectively from the patient files.
Results: There were 13 patients with systemic rheumatic disease who were diagnosed with interstitial lung disease during the course of the disease. Seven (53.8%) of these patients were female and 6 (46.2%) were male. The median age at the diagnosis of the rheumatic disease was 8 years. Primary rheumatic diseases were as follows; systemic juvenile idiopathic arthritis (JIA) (n=4; 30.8%), systemic sclerosis (n=2; 15.4%), mixed connective tissue disease (n=2; 15.4%), juvenile dermatomyositis (n=1), sarcoidosis (n=1), granulomatous polyangiitis (GPA) (n=1), Sting-associated vasculopathy with onset in infancy (SAVI) (n=1), and oligoarticular JIA (n=1). Respiratory symptoms were present in 6 (46.2%) patients at the time of primary diagnosis. In other patients, the time period between the diagnosis of the rheumatic disease and the onset of the respiratory symptoms ranged from 1 to 12 years. Cough, the most common symptom, was present in 10 (76.9%) patients. Six patients manifested with cough and sputum. Six (46.2%) patients had shortness of breath and one patient had hemoptysis. On the physical examination of one patient, rales and clubbing were detected. High resonance computerized tomography (HRCT) was performed in all patients. HRCT findings were as follows; lymphadenopathy in 8 patients (61.5%), ground glass appearance in 10 patients (76.9%), consolidation in one patient, pleural effusion in one patient, pulmonary nodule in 4 patients (30.8%), fibrosis in one patient, cystic lesions in 3 patients (23.1%), septal thickening in 5 patients (38.5%), bronchiectasis in one patient, and reverse halo sign in one patient. In echocardiographic examination, only one patient had pulmonary hypertension.
Three patients underwent open lung biopsy, and diagnosis was made with pathological examination of the lung tissue. Of these three patients, two (15.4%) had lymphocytic interstitial pneumonia (LIP), and one patient had chronic inflammation and focal fibrosis. Infectious lung disease was not detected in any patient. Ten patients (76.9%) had interstitial lung disease associated with rheumatic disease, one patient had pulmonary hemorrhage, one patient had pulmonary involvement of GPA, one patient had pulmonary involvement of sarcoidosis. There was no statistically significant difference between the first and last spirometry and DLCO values during the follow-up period. Mortality was 7.5% (1/13) in this cohort.
Conclusion: Although pulmonary complications of rheumatic diseases are rare in childhood, they can cause significant morbidity and mortality.

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Disclosure of Interest: None declared

P189

ASSESSMENT OF LIPID PROFILE IN CHILDREN WITH PAEDIATRIC RHEUMATIC DISEASES

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Introduction: Dyslipidemias are well-recognized risk factors for cardiovascular diseases (CVD) and are very common in patients with autoimmune rheumatic diseases. Lipid profile disorders are one of the most studied problems in adult patients with rheumatic diseases. However, few studies addressed this problem in paediatric rheumatic diseases patients.
Objectives: To assess the lipid profile in children with paediatric rheumatic diseases
Methods: Ninety patients diagnosed with pediatric rheumatic diseases were included. Exclusion criteria were patients previously treated with lipid lowering drugs, history of diabetes mellitus, thyroid disease and familial hyperlipidemia. After fulfilling the inclusion criteria, detailed history was taken. Data included age, sex, weight, body mass index (BMI), and duration of disease. Fasting lipid profiles were measured after overnight fasting and consumption of normal diet for previous 2 days (without fat restriction). Fasting lipid profiles included total cholesterol (TC), triglycerides (TG), low density lipoprotein cholesterol (LDL) and high density lipoprotein cholesterol (HDL). Normal values were considered according to reference values. Disease activity was classified according to clinical assessment and laboratory tests like ESR, CRP, complement levels and anti-ds DNA titres.
Results: The study included 90 children, suffering from rheumatic diseases. Out of them, 13 were males and 77 were females. Sixsty-seven patients had juvenile idiopathic arthritis (JIA) of them, 48 patients Polyarticular type, 16 patients systemic onset type and 3 patients oligoarticular type. Twenty children were diagnosed with Juvenile systemic lupus erythematosus (jSLE), 2 children with Vasculitis (henoch schonlein purpura) and 1 child with juvenile scleroderma. Mean age was 11.58±3.6 years. Mean age at diagnosis was 7.2± 1.3 years. Mean disease duration was 3.60±1.2 years. Mean BMI was 20.55±8.42 Kg. Twenty-nine patients had active disease while sixty-one patients had inactive disease. Mean TC was 170.65±51.38 mg/dl, mean HDL was 45.2±11.3mg/dl, mean LDL was 88.45±15.1 and mean TG was 88.15±26.1 mg/dl. The most common lipid abnormality was disturbed HDL, it was found in 29 patients followed by disturbed TC in 22 patients. Abnormal triglycerides was found in 22 patients and abnormal LDL in 16 patients. 14.9% of JIA patients had abnormal TC, 40.3% had abnormal LDL, 11.9% had abnormal LDL and 20.9% had abnormal TG. Sixty percent of jSLE patients had abnormal TC levels, 10% had abnormal HDL level, 40% had abnormal LDL and 40% had abnormal TG levels. Presence of jSLE and JIA was significantly associated with abnormal TC ($p<0.001$*), abnormal HDL ($p=0.005$*), abnormal LDL ($p=0.01$*) and abnormal TG ($p=0.07$).
Active disease was significantly associated with abnormal TC, HDL, and TG levels ($p=0.04$*), ($p=0.03$*) and ($p=0.04$*) respectively. Multivariate analysis of the factors affecting abnormal cholesterol level revealed that SLE is a significant predictor of abnormal cholesterol level . Presence of jSLE increase risk of abnormal cholesterol 9 times more than cases without jSLE. The overall percent predicted was 80%. Active disease is a significant risk factor for abnormal TG with increased risk of abnormal TG by 3.2 among cases with active disease than cases with inactive disease. The overall percent predicted was 75.6%.
Conclusion: children with rheumatic diseases showed significant lipid profile abnormalities. Abnormal TC, HDL and TG are significantly associated with active disease. Presence of jSLE increase risk of abnormal cholesterol. Active disease is a significant risk factor for abnormal TG. Therefore, lipid levels should be monitored regularly and managed in patients with paediatric rheumatic diseases to minimize the longterm risk of CVD.
Disclosure of Interest: None declared

P190

DEFINITIONS AND CONCEPTS OF MUSCULAR SKELETAL PAIN - WHAT DO PHYSICIANS KNOW?

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Introduction: Musculoskeletal pain (MSP) is the most frequent reason for seeking health care in adult and paediatric rheumatology. Semiological accuracy and the use of a standardized language will allow correct communication, avoiding ambiguities in definition and interpretation that may culminate in diagnostic errors. At least 82 concepts / definitions and clinical situations associated with musculoskeletal pain are known.
Objectives: Evaluate physicians' knowledge of the most used definitions of MSP in order to improve patient attendance.
Methods: Non-experimental, cross-sectional and descriptive study. A confidential survey was conducted online, aimed at residents and attendings who deal with musculoskeletal pain. Were addressed with the definitions of arthralgia, arthritis, myalgia, allodynia and hyperesthesia (between five to seven options) with only one correct answer.
Correct definitions: arthralgia (pain localized to the joint or periarticular structures, as a only manifestation); arthritis (Criterion one or criterion two: 1 - Joint swelling or intra-articular effusion / 2 - Limitation of joint mobilization associated with at least one of the following: a) Pain b) Tenderness c) Swelling d) Heat); myialgia (pain with muscular origin or referred to muscle, regardless of its etiology); allodynia (pain resulting from usually non-painful stimulus); hyperesthesia (coexistence of allodynia plus hyperalgesia - exaggerated responses to tactile and thermal nociceptive and nonnociceptive stimuli). The study took place between September and October 2018.
Results: A total of 193 physicians participated, 71.5% (138) attendings and 28.5% (55) residents. Distribution by specialty: Paediatrics 51.3% (99), Rheumatology 14% (27), General and Family Medicine (GFM) 14% (27), Orthopedics 8.8% (17), Paediatric Rheumatology 4.2% (8), Physical and Rehabilitation Medicine (PRM) 2% (4), other specialties 5.7% (11). Overall, the correct answers to each assessed item have the following distribution: isolated arthralgia 41.5% (80), arthritis 17.6% (34), myalgia 54.9% (106), allodynia 61.1% (118), hyperesthesia 64.8% (125). By specialty, the percentage of correct answers is shown in table 1.

Table 1: Concept and percentage of correct answers by specialty

	Isolated arthralgia	Arthritis	Myalgia	Allodynia	Hyperesthesia
Paediatrics	51.5% (51)	18.2% (18)	46.5% (46)	50.5% (50)	59.6% (59)
Rheumatology	77.8% (21)	25.9% (7)	55.6% (15)	81.5% (22)	77.8% (21)
GFM	25.9% (7)	7.4% (2)	77.8% (21)	66.7% (18)	70.4% (19)
Paediatric Rheumatology	75.0% (6)	50.0% (4)	50.0% (4)	75.0% (6)	50.0% (4)
Orthopedics	29.4% (5)	5.9% (1)	58.8% (10)	70.6% (12)	58.8% (10)
PRM	25.0% (1)	0.0% (0)	75.0% (3)	75.0% (3)	75.0% (3)
Overall	41.5% (80)	17.6% (34)	54.9% (106)	61.1% (118)	64.8% (125)

Conclusion: The low percentage of correct answers, allows us to conclude that many physicians are unaware of the correct concepts / definitions related to MSP and do not evaluate the musculoskeletal system routinely, or in an appropriate way. This tendency must be counteracted through continuous medical training.
Disclosure of Interest: None declared

e-Poster viewing: New diseases

P191

PURE RED CELL APLASIA, TYPE 1 DIABETES AND POLY ARTHRITIS IN A 2.5 YEARS OLD GIRL WITH A SYNDROMIC FACE – A NEW DISEASE.

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Introduction:

The association of pure red cell aplasia (PRCA) with thymoma led to the discovery of the autoimmune mechanisms involved in the pathogenesis of this rare disease. Till date many adult case reports have revealed a strong link between PRCA and autoimmune diseases, endocrine disorders, rheumatic diseases, autoinflammation and immune dysregulation.[1-5]

Objectives:

To stimulate a search for the genetic and immunological roots for a 2.5 years old girl with syndromic face, pure red cell aplasia, type 1 diabetes and polyarthritis.

Methods:

This is a story of a 2.5 years old girl with pure red cell aplasia, type 1 diabetes and polyarthritis. She was normal till 7 months of age. At the age of 8 months, she was diagnosed with type 1 diabetes. She was evaluated by her paediatrician in view of generalized hypotonia, deformed pinna, low set ears, midfacial hypoplasia, blue sclera, umbilical hernia and retracted eyelids. She had multiple episodes of seizures during next few months. To me, she was presented with one year history of polyarthritis with severe pallor requiring frequent blood transfusions. Family history was inconclusive. Musculoskeletal examination showed polyarthritis involving right knee, bilateral ankles, fingers and toes. Further examination revealed haemolytic facies and hepatosplenomegaly. I was not able to make out any facial dysmorphism mentioned earlier by her paediatrician.

Results:

Table 1 showed available investigation reports

Haemoglobin (11.5-14.5 gm/dl) RBC Count (4-5.3 mill/cumm) PCV (33-43%) WBC count(4000-12000 cells/cumm) ANC (1800-6800 cells/cumm) ALC (1100-4700cells/cumm) Platelet count (1,50,000-4,50,000/ul) MCV (76-90 Fl) Peripheral smear	3.6 1.16 10.4 9100 5551 3185 5,62,000 89.8 Normocytic Normochromic RBCs
Reticulocyte count (0.8-2%) Absolute reticulocyte count (0.02-0.1 * 10^6 cells/ul)	0.5% 0.0005
ESR (0-20 mm/hr) CRP (0-5 mg/L)	135 1.1
HBA1c (<5.6%) TSH (0.45-4.5 microIU/ml) Free T4 (0.91-1.44 ng/dl)	12.6 4.04 1.24
Bone Marrow Examination	Normocellular marrow with markedly reduced erythropoiesis and occasional lymphoid aggregates)
ANA by IIF RF GAD antibody	Negative Negative Negative
MRI Brain	Normal

Conclusion:

Early age of onset, pure red cell aplasia, autoimmune and endocrine manifestations with some doubtful facial dysmorphism inspired me to suspect some known or unknown immune dysregulation syndrome in this child. Genetic analysis would be the best possible option in this scenario if financial condition permits.

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Disclosure of Interest: None declared

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INFLAMMATORY ARTHRITIS COMPLICATING GALACTOSIALIDOSIS : A CASE REPORT AND REVIEW OF THE LITERATURE

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Introduction: Galactosialidosis (GS) is a rare inherited lysosomal storage disorder (LSD) which is characterized by a defect in the lysosomal glycoprotein catabolism. Here we report, for the first time, a case of a child affected by GS who presented with recurrent episodes of extensive joint inflammation in both knees. Knowledge on GS related inflammatory joint pathology is lacking, which hampers evaluation of possible mechanisms that could give an explanation for the significant arthritic joint abnormalities as observed in our patient.
Objectives: The aim of this study is to describe the clinical presentation as well as the laboratory, radiologic and microscopic features of this extremely rare presentation of GS. Furthermore, we conduct a literature review on LSD's complicated by arthritis in order to evaluate potential mechanisms that could explain the extensive inflammatory joint swelling observed in our patient.
Methods: In this study we present a 12-year-old Turkish boy who was diagnosed with GS (late infantile form) at 17 months of age. From the age of 8 years, the boy presented with episodes of inflammatory joint pathology of the knee. Informed consent was obtained.
Alongside the case report, a literature review using Medline was conducted. An extensive list of known LSD's was combined with the terms: "arthritis", "joint inflammation", "synovitis" and "synovial inflammation". Cases in which joint inflammation was based on a probable cause other than the underlying LSD were excluded.
Results: In the present case, owing to comprehensive examinations (i.e. laboratory tests, imaging and microscopic examination) multiple possible causes for the recurrent inflammatory joint pathology could be rejected (i.e. no signs of infectious arthritis, reactive arthritis, osteoarthritis, arthritis secondary to a malignancy or crystal induced arthritis). A diagnosis which could explain the clinical picture is the JIA subtype: ANA negative oligo-articular JIA. However, microscopic examination showed numerous foamy macrophages with extensive vacuolization in the synovial tissue of the inflamed joint, which is not associated with JIA. Given the evidence of storage products within the macrophages of the inflamed synovial tissue and no conclusive diagnosis, GS itself should be considered as the primary cause for the recurrent arthritis.
An in-depth literature review using Medline for data on inflammatory joint pathology in LSD's showed that 7 LSD subtypes (i.e. Fabry disease, Farber lipogranulomatosis, Gaucher disease type 1, Mucopolysaccharidosis IX, a-Mannosidosis, Fucosidosis and Cystinosis) could present with disease related arthritis. Multiple potential arthritic mechanisms secondary to storage product accumulation in LSD's have been described, such as: dysregulation of innate immunity and increased upregulation of numerous pro-inflammatory proteins.

Conclusion: Given the evidence of storage products within macrophages of the inflamed synovial tissue and the absence of other etiological clues, our hypothesis is that GS itself is the primary cause for the inflammatory joint pathology in our patient. Although, GS cannot be linked directly to joint inflammation, lysosomal defects have been associated to pro-inflammatory effects that possibly could result in arthritic disease. Future identification of other patients with GS is required to support the hypothesis of an arthritic clinical phenotype of GS and to assess underlying pathophysiology.
Disclosure of Interest: None declared

P193

RECURRENT ORAL ULCERS-A NOVEL MUTATION

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Introduction: A 1 year old male infant presented with h/o recurrent oral ulcers and fever since 6 months of age. Provisional diagnosis were 1. Cyclic neutropenia. 2.Infantile behcet.3.A20 Haploinsuffiency
Objectives: To establish cause of recurrent fever and oral ulcers, to rule out immune deficiency
Methods: Blood sent for-Complete blood count, primary immune deficiency work up which included immunoglobulin levels, flow cytometry for lymphocytes subsets and phagocytic defects
Results: Thinking of cyclic neutropenia, a complete blood count was done twice a week for 6 weeks.There was no evidence of neutropenia.Primary immune deficiency work up was negative.Genetic analysis was sent to rule out A20 haploinsuffiency. However clinical exome sequencing showed homozygous deletion of MAG TI gene.
Conclusion: So this was a case of MAGTi deficiency .
The infant showed homozygous deletion and later on may be complicated with recurrent EBV infection and lymphomas.MAGT1deficiecy is an x linked immunodeficiency characterized by CD4 lymphopenia, and defective Tcell activation. These individuals have recurrent viral infections especially with Ebstein Barr Virus. They also have associated lymphoprolifeerative diseases especially lymphoma. Sometimes magnesium salts may prove useful in treatment. The index case is on magnesium and doing well. Though the usual age of presentation I 3to 45 years ,our patient presented very early.
Later on they may have viral skin infections like molluscum,sinopulmonary infections and viral pneumonia.
The main aim of presentation is to
1.recognize immune deficiency early in life and not to ignore them
2.treat them accordingly
Disclosure of Interest: None declared

e-Poster viewing: Pain, fatigue, disease experience and quality of life

P195

JOINT PAIN IN CHILDREN AND ADOLESCENTS: OCCURRENCE, CAUSES AND AGE PROFILE.

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Introduction: Joint pain (JP) is a relatively common complaint among children and adolescents. A painful joint in children for many years continues to maintain the status of the most common symptom of juvenile arthritis. However this symptom should not always be interpreted as a manifestation of rheumatic diseases.
Objectives: The aim of current review is to debate of the structure in children with the chief complaint of JP.
Methods: We retrospectively analysed our series of 600 children which attending outpatient department with complaint about pain lasting longer than two months in one or more joints. The clinical, instrumental and laboratory pictures were collected. Special attention was paid to certain aspect of medical complaints, a complete and accurate history and physical examination. Different categories as possible etiologies of JP in children were systematize and detailed.
Results: All children were divided into several groups based on their anatomical and physiological characteristics of osteoarticular system: the first group consisted of 240 children under 6-7 years old, the second group – 220 children 7-12 years old, the third group – 140 children over 12 years old.
Research suggests that more preschool children were experience bilateral lower extremity pain by “post-walk genesis” due to natural hypermobility, immaturity of sensory innervation of the joints and imbalance of the leg muscles (e.g. growing pains). The second most common cause of JP was associated with intra - or postinfectious factor (viral, streptococcal and chronic focal of infection). The frequency of juvenile arthritis and other rheumatic diseases in children of this age group did not exceed 10%. Special attention was paid to fever, chills, malaise, nightpain and constitutional symptoms with changes in blood lab tests to exclude osteomyelitis (inc specific cause), malignancies manifestation and other bone tumors (less 5%).
The most common causes of joint pain of school-age children were hypermobility syndrome and enthesopathy (primary, secondary). Secondary enthesopathy were result of changes in nutrition, rapid growth and excessive exercise. Also enthesopathy were manifestation of endocrine, gastrointestinal or infectious diseases. The proportion of children with the onset of chronic inflammatory arthropathy also did not exceed 10%. Hypermobility child’s syndrome was characterized by harmless pain (inc low back pain), linked to physical activity (less morning stiffness).
Over the past decade, we've seen a gradual increase in the number of children (95% were girls) with knee pain by diagnosed patellofemoral and mediopatellar plica syndromes, patellar tendinitis or idiopathic cause. In most cases children was complicated by syndrome of increased anxiety. The share of true chronic inflammatory arthropathies, including spondylitis, in children of this age group did not exceed 10%. Fibromyalgia were diagnosed less 5%.
Conclusion: Despite continuous improvements in examination technique and image quality there is no universal test to diagnose cause of chronic childhood arthralgia. Age features, individual nature of pain perception, the high frequency of incomplete and transient forms of arthropathy, cases atypical joint diseases have been intriguing problems for diagnostic pathology. Integrated assessment modelling framework of the clinical and instrumental pictures with understanding of the anatomical and physiological characteristics of childhood will help identify the true cause of chronic musculoskeletal pain.
Disclosure of Interest: None declared

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THE MAIN DIFFERENCES BETWEEN CHILDREN WITH INFLAMMATORY AND NON-INFLAMMATORY PAIN GENESIS

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Introduction: A significant part of patients in rheumatologist's practice is children and teenagers with complaints of pain. The further volume of examination and the choice of treatment course depends on the capability of the rheumatologist to define the inflammatory and non-inflammatory genesis of pain. That makes the problem of differential diagnosis very important.
Objectives: To conduct a comparative analysis of patients with a principal pain complaint to determine if there are significant differences in the groups with the inflammatory and non-inflammatory pain genesis.
Methods: The retrospective study included children who consulted a rheumatologist in the outpatient clinic in the period 2018-2020 without preliminary selection (n = 176). Of them there were selected children with principal pain complaint (n = 120). According to the diagnosis, the children were divided into 2 groups: those who have inflammatory genesis of pain (A, n =59) and those with non-inflammatory genesis of pain (B, n =61). The group A included children with such diagnoses as: reactive, poststreptococcal and juvenile idiopathic arthritides. The group B included children with arthralgia, chronic pain syndrome, orthopedic pathology, fibromyalgia.
Results: 1. Groups A and B differ in the average age of the first complaints onset (t-criterion for equality of means) with a high degree of statistical significance (Group A = 7,4 years; Group B = 9,3 years; p = 0.019). Which means that in Group A more often than in Group B first complaints appear in the age between 1 to 10 while in Group B more often than in Group A it happens in the age between 11 to 16.
2. There was a statistically significant difference in the means between Groups A and B in time between the onset of first complaints and the first visit to a rheumatologist (p = 0.03)
Also in favor of this conclusion speaks the fact that in Group A the number of visits to a rheumatologist in the same year when the first complaints appear is almost 2 times higher than in Group B.
56% of cases in Group A consulted the rheumatologist the same year when the first complaints appeared in comparison to Group B where only 31% of patients did the same.
Below is the table with distribution of cases by the number of years between the first complaints onset and the first visit to a rheumatologist in both groups:

Number of years	Group A	Group B
0	56%	31%
1	24%	30%
2	10%	16%
3	7%	7%
4	2%	5%
5	2%	7%
6	0%	0%
7	0%	3%
8	0%	0%

Conclusion: In children with arthritides, the first pain complaints appear at an earlier age (an average of 7.4), and in Group B (an average of 9.3). Patients with arthritis more often visit a rheumatologist earlier (within 1 year after the first complaints) than those with non-inflammatory genesis of pain complaints.
Disclosure of Interest: None declared

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CAN ARTIFICAL INTELLIGENCE HELP WITH DIAGNOSING GROWING PAIN?

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Introduction: The most common cause of recurrent musculoskeletal pain is growing pain (GP) in children. Differential from rheumatic diseases could be challenging in some cases since there are no diagnostic criteria for GP.

Objectives: To analyze GP characteristics in a large cohort of patients in comparison with other non-inflammatory and inflammatory diseases causing limb pain, and to simplify the GP's diagnosis process by using machine learning (ML) techniques.

Methods: This is a multicenter cross-sectional study. From February 2019 through August 2019, patients with GP and diseased controls were enrolled at the pediatric rheumatology units of three centers from Turkey. The gold standard for diagnosis of GP was the expert opinion.

A total of 398 patients with growing pain were enrolled (157 from Ankara Training and Research Hospital, Ankara; 128 from Umraniye Research and Training Hospital, Istanbul; and 113 from Kanuni Sultan Suleyman Training and Research Hospital, Istanbul, Turkey). The control group consisted of 254 patients with diseases causing limb pain other than GP; 212 of these had inflammatory diseases (e.g., juvenile idiopathic arthritis), while the etiology of limb pain was non-inflammatory in 42 patients (e.g., trauma).

Once the data obtained from the participating hospitals as an Excel table, we performed exploratory data analysis. Consequently, columns with the missing value rate of more than 20% were removed. Iterative imputation methods were used to complete the rest of the missing values. Afterward, correlations among columns were investigated, and collinearity was removed. Finally, the data set used in this study consisted of 652 rows and 29 columns. We refer to columns as features as in ML vocabulary. Next, we developed several ML models by using a 10-fold cross-validation method with algorithms frequently used in similar problems in literature.

Results: The female-to-male ratio was 1.3, and the median age was 102 (22-213) months in the GP group (n=398). The pain was bilateral (86.2%), localized at lower extremities (89.7%), nocturnal (74%), and led awakening at night (60.8%) in the majority of GP patients. The pain was not daily (58.4%) and was exacerbated by increased physical activity during the day (57.3%) in more than half of the patients. History of arthritis, trauma, morning stiffness, limping, limitation of activities, and school abstinence were more prevalent among diseased controls then GP patients ($p=0.016$ for trauma and $p<0.001$ for others). Hypermobility and pes planus were more frequent in the GP group than controls ($p<0.001$ and $p=0.02$, respectively). Anemia, leukocytosis, thrombocytosis, and elevated acute phase reactants were more prevalent among diseased controls than GP patients ($p=0.013$ for thrombocytosis and $p<0.001$ for the rest).

Our experiments with different ML models revealed that the Random Forest (RF) algorithm provided with 0.98 accuracy, 1.0 sensitivity, and 0.97 specificity in our test set.

Conclusion: In our cohort, GP was bilateral, localized at lower extremities, nocturnal, and led awakening at night, which were consistent with the previous reports. Our cohort is the largest cohort of children with GP. We also developed an ML model to identify GP patients based on clinical features. The results show that our RF model can be used to facilitate diagnosing GP disease. To the best of our knowledge, this is the first study that attempts to diagnose GP in children by using ML techniques.

Disclosure of Interest: None declared

P198

STRUCTURAL AND FUNCTIONAL STATUS OF THE BONE TISSUE IN CHILDREN DURING GROWTH SPURT

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Introduction: It is a well-known fact that the period of intensive growth in children is associated with the processes of active bone mass accumulation and coincides with them in time. One of the most distinctive indicators of an increase in the disease incidence among children for the recent decade (+105,3%) can be found in the skeletal disorders resulting from disrupted calcium metabolism and vitamin D deficit. The latter is widespread in Ukraine as it is observed in 92% of schoolers.
Objectives: Establish the specifics of the structural and functional status of the bone tissue in children during the growth spurt, taking account of the degree of vitamin D3 sufficiency.
Methods: The examination covered 147 children aged 9-17 who were divided into three groups depending on the presence of the growth spurt (GS) and its intensity: group 1 - 35 children who had become 8-12 cm taller for the year in question; group 2 – 32 children who had become taller by 12 cm or more, group 3 – 80 children who had experienced no growth spurt. Inclusion criteria were the following: no chronic somatic or endocrine pathologies, no musculoskeletal disorders or mineral homeostasis disruptions; physical exertion corresponding to their age; the children had not been taking any complexes of vitamins and minerals, including vitamin D_3 for 6 months before the examination.
The examination included analysis of the medical history, general clinical examination and assessment of physical development (WHO “Child Growth Standards”, 2007). Additional tests included ELISA aimed at determining the 25(OH)D_3 level as well as Ultrasound densitometry (Sonost -2000, Korea) and X-ray densitometry(DXA) (HOLOGIC QDR W Explorer, USA). Z-score ≤ -2 was used as a criterion determining reduced bone mineral density (BMD) (The International Society For Clinical Densitometry, 2013).
Results: Reduced BMD was found in 51,42% of the children in 1st group, 62,5% of the children in the 2nd group and 35,0% of the children in the control group. All the children under examination experienced a deficiency of 25(OH)D_3 (M.F. Holicke at all., 2011). In the children of the 1st group, the average 25(OH)D_3 level reached 38,87±9,96 nmol/L. In the children of the 2nd group, the average 25(OH)D_3 level was 42,58±8,99 nmol/L. In the 3rd group, the 25(OH)D_3 level reached 40,68±9,29 nmol/L on average.
Spearman’s correlation showed that in groups 1 and 2 there was no interrelation between the levels of 25(OH)D_3 and BMD; in group 3, it revealed a positive relation between the 25(OH)D_3 level and BMD (r=0,45).
Conclusion: Children aged 9-17 showed deficiency of vitamin D_3 reaching 100% which had no correlation with the presence or intensity of the growth spurt. In children who experienced growth spurt, a reduced BMD proved more frequent and correlated with the spurt intensity, however, it did not depend on sufficiency of vitamin D_3.Therefore, during the growth spurt, disrupted mineralization of the bone tissue was influenced not only by the vitamin D deficit but also by the correlation between the bone tissue mineralization rate and intensity of growth in the children.
Disclosure of Interest: None declared

P199

PATIENT PERSPECTIVES ON LIVING WITH SJIA OR STILL'S DISEASE: IMPACT ON QUALITY OF LIFE

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Introduction: Systemic juvenile idiopathic arthritis (SJIA) and Adult-onset Still's Disease (AOSD) are related arthropathies with features of autoinflammation and onset in children and adults, respectively. Due to their chronic course, we hypothesized that SJIA and AOSD have negative impact on quality of life (QOL). We also hypothesized that children with SJIA, adults diagnosed with SJIA as children, and adults with AOSD have differing effects on QOL.
Objectives: To investigate patient-reported factors underlying the negative impact of SJIA and AOSD on QOL.
Methods: A self-reported 25 question online survey on QOL of patients with SJIA and AOSD was developed by the non-profit organizations, the Autoinflammatory Alliance, KAISZ/VAISZ, ENCA and SJIA Foundation in English and translated to Dutch. Respondents were recruited by convenience sampling through online social media posts. Data on flares, triggers, family history, and correlation of symptoms with labs were collected in addition to detailed information on QOL during and in-between flares.
Results: Between 2017 and 2019, there were 109 responses; 54 were from parents of children with SJIA, 18 from adults with SJIA, and 37 from adults with AOSD. Interestingly, adults (whether diagnosed with SJIA or AOSD) were more likely to report pain, fatigue, joint swelling or arthritis, nausea & vomiting, and diarrhea during flares than children. Adults were also more likely to describe flares >one month. 80% of patients reported being "greatly" or "severely" limited during flares. Between flares, 20% reported being "greatly" or "severely" limited while 59% were "somewhat" limited. 80% felt their condition affected their studies, job, and career, including 66% of children with SJIA, 100% of adults with SJIA, and 92% with AOSD.
Respondents were asked open-ended questions regarding their experience with disease flares and impact on their lives, and specifically how SJIA and AOSD affected work, career and schooling. Responses regarding the disease experience were classified into 7 theme areas: 1) experience with disease onset and process of diagnosis; 2) health care access, quality, and drug safety concerns; 3) physical impact of the disease including pain and chronic fatigue; 4) social impact of the disease; 5) mental health and emotional impact of the disease; 6) impact on work, career, and employment; and 7) broad impact on life and lifestyle. Responses regarding effect on work, career, and schooling were categorized into 3 theme areas: 1) physical impact negatively influencing school/work productivity; 2) lost work and wages, including unemployment and needing disability benefits, and parents missing work to care for the child; and 3) the social-emotional impact as well as negative effects on mental health. About half of patients regardless of age reported the name SJIA did not represent well the disease, specifically that it did not emphasize the systemic symptoms, and that the disease gets confused with other types of arthritis. Adult patients with SJIA did not like to have juvenile in the name.
Conclusion: Children and adults with SJIA and AOSD report high levels of QOL limitation and effect on school, work, and career, both during and between flares. Our qualitative data emphasizes the importance of multidimensional evaluation of disease with ongoing input from the patients, which will provide a foundation for asking more relevant research questions to foster better care and improve QOL.
Disclosure of Interest: R. Sinha: None declared, K. Durrant: None declared, M. Marques: None declared, N. Tennermann: None declared, P. Reardon: None declared, J. Tousseau: None declared, S. Angevare : None declared, S. Lapidus: None declared, G. Schulert Consultant for: Novartis and SOBI, F. Dedeoglu Consultant for: Novartis

P200

REDUCING FATIGUE IN PAEDIATRIC RHEUMATIC CONDITIONS: A SYSTEMATIC REVIEW

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Introduction: Although fatigue is a generic and profound symptom among children and adolescents with Paediatric Rheumatic Conditions (PRCs), intervention studies designed for reducing fatigue in PCRs are limited.
Objectives: To systematically review contemporary evidence regarding the efficacy of interventions intended to reduce fatigue in patients with PRCs.
Methods: Comprehensive electronic searches were performed in PubMed/ MEDLINE, Embase, Web of Science and Cinahl. Risk of bias was assessed using the '*Revised Cochrane risk-of-bias tool for randomized trials*' and '*Quality Assessment Tool for Before-After Studies With No Control Group*' for respectively studies with and without a control group. Level of evidence was assessed according to the rating system of Proper et al.
Results: Eight out of 385 studies were included for review with a total of 213 participants (age range 5-23 years). Applied interventions included exercise therapy, prednisolone therapy, vitamin-D supplementation, psychological therapy and a transition programme. Fatigue was assessed with self-reported questionnaires in all included studies. Four studies displayed a small but significant positive effect, one study a small non-significant positive effect and three studies found no effects in reducing subjective fatigue. Five studies showed a high risk of bias and three studies showed a moderate risk of bias.
Conclusion: Insufficient evidence is provided to substantiate the efficacy of current interventions to reduce fatigue in PCRs. The low number of studies, non-comparable interventions, risk of bias and inclusive outcomes of the included studies denote future research should focus more on understanding the underlying mechanisms of fatigue. Identification and development of and need to effective multifactorial interventions to reduce complaints of fatigue in children and adolescents with PCRs is warranted.
Trial registration identifying number: NA
Disclosure of Interest: None declared

P201

QUALITY OF LIFE IN JUVENILE IDIOPATHIC ARTHRITIS PATIENTS IN LATVIA

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Introduction: Dimensions of health releated quality of life (HRQoL) includes both physial and psychosocial well-being and reveals how health status influence on the patient's well-being. Juvenile idiopathic arthritis can be a reason for children's low indicators of quality of life.
Objectives: The objective of the study was to analyse health releated quality of life in Juvenile idiopathic arthritis patient comparing to their parents opinion`s and healthy children's answers about their health releated quality of life.
Methods: In this study, juvenile idiopathic arthritis patients aged 8 to 17 years old and their parents were surveyed at the Children`s Clinical University Hospital outpatient department. The participants voluntarily filled Kidscreen - 52 questionnaire[1]. Survey includes 10 HRQoL dimensions such as physical, psychological and social life well-being. Control group consisted of 100 healthy children. Statistical analysis was performed using Mann–Whitney U-test (SPSS Statistics 22). The level of statistical significance was set at $p < 0.05$.
[1]Ravens-Sieberer U. et al., 2004, The …KIDSCREEN Group" Europe, 2006
Results: In total 111 participants were included in the study : 62 Juvenile idiopathic arthritis (JIA) patients, and 49 their parents. The mean age of the patients was 13.7 ± 2.3 years. Significant differences were found between patients and healthy children in such HRQoL survey categories like "Autonomy" and "Financial resources" ($p < 0.05$). Although quality of life in children's with Juvenile idiopathic arthritis was lower than in healthy children in HRQoL survey category "Self perception" ($p < 0.05$). After analyzing data no significantly differences were found between patients and parents' assessment scores in HRQoL survey categories ($p > 0.05$).
Conclusion: Juvenile idiopathic arthritis has a moderate negative influence on HRQoL survey categories "Self perception", "Autonomy" and "Financial resources" ($p < 0.05$) according KIDSCREEN-52 queationnaire. The evaluation of children and their parents' opinions in their children's quality of life did not differ significantly. We need to continue study about children's with Juvenile idiopathic arthritis quality of life.
Disclosure of Interest: None declared

P202
"TOMATO FACE" –
THE VISIBLE / INVISIBLE IMPLICATIONS OF JDM FROM A CHILD AND YOUNG PERSON'S PERSPECTIVE

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Introduction: Juvenile Dermatomyositis (JDM) is often first identified by parents and carers as the red facial rash develops. The rash can progress and lead to young people being misdiagnosed with eczema, scarlet fever or psoriasis. However, over time the obvious signs of JDM can become "invisible" as treatment calms the rashes and masks the outward signs of JDM, until a flare occurs, when the rashes can be a marker for disease activity or progression. As part of a larger study, children around the United Kingdom were asked to discuss their views on whether they wanted people to be able to see their JDM.
Objectives: To understand the implications for children and young people from having a disease that has visible and invisible phases and whether they want others to see their JDM, or not.
Methods: Children and young people around the United Kingdom who were already consented and enrolled into the UK Juvenile Dermatomyositis Cohort and Biomarker Study were asked to complete a bespoke questionnaire. There was a mix of open and closed questions, and it was administered in paper format to all children and young people between the ages of 8 and 19 years of age for self-completion, either on the paper forms, or via a secure web-based software system. The questionnaires were administered at the end of 2018. Numeric data were described and qualitative data were analysed using standard content analysis.
Results: 246 questionnaire packs were sent out, with 127 (52%) being returned. Of these 4 could not be used due to practical reasons, such as only demographic data being completed, which left a sample of 123. 98 (80%) of the 122 who responded said other people could not see their JDM, with only 11 (9%) saying it was visible and 13 (11%) saying they did not know if others can see it. 1 did not respond to the question as said their JDM has gone away. They were then asked whether it was a good or bad thing for others to be able to see their JDM or for others not to be able to see it. 41 young people left comments as to why it was a good thing, 36 left comments as to why it was a bad thing and 14 left comments to why they said don't know, table 1 presents the top ranking response for the three multi-choice answers.
Table 1: Presenting the top coded theme for each ranked answer

Answer Option	Theme	Number
Good	So others can understand	23
	So I can be the same as others	10
	Both/neither	4
Bad	Makes me embarrassed	14
	I get treated negatively	11
	It means I don't get any leeway or understanding	5
No answer	Don't mind	6
	Neither	4
	Don't know	4

Conclusion: This study has highlighted the disparity between young people wanting others to see their JDM so that they gain more understanding and empathy from those around them, but equally, wanting their JDM to be invisible, so that they feel the same as their peers. Whilst many paediatric rheumatic conditions are in fact invisible, our data illustrate that JDM often gives children and young people a taste of both visible and invisible phases of disease activity. As one young person said "It's not good, nor bad – it's good that it's invisible sometimes so I can blend in without the disabled stereotype. However, sometimes it needs to be seen so I can be understood and not challenged".
Disclosure of Interest: None declared

P203

A NOVEL MULTIDIMENSIONAL ASSESSMENT TOOL FOR CLINICAL CARE OF PATIENTS WITH JUVENILE FIBROMYALGIA SYNDROME

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Introduction: Juvenile fibromyalgia syndrome (JFS) is a chronic disabling condition characterized by widespread musculoskeletal pain in combination with several somatic symptoms including fatigue, non restorative sleep, headaches. Although 2-6% of school age children are estimated to suffer from JFS, patients often go undiagnosed for years; in addition, recommendations for the treatment and validated outcome measures for JFS are currently lacking.

Objectives: 1) To describe clinical features of JFS patients followed at our Centre

2) To develop a new multidimensional outcome measure for the assessment of patients with JFS in standard clinical care.

Methods: We included 43 patients diagnosed with JFS according to the 2010 criteria of the American College of Rheumatology. All patients were administered the Juvenile Fibromyalgia Multidimensional Assessment Report (J-FiMAR) which includes comprehensive patient self-report questionnaire and numerical rating scales to measure pain, fatigue, headache, sleep quality, physical function, psychological state, health-related quality of life, satisfaction with illness course. The J-FiMAR has been devised according to the Outcome measure in Rheumatology (OMERACT) guidelines. Discriminant ability of the multidimensional tool was evaluated by testing it in a control group including healthy controls and patients affected by active juvenile idiopathic arthritis (JIA). The psychosocial consequences of chronic pain were evaluated by using the Children Depression Index (CDI) and the Multidimensional Anxiety Scale for Children (MASC). The objective sleep quality was measured by overnight polysomnography.

Results: Table 1 shows characteristics and the most represented somatic symptoms in our cohort of JFS patients at the study enter. Polysomnography was performed in 21 patients with sleep disturbance; 8/21 (38.1%) showed an electroencephalographic pattern of alpha wave intrusion in slow wave sleep (SWS). The presence of objective sleep disorders was significantly correlated to CDI score rs -0,775 (p≤0,0001) and MASC 0,61 (p=0,005). From November 2016 to April 2020 J-FiMAR was completed by 43 JFS patients (F 35 (81.4%), median age 14.7 years [7.1-17.6], median disease duration 1.9 years [0.1-7.8]) in 125 visits. All patients filled out the questionnaire in a short time (<15 minutes) and considered it simple and easy to understand. JFS patients showed significantly higher score for pain, fatigue, poor physical function and measure of psychological distress than healthy controls and JIA patients (p<0.05 for each item).

Table 1

Widespread musculoskeletal pain	38 (88.4%)
Fatigue	37 (86%)
Headache	27 (62.8%)
Concentration or Memory Problems	22 (55%)
Sleep disturbance	22 (51.7%)
Anxiety and/or depression	17 (39.5%)
Irregular School attendance	15 (34.9%)
IBS and abdominal pain	11 (25.6%)
Body mass index >25	12 (27.9%)
Family history of fibromyalgia	11 (25.6%)

Conclusion: JFS patients presented significantly higher pain experience, functional disability, and impaired quality of life than patients with active JIA. A relevant percentage of JFS patients experience sleep disturbances, which were correlated with mood and anxiety disorders. Our multidimensional tool was feasible and able to quantify global JFS severity. This multidimensional tool, by measuring the main domains affected by the disease, could be promising to individualize treatment strategy and to test its efficacy.

Disclosure of Interest: None declared

e-Poster viewing: Patient/parent organisation initiatives

P204

FATIGUE IN CHILDREN AND TEENS WITH AUTOINFLAMMATORY DISEASE.

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Introduction: Fatigue is a subjective state of overwhelming, sustained exhaustion and decreased physical and mental capacity, which is not relieved by rest. Fatigue is the most common complaint in children and teens with an autoinflammatory disease, besides the disease related flares. The purpose for this study was to show that fatigue is a serious issue for children and young people with autoinflammatory diseases. We hypothesized that age, gender and/or the type of autoinflammatory disease could have differing effects on the fatigue experience.

Objectives: We aimed to investigate fatigue in children and young people (CYP) with autoinflammatory disease, including how this affected them on a daily basis.

Methods: CYP with autoinflammatory diseases were invited to complete an online survey, providing details about their fatigue and how it affected them. The survey was developed by the non-profit organizations Autoinflammatory Alliance and KAISZ/VAISZ, in English. Respondents were recruited by convenience sampling through online social media posts. Data on age, gender and disease were collected in addition to information on their experience of fatigue on school and social interaction.

A total of 114 CYP (age range 7-18 years) with an autoinflammatory disease responded to the survey (52% female).

Results: The majority of respondents (81%) reported experiencing both mental and physical fatigue. Respondents were asked how much their fatigue affected them, on a scale of 0 to 10; overall, the mean fatigue score was 6.6. However, young people aged 15 or over reported a significantly higher impact than those aged 11-14 years (mean 7.5, p=0.012). Different autoinflammatory diseases were surveyed: CRMO 25%, CAPS 20%, PFAPA 12% also Unclassified SAID (uSAID) with 23%.

In the open-response portion of the survey, 81% of respondents reported that fatigue was physical, as well as mental, in their experience.
Most (89%) reported that someone had doubted their fatigue in the past; 29% had found their teachers had doubted them, 26% had friends who doubted them, and 24% reported that they felt their doctors had doubted them. Children and young people also felt a number of activities made their fatigue worse (table 1)."

Table 1: Proportion of respondents reporting what they felt makes their fatigue worse.

	Total	%
School	77	20%
Extracurricular activities	76	20%
Sports	72	19%
Social interaction	62	16%
Family activities	50	13%
Medication	16	4%
Don't know	16	4%
Nothing	8	2%
Total	377	

Conclusion: CYP with autoinflammatory diseases experience physical and mental fatigue. Health professionals and teachers should listen to patients reporting fatigue, validate their experience, and help find ways to support them. Identifying

resources to help the patients with fatigue, and referrals to therapy and mental health resources as needed may help the patients to better cope and manage their chronic disease.
Further studies will include patient engagement in designing questionnaires about all aspects of life and autoinflammatory disease will help our understanding of these complex conditions and how they affect patients.

Disclosure of Interest: None declared

e-Poster viewing: Psycho-social aspects and rehabilitation

P205

PSYCHOLOGICAL INVOLVEMENT IN YOUNG PEOPLE WITH CHRONIC RHEUMATOLOGICAL DISEASE: WHAT INPUT DO PATIENTS NEED?

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Introduction: Paediatric rheumatological diseases increase the risk of co-morbid mental health disorders and symptoms, yet the optimum psychological intervention to address mental health symptoms in this patient group has not been established.
Objectives: This study set out to establish patient and parent views on the suitability of different interventions that seek to support the mental health of patients with paediatric rheumatological diseases.
Methods: Patients with inflammatory diseases and their parents attending the Paediatric Rheumatology Department or Young Adult Clinic (YAC) at the University Hospital Southampton were invited to take part in the study. Questionnaires and semi-structured interviews, developed with paediatric psychologists, and a medical anthropologist, were used to examine the experience of emotional difficulties amongst patients and views on suitability of different intervention formats. Patients and their parents were invited to complete the questionnaires however only patients were invited to take part in the interviews. Interviews were audio recorded and transcribed verbatim by the interviewer. Codes were generated inductively from the interview transcripts and manually grouped into themes.
Quantitative data from completed forms were analysed descriptively using SPSS and Excel. Qualitative data from extended answer responses and patient interviews were thematically analysed.
Results: 72 patients, (IQR of age in years 12.25 – 17.00) and 47 parents (IQR of age in years 12.00 – 15.25) completed questionnaires. 80% of patients reported experiencing at least one emotional difficulty, related to their rheumatological condition. Sleeping problems (49.3%) and anxiety (46.5%) were the most commonly reported symptoms in patient participants. 91.4% of patient participants agree or strongly agree that intervention deliverers should understand their condition. 50% of patients and 64.4% of parents reported psychologists as suitable interventionists for emotional difficulties followed by paediatric rheumatologists (29.4% and 57.8%, respectively).
Five patients were interviewed. Key themes from the interviews include experience with emotional difficulties (e.g. anxiety around taking medication and the effect of disease on future life); variety of interventions (e.g. educational and psychological support to overcome emotional challenges related to disease), and awareness of available support.
Conclusion: This study highlighted there are high levels of emotional difficulties in paediatric rheumatology patients. Psychologists and paediatric rheumatologists are deemed the most suitable interventionists by participants. Patients demonstrate a need for emotional and educational support to overcome emotional difficulties associated with their rheumatological disease.
Disclosure of Interest: None declared

e-Poster viewing: Scleroderma and related syndromes

P206

SCLERODERMA-POLYMYOSITIS OVERLAP SYNDROME IN PEDIATRIC AGE: A CASE REPORT

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Introduction: Scleromyositis is the most common overlap syndrome but is rarely observed in childhood. This disorder involves two different autoimmune diseases: systemic scleroderma (SSc) and polymyositis (PM).
Objectives: To describe the clinical course of a SSc/PM syndrome in a young girl.
Methods: Case report
Results: An 11-year-old female was admitted to the Neurological Unit of our hospital for creatine phosphokinase (CPK) increase and hypertransaminasemia associated to sporadic episodes of right calf pain. Familiarity for muscular dystrophy was reported in the maternal branch. Muscle tone and trophism were preserved at initial neurological evaluation. Laboratory investigation confirmed increased muscle enzyme levels, including CPK (x70) (CK-MM 94.5%, CK-MB 5.5%), aldolase (x7), cardiac troponin (x10) and myoglobin (x10). Suspecting a primary muscle disease, she underwent a total body STIR-MRI which showed a diffuse edema of gluteus medius bilaterally and a muscle biopsy revealing a marked muscle damage with dystrophic aspects and normality of the tested proteins. A genetic extended panel for congenital myopathies resulted negative.
After 4 months, a new clinical examination showed the occurrence of general skin induration, sclerodactyly and tightening of the face skin. Appearance of dysphagia was also reported, and muscle enzyme increase persisted. In suspicion of an SSc/PM overlap syndrome, she was referred to our Unit. Nailfold capillaroscopy showed capillary dilatation and branching, megacapillaries and diffuse microhemorrhages. Reduction of esophageal contractions amplitude and hypotensive lower esophageal sphincter pressure were observed at esophageal manometry test. High-resolution CT of lungs and pulmonary function testing were normal. Skin biopsy showed sclerodermiform findings. Immunological studies revealed a positivity of antinuclear antibody (1:320) and anti-Ku. Anti-PM-Scl resulted negative. An oral corticosteroid therapy (prednisone, 1.5 mg/kg/day) was started in association with subcutaneous Methotrexate (15 mg/m^2/week) and intravenous immunoglobulins (IVIG) (2gr/kg every two weeks). Improvement of skin manifestation, joint mobility, as well as normalization of serum CPK levels were observed. Over 3 months, prednisone and IVIG were slowly discontinued up to the ongoing dosage of 0.9/mg/day and 2 gr/kg every 4 weeks, respectively. MTX is still ongoing at the same dosage.
Conclusion: The diagnosis of overlap connective tissue disease syndromes may be challenging in pediatric age. Different symptoms may be prevalent at different stages throughout the course of the disease. In our patient, a localized myositis preceded the SS onset by about four months. Even though the use of high dose of corticosteroids is associated to a higher incidence of renal crisis in patients with cSS, a combined therapy with high doses of oral steroids, IVIG and MTX was safe and effective in skin, muscle and joint symptoms in our patient.
Disclosure of Interest: None declared

P207

TOCILIZUAB AS A TREATMENT OPTION FOR A LIBYAN FEMALE CHILD WITH JUVENLE SYSTEMIC SCLEROSIS

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Introduction: Juvenile systemic sclerosis is a rare autoimmune disease characterized by skin stiffness and fibrosis of internal organs (e.g.lung,heart,and gastrointestinal system).The efficacy and safety of tocilizumab (TCZ),an interleukin 6 receptor- inhibitor,and reports on its efficacy among children have been the subject of a few recent studies.This is a first report on the treatment of a JSS patient with TCZ in Libya.
Objectives: We aimed to present a case with Juvenile systemic sclerosis to evaluate the efficacy of tocilizumab in the treatment of systemic sclerosis in children.
Methods: DESIGN AND methods: Case report study
Results: A 16-year-old female who was diagnosed with juvenile scleroderma was referred to our rheumatology clinic in September 2018 due to progressive dysphagia specifically for solid food associated with coffee ground vomiting and sometimes,shortness of breath during exertion.The patient had been diagnosed with juvenile scleroderma 3 years ago based on skin tightness,Raynaud phenomena,sclerodactly with digital ulcers,an upper GIT endoscopy which revealed lower esophagus ulceration,decreased pulmonary function test,a high resolution CT scan chest which showed interstitial pneumonitis,holter ECG showed ventricular arrhythmia with normal conduction,and an EMG revealed myopathy.She had been treated with a B.bloker (Nebiodol 5mg) 1\4tab once per day and flecaine tab 50mg,in addition to a methotrexate tab and an omeprazole capsule by a rheumatologist.She showed generalized fatigability,increased tightness of skin on her face as well as her upper and lower extremities,limitation of range of motions of most joints,and an abnormal handgrip.Laboratory tests revealed the following: low CBC at HGB 9.6,ANA 1:1280 positive and antids DNA was negative,ENA was negative,SCL-70 was positive,holter ECG showed ventricular arrhythmia,EMG revealed myopathy,high resolution chest showed fibrosing alveolitis worse than the first one,PFT was decreased.A diagnosis of diffuse systemic sclerosis (JSS) was made,and cyclophosphamide IV was administrated for 6 months.Methotrexate 15mg\m\week SC was initiated,well as a,low dose of steroids for 3 months,along with B blocker tab and an omeprazole capsule; however,there was no improvement.In April 2019,she started using Tocilizumab infusion once per month accompanied with methotrexate SC and MMF tab,and the effects of therapy have been very good.
Conclusion: JSS is a rare condition characterized with internal organ involvement.Tocilizumab represents an efficient treatment option for patients unresponsive to standard treatment.
Disclosure of Interest: None declared

P208

HOW THE ADULT CRISS WORKS IN PEDIATRIC JSSC PATIENTS - RESULTS FROM THE JUVENILE SCLERODERMA INCEPTION COHORT

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Introduction: The Composite Response Index in Systemic Sclerosis (CRISS) was developed by Dinesh Khanna as a response measure in patients with adult systemic sclerosis. CRISS aims to capture the complexity of systemic sclerosis and to provide a sensitive measure for change in disease activity. The CRISS score is based on a two-step approach. First, significant disease worsening or new-onset organ damage is defined as non-responsiveness. In patients who did not fulfill the criteria of part one, a probability of improvement is calculated for each patient based the Rodnan Skin Score (mRSS), percent predicted forced vital capacity (FVC%), patient and physician global assessments (PGA), and the Health Assessment Questionnaire Disability Index (HAQ-DI). A probability of 0.6 or higher indicates improvement.

Objectives: to validate the CRISS in a prospectively followed cohort of patients with juvenile systemic sclerosis (jSSc)

Methods: Data from the prospective international inception cohort for jSSc was used to validate the CRISS. Patients with an available 12-months follow-up were included in the analyses. Clinically improvement was defined by the anchor question about improvement (much better or little better versus almost the same, little worse or much worse) in patients overall health due to scleroderma since the last visit provided by the treating physician.

Results: Forty seven jSSc patients were included in the analysis. 74.2% had diffuse subtype. The physician rated the disease as improved in 34 patients (72.3%) since the last visit. No patient had a renal crisis or new onset of left ventricular failure during the 12-months follow-up. Three patients (3.4%) each had a new onset or worsening of lung fibrosis and new onset of pulmonary arterial hypertension. In total, 6 patients resulted in a rating of not improved based on the CRISS in part I. The mRSSS, FVC%, CHAQ and PGA significantly improved during the 12-months follow-up in patients who were rated as improved. The predicted probability based on the CRISS algorithm resulted in an area under curve of 0.77 predicting the anchor question of improvement. In summary, 33 (70.0%) patients were correctly classified by the adult CRISS score resulting in an overall area under curve of 0.7.

Conclusion: The CRISS score was evaluated in a pediatric jSSc cohort for the first time. It showed a good performance. However, it seems that the formula of part II of the CRISS score needs a calibration to pediatric jSSc patients.

Disclosure of Interest: None declared

P209

DESCRIPTION OF THE CHARACTERISTICS OF THE NAILFOLD CAPILLARY STRUCTURE IN HEALTHY CHILDREN: A PILOT STUDY

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Introduction: Nailfold capillaroscopy is the best method for the early diagnosis of connective tissue diseases, especially systemic sclerosis, and evaluation of microcirculation in children and adolescents. Although there are many studies to identify normal capillaroscopic findings in healthy adults, there are limited number of studies for normal reference ranges by age and gender in the children and adolescents.

Objectives: The aim is to define and standardize the nail bed capillary properties in healthy Turkish children and adolescents.

Methods: This multicenter cross-sectional pilot study included; 118 healthy children and adolescents from 5 pediatric rheumatology centers. Using the *Dino-Lite CapillaryScope 200 Pro / MEDL4N Pro capillaroscopy* device, two images of 1mm radial and ulnar edge were obtained from the 4th fingernail bed of the non-dominant hand at 200x magnification. Capillary density, capillary morphology (*i.e.,* capillary tortuosity, capillary crossing, giant capillary, capillary meandering and branched capillary), microhemorrhage and avascular area were the parameters. Also 3 consecutive capillaries from each image; capillary length, capillary width, apical loop, arterial and venous width, and distance between capillaries were measured. The children included in the study were classified according to their age; Group 1: 5-7 years, Group 2: 8-10 years, Group 3: 11-14 years, and Group 4: 15-18 years old.

Results: A total of 336 images were obtained from 118 healthy children included in the study and 708 capillary measurements were made. Capillary density was significantly higher in *Group* 4 than in *Groups* 1 and 2. Arterial width was significantly lower in *Group* 1 as compared to *Group* 3 and 4, and in *Group* 2 as compared to *Group* 4. Apical loop width and capillary distance were significantly lower in *Group* 1 compared to *Group* 2 and 3 and 4. There was no significant difference between the age groups in terms of capillary length and venous width. There was no difference between the groups in terms of capillary morphology. In total 336 image evaluations, capillary tortuosity was <50% in 67.8%, and > 50% in 4.2%, and capillary crossing were <50% in 52.5% and> 50% in 3.4%. While the enlarged capillary was 4.7% and the avascular area was 4.2%, capillary branching, capillary meandering, microhemorrhage, and giant capillary were not detected in any case. There was a good level of agreement between the researchers, as 20 cases with 120 capillaries were evaluated with a good level of agreement (Table 1).

Table I. Evaluation of compatibility between the researchers for capillary density / mm, capillary length, capillary width, arterial width, venous width, apical width and intercapillary distance measurements.

	ICC (%)	Confidence Interval (%95)	p
Capillary density	96.1	0.944-0.975	<0.001
Capillary length	94.3	0.895-0.974	<0.001
Capillary width	90.6	0.866-0.937	<0.001
Arterial width	90.7	0.868-0.938	<0.001
Venous width	89.6	0.853-0.930	<0.001
Apical loop width	91.1	0.874-0.941	<0.001
Capillary distance	94.3	0.918-0.962	<0.001
ICC: Interclass correlation coefficient			

Conclusion: This is the first study to evaluate capillary morphology in healthy Turkish children. This study also adds that some special forms such as enlarged capillary and avascular area, which is always named as pathological in adult age, can be seen in healthy children. These data will be guiding in capillaroscopic studies in various patient groups, particularly in children with collagen vascular diseases.
Disclosure of Interest: None declared

P210

IS THERE A DIFFERENT PRESENTATION OF JUVENILE SYSTEMIC DIFFUSE AND LIMITED SUBSET? DATA FROM THE JUVENILE SCLERODERMA INCEPTION COHORT. WWW.JUVENILE-SCLEORDERMA.COM

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Introduction: Juvenile systemic scleroderma (jSSc) has a prevalence of 3 per 1 000 000 children. There are limited data regarding the clinical presentation of jSSc. The Juvenile Systemic Scleroderma Inception Cohort (jSScC) is the largest multinational registry that prospectively collects information about jSSc patients.

Objectives: To assess of there is a difference in the clinical characteristics in diffuse and limited subtype jSSc patients at the time of inclusion in the jSScC

Methods: Patients were included, if they fulfilled the adult ACR/EULAR classification criteria for systemic scleroderma, if they presented the first non-Raynaud symptom before 16 years of age and were younger than 18 years of age at time of inclusion. Patients' characteristics at time of inclusion were evaluated.

Results: Until December 2019 hundred fifty patients were included, 83% of them being Caucasian and 80% female. The majority had the diffuse subtype (72%) and 17% of all jSSc had overlap features. The mean age of first presentation of Raynaud´s phenomenon was 9.8 years in the diffuse subtype (djSSc) and 10.7 years in the limited subtype (ljSSc) (p=.197). The mean age at first non-Raynaud's symptoms was 10.0 years in the djSSc and 11.2 years in the ljSSc (p=0.247). Mean disease duration at time of inclusion was 3.4 years in the djSSc and 2.4 years in the ljSSc group.

Significant differences were found between the groups regarding mean modified Rodnan skin score, 18.2 in the djSSc vs 6.2 in the ljSSc (p=0.02); presence of Gottron´s papulae (djSSc 30% vs ljSSc 13%, p=0.43);presence of teleangiectasia (djSSc 42% vs 18% ljSS, p=0.01); history of ulceration (djSSc 42% vs 18% ljSSc,p=0.008); 6 Minute walk test below the 10th percentile (djSSc 85% vs ljSSc 54%, p=0.044), total pulmonary involvement (djSSc 49% vs ljSSc 31%, p=0.045), cardiac involvement (ljSSc 17% vs djSSc 3%, p=0.002). djSSc patients had significantly worse scores for Physician Global Assessment of disease activity compared to ljSSc patients (VAS 0-100) (40 vs 15) (p=0.001) and for Physician Global Assessment of disease damage (VAS 0-100) (36 vs 17) (p=0.001).

There were no statistically significant differences in the other presentations. Pulmonary hypertension occurred in approximately 6% in both groups. No systemic hypertension or renal crisis was reported. ANA positivity was 90% in both groups. Anti-Scl70 was positive in 35% in djSSc and 36% in the ljSSc group. Anticentromere positivity occurred in 3% in the djSSc and 7% in the ljSSc group.

Conclusion: In this unique large cohort of jSSc patients there were significant differences between djSSc and ljSSc patients at time of inclusion into the cohort regarding skin, vascular, pulmonary and cardiac involvement. According to the physician global scores the djSSc patients had a significantly more severe disease.

Supported by the "Joachim Herz Stiftung"

Disclosure of Interest: None declared

e-Poster viewing: Spondyloarthritis (SpA) and enthesitis related arthritis (ERA)

P211

THE COMPARISON OF THE HLA-B27-POSITIVE AND HLA-B27-NEGATIVE PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS IN THE SINGLE CENTER

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Introduction: Juvenile spondyloarthropathies (JSA) are the group of diseases with axial involvement in childhood. EULAR and ASAS classifications are known for diagnosis of JSA, the last one is less sensitive. The 70% of patients are HLA-B27 positive and have sacroiliitis or cervical involvement in the onset or developing of the disease. There's limited information about seronegative JSA in childhood.
Objectives: to compare the patients with JIA depending on HLA-B27 positivity. To identify the rate of axial involvement depending HLA-B27 positivity.
Methods: 308 patients with JIA were tested for HLA-B27. They were divided into 2 groups: 1) HLA-B27 positive and 2) HLA-B27 negative.
Results: 100 patients (32,5%) were HLA- B27 positive and all of them are fulfilled the EULAR criteria of entesitis-related arthritis (ERA). The group 2 consists of 208 patients (67.5%). There's no statistical difference between both groups in active joint count, ANA-positivity and uveitis frequency, the rate of use methotrexate and time before biologics. No difference in axial cervical spine 12 (12.0%) *vs* 21 (10.1%) (p=0.613) and sacroiliac joints 18 (18.0%) *vs* 23/207 (11.1%) (p=0.097) involvement was observed. HLA B27(+) patients often received pulse therapy with methylprednisolone due to increased inflammatory activity and severe arthritis (22% *vs* 11.1%, p=0.011). Other parameters are listed in Table1.
Table1. The difference between HLA-B27 positive and negative arthritis.

Parameters	HLAB27 (+) (n=100)	HLAB27 (-) (n=208)	p
Onset age, years	9.3 (6.4; 11.8)	6.1 (3.5; 10.3)	0,00001
ESR, mm/h	16.0 (4.0; 30.0)	5.0 (3.0; 14.0)	0,00002
CRP, g/l	2.2 (0.2; 15.7)	0.8 (0.0; 5.2)	0,016
PLT, $x10^9$/l	336.0 (257.0; 430.0)	303.5 (255.0; 366.5)	0,034
Male, n (%)	66 (66.0)	93 (44.7)	0,001
Hip arthritis	34 (34.0)	41 (19.7)	0.007
Knee arthritis	56 (56.0)	155 (74.5)	0.002
Sulfasalazine	42/64 (65.6)	34/156 (21.8)	0,001
Biologics	61 (61.0)	82 (39.4)	0,001

Conclusion: patients with HLA-B27 positivity were characterized by male predominance, more often hip involvement, higher laboratory activity and the need for more frequent use biologics. The rate of axial involvement wasn't different in HLA-B27 positive and negative patients, that needs further study and creating more accurate classification criteria for JSA.
Disclosure of Interest: None declared

P212

CROSS-SECTIONAL STUDY OF FECAL CALPROTECTIN IN CHILDREN WITH VARIOUS FORMS OF ARTHRITIS AND NON-INFLAMMATORY MUSCULOSKELETAL DISORDERS: A SINGLE CENTRE EXPERIENCE

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Introduction: Although gut is increasingly recognized as origin and/or target of inflammation in adult onset spondyloarthritis (SpA), the incidence of gut involvement in juvenile SpA (jSpA) patients is still largely unknown, mostly due to the lack of reliable non-invasive tests.
Objectives: We performed a cross-sectional study of fecal calprotectin (fCAL), a surrogate marker of gut inflammation, in patients with jSpA, other forms of juvenile idiopathic arthritis (JIA) and non-inflammatory (NI) conditions.
Methods: fCAL was measured by commercially available assay in stool samples of enthesitis related (ErA), psoriatic (PsA) and patients with other JIA subtypes (oligo- and poly- articular) who fulfilled ILAR criteria, as well as in children with NI causes of musculoskeletal pain (NI-MSD), regardless of the gastrointestinal (GI) symptoms (Table 1). fCAL was compared among different groups of patients and correlated with demographic data, clinical characteristics, treatment modalities and disease activity measured by jSpADA. The values were also dichotomized to <50 mg/kg, 50-200 mg/kg, and >200 mg/kg, which was regarded as normal, slightly increased and increased, respectively. Ileocolonoscopy was performed in one patient.
Results: The median fCAL levels were highest in ErA patients (p=0.04). Moreover, in ErA patients moderate correlation between fCAL levels and MRI signs of SI inflammation (r=0.4, p=0.39) was found, while the patients with inflammation had higher fCAL concentrations than those without (22.6 vs 54.3, p=0.048). There was no significant difference in fCAL concentration between ErA patients with inactive (jSpADA ≤ 1) or active (jSpADA ≥ 1) disease (39.7 vs 30.9, p=0.66). In all patients, NSAID use was not associated with increased fCAL (20 vs 23, p=0.18), although weak correlation was found with the duration of the use (r=0.25, p=0.03). No correlation was observed between fCAL level and age at the time of sampling, duration of the disease, CRP or ESR, number of active joints and/or enthesis, physician global assesment, morning stiffnes, uveitis, back mobility, abdominal pain, diarrhea, B27 presence in a patinet or a faimly and disease activity in ErA and other JIA patients measured by jSpADA and JADAS, respectively. Microscopic gut inflammation was observed in one ErA patient with fCAL concentration of 839 mg/kg.

		ErA	**PsA**	**JIA**	**NI-MSD**
N (% female)		26 (65%)	4 (100%)	29 (57%)	12 (67%)
Age* (yrs)		12 (7.7-14.5)	10.8 (8 – 13.9)	11 (7 – 14)	13 (6.1 – 14)
fCAL* (mg/kg)		33.20 (20-84.8)	20 (20-30.7)	20 (20-31.5)	20
fCAL (mg/kg)	<50	18	4	24	10
	50-200	5	/	4	2
	>200	3	/	1	/
TREATMENT	NSAIDS	14	2	23	0
	DMARDS	2	0	9	0
	GC	1	0	1	0

*median, IQR
Conclusion: Our study has shown that fCAL levels are significantly higher in ErA patients compared to other JIA (p=0.03) and/or NI-MSD (p=0.03) patients. Moreover, almost a third of patients with ErA had levels of fCAL above the range regarded as normal, which adds to the number of evidences for a gut inflammation in this particular type of JIA. Besides, the fCAL levels were higher in those with axial involvement, which further suppots the association of gut and axial inflammation in children with ErA. Although endoscopy remains a gold standard for the diagnosis of gut inflammation, fCAL can help to select children with ErA who might benefit from this invasive procedure, regardless of the GI symptoms, as shown in one patient with the highest fCAL concentration in our study. Moreover, fCAL levels seems not to be influenced by disease characteristic and/or concomitant therapy intake. Therefore, fCAL should be a part of diagnostic workup in children with any type of JIA, but most importantly in those with ErA.
Disclosure of Interest: None declared

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THE FEATURES OF THE JUVENILE IDIOPATHIC ARTHRITIS IN SAKHA REPUBLIC (YAKUTIA).

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Introduction: Juvenile idiopathic arthritis (JIA) is not uncommon disease among aboriginals in Sakha Republic (Yakutia) - SR(Y), which can be related to high spreading of HLA B27 antigen. Adult aboriginals of SR(Y) have ankylosing spondylitis several times higher than Caucasians. According the epidemiological studies HLA B27 antigen distributes in 33% of healthy aboriginals.
Objectives: The aim of our study was to describe features of JIA in aboriginals of RS(Y).
Methods: In the retrospective study were included 184 JIA patients before age 18 consisted of 155 SR(Y) aboriginals, 26 Caucasians and 3 mixed (Yakutia and Caucasians) whom have been living in SR(Y). We compare data of clinical course and compare aboriginals with Caucasians.
Results: The JIA prevalence in aboriginals is approximately 137/100 000 children and 30/100 000 in Caucasians. Clinical features describes in the table. HLA B27 distributed in aboriginals with JIA two times higher than in Caucasians and in healthy aboriginals. Positive family history in HLA B27 related diseases in 78 (53.1%) of aboriginals compare to 8 (36.4%) in Caucasians. ANA positivity was only in 4/53 (7.6%) that is less than in other populations. Uveitis is in 16 (10.5%) of aboriginals, usually associated with HLA B27 rather than ANA-positivity. Biologics received 44.5% of JIA aboriginals, 91.3% received TNF-a inhibitors. HLA B27 presented in all JIA categories, 48.7% in oligoarthritis, in 42.9% of RF(-) polyarthritis, in 50% of RF(+) polyarthritis, 66.7% of systemic JIA, 71.3% of enthesitis-related arthritis and in 40% of psoriatic arthritis patients. 70.3% of biologic users had HLA B27 antigen (p=0.028).

Parameter	Aboriginals (n=155)	Caucasians (n=26)	p
Males, n (%)	92 (85.6)	10 (38.6)	0.047
HLA B27, n (%)	87/145 (60.0)	6/20 (30.0)	0.012
JIA categories			
Oligoarthritis	39 (25.1)	6 (23.1)	0.137
Polyarthritis, RF (-)	25 (16.1)	4 (15.4)	
Polyarthritis, RF (+)	2 (1.3)	0 (0.0)	
Systemic	4 (2.6)	4 (15.4)	
Enthesitis-related arthritis	79 (51.0)	10 (38.5)	
Psoriatic arthritis	6 (13.9)	2 (7.7)	

Conclusion: Aboriginals in SR(Y) have higher prevalence of JIA, HLA B27 antigene, enthesitis-related category of JIA and juvenile ankylosing spondylitis, increased family history of rheumatic diseases, especially arthritis and have higher requirement in biologic medicine (anti-cytokine antibodies) for arthritis control compare to Caucasians.
Trial registration identifying number: This work was supported by the Budget Projects of YNC CMP “Monitoring the state of children's health of the Republic of Sakha (Yakutia)” (#0120-128-07-98), by the Project of the Ministry of Science and Higher Education of the Russian Federation (basic part of funding to M.K. Ammosov North-Eastern Federal University #FSRG-2020-0016) and by the RFBR grant #18-05-600035_Arctika.
Disclosure of Interest: None declared

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ACHIEVING INACTIVE DISEASE IN ERA WITH SECUKINUMAB FOLLOWING TNF INHIBITOR FAILURE; A REAL-LIFE, DUAL-CENTER EXPERIENCE

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Introduction: TNF- inhibitors (TNFi) have greatly improved the clinical outcome of patients with Enthesitis-Related Arhtritis (ERA), there is however a minority of patients who fail to respond to standard treatment.
Objectives: We describe the efficacy and safety results of a secukinumab (monoclonal antibody neutralizing interleukin-17A) compassionate use in patients with active ERA following failure of disease remission by TNFi.
Methods: In this case-series, 4 patients diagnosed with ERA (based on ILAR criteria) with a mean age of 16.2 years (range 15-17) received secukinumab 150 mg subcutaneously at weekly intervals and each 4 weeks thereafter for a total period of 18 months. All patients showed mild/no improvement to treatment with adalimumab (TNFi) received for at least six months. Clinical response was assessed at weeks 24, 52, 76(jSpADA). Safety and tolerability were also assessed at the same key time points during the course of the study
Results: Clinical and demographic data were collected. The jSpADA response rate was 70% at week 24, which was sustained and further improved until week 76. Secukinumab was effective in multiple clinical outcomes including physician's global assessment of disease activity, CHAQ score and CRP level (table 1). Secukinumab was well-tolerated with a safety profile consistent with reports in adult studies. Disease duration, prior use of NSAIDS, age and gender did not affect the clinical outcome. There have been no reports of uveitis, psoriasis, IBD or any new-onset autoimmune disease. No major adverse events were reported.

Table 1: Patient and disease characteristics at inception and at one year follow-up First line indicates initial assessment and second line (in bold) follow up assessment.

Patient Characteristics	Gender	Age (years)	CRP (mg/L)	SI involvement	Physician global assessment	Spinal Pain VAS (0-10 scale)	CHAQ	jSpADA
Patient 1	male	16	32 **5**	bilateral	4.5 **1**	6 **0.3**	3 **0**	7 **0.5**
Patient 2	male	17	45 **4**	bilateral	8 **2**	7 **0**	2 **0.5**	5 1
Patient 3	female	15	76 **5**	bilateral	7.2 **1.5**	6 **1**	6 **1**	6 **1**
Patient 4	male	17	19 **3**	unilateral	5 **1**	4 **0**	2 **0**	5 **0**

Conclusion: This was a retrospective study regarding secukinumab effectiveness in patients with ERA who failed TNFi treatment, showing optimistic results. Secukinumab is usually effective in inducing and maintaining remission in Ankylosing Spondylitis and psoriatic patients and thus long-term therapy is recommended. Overall, biologic-naïve patients demonstrate a swift and sustained response to biologics (TNFi); however not all patients who receive TNFi will reach a state of inactive disease. Further studies are required to address the effectiveness of secukinumab treatment in patients with ERA, with the aid of appropriate disease-associated risk-assessment markers. Our study demonstrated that secukinumab is safe and effective in ERA patients, provided it is initiated promptly following TNFi failure. In addition, prolonging the duration of treatment in clinical remission prior to attempting discontinuation may show favorable results in contrast to other studies endeavoring earlier discontinuation. Minimizing exposure to TNFi especially within the case of partial response or no response may lead to decreased adverse events and costs. In addition, secukinumab provided sustained improvement in the signs and symptoms of ERA patients through 18 months, with no new or unexpected safety signals.
Disclosure of Interest: None declared

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IMPACT OF ANTI-TUMOR NECROSIS FACTOR THERAPY ON SPONDYLOARTHRITIS RESEARCH CONSORTIUM OF CANADA SACROILIAC JOINT INFLAMMATION SCORE IN CHILDREN WITH ENTHESITIS-RELATED ARTHRITIS

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Introduction: Enthesitis-related arthritis (ERA) is a category of Juvenile idiopathic arthritis considered to be a form of Juvenile Spondyloarthropathy (jSpA). Tumor necrosis factor (TNF)-blocking strategies have proven to be effective in the treatment of jSpA. The Spondyloarthritis Research Consortium of Canada sacroiliac joint score (SPARCC- SIS), measures inflammation in sacroiliac joints (SIJ). It has been used in adults as a tool to assess response to anti-TNF agents, however, limited experience exists in JSpA cohorts

Objectives: To evaluate effectiveness of anti-TNF treatment in SIJ inflammation in a cohort of patients with ERA using SPARCC-SIS. To quantify the effect size of TNF-blockers on SIJ inflammation. To evaluate potential predictor variables of Magnetic Resonance Imaging (MRI) SIJ remission

Methods: Retrospective review of prospectively collected data. We included patients with ERA (according to ILAR criteria) continuously treated with anti-TNF agents for ≥ 12 months who had at least two MRIs of the sacroiliac joints performed before starting anti-TNF therapy (baseline) and during the follow up (> 12 months after anti-TNF treatment). SI joints were examined using T1-weighted images, T2 fast-suppressed and short-tau inversión recovery. The SPARCC-SIS was scored by two pediatric radiologists. SPARCC-SIS assessed the presence, depth and intensity of bone marrow edema (BME) on consecutive six slices in the iliac and sacrum bones . Scoring is composed by: BME (0-48), BM intensity (0-12), BM depth (0-12).Maximum:72. MRI SIJ remission was defined as SPARCC-SIS score < 2. Magnitude of change on MRI SIJ score was assessed. Treatment with TNF-blockers and exposure time were recorded. Outcome measures were collected: pain score (0-10), wellbeing according to the patient using a visual analogue scale (VASp, 0-10), disease activity according to the physician (VASphy, 0-10), JADAS-10, JSpADA. Functional capacity was assessed by CHAQ. Statistical analysis included: Intraclass Correlation Coefficient (ICC) for readers, magnitude of change using Cohen`s d test, comparisons by Wilkoxon Signed Rank test and Mc Nemar test.

Results:

Twelve (75% male) patients fulfilled inclusion criteria. Median (range) age at start of TNF-blocker therapy was 10.5 years (6-15) and disease duration 8 years(4-14). Presence of HLA-B27 positive 33%. Anti-TNF therapy consisted of: etanercept (7, two of them were later switched to adalimumab) and adalimumab (5). Median (range) exposure to anti –TNF was 30.5 months (12-60). All patients had evidence of SIJ inflammation at baseline on MRI. SPARCC-SIS at baseline was (median±SD) = 36±16.87. SPARCC-SIS over time (post treatment) was 12±7.44. Magnitude of change on score (Cohen`s:1.84, r: 0.68). MRI SIJ remission was achieved on 33%. ICC for concordance between readers= 0.73. Outcome measures are shown in table1.

Table1	Before TNF- blockers	After TNF -blockers	p value
Pain Score (0-10)*	3.5(0-7.5)	0.25(0-5)	0.019
VASp (0-10)*	4(0-9.5)	0 (0-6)	0.03
VASphy (0-10)*	3.5(0-7.5)	0.5(0-6)	0.009
CHAQ≥0.5**	6(50%)	1(8%)	ns
JADAS-10*	14.8 (1-28)	1(0-18)	0.003
JSpADA*	2.5(0.5-6)	0.75(0-3.5)	0.013

*median (range) ** n(%)

There was no significant association between exposure time to anti-TNF treatment and MRI SIJ remission. Neither predictor variables on MRI SIJ remission were found.

Conclusion: Anti-TNF blockers showed to be effective in reducing MRI SIJ inflammation. Magnitude of change in SIJ inflammation had a large effect size. One third of patients achieved MRI SIJ remission on TNF-agents

Disclosure of Interest: None declared

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DISTINCT DISEASE PROFILE IN HONG KONG JUVENILE IDIOPATHIC ARTHRITIS (JIA) PATIENTS

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Introduction: The prevalence and disease pattern of JIA vary across different ethnicities. Up till now, data on Chinese children is lacking. Different disease profile may potentially impact management strategies and resource allocation.
Objectives: To study the characteristics of JIA in Hong Kong.
Methods: A retrospective review of patients being seen at the rheumatology clinic of a tertiary referral centre from 1990 to 2020 was performed. Eligible patients were: 1) diagnosed JIA according to the ILAR criteria; 2) those having more than 1 clinic visits; 3) those data retrievable from hospital record. Results were presented in descriptive manner.
Results: 94 of 100 patients were eligible for analysis. The mean duration of follow up was 7.5±5.5 years. The mean age at diagnosis was 11.6±4.5 years. There were more boys than girls (55 vs 39, 1:1.28).

Among them Enthesitis Related Arthritis (ERA) was the most prevalent subtype (39.4%), followed by Oligoarticular JIA (20.2%). Undifferentiated JIA accounted for 10.6% of the total cases.

The data also reveal a large proportion of HLA B27+ individuals develops axial disease early. It is our practice to perform imaging to look for SI joint involvement if there is any suggestive signs and symptoms. Among ERA (all were HLA B27+), 78% had sacroiliitis and 57% low back pain. 4 of the 10 undifferentiated JIA were HLA B27+, 2 had sacroiliitis. For the 13 patients who are still being managed by paediatricians, sacroiliitis are already established in 10 (77%). Taking together, an overwhelming proportion of paediatric patients had established axial involvement.

70.2% patients required treatment other than NSAIDs. DMARDs was used as 57.4%. Biologics was used in 20% . Despite the fact that many ERA had axial disease, biologic was prescribed in only 22% of them. This proportion is lower than other ERA cohorts[1].

72 of 94 (77%) patients still have rheumatology clinic FU at the end of the review period.

Category	Number (%)
Oligoarticular JIA	19 (20.2%)
Polyarticular RF negative JIA	10 (10.6%)
Polyarticular RF positive JIA	6 (6.4%)
Psoriatic arthritis	3 (3.2%)
Systemic JIA	9 (9.6%)
Undifferentiated JIA	10 (10.6%)
Enthesitis related arthritis	37 (39.4%)
Sacroiliitis	29 (78.4%)
Low Back Pain	21 (56.8%)
Treatment other than NSAIDs	66 (70.2%)
DMARDs	54 (57.4%)
Prednisolone	4 (4.3%)
Intra-articular steroid	8 (8.5%)
Biologics	18 (19.1%)

Discussion: In Hong Kong ERA is the most prevalent JIA subtype. A striking 78% develop sacroiliitis early in the course. This is somewhat different from what being suggested by a recent Taiwanese cohort, in which only 16% has sacroiliitis[2]. It was not mentioned in their study how SIJ was assessed. The possible difference in SIJ assessment may explain the discrepancy.

Biologics, instead of DMARDs, is indicated when the sacroiliitis fails to response to NSAIDs[3]. The finding of such a sizable number of sacroiliitis in ERA may have an impact on treatment algorithm and resource justification in the future.
Conclusion: ERA is the predominant JIA subtype in Hong Kong. Sacroiliitis development are common and probably early.
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Disclosure of Interest: None declared

P217

ENTHESITIS-RELATED ARTHRITIS: IS THERE A RELATIONSHIP BETWEEN STRUCTURAL HIP DAMAGE AND ULTRASOUND SYNOVITIS?

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Introduction: Juvenile idiopathic arthritis (JIA) includes all inflammatory joint damage starting before the age of 16, lasting more than or equal to 6 weeks and with no identifiable cause. Enthesitis-related arthritis (ERA) accounts for 15-20% of all JIAs. Hip involvement is particularly important in this disease as it represents a major functional prognostic factor.
Objectives: The objective of our study is to clarify the correlation between the presence of a structural hip damage on X-Ray and the presence of synovitis on hip ultrasound.
Methods: This is a monocentric retrospective study, 35 patients with ERA were enrolled (ILAR Criteria). We have identified the epidemiological, clinical and radiological characteristics. The damage of hip was assessed by the Bath Ankylosing Spondylitis Radiology Index hip (BASRI) score.
Results: Our study included 35 patients, 91,4% of whom were male. The average age at diagnosis was 13.08 years [6-16]. At the time of inclusion, 88, 5% of patients had coxitis, 77, 1% of which had bilateral coxitis. The median time to onset of coxitis from the onset of ERA was 0,2 years [0-3,4]. Nearly 60% of patients had destructive coxitis. The average BASRI was 2.57 [0.4]. The ultrasound performed in 17 patients had demonstrated synovitis in 6 cases (n = 6) and effusion in 3 cases. There was no statistically significant correlation between the BASRI Hip Score and hip synovitis (p = 0.053).
Conclusion: According to our study, there was no correlation between structural hip damage assessed by BASRI and ultrasound synovitis in ERA. These two examinations must be complementary and if necessary supplemented by an MRI in order to better document the involvement of the hip.
Disclosure of Interest: None declared

e-Poster viewing: Systemic JIA

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SPIDER BITE MIMICKING PYODERMA GANGRENOSUM IN SJIA: A CASE REPORT

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Introduction: Several paediatric patients manifest conditions commonly misdiagnosed as spider bites, which however, can include other arthropods bites; bacterial, viral, and mycotic infections; vasculitis; dermatological diseases; miscellaneous conditions as drug reactions, chemical injuries.
Objectives: In Italy, spiders which are likely to be associated with severe toxin mediated tissue damage are uncommon, especially in urban zones. However, a minor trauma may be a precipitating factor for pyoderma gangrenosum particularly over the legs, in association with inflammatory bowel disease, haematologic diseases and Juvenile Idiopathic Arthritis (JIA).
Methods: We describe a 11-years old boy with pyoderma gangrenosum complicated spider bite in association with systemic JIA (sJIA). The patient was in clinical remission after the start of the sJIA, occurred two months before, still treated with tapering doses of steroids and canakinumab, with the normalization of inflammatory parameters (CRP, ESR, SAA, ferritin) and clinical manifestations. Only a mild arthritis of the knee persisted and for this reason he was still treated with steroids. Furthermore, he developed hyperglycemia, requiring insulin treatment. The first dermatological manifestation which he referred was a red dot of the leg skin. In a few days, the erythema enlarged, involving an area of 7 x 7 cm, with oedema, pain, and blisters, evolving in a necrotic lesion, with purulent exudate, surrounded by a haemorrhagic zone.

Results: Haematological controls revealed neutrophilic leucocytosis, increased CRP and procalcitonin. He started treatment with intra venous administration of teicoplanin plus ceftriaxone, with no resolution of the clinical manifestations and the reduction of leukocytosis, CRP, procalcitonin.
A culture swab was performed and was positive for Pseudomonas Aeruginosa, confirmed by PCR on the culture. He started ciprofloxacin and surgical curettage of the lesion, with the resolution of the lesion and the normalization of biochemical parameters.
Conclusion: The aspect of the lesion and its evolution were evocative of a spider bite suggested by anamnestic records, complicated by a pyoderma gangrenosum secondary to Pseudomonas Aeruginosa. The underlying disease, the immune suppressive treatment, with steroids and biological drugs, the hyperglycaemic pattern of the patient allowed the severe evolution of the spider bite.
Children in treatment with immune suppressive and/or biologic drugs are at high risk of infections. Skin lesions, as arthropods bites, can be a facility for superinfection, with possible haematological and systemic diffusion.
Disclosure of Interest: None declared

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APPLICATION OF PRELIMINARY PRINTO CLASSIFICATION CRITERIA FOR SJIA IN AN INDIAN COHORT

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Introduction:
The strict application of the ILAR[1] requirement for the presence of documented arthritis for the diagnosis of sJIA, early in the disease course, may result in unnecessary delays in initiating appropriate treatment. In preliminary PRINTO[2] classification criteria for sJIA, this mandatory requirement of documented arthritis has been modified.

Objectives:
To measure performance of preliminary PRINTO classification criteria for sJIA in our Indian cohort.

Methods:
I gathered a data of seven sJIA patients who attended dev children's hospital between Jan 2019 and Jan 2020. My data included demographics,clinical presentation, laboratory parameters and outcome of these patients. All these patients were diagnosed at an early stage by clinical judgement irrespective of fulfilment of ILAR criteria. I applied preliminary PRINTO classification criteria for all.

Results:
Average age of selected children (4 girls and 3 boys) was 5.1 years.
Table 1 showed performance of preliminary PRINTO classification criteria for sJIA in our cohort

sJIA	Preliminary PRINTO Classification Criteria	No of patients fulfilled respective criteria N (total=7) (%)
Mandatory criterion	**Fever** of unknown origin that is documented to be daily , **quotidian**; fever that rises >/= 39 C once a day and returns to	7 (**100%**) at diagnosis
Major criteria	***1.Evanescent (nonfixed) erythematous rash*** ***2.Arthritis***	*6 (**86%**) at diagnosis* *2 (**28%**) at diagnosis* *4 (57%) within 4 months of diagnosis*
Minor Criteria	1.Generalized lymph node enlargement and/or hepatomegaly and/or splenomegaly 2.Serositis 3.Arthralgia lasting 2 weeks or longer (in absence of arthritis) ***4.Leukocytosis*** (>/= 15,000/mm3) with neutrophillia	3 (43%) at diagnosis 3 (43%) at diagnosis 3 (43%) at diagnosis 7 **(100%)** at diagnosis
Exclusions(ruled out in our cohort)	**EBV** Neoplastic conditions Autoimmune conditions Monogenic auto-inflammatory condition- **CAPS** **PID**	**3 (43%)** 2 (28%) 2 (28%) **3 (43%)** 1 (14%)
Common laboratory parameters	***Anaemia of chronic disease (age matched)*** ***Platelet count (> 5 lakhs/ul)*** ***ESR (>80mm/hr)*** ***CRP (>60mg/L)*** Ferritin (>500ug/dl)	***7 (100%)*** ***5 (71%)*** ***5 (71%)*** ***6 (86%)*** 2 (28%)
Medicines used in our cohort	Oral Naproxen with oral steroids SC Methotrexate IV Methylprednisolone IV Tocilizumab	7 (100%) 5 (71%) 1 (14%) 2(14%)

	IV Ig (in one case of suspected incomplete KD)	1 (14%)
Final Outcome	Death (due to MAS) Monocylic course Chronic persistent course	1 (14%) 2 (28%) 4 (57%)

(Abbreviations: PRINTO: Paediatric Rheumatology INterrnational Trail Organization, sJIA: systemic juvenile idiopathic arthritis, ILAR: International League of Associations for Rheumatology, EBV: Epstein-Barr-virus, CAPS: Cryopyrin Associated Periodic Syndromes, KD: Kawasaki Disease, MAS: Macrophage Activation Syndrome, PID: Primary Immunodeficiency Disease)

Conclusion:

A preliminary PRINTO classification criteria for sJIA has been validated in our cohort. There are many raised inflammatory markers in most of these patients other than WBC count. These markers should be considered to be added in supportive laboratory criteria to be more specific towards the diagnosis. It is important to add PID in exclusion list especially in a case of sJIA with MAS at onset.[3]

Trial registration identifying number:

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Disclosure of Interest: None declared

P220

ALLOGENIC HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR REFRACTORY CHILDHOOD RHEUMATIC DISEASES

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Introduction: Patients with refractory rheumatic diseases face poor quality of life, long-term sequelae and life-threatening complications. With advances in allogenic hematopoietic stem cell transplantation (allo-HSCT), this procedure becomes an interesting therapeutic option, allowing patients to achieve complete remission (CR) and withdrawal of most medications.
Objectives: Report two cases of allo-HSCT performed in children with refractory rheumatic diseases at a tertiary care paediatric hospital since 2017.
Methods: Patients' demographics, disease course, allo-HSCT course and outcome are described. A review of the literature was performed, and clinical outcomes were compared to our local experience. Patients/parental consent was obtained from both subjects.
Results: Two patients with systemic-onset juvenile idiopathic arthritis (sJIA) underwent allo-HSCT. Patients' characteristics are shown in Table 1. Both had failed multiple lines of immunosuppressive treatments and experienced severe disease and treatment-related complications. Both experienced early complications following HSCT but recovered without major sequelae. Patient 1 is in CR off all immunosuppressive medications at 2.6 years post-HSCT. Patient 2 experienced a disease flare at 11 months post-HSCT. He received one pulse of methylprednisolone and was started on tofacitinib. At 1.3 years post-HSCT, he is now in CR on tofacitinib monotherapy, which represents a significant improvement from his pre-HSCT status. Engraftment was excellent with most recent chimerism at 100% (2.6 years post-HSCT) and 95% (1.1 years post HSCT), for Patient 1 and 2, respectively. Allo-HSCT is reported as a treatment option in very few paediatric JIA patients. In a recently described cohort of 16 JIA patients who underwent allo-HSCT (11/16 had sJIA), CR was achieved in 90% and 9% had transplantation-related mortality (TRM) (median follow-up 2.4 [range 0.2-8.0] years) [1].
Table 1 sJIA patients characteristics and evolution post-HSCT

	Patient 1	Patient 2
Sex	F	M
Refractory disease manifestations	Fever, polyarthritis, MAS	Fever, polyarthritis
Previous medications	NSAID, Corticosteroids, Methotrexate, Tocilizumab, Anakinra, Canakinumab, Cyclosporine, Tofacitinib.	NSAID, Corticosteroids, Methotrexate, Tocilizumab, Canakinumab, Infliximab, Tofacitinib, Siltuximab
Age at HSCT, years	5	8
Disease duration at HSCT, years	2	3
Donor type	MUD	MRD
Time to stop IS post-HSCT, months	14	Ongoing
Disease outcome (years post-HSCT)	CR off IS (2.6)	Relapsed at 11 months; CR on Tofacitinib (1.3)

F: Female; IS: Immunosuppression; M: Male; MAS: Macrophage Activation Syndrome; MRD: Matched-Related Donor; MUD: Matched Unrelated Donor; NSAID: Non Steroidal Anti-Inflammatory Drugs
Conclusion: Allo-HSCT should be considered as an alternative therapeutic option early in the course of severe paediatric rheumatic diseases refractory to conventional treatments as it is currently the only curative treatment. The decision to proceed to allo-HSCT should not be delayed since it increases TRM, and allo-HSCT does not correct disease and treatment's sequelae. With current TRM rates < 10 %, allo-HSCT should be considered sooner after failure of conventional lines of treatment, and not only in patients with no other therapeutic options. Our data may suggest that full donor chimerism is necessary in some patients to maintain CR off immunosuppression.
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Disclosure of Interest: None declared

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THE ROLE OF INTRA-ARTICULAR GLUCOCORTICOID INJECTIONS (IAGI) IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS (SJIA): A SINGLE CENTER EXPERIENCE

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Introduction: IAGI are a safe and widespread treatment option in patients with JIA. Little is known about the benefits of IAGI in sJIA

Objectives: The aim of the study is to explore whether IAGI can spare the amount of systemic glucocorticoids (GC) in achieving remission of arthritis in sJIA

Methods: Records of patients with sJIA at the study center were retrospectively reviewed. All sJIA patients at their first assessment of arthritis (baseline) and treated with systemic GC (with or without c/bDMARDs) were included and divided into two groups: group A comprised children who were also treated with IAGI within the first five months of arthritis occurrence; group B the others. Patients with disease onset before 2015 or treated for more than 3 months before accessing to the study center were excluded. Demographic and clinical features, administration of intravenous (IV) GC pulses from baseline to six months from arthritis occurrence (T6), total amount of systemic GC (mg/kg), remission of arthritis and achievement of clinical inactive disease (CID, according to Wallace criteria) at T6 were registered and compared in the two groups

Results: From a total of 23 sJIA patients at first assessment of arthritis at the study center, 11 were excluded because of treatment before 2015 (n=2), treatment for more than 3 months before coming at the study center (n=6), no systemic GC (n=2) or follow-up less than six months from IAGI (n=1). Twelve patients were included in the study. In group A (n=6, F 83.3%) IAGI was performed in a median of 3.8 months (range 1.6-4.9) from baseline, with a median of 12 injected sites/IAGI procedure (range 2-26), including 30 large joints, 19 small joints and 24 tendon sheaths. Triamcinolone hexacetonide and methylprednisolone acetate were injected in large joints and small joints+tendon sheaths, respectively. Children in group B (n=6, F 33.3%) presented arthritis of large joints (2 wrists, 2 knees, 1 ankle, 1 elbow). In both groups 4/6 (66.7%) patients received IV GC pulses from baseline to T6. Table 1 shows demographic features at baseline and clinical assessment at T6 of the two groups

Table 1. Demographic features at baseline and clinical assessment at T6 in sJIA patients with arthritis.

	Group A (IAGI; N=6)	**Group B (No IAGI; N=6)**
Age at baseline, years*, median (range)*	3.5 (1.0-7.9)	7.4 (0.8-15.1)
Concomitant systemic treatment at baseline*, n (%)*	3 (50.0)	5 (83.3)
Systemic treatment (apart from GC) baseline-T6*, n (%)*	6 (100)	6 (100)
Systemic GC baseline-T6*, n (%)*	5 (83.3)	6 (100)
Cumulative systemic GC baseline-T6 (mg/Kg)*, median (range)*	54 (21-147)	102 (54 -200)
Triamcinolone hexacetonide (mg/kg)*, median (range)*	2.7 (1.1-6.7)	-
Methylprednisolone acetate (mg/kg)*, median (range)*	4.8 (1.1-8.0)	-
Remission of arthritis at T6*, n (%)*	5 (83.3)	6 (100)
CID at T6*, n (%)*	4 (66.7)	5 (83.3)

Conclusion: Our study represents the first attempt to define the role of IAGI in children with sJIA. Despite a clear trend in sparing systemic GC in achieving remission in children with sJIA treated also with IAGI, our results highlight the complexity of sJIA features presentation and treatment. This limits the possibility of comparing the therapeutic strategies in our cohort. Nonetheless, IAGI appear to represent an efficacious option in sJIA, particularly in those patients with widespread articular involvement. Prospective randomized studies may further explore this benefit

Disclosure of Interest: None declared

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COXARTHROSIS RISK FACTORS IN SYSTEMIC AND NON-SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS.

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Introduction: Hip involvement in juvenile idiopathic arthritis (JIA) is an alarming sign for patients and physicians. It can lead to coxarthrosis (CA), severe loss of function and decreased quality of life, and may require total hip arthroplasty (THA).
Objectives: To compare the frequency of hip involvement, progression to CA and a requirement for THA in patients with systemic and non-systemic JIA categories.
Methods: 753 JIA patients aged 2 to 17 years included in the retrospective study. JIA was diagnosed by ILAR criteria. Patients divided into two groups: systemic-onset JIA (n=58) and non-systemic, included other JIA categories (n=695). We compared demographic and clinical data, frequency and character of hip damage (coxitis, CA and THA), and treatment regimens too, especially, corticosteroid (CS) administration.
Results: the data presented in table 1. Patients with soJIA developed CA earlier than non-systemic 13.7 (9.5; 15.4) vs 15.2 (13.5; 16.4) years (p=0.045). There were no differences in time to CA (4.5 vs 5.1 years, p=0.956), time to THA (7.4 vs 9.5 years, p=0.571) and time since CA to THA (2.1 vs 1.1 years, p=1.0). Patients with soJIA had more markers of inflammation (ESR, CRP, PLT, WBC) and lower Ca (2.35 vs 2.4 mmol/l, p=0.006) and 25OHD (14.0 vs 19.0 ng/ml, p=0.039). Systemic JIA increased the cumulative probability of CA development in Cox-regression model: RR=2.7 (1.4; 5.4), p=0.009. For whole studied population CS per os (PO) (p=0.008), pulse-therapy with CS (p=0.012), cumulative doses of CS (p=0.023), WBC (p=0.044), soJIA (p=0.007) and delayed hip involvement (p=0.00002) were predictors of CA in univariate regression analysis. In multiple regression analyses only delayed hip involvement (p=0.023) and cumulative doses of CS>2700 mg (p=0.02) were independent risk factors of CA development. In logistic regression delayed hip involvement (OR=4.9 [95%CI: 1.2; 20.4], p=0.027) and cumulative doses of CS>2700 mg (OR=5.7 [95%CI: 1.2; 27.9], p=0.025) increase the risk of CA development. Patients with systemic and non-systemic JIA had different risk factors of coxarthrosis: onset age (p=0.049), CS PO (p=0.033), CS pulse-therapy (p=0.023), CS>2700 mg (p=0.025) and WBC (p=0.013) were risk factors in systemic JIA; alkaline phosphatase (AP) (p=0.013), CS PO (p=0.047), CS pulse-therapy (p=0.026), CS>2700 mg (p=0.01) were risk factors in non-systemic JIA. In discriminant analysis only CS>2700 mg (p=0.008) and WBC (p=0.024) were CA predictors in systemic JIA and calcium (p=0.026), AP (p=0.019), CS PO (p=0.041), CS pulse-therapy (p=0.031), CS>2700 mg (p=0.012) were risk factors in non-systemic JIA.

Investigated parameters	soJIA, n=58	non-systemic JIA, n=695	p-value
JIA onset age, years	4.3 (2.6-7.3)	6.15 (3.0-10.5)	0.022
Any hip involvement, n (%): Coxitis CA	19 (32.8) 8 (13.8) 11 (19.0)	134 (19.3) 97 (14.0) 37 (5.3)	0.015 <0.001
THA, n (%)	5 (8.6)	16 (2.3)	0.005
Delayed hip involvement, n (%)	11/19 (57,9)	41/134 (30,6)	0,019
CS, PO, n (%)	47 (81)	105/694 (15,1)	0,000001
Pulse-therapy of CS, n (%)	46/57 (80,7)	89/693 (12,8)	0.000001
Total CS, mg	3085 (1500-7000)	2000 (750-4500)	0,005

Conclusion: to avoid coxarthrosis development required excluded corticosteroids as well as possible or applied steroid-sparing agents, e.g., biologics, especially in soJIA.
Trial registration identifying number: This work supported by the Russian Foundation for Basic Research (grant № 18-515-57001).
Disclosure of Interest: None declared

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DRUG SURVIVAL FOR IL-1 INHIBITOR CANAKINUMAB: DATA FROM A SINGLE-CENTER OBSERVATION

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Introduction: The efficacy of canakinumab for treatment patients with systemic juvenile idiopathic arthirtis (sJIA) was demonstrated before. Our aims was to describe canakinumab drug survival based on data from a single-center observation.
Objectives: To analyze the drug survival of canakinumab in patients with sJIA treated at the National Medical Research Center of Children`s health, Moscow, Russia.
Methods: Medical records from sJIA patients treated with canakinumab (CAN) were analyzed retrospectively from the National Medical Research Center of Children`s health, Moscow, Russia.
Results: Seventy-four patients presenting with sJIA were included in this observation, with a median age at treatment initiation of 8,2 (interquartile range, IQR 3,9 -12.7) years and a median disease duration of 5,3 (IQR 2,9-10,7) years. Most patients (66/74) had been treated previously with one or more biologic agents for sJIA, 44/74 patients have received cDMARDs. As of 30 March of 2020, the median time of follow up was 97,3 (37,4-153,8) months, with all patients being followed for at least 6 months. The most patients (66/74) were previously treated with other biologic drugs. Eleven (11/74) patients stopped treatment with canakinumab, three of them - because of achievement of remission. Two patient stopped treatment within 6 months from therapy start: due to primary inefficiency (1) and allergic reaction (1). Five (5/11) patients were-co-administered with cDMARDs, other 5 – with oral GC, and 6 subjects had been previously exposed to other biologic drugs. Whole 5 patients stopped therapy due to secondary inefficiency: 2 patients were switched on TOC, other children were switched on ETA (1), RIT (1), ADA (1). There were 1 death recorded because of MAS, not associated with receiving CAN.
Conclusion: Our results have shown an excellent survival of the IL-1 inhibitor CAN. Survival was not affected by the concomitant use of cDMARDs. These data underline the effectiveness of CAN in sJIA patients as monotherapy.
Disclosure of Interest: E. Krekhova: None declared, E. Alexeeva Speaker Bureau of: Novartis, Pfizer, Sanofi, MSD and Roche, T. Dvoryakovskaya Speaker Bureau of: Novartis, Pfizer, MSD and Roche, A. Mamutova Speaker Bureau of: Novartis, K. Isayeva: None declared, R. Denisova Speaker Bureau of: Novartis, MSD and Roche, A. Chomahidze: None declared, A. Fetisova: None declared, O. Lomakina: None declared, K. Chibisova: None declared, M. Gautier: None declared, D. Vankova: None declared, I. Kriulin: None declared, M. Shingarova: None declared

P224
THE SHARE RECOMMENDATIONS ON DIAGNOSIS AND TREATMENT OF SYSTEMIC JIA

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Introduction: Systemic juvenile idiopathic arthritis (sJIA) is a rare, complex auto-inflammatory disease with significant morbidity including fever, rash, serositis and articular problems. With the availability of interleukin-1 (IL-1) and IL-6 inhibitor treatment, morbidity has significantly reduced and the outcome for sJIA patients has improved. However, differences in access to care and differences in treatment strategies between countries in and outside of Europe remain a concern.
Objectives: The Single Hub and Access point for paediatric Rheumatology in Europe (SHARE) consortium aimed to develop best practices for paediatric rheumatic diseases in order to decrease differences in care between European countries. Here, we present the final results of the literature review and a series of consensus meetings on defining overarching, diagnostic and therapeutic recommendations for diagnosis and treatment of sJIA.
Methods: The SHARE methodology has been previously published, including the use of the EULAR standardized operating procedure for developing best practice recommendations. As per these guidelines, a methodologist provided supervision during the process and consensus meetings.
A systematic literature search of Medline, Embase and Cochrane databases was performed in 2013 and again in November 2019. Results were used to develop and support recommendations on diagnosis, treatment and complications of systemic JIA. These recommendations were presented in an online survey to a task-force of expert paediatric rheumatologists to assess potential agreement and enable rewording. The participating experts convened in 3 consensus meetings (Genoa 2014, Barcelona 2015 and Utrecht 2020) to develop the recommendations. Making use of the Nominal Group Technique, recommendations were proposed, discussed and voted on. Recommendations that reached ≥80% were accepted.
Results: The 2-step systematic literature review included 98 papers on sJIA. Quality and grade of evidence was assessed and a categorized overview was used as backbone during the consensus meeting. In total, 15 recommendations were developed and accepted: 4 overarching principles, 3 diagnostic recommendations and 8 recommendations on management of sJIA and its complications. Recommendations were presented with accompanying level of evidence (LoE), strength of recommendation (SoR) and percentage of agreement (PoA). In addition, adherence to the 2018 EULAR Treat-to-Target principles on JIA was confirmed by the expert panel.
Conclusion: These SHARE best practice recommendations for sJIA are based on the best available evidence and expert opinion, and provide guidance for the diagnosis and management of sJIA, aiming to improve the outcome for all sJIA patients in Europe and beyond.
Disclosure of Interest: A. Leek: None declared, J. Anton Consultant for: SOBI, Roche, Novartis, Speaker Bureau of: SOBI, Roche, Novartis, T. Avcin Consultant for: AbbVie, Octapharma, Takeda, Alexion, F. De Benedetti Consultant for: Institutional grants from Abbvie, SOBI, Novimmune, Novartis, Roche, Pfizer, Abbvie, SOBI, Novimmune, Novartis, Roche, Pfizer, Employee of: Family member SOBI employee, V. Boom: None declared, C. Bracaglia Consultant for: SOBI and Novartis , P. Brogan Consultant for: SOBI, Roche, Novartis; UCB, institutional grants from SOBI, Roche, Novartis, A. Consolaro

Speaker Bureau of: AbbVie, T. Constantin: None declared, P. Dolezalova Consultant for: SOBI, Novartis, Sanofi Genzyme, D. Eleftheriou: None declared, H. Foster Consultant for: Unrestricted educational grants from Pfizer, SOBI, Sanofi-Genzyme, C. Hinze Consultant for: Novartis, I. Kone-Paut: None declared, K. Minden Consultant for: Abbvie, Sanofi, gsk, Roche, F. Minoa Consultant for: SOBI, P. Quartier Consultant for: consultancy or speaking fees from AbbVie, Bristol-Myers Squibb, Chugai-Roche, Lilly, Novartis, Novimmune, and Swedish Orphan Biovitrum, A. Ravelli Consultant for: SOBI, Novartis and Roche, N. Ruperto Consultant for: consultancy or speakers fee from: Ablynx, Astrazeneca-Medimmune, Aurinia, Biogen, Boehringer, Bristol Myers and Squibb, Centrical Global, Domain Therapeutics, Eli-Lilly, EMD Serono, Glaxo Smith and Kline, Hoffmann-La Roche, Idorsia, Janssen, Merck, Novartis, Pfizer, R-Pharma, Sanofi, Servier, Sinergie, and Sobi, J. Swart Paid Instructor for: SOBI, Y. Uziel Speaker Bureau of: Pfizer, Abbvie, H. Wittkowski Speaker Bureau of: Novartis, Shire/Takeda and CSL-Behring, C. Wouters Consultant for: institutional grants from Roche, Novartis, Sobi, GSK, M. Zajc Avramovitz: None declared, N. Wulffraat Consultant for: SOBI, Novartis, Roche, institutional grants from SOBI , S. Vastert Consultant for: SOBI, Novartis, unrestricted institutional grant SOBI

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EFFECT OF DOSE AND DURATION OF GLUCOCORTICOID TREATMENT ON PROGNOSIS OF SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Systemic Juvenile idiopathic arthritis(SJIA) is characterised with high level of inflammation, high disease activity, and risk of development of macrophage activation syndrome that is high life threatening condution. Due to all of these reasons,the rate of glucocorticoid usage is very higher in SJIA than other JIA subtypes. Although the cessation of glucocorticoid was recommended as soon as possible, there is no consensus on the duration and dosage of glucocorticoid treatment.
Objectives: We aimed to investigate to effect of dose and duration of glucocorticoid treatment on SJIA disease prognosis.
Methods: Forty two patients diagnosed with SJIA and had duration of disease upper than 2 years were involved in this study. Demographic, clinic, laboratory data, and treatments were collected from patients records. Affecting factors which were patients clinical, labaratory findings, treatment options, dose and duration of steroid treatments were evaluated on the duration of achieving remission period (period of active disease) and duration of remission period with cox regression analysis.
Results: Half of patients had monophasic course. **Age at diagnosis**; HR(95% CI):1,095 (1,006-1,192),p: 0,036, **platelet values;** HR (95% CI): 0,997 (0,995-0,999), p: 0,008, **duration of steroid treatment**;HR (95% CI): 0,837 (0,754-0,929),p: 0,001 were determined as risk factors on duration of achieving remission period (period of active disease) with multivariate cox regression analysis (table). There was no determined risk factors on duration of remission period.

Table. Factors Affecting on the Duration of Achieving Remission Period

Variables	**Univariate Cox Regression**			**Multivariate Cox Regression***	
	n	**HR (95% CI)**	**p**	**HR (95% CI)**	**p**
Age at diagnosis	42	1,098 (1,015-1,188)	**0,019**	1,095 (1,006-1,192)	**0,036**
Gender	42	0,986 (0,530-1,835)	0,965		
Features at first flare					
Fever	42	1,460 (0,556-3,830)	0,442		
Serositis	25	1,594 (0,846-3,001)	0,149		
Rash	23	0,644 (0,223-1,864)	0,417		
Joint involvement	38	0,440 (0,189-1,026)	0,057		
Morning stiffness	39	1,603 (0,653-3,936)	0,303		
Lymphadenopathy	96	2,099 (0,963-4,574)	0,062		
Hepatosplenomegaly	61	1,108 (0,578-2,125)	0,757		
Macrophage activating syndrome	10	0,846 (0,648-1,105)	0,219		
Patient/parent VAS	14	1,002 (0,777-1,293)	0,987		
PGA	42				
Laboratory parameters at first flare					
HGB (g/dL)	42	0,885 (0,677-1,158)	0,374		
WBC (/µL)	42	1,000 (1,000-1,000)	0,407	0,997 (0,995-0,999)	**0,008**
PLT (/µL)	42	0,998 (0,997-1,000)			
ESR (mm/h)		1,000 (0,991-1,008)			
CRP (mg/L)		1,000 (0,995-1,006)			

AST (U/L) ALT (U/L) BUN (mg/dL) Creatinine (mg/dL) Ferritin (ng/mL) Fibrinojen (mg/dL) LDH (U/L) Trigliserid (mg/dL)	4 2 4 2 4 2 4 2 4 2 2 4 1 7 2 7 1 7	1,001 (0,998-1,005) 1,002 (0,999-1,005) 1,014 (0,945-1,089) 1,133 (0,429-2,992) 1,000(1,000-1,000) 1,001 (0,997-1,004) 1,000 (0,999-1,001) 1,000 (0,998-1,002)	**0,02 8** 0,92 5 0,89 2 0,47 1 0,13 4 0,69 4 0,80 2 0,66 2 0,71 1 0,92 4 0,99 9		
Treatments at the first flare					
PMP treatment Oral steroid DMARDs Biologic drugs Dosage of corticosteroid treatment (g/m^2) Duration of corticosteroid treatment (months)	1 5 4 0 3 1 7 4 0 4 0	0,561 (0,282-1,115) 1,295 (0,308-5,444) 0,761 (0,367-1,579) 0,552 (0,243-1,261) 0,890 (0,808-0,980) 0,894 (0,824-0,970)	0,09 9 0,72 4 0,46 4 0,15 9 **0,01 8** **0,00 7**	**-** 0,837 (0,754-0,929)	**- 0,00 1**
*Age at diagnosis, PLT values, dose of corticosteroid treatment and duration of corticosteroid treatment were assessed in multiple cox regression PMP, pulse methylprednisolone; DMARDs, disease modifying anti-rheumatic drugs					

Conclusion: In our preliminary study showed that duration and dose of glucocorticoid treatment did not change prognosis and disease course. The best dose and duration of the treatment should be evaluated further studies.

Disclosure of Interest: None declared

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PERFORMANCE OF THE "MS-SCORE" AND "HSCORE" IN THE DIAGNOSIS OF MAS IN SYSTEMIC JIA PATIENTS

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Introduction: Macrophage activation syndrome (MAS) is a very devistating complication of Systemic JIA (sJIA), seen in approximately 15-25% of the sJIA patients. There are many tools to differentiate activation of sJIA and MAS including HScore and the recently proposed MS-score. This is the first study comparing MS-score and HScore in sJIA.
Objectives: We aimed to compare the performances of MS-score[1]and HScore[2]for the diagnosis of MAS in sJIA patients
Methods: Systemic JIA patients followed at Hacettepe University Pediatric Rheumatology Department were included in the study. Clinical features and laboratory findings at the time when patients were most active or diagnosed as MAS were recorded retrospectively. HScore and MS-score were calculated respectively and the diagnostic capacity of MAS was compared by means of receiver operating characteristic (ROC) curve analysis.
Results: Seventy-one sJIA patients were included (23 MAS, 48 activation). There was no difference in the age of onset (median 4.7 vs 5.0) and gender (73.9% vs 54.2%) between patients who had MAS and sJIA activation. There was no significant difference in the frequency of fever, rash and LAP between the two groups, but the frequency of fever ≥39.4^{o}C was higher in the MAS group. Hepatomegaly, splenomegaly, central nervous system involvement, haemorrhagic manifestations, and hemophagocytosis in the bone marrow were also common in the MAS group, while the presence of active arthritis and the number of affected joints were higher in the sJIA activation group. Hemoglobin, white blood cell count, platelet count, fibrinogen, erythrocyte sedimentation rates were lower; ALT, AST, LDH, triglyceride and ferritin were higher in the MAS group as expected. There was no significant difference in C-reactive protein levels between two groups. While 47.8% of MAS patients required intensive care hospitalization, this rate was 6.5% in patients who had disease activation. Although there was no significant difference between two groups in terms of mean intensive care stay (11.7±12.3 vs 8±4.2 days; p=0.23), the total duration of hospital stay was longer in the MAS group (25.9±17.9 vs 10.1±8.6 days; p<0.0001). The most common disease course in both the MAS group and the activation group was monocyclic disease (43.5% vs. 45.8%). Polycyclic course was observed more frequently in MAS group (43.5% vs 10.4%), polyarticular course was more common in activation group (13% vs 43.8%).
MS-score (median [range] 1.8 [(-5.7)-(9.3)] vs (-4.0) [(-7.2)-(3.8)] p<0.0001) and HScore (median [range] 241 [51-337] vs 51 [18-202] p<0.0001) were higher in the MAS group. ROC curve analysis revealed that HScore performed slightly better in diagnosing MAS, compared with MS-score (AUC=0.965 and 0.901 for HScore and MS-score repectively, P<0.001). In our cohort, MS score≥-1.64 yielded a sensitivity of 91.3% and a specificity of 83.8%; HScore≥162.5 yielded a sensitivity of 91.3% and specificity of 90.2%.
Conclusion: HScore seems to perform slightly better than MS-score for the diagnosis of MAS in our cohort.
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Disclosure of Interest: None declared

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A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF ANAKINRA IN PEDIATRIC AND ADULT PATIENTS WITH STILL'S DISEASE

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Introduction: Still's disease, including both systemic juvenile idiopathic arthritis (SJIA) and adult-onset Still's disease (AOSD), is a rare systemic auto-inflammatory disorder associated with an activated IL-1 pathway.
Objectives: To build on earlier evidence and evaluate in a controlled setting the efficacy and safety of anakinra, an IL-1 receptor antagonist, in patients with active, newly diagnosed Still's disease across all age groups.
Methods: The anaSTILLs study (anakinra in Still's disease) was a randomized, double-blind, placebo-controlled, 12-week study including patients with active and newly diagnosed Still's disease (adapted ILAR criteria if <16 years of age, Yamaguchi criteria if ≥16 years of age at disease onset). Patients were randomized to anakinra 2 mg/kg (max 100 mg/day), 4 mg/kg (max 200 mg/day) or placebo. The primary objective was to demonstrate the efficacy of anakinra versus placebo as assessed by ACR30 response with an absence of fever at Week 2. Secondary objectives included: early onset of efficacy, sustained efficacy, time to study drug discontinuation, safety, pharmacokinetics (PK), clinical signs and biomarkers.
Results: Twelve patients were randomized and received study treatment: 6 to anakinra (2 mg/kg n=2, 4 mg/kg n=4) and 6 to placebo. Due to slow recruitment the study was terminated early. One patient was excluded from the efficacy analyses since he/she was later diagnosed with lymphoma, not Still's disease. 11 patients were analyzed for efficacy (anakinra n=6, placebo n=5), 8 children (median [range] age=4.0 [1-11] years) and 3 adults (median [range] age=32.0 [25-51] years). 55% were male and the mean (range) symptom duration was 74.2 (12-222) days. All patients on anakinra but none on placebo achieved ACR30 response with absence of fever at Week 2 (p-value=0.0022). The efficacy of anakinra was supported by superiority to placebo in ACR50/70/90 responses with absence of fever at Week 2. All placebo patients discontinued the study within 6 weeks, 2 due to progressive disease, 2 due to lack of efficacy and 1 due to withdrawal by the patient. A numerically greater proportion of patients in the anakinra group had early onset of efficacy (Week 1) compared to placebo, as assessed by ACR30. ACR30/50/70/90 responses in anakinra-treated patients were sustained throughout the study period. No unexpected safety findings were observed. Based on serum anakinra concentrations Week 12, Cmax was 2920 ng/mL at 4.0 hours (dose: 4.1 mg/kg) in a 1-year-old patient, and Cmax was 1060 ng/mL at 2.1 hours (dose: 1.5 mg/kg) in a 6-year-old patient.

ACR response with absence of fever at Week 2

Primary & secondary endpoints	Response (Anakinra) n (%) N=6	Response (Placebo) n (%) N=5	Difference (Anakinra-Placebo)	95% exact CI for difference	Fisher's exact test p-value
ACR30*	6 (100.0)	0 (0.0)	1.00	0.42, 1.00	0.0022
ACR50*	6 (100.0)	0 (0.0)	1.00	0.42, 1.00	0.0022
ACR70*	6 (100.0)	0 (0.0)	1.00	0.42, 1.00	0.0022
ACR90*	5 (83.3)	0 (0.0)	0.83	0.24, 1.00	0.0152

*With absence of fever at Week 2

Conclusion: Anakinra is superior to placebo in the treatment of Still's disease. The safety and PK results are consistent with previous anakinra experience. These results confirm the benefits of anakinra treatment in patients with active, newly diagnosed Still's disease across ages.
Trial registration identifying number: NCT03265132
Disclosure of Interest: L. Schanberg Consultant for: Sobi, P. Nigrovic Consultant for: Novartis, BMS, Pfizer, Sobi, Miach Orthopedics, Simcere, XBiotech, Quench Bio, Siglion, Cerecor, A. Cooper: None declared, W. Chatham Consultant for: Sobi, S. Akoghlanian: None declared, N. Singh: None declared, E. Rabinovich: None declared, A. Thatayatikom: None declared, A. Taxter: None declared, J. Hausmann Consultant for: Novartis , M. Zdravkovic Shareholder of: Sobi, Employee of: Sobi, S. Ohlman Shareholder of: Sobi, Employee of: Former employee of Sobi, H. Andersson Employee of: Sobi, S. Cederholm Shareholder of: Sobi, Employee of: Sobi, G. Huledal Employee of: Sobi, R. Schneider Consultant for: Novartis, Novimmune, Sobi, F. De Benedetti Speaker Bureau of: AbbVie, Novartis, Roche and Sobi

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CANAKINUMAB AS FIRST- OR SECOND-LINE DMARD IN SYSTEMIC-ONSET JUVENILE IDIOPATHIC ARTHRITIS (SJIA) - DATA FROM THE GERMAN BIKER REGISTRY

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Introduction:
Early inhibition of IL-1 is discussed to play an important role in the disease course of sJIA[1]. Assuming that pretreatment with other DMARDs leads to a later start of therapy with canakinumab, this analysis evaluates the effectiveness of canakinumab as first-line vs. second-line DMARD.

Objectives:
To evaluate the effectiveness of canakinumab as first used biological DMARD in sJIA compared to canakinumab in sJIA-patients pretreated with other DMARDs.

Methods:
SJIA-patients documented in the German Biologic Registry for Pediatric Rheumatology (BiKeR), who were exposed to canakinumab, were identified. For the first-line (FL) group DMARD naïve patients were selected, prior treatment with corticosteroids and/or NSAIDs was allowed. Patients receiving any DMARD prior to canakinumab entered the second-line (SL) group. Both groups were compared in a retrospective intention-to-treat-analysis. Effectiveness was determined by analyzing JIA American College of Rheumatology (ACR) Inactive Disease (defined by Wallace et al.[2]), 10-joint Juvenile Arthritis Disease Activity Score Remission (JADAS-10-Remission) and JADAS-10-Minimal Disease Activity (-MDA). Safety was analyzed based on adverse event (AE) reports.

Results:
Altogether 60 patients with sJIA were included, 13 patients (21.7%) in the FL-group, 47 (78.3%) in the SL-group. Mean disease duration until baseline was 10.3±22.9 months in the FL- and 35.7±46.7 months in the SL-group (p=0.0647). Patients in the FL-group had significantly higher scores for CRP (FL 76.7±56.8 mg/l, SL 27.2±46.5 mg/l, p=0.002) and JADAS-10-mean (FL 17.7±7.0, SL 10.5±8.5, p=0.0073) at baseline than patients in the SL-group. In both groups a significant improvement in the number of patients reaching JADAS-10-MDA, JADAS-10-Remission and ACR-Inactive-Disease was achieved from month 0 to month 3. Significantly more patients in the FL-group reached ACR-Inactive-Disease (FL 81.8%, SL 40.0%, p=0.0351) at month 6 than in the SL-group. 122 adverse events (AE) were reported, 22 of them were serious (SAEs). Most events were classified as infections and infestations (49 AEs, 5 SAEs).

		First Line (n=13)	Second Line (n=47)	P-Value
ACR-Inactive Disease, n (%)	Mo 0	0 (0.0)	7 (14.9)	0.3288
	Mo 3	6 (60.0)	18 (64.3)	1.000
	Mo 6	9 (81.8)	14 (40.0)	0.0351
JADAS-10-Remission, n (%)	Mo 0	0 (0.0)	11 (23.4)	0.0998
	Mo 3	8 (80.0)	16 (57.1)	0.2685
	Mo 6	9 (81.8)	17 (48.6)	0.0821

Conclusion:
Canakinumab treatment showed good effectiveness in sJIA both as first- and second-line DMARD. After 6 months the use of canakinumab as first-line DMARD is associated with higher response rates compared to second-line use. Our data support the hypothesis that early treatment with canakinumab is associated with good therapeutical response and a positive effect on the disease course of sJIA.

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Disclosure of Interest: R. Heidebrecht: None declared, A. Klein: None declared, K. Minden Speaker Bureau of: Abbvie, GSK, Roche, Sanofi & Biermann, F. Dressler Speaker Bureau of: Novartis, Pfizer & Abbvie, G. Horneff Speaker Bureau of: Pfizer, Abbvie, Novartis, Chugai

e-Poster viewing: Systemic lupus erythematosus and antiphospholipid syndrome

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CHILDHOOD SYSTEMIC LUPUS ERYTHEMATOSUS: EXPERIENCE FROM SUB -HIMALAYAN REGION OF NORTH WEST INDIA

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Introduction: Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease. Clinical presentation can vary from mere cutaneous involvement to more severe multisystem involvement. SLE usually presents with rash, fatigue and fever but may sometimes present with unusual, non-specific manifestations in children.
Objectives: To describe a cohort of children with SLE from tertiary care centre in a resource limited setting in North west India
Methods: Retrospective case review of all children diagnosed as SLE from July 2017-December 2018 at a single tertiary care hospital in north India was done. Diagnosis of SLE was based on Systemic Lupus International Collaborating Clinics(SLICC) classification criteria.

Results: A total of 11 children (9 girls) with SLE were identified. Median age of symptom onset and diagnosis was 14 years(range 8-17 years) and 11 years respectively. The presenting manifestations were fever(5), oral ulcers(3), alopecia(3), malar rash(4), photosensitivity(5), renal involvement(5), seizures(1) and gastrointestinal complaints (1) apart from some unusual manifestations of isolated peripheral arthritis(1), isolated bilateral pleural effusion(1), macrophage activation syndrome(2).
Laboratory investigations: Hemogram revealed anemia in 8 children and thrombocytopenia in 5. Urine examination showed nephrotic range proteinuria in 1 child and subnephrotic proteinuria in 2. Microscopic hematuria was noted in 2 pateints. Renal function tests were deranged in 2 cases. ANA, Anti dsDNA positivity and hypocomplimentemia were present in all. Renal biopsy was done in 4 patients, 2 had class IV, one class III and one had class V lupus nephritis.
All patients were initiated on hydroxychloroquine and photoprotection. Children with renal involvement were given pulse methylprednisolone followed by tapering doses of oral prednisolone and intravenous, monthly cyclophosphamide. Azathioprine was used as maintenance therapy in all. Subcutaneous weekly methotrexate was used in 2 patients. One child (MAS) died during disease course. Disease continues to be in remission in rest.

Conclusion: We found a significant female preponderance in our study group. Renal involvement was the commonest presentation. Some unusual presentations were also seen. Early recognition of SLE is critical for timely initiation of appropriate treatment. This is the first report of a cohort of Pediatric SLE from this part of India.
Disclosure of Interest: None declared

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A RARE CASE OF MIXED TYPE AUTOIMMUNE HEMOLYTIC ANEMIA IN A 15-YEARS OLD ADOLESCENT– DON'T ALWAYS BLAME LUPUS

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Introduction: Autoantibodies in AHAI may be IgG/IgM/IgA. AHAI can be divided into primary or secondary (e.g. SLE, lymphoproliferative diseases, infections, medications). It is also classified based on the temperature at which the antibody reacts to erythrocytes, and can be warm (IgG or IgA) or cold (IgM or C3). In warm AHAI, the antibodies react at temperatures ≥37ºC, not activating the complement system and not undergoing agglutination *in vitro*. In cold AHAI, antibodies react at temperatures below 37ºC, activating the complement system with *in vitro* agglutination.Mixed AIHA (warm and cold) is rare and occurs in <10% of AIHA cases and can occur at any age, but is extremely rare in children. The prevalence of the mixed form is less than 1/1,000,000 patients with AHAI.
Objectives: To report a rare case of mixed AHAI and idiopathic intracranial hypertension(IIH) in a 15-years old female patient with a previous diagnosis of SLE and APS.
Methods: Case report and literature review.
Results: A 15-years old female adolescent previously diagnosed with SLE/APS since 2017 was in remission on hydroxychloroquine(400mg);azathioprine(150mg);aspirin(100mg);vitaminD3(1.000IU);calcium(1g), and sunscreen. In April 2020, she had a relapse presenting with fatigue, myositis, headache, hypocomplementemia, and severe autoimmune hemolytic anemia (Hb of 4g/dL) (SLEDAI-2K=18 points). Mixed AHAI was diagnosed base on a Direct/Indirect Coombs test 4/4+;DirectAntiglobulinTesting showing anti-IgA(weak),anti-IgM(3+/4+),anti-IgG(3+/4+),anti-C3c(weak),anti-C3d (3+/4+);IgG1/3subclasses with a reaction of 1:100(2+/4+);an eleven cell antibody panel positive revealing a cold and warm antibody, and adsorption technique revealing a cold and warm autoantibody. Chest CT showed bibasilar subsegmental atelectasis, head CT/MRI was normal and LP showed a high opening pressure of 45cmH2O with a normal cell count. After the procedure, the patient reported improvement in the pain and was diagnosed with IIH. The patient was screened for secondary causes for AHAI (table 1) due to the unusual mixed type pattern and serology was positive for *Chlamydia trachomatis* (IgM) and *Mycoplasma pneumoniae* (indeterminate-IgM/positive-IgG) suggesting a recent infectious trigger causing reactivation of the underlying disease with a probable cross-reactivity. The patient treated with 10-days of clarithromycin. Before the infectious screening came back negative, AHAI was treated with a single dose of IVIG(1g/kg) and then, with 3-days of methylprednisolone(1g/day). Azathioprine was replaced by mycophenolate mofetil. Due to headache recurrence, acetazolamide(500mg/day) was started, and the patient referred no pain. The patient was discharged with a resolution of the symptoms.
Conclusion: The diagnosis of AHAI should alert pediatricians for the possibility of underlying causes other such as infectious, autoimmune diseases or neoplasms. In this case, SLE reactivation was a clear cause of AHAI but the mixed type is not what usually occurs in SLE. AHAI in SLE presents with a warm type(IgG). The presence of a cold antibody(IgM) is usually associated with infectious diseases such as *Mycoplasma pneumoniae*. This could contribute to the disease relapse. Atypical patterns of AHAI should be investigated for other causes even if a clear cause such as SLE is identified.
Disclosure of Interest: None declared

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BICKERSTAFF ENCEPHALITIS WITH OVERLAPPING GUILLAIN-BARRÉ SYNDROME AS A FIRST MANIFESTATION OF JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS: A CASE REPORT

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Introduction: Pediatric systemic lupus erythematosus (pSLE) is an autoimmune disease with multisystemic involvement. More than 50% of the patients present neurological or psychiatric manifestations, with 43.9% of them presenting these symptoms at the time of diagnosis (REF). Rarely, Guillain-Barré syndrome (GBS) and its subtypes have been described in association with active SLE. Bickerstaff's brainstem encephalitis (BBE) is a rare immune-mediated disorder characterized by ophthalmoplegia, ataxia and disturbance of consciousness, which symptoms may overlap with GBS.
Objectives: To our knowledge, the association of GBS and BBE has been described in adults only.
Methods: We here describe a child presenting at SLE disease-onset with an overlap of peripheral (GBS) and central (BBE) nervous system manifestations, highlighting the possible association between these two entities in children.
Results: An 11-year-old healthy girl presented with acute ataxia, ophtalmoparesis and altered level of consciousness, rapidly followed by areflexia, facial paresis, swallowing difficulties, sensory deficits, paresis in all four limbs and respiratory insufficiency. These symptoms were accompanied by pleuro-pericardial serositis, proteinuria and hypertension. Immunological investigations revealed the presence of positive ANA and ds-DNA antibodies. The renal biopsy showed a stage III lupus nephritis. Hence, the clinical, laboratory findings and biopsy report led to the diagnosis of pSLE. Brain and spine MRI did not show any abnormalities; diffuse slowing compatible with nonspecific encephalopathy was seen on EEG. Nerve conduction studies (NCS) confirmed the clinical suspicion of acute polyradiculoneuropathy with proximal interruption of motor nerve conduction, compatible with Guillain-Barré-like syndrome. CSF analysis (performed twice) remained normal. The patient was treated with glucocorticoids, intravenous immunoglobulins, cyclophosphamide as well as plasmapheresis. The neurological and physical symptoms improved gradually with complete neurological recovery four months after onset.
Conclusion: Overlapping forms of BBE/GBS have never been described in association to SLE in children. Our patient's presentation and evolution fulfilled the criteria for such an overlap, occurring at pSLE onset. Although SLE and BBE/GBS are rare entities, our case suggests that there may be a common underlying immune background. This association should be recognized early for rapid and appropriate treatment initiation.
Disclosure of Interest: None declared

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INFANTILE ANTIPHOSPHOLIPID ANTIBODY SYNDROME: ACQUIRED AND DE NOVO APL APPEARANCE IN FOUR INFANTS.

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Introduction: Antiphospholipid syndrome (APS) is a rare condition in the neonatal age. In most cases it is considered a passively acquired autoimmune disease, due to a transplacental passage of maternal antiphospholipid antibodies (aPL). Exceedingly unusual is the *de novo* production of aPL in newborns and infants.

Objectives: To describe four infants who developed an early brain stroke with increased and persistent levels of aPL, even after six months of life.

Methods: We reviewed the clinical charts of four such infants, followed from diagnosis up to two years after the disappearance of aPL.

Results: Four babies (3 F and 1M) came to our attention at 5, 7, 9 and 22 months of life, respectively, because of perinatal stroke and presence of aPL. Clinical and laboratory data of mother-infant pairs are described in the table. Three out of 4 children (cases 1-2-3) had only IgG antibodies. One mother had both aCL and anti-beta2GP1 IgM and IgG. In the first 3 cases antibodies disappeared within 2 years of life (6, 16 e 20 months respectively), in the last case at 26 months of life. Two cases (1 and 3) had genetic pro-thrombotic factors and received baby aspirin until the disappearance of aPL. Case 4 had a perinatal risk factor and was the only one to have positive aPL IgM.

Case	**Prenatal risk factors**	**Type of delivery**	**Age at symptoms onset**	**Laboratory (babies)**	**Laboratory (Mothers)**	**Disappearance of APL**	**Outcome**
1 Male	Abruption placentae and premature uterine contraction	vaginal	10 days: poor feeding, hyposthenia; 4 weeks: jerking movements, partial seizure	- aCL IgG 45 U/ml; *β*2GPI IgG 60 U/ml - Heterozygous for FVL mutation	ANA 1:160	9 months	right hemiplegia, psychomotor development delay
2 Female	Gestational diabetes	vaginal	5 months: hemiparesis	At 6 months: - aCL IgG 20 U/ml; β2GPI IgG 120 U/ml	ANA 1:80	16 months	Hemiparesis
3 Female		elective caesarian	5 months: hyposthenia of right side	At 9 months: - aCL IgG 101,6 U/ml, β2GPI IgG >100 U/ml -protein C 53%, (nv 70-140), protein S 39,64%, (nv 54-124), - plasminogen	aCL IgM 38 U/ml, IgG 30 U/ml, β2GPI IgM 20 U/ml, and IgG 20 U/ml	20 months	hemiparesis

				67%, (nv 80-120), - Heterozygosis MTHFR			
4 Female	Dichorionic-diamniotic twin pregnancy Gestational diabetes Prematurity (31+6 gw)	Emergency cesarean	sonography signs of periventricular suffering 21 months: acrocyanosis	22 months: β2GPI IgG 70 U/ml, and IgM 35 U/ml		26 months	none

Conclusion: Common characteristics of these four children are the development of brain stroke and the increased and persistent aPL levels even after six months of life. This opens the window on a gray zone related to the origin of these antibodies (maternal or neonatal) and on their role in the pathogenesis of the infantile brain stroke.
Disclosure of Interest: None declared

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SPECTRUM OF CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS AND ITS CLINICAL COURSE

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Introduction: Childhood systemic lupus erythematosus (cSLE) is an autoimmune systemic disease diagnosed in children under the age of 18 years old, leading to an important morbidity and mortality. Typically in the literature, cSLE is described in the literature with a more severe clinical course compared to adult-onset.
Objectives: To analyze clinical manifestations within the first year after the diagnosis of cSLE and its subsequent clinical course.
Methods: A descriptive, observational, cross-sectional study was carried out. Inclusion criteria: all patients with diagnosis of cSLE based on 1997 updated American College of Rheumatology (ACR) criteria or 2012 Systemic International Collaborating Clinics (SLICC), in a tertiary hospital. Exclusion criteria: patients with a diagnosis of cSLE in another center, as data of the onset of the disease was not available. Demographic, clinical and analytical data were collected.
Results: 42 patients were included, 38 (90.5%) girls and 4 (9.5%) boys. 39 (92.9%) were Caucasians. Mean age at diagnosis was 13.3 years (range: 7-18). Clinical manifestations within the first year of cSLE and complementary tests are shown in Table 1.
31 (73.8%) children developed a major organ involvement within the first year of the disease. Renal impairment was the most frequent manifestation (20 patients, 47.6%); followed by neurological (8 patients, 19%), lung (2 patients, 4.8%), and cardiac (1 patient, 2.4%) involvement.
Class IV lupus nephritis, based on 2003 International Society of Nephrology and the Renal Pathology Society (ISN/RPS) classification, was the most frequent (50%). The most common neurological manifestations was the presence of seizures (4 patients, 9.5%), followed by: 1 pseudotumor (2.4%), 1 chorea (2.4%), 1 aseptic meningitis (2.4%), 1 peripheral nervous system (2.4%) and 1 lupus psychosis (2.4%). Regarding lung disorders, 2 (4.8%) lupus pneumonitis were registered; and within cardiac involvement, 1 (2.4%) tamponade.
Following the first year of the onset (maximum follow-up period: 46 years), just 6 (14.2%) patients suffered from major organ involvement, with a mean time of 29.5 months (range 12 months – 17 years).
20 (47.6%) children required a strong immunosuppressant drug as mycophenolate, cyclophosphamide, azathioprine or biologic therapy within the first year. 1 death was registered.

Joint	34 (81%)		Total (n=42)
Mucocutaneous	31 (73.8%)	**ANA+**	41 (97.6%)
Hematological	29 (6%)	**antiDNA+ (IU/ml)**	132 (12-624)
Renal	20 (47.6%)	**C3 (mg/dL)**	38.7 (9.8 - 75.8)
Systemic	19 (45.2%)	**C4(mg/dL)**	6 (1.34 - 9.9)
Neurological	8 (19%)	**ESR (mm/1ªh)**	44 (4 - 120)
Serositis	6 (14.3%)	**PCR (mg/L)**	2.44 (0.2 - 17.8)
Pulmonary	5 (11.9%)		
Cardiac	4 (9.5%)		
Raynaud's phenomenon	2 (4.8%)		

Table 1. Clinical manifestations and complementary tests within the first year of cSLE. ANA: antinuclear antibodies (>1:80); ESR: erythrocyte sedimentation rate; PCR: protein-C reactive.

Conclusion: In our patient cohort with cSLE, 88% patients developed a major organ involvement. 73% children suffered from this kind of manifestations during the first year after diagnosis, being less frequent (14.2%) as the disease progresses. Renal impairment was the most common, followed by neurological, lung and cardiac involvement.
Disclosure of Interest: None declared

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THE USE OF 'THE LUPUS CHECKLIST' IN CONSULTATIONS WITH PAEDIATRIC PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN IMPROVING PATIENT MONITORING OUTCOMES

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Introduction: The Lupus Checklist is designed for use in a Paediatric Rheumatology Clinic to help doctors keep track of the monitoring of patients with Juvenile Systemic Lupus Erythematosus, a complex, multi-organ condition which requires rigorous and regular monitoring.[1] Juvenile Systemic Lupus Erythematosus (JSLE) patients in South Africa are at high risk of poor outcomes, so stringent monitoring of disease activity, vaccination, and medication safety are important.[2]
Objectives: The two objectives of this audit were, firstly, to determine if the appropriate level of rigorous monitoring (as set out by the Lupus Checklist) for each patient was completed and secondly, to determine whether the Lupus Checklist was useful in assisting doctors in monitoring their patients' condition.
Methods: All patients treated in the Paediatric Rheumatology Clinic at the Red Cross War Memorial Children's Hospital, Cape Town with JSLE were included (20 patients). Patient notes and laboratory records were used to determine if the appropriate monitoring checks, as laid out by the Lupus Checklist, had been completed.
Results: Overall 37.7% of audited checks were completed. 19 patients had over 20% of their monitoring completed but only 2 had over 80%. Aspects of monitoring that were more time intensive or were required less regularly were most frequently overlooked. There was a statistically significant increase in the percentage of completed monitoring in those patients for whom the Lupus Checklist was used compared to patients where a checklist was not used (p=0.00).
Conclusion: There is significant room for improvement in the monitoring of these patients with JSLE in the rheumatology clinic. This audit illustrates that more diligent use of the Lupus Checklist and an overall improvement in sustained use of the checklist will help to improve monitoring of these patients. Evidence suggests that checklists are underutilised in medicine and wider implementation of this simple tool could improve patient outcomes.[3,4,5] Interventions such as in person or electronic reminders, or audits with feedback to physicians could improve usage over time. The application of the Lupus Checklist or a similar document in other paediatric clinics is important for comprehensive monitoring of a condition as complex as JSLE and has the potential to prevent ongoing damage and medication toxicity in this high-risk population.

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Disclosure of Interest: None declared

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DISEASE COURSE AND TREATMENT RESPONSES IN JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS; A SINGLE CENTER EXPERIENCE

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Introduction: Systemic lupus erythematosus (SLE) is a chronic autoimmune inflammatory disease that may cause morbidity and mortality by affecting multiple systems. The 10-20% of patients have juvenile onset and this cluster have may more severe kidney, neuropsychiatric or hematological involvement.
Objectives: The aim of this study was to assess the clinical and laboratory characteristics, disease activity, and treatment response of patients with juvenile SLE (jSLE).
Methods: This is a retrospective study involving patients between 1 July 2016 and 1 January 2020. The data of patients diagnosed with jSLE and followed up for a minimum of 6 months, were collected. The SLEDAI-2K scores at initiation and at the follow-up (1st, 3rd, 6th, and 12th months of treatment) were examined. The SLEDAI-2K score was considered to be ≤4, for disease remission status.
Results: A total of 49 children were included in to the study. The female/male ratio was 4.4/1 and the median age of the patients at the diagnosis was 13 (IQR: 11.1–15.2) years. The median follow-up of patients was 19 (IQR: 12–25) month. Four of the patients were diagnosed with monogenic SLE. Two siblings were diagnosed with c3 deficiency and two were diagnosed with familial chilblain lupus. The most common clinical findings were found musculoskeletal complaints (69.4%), malar rash (51%), oral ulcers (38.8%), and fever (30.6%), respectively in over all the group. The frequency of involvement of the system and organs was as follows; mucocutaneous 77.6%, musculoskeletal 69.4%, renal 44.9%, hematological 34.7%, serous membranes 16.3%, neuropsychiatric 12.2%, respectively. All patients had anti-nuclear antibody positivity, while 46.9% had anti-ds DNA, 14.3% had anti-Sm and 8.2% had antiphospholipid antibody positivity. While all patients received hydroxychloroquine treatment, 22.4% of the patients were received were mycophenolate mofetil, 22.4% were azathioprine, 14.3% cyclophosphamide, 12.2% methotrexate and 10.2% were rituximab. The median SLEDAI-2K score was 14 (IQR: 10–18.5) at admission, besides it was found to 6 (IQR: 4–12), 4 (IQR: 2–6), 2 (IQR: 0–6) in the 1st, 6th and 12th months of treatment, respectively. While 98% of the patients had active disease at admission, 67.3% at 1 months, 32.7% at 6 months and 22.4% at 12 months still had active disease (SLEDAI-2K >4). Patients with initially high SLEDAI-2K scores had significantly lower remission rates in the first month (p=0.003). It was observed that patients with high SLEDAI-2K scores in admission were more resistant to conventional immunosuppressive treatments and the use of rituximab was more frequent in these patients. At least one major organ (renal, hematological, neurological) were affected in 57% of patients. The remission rate of these patients at 6 months was found significantly decreased compared to the others (p <0.005). Renal biopsy was performed in 21 patients (42.9%). 12 of them had type 4 lupus nephritis (LN), 5 had type 2, 2 had type 3, and 1 had type 5. It was observed that patients with renal involvement were the group that reached remission latest.
Conclusion: The presence of high initial SLEDAI-2K scores and the major organ involvement have poor predictive value to achieve inactive disease.
Trial registration identifying number: None
Disclosure of Interest: None declared

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HYPOPHOSPHATEMIA SECONDARY TO FGF23 INCREASE ASSOCIATED WITH SYSTEMIC AUTOIMMUNE DISEASE : A REPORT OF 2 CASES

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Introduction: Fibroblast Growth Factor 23 (FGF23) is a hypophosphatemic hormone playing a key role in phosphatemia homeostasis. Antibodies blocking FGF23 signaling can cause hyperphosphatemic tumoral calcinosis. To our knowledge, there is no description of systemic autoimmune disease associated with FGF23 signaling excess.

Objectives: To report two patients with systemic autoimmune diseases and severe hypophosphatemia secondary to FGF23 level increase.
Methods:

Results: The first patient was diagnosed with an early-onset Sjogren syndrome at 4 years old with anti-SSa and SSb antibody positivity and focal lymphocytic sialadenitis with a focus score of ≥1 foci/4 mm^2, as well as joint, parotid, hepatic, hematological and neurological involvement. During a disease flare, hypophosphatemia occurred (0.51mmol/L (Normal values:1.3-1.85)) with intact FGF23 level at 215ng/mL (N=23.2 – 95.3) associated with hyperphosphaturia with a normal renal function. FGF23 level normalized at 62.4ng/mL and phosphatemia went back up at 1.19mmol/L after intensification of immunosuppressive drugs. The second patient suffers from systemic erythematous lupus diagnosed at age of 10 year, with cutaneous, joint, and hematological involvement, positive anti-Sm, anti-SSA, anti-RNP, , anti-DNA antibodies. She developed hypophosphatemia at 0.35 mmol/L with a 70% phosphate reabsorption rate, resulting from a renal phosphate leak. An elevation of intact FGF23 to 135.7 ng / L without renal dysfunction was demonstrated. The level of intact FGF23 then normalized with the intensification of immunosuppression.
Conclusion: Conclusion: We report for the first time the occurrence of severe hypophosphatemia secondary to an increase of intact FGF23 level in two patients with systemic autoimmune disease. Correlation between disease activity and the level of FGF23 suggests that this secretion may be secondary to an activating autoimmune mechanism.

Disclosure of Interest: None declared

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LONGITUDINAL EVALUATION OF EXECUTIVE FUNCTIONS IN PATIENTS WITH CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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Introduction: Among the neuropsychiatric manifestations of Childhood-onset Systemic Lupus Erythematosus , cognitive losses are frequent.
Objectives: To analyze the fluctuation of executive functions these patients in treatment at a tertiary hospital rheumatology outpatient clinic.
Methods: This is a longitudinal study with application of validated instruments: Coding subtest, Picture Arrangement , Block Design, Vocabulary and Picture Completion in patients with confirmed diagnosis of Childhood-onset SLE . In this study 24 patients were included, with a mean of 16.83 years, of whom 23 were women and 1 were man. The subjects were evaluated in two different periods with mean separation time of 9.5 months.
Results: The Coding subtest showed the largest difference between the scoring means, with the first being 58.83 ± 15.18 (mean ± SD) and the second 55.20 ± 20.63, followed by the arrangement of figures, with 22.87 ± 12.69 and 20.5 ± 8.88, and Block Design with 42.37 ± 13.73 and 41.62 ± 13.66. On the other hand, when analyzing the substandard Vocabulary and Picture Completion, there is an increase in the mean between evaluations, the first one being from 26 ± 3.21 to 26.41 ± 6.48, and the second from 22.79 ± 3.28 to 23.95 ± 9.03. When performed the T-test for paired samples, with a 95% confidence interval, it was not possible to prove the statistical significance when comparing the data obtained in the two evaluations. The Block Design subtest was closest to significance, with a result of 0.328, followed by Coding with 0.524.
Conclusion: Although the data analyzed do not have statistical significance it's possible to realize a tendency in the decrease of the ability to perform tasks. In this way, the study provides an indication of impairment in spatial visualization capabilities, selective and focused attention, and mental flexibility and perceptual and visual organization. Further studies are needed to better evaluate the long-term impairment of executive functions on patients with Childhood-onset SLE
Disclosure of Interest: None declared

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NEUROLOGICAL MANIFESTATIONS OF PEDIATRIC SYSTEMIC LUPUS ERYTHEMTOSUS

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Introduction: SLE is a complex autoimmune disorder, characterized by multisystem involvement including the nervous system, juvenile onset SLE has more aggressive clinical course in comparison with adult-onset SLE. Neuro Psychatric (NP) symptoms may be the initial presentation of SLE in children. The mortality rate is relatively low, but morbidity may be significant and permanent damage can occur.Early recognition of symptoms is crucial in prevented of permanent neurological sequalae and patients' quality of life.
Objectives: The aim of the work is to study the neurological manifestations of pediatric SLE in a sample of Egyptian children.
Methods: We studied 54 children and adolescents <18 years old who were undergoing treatment or follow-up at the paediatric neurology unit, neurology department at Al-Azhar University Hospitals (Al-Hussein and Bab-Al-Shaaria), and children referred from rheumatology department from June 2018 to November 2018. All patients fulfilled the new EULAR/ACR SLE classification criteria 2017.Patients were excluded from the study when their NP manifestations were secondary to other causes, such as hypertensive encephalopathy uremia infection or congenital or acquired CNS disease not related to SLE.
Results: out of 54 children with SLE, 30 (55.6%) had neuropsychiatric (NP) manifestations, the mean age at onset of the disease was 13.6 years. The mean period between onset of SLE and NP manifestations 15.5 months. NP manifestations was the presenting feature in 3 patients. Headache was the initial symptom of central nervous system (CNS) involvement in 35% of patients seizures was the most frequent CNS finding seen in 7(23.3%) patients, 6 (20%) patients had congnifive impairment, 6(20%) patient had cognitive impairment, 6(20%) patients had CVA, 2(6.7%) had chorea, 2(6.7%) had psychosis, 2(6.7%) had depression, 1(3.3) had cerebritis, 1(3.3%) had peripheral neuropathy. Lupus anticoagulant was high in patients with chorea, seizures or cerebrovascular accidents (CVA). Electroencephalogram (EEG) was abnormal in 30% of patients presented by seizures and rarely helpful in patients with diffuse NP symptoms. Magnetic resonance imaging (MRI) was abnormal in 13 cases, long term outcome was good, 3 patients had significant persistent CNS deficits, the majority of patients (90%) had excellent recovery from neuropsychiatric SLE.
Conclusion: NPSLE is one of the most common serious complications of pediatric SLE, so early recognition and management are of paramount importance. CNS involvement was observed in 55% of our pediatric patients with SLE, 76 % of whom developed symptoms during the first year of onset of the disease Headache and seizures were the most common neurological manifestations of pediatric SLE, followed by Cerebro Vascular Accident CVA and intellectual disability. Psychosis, depression and chorea were less frequent in our study group, while peripheral neuropathy and cerebritis were rare. Neuroimaging were generally unhelpful in patients with diffuse CNS disease, in contrast, it was more helpful in patients with focal neurological findings such as CVA. Patients with CVA or chorea, usually had positive lupus anticoagulant (LAC) antibody, and all of these patients should be investigated thoroughly for the presence of antiphospholipid antibodies. Thus, the clinicians should make a reasonable prediction of individual patients to reduce morbidity and mortality of SLE in children and improve patients' outcome
Disclosure of Interest: None declared

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LUPUS MANIFESTATIONS IN CHILDREN WITH PRIMARY IMMUNODEFICIENCY DISEASES: PHENOTYPIC AND GENETIC FEATURES AND OUTCOME

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Introduction: Systemic lupus erythematosus (SLE) is a complex systemic inflammatory disease with a wide spectrum of clinical and laboratory features. Increasing evidence has shown a strong association between autoimmune diseases and primary immunodeficiency diseases (PIDs).
Objectives: To report the phenotypic features, underlying genetic defects and outcome of patients with SLE and SLE-like associated with PIDs.
Methods: Data retrospectively collected on patients with lupus manifestations and clinically/ or genetically proven PIDs seen between 1998 to 2019. The collected data comprised the clinical findings and diagnostic evaluation including genetic testing, the response to therapeutic intervention and the accrual damage related to SLE.
Results: A total of 40 patients (22 female) with a median age of 13 (range of 2- 24) years were reviewed. Thirty-four patients had SLE and 6 with SLE-like. Genetic analysis was performed in 23 patients, all had positive results for monogenic PIDs. Complement deficiency was the most frequent PIDs; 26 patients were C1q deficient, 3 patients had C3 deficiency, 2 patients had C4 deficiency and one patient with heterozygous *C8b* variant. The other 8 patients had different PIDs genetic defects that include severe combined immunodeficiency caused by PNP deficiency, chronic granulomatous disease, common variable immunodeficiency (*PIK3CD)*, IL-2RB mutation, DNase II deficiency, *STAT1* mutation and Griscelli syndrome type 3, in addition to a possible novel genetic defect in FGL2. Mucocutaneous lesions, arthritis and lung involvement were the main clinical features. Most of the patients (84.2%) experienced recurrent infections. Complement-deficient patients were younger and more likely to have a familial disease with severe mucocutaneous lesions. All patients treated with corticosteroid and immunosuppressive medications. Seven patients received biologic agents, either rituximab or belimumab. The mean accrual damage was 2.7 ± 2.2. There were 5 deaths because of infection.
Conclusion: This study showed a variable pectrum of SLE associated with heterogeneous group of PIDs. Our data suggest that SLE patients with early onset disease, family history of SLE or recurrent infections should undergo immunological work-up and genetic testing to rule out PIDs.
Disclosure of Interest: None declared

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OFATUMUMAB USE IN JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS: A SINGLE CENTRE EXPERIENCE

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Introduction: Ofatumumab is a fully humanized anti-CD20 monoclonal antibody (mAb) which has been licensed for use in haematological malignancies, rheumatoid arthritis and paediatric nephrotic syndrome. There are limited data on the off-label use of Ofatumumab as an alternative B-cell depletion agent for patients with systemic lupus erythematosus (SLE) allergic to Rituximab, particularly juvenile SLE (jSLE).
Objectives: To describe a single-centre experience of use of ofatumumab for jSLE.
Methods: A single-centre retrospective case series of patients treated with off-label ofatumumab for jSLE between June 2018-April 2020 at Great Ormond Street Hospital, UK. Demographics, clinical and laboratory characteristics and treatment were collected.
Results: Three patients were identified: Laboratory and clinical data including active organs/systems involved prior to ofatumumab are summarized in **Table 1**. All patients received Rituximab, Mycophenolate Mofetil (MMF) and steroids prior to Ofatumumab. 2/3 patients had cyclophosphamide (cases 1 and 2). Post-Ofatumumab, all patients remained on MMF maintenance therapy, and weaning course of steroids. The indication for ofatumumab in 3 patients was active SLE, with severe prior reaction to Rituximab. The median number of Rituximab infusions received was 2 (range 1-4).
Cases 1 and 3 received one course of Ofatumumab (700 mg/dose, 2 doses, administered on day 0 and day 14); case 2 received 2 courses, same dose, 9 months apart. The median follow up post-Ofatumumab was 14 months (range 8-23 months).
Ofatumumab was well tolerated without any infusion reactions or other adverse events for all 3 patients. B cell depletion was achieved in 3/3 patients within three months (range 1-3 months). Significant clinical improvement was observed in all cases (Table 1), mirrored by improved laboratory markers of disease activity including anti-dsDNA antibody, complement levels, and proteinuria. At 6 months follow up, BILAG-2004 index had improvement for all patients (Table 1) At 6 months follow-up, the disease remained well-controlled for 2/3 patients, whereas 1/3 patient had a disease flare 9 months after the Ofatumumab course and received a second course with good response. Lymphocyte subsets were only available for 2/3 patients at 6 months post Ofatumumab. Two of the patients had repopulated B cells at this time point.

	Case 1	**Case 2**	**Case 3**
Age, gender	14 years, F	16 years, F	12 years 8 months, F
Ethnicity	Asian	Afro-Caribbean	Asian
Duration jSLE (months)	31 months	71 months	16 months
Disease manifestations Pre Ofatumumab	Neurological (headaches, memory loss, non-specific white matter changes on MRI Brain) Renal (Lupus nephritis, ISN/RPS Class III)	Lupus nephritis, ISN/RPS Class III Serositis (pleural and pericardial effusions) Haematological	Haematological (ITP, anaemia) Arthritis

	Haematological		Arthritis Chronic cutaneous lupus Non-scarring alopecia			
Ofatumumab	**Pre**	**Post**	**Pre**	**Post**	**Pre**	**Post**
BILAG-2004	A	D	B	D	A	D
dsDNA	318.0	104.0	412	156	3.5	1.8
Urine Alb/Cr ratio (RR: 0.7-7.4 mg/mmol)	561.9	172.6	1.4	3.7	2.0	1.1
B cell repopulation (months/CD19)	N/A		5 months CD 19: 4.1%		6 months CD19: 13.5%	

Conclusion: In this small series, treatment with Ofatumumab for patients with jSLE allergic to Rituximab was a safe and well-tolerated alternative to Rituximab therapy for B cell depletion. The clinical and serological outcomes were favourable. Clinical trials of Ofatumumab in jSLE are needed to prove efficacy and to determine the optimal treatment regimen.

Disclosure of Interest: None declared

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A NOVEL MUTATION IN THE C1QA GENE IN A TODDLER WITH C1Q DEFICIENCY ASSOCIATED WITH MONOGENIC LUPUS AND RECURRENT INFECTION

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Introduction: C1q deficiency is a rare hereditary disorder, which is strongly associated with Systemic Lupus Erythematosus (SLE).To date more than 60 cases of C1q deficiency have been published with various mutations
Objectives: We are reporting a novel homozygous mutation in the C1qA gene in a two year old girl who presented with SLE
Methods: Chart review of clinical data, laboratory data and molecular analysis
Results: A two year old girl of consanguineous parents presented to hospital at 13 months of age with fever and erythematous macular rash on her cheeks which spread to her nose, chin, and ears. The rash started a month prior, and progressed over her entire body. A skin swab grew staphylococcus aureus but the rash didn't respond to topical antibiotics. Review of systems was unremarkable except for longstanding oral thrush and diaper rash. Birth and family history were unremarkable. On exam she had a diffuse, erythematous, morbilliform eruption over her face and body. She had facial swelling, orbital edema and vasculitic oral ulcers. She had leukopenia mainly neutropenia, low hemoglobin, with normal platelets. Her liver enzymes and erythrocyte sedimentation rate (ESR) were high while C-reactive protein, immunoglobulins, C3 and C4 were normal. Cultures were negative, however she was positive for adenovirus, mycoplasma and EBV (EBV load was 6000 IU/ml). Autoimmune hepatitis work up was negative. The direct coombs test, antinuclear antibodies (1:640), Ro, RNP and SmD were positive. CH50 came low as well as C1q level of 4 mg/dL (normal range 12-22 mg/dL). Lymphocyte subsets showed reduced CD4 and NK cells. Bone marrow aspiration showed active marrow. Skin biopsy showed chronic non-specific inflammation (immunofluorescence and electron microscopy were not available). Echocardiogram showed dilatation of the left coronaries. She was treated with intravenous immunoglobulin (IVIG) for Kawasaki disease with no improvement. Therefore pulse steroid 30mg/kg followed by 2 mg/kg was initiated. Her rash, facial swelling and abnormal blood counts improved dramatically. Whole Exome sequence showed homozygous variant c.469G>T p.G157C at the C1QA gene. While tapering steroids she flared so subcutaneous methotrexate was started. Unfortunately, she continued to have rash, leukopenia and high liver enzymes, so treatment was switched to mycophenolate mofetil and hydroxychloroquine. However she did not improve and started to have recurrent bacterial and viral infections that included cellulitis, gastroenteritis and upper respiratory tract infection. We started her on regular IVIG, which helped with infections and allowed for weaning of steroids. However she developed alopecia and lower limb spasticity with delayed walking. MRI brain and spine was normal. Upon reanalysis of the WES, two other homozygous mutations at KIF1C and APG7 were identified and associated with spastic paraplegia, but reported as variants of unknown significant. Fresh frozen plasma (FFP) transfusions were started, initially weekly, then every two weeks and subsequently every four weeks. The rash disappeared, leukopenia and ESR improved and we were able to discontinue steroids
Conclusion: Early-onset SLE with a severe course of disease raises the possibility of a genetic etiology. We are reporting, for the first time, a rare missense mutation G>T in exon 3 of the C1QA gene that resulted in an amino acid substitution that is pathogenic. Interestingly, she had other mutations associated with neurological manifestation that never reported together before and altered her phenotype. She has responded well to FFP as has been reported in a few case reports
Disclosure of Interest: None declared

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HOW DO NOT TO MISS THE SYSTEMIC LUPUS ERYTHEMATOSUS IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS: PRELIMINARY RESULTS OF A RETROSPECTIVE STUDY.

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Introduction: Systemic lupus erythematosus (SLE) - is an autoimmune disease with a multisystem lesion. In some cases, mild SLE may resemble juvenile idiopathic arthritis (JIA), leading to misdiagnosis. Both diseases have common features, such as arthritis and antinuclear antibodies (ANA) seropositivity.
Objectives: To conduct a comparative study analysis of patients with SLE and JIA, to develop discriminating criteria for both conditions.
Methods: In a retrospective study, ANA-positive children (≥1/160) from laboratory reports (n=281) selected. We chose patients meeting the criteria for SLE (n = 55) aged 4-18 years and selected RF-negative ANA-positive polyarticular JIA patients (n = 52) of the same age. We exclude patients with other reasons for ANA-positivity. Clinical and laboratory characteristics compared using descriptive statistics, Mann-Whitney test, χ^2 test, AUC-ROC analysis, calculation of odds ratio (OR), analysis of sensitivity (Se) and specificity (Sp). Univariate, multivariate, and logistic regression analysis applied.
Results: The results of comparison of studied groups in the table. The cut-offs of continued variables and their OR associated with SLE are: onset age>9,5 years (OR=9,0 (95% CI: 3,6; 22,6), Se=89,3, Sp=63,3, p=0,000001), ANA>1280 (OR=4,2 (95% CI: 1,5; 11,7), Se=48,2, Sp=81,8, p=0,005); platelets ≤267x109/l (OR=7,3 (95% CI: 2,6; 20,4), Se=89,3, Sp=46,8, p=0,00004) and active joints<7 (OR=3,7 (95% CI: 1,6; 8,5), Se=61,8, Sp=69,6, p=0,002). In univariate, multivariate regression analysis, only onset age>9.5 years (p=0.00002) and active joints<7 (p=0.009) were independent discriminators between SLE and JIA. In logistic regression onset age>9.5 years (OR=9.1 [95%CI: 2.8; 29.8], p=0.0002) and active joints<7 (OR=5.4 [95% CI: 1.4; 20.1], p=0.012) increase the probability of SLE in JIA-like cohort. The presence of 2 mentioned above criteria has Se=75.0, Sp=87.5, OR=18.0 (95% CI: 6.6; 49.1) for discrimination of SLE from JIA.
Table 1. Comparison SLE and JIA patients

Parameter	SLE (n=49)	JIA (n=56)	p
Onset age, year	12.3 (10.1;14)	8.0 (6.2; 11.0)	0.00004
ANA (titer)	1/1280 (1/640; 1/5120)	1/1280 (1/640; 1/1280)	0.007
Active joints, n	0.5 (0; 3.5)	5.0 (1.0; 10.0)	0.00009
CRP, mg/l	1.0 (0.3; 3.9)	1.4 (0.5; 4.5)	0.345
ESR, mm/h	10.5 (5; 20.5)	8.0 (4.0; 18.0)	0.282
WBC $x10^9$/l	6.0 (4.4; 8.2)	6.7 (5.7; 8.1)	0.164
Platelets $x10^9$/l	245.5 (217.5; 333.0)	298.0 (251.0; 363.0)	0.015
Hemoglobin, g/l	121.5 (113.0; 131.5)	124.0 (118.0; 130.0)	0.256
Absolute lymphocyte count, $x10^3$/l	1845.8 (1320.5; 2459.0)	2046.0 (1711.0; 2557.8)	0.137

Conclusion: In ANA-positive patients with arthritis older than 9.5 years with active joints<7, it should be included in the differential diagnosis with the obligatory determination of all immunological tests specific for SLE.
Trial registration identifying number: This work supported by the Russian Foundation for Basic Research (grant № 18-515-57001).
Disclosure of Interest: None declared

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HYPOCOMPLEMENTEMIC URTICARIAL VASCULITIS IN PEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS

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Introduction: Urticarial vasculitis (UV) is a clinico-pathologic entity typified by recurrent episodes of urticaria that have the histopathologic features of leukocytoclastic vasculitis. In additions, patients with hypocomplementemic urticarial vasculitis (HUV) exhibit systemic manifestations, including constitutional symptoms, arthralgia or arthritis, serositis, glomerulonephritis, conjunctivitis and recurrent abdominal pain.

An association between HUV and SLE is hypothesized as both share similar clinical anf pathological features. Low serum complement measurements (C3, C4 and C1q) as well as anti C1q autoantibodies are also observed in both conditions. Some authors suggest the possible progression of HUV to SLE and others have defined HUV as an SLE subtype. HUV is present in 7-8% of SLE patients and 54% of HUV patients are diagnosed with SLE upon follow-up.
Objectives: To determine the prevalence HUV in pediatric systemic lupus erythematosus (pSLE) cohort of Arab ethnicity from Oman and to describe their demographic, clinical and laboratory features.
Methods: We conducted a retrospective multicenter study among pediatric rheumatology centers in Oman over a 10-year period from 2008-2018. Analyses were performed using univariate statistics.
Results: A total of 148 pSLE under the age of 13 years were included, 30% (n = 44) were males. The overall mean age at diagnosis was 7.6 ± 3.5 years and median disease duration was 9.5 (5-13) years. HUV was diagnosed in 34.5% (n = 51) of pSLE cohort. pSLE with UV were more likely to be males (57% *vs* 15%; $P < 0.001$), diagnosed at a younger age (5.9 *vs* 8.5 years; $P < 0.001$), have a family history of SLE (53% *vs* 36%; $P = 0.044$) and have conjunctivitis more frequently (32% *vs* 5.3%; $P < 0.001$) than pSLE without UV. pSLE with UV were also less likely to have CNS involvement (7.6% *vs* 20%; $P = 0.045$) and hematological manifestations such as leukopenia (9.4% *vs* 24%; $P = 0.028$) and thrombocytopenia (5.7% *vs* 18%; $P = 0.045$). In addition, pSLE with UV were more likely to be associated with low C3 complement count (94% *vs* 66%; $P < 0.001$) and positive cytoplasmic ANCA (11% *vs* 0%; $P = 0.022$).However, the pSLE with UV cohort were less likely to be associated with ANA (65% *vs* 83%; $P = 0.016$), DsDNA (56% *vs* 72%; $P = 0.042$) and perinuclear anti-neutrophil cytoplasmic antibodies (33% *vs* 55%; $P = 0.047$).
Conclusion: We report a high occurrence of HUV in pSLE cohort (34.5%) associated with unique demographic, clinical features and laboratory features. The debate regarding whether HUV is a rare subset or unusual type of SLE, or is a separate entity altogether, continues. However, the overlap in clinical, laboratory and genetic mutation supports the notion that HUV and SLE fall into the same spectrum of autoimmune disease with similar disease pathogenesis. However, further studies are needed to reach clear conclusions regarding the relationship between HUV and SLE.
Disclosure of Interest: None declared

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CLINICAL FEATURES AND LONG-TERM OUTCOME IN JUVENILE-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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Introduction: Juvenile-onset Systemic Lupus Erythematosus (jSLE) is a rare multisystem, autoimmune/inflammatory disease with onset before the age of 18, that accounts for 15-20% of all SLE patients. Clinical manifestations are extremely heterogeneous and disease course is unpredictable, varying from mild to life-threating disease. jSLE has been associated with a worse prognosis than adult-onset disease and can be a life-long disease. However, long term outcomes are poorly described.

Objectives: The aim of this study was to describe clinical features and long-term outcome of a cohort of adult patients diagnosed with jSLE and to evaluate their long-term outcome.

Methods: Charts of adult patients diagnosed with jSLE in two tertiary centres in Milan were analyzed. Data regarding clinical features, laboratory findings, treatments, long-term complications and long-term outcome were recorded retrospectively.

Results: In total, 183 patients with jSLE were included, 88% were female. Mean age at diagnosis was 12.5 years, while median disease duration at last clinical evaluation was 26 years.

At the time of diagnosis 102 patients (55.7%) presented cutaneous involvement, 115 patients (62.8%) showed heamatologic manifestations, while renal disease was described in 59 patients (32.2%); neurologic involvement was less frequently observed (14.2%).

We reported deaths in nine patients: two patients died due to infectious complications, one of kidney failure; two of myocardial infarctions and two of malignancies.

Corticosteroids were used in 74 patients (40.4%); 62.8% of patients received hydroxycloroquine, 35.5% azathioprine, 9.2% cyclosporine A and 30.6% cyclophosphamide. Four patients required the use of biologic agents (2 Rituximab and 2 Belimumab).

Major long term complications were hypercorticism due to long use of corticosteroids and infections.

Conclusion: In our cohort of patients, heamatologic, cutaneous and renal involvement were the most common clinical features, while neurologic manifestations were rarer. Our patients showed active disease also during adulthood confirming that jSLE is a life-long multisystem disease with an important impact on health-related quality of life. Moreover treatment strategies contribute to the development of irreversible damage, determining hypercorticism and higher risk of infections.

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Disclosure of Interest: None declared

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GENETIC ANCESTRY AND ITS CONTRIBUTION TO COMPLEX TRAITS IN CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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Introduction: Several studies have shown that ancestry influences the susceptibility and development of systemic lupus erythematosus (SLE). However, determining ancestry in an admixture population like Brazilians is difficult.
Objectives: To evaluated the role of admixture degree in clinical manifestations of childhood-onset systemic lupus erythematosus (cSLE) in a tri-hybrid population.
Methods: The genome-wide human Cytoscan HD array was applied to genotype 2.6K markers in 107 cSLE Brazilian patients and 110 healthy controls. Quality control of the chip was carried out using Chromosome Analysis Suite software. A panel of 345 ancestry informative markers (AIMs) based on SNP data from Cytoscan HD array was used to infer the proportion of European, African and Amerindian ancestries of each cSLE and control subjects. The individual ancestral composition based on the SNP-AIMs set was estimated using Admixture. Statistical analyses to associate the genetic ancestry with different clinical traits were performed using the computing environment R.
Results: Ancestral composition analysis revealed that the main component of patients and control group was European (66.9% and 80.2%), followed by African (21.6% and 11.5%) and Amerindian (11.5% and 8.4%). Comparisons using the proportions of each ancestral component showed significant differences in European ($p = 4.7 \times 10\text{-}11$, 95% CI -0.18− -0.10), African ($p = 4.1 \times 10\text{-}9$, 95% CI 0.05 − 0.12) and Amerindian ($p = 1.9 \times 10\text{-}6$, 95% CI -0.03 − 0.06) ancestries between cSLE and control groups.
A higher proportion of Amerindian ancestry in cSLE was associated to development of photosensitivity ($p = 0.035$) and hematologic alterations ($p = 0.025$). Otherwise, a higher African component was protective against hypocomplementemia ($p = 0.021$).
Conclusion: Results described here show novel associations to clinical manifestations in cSLE according to the ancestry profile. The deeper investigation of its relation to the pathogenesis may contribute to the understanding of the genetic basis of the disease.
Disclosure of Interest: None declared

P246

RELIABLE DETECTION OF SUBTYPES OF NAILFOLD CAPILLARY HAEMORRHAGES IN CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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Introduction: Systemic Lupus Erythematosus (SLE) is a severe chronic disease for which it is necessary to obtain more indicators of disease severity that predict disease damage. Nailfold capillary abnormalities could be such an indicator or biomarker in SLE. Nailfold capillary haemorrhages have been observed in adults and children with SLE as an abnormality that was significantly correlated with disease activity. Recently, different subtypes of capillary haemorrhages have been described in a cross-sectional case-control study of childhood-onset (c)SLE.

Objectives: The aim of this current study was to evaluate the inter- and intra-observer reliability for detection of different subtypes of capillary haemorrhages, as identified by nailfold videocapillaroscopy (NVC) in cSLE patients.

Methods: Five raters from three different centres blindly evaluated 140 NVC images from 35 cSLE-patients, diagnosed according to the Systemic Lupus International Collaborating Clinics (SLICC) criteria. The raters assessed the anonymized NVC images qualitatively (present or absent) and quantitatively (total number) on four different subtypes of haemorrhages:
1) punctate extravasations; point-shaped, localized around, or in the apical centre of capillary loop
2) perivascular haemorrhage; as 1) but in grouped/confluent aspect
3) large confluent haemorrhage; migrating in line with the capillary to distal towards the cuticle
4) non-definable; not matching criteria 1-3

As punctate extravasations and perivascular haemorrhages were interpreted as a continuous spectrum, an analysis with groups 1-2 merged (mean) kappa/ICC was also calculated as one sub-group. For qualitative data, Fleiss' and Cohen's kappa analyses were calculated. For quantitative data, the intraclass correlation coefficient (ICC) was calculated.

Results:

Inter-rater scores	**Fleiss' kappa** (qualitative counts)	95% CI	**ICC** (quantitative counts)	95% CI
Punctate&perivascular haemorrhages	0.62	0.57-0.67	0.82	0.76-0.87
Large confluent haemorrhages	0.78	0.72-0.83	0.93	0.91-0.95
Intra-rater scores	**Mean Kappa** (qualitative counts)		**Mean ICC** (quantitative counts)	
Punctate&perivascular haemorrhages	0.70		0.84	
Large confluent haemorrhages	0.86		0.96	
CI = Confidence Interval	Kappa interpretation: 0.61-0.80 substantial agreement >0.81 almost perfect agreement		ICC interpretation: 0.76-0.90: good >0.90 excellent	

Conclusion: This is the first study on intra- and inter-rater reliability for different subtypes of nailfold capillary haemorrhages in (c)SLE. Our findings show that different subtypes of capillary haemorrhages in cSLE-patients can be reproduced with a good inter- and intrarater reliability. This confirms our recent observation of two haemorrhage-subtypes in a cross-sectional case-control study. Thus, it also indicates the potential diagnostical value for NVC in cSLE. Future observational studies should elucidate whether the different subtypes of capillary haemorrhages are specific for (c)SLE compared to (juvenile) dermatomyositis and (juvenile) systemic sclerosis. Longitudinal studies are needed to investigate the role of capillary haemorrhages as a prognostic biomarker for disease damage in (c)SLE.

Disclosure of Interest: None declared

P247

THE PERFORMANCES OF DIFFERENT CLASSIFICATION CRITERIA IN PEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS

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Introduction: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease. The three available classification criteria for SLE are ACR 1997, SLICC 2012, and EULAR/ACR 2019 all of which are formed based on data mainly derived from adult SLE cohorts.

Objectives: We aimed to test the performances of ACR 1997, SLICC 2012, and EULAR/ACR 2019 SLE criteria among pediatric SLE patients.

Methods: One hundred and eleven SLE patients from Hacettepe University, Ankara; 102 from Erciyes University, Kayseri; and 49 SLE patients from Umraniye Training and Research Hospital, Istanbul, Turkiye were included. As controls, 172 children with different rheumatic diseases (including mixed connective tissue disease and juvenile dermatomyositis) who had ANA test were included. The disease onset was before 18 years of age in all patients. The sensitivity and specificity of the ACR 1997, SLICC 2012, and EULAR/ACR 2019 criteria were evaluated based on the features of the patients at the time of diagnosis. The gold standard for the diagnosis of SLE was expert opinion at each center.

Results: In total, 262 SLE (80.9% female) and 172 control patients were included. The sensitivities of ACR 1997, SLICC 2012, and EULAR/ACR 2019 criteria were 68.7%, 95.4%, and 92%, respectively. The specificities of ACR 1997, SLICC 2012, and EULAR/ACR 2019 criteria were 94.8%, 89.5%, and 87.8%, respectively. There were 17 SLE patients who met SLICC criteria but did not fulfill ACR/EULAR 2019 criteria. Among these patients, hematologic involvement was prominent (12/17; 70.6%). On the other hand, there were 8 SLE patients fulfilling ACR/EULAR 2019 criteria but not SLICC 2012 criteria. In these patients, joint involvement was prominent (6/8; 75%). The characteristics of these patients are presented in Table 1.

Table 1. SLE (systemic lupus erythematosus) patients who met either one of the SLICC 2012 or EULAR/ACR 2019 criteria but not the other

Characteristics, n (%)	**SLE patients who met SLICC 2012 but not EULAR/ACR 2019 (n=17)**	**SLE patients who met EULAR/ACR 2019 but not SLICC 2012 (n=8)**
Joint involvement	3 (17.6)	6 (75)
Oral ulcers	8 (42)	0 (0)
Hematologic involvement	12 (70.6)	1 (12.5)
ANA positivity (≥1/80)	15 (88.2)	8 (100)
Anti-cardiolipin antibodies	6 (35.3)	0 (0)
Anti-β2 glycoprotein	3 (17.6)	0 (0)
Lupus anticoagulant	4 (23.5)	0 (0)
Renal biopsy	2 (11.8) (class I; class III lupus nephritis)	0 (0)
SLE according to the ACR 1997 criteria	7 (41.2)	2 (25)

ACR, American College of Rheumatology; ANA, anti-nuclear antibody; anti-dsDNA, anti-double stranded DNA; EULAR, European League Against Rheumatism; SLE, systemic lupus erythematosus; SLICC, Systemic Lupus International Collaborating Clinics

Conclusion: In our study, the sensitivity of SLICC 2012 criteria was the best, while the best specificity was that of ACR 1997 criteria. SLICC 2012 criteria performed better than EULAR/ACR 2019 criteria with higher sensitivity and specificity. Separation of different hematological manifestations in SLICC 2012 criteria might have contributed to the higher performance of this criteria set.

Disclosure of Interest: None declared

P248

VALIDATION OF THE 2019 ACR/EULAR CLASSIFICATION CRITERIA OF SYSTEMIC LUPUS ERYTHEMATOSUS IN A MEXICAN PEDIATRIC POPULATION

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Introduction: Systemic Lupus Erythematosus (SLE) is the prototype autoimmune disease, characterized by the presence of multiple autoantibodies with the consequent formation and deposition of immunocomplexes, and other immune processes, causing a multisystemic disease. Over the years, various classification criteria have been published with variable performance. In 2019 the European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR) developed a set of criteria, which the validity has not been studied so far in the pediatric population with juvenile Systemic Lupus Erythematosus (SLEj).
Objectives: To determine the sensitivity, specificity, positive predictive value and negative predictive value of the 2019 EULAR / ACR criteria for SLE in children who attended in the pediatric rheumatology service of the Hospital Infantil de México Federico Gómez and compare them with the ACR criteria of 1997 and the International Collaborating Clinics of Systemic Lupus (SLICC) 2012.
Methods: Retrospective collection of clinical and paraclinical data during the first month of illness in patients with SLEj and control group with rheumatologic disease other than SLE who have a positive determination of antinuclear antibodies. The ACR 1997, SLICC 2012 and 2019 EULAR / ACR classification criteria were applied to each patient to determine the sensitivity, specificity, positive predictive value and negative predictive value for each classification criteria.
Results: A total of 100 patients with LESj diagnosis and 100 patients in the control group were included. 88% of the cases and 76% of the controls were female. The average age at diagnosis was 10.5 ± 3.78 years (2 - 17 years). When comparing the criteria proposed by 2019 EULAR-ACR, ACR 1997 and SLICC 21012, greater sensitivity, specificity, positive predictive value and negative predictive value were obtained in the 2019 EULAR-ACR criteria (98%, 100%, 100% and 98% respectively) as reflected in Table 1.

Table 1. Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value of the Classification Criteria of the European League Against Rheumatism and the American College of Rheumatology of 2019, American College of Rheumatology 1997 and the group of International Collaborating Clinics of Systemic Lupus from 2012.

Criteria	**Sensitivity (%)**	**Specificity (%)**	**PPV (%)**	**NPV (%)**
2019 EULAR-ACR	98	100	100	98
ACR 1997	91	98	98	92
SLICC 2012	88	97	97	89

Conclusion: It is the first study in pediatric population where a comparison of the three groups of classification criteria is performed and reveals a sensitivity of 98% and specificity of 100% for the 2019 EULAR-ACR criteria, demonstrating greater sensitivity and specificity in comparison with the criteria of ACR 1997 and SLICC 2012. The report identifies the applicability of the 2019 EULAR / ACR criteria and sets a guideline for future studies.

Disclosure of Interest: None declared

P249

MOLECULAR FINDINGS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS FROM SAKHA REPUBLIC (YAKUTIA)

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Introduction: In the last few years, many monogenic defects leading to a lupus-like phenotype have been described. Sakha Republic (Yakutia) is a large north – eastern region of Russia where an increased incidence of systemic lupus erythematosus (SLE) is reported. In general, like the native Americans from Alyaska, the Yakutia aboriginals have a load of autoimmune diseases, especially HLA-B27-associated conditions.
Objectives: Yakut population of 500000 has peculiar genetic background and high level of consanguinity; thus, we expected to reveal specific lupus - associated genes and founder variants characteristic for this ethnic group.
Methods: We performed clinical exome sequencing of 14 Yakut SLE patients (9 – 18 years old) primarily focusing on analysis of the 51 genes currently associated with monogenic lupus and lupus – like conditions.
Results: Likely causative variants of SLE-associated genes were detected in 7 of 14 patients. Rare variants of RNASEH2B, TREX1, PTPN22, DNASE1L3, TMEM173 and SAMHD1 including some recurrent alleles have been revealed. It is also of interest that TNFRSF13C c.62C>G (p.P21R) polymorphism having reported frequency of 1 – 7% in different world populations was apparently overrepresented in the group of SLE patients.
Conclusion: Genetic defects may be detected in a substantial fraction of non-early onset Yakut SLE thus making this population worthy of further analysis. This pilot study extends existing data on spectrum of genetic variants associated with SLE.

This work was supported by the RSF grant № 20-45-01005
Disclosure of Interest: None declared

e-Poster viewing: Treatment

P251

RATES OF TUBERCULOSIS INFECTION IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS PRECEDING ANTI-TNF THERAPY FOR MORE THAN 2 YEARS: A SINGLE-CENTER OBSERVATIONAL STUDY.

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Introduction: Currently, the assessment of the incidence of tuberculosis infection in patients with juvenile idiopathic arthritis (JIA) receiving therapy with TNF-alpha inhibitors remains relevant.
Objectives: To evaluate the incidence of tuberculosis infection in patients with JIA receiving anti-TNF therapy (Adalimumab (ADA), Etanercept (ETA)) for 2 years or more.
Methods: This was a retrospective study that included JIA patients treated with anti-TNF therapy for more than 2 years. 48 JIA patients with current age 9.2±4.0 years, mean disease duration of 3.4±1.8 years were included. All patients received a single anti-TNF therapy: 28(58%) patients were treated with etanercept, 20(42%) patients were treated with adalimumab. All patients were screened for latent tuberculosis infection(LTBI) prior to anti-TNF therapy using tuberculin skin test (TST), chest computer tomography (CT) and history of exposure to tuberculosis. Patients were regularly followed at 6-month intervals. Before patients started receive anti-TNF therapy, LTBI screening (solely TST-positive) was positive in 8(16.6%) patients: 5 patients in group of ETA and 3 in group of ADA, no one had active tuberculosis (TB) or history of TB exposure.
Results: After 2 years of therapy with ADA latent tuberculosis infection (LTBI) was diagnosed in 6(12.5%) patients (10.3/100 patient-years); spontaneously cured primary tuberculosis was diagnosed in 1(2%) patient (1.7/100 patient-years); pulmonary tuberculosis (positive TST and changes on chest CT) was diagnosed in 1(2%) patient (1.7/100 patient-years). After 2 years of ETA therapy LTBI was diagnosed in 4(8.3%) patients (4.6/100 patient-years); spontaneously cured primary tuberculosis developed in 1(2%) patient (1.1/100 patient-years).
Conclusion: According to the obtained data it can be concluded that the risk of developing tuberculosis infection among patients receiving anti-TNF therapy remains. Our observation shows that the risk of developing tuberculosis infection is slightly higher in the group of children receiving ADA, compared with patients treated with ETA.
Disclosure of Interest: None declared

P252

HYPERSENSITIVITY REACTIONS WITH DMARDS

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Introduction: Disease-modifying antirheumatic drugs (DMARDs), are widely used for the treatment of rheumatologic diseases including juvenile idiopathic arthritis (JIA), psoriatic arthritis (PsA), entesitis related arthritis (ERA), systemic sclerosis (SSc), systemic lupus erythematosus (SLE), and Sjogren syndrome (SS), juvenile dermatomyositis, Behçet Disease. We aimed to study the hypersentivity reaction findings associated with the commonly used conventional DMARDs include methotrexate, leflunomide, hydroxychloroquine and sulfasalazine.
Objectives: We aimed to study the hypersentivity reaction findings associated with the commonly used conventional DMARDs include methotrexate, leflunomide, hydroxychloroquine and sulfasalazine.
Methods: We evaluated the patients followed up between January 2019 and January 2020 in Department of Pediatric Rheumatology in Hacettepe University, Ankara, Turkey. 128 pediatric patients used DMARDs were accommodated in the study. The demographics, disease course, atopy history, familial history of atopy and drug allergies were analysed.
Results: 128 pediatric rheumatology patients including 46 juvenile idiopathic arthritis, 23 familial mediterranean fever patients, 19 polyarteritis nodosa, 17 systemic lupus erythematosus, 7 Behçet' s disease, 5 juvenile dermatomyozitis, 5 enthesitis-related arthritis, 4 scleroderma, and 2 psoriatic arthritis were the subject of this study. Drug allergy was found in 14 patients: 7 against to antibiotics, 4 against to biologic agents and 3 to DMARDs. The use of DMARDs agents among the group were: 62 patients (48%) using methotrexate, 38 patients (29%) colchicine, 18 patients (14%) hydroxychloroquine, 18 patients (14%) mycophenolate mofetil,12 patients (9%) cyclosporine A, 19 patients (14.8%) AZA, 2 patients sulfasalazine. No allergic reactions to MTX, AZA, MMF were detected. On the other hand, 1 patient developed a hypersensitivity reaction against hydroxychloroquine similar to erythroderma, and another patient developed allergic reactions to sulfasalazine, one to infliximab, one to colchicine and one to rituximab.
Conclusion: DMARDs are commonly used agents in rheumatology departments, hypersensitivity reactions against them are seldom reported. It is usually known that the subcutaneous form results in more allergic reactions than the oral form, however it is discovered that oral forms of DMARDs is very likely to lead to allergenic reactions.
Key words: childhood, DMARDs, hypersensitivity reactions, rheumatologic disease, methotrexate
Disclosure of Interest: None declared

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DRUG SURVIVAL AND SAFETY OF BIOLOGICAL THERAPIES IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Biological treatment (BT) has changed perspectives of JIA patients. Increasing data from real life experience have been reported.
Objectives: To compare drug survival, safety and efficacy of BT in patients with Juvenile Idiopathic Arthritis (JIA).
Methods: A retrospective observational study was conducted on JIA patients followed in a referal hospital and who had received at least one BT between 1999 and 2019.
Results: 218 BT in 130 JIA patients were analyzed. 67.7% were women with a median age at diagnosis of 8 years old IQR (3-13) and a median age at the beginning of the BT of 15 years old IQR(7.8-21). 21.5% of the patients had uveitis during follow-up. BT were indicated due to: arthritis (73.9%), uveitis (10.1%), arthritis and uveitis (2.7%), systemic activity (8.3%) and macrophage activation syndrome (1,8%).There were 130 BT started in 1st line, 55 in 2nd line, 20 in 3rd line, 10 in 4th line and 3 in 5th line.
The 1st line BT most frequently indicated was Etarnecept (ETN) up to 40%, followed by 30% Adalimumab (ADA) and 16,2% Infliximab (INF). The median duration of the 1st line was 51 months IQR (14-109,3). However, 53.8% of the 1stline BT were swiched: 28.3% due to adverse events, 25.7% due to 1º failure and 25.7% due to 2º failure. The BT that were discontinued were: INF (76.2%) and Anakinra (ANAK) (75%) due to adverse events and ETN (59.6%) due to 1º and 2º failure. 55 patients started a 2nd BT: 43.6% received ADA and 20% Tocilizumab (TCZ) with a median duration of 43 months IQR (12-90). 22 of 55 BT required a change: 75% of ETN and 59% of INF prescribed in 2nd line were discotinued. The causes were: 40% 1º failure, 28% 2º failure and 12% remission. In 1st line 87,6% of patients received TNF inhibitors, 74% mantained the target in 2nd line. In 3rd line TCZ was the most frequent BT. 71.5% of patients continue on BT. BT was withdrawn in 20 of 130 patients due to remission (40%), adverse events (30%), and pregnancy (10%).
In the analysis by decades, 80 BT (36.7%) were started from 1999 to 2008 and 138 BT (63.3%) from 2009 to 2019. In the 1st decade ETN and INF were the most frequently prescribed and in the 2nd decade, ADA and TCZ (p <0.0001). The 1st BT in the 2nd decade were indicated sooner compared to the 1st decade (1st decade: mean 119.5months SD(109.2); 2nd decade: mean 53.9 months SD(99.7); p <0.0001). In 1st line BT, the BT prescribed in the 2nd decade had a shorter duration than those in the 1st decade (1st decade: mean 84.1 months SD(71.8); 2nd decade: mean 51.7 months SD(5); p <0.0001).
In the survival analysis, TCZ and ADA were the BT with the highest survival (p=0.001). Of the 31 patients that startedTCZ, 61.3% continue on TCZ, with a median duration of 46 months IQR(25-99) and 36/68(52,9%) still on ADA with a median duration of 61,5 months IQR(30.5-98).
Conclusion: 42.3% of patients required more than one BT. Since the onset of the BT there has been a change in prescription, probably related to the emerge of new targets and the evidence provided by clinical trials and guidelines. TCZ and ADA were the BT with the highest survival rate. On the other hand, INF and ANAK were the ones with the lowest survival rate. The most common causes of BT change in 1st line were adverse events in relation to INF and ANAK. In 2nd line there was a high rate of change in those patients who maintained TNFi, related to 1º failure.
Disclosure of Interest: None declared

P254

REVISING THE WHO ESSENTIAL MEDICINES LIST FOR PAEDIATRIC RHEUMATOLOGY

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Introduction: The World Health Organisation (WHO) Essential Medicines List (EML) informs countries about the minimum medicine items necessary to meet priority health needs of the population (both adults and children). The EMLs guide national and institutional medicine lists, especially in Low and Middle Resource Income Countries. The current EML for paediatric rheumatology does not reflect current best practice (*Foster and Scott 2020 Nature Reviews Rheumatology*). The Paediatric Global Musculoskeletal Health Task Force (TF) is working to revise the WHO EML.

Objectives: To explore which drugs are considered 'essential' and 'ideal' for listing in the EML under paediatric rheumatic diseases.

Methods: Healthcare professionals working in paediatric rheumatology and who are TF members were invited to take part in an anonymous online survey. We had 97 responses from 43 countries (across all continents), with 1-35 years of clinical practice including: consultant grade paediatric rheumatologists (n=77), consultant general paediatricians with interest in rheumatology (n=13), paediatric rheumatology trainees (n=3), adult rheumatologists (n=3) and a nurse working in paediatric rheumatology (n=1). The survey data was analysed applying descriptive statistics and free-text comments using qualitative techniques.

Results: Most respondents (n=70/97, 72%) reported that a revised EML would improve access to medicines in their country, improve drug provision and accessibility within their clinical practice, provide assistance when negotiating with healthcare agencies, funding bodies or insurance companies and inform paediatric trainees and adult rheumatologists about paediatric rheumatology issues. They deemed that the EML should list the following drugs (Table 1).

Table 1: Rheumatic disease drug inclusion within the WHO EML

Drug	Should Include (Ideal)	Inclusion 'Essential'	Drug	Should Include (Ideal)	Inclusion 'Essential'	Drug	Should Include (Ideal)	Inclusion 'Essential'
Oral prednisolone	100%	92%	Intravenous cyclophosphamide	91%	77%	Subcutaneous Tocilizumab	81%	46%
Oral NSAIDs	99%	93%	Adalimumab	91%	71%	Infliximab	80%	52%
Hydroxychloroquine	98%	88%	Anakinra	90%	60%	Intravenous bisphosphonate (e.g. pamidronate)	76%	37%
Intravenous Methylprednisolone	98%	83%	Etanercept	87%	70%	Intra-articular corticosteroid Triamcinolone Acetonide	72%	28%
Methotrexate oral	96%	81%	Intra-articular corticosteroid Triamcinolone Hexacetonide	86%	64%	Intra-articular corticosteroid Methylprednisolone	45%	25%
Mycophenolate Mofetil	95%	77%	Intravenous Tocilizumab	86%	63%	Oral cyclophosphamide	41%	16%
Azathioprine	94%	71%	Oral prednisolone (soluble)	86%	55%	Inhaled analgesia (nitrous oxide)	36%	15%

Methotrexate subcutaneous	91%	80%	Ciclosporin	85%	52%	Thalidomide	34%	8%
Total Respondents: 97								

Conclusion: Respondents confirmed the need to update the WHO EML and anticipate considerable impact on clinical practice in many countries around the world. More than 80% of respondents identified 5 agents as 'essential' (oral, intra-articular and intravenous steroids, NSAIDS, Hydroxychloroquine and Methotrexate [oral and subcutaneous]) and indicated that the EML should include a wide range of synthetic and biologic DMARDS as well as other immunosuppressive agents used in the management of rheumatic diseases in children. This data will form the basis of the TF application to the WHO to revise the EML with submission planned for 2020.
Disclosure of Interest: None declared

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THE RANGE OF BIOLOGICAL DRUGS USED IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS, SARATOV REGION EXAMPLE.

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Introduction: The last decade has brought a lot to the approaches to the diagnosis and treatment of juvenile arthritis. In Russia, the actualization of the problem of diagnosis and treatment of JIA required the development of federal standards, which provide the most detailed algorithms for medical care, both at the stage of inpatient and outpatient care. In the regions of the Russian Federation, the effective use of these documents required a whole range of additional educated activities, both with students of medical universities, as well as with the medical and nursing community, in addition, a set of work was carried out to create a regional regulatory framework. The first genetically engineering drug with children's indications in the Russian Federation was registered at the end of 2009. Over the past decade, the range of biological agents used in pediatrics has expanded significantly and requires constant replenishment of the level of knowledge of doctors.
Objectives: To analyze the structure of biological therapy in patients with juvenile idiopathic arthritis living in the Saratov region of the Russian Federation.
Methods: The study included generalized information on 253 patients aged 1-17 years with a diagnosis of JIA verified by the ILAR criteria and living in the Saratov Region on January 1, 2019.
Results: According to medical statistics in the region, a diagnosis of JIA has been made in 253 children and adolescents. A significant increase is noted annually in children receiving biological therapy, so in 2014 there were 30 patients, which accounted for 9,3% of the total number of patients with JIA, at the beginning of 2019 this figure was 19% (n = 48), and by the end of 2019 – 22,1% (n = 56). In the total biological therapy pool, 67% of patients receive TNF-alpha inhibitors, antibodies to IL-6 receive 27% of patients, antibodies to IL-1 – 6,25%. It is worth noting that when using biological agents in 60% of cases, the criterion of an inactive disease was achieved by 4-5 months, which was characterized by the absence of acute inflammatory symptoms, normalization of ESR and CRP. Monitoring of patients with JIA receiving biological agents required the conduct of a number of educational activities for medical personnel, the creation of an additional methodological base. For further training of young specialists at the regional medical university, a program of an additional educational course in pediatric rheumatology was developed and introduced. A regional patient organization was established and also required a set of information activities by the medical community.
Conclusion: In the Saratov region of the Russian Federation, about 20% of patients with JIA receive biological therapy, which corresponds to the average indicators according to the literature. In the structure of the biological drugs used, the group of TNF-alpha inhibitors is preserved - 67%. The introduction of modern methods of treatment using biological agents in JIA has significantly increased the effectiveness of treatment, but it required the organization of additional information support for medical personnel.
Disclosure of Interest: None declared

P257

BIOLOGICAL THERAPIES IN JUVENILE IDIOPATHIC ARTHRITIS: ARE THERE ANY DIFFERENCES BETWEEN CATEGORIES?

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Introduction: Juvenile Idiopathic Arthritis (JIA) is a heterogeneous group of pediatric diseases. Different response to biological treatment (BT) has been reported according to disease subtype.
Objectives: to analyze the presctiption and withdrawal of BT in JIA patients with focus on JIA category.
Methods: A retrospective observational study was conducted on JIA patients followed in a referal hospital and who had received at least one BT between 1999 and 2019.
Results: 130 JIA patients were analyzed: 29 (22,4%) were Oligoarticular Persistent (OligP), 22 (16,9%) Enthesitis related Arthritis (ERA), 20 (15,4%) Systemic (sJIA), 19 (14,6%) Polyarticular RF- (PolyRF-), 14 (10,8%) Polyarticular RF+(PolyRF+), 13 (10%) Oligoarticular-Extended (OligE), 11 (8,4%) Psoriatic Arthritis (APso) and 2 (1,5%) Undifferentiated (Und).
The main characteristics are summarized in table 1.
The first line BT most frequently indicated was Etanercept up to 40% in all the categories except for ERA, where the most frequent BT was Adalimumab and sJIA, where the most frequent BT was Anakinra. The time between diagnosis and start of BT was different among the categories (p=0,007). In the Und category, the time until BT was the shortest (median: 1 month), since both patients had coxitis, followed by APso [median: 9 months IQR(1-57)] and sJIA [median: 17,5 months IQR(0,3-146,8)].
The survival of the first BT was different among the categories (p=0,006): 94,7% of the ERA continue receiving the first BT, followed by 76,2% of OligP and 50% of PolyRF+ and APso. Only 42% of sJIA continue on the first BT prescribed [up to 53,3% were TNF inhibitors (TNFi)]. The categories with less retention of the first BT were: OligE (25%) ; PolyRF- (27,3%) and Und (0%). The most frequent cause of discontinuation, among these categories, was secondary failure.
In the survival analysis between categories, there were differences on OligP (p=0,004), OligE (p=0,042) and PolyRF- (p=0,017). Tocilizumab and Adalimumab were the BT with highest survival with regards to Infliximab, Etanercept, Rituximab (OligE, PolyRF-), Abatacept (OligE, PolyRF-) and Certolizumab (OligP). The survival rate of IL1 inhibitiors and IL6 inhibitiors was higher regarding to TNFi in sJIA patients (p=0,013).

Table 1	OligP	ERA	sJIA	PolyRF-	PolyRF+	OligE	Apso	UND
Sex,n% M F	4(13,8) 25(86,2)	17(77,3)5(22,7)	11(55) 9(45)	2 (10,5) 17(89,5)	2(14,3) 12(85,7)	1(7,7) 12(92,3)	4(36,4) 7(63,6)	1(50) 1(50)
Age at diagnosis me, IQR	4 (2,6-5)	12 (9,8-15)	7 (3-13)	8 (2-13)	12 (8,5-15)	3,5 (2-8,3)	12 (3-15)	. 12,5
Uveitis,n%	12(41,4)	7(31,8)	0(0)	3 (15,8)	0 (0)	3(25)	2 (18,2)	1(50)
ANA, n (%) ACPA, n (%) B27, n (%)	22(75,9)	18(81,8)		8 (42,1)	12 (85,7) 9(64,3)	9(75)	5 45,5) 3(27,3)	
BT lines: n	1ª: 29 2ª: 11 3ª: 1	1ª: 22 2ª: 2	1ª: 20 2ª: 10 3ª: 5 4ª: 1 5ª: 1	1ª: 11 2ª: 9 3ª: 6 4ª: 3	1ª: 14 2ª: 7 3ª: 2 4ª: 2	1ª:13 2ª: 9 3ª: 2 4ª: 1 5ª: 1	1ª:11 2ª: 5 3ª: 4 4ª: 3 5ª: 1	1ª:2 2ª:2

Conclusion: Taking into account JIA category is mandatory to choose BT and to understand the response and discontinuation of BT. OligE and PolyRF - showed a high rate of change of the first BT related to secondary failure of Etanercept and Infliximab when compared to Adalimumab and Tocilizumab, as described in the survival analysis. The category with the highest retention of the first BT was ERA. UND patients started sooner BT due to the presence of coxitis. In sJIA, IL1 inhibitors and IL6 inhibitors were superior to TNFi in the survival analysis, as reported in existing literature.
Disclosure of Interest: None declared

P258

COMPARISON OF DIFFERENT PHARMACEUTICAL PREPARATIONS OF COLCHICINE IN CHILDREN WITH FMF: IS COLCHICINE OPOCALCIUM A GOOD ALTERNATIVE?

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Introduction: Familial Mediterranean fever (FMF) is the most common autoinflammatory disease among Mediterranean populations that can cause serious complications such as amyloidosis, without proper treatment (1). Colchicine is an anti-inflammatory agent used for preventing FMF attacks and amyloidosis. Remarkable numbers of patients are non-responsive or intolerant to domestic drug colchicum dispert (2).
Objectives: This study aimed to compare the efficacy and side effects of colchicum dispert (CD) and colchicine opocalcium (CO) in children with FMF.
Methods: Twenty-nine children with FMF, who used CD at least six months initially, and another consecutive 6 months of CO were included. Clinical features, visual analog scale (VAS) for pain scores, exercise induced leg pain (EILP), and FMF severity scores with laboratory parameters were evaluated for both treatment periods. Bristol stool chart and number of stools per 24 hours were recorded for comparing gastrointestinal side effects.

Results: There were 13 female (43.4%) and 16 male (56.6%) patients and the mean age was 14 ± 3.8 years. Non-responsiveness to CD was the major indication for switching preparation in 18 patients (62 %), and also intolerance was noted in 11 patients (38 %) due to gastrointestinal symptoms, i.e. diarrhea. 19 patients had homozygous M694V mutation (62 %) and 27 patients had exon-10 mutation in at least one allele of MEFV gene (93 %). The median duration for CD treatment was higher than that for CO.
The mean dosage of CO was higher (1.71 ± 0.44 mg/day) than CD (1.49 ± 0.41 mg/day), and the difference was statistically significant ($p<0.001$). Besides, usage of CO (significantly higher dosage than CD) showed beneficial effects on number and duration of attacks, VAS for pain and EILP scores, also on FMF severity scores, statistically significantly ($p<0.05$ for each parameters) (Table 1).
Usage of colchicine opocalcium was successful also in terms of controlling gastrointestinal symptoms. Bristol stool chart questionnaire scores decreased from 5.62 ± 1.56 to 4.15 ± 1.73 points, and scores of daily stool number decreased from 0.46 ± 0.894 points to 0.03 ± 0.118. Decrease in gastrointestinal complaints were statistically significant ($p<0.05$) (Table 1).
There were 12 patients in which colchicine dose remained the same. We further analyzed this group separately to see if there was a bias in terms of change of dosage. The results were similar to the whole group analysis. There was a significant decrease of the clinical findings such as number of attacks at the last six months, average duration of attacks, FMF severity score and VAS scores of EILP ($p<0.05$). Also, the laboratory findings such as NLR, ESR and CRP values were decreased following switch.

Table 1. Comparison of clinical results for both preparations (n=29).

	Colchicum Dispert	*Colchicine Opocalcium*	*p value*
Duration of treatment (months)	**59.54 ± 36.43**	**26.39 ± 16.64**	**<0.001**
Dosage (mg/day)	**1.49 ± 0.41**	**1.71 ± 0.44**	**<0.001**
Number of attacks at the last 6 months	**4.83 ± 2.1**	**1.89 ± 1.50**	**<0.001**
Average duration of FMF attacks (hours)	**63.98 ± 25.84**	**44.41 ± 21.81**	**<0.001**
EILP (attack-free period)	**7.36 ± 1.43**	**2.84 ± 1.77**	**<0.001**
FMF severity score	**8.88 ± 2.08**	**6.52 ± 1.83**	**<0.001**
Bristol stool scale	**5.62 ± 1.56**	**4.15 ± 1.73**	**0.044**
Number of stools/24 h	**0.46 ± 0.894**	**0.03 ± 0.118**	**<0.001**

Conclusion: The patients with FMF in pediatric age group who have active disease and/or gastrointestinal complaints during the use of colchicum dispert, may benefit from colchicine opocalcium. It might be a valuable treatment option before considering biological agents.

Disclosure of Interest: None declared

P259

ANTI-ADALIMUMAB ANTIBODIES DETECTION USING A NOVEL PEPTIDE-BASED ASSAY IN A COHORT OF PEDIATRIC PATIENTS WITH CHRONIC RHEUMATIC DISORDERS : A PILOT STUDY

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Introduction: Immunogenicity and development of anti-drug antibodies have been associated with treatment failure and adverse events during biologic treatment. Anti-drug antibodies (ADAs) have been reported in 21% of Juvenile Idiopathic Arthritis patients treated with Adalimumab. However, their role in reducing adalimumab efficacy is still debated due to conflicting results. No study has been directed toward identification of neutralizing ADAs in paediatric rheumatic disorders.
Objectives: Aim of our study was to detect ADAs, along with their clinical relevance, using a new theranostic peptide-base assay in a cohort of children with inflammatory chronic diseases on Adalimumab treatment.
Methods: Six candidate Adalimumab derived peptide antigens (HC-CDR1, HC CDR2, HC CDR3, LC CDR1, LC CDR 2, LC CDR3) have been developed and optimized to be tested. Their performance has been compared with commercial ELISA kit and a SPR-based optical assay (Biacore®). Assays have been performed in sera of a cohort of children receiving Adalimumab due to an inflammatory chronic disease. Mean age, disease duration, concomitant treatment with methotrexate (MTX), ANA positivity, disease activity parameters and scores at the time of ADA determination have been recorded. Chi-square, and Fisher exact test were used to compare data. Pearson's and Spearman's correlation tests were used to determine correlation coefficients for entered variables.
Results: Eighteen (14 F, median age 12.6, range 3.8-16, yrs) patients were enrolled: 16 affected by Juvenile Idiopathic Arthritis, 7 of whom complicated by JIA -associated chronic uveitis, and 2 patients affected by chronic idiopathic uveitis. Peptide assay revealed ADAs in 8 children, Biacore in 6, commercial Elisa in 5. Of note, we found total concordance among the 3 tests just in 2 patients. No significant correlation has been proven among the 3 ADA determinations. Biacore and ELISA determination showed significant concordance (r_S: 0.72, $p<0.006$). The presence of HC CDR3 and LC CDR 3 resulted significantly correlated with disease activity (r_S: 0.57, $p<0.05$), and, inversely, with disease remission on treatment (r_S= -0.523, $p<0.05$). No patient experienced severe adverse events and no correlation with ADAs has been revealed
Conclusion: In chronic rheumatic disorders, novel reliable methods are urgently required to guide clinical decision and support decisions about switching within or between drugs in refractory children. The 3 different methods, since based on different antigenic probes, detect different antibody populations. The present peptide-based assays might contribute to identify neutralizing ADAs in patients treated with Adalimumab. Further validation in larger cohort is required.
Disclosure of Interest: None declared

P260

TNF-INHIBITORS THERAPY IN 13 PATIENTS WITH NON-BACTERIAL MULTIFOCAL OSTEOMYELITIS: LESSONS FROM REAL CLINICAL PRACTICE OF THE SINGLE CENTER

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Introduction: Non-bacterial multifocal osteomyelitis (NBO) is a rare polygenic autoinflammatory disease, which is difficult to diagnose and treat. Because of combination of bone lesions with arthritis and/or axial skeleton damage in most cases the diagnosis of juvenile idiopathic arthritis (JIA) or juvenile ankylosing spondylitis (JAS) may be establish as a concurrent diagnosis, so this allows to legal use of Biologics (BA) for the treatment.
Objectives: To analyze the single center experience of clinical and laboratory features of multifocal NBO in patients (pts) who were treated by BA for the last 8 years.
Methods: The study involved a retrospective cohort of multifocal NBO pts treated by different BA in our clinic from 2013 to 2020. All of them underwent standard rheumatological examination. In order to examine all localizations of the bone damage, a scintigraphy and/or "whole body" MRI scan was performed.
Results: Among the whole group of pts with NBO (n=40) we identified 13 pts treated by BA (TNF-inhibitors only). The majority were girls (n=9, 69 %). Age at disease onset was 10.2 years in average (Me 10.2 range 1.3-16.5). For legal reason of BA administration, we classified our patients according to rheumatological features as JIA or JAS. 7 pts had JIA (5 girls), 6 pts had JAS (4 girls). Among 13 pts 9 had oligoarthritis (69%), 4 had polyarthritis of low limbs (hip, knee, ankle). Axial involvement was represented by active erosive sacroiliitis with deep bone marrow edema on MRI scan in 9 pts (69%), active spondylitis of several bodies in thoracic spine – in 2; erosive arthritis with partial ankyloses of facet joints of neck in 3 pts, multiple syndesmophytes in 1 girl. We found that definite axial lesions in NBO developed in very young children (in 2 y.old at minimum), much earlier than in “idiopathic” JAS. HLA B27 was presented in 5 pts (39%), 5 pts had ANA in high titer (all of those HLA B27-negative). The pts had bone lesions in different parts of skeleton: vertebral bodies - 5 pts, clavicle - 1, sternum, ribs – 1, extremities bones, metaphysic mostly (tibial, fibular - 7 pts), sacroiliac region – 4 pts. Extraskeletal manifestations were observed in 3 pts, one in each condition - uveitis, psoriasis pustulosus, acnae conglobate. In a girl with very severe course of disease, not responded to any therapy NBO was combined with familial Mediterranean fever. High level of laboratory activity were detected before biologics in 10 pts (77%): ESR acceleration up to 60 mm/h, increase of CRP – up to 80 mg/l. Treatment included NSAIDS (all), methotrexate (7 pts), sulfasalazine (6 pts, but it was withdrawn in all pts), bisphosphonates (1 pt), prednisolone (3 pts). Because of high activity of NBO with appearance of new bone lesions and persistent arthritis TNF inhibitors were administrated: etanercept in 10 pts, adalimumab – 4 (2 as first line, 2 – second line), golimumab – 1. At the start of BA the average age was 13.7 years (range 7.2-17.9); mean disease duration was 3,4 years (range 0.3-8.1). There were 2 cases of withdrawals. Due to inefficacy etanercept was switched to adalimumab. Disease activity decreasing was reached in the most of the patients (12 from 13). Among them 2 pts developed the whole remission with resolving of active arthritis and bone marrow edema spots. Skin lesions (psoriasis pustulosis and acnae conglobate) were significantly improved. There were no adverse events during the TNF therapy.
Conclusion: Our experience of the therapy with TNF inhibitors in patients with high NBO activity has shown that this is a good and safe therapeutic option that is expected to prevent progression and bone destruction.
Disclosure of Interest: None declared

P261

SAFETY ON THE USE OF BISPHOSPHONATES IN PAEDIATRICS

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Introduction: The use of bisphosphonates has increased in paediatrics in the last twenty years.
Objectives: The study describes safety of bisphosphonate therapy in children in Montpellier and Nimes University Hospitals, France.
Methods: In our retrospective study, all patients treated with bisphosphonates between January 2012 and August 2018 were included. The main endpoint was safety using adverse events (AE) and serious adverse events (SAE) reported in medical files.
Results: 120 children, median age [IQR 25%>75%] of 13 years [1 month-18 years], with osteogenesis imperfecta (22), secondary osteoporosis (77: 63 immobility, 5 nutritional diseases, 7 corticosteroids, 1 sickle cell anaemia, 1 growth hormone deficiency) and non-fragility bone disorders (21: 10 fibrous dysplasia, 4 bone cysts and tumour, 7 inflammatory bone diseases), were included: 29 using zoledronate, 91 using pamidronate. The median duration of treatment [IQR 25%>75%] was 12 months [6-27 months]. AE were reported for 71.7% of patients, most within 24 to 48 hours after the first or second injection: flu-like symptoms (57.5%), hypocalcaemia (37.5%) and hypophosphatemia (20%). Underweight patients (body mass index < 18.5 kg/m²) accounted for 50% of hypocalcaemia. The frequency of all the AE not significantly decreased with the reduction of the first dose. Only one serious hyponatremia occurred corresponding to a patient with renal failure before treatment.
Conclusion: Our results were similar to those previously published: bisphosphonates are safe for osteoporosis in children. In the literature, SAE are very rare in children, being limited to anecdotal osteopetrosis in cases of higher doses and long-term treatment, and delayed bone healing. Anecdotal osteonecrosis of the jaw in adults has never been described in children. The use of bisphosphonates beforehand requires dietary measures (vitamin D and calcium supplementation). Furthers systematic collection on efficacy and safety parameters for each Bisphosphonates drug should confirm these data.
Disclosure of Interest: None declared

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A REAL-LIFE STUDY OF EFFECTIVENESS AND TOLERABILITY OF ADALIMUMAB BIOSIMILAR IN JIA-A SINGLE CENTRE EXPERIENCE

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Introduction: The use of biosimilars in rheumatology has increased significantly over the last 5 years and has resulted in considerable cost savings.
Objectives: To assess the effectiveness and tolerability of the Adalimumab biosimilar ABP 501 in patients with JIA.
Methods: A database of patients prescribed Adalimumab in our service has been screened to identify patients with JIA, who switched from the originator to the biosimilar. Only patients who had a clinical review since they had started the biosimilar were included. A paired-samples t-test was conducted to compare the number of active joints at the clinic appointment before and after the initiation of the biosimilar treatment. The frequency and type of side effects, the clinical response and the number of patients who switched back to the originator have been collected.
Results: Sixty-one patients who switched to the biosimilar ABP 501 between February 2019 and February 2020 were included. They were comprised of 30 enthesitis-related arthritis (ERA), 13 polyarthritis, 9 oligoarthritis, 6 psoriatic and 3 systemic JIA patients. Their baseline characteristics and outcomes are summarised in Table. The mean duration of follow-up after the switch to biosimilar was 10 months (range 2-23). Eleven patients (18%) reported side effects; the most common side effect (n=7, 63.6%) was injection site reactions and the remaining 4 consisted of anaphylaxis, drug-induced lupus, dizziness and bone pain, respectively. Seven patients (11.5%) reverted to the Adalimumab originator, 4 as a result of side effects, 3 because of ineffectiveness and one patient for both reasons. In addition, 3 patients were changed to a different biologic, one patient due to allergy to both the originator and biosimilar and the other two patients had active disease on the originator and biosimilar Adalimumab. Two patients stopped the biosimilar and remained off any biologic, in the first case this was due to a side effect and in the second case it was patient's choice. On the whole, 78.7% of patients had remained on ABP 501 at their last visit. There was no significant difference in the active joint count before the biosimilar was started (mean 0.55+/-1.11) and after the switch (mean 0.6+/-1.59), (p=0.855).

Age, mean (range)	21 (15-36)
Female, n (%)	40 (65.6%)
Disease duration in years, mean (range)	11.5 (0-29)
Prior exposure to biologics other than the originator, n (%)	25 (40.9%)
Concomitant Methotrexate, n (%)	31 (50.8%)
Side effects, n (%)	11 (18%)
Switched back to originator	5 (45.4%)
Remained on biosimilar	4 (36.4%)
Changed to different biologic	1 (9.1%)
Not on biologic	1 (9.1%)
Patient-reported reduced effectiveness, n (%)	6 (9.8%)
Switched back to originator	3 (50%)
Remained on biosimilar	3 (50%)

Conclusion: During a mean follow-up period of 10 months, 78.7% of JIA patients who switched to the Adalimumab biosimilar have remained on treatment with no significant difference in their disease activity. Overall, the tolerability and effectiveness of the Adalimumab biosimilar is acceptable, but 11.5% of patients required to be switched back to the originator.
Disclosure of Interest: None declared

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MATCHED CONTROLLED SURVEILLANCE OF GOLIMUMAB TREATMENT FOR POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS–AN INTERIM ANALYSIS

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Introduction: Golimumab (GOL) is approved for polyarticular juvenile idiopathic arthritis (pJIA) in patients of ≥2years but long-term safety data are limited.

Objectives: Prospective monitoring of long-term safety and effectiveness of GOL in routine care using the BIKER-registry.

Methods: Baseline demographics, clinical characteristics, disease activity and safety parameters were compared to a contemporary 1:2 matched control cohort using alternative TNF inhibitors or methotrexate without exposure to a biologic. Efficacy outcomes were JADAS10, joint counts and functional status. Safety assessments were based on adverse events (AE) reports.

Results: In this ongoing study, 65 pts initiating GOL were matched to 130 with alternative TNFi and 65 biologic-naïve pts. Pts starting GOL had a longer disease duration (p<0.0001) and use of GOL was significantly more often second line (84.6% vs 22.3%, p< 0.0001) and thus disease activity was lower at baseline. Pts in the GOL cohort used less corticosteroids, otherwise patients were comparable with pts treated with other TNFi (Table 1).

In GOL treated ps a marked clinical response was noted at 6 months and beyond, indicating the effectiveness of GOL in the treatment of pJIA. A significant decrease of the mean JADAS 10 11.3 to 5.3 (p=0.0008) after 6 months of treatment was observed, as well as JIA ACR 30/50/70/90 response rates of 61/59/42/29%. JADAS remission and minimal disease activity was observed in 27% and 53.7% after 6 months and in 39% and 54% after 12 months of treatment.

Rates of AE, SAE and infectious AE were comparable in the GOL cohort (87.5/100PY, 3.4/100PY and 11.1/100PY), the alternative TNFi cohort (92.3/100PY, 2.9/100PY and 9.7/100PY) and the MTX only cohort (121.2/100PY, 2.1/100PY and 18.5/100PY). SAE reported in the GOL cohort were flares of uveitis and of JIA (each 1) and fibromyalgia syndrome (1). SAE reported in the alternative TNF cohort was two serious infections (both influenza), one knee ligament injury, one flare of arthritis and one hyperventilation . No case of pregnancy, malignancy or death was reported.

	GOL N=65	Other TNFi N=130	MTX N=65	p# GOL vs TNFi/GOL vs. MTX
Disease duration, mean (SD), years	7.0(4.4)	4.2(3.8)	1.2(2.2)	<0.001/<0.001
RF - Poly/RF+ Poly/ext Oligo/PSA, n(%)	32(49.2)/ 6(9.2)/ 24(36.9)/ 3(4.6)	63(48.5)/ 20(15.4)/ 44(33.8)/ 3(2.3)	43(66.2)/ 12(18.5)/ 9(13.8)/ 1(1.5)	ns
Pretreatment bDMARD n(%)	56(86.2)	29(22.3)	0	<0.001/<0.001
Concomitant steroids, n(%)	9(13.8)	33 (25.4)	32 (49.2)	ns/<0.001
Active joints, mean (SD)	4.3 (3.8)	5.2 (5.8)	10.1 (6.7)	ns/<0.001
JADAS10, mean (SD)	11.3 (5.6)	12.2 (6.0)	17.1 (5.4)	ns/<0.001
AE,n (rate/100PY)	71 (87.5)	161 (92.3)	59 (121.2)	ns
SAE, n (rate/100PY; 95%CI)	3 (3.4; 1.2-8.3)	5 (2.9; 1.2-6.9)	1 (2.1;0.3-14.6)	ns
Serious infections, n (rate/100PY; 95%CI)	0	2 (1.1; 0.3-4.6)	0	na

Table 1 Baseline parameters and adverse events. Comparison of GOL cohort with 1st Other TNFi cohort and 2nd MTX cohort. # t-test or c2-test as appropriate. SD standard deviation, RF rheumatoid factor, bDMARD biologic disease modifying antirheumatic drug,

Conclusion: Golimumab seems an effective in treatment of pJIA. Tolerability was acceptable and comparable to alternative TNFi or MTX. Recruitment to the project is ongoing.

Trial registration identifying number: EUPAS20781

Disclosure of Interest: None declared

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METHOTREXATE INTOLERANCE: CHILDREN VS ADULTS

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Introduction: Methotrexate (MTX) is one of the most commonly used disease-modifying anti-rheumatic drug in rheumatology practice. It has some side effects that can impair quality of life. The most common of them is associated with the gastrointestinal tract.

Objectives: The aim of the study is to evaluate and compare the frequency of methotrexate intolerance in adult and pediatric patients.

Methods: Patients with rheumatologic diseases followed in Hacettepe University Pediatric Rheumatology and Rheumatology departments who used oral or parenteral methotrexate for at least 3 months were included in the study. Methotrexate intolerance was assessed using 'Methotrexate Intolerance Severity Score (MISS) questionnaire. The MISS questionnaire consisted of 5 parts: abdominal pain, nausea, vomiting, fatigue and behavioral symptoms. The patients scored the severity of each symptom separately; 0: no symptoms, 1: mild symptoms, 2: moderate symptoms, 3: severe symptoms. A total score of 6 or more was defined as MTX intolerance. Visual analogue scale (VAS) ranging from 0 cm to 10 cm was performed to each patient concurrently with the MISS questionnaire. In the pediatric patient group, MISS questionnaire and VAS assessment were applied to both patients and families.

Results: A total of 100 patients, 50 of whom were children, enrolled in the study. The mean age for children and adults were 11.78 (**±** 3.4) and 52.9 (**±** 11.8) respectively. The most frequent diagnosis of patients was juvenile idiopathic arthritis (78.0%) in children and rheumatoid arthritis in adults (68.0%). The mean MTX dose in adults and pediatric group was 12.5 (**±**3) mg vs 14.5 (**±** 3.6) mg (p: 0.004).

The prevalence of MTX intolerance in children and adults were 66.0% (n:33) and 14.0% (n:7) respectively. The mean MISS score in the pediatric group was higher compared with the adults (12.4±9.4 vs 1.84±4.5, p<0.001). Similarly, the mean VAS scores were higher in pediatric group (1.2±2.4 vs 4.2±3.2 (p<0.001)). There was a strong correlation between MISS and VAS scores between family and child evaluations (p <0.01, r = 0.95 / p <0.01, r = 0.94).

Abdominal pain, nausea, vomiting and behavioral symptoms were observed more frequently in children compared to adults. The rate of subcutaneous use of MTX was 74.0% in pediatric patients and 4.0% in adult patients. Of 61 patients receiving oral MTX, 17 (27.8%) experienced MTX intolerance, whereas 23 (58.9%) of 39 patients receiving parenteral MTX experienced intolerance to the drug symptoms (p=0.001). Complaints were started after the first dose in 2/7 in adults and 8/33 in children. MTX intolerance decreased with increasing folic acid dose (r = -0.26, p = 0.007).

MTX intolerance developed in 16 of 21 pediatric patients who were informed about side effects of drug by their families. In addition, 17 of 45 patients (%37.7) who read the drug prospectus had MTX intolerance.

Conclusion: Methotrexate intolerance was higher in childhood. Folic acid supplementation should be recommended for patients taking MTX treatment.

Disclosure of Interest: None declared

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RATES OF PSORIASIS DE-NOVO IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS PRECEDING ANTI-TNF THERAPY: A SINGLE-CENTER OBSERVATIONAL STUDY

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Introduction: nowadays there are known cases of psoriasis de-novo in patients with juvenile idiopathic arthritis(JIA) receiving therapy with TNF-alpha inhibitors.
Objectives: to evaluate frequency of psoriasis de-novo in patients with JIA receiving TNF-alpha inhibitors.
Methods: this prospective study included 73 patients with different types of JIA (persistent or extended oligoarthritis, RF-negative polyarthritis, enthesitis-related arthritis and undifferentiated arthritis) who were treated with TNF-alpha inhibitors. Children with psoriatic JIA were excluded from this study. All patients had no previous clinical manifestations of psoriasis. TNF-induced psoriasis had been identified as a case of psoriasis development after initiation of TNF-alpha inhibitors.
The average age of patients was 11.7±3.7 years, the average duration of the disease was 4.1±2.1.
24 (33%) children received Adalimumab(ADA), 49(67%) – Etanercept (ETA). The average duration of ADA therapy was 2.1±0.7 years. The average duration of ETA therapy was 2.9±1.1 years. All children received methotrexate (the average duration of methotrexate therapy was 3.4±0.7 years.
Presence of HLA B27 antigen had been detected in 14 (19%) patients: 9(64%) boys, 5(36%) girls.
Antinuclear factor (ANF) had been detected in 38 (52%) patients: 31(81%) girls, 7(19%) boys.
Results: 3(4%) out of 73 patients were diagnosed with psoriasis de-novo. One patient was treated with ADA (a girl with undifferentiated arthritis who had positive HLA-B 27, ANF and family history of psoriasis - her grandmother had psoriasis), 2 patients were treated with ETA (both female, one patient had undifferentiated arthritis, the other had enthesitis-related arthritis; both patients had positive HLA – B 27 and ANF negative).
2 patients achieved significant improvement after changing TNF-alpha inhibitor (1-ADA, 1-ETA), 1 patient (was treated with ETA) had significant improvement after discontinuation of biological therapy.
Conclusion: This single-center observational study demonstrates the possibility of developing psoriasis de-novo in patients with JIA receiving TNF-alpha inhibitors.
Although more extensive research is needed, our data suggest that discontinuing the TNF-alpha inhibitor or switching to another TNF-alpha inhibitor in patients with psoriasis de-novo should be considered as a treatment strategy in such cases.
Disclosure of Interest: None declared

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THE POSSIBILITY OF INCREASING THE INTERVALS BETWEEN INJECTIONS OF TNF-ALFA INHIBITORS IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS: A SINGLE-CENTER OBSERVATIONAL STUDY

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Introduction: Nowadays many patients who are suffering from juvenile idiopathic arthritis (JIA) are treated with TNF-alpha inhibitors. The question of the duration of therapy with TNF-alpha inhibitors in children receiving TNF-alpha inhibitors and achieving remission on it is relevant.
Objectives: To evaluate the efficacy of therapy with TNF-alpha inhibitors in children suffering from JIA on different therapy regimens after 2 years of treatment with TNF-alpha inhibitors and having a remission for at least one year, which was achieved after prescribing TNF-alpha inhibitors.
Methods: This single-center observational study included 44 children suffering from JIA receiving anti-TNF therapy for 2 consecutive years in standard dose and standard scheme and reached remission on it (average age 9.6±1.7, average disease duration 5.2±1.4): 20(45%) children were treated with adalimumab(ADA), 24(55%) – etanercept(ETA); all children received methotrexate (the average duration of methotrexate therapy was 4.7±0.4. The first group included children who after 2 years of therapy with TNF-alpha inhibitors, was continued this therapy at the standard dose and standard scheme (10 children treated with ADA and 10 children treated with ETA). The comparison group included children who after 2 years of therapy with TNF-alpha inhibitors was continued this therapy at the standard dose, but the intervals between injections of TNF-alpha inhibitors were doubled (this group included 10 children treated with ADA and 14 children treated with ETA). Effectiveness was determined by using the Pediatric American College of Rheumatology Criteria (PedACR) and the Juvenile Disease Activity Score 27 (JADAS-27) at the time of inclusion in the study and after 12, 24, 36 and 52 weeks of therapy. The criteria for exclusion from the study was absent 30% improvement according to PedACR.
Results: In both groups at the time of inclusion all patients had a 90% improvement according to PedACR criteria, JADAS 27 less than 1.
After 12 weeks in the first group and in the comparison group JADAS 27-0.75(0.1; 1.5) and 0.7 (0.2; 1.5), respectively; 100% of children in the first group had 90% improvement according to PedACR criteria, in the comparison group - PedACR 70/90 improvement registered in 24(100%)/22 (90%) children.
After 24 weeks in the first group JADAS 27-0.75(0.1; 1.5), in the comparison group - 2(1.5;5). In the first group 100% of children had 90% improvement according to PedACR criteria, in the comparison group - 2(8%) children didn't achieved 30% improvement according to the PedACR criteria (1 child was treated with ADA, 1-ETA), PedACR 70/90 improvement registered in 22(92%)/17 (71%) patients.
After 36 weeks in the first group JADAS 27-1.5(0.5; 2.5), in the comparison group- 2(1.5; 2.5). In the first group 18(90%) children maintained a 90% improvement PedACR criteria, 2 (10%) children (1 were treated with ADA, 1 – ETA) didn't reached 30% improvement according to the PedACR criteria; in the comparison group PedACR 70/90 improvement registered in 22(92%)/19(79%) patients.
After 52 weeks JADAS 27 in the first group - 0.75(0.1; 1.5), in the comparison group - 1(0.5; 2.0). In the first group 18(90%) children have a 90% improvement in PedACR criteria, in the comparison group - PedACR 70/90 improvement registered in 22(92%) /20(83%) patients.
Conclusion: According to the obtained data, it can be concluded that after 2 years of therapy with TNF-alpha inhibitors at the standard dose and standard scheme and if there is a remission on this therapy for at least a one year, it is possible to correct therapy with TNF-alpha inhibitors in the form of doubling the intervals between the injections of TNF-alpha inhibitors.
Disclosure of Interest: None declared

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MATCHED CONTROLLED SURVEILLANCE OF TOCILIZUMAB TREATMENT FOR POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS–AN INTERIM ANALYSIS

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Introduction: Tocilizumab (TOC) is approved for treatment of polyarticular JIA. Data out of clinical practice are limited.
Objectives: Long-term surveillance of patients newly initiating TOC treatment for at least 5 years compared to a cohort of patients newly initiating a comparator biologic using the BIKER-registry.
Methods: Baseline demographics, clinical characteristics and disease activity, efficacy and safety parameters were compared. Efficacy outcomes were JADAS10, joint counts and functional status Safety was assessed by adverse events (AE) reports.
Results: 161 patients with 161 matched controls have been recruited. Patients starting on TOC were older at treatment start (12.1 vs. 10.1 years (y); p<0.0001) and had a longer disease duration (p<0.0001). TOC was significantly more often a second line biologic (p< 0.0001). Baseline JADAS10 (17+/-10 vs 15+/-6), CHAQ-DI (0.63+/-0.63 vs 0.65+/-0,64), ESR 18+/-15 mm/h vs. 21+/-21 mm/h and active joint counts (7+/-7 vs. 6+/-5) were comparable.
Upon TOC a substantial response with a significant reduction in JADAS 10 from 16.8 to 3.4 (p<0.0001) after 12 months of treatment was observed. There were no significant differences between patients from the TOC cohort and their matched controls in the JIA ACR 30/50/70/90 criteria, JADAS 10, JADAS remission and minimal disease activity was reached by comparable numbers (TOC 37% and 58%; control cohort 37% and 60%).
The total number of AE was comparable (TOC cohort n=201 AE; (77/100PY); control cohort n=207; (65/100PY; RR 1.2; 95%CI 0.99-1.4). More serious AE (SAE) were reported with TOC. Serious infections were documented at lower frequency with TOC. Uveitis events were documented at significantly higher frequency with TNF inhibitors most likely due to a selection bias(Table 1). SAE with TOC were depression (n=3) in 2 with suicidal intent, exacerbation of JIA (n=2), septic arthritis, gastrointestinal infection, abdominal pain, colitis, paronychia and fracture. SAE in the control cohort were depression, osteomyelitis, gastrointestinal infection and disease flare. No significant differences regarding cytopenias and elevated transaminases were observed. No gastrointestinal perforation, no vascular events and no deaths occurred.

	TCZ mono N=161	Matched controls N=161	p
RF neg. Poly/RF pos. Poly/ext.Oligo n (%)	110 (68)(15(9)/36(22)	97 (60)/19(12)/45(28)	n.s.
Pretreatment with biologics, n(%)	127 (83.5)	20 (13.2)	**<0.0001**
Efficacy Month 12	N=87	N=105	
JADAS MDA/REM, n (%)	50 (57.5)/32 (36.8)	63 (60.0)/39(37.1)	n.s.
JIA ACR 30/50/70/90, %	80/75/61/53	86/84/70/56	0.34/0.15/0.17/0.66
AE, N(rate/100PY/95%CI)	Observation: 260 PY	Observation: 312 PY	RR (95%CI); p
Serious AE (SAE)	13 (5; 3-9)	4 (1.3; 1-3)	**3.9 (1.3-12.0); 0.02**
SAE infection	3 (1.2; 0.4-3.6)	6 (1.9; 0.8-4.2)	0.6 (0.2-2.4); n.s.
Uveitis event	2 (0.8; 0.2-3.1)	12 (3.8; 2.2-6.8)	**0.2 (0.04-0.9); 0.03**

*Number and rate of patients are given # t-test or c2-test as appropriate
Conclusion: TOC was effective and comparable to treatment with alternative biologics. Tolerability was acceptable. As TOC was given as a second-line biologic in the vast majority of patients comparisons between the 2 cohorts have to be interpreted carefully. Observation is ongoing.
Disclosure of Interest: G. Horneff Speaker Bureau of: Pfizer, Abbvie, Novartis, Chugai, A. Hospach: None declared, F. Weller-Heinemann: None declared, J. Kuemmerle-Deschner: None declared, M. Fasshauer: None declared, K. Minden: None declared, I. Foeldvari: None declared, C. Rietschel: None declared, T. Schwarz: None declared, R. Trauzeddel: None declared, M. Hufnagel: None declared, D. Foell: None declared, R. Berendes: None declared, P. Oommen: None declared, F. Dressler: None declared, A. Helling-Bakki: None declared, A. Klein: None declared

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SECUKINUMAB EFFICACY AND SAFETY IN JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in children, characterized by chronic inflammation of synovium, cartilage and bones destruction and wide spectrum of extra-articular manifestations. Often JIA is associated with eye damage –uveitis. Rheumatoid uveitis is the most common extra-articular JIA manifestation. Currently there is a large number of biological monoclonal antibodies therapy for the treatment of JIA. Monoclonal antibodies now represent an important series of options in the treatment of rheumatoid arthritis. However, some patients do not response to standard biologic therapy. However, in some cases there is no response to standard therapy. Secukinumab is a human anti–interleukin-17A monoclonal antibody, which is used in JIA. Secukinumab is being used off-label in Russia for JIA, so it is important to evaluate efficacy and safety in children.
Objectives: To evaluate efficacy and safety of Secukinumab in children with JIA.
Methods: 25 children (13 boys (52%) and 12 girls (48%)) with JIA who received Secukinumab in the rheumatological department of the National Medical Research Center for Children's health of Ministry of health were included. Efficacy of therapy was evaluated by uveitis activity, joint inflammation activity according to pediatric criteria of the American College of rheumatologists (ACRpedi), juvenile arthritis disease activity score (JADAS).
Results: Secukinumab was used in children with following types of JIA: enthesitis-related arthritis – 9 (36%), oligoarthritis – 4 (16%), RF(-) polyarthritis – 6 (24%), psoriatic arthritis – 4 (16%), undifferentiated arthritis – 2 (8%). Among these patients 4 (16%) children had rheumatoid uveitis and 15 (60%) children were HLA-B27 positive. We consider important to notice that 17 (68%) patients were switched on Secukinumab from another biologic agents, the average number of switches was 1,3 [min 0; max 3]. Secukinumab demonstrated high efficacy in treatment of JIA and rheumatoid uveitis. Average treatment duration was 17,6 months [min 0; max 28,5]. From 20 patients who received Secukinumab more than 6 months after six months 20 (100%), 18 (90%), 16 (80%), 9 (45%) patients achieved 30%, 50%, 70%, 90% improvements in ACRpedi and 8 (40%) children reached inactive disease stage in JADAS (less than 1 point). 2 (50%) patients out of 4 with rheumatoid uveitis achieved remission. 5 (20%) patients developed adverse effects: in 3 (12%) children high levels of hepatic transaminases was observed (in 1 child it required to stop therapy), in 1 (4%) patient – leucopenia and neutropenia and in 1 (4%) patient – an severe allergic reaction and secondary MAS.
Conclusion: High efficiency and safety of Secukinumab in patients with JIA was demonstrated and we consider Secukinumab can be used as first-line therapy for JIA, associated with HLA-B 27 gene and as an alternative therapy when standard biologic ani-TNF therapy is ineffective. Only one serious adverse effect was reported.
Disclosure of Interest: I. Kriulin: None declared, E. Alexeeva Speaker Bureau of: Novartis, Pfizer, Sanofi, MSD and Roche, T. Dvoryakovskaya Speaker Bureau of: Novartis, Pfizer, MSD and Roche, R. Denisova Speaker Bureau of: Novartis, MSD and Roche, A. Fetisova: None declared, A. Mamutova Speaker Bureau of: Novartis, K. Isayeva: None declared, A. Chomahidze: None declared, O. Lomakina: None declared, K. Chibisova: None declared, M. Gautier: None declared, D. Vankova: None declared, E. Krekhova: None declared, M. Shingarova: None declared

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NEUTRALIZING ANTI-RITUXIMAB ANTIBODIES IN CHILDREN WITH IMMUNE MEDIATED DISEASES

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Introduction: Rituximab is frequently used as a therapeutic drug in different B-cell mediated autoimmune diseases and leads to B cell depletion. Different treatment responses have been observed in patients with B-cell mediated diseases. It has been suggested that a lack of efficacy may be related to the formation of anti-drug antibodies (ADA). The presence of ADA has been correlated with the failure of B cell depletion as well as the occurrence of infusion-related reactions. It is unknown if these ADA neutralize in-vivo rituximab levels.

Objectives: The primary objective of this study is to determine if ADA neutralize rituximab levels and if a specific patient-group has a higher susceptibility for developing ADA. The secondary objective is to correlate ADA with B-cel depletion and infusion-related reactions.

Methods: Retrospectively, children with different B-cell mediated diseases, treated with rituximab between December 2006 and November 2019, were included. Plasma samples for B-cell measurments had been collected at standard clinical visits every three months until six months after rituximab treatment. Rituximab-specific ADA levels and rituximab serum concentrations were determined, from frozen rest material, by radio-immunoassay and enzyme-linked immunosorbent assay, respectively. ADA presence was defined as a titer above 12 AU/ml. Patient charts were screened for infusion-related reactions.

Results: ADA levels were measured in 29 patients (n=9 nephrotic syndrome, n=8 Systemic Lupus Erythematosus (SLE), n=2 systemic vasculitis, n=2 pulmonary hemosiderosis, n=2 juvenile systemic sclerosis, n=2 other renal disease, n=1 juvenile dermatomyositis, n=3 other).

Of these, 35.4% (n=10/29) tested ADA-positive, after a median of 93 days after RTX infusion (IQR 127.5 – 108.5). Median ADA-titer was 345.0 AU/ml.

RTX concentrations were measured in 28 patients after a median of 92 days after RTX infusion (IQR 62–113). Rituximab concentrations in seven ADA-positive patients were measured and all (n=7) showed undetectable low RTX-concentrations. These RTX-levels differed significantly when compared to ADA-negative patients ($p<0.005$).

Three autoantibodies were significantly more present in ADA-positive patients (anti-ds-DNA (OR 12.5, p=0.045), anti-RNP (OR 14.7, p=0.038) and anti-Sm (only present in ADA-positive patients, p=0.036)).

Five ADA-positive patients (n=5/8, 62.5%) did not show B-cell depletion after RTX-treatment, compared to one of 19 (5.3%) ADA-negative patients (p=0.002; OR 26.7; 95% CI, 2.24–317.25).

Severe anaphylaxis during rituximab infusion occurred only in the ADA-positive patients.

Conclusion: In this retrospective cohort study in pediatric patients on RTX-treatment, we found undetectable low drug levels in ADA-positive patients, indicative for their neutralizing capacity. Consequently, the lack of B-cel depletion leads to reduced treatment efficacy. Patients with SLE seem more susceptible to develop ADA. If ADA are detected, continuation of treatment seems non-effective and changing medication is advised. Certainly when considering that, in this study, anaphylactic reactions only occurred in ADA-positive patients.

Disclosure of Interest: None declared

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SWITCHING FROM REFERENCE TO BIOSIMILARS DOES NOT REDUCE EFFICACY AND SAFETY IN JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Limited data about the use of biosimilar are available in children with Juvenile Idiopathic Arthritis (JIA).
Objectives: To evaluate the long-term efficacy and safety of switching from the etanercept (ETA) and adalimumab (ADA) originators to their biosimilars, in children with JIA.
Methods: Medical charts of JIA children who switched from ETA or ADA originators to the biosimilars were retrospectively evaluated. Efficacy of anti-TNF therapy was evaluated at last follow-up during the originator therapy and at 3, 6 and 12 months following the switch to biosimilar, assessing number of inflamed joints, CRP, ESR, Juvenile Arthritis Disease Activity Score (JADAS 10), Visual Analog Scale (VAS) and Childhood Health Assessment Questionnaire (CHAQ). Occurrence of adverse event (AE) during treatment was evaluated. Continuous variables were reported as median value and interquartile range (IQR) and compared using the Wilcoxon test for paired data, and csquare analysis.
Results: 43 children (31 Female, median age at onset 65 months (IQR 31-125) received originator ETA (n=14) or ADA (n=29), as first-line anti-TNF treatment for refractory JIA. Due to healthcare politics, patients have been switched to the biosimilar: Benepali®(n=13), Erelzi® (n=1) for ETA; Imraldi® (n=24), Amgevita® (n=5) for ADA, after 40.5 months (IQR 19.1-73.8) duration of originator treatment. At time of switch, 10/14 patients on ETA and 19/29 on ADA were on complete disease remission. No significance difference of entered parameters has been found at 3, 6 and 12 months thereafter the switch. Nine patients discontinued biosimilars, due to disease remission (5), to family willing (2), to occurrence of burning at injection site (2, on Benepali). The number of patients who experienced an AE was not different in different frame follow-up when comparing exposure to the originator and that to biosimilar, respectively: during 0-3 months, 15/42 (35.7%) *vs* 7/37 (18.9%), c^2: 2.76; during 3-6 months, 16/40 (40.0%) *vs* 17/31 (54.8%), c^2: 1.54; during 6-12 months, 15/39 (38.5%) *vs* 11/24 (45.8%), c^2: 0.33 . Most frequent AEs were upper respiratory tract infections (31) and injection site reactions (7).

		0 Time of switch	3 months	6 months	12 months
Amgevita (N=5)	n	5	5	3	2
	Number of active joints	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)
	JADAS10	0 (0-0.1)	0 (0-1)	0 (0-0)	0.1 (0-0.2)
Benepali (N=13)	n	13	11	9	10
	Number of active joints	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)
	JADAS10	0 (0-6)	0 (0-0.8)	0 (0-0.4)	0 (0-0.8)
Imraldi (N=24)	n	24	20	19	12
	Number of active joints	0 (0-0.5)	0 (0-0)	0 (0-0)	0 (0-0)
	JADAS10	0 (0-3.4)	0 (0-2.8)	0 (0-0)	0 (0-0)

Conclusion: Data from this small, retrospective inception cohort, showed similar efficacy and safety of the originator and a type of ETA and ADA biosimilars in JIA.
Disclosure of Interest: None declared

e-Poster viewing: Uveitis

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LONG TERM TREATMENT WITH ADALIMUMAB IN JUVENILE IDIOPATHIC ARTHRITIS ASSOCIATED UVEITIS - OUR EXPERIENCE

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Introduction: Juvenile idiopathic arthritis (JIA) associated uveitis is one of the most severe extra-articular manifestations in JIA. Delayed diagnose time and inadequate treatment could lead to serious structural consequences. In the last years new treatment novelties and TNF inhibitors have shown excellent control of ocular inflammation.
Objectives: The aim of this study was to evaluate retrospectively the long-term efficacy and safety of adalimumab in patients with JIA-associated uveitis.
Methods: We have retrospectively analysed nineteen JIA patiens data with associated uveitis from our centre registry between 2010 and 2020, treated with adalimumab after failure of treatment with corticosteroids and metotrexate. Demografic data and blood samples were collected at different time points while uveitis activity was evaluated by slit-lamp biomicroscopy. Adverse events were recorded.
Results: Registry records provided 10 years follow up of 19 JIA patients data with associated uveitis. Eleven patients were females (57.90 %) diagnosed as oligo/extended oligoarticular JIA while eight (42.10 %) were males diagnosed as enthesitis related arthritis (ERA). Before adalimumab was prescribed, all patients were previously treated with metotrexate during 3.5 years in avarage dose of 10 mg/m^2 weekly. The mean uveitis duration, before adalimumab administration was 9 months. Ten years long follow up period have showed that there were no new relapsis of uveitis while patients were receiving adalimumab and metotrexate. All of our patients were able to gradually tapper and stop treatment with topical steroids two months after adalimumab commencing. Seven patients were able to stop biological treatment after 4.3 years of adalimumab usage. Uveitis relapsed three monts after the adalimumab discontinuation only in one patient. Two patient were lost to follow up during the transitional period. No serious adverse events were recorded.
Conclusion: During the long term follow up period adalimumab have shown good efficacy and safety profile in JIA patients with active inflammatory ocular disease.
Disclosure of Interest: None declared

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PROLONGED FEVER, ARTHRITIS AND UVEITIS: A SURPRISING DIAGNOSIS

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Introduction: Post-streptococcal syndrome is a systemic immune-mediated complication of beta-haemolytic streptococci infection, mostly seen as post-streptococcal arthritis, rheumatic fever or glomerulonephritis. Uveitis is an uncommon manifestation of this syndrome.
Objectives: Case report
Methods: Case report
Results: A previously healthy 7-year-old female was admitted at the emergency department with prolonged fever, arthritis and red eye. She had a 4-month history of febrile episodes every two weeks, with axillary temperature ranging from 37,8 to 39ºC. Migratory arthralgia affecting both knees and tibiotarsal joints showed up two months after the fever onset and worsened in the previous week, with refusal to walk. Non-painful bilateral red eye for several weeks was mentioned. Other symptoms were absent. Recent infections were denied and family history was irrelevant.
Physical examination revealed lower limb muscular atrophy, knees pain and impaired function and bilateral tibiotarsal arthritis with inability to walk. Ophthalmological observation showed a bilateral non-granulomatous anterior uveitis. Sequential laboratory work up revealed a maximum eritrocitary sedimentation rate of 135 mm/h, maximum c-reactive protein of 5,3 mg/dL, microcytic hypochromic anemia, positive antistreptolysin O titer (ASOT) (initial result of 1250 that increased to 2500 in 4 weeks and later decreased to 500) and negative anti-nuclear antibodies. Cardiac involvement was excluded. The diagnosis of rheumatic fever with concomitant post-streptococcal uveitis was assumed and the patient was treated with oral and topical ophthalmic corticosteroids with prompt clinical resolution of fever, acute polyarthritis and uveitis. No relapse occurred in a 5-year follow-up.
Conclusion: Juvenile idiopathic arthritis (JIA) is the most common cause of uveitis in childhood. Although our patient clinical course could initially raise the possibility of systemic JIA (sJIA), the criteria that define this entity weren't all present and clinical and laboratory findings were more supportive of rheumatic fever. Besides, uveitis occurs exceptionally in sJIA, which turned this diagnosis even less reasonable. In our Rheumatology Unit, among 563 patients diagnosed with JIA in 32 years, 89 had uveitis. However, in the group of 51 patients with sJIA only one had ocular involvement, a boy with isolated vitritis. Post-streptococcal uveitis (PSU) typically presents as bilateral, non-granulomatous anterior uveitis, as described in this case. As streptococcal infection is very common among children and many patients may experience subclinical infection. PSU should be considered in all patients with uveitis along with positive ASOT and negative routine investigations for other causes.
Although PSU has been described in literature, to the best of our knowledge, this is the first reported case of concomitant rheumatic fever and PSU.
Disclosure of Interest: None declared

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TO TAPER OR NOT TO TAPER IN JUVENILE IDIOPATHIC ARTHRITIS: IS THERE A RISK OF DEVELOPMENT OF UVEITIS FLARES?

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Introduction: Juvenile Idiopathic Arthritis (JIA) is the most common extra-ocular disease and is associated with chronic anterior uveitis during childhood. JIA-associated uveitis (JIAU) is a serious, sight-threatening disease with multiple complications and even blindness if untreated. Although most treatments used improve simultaneously both arthritis and uveítis, there is low correlation between the activity and damage for both conditions.
Objectives: To determine the association between the occurrence of uveitis flares in patients with Juvenile Idiopathic Arthritis (JIA) and the de-intensification of immunosuppressive treatment.
Methods: We conducted a retrospective longitudinal cohort study, including a single-centre consecutive cohort of patients diagnosed with oligoarticular JIA antinuclear antibody (ANA) positive, who had had at least one uveitis flare during their follow-up up to 19.5 years. Patiens with the same JIA category, ANA positive, with no history of uveitis flare were considered controls. Epidemiological data, age of first uveitis flare, number of previous episodes, treatments prescribed at the time of the flare and time since the last treatment modification were recorded. Treatment tapering was defined as a reduction in dose or increase in the inter-doses period, according to datasheet of the corresponding treatment. The relative risk (RR) for the development of uveitis flare and treatment tapering were determined by contingency tables.
Results: We included 68 patients of which 22 had had uveitis flares during their follow-up, and 46 controls. The mean age of patients at JIA diagnosis was3.56 ± 2.17 years. A total of 107 uveitis flares were recorded with an average of 4.54 ± 4.70 episodes per patient. The first uveitis flare was registered at an average age of 6.57 ± 5.79 years. Four patients (18.1%) had had only one episode. Among patients with more than one flare, the inter-flare period was 17.84 ± 21.8 months. Thirty flares (27%) were registered in patients without immunosuppressive treatment. Twenty patients (90%) required the initiation of biological therapy specific for uveitis. Adalimumab (ADA) was chosen in 19 (86.3%) patienst and avoided further uveitis flares in 15 (68%) cases. Treatment with Tocilizumab (TCZ) was used in 6 (27.7%) cases and avoided further uveitis flares in 5 (27.3%). Thirty-three episodes (33.1%) were registered in patients with Methotrexate (MTX) of which, 8 (7.5%) were receiving doses below datasheet (<10mg/m2). Forty-four uveitis flares (41%) took place in patients on biological treatment, of which 27 were receiving ADA (25.3%), 2 (1.9%) TCZ and 15 (14%) other therapies. Thirty-seven flares (32.1%) took place in patients on tapered treatments and 11 (10.3%) after non scheduled withdrawal. In terms of risk of developing a new uveitis flare, tapering had a RR of 2.79 (CI 2.01-3.7; P<0.05) while therapy withdrawal had a RR of 5.91 (CI 3.23-10.8; p<0.05). MTX tapering had a RR of 12.5 (CI 6.4-24.5 p<0.05). Patients with ADA had a RR of 0.88 (CI 0.4-1.6; P=0.84) of developing uveitis flares, with TCZ a RR of 4,65 (CI 1.2-17.8; P<0.05) and with other biological therapy (Etanercept, Infliximab, Abatacept) a RR of 3.56 (CI 2.05-6.2; P<0.05).
Conclusion: Tapering immunosuppressive treatment in oligoarticular JIA ANA positive patients, increases the risk of developing uveitis flares.
Disclosure of Interest: None declared

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PRACTICE PATTERNS FOR TAPERING MEDICATIONS IN THE TREATMENT OF JIA-ASSOCIATED UVEITIS

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Introduction: Juvenile idiopathic arthritis associated uveitis (JIAU) is the most common extra-articular manifestation of JIA, and occurs in approximately 10% of affected children. Although there are effective medications to treat JIAU, guidelines and large studies that inform of tapering treatment after disease remission are lacking.
Objectives: To understand the current medication tapering practice patterns of pediatric rheumatologists and pediatric ophthalmologists specialized in children with JIAU.
Methods: We surveyed vie email international pediatric rheumatologists: 1. Multinational Interdisciplinary Working Group for Uveitis in Childhood (MIWGUC), 2. Pediatric Rheumatologic Email-Listserve, 3. CARRA uveitis workgroup, and international
ophthalmologic specialized in children with JIAU. Survey questions focused on the definition of remission, duration of remission prior to initiation of medication tapering, and method of tapering. Specific medications included methotrexate (MTX), adalimumab (ADA), infliximab (IFX), abatacept (ABA), and tocilizumab (TOC).
Results: Of 45 responses, 88% were from pediatric rheumatologists with a mean work experience of 18 years. The regional distribution was 31 form Europa, 9 from North-America, 3 from South-America and 2 from Asia. The responding colleagues managed a mean number of 43 JIAU patients. Remission on medication was defined as no cells in the anterior chamber (78%), followed by no need for eye drops (36%), and no uveitis flares (32%). Tapering practices were described for MTX monotherapy (100%) ADA (100%), IFX (80%), TOC (56% [25% s.c.]) and ABA (46% [30% s.c.]).
Standardized protocol for tapering exists in 32% of centers for MTX, in 26% for ADA, and 20% for IFX. The timepoint for tapering was after 6 months of remission on medication by 14% of respondents, 12 months for 38%, 24 months for 56% and 36 months for 12%.

MTX was tapered by dose in 42%, dose and interval in 40%, and interval in 15%. The lowest dose of MTX was 6mg/m2/week at the time of tapering and the longest mean interval 2.5 weeks (1 to 4 weeks). ADA was first tapered to every 3 weeks by 76% of the responders and then to every 4 weeks by 49% before discontinuing. Fewer respondents used or tapered IFX, TOC or ABA. Around 65% tapered the interval and 20% tapered the dose and interval for ABA, 26% for TOC and 37% IFX

There were differences in the duration of tapering prior to discontinuation of specific medications. For ADA it was 6 months in 62%, 12 months in 36% ,and 24 months in 10%. For IFX it was 6 months in 27%, 12 months in 45%, and 24 months in 33%. For TOC it was 40% after 4 weeks, 87% after 6 weeks and 53% after 24 weeks. For ABA i.v. it was 30% after 8 weeks, and 90% after 12 weeks.
If combination therapy was used, 36% tapered the bDMARD first, 62% csDMARD first, and 12% both simultaneously.
Conclusion: This is the first survey to describe “real world” medication tapering and discontinuation practices of pediatric rheumatologists and ophthalmologists globally. Most physicians start to taper medication after 24 months of remission on medication and discontinue after the 6 to 12 months of tapering.
Acknowledgement:
We would like to thank all the participating colleagues, who took time to fill out our surve
Disclosure of Interest: None declared

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THE CLINICAL FEATURES OF UVEITIS DE-NOVO IN JUVENILE IDIOPATHIC ARTHRITIS PATIENTS DEVELOPED ON BIOLOGIC TREATMENT

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Introduction: Uveitis *de-novo* means the new cases of uveitis, developed after the initiation of the biologic treatment. More often uveitis *de-novo* occurred in the juvenile idiopathic arthritis patients and after etanercept.
Objectives: The aim of our study was to evaluate clinical features of uveitis *de novo* and compare to other autoimmune uveitis.
Methods: in the retrospective study 225 pediatric autoimmune uveitis included. The onset age ranged from 1 to 16 years, 144 girls (64%) and 81 boys (36%), ANA positivity was in 106/180 (58.9%), HLA B27 was in 23/107 (21.4%). JIA-associated uveitis was in 90% (59.2% - oligoarthritis, 21.6% - polyarthritis, 9.2% enthsytis-related arthritis) and 10% of the patients had uveitis solely. The distribution of uveitis types: anterior 78%, peripherial and posterior uveitis in 2.8% each, and panuveitis in 16.4%. Unilateral uveitis at onset was in 34.7% and bilateral in 65.3%.
Results: uveitis *de-novo* occurred in 12 (5.3%) patients of all uveitis in 1-48 months (median=26 months, 25-75%: 17-41 months) after start of biologic. Gender distribution: 4 boys (33.3%) and 8 girls (66.7%). Anterior uveitis was in 11/12 (91.7%) patients and 1/12 (8.3%) had panuveitis; unilateral involvement in 5 (41.7%) and bilateral in 7 patients (58.3%). HLA B27 antigen was in 3/10 (30%) in uveitis *de-novo* and in 20/98 (20.4%) in other uveitis (p=0.366), ANA positivity in 4/12 (33.3%) in uveitis *de-novo* and in 102/171 (59.7%) in other uveitis (p=0.366). The main features in both studied groups are in the table 1. All cases of the uveitis de-novo developed under etanercept (100%) and 4 of them (33.3%) discontinued methotrexate before uveitis. Before uveitis 10/12 (83.3%) had remission in arthritis. All patient discontinued etanercept and 10 patients switched etanercept on adalimumab: eight patients with methotrexate and 2 pattients – adalimumab monotherapy. In two remaining patients, one only discontinued etanercept and continue methotrexate with mild flares and using the topical steroids, and second patient discontinued etanercept and restarted methotrexate. Remission in uveitis achieved in 6/10 (60%) who switched etanercept on adalimumab, 4/10 (40%) experienced flares despite adalimumab treatment with methotrexate (n=3).

Parameter	Uveitis *de-novo* (n=12)	Other uveitis (n=213)	p
JIA category OA PA ERA	 2 (16.7) 6 (50) 4 (33.3)	 127 (69.5) 40 (21.9) 16 (8.6)	0.002
ESR, mm/h	30 (19; 57)	20 (7; 28)	0.03
Arthritis before uveitis, n (%)	12 (100)	123/202 (60.9)	0.007
Biologics for uveitis treatment, n (%)	10 (83.3)	113/206 (54.9)	0.042
Time before uveitis, years	3.5 (2.4; 4.9)	0.2 (0.0; 1.7)	0.000008
Time before biologics treatment (indication: uveitis), years	0.2 (0.1; 0.6)	2.1 (0.8; 4.9)	0.002

Conclusion: uveitis de-novo is a challenging problem, associated with biologic treatment. Further investigation required for finding the predictors of this condition.
Trial registration identifying number: This work supported by the Russian Foundation for Basic Research (grant № 18-515-57001)
Disclosure of Interest: None declared

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CHANGING EVIDENCE OVER TIME: UPDATED META-ANALYSIS REGARDING ANTI-TNF EFFICACY IN CHILDHOOD CHRONIC UVEITIS

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Introduction: Childhood uveitis is a sight-threatening condition and it may lead to ocular complications. In the last 15 years the biologic therapy, specifically anti-TNF, has revolutionised the management of uveitis refractory to conventional immunomodulatory approaches.
Objectives: To summarize evidence regarding efficacy of anti-tumour necrosis factor-α (anti-TNFα) in childhood autoimmune chronic uveitis (cACU), refractory to common disease modifying antirheumatic drugs (DMARDs).
Methods: An updated systematic search was conducted between November 2012 and January 2020. Studies investigating the efficacy of anti-TNFα therapy, in children ages <16 years, as the first biologic treatment for cACU, refractory to topical and/or systemic steroid and at least one DMARD, were eligible for inclusion. The primary outcome measure was the improvement of intraocular inflammation according to Standardization of Uveitis Nomenclature Working Group criteria. A combined estimate of the proportion of children responding to etanercept (ETA), infliximab (INF), and adalimumab (ADA) was determined.
Results: We identified 1677 articles and 37 articles were eligible. Three were randomized clinical trials (RCTs), one on ETA and 2 on ADA, and were excluded from pooled analysis. From the observational studies, a total of 487 children were identified: 226 received ADA, 213 INF and 48 ETA. The proportion of responding children was 86% (95% CI 76–95%) for ADA, 68% (95% CI 50–85%) for INF, and 36% (95% CI 9–67%) for ETA. Pooled analysis showed clear differences ($\chi 2 = 32.2$, $p<0.0001$): ADA and INF were both significantly superior to ETA ($\chi 2 = 26.8$, $p<0.0001$, and $\chi 2 = 7.41$, $p<0.006$ respectively), ADA significantly superior to INF ($\chi 2 = 13.4$, $p<0.0002$).
Conclusion: This metanalysis, consistent with recent RCT data, suggests the efficacy of ADA and INF in cACU treatment. However, ADA results superior to INF in this clinical setting.
Disclosure of Interest: None declared

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DRUG SURVIVAL OF THE INFLIXIMAB BIOSIMILAR (CT-P13) IN PEDIATRIC PATIENTS WITH NON-INFECTIOUS UVEITIS

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Introduction: Uveitis is uncommon in the children, accounting for 2 to 14% of all uveitis cases Pediatric non-infectious uveitis (NIU) is an important cause of significant long term complications and blindness in children. Biosimilar drugs are reproductions of their originator counterparts, are usually less expensive
Objectives: In this report, we studied children with uveitis who had Infliximab Biosimilar (CT-P13) therapy focusing on demographics, anatomic distribution, etiologies, outcome, and complications.
Methods: This non-interventional, retrospective, single center analysis collected medical record data for pediatric patients with non-infectious uveitis who received CT-P13 treatment at the referral center for pediatric rheumatology between January 2016 and January 2020.
Results: Forty six eyes of twenty six patients were enrolled in this study. The gender distrubiton was equal The median age at presentation was 9.7 years. The median age (IQR) at diagnosis of uveitis was 9.41 (5-12.3) years, the median age at primary diagnosis was 7.8 years and the median age at the beginning of the symptoms was 6.6 years. The median time between primary diagnosis and uveitis was 1 months.The mean number of uveitis episodes was 5.4±2.75. Bilaterally was more commonly encountered in the older age group, p = 0.32. Anterior uveitis was the most common site of inflammation followed by panuveitis then posterior and finally intermediate uveitis. Of the 26 patients evaluated, the primary diagnosis of 16 was JIA, 3 was Behcet disease, 6 were idiopathic and 1 was sarcoidosis. In the patients with BD, the mean age (IQR) at diagnosis was 17.7 (12.9-17.7) years and the mean age (IQR) at diagnosis was 8.2 (7.3-12.3) years in patients with idiopathic uveitis. Both the age at uveitis and primary diagnosis were detected younger in JIA groups than others (p=0,04). While the rate of patients with controlled uveitis was 80.7%, disease control was not achieved in 7 patients with INF treatment. At presentation, there was good VA (LogMAR VA < 0.3, >20/40) in sixty percent of the eyes and significant improvement in VA during follow-up in most eyes (81%).Overall, all patients were treated with CT-P13 (22 patients infliximab-naïve; 4 switched from adalimumab). Drug survival was similar in naïve and switched patients. Treatment-emergent adverse events (TEAEs) occurred in 26,9%.
Conclusion: In our present study, we report the 4-year follow up results on the safety and efficacy of biosimilar infiliximab of pediatric non-infectious uveitis. This is first report about biosimilar infliximab (CT-P13)-efficacy and safety in pediatric patients with uveitis. IFX biosimilar (CT-P13) is remarkably safe and effective for long-term treatment of non-infectious pediatric uveitis. Higher dosage and shorter intervals may be necessary to achieve successful control in a greater percentage of patients.
Disclosure of Interest: None declared

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MORBIDITY OF JIA-ASSOCIATED UVEITIS: HALF OF PATIENTS DESPITE SYSTEMIC TREATMENT STILL SHOW OCULAR DAMAGE DURING A LONG-TERM FOLLOW-UP

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Introduction: Uveitis is the most common extra-articular complication of juvenile Idiopathic arthritis (JIA). Due to its typical indolent and chronic course, children with this condition are at risk for ocular morbidity with a significant impact on their quality of life.
Objectives: To describe demographic and clinical features, treatment approaches and outcome of a population of patients with JIA-associated uveitis.
Methods: Charts of patients with JIA-associated uveitis, followed in two tertiary Pediatric Rheumatology Centres were retrospectively reviewed with regard to clinical features, therapeutic choices and outcome.
Results: Data from 162 JIA patients with uveitis were analysed (81.5% female), with a mean follow up of 8.9 years (SD ± 2.56). Mean age at JIA onset was 3.6 years (SD± 3.1) and the mean JIA duration at uveitis onset was 2.5 years (SD ± 4.3). Uveitis was diagnosed at JIA onset in 9.9% of patients. The most frequent JIA category was oligoarthritis (88.9%), which was persistent in 72.8% of cases, followed by RF- polyarthritis (9.3%). No systemic JIA was reported. Uveitis was predominantly anterior (96.9%) and reported bilateral in 65.4% of cases. In almost all patients (87.6%) antinuclear antibodies (ANA) were positive. Systemic medications were required in 134 (82.7 %) patients. Methotrexate and cyclosporine were used in 66.0% and 7.4% of cases, respectively, while 86 patients (53.1%) required biologic therapy, mainly adalimumab (34.6%), followed by infliximab (10.5%) and tocilizumab (3.7%). In 28.4% of cases more than 1 biologic was needed. Mean recurrence rate in our cohort was 1.3 per year (SD ±1.1). In 79 patients (49.8%) uveitis was complicated by ocular damage, which is summarized in Table 1. A best-corrected visual acuity (BCVA) ≤ 0.4 and ≤ 0.1 were observed in 14.2% and 10.5% of patients, respectively. Clinical remission at last follow-up was reached in 26 (70.3%)/37 patients with available data.

Table 1.

Ocular damage, n (%)	**JIA patients with uveitis N 162**
Synechiae	56 (34.6%)
Glaucoma	9 (5.6%)
Cataract	29 (17.9%)
Band keratopathy	32 (19.8%)
Cystoid macular edema	7 (4.3%)
Any surgery	28 (17.3%)
Cataract	24 (14.8%)
Synechiotomy	2 (1.2%)
Other (band keratopathy, glaucoma)	2 (1.2%)

Conclusion: Despite continue improvement in therapeutic options, uveitis remains a high morbidity complication of JIA. Clinical predictors and biomarkers are needed to identify patients at higher risk of unfavourable outcome. Careful monitoring and follow-up are crucial for timely detection of ocular inflammation and prevention of damage.
Disclosure of Interest: None declared

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ASSESSING S100 PROTEINS AND CYTOKINES IN TEARS AS POTENTIAL BIOMARKERS FOR UVEITIS DIAGNOSIS AND ACTIVITY IN JIA PATIENTS

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Introduction: JIA-associated uveitis (JIA-U) occurs in 10-20% of children with Juvenile Idiopathic Arthritis (JIA) and typically asymptomatic, and sight-threatening complications occur in 50% of children, (i.e. cataracts, vision loss). Frequent ophthalmic examinations are important for early diagnosis and monitoring of uveitis activity. Even after uveitis is controlled, risk of disease exacerbation still exists. Therefore, frequent ophthalmic screening and monitoring is important for detection and management of JIA-associated uveitis (JIA-U). S100 proteins, cytokines, and chemokines detected in aqueous humor of patients with uveitis are also detected in tears. Biomarker discovery using tears is promising since collection is noninvasive, feasible, well-tolerated, and close to the target organ.
Objectives: We aim to determine if S100 proteins, cytokines, and chemokines levels differ in tears of children with JIA and JIA-U and in children with JIA-U by uveitis activity.
Methods: Tears were collected using Schirmer strips from children ≥5 years old with oligo- or polyarticular RF negative JIA with (JIA-U) and without uveitis (JIA-no-U), and in children with JIA-U at time of active and inactive eye disease. Activity was defined by Standardization of Uveitis Nomenclature (SUN) criteria. Active uveitis was anterior chamber inflammation grade ≥0.5+ cells. S100A8, A9, and A12 were measured by ELISA, and IL-18, IL-8, IP-10, MCP-1, RANTES, and sICAM-1 by Luminex assays. Biomarker levels were compared in children with 1) JIA-no-U (n=8) to active JIA-U (n=8), and 2) JIA-U (n=8) at time of active and inactive uveitis.
Results: Children with JIA-no-U and JIA-U were matched by JIA subtype and arthritis activity. They had primarily oligoarticular JIA (63%), active arthritis (25%), and were on systemic medication (75%). At time of active uveitis, 75% had grade 0.5+, and 25% had 1+ and mean interval between time of active and inactive disease was 11 months. We found that levels of biomarkers in tears of children with JIA-no-U compared to active JIA-U were similar. Although not statistically significant, levels of S100A12 (mean difference 12,190 pg/ML [95% CI -4847 to 29,227], P=0.14) and sICAM-1 (5329 pg/ML [95% CI -5372 to 16,031], P=0.28) were higher when uveitis was active compared to inactive.
Conclusion: Our results suggest that S100A12 and sICAM-1 are potential biomarkers of uveitis activity in JIA-U, but not uveitis diagnosis. Thus, neutrophils may play a role in the pathogenesis of anterior uveitis which has been reported in an animal model of acute anterior uveitis. Identifying biomarkers using tears provides a noninvasive and objective method of monitoring uveitis. Limitations are our heterogeneous cohort that varied by arthritis severity and immunosuppression, and minimally active uveitis. We were underpowered to detect statistically significant differences and continue to collect tears prospectively in children with JIA-U with goal of n=28. Despite low uveitis activity, we were still able to detect differences. Further studies in larger and diverse cohorts are necessary to assess the role of S100A12 and sICAM-1 in JIA-U.
Disclosure of Interest: J. Rodriguez-Smith: None declared, V. Miraldi Utz : None declared, S. Thornton: None declared, G. Schulert Consultant for: Novartis, SOBI, A. Sproles: None declared, N. Mwase: None declared, T. Hennard: None declared, A. Grom Consultant for: AB2Bio, Novartis, SOBI, M. Altaye: None declared, S. Angeles-Han: None declared

e-Poster viewing: Vasculitides

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CASE REPORT OF ACUTE DIGITAL ISCHAEMIA IN A 12 YEAR OLD BOY WITH GRANULOMATOSIS WITH POLYANGIITIS

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Introduction: Granulomatosis with polyangiitis(GPA) is a rare vasculitis involving medium and small arteries, affecting predominantly upper and lower respiratory tracts, often with glomerulonephritis. Typically it is characterised by necrotising granulomatous inflammation and the presence of anti-neutrophil cytoplasmic antibodies(ANCA).
Objectives: To report an extremely rare presentation of GPA in a 12 year old with acute digital ischemia.
Methods: A 12 year old boy, with a background of poorly controlled type 1 diabetes and hypothyroidism, initially presented to hospital unwell with diabetic ketoacidosis. Treatment was initiated promptly with good response. Furthermore, he was found to have weight loss, productive cough and hearing loss over the past 3 months.
He was haemodynamically stable, but very pale and cachectic. He had reduced air entry and crackles on the right. There was hypertonia and clonus in his lower limbs.
Blood tests showed microcytic hypochromic anaemia (Hb 82g/L), normal white cell count, thrombocytosis and raised inflammatory markers (CRP 138mg/L and ESR 68 mm/hr). His chest x-ray showed enlargement of the right hilum with consolidation/ atelectasis extending into the middle and lower lobes. MRI scans of head and spine were normal apart from fluid opacification in the paranasal sinuses. He was screened for infections including Tuberculosis and started on intravenous antibiotics.
On day 13, he developed painful bluish discolouration of his left hand, particularly his thumb, index and middle fingers. His left radial and brachial pulses weren't palpable. A heparin infusion was started. A Doppler scan showed occlusion of radial and ulnar arteries proximal to the wrist with no clear thrombus.
He had a CT thoracic aorta with contrast which showed proximal left radial artery occlusion and distal ulnar artery occlusion with no evidence of proximal embolic source or vasculitis. It showed multiple perihilar masses (lymph nodes) in the right lung and peripheral parenchymal masses in both lungs, suggestive of atypical infection or connective tissue disease.
Blood tests still showed raised inflammatory markers(CRP 107mg/L, ESR 86 mm/hr and platelets 658 10^9/L). An autoantibody screen showed positive ANCA with strongly positive anti PR3(>100 U/mL); other autoantibodies, including ANA, ds DNA and anti-phospholipid antibodies, were negative.
He developed further ischaemia with bluish, painful discoloration of his right foot, especially right great toe, with a weakly palpable dorsalis pedis pulse. Doppler scan revealed occlusion/narrowing of the posterior tibial artery 6cm proximal to the ankle. Following vascular team advice, he was started on ilioprost infusion to aid re-perfusion of the extremities involved, with good results.
Based on clinical and lab features of systemic inflammation, evidence of upper airway involvement(bilateral conductive hearing loss and sinusitis on MRI scan), parenchymal lesions on CT chest and strong PR3 positivity, a diagnosis of GPA was made.
Results: Our patient responded well to therapy including multiple pulses of high dose methylprednisolone and cyclophosphamide, with improvement of all organs involved and no further digital ischemia.
Conclusion: Although GPA is very rare in children, it is associated with high morbidity and mortality. Many studies show that the spectrum of paediatric GPA is not vastly different from adults, except for higher gender bias towards female, more constitutional and musculoskeletal symptoms and higher risk of subglottic stenosis. Although there are a handful of case reports of digital ischaemia in adults with GPA, to our knowledge this is the first case report of acute digital ischaemia in paediatric GPA. Early diagnosis and prompt treatment with a multidisciplinary team approach is paramount for good outcome.
Disclosure of Interest: None declared

P281
CHILDHOOD POLYARTERITIS NODOSA –
DIAGNOSIS USING SELECTIVE VISCERAL ANGIOGRAPHY

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Introduction: To diagnose polyarteritis nodosa (PAN), either histopathological or imaging evidence of vasculitis is necessary. In our case, the diagnosis could not be confirmed either by histology or by angiography MRI. It was only when conventional selective visceral angiography was carried out that the decisive evidence about the diagnosis was made
Objectives: To report on the difficulties in diagnosing childhood PAN:
Methods: Case report: This 10 year old girl with parents of Turkish origin presented with fever up to 40 °C over 14 days, distinct myalgia and cutaneous efflorescences. The general condition was massively impaired, the girl could not turn around in bed without foreign help. The CRP was 24 mg/dl, the ESR 100 mm/h. The girl had microscopic hematuria, the blood pressure was intermittently greater than 95th centile for height. The MRI showed distinct increased signal intensity in the muscles of the lower limbs. Under the suspected diagnosis of PAN, a deep muscle biopsy in the area of the signal intense muscles was performed. However, no arteries were detectable in the biopsy, so that a diagnosis could not be made. The angiography MRI performed afterwards was normal. It was only through conventional selective visceral angiography that the diagnosis could be confirmed by detecting multiple aneurysms.
Results: Discussion: To ensure the diagnosis of a PAN, one of the two mandatory criteria must be met. A definitive confirmation of the diagnosis is of crucial importance, since the disease can be complicated and result in intensive and aggressive therapy. In our case, the high degree of clinical suspicion could not be confirmed histopathologically or by angiography MRI. Conventional selective visceral angiography. This method offers the advantage of a good detailed representation of small aneurysms and is superior in resolution to MRI and - although less – to CT angiography. It should be noted that all intra-abdominal vessels (Celiac trunk, renal-, mesenteric-, hepatic- artery) are examined. However, at an early stage of the disease or under therapy, aneurysms may not be detectable by imaging. However, as an invasive procedure, conventional selective visceral angiography may have complications and should therefore only be carried out by experienced examiners. It is generally recommended that an MRI-based targeted deep biopsy should be performed. This should measure a size of at least 2.5 x 0.5 cm to capture arterial vessels as possible. If the biopsy is negative, a CT or conventional selective visceral angiography can be performed afterwards.
Conclusion: To ensure the diagnosis of a PAN, all diagnostic options - including conventional selective visceral angiography - should be consistently exhausted. Therefore a close cooperation between the involved different disciplines is recommended.
Disclosure of Interest: None declared

P282

DIFFERENT CLINICAL PRESENTATION OF ADENOSINE DEAMINASE-2 DEFICIENCY IN TWO SISTERS

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Introduction: Adenosine deaminase-2 deficiency (DADA2) is a monogenic vasculitis syndrome whose presentation ranges from recurrent fevers and livedo reticularis to systemic vasculitis, hematologic and immunologic abnormalities, and early-onset stroke. It is characterized by biallelic loss-of-function mutations in the encoding gene of ADA2 protein and low levels of ADA2 enzymatic activity in the peripheral blood. The genotype and phenotype features of DADA2 has a wide spectrum. Treatment with anti-TNF inhibitors is effective in controlling vascular inflammation and reducing strokes.
Objectives: To describe two sisters with different presentations of DADA2 and a deletion mutation on exon 7 of the ADA2 gene.
Methods: Medical data was used to describe the clinical manifestations of two siblings. Parental informed consent was obtained.
Results: Patient 1: A 10-year-old female had presented with fever, rash, arthralgia, hepatosplenomegaly, and coombs positive autoimmune hemolytic anemia (AIHA) at the age of 7 years. She had been followed with a suspected diagnosis of systemic lupus erythematosus (SLE) and steroids, azathioprine, mycophenolate mofetil had been used. Her ANA and complement levels were normal. Because of unmet classification criteria of SLE, genetic testing had been done, and no mutation found in the ADA2 gene. Cranial MR and MR angiography was normal.
She was referred to our clinic after 2.5 years of the first manifestation. Physical examination revealed Raynaud phenomenon on both hands and feet, livedo reticularis, arthritis, and splenomegaly. Laboratory tests indicated an increase in acute phase reactants, CD19, CD20, and switched memory B cell lymphopenia, and hypogammaglobulinemia. Because of prolonged fevers, a thorax CT was obtained and aneurisms of the renal artery were seen. Abdominal CT angiography indicated multiple aneurysms of both renal, intercostal, and hepatic arteries. Repeated genetic analysis of the ADA2 gene showed a homozygous deletion mutation on exon 7. She has been followed on anti-TNF and IV immunoglobulin without severe symptoms for a year.
Patient 2: The older sister had been followed with a diagnosis of familial Mediterranean fever with E148Q heterozygous mutation because of recurrent fever, abdominal pain, erysipelas-like erythema, elevated acute phase reactants, and splenomegaly. She did not have any other cutaneous or systemic findings. Because of parental consanguinity, the ADA2 gene was analyzed and a homozygous deletion mutation on exon 7 was found. She has been followed without any symptoms after anti-TNF treatment.
Conclusion: We presented two siblings from a consanguineous marriage with different clinical presentations of DADA2. Further, we emphasize that genetic testing should be repeated in the presence of clinical suspicion.
Disclosure of Interest: None declared

P283

GASTROINTESTINAL HENOCH-SCHÖNLEIN PURPURA TREATED WITH MYCOPHENOLATE MOFETIL: DESCRIPTION OF TWO CASE REPORTS.

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Introduction: Henoch Schönlein purpura (HSP) is the most common vasculitis in children. HSP prognosis is generally good, recurrence is common among children. Morbidity and mortality are associated with gastrointestinal erosions and nephritis.Treatment is supportive,with control of pain with analgesics.There are retrospective studies that suggest a benefits of steroids to treat abdominal,renal involvement and severe orchitis. Immunosuppressive treatment of HSP nephritis is used in patients with severe renal involvement. There are few data in literature about immunosuppressive treatment of recurrent HSP without kidney involvement
Objectives: We report the successful use of Mycophenolate Mofetil(MMF) in two patients affected from recurrent gastrointestinal HSP
Methods: Case 1: A 15 years old girl after a pharyngitis presented rash, so she was hospitalized, vasculitis was diagnosed, and steroids treatment was started. At steroids suspension patient presented hematemesis and purpuric lesions, so underwent both to an esophagogastroduodenoscopy that was negative and to a skin biopsy, suggestive of leukocytoclastic vasculitic with IgA deposition. HSP was confirmed and oral prednisone was prescribed. At steroids reduction purpuric lesions, hematemesis, abdominal pain came again, so she came to our observation. She presented purpuric lesions and abdominal pain. Blood tests were unremarkable for: complete blood count,ANA, ENA,ANCA, RF,immunoglobulins, complement C3 and C4. Factor XIII activity was reduced. Inflammatory parameters were slightly increased: ERS 25 mm/h, CRP 1 mg/dL. Urinalysis was normal. Occult blood in the stool was present. Throat swab was negative. Abdomen ultrasound showed bowel wall thickening. Oral prednisone was prescribed, with initial improvement of symptoms. After few days she presented new purpuric lesions and abdominal pain. Due to the recurrent nature of her symptoms and the lack of a sustained response to steroids, MMF(600mg/m^2 twice a day) was started and prednisone was gradually tapered in a month
Case 2: After a respiratory tract infection a 13 years old boy presented purpuric lesions on the limbs with spontaneous resolution in 3 days. After a week purpuric lesions and abdominal pain came again so he was evaluated to emergency department. Abdominal ultrasound was normal, urinalysis revealed proteinuria. HSP was diagnosed, but no treatment was prescribed. Due to the persistence of vasculitic lesions, abdominal pain and the onset of gastrointestinal bleeding patient was hospitalized to our Department. On examination purpuric lesions were detected. Patient referred both abdominal and testis pain. Blood tests were unremarkable for: complete blood count, ERS, CRP,ANA,ENA, ANCA, RF, immunoglobulins, complement C3 and C4. Factor XIII activity was reduced. Virological screening showed Immunoglobulin M versus Influenza Virus. Urinalysis revealed proteinuria. Throat swab was negative. Abdomen ultrasound showed bowel wall thickening, testis ultrasound was normal. HSP diagnosis was confirmed. Methylprednisolone iv was administered for three days, then oral prednisone was started. Purpuric lesions, abdominal pain persisted, so we decided to add MMF (600mg/m^2/day) and prednisone was tapered in a month.
Results: Thanks to MMF vasculitis lesions and abdominal symptoms disappeared in few days. MMF was continued for a month, tapered in 6 months. There was no evidence of relapse in a 6 months follow up.

Conclusion: These cases suggest that MMF may be useful to induce and maintain remission of recurrent HSP with gastrointestinal involvement. Multicenter clinical trials with long-term follow up to confirm the efficacy of MMF in the treatment of HSP with gastrointestinal involvement are needed.
Disclosure of Interest: None declared

P284

HENOCH–SCHÖNLEIN PURPURA COMPLICATED BY CALCULUS CHOLECYSTITIS

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Introduction: Henoch–Schönlein purpura (HSP), the most common childhood vasculitis. Cholecystitis is extremely rare in patients with HSP. This is the first case of a Libyan child presenting with HSP complicated by calculus cholecystitis HSP nephritis.
Objectives: our aim is to present an unusual case of gall bladder involvement in an 8-year-old Libyan female affected by HSP.
Methods: a case reports study
Results: : we report an unusual case of gall bladder involvement in an 8-year-old Libyan female with HSP. She was referred to a rheumatology clinic due to HSP with chronic calculus cholecystitis and distended small bowel with fluid-like fecal material with no evidence of intussusception on an abdominal ultrasound.
The patient had a one-month history of abdominal pain, purpuric lesion on lower limbs and swelling in both feet. She was admitted 3 times to another hospital before being referred to the rheumatology clinic. An abdominal sonography revealed a distended small bowel with fluid-like fecal material with no evidence of intussusception and chronic calculus cholecystitis; they treated her with Urosdoxycholic acid tab at 250mg per day and ibuprofen syrup. Then referred to our rheumatology clinic. After 40 days, she showed a purpuric rash over her lower extremities, mainly over her thighs and buttocks, microscopic hematuria, no arthritis, no fever, no abdominal pain; her blood pressure was normal at90\55mmHg, and she had normal laboratory tests (CBC, WBC 7.7, HGB 10.8, Platelets 356 ESR 20ml\hour, CRP 1mg\dl was negative, C3 was 150mg\dl within normal range 90-180mg\dl, C4 was 35.4 mg\dl within normal range 10-40, ANCA, ANA, as well AntidsDNA Ab yielded negative, Antistreptolysin-O (ASO) titer was 250 Todd , LFT included total bilirubin , direct , indirect GPT,GOT, U\E, creatinine) except urine routine showed mild microscopic hematuria RBC 100 HPF , protein was Nil) urine for protein\creatinine ratio was 0.16 normal range <0.5). An abdominal sonography showed multiple stones, with faint acoustic shadow, the largest of which were 7mm, no signs of acute inflammation. We initially treated her with oral prednisolone tab at 1mg\kg\day and enalopril tab 2.5mg once per day, All clinical manifestations resolved within one week, including normal gallbladder sonography finding, besides microscopic hematuria RBS was 80-85HPF; she had nephrotic syndrome urine protein\creatinine ratio was 1.99 (normal range is <0.5) in spite of taking prednisolone tab for 4 weeks. The treatment with MMF 30 mg/kg/day commenced and the oral prednisolone (2 mg/kg/every other day for 2 months only) after treatment with MMF for two months, microscopic hematuria continued for 3 months and recovery from nephrotic syndrome within 2 weeks. After six months, MMF was discontinued and there was no clinical or laboratory abnormalities .The patient achieved complete remission at the end and after discontinuation of the therapy. There was no evidence of recurrence over one-year follow-up.
Conclusion: Physicians should be aware that HSP might present initially as calculus cholecystitis. Repeat abdominal ultrasonography is essential in order to detect complications in patients with HSP. MMF was found to be a useful immune-suppressant and effective for maintenance of remission in HSP patients.

Disclosure of Interest: None declared

P285

INFLAMMATORY BOWEL DISEASE AND TAKAYASU ARTERITIS: A CASE REPORT.

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Introduction: Takayasu's arteritis (TA) is extremely rare, especially in childhood, and its occurrence with inflammatory bowel disease (IBD) is even rarer. There have been suspected associations between TA and IBD in adult literature, but only a few paediatric case reports.
Objectives: We describe a case of a girl (X) with Pakistani origin, diagnosed with indeterminate pan colitis, age 4 following her presentation with abdominal pain, weight loss, blood and mucus PR. Rescoping 2 years later, as steroid dependant, confirmed ulcerative colitis and she subsequently went into remission with Sulfasalazine and Azathioprine. Age 12, X presented with 3 months history of right sided neck pain, fatigue, pain in her lower limbs, intermittent fevers, night sweats and weight loss but no changes in her bowel symptoms. On examination she was pale, tachycardic at 135 bpm, BP 101/61 mmHg with no discrepancy between limbs. She had right sided torticollis despite full range of neck movements.
Methods: X was admitted for pain management and noted to have raised inflammatory markers, anaemia and thrombocytosis. She had a neck ultrasound which revealed evidence of large vessel arteritis. CT angiogram showed arteritis of the thoracic aorta with aneurysmal change with involvement of the proximal arch vessels and proximal superior mesenteric artery; consistent with a diagnosis of Takayasu arteritis. MRI confirmed the findings. X was started on IV pulsed Methylprednisolone 30mg/kg for 3 days followed by weaning dose of oral Prednisolone, weekly SC Methotrexate and low dose Aspirin therapy. Treatment was switched to Mycophenolate Mofetil and later Tocilizumab, due to inadequate control of TA with SC Methotrexate, suggested by blood tests and serial US of large artery walls. Her disease remains stable and Prednisolone has been weaned to 5mg daily.
Results: The exact causative mechanism for both IBD and TA is unclear; however there may be genetic markers which link both diseases. A significantly higher proportion of patients with IBD and TA were HLA-B52 positive compared to TA alone. Other genetic markers including HLA-DR2 and IL-12B have also been shown to be present in both diseases. There are reports that Infliximab has been effective to treat combined IBD and TA; this could support the theory that TNF-alpha may have a role in both conditions leading to mucosal and vessel inflammation. There is currently no NHS England funding pathway for anti-TNF alpha medications for TA, however Tocilizumab can be used.
Conclusion: TA and IBD is extremely rare and requires a high degree of suspicion. Ongoing symptoms of pain, weight loss, fever and high inflammatory markers, in patients with otherwise well controlled IBD, should raise suspicion of alternative pathologies such as Takayasu arteritis. Neck and back pain in this child aided the journey to a diagnosis of TA due to direct pressure effects of enlarged arteries, but these symptoms are unusual. Early diagnosis and prompt treatment are likely to reduce morbidity and mortality in these patients who already suffer a high disease burden.
Disclosure of Interest: None declared

P286

KAWASAKI DISEASE IN EARLY INFANCY - CASE SERIES

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Introduction: Kawasaki disease in infants typically presents as an incomplete or atypical form, which often results in delayed diagnosis and treatment thereby increasing the risk of coronary artery involvement.
Objectives: To draw attention to diagnostic and therapeutic challenges posed by patients with Kawasaki disease manifesting at very early age.
Methods: Medical reports and laboratory and echocardiographic findings of three infants treated at our centre for Kawasaki disease presenting below four months of age were analyzed retrospectively.
Results: The first patient presented at the age of almost four months with fever and shock that required inotropes and artificial ventilation. Due to the atypical presentation the diagnosis was delayed until day seventeen of the illness when the patient developed giant coronary aneurysms and severe mitral valve insufficiency. Another patient manifested at three months of age and fulfilled most of the clinical criteria and received appropriate treatment already on the fifth day of the illness. He exhibited multiple risk factors for an adverse outcome including low age, very high CRP, thrombocytopenia, hyponatremia and hypalbuminemia with pronounced vascular leakage. After administration of IVIG and corticosteroids his clinical condition improved significantly. He was afebrile but his CRP remained mildly elevated and he experienced another flare of the disease within four weeks after the initial treatment with newly formed giant coronary aneurysms. He received adalimumab and pulsed methylprednisolone that finally terminated the inflammation. The last patient manifested at two months with a complete form of Kawasaki disease that prompted timely IVIG treatment. Despite repeated administration of IVIG only partial improvement was achieved and the patient developed giant coronary aneurysms during the second week of illness. Further therapeutic decision was complicated by the patient´s concurrent primary CMV infection.
Conclusion: The first case demostrates a diagnostic challenge posed by patients presenting with Kawasaki disease shock syndrome. The second patient shows the need for very close follow-up of high risk patients. Even though our patient was afebrile after the initial treatment, his CRP remained elevated and the inflammatory process continued requiring biological therapy and escalation of antiaggregation to anticoagulation. The last patient emphasizes the importance of treating both Kawasaki and the concurrent illness that may potentiate the vasculitis as a trigger.
Supported by Ministry of Health of the Czech Republic, grant nr. NV18-02-00237.
Disclosure of Interest: None declared

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KAWASAKI DISEASE COMPLICATED BY MACROPHAGE ACTIVATION SYNDROME AND PARVOVIRUS B19 INFECTION: WHICH RELATIONSHIP?

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Introduction: Macrophage activation syndrome (MAS) is characterized by massive production of cytokines leading to macrophage activation and haemophagocytosis presenting with prolonged fever, rash, hepatosplenomegaly, pancytopenia, liver dysfunction, hypertriglyceridemia, hyperferritinemia and coagulopathy that can complicate rheumatic conditions such as Systemic Juvenile Idiopathic Arthritis (sJIA) and Systemic Lupus Erythematosus (SLE). Incidence of MAS in Kawasaki Disease (KD) has been estimated in about 1.1% patients but subclinical MAS may be detected in 30-40% of KD.
Objectives: Case description
Methods: A previously healthy 10 years-old girl presented high grade fever for 4 days, pharyngitis and vomiting. After 24 hours, she developed diffuse maculo-papular rash and oedema on extremities. She presented progressive worsening of general conditions and bilateral bulbar conjunctivitis, mucositis with strawberry-like tongue and left cervical lymph nodes enlargement. On admission remarkable laboratory tests were increased C reactive protein (CRP), neutrophilic leucocytosis, low sodium and albumin, increased gGT and gallbladder hydrops on abdominal ultrasound. Suspecting Kawasaki disease 2 gr/kg IVIG were administered with salicylic acid (50 mg/kg/day). Nevertheless, she presented persistent remitting fever, low consciousness, diffuse vasculitic rash, worsening of mucositis and pericardial and pleural effusion. Lab tests showed low haemoglobin, platelets and fibrinogen (9,3 g/L, 65.000/ml and 1.05 g/L, respectively), ferritin 16.492 g/L, SGOT 487 U/L, SGT 351 U/L, triglycerides 345 mg/dl , D-dimers 10.353 microgr/L and soluble interleukin-2 receptor (sIL-2R), 6464 kU/L. Active haemophagocytosis was retrieved in bone marrow and cerebrospinal fluid (CSF) so MAS was diagnosed. Three consecutive iv methylprednisolone pulses (30 mg/kg) were administered followed by dexamethasone 10 mg/m2/day and cyclosporin A 2 mg/kg/day as well as plasma infusions and oxygen supplementation (6 l/min) for 48 hours. Parvovirus B19 (HPVB19) DNA was found in peripheral blood, bone marrow and CSF, while other microbiological analysis (EBV, CMV, HHV6, VZV, Influenza A-B, Measles, Adenovirus, HSV) were negative. The patient progressively improved with reduction of fever, oedema of extremities and skin rash and after 6 days presented extensive desquamation on hands, feet and limbs. Lab tests slowly improved and normal values were achieved on day 23. Echocardiogram did not show any coronary aneurism or dilatation, cerebral MRI was normal and neurological impairment gradually disappeared. Primary HLH mutations for UNC13D, STXBP2, STX11, RAB27a, SH2D1A, XIAP were not found. Corticosteroids and Ciclosporin were gradually tapered and discontinued after 7 and 12 months respectively, whilst acetylsalicylic acid was stopped after 2 months.
Results: MAS is a relatively infrequent complication in KD and may be associated with severe course and poor outcome. Several potential infectious agents have been suggested as trigger factors of both MAS and KD, such as Epstein Barr virus, Influenza virus etc. and, more recently, the SARS-CoV-2 epidemic has been associated with severe forms of systemic inflammatory syndrome resembling KD and MAS.
Conclusion: To the best of our knowledge, this is the first case in which demonstration of HPVB19 DNA in peripheral blood, bone marrow and CSF during acute phase strongly suggests a direct role of the virus in triggering both KD and MAS rather than an antibody or immune-complex mediated mechanism.
Disclosure of Interest: None declared

P288

SPECTRUM OF VASCULITIS IN 27 CHILDREN FROM A SINGLE CENTER IN AN INDIAN STATE OF GUJARAT

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Introduction:

There is a limited awareness about vasculitis amongst primary physicians in our region. There is not a single exclusive pediatric rheumatology center in our region catering around 20 million people.[1-3]

Objectives:

To unveil characteristics of vasculitis in children in our region.

Methods:

I gathered a data of 27 children with confirmed diagnosis of some form of vasculitis who attended Dev Children's Hospital between January 2019 and January 2020. It included demographics, clinical presentations, laboratory results, treatment and follow up.

Results:

Table 1 showed detailed analysis of children with Vasculitis at Dev Children's Hospital

Parameter	No (%) of children fulfilled a respective parameter
Age < 3 months 3 months- 2 years 2 years-5 years >5 years	1 (3.5%) 8 (29.5%) 9 (33.5%) 9 (33.5%)
Sex : Male Female	18 (66.6%) 9 (33.5%)
Incomplete Kawasaki disease (KD) Complete Kawasaki disease IgA Vasculitis (IgA-V)	8 (29.5%) 9 (33.5%) 10 (37%)
Coronary artery involvement in KD patients at onset Renal involvement in IgA-V patients at onset Gastrointestinal complications in IgA-V patients	None 1 (10%) 4 (40%)
Echocardiography findings at diagnosis in KD Pericarditis	 7 (44%)
Treatment (IV Ig within 12 days of fever in all KD patients) Intravenous Immunoglobulin Infusion (IV Ig) – single dose IV Ig – two doses IV methyl prednisolone Oral steroids	 15 (88%) 2 (12%) 2 (KD and IgA-V patient each) 9 (IgA-V patients)
Coronary artery involvement in KD patients at 2,4,6 weeks Renal involvement in IgA-V patients at 1,2,3 months	0 1 (10%)

Conclusion:

The most common vasculitis in our cohort is Kawasaki disease. The number of incomplete KD patients was almost same as complete KD. Almost all our KD patients responded to IV Ig. None of the children with KD developed coronary artery abnormalities. Gastrointestinal complications were seen to be associated with four patients of IgA vasculitis at onset. Two children with IgA vasculitis developed renal complication within 3 months of disease onset.

Trial registration identifying number:

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Disclosure of Interest: None declared

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AUTOIMMUNE DISEASES AS NON-CARDIOGENIC COMPLICATIONS OF KAWASAKI DISEASE

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Introduction: Kawasaki disease (KD) is an acute, immune-mediated multisystem vasculitis of unknown etiology that most frequently affects infants and young children. Immunological abnormalities during the acute phase of KD have been described extensively and coronary artery aneurysms (CAA) identified as a main long term complication. The occurrence of non-cardiac, autoimmune complications in patients with history of KD was rarely reported.
Objectives: Our aim was to evaluate the presence of autoimmune diseases (AID) in patients after KD diagnosis and to compare clinical, demographic and laboratory characteristics between patients who developed AID (group 1) and patients who did not (group 2).
Methods: A single-center, retrospective cohort study with longitudinal follow-up of all children newly diagnosed with KD between June 2006 and December 2018 was performed. In total, 151 children (91 males and 60 females, median age 3.4 years) with KD were enrolled. Range of follow up was from 1 to 13 years after KD (mean follow-up 16.8 months).
Results: Of 151 children with KD, 16 (10.6%) developed AID after KD including: 6 juvenile idiopathic arthritis (JIA), 6 macrophage activation syndrome (MAS), 3 coeliac diseases, 1 ulcerative colitis, 1 psoriasis, 1 hypothyroidism and 1 demyelination. Three patients presented with more than one AID. The mean time interval between diagnosis of KD and diagnosis of AID was 30.5 months (range 0.2 − 149 months). We found no difference in age distribution, clinical characteristics and incidence of CAA between the two groups. Group 1 had significantly lower median serum sodium (135 vs 137 mmol/L, p = 0.002), lower median platelet count (262 vs 363 $x10^9$/L, p = 0.026) and higher neutrophil to lymphocyte ratio (9.4 vs 4, p = 0.009). There was also significantly higher percentage of IVIG resistance in group 1 (37.5% vs 12.6%, p = 0.022). Moreover, we found that children with KD had twice as many AID compared to CAA on long term follow-up (10,6% and 5,3% respectively).
Conclusion: In our cohort, children with KD had twice as many AID when compared to CAA on long term follow up. Monitoring of children after KD for AID should be considered, especially in patients who were resistant to IVIG treatment. Additional studies are necessary to clarify the possible role of sodium, platelet count and neutrophil to lymphocyte ratio for risk stratification of AID after KD.
Disclosure of Interest: None declared

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CLINICAL FEATURES AND THERAPY IN CHILDREN WHO HAVE GRANULOMATOSIS WITH POLYANGIITIS (WEGENER'S) IN ONE RUSSIAN CENTER

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Introduction: The clinical presentation of Granulomatosis With Polyangiitis (GPA) is often heterogeneous, with frequent involvement of the respiratory tract, the kidney, the skin and the joints. GPA vasculitis is rare in childhood but cohort studies performed during the last decade have clarified their phenotype, patterns of renal involvement and their prognostic implications, and outcome. We provided preliminary data on demographic characteristics and organ manifestations of Russian cohort in one center.
Objectives: To describe demographic characteristics, presenting clinical features, and initial treatments in patients with granulomatosis with polyangiitis (Wegener's) (GPA).
Methods: The European Medicines Agency (EMA) classification algorithm was applied. The EMA algorithm was used to uniquely distinguish children with GPA from children with other vasculitis, whose diagnoses had been classified according to both adult- and pediatric-specific criteria. Descriptive statistics were used for comparisons.
Results: In total, 15 patients (67% female) fulfilled the classification criteria for GPA (n = 15). The median time to diagnosis was 3.5 months (ranging to 24 and 46 months, respectively). The median age was 13 years. Pulmonary manifestations were in 53 % (n=8) of patients (alveolar hemorrhage (n=2), dyspnea (n=5), chronic cough (n=4), pleural effusion (n=1), lung nodules or cavity (n=3), lung infiltration (n=6). Renal pathologic features were found in 53% (n=8). Eye involvement was in 33 % (n=5), ENT involvement was in 67 % (n=10), cutaneous involvement was in 26 % (n=4), CNS involvement was in 6% (n=1), cardiovascular involvement was in 6% (n=1), musculoskeletal involvement was in 60% (n=9), gastrointestinal involvement was in 13 % (n=2), fever, fatigue were in 87 % (n=13). All patients with GPA for induction remission received combination therapy with corticosteroids plus immunosuppressive agents (cyclophosphamide (n=4), mycophenolate (n=10), rituximab (n=6), tocilizumab (n=1)), for maintenance therapy - combination therapy with corticosteroids plus immunosuppressive agents (azathioprine (n=5), mycophenolate (n=10), rituximab (n=2)).
Conclusion: GPA is rare disease in childhood. Their clinical presentation is often similar to that adult patients, although some differences exist. Renal involvement drives the prognosis of pediatric GPA. The treatment of pediatric GPA still relies on the studies performed in adults.
Disclosure of Interest: E. Alexeeva Speaker Bureau of: Novartis, Pfizer, Sanofi, MSD and Roche, R. Denisova Speaker Bureau of: Novartis, MSD and Roche, T. Dvoryakovskaya Speaker Bureau of: Novartis, Pfizer, MSD and Roche, A. Mamutova Speaker Bureau of: Novartis, K. Isayeva: None declared, A. Chomahidze: None declared, A. Fetisova: None declared, O. Lomakina: None declared, K. Chibisova: None declared, M. Gautier: None declared, D. Vankova: None declared, I. Kriulin: None declared, E. Krekhova: None declared, M. Shingarova: None declared

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ERYTHROCYTE GLUTATHIONE S-TRANSFERASE ACTIVITY IN CHILDREN WITH HENOCH-SCHÖNLEIN PURPURA

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Introduction: Henoch-Schönlein purpura (HSP) is the most common vasculitis of the childhood. Among all possible symptoms / complications, nephritis (HSPN) is the main and almost only cause of morbidity and mortality in HSP.
Objectives: The aim of this study was to investigate the value of erythrocyte glutathione S-transferase (e-GST) activity as an early predictor of nephritis development in HSP.
Methods: Ninety-seven children with HSP were enrolled into the study. The control group consisted of 52 children without clinical and laboratory signs of inflammation. In all patients e-GST activity was determined spectrometrically for three times during six-month period and corelated with clinical characteristics of the disease, routine blood and urine laboratory findings as well as with e-GST activity in healthy children.
Results: At the beginning of the disease the e-GST activity values were significantly higher in the group of HSP patients who developed proteinuria above 0.15 g/dU and/or haematuria above 5 E/mm^3 (i.e. HSPN) during six-month follow-up period, compared to the group of HSP patients without nephritis during same time span: median (interquartile range) 5,70 U/g_{Hb} (4,38-7,50 U/g_{Hb}) compared to 3,10 U/g_{Hb} (2,20-4,20 U/g_{Hb}); P<0,001. Similar results were obtained after the comparison of the patients with HSPN and control group: 5,70 U/g_{Hb} (4,38-7,50 U/g_{Hb}) vs. 3,13 U/g_{Hb} (1,91-4,20 U/g_{Hb}); P<0,001. There were no statistically significant differences between the group of HSP patients without nephritis and a control group (P=0,837). After the period of three and six months, a decrease of e-GST activity was observed in the HSPN patients, but it was still significantly higher compared to the group of HSP patients without nephritis (P<0,001 / P<0,001).
In the ROC analysis of the e-GST activity determination value in the prediction of HSP nephritis, for the e-GST values >4,1 U/g_{Hb} a significant area under the curve (AUC) of 91.1% (P < 0.001) and sensitivity of 90.5% and specificity of 72.7% was found at the beginning of the study. The sensitivity of the nephritis detection tests decreased, and the specificity increased during the follow-up period. No significant correlation between e-GST activity and severity of skin changes, abdominal pain and arthralgia/arthritis, or used therapy was found. Among the routine laboratory tests, a consistent, statistically significant, positive correlation was found only between e-GST activity and the number of erythrocytes per mm^3 in urine samples.
Conclusion: e-GST activity is a reliable, independent marker of early nephritis risk assessment in children with HSP. As a sensitive and specific, feasible and inexpensive laboratory test, it has potential practical utility in the diagnostic algorithm and monitoring of the children with HSP.
Disclosure of Interest: None declared

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GASTROINTESTINAL MANIFESTATIONS AND THEIR ASSOCIATION WITH THE RISK FOR RENAL DISEASE IN PATIENTS WITH HENOCH-SCHÖNLEIN'S PURPURA

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Introduction: Henoch-Schönlein's purpura (HSP) is the most frequent systemic vasculitis in childhood. Although the disease is most often self-limiting, more than 50% of children may develop gastrointestinal (GI) symptoms, most commonly manifested by nausea, vomiting, and blood in the stool, while in about 10-20% of patients serious complications such as intussusception, bowel perforation, and massive bleeding occur.

Objectives: The aim of this research was to analyze clinical and biochemical parameters in patients with HSP and GI manifestations.

Methods: This retrospective study included children with HSP reviewed in five Croatian University Centers for pediatric rheumatology in the period 2009 to 2019. Differences between categorical variables were examined using the χ^2 and Fisher exact test, and among the numerical using the Mann Whitney U test.

Results: Out of 611 children with HSP, 320 were males and 291 were females. The overal GI prevalence was 45.9% with a 95% CI of 41.9 to 50% and the median (range) age at diagnosis was 6.42 (4.5-8.83) years. Among patients with GI symptoms there were 1.44 times more males (N = 166) than females (N = 115), which was statistically significant ($p = 0.003$), higher proportion of patients came from the Mediterranean area (54% vs. 42%, $p = 0.007$). Patients with GI simptoms had less prodromal infections before the appearance of purpura (59.8% vs. 70.9%, $p = 0.005$) and less respiratory infections (35.6% vs. 45.2%, $p < 0.001$), while regarding intestinal infections there was no difference. Patients with GI symptoms were 1.68 times more likely to develop renal symptoms, and if GI symptoms occured before other symptoms of HSP, then this probability was 3.55 times higher. There was no difference in involvement of the joints and central nervous system, whereas patients suffering from HSP with GI symptoms were found to be significantly more likely to have rash distributed on the trunk (61.9% vs. 48.5%, $p = 0.001$), and upper extremities (35.2% vs. 24.7%, $p = 0.006$), as well as generalized rash (38.8% vs. 28.3%, $p = 0.008$). These patients also had statistically significant higher values of C-reactive protein, leukocyte count, erythrocytes and platelets, hemoglobin, hematocrit and D-dimer concentrations and lower levels of IgG and IgM. In our cohort 42 out of 281 children (14.9%) had the most severe GI manifestations (intussusception and/or massive GI bleeding) with statistically significant higher values of 24-hour urine protein levels and D-dimer concentrations and lower total serum protein, albumin, IgG, IgM and C3 levels in comparison with children whose GI manifestations were less severe (abdominal pain, vomiting, and blood in the stool).

Conclusion: We detected a group of patients with HSP and GI symptoms that differed in their demographic, clinical, and biochemical characteristics from patients without GI symptoms. This group of patients was found to be significantly more likely to develop renal disease and thus cumulatively have a higher risk of acute and chronic complications of HSP.

SUPPORT: Croatian Science Foundation project IP-2019-04-8822.

Disclosure of Interest: None declared

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DOES THE PATIENTS WITH KAWASAKI DISEASE DIAGNOSED BEFORE ONE YEAR OF AGE HAVE DISTINCT PRESENTATIONS?

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Introduction: Kawasaki disease (KD) is one of the most common vasculitidis of childhood. It may present at an early age with atypical findings and even more severe course.
Objectives: In this study, we aimed to examine the clinical and laboratory features of patients diagnosed with KD below one year of age and compare the data with KD patients diagnosed over one year of age.
Methods: The demographic data, clinical features, laboratory findings and treatment modalaties of patients diagnosed with KD between January 2009 and January 2019 were reviewed retrospectively. Patients were goruped according to age of presentation as group 1 (diagnosed before 1 year of age) and group 2 (diagnosed after 1 year of age).
Results: The study included 68 patients (37 boys / 31 girls) below one year of age and 97 (60 boys / 37 girls) patients over one year of age. The mean age of diagnosis was 7 months (1-12) in patients under one year and 50 months (12-119) in patients over one year of age. Twenty-six of all patients (%15,7) were atypical KD; 18 of these children were below one year and 8 were over one year of age (p=0,001). Fifty-eight of all patients (%35,1) were diagnosed with incomplete KD; 34 of these children were in group 1 and 24 were in group 2 (p<0,001). Unilateral cervical lymphadenopathy was obviously more common in group 2 (p<0.001), while aseptic meningitis and BCG scar erythema was significantly more common in group 1. Coronary artery involvement was present in 27 of 68 patients (%39,7) in group 1 and in 15 of 97 patients (%15,4) in group 2; (p<0,001). IVIG resistance was detected in 23/165 (%13,9) of the patients, 12 of whom were in group 1 (p=0,178). In addition to IVIG treatment, steroid therapy was commenced to 17 patients in group 1 and 12 patients in group 2 (p=0,30) Aspirin was started to all patients (40-80 mg / kg / day) and saliciliysm findings were observed in 3 patients in group 1 and 3 patients in group 2.
We applied Kobayashi, Harada, Egami and Formosa risk score systems for each of the two groups and analyzed the accuracy of each score in detecting high risk patients for coronary artery aneurysms and IVIG resistance. None of the scores could predict high risk patients in both of the groups. When we use Harada score to predict coronary artery involvement it was statistically high in both groups that had CALs (p=0,001)
Conclusion: In our cohort, incomplete KD, atypical KD and cardiac involvement were more common in children diagnosed before one year of age, So, while evaluating patients under 1 year of age, phyicians should be aware of the distinctive features of presentation, severe course of disease and follow these patients accordingly.
Disclosure of Interest: None declared

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IS KAWASAKI DISEASE OR SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS IN CHILDREN WITH FEVER WITHOUT A SOURCE ?

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Introduction: Fever without a source (FWS) is caused by various diseases, making differential diagnosis difficult. Clinical similarities between Kawasaki disease (KD) and systemic Juvenile Idiopathic Arthritis (sJIA) are well known. Kawasaki disease (KD), a self-limiting systemic vasculitis, remains of unknown etiology and can cause irreversible coronary artery aneurysms (CAAs). SoJIA is sometimes confused with incomplete KD because both diseases have overlapping clinical features and can be accompanied with CAAs and/or SJIA with macrophage activation syndrome (MAS).

Objectives: In this study, the frequency of both KD and SJIA among the patients evaluated with FWS and the clinical features of patients diagnosed with Kawasaki disease.

Methods: Medical records of patients who first visited our department between January 2016 and December 2019 were reviewed

Results: A total of 107 patients were enrolled in this study, including 43 patients (40.2%, 23 males) who fulfilled the criteria of Kawasaki disease and 64 patients (59.8%, 39 males) who did not fulfill them. In patients who fulfilled the criteria of classical FWS, 36(33.6%, 20 males) patients were diagnosed with systemic juvenile idiopathic arthritis. The mean age of the patients with Kawasaki disease was 30.0±20,4 months (median 25 months), the mean age of other patients was 52,6±40 months (median 39,5 months). The mean age of the patients with sJIA patients was 87,6±49,8 (median 80months). Kawasaki patients were younger than others (p=0.01). There was no difference in gender between groups.
In Kawasaki patients, the most common clinical feature at diagnosis was fever (100%) followed by conjunctival congestion and mucosal changes (69%). The last two findings are more significant in kawasaki patients than others (p<0,00). Twenty-six (59%) patients had completed KD while 25% had incomplete KD. 7 (16%) patients had atypical KD. The mean fever duration was longer in sJIA patients than KD and others (median 14,8 and 7 days, p<0.00). All patients with KD received IVIG (2 g/kg, infusion in 12 h) and aspirin (60 mg/kg/day). 13.6% of the patients also received oral corticosteroids because of IVIG resistance. Thirty-one patients (72.1%) responded to IVIG treatment, whereas 12 (6 female, 6 male) were IVIG resistant. CAI was detected in echocardiography at diagnosis in 10 (22.7%) (6 female ; 4 male) patients. We also detected 4 patients pericarditis with /without CIA.

Conclusion: The clinical presentations of KD and sJIA are quite similar with fever, rash, hepatomegaly, and lymphadenopathy. All 2 entities may provide clues to potentially shared immunopathology.
Disclosure of Interest: None declared

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JAPANESE PREDICTIVE SCORES IN SLOVENIAN POPULATION OF CHILDREN WITH KAWASAKI DISEASE

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Introduction: There are several scoring systems developed in Japan that are clinically used to stratify high risk KD patients and thus identify the ones that may benefit from early adjunctive therapy. There are increasing reports from all over the world on poor performance of these scores in other ethnic populations.
Objectives: The aim of our study was to evaluate the Kobayashi, Egami, Sano and Kawamura scores in our population which is homogenous Caucasian.

Methods: Hospital database was retrospectively searched for code M30.3 of the International Classification of Diseases, 10th Revision, Clinical Modification Code: Mucocutaneous lymph node syndrome [Kawasaki], over the period from January 2006 to December 2019. All patients who were seen in this period for the first time for complete or incomplete Kawasaki disease, as defined by the American Heart Association, were included.
We applied IVIG resistance prediction scores (Kobayashi, Sano, Egami and Kawamura scores) to our cohort. Only patients who received 2g/kg IVIG within the first 10 days of the disease were included in this analysis. The scores of prediction models were calculated for each patient and patients were assigned to high- or low-risk group accordingly.
Results: During the study period a total of 169 children were diagnosed with KD (61.5 % males, median age 3.28 years). All of them were Caucasian except one child who was biracial (Caucasian and African American). Among them, 158 children were hospitalized in the acute phase of the disease and 11 children were seen in the subacute phase of the disease. 151 children were followed-up for at least one year to evaluate persistent coronary artery aneurysms (CAA), which were observed in 8 (5.3 %) patients. Among them, 2 were not treated with IVIG and 2 received IVIG after 10 days of illness. 125 patients were treated with IVIG within first 10 days of illness and were included in the calculation of IVIG resistance prediction scores. 24 (19.2 %) were IVIG resistant.
Sensitivity of Kobayashi, Sano, Egami and Kawamura scores were 0.53, 0.47, 0.61and 0.58, respectively. Specificity of those scores were 0.77, 0.87, 0.75 and0.58, respectively. We found no difference in demographic or clinical characteristics between IVIG resistant and IVIG responsive patients. Patients with IVIG resistance had significantly higher ALT (p = 0.025), neutrophil-to-lymphocyte ratio (p = 0.036) and lower serum sodium (p = 0.009).
Conclusion: By applying the Japanese scores to our population, we were able to identify most of the low-risk, but missed many of the high-risk patients. Our results are consistent with Caucasi n based population studies available to date.
Disclosure of Interest: None declared

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LONG TERM OUTCOME OF POST-VARICELLA ARTERIOPATHY IN CHILDREN

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Introduction: Varicella zoster virus (VZV) related arterial ischemic stroke (AIS) has been described in literature in pediatric age. However, the long-term course of post-VZV vasculopathy need to be inquired: clear information about prevalence of recurrence and severity of clinical outcome are lacking, even if a favorable evolution was initially described, and therapeutic protocols are not currently standardized.

Objectives: We aimed to describe the clinical, laboratory and neuroradiologic features of children affected by AIS due to post-VZV referred to our Institute and to present our experience in their therapeutic management.

Methods: We selected 22 pediatric patients (6 females) with AIS and a CNS confirmed VZV reactivation and/or with a VZV history in the previous 12 months. Other causes of pediatric stroke (systemic disease, cardiac disease, trauma, major thrombophilia) were excluded. Clinical, neuroimaging, laboratory and treatment data were reviewed, focusing on pediatric score outcome measure (PSOM) and executive functions final outcome.

Results: Average age of AIS onset, VZV primary infection and interval between infection and AIS were: 4 years 10mo (range: 1 year and 8 mo-9 years and 11 months), 4 years and 5 months (range 8 months-9.4 years), and 7 months (range 10days-34 months), respectively. The AIS involved the nucleo-capsular region in 18 cases, the cerebral cortex in 9 cases, the thalamus in 4 cases, and the pons in 3 subjects. Seventeen patients had inflammatory focal cerebral arteriopathy (iFCA). Virological confirmation (VZV-DNA or anti-VZV IgG in the cerebrospinal fluid) was obtained in 11 patients. Three patients were treated with trombectomy and one with rTPA. Thirteen patients were treated with antiviral agents associated with steroids in 8 cases, with different administration schedules. Only in one case steroid treatment was given without association with antiviral agents. One patient received a short course of steroid and antiviral treatment at the time of the stroke and then a more prolonged course after six months at the time of the virological diagnosis. Prophylactic antiaggregants were administered to all patients. Mean follow-up was 2 years and 5 months (range 6 mo -10 years) ; iFCA was persistent in 12 cases and transient in 5 subjects. Four patients presented a recurrence of post VZV arteriopathy, two of them presenting new stroke events. Twelve patients presented a variable motor deficit at last follow up. The mean PSOM score of the cohort at the last visit was 1 (range 0-2). Executive functions were evaluated at last follow up in twelve patients, showing no deficit in seven patients, a mild deficit in two patients and a severe deficit in the last three.

Conclusion: Albeit a favourable evolution was initially described, our experience suggests that VZV-related AIS may result in persistent FCA and significant neurological impairment in the majority of cases. Therapeutic approach, particularly involving steroid administration, still need to be validated.

Disclosure of Interest: None declared

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CAN WE PREDICT CORONARY ARTERY INVOLVEMENT IN KAWASAKI DISEASE?

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Introduction: Coronary artery involvement is the most important complication of Kawasaki disease (KD). While 25% of the untreated patients develop coronary artery aneurysms, this rate decreases to 3-5% in patients who started treatment rapidly.
Objectives: We aimed to evaluate the clinical and laboratory features which could predict coronary artery involvement in these patients.
Methods: This study included retrospective analysis of patients who diagnosed with Kawasaki disease at the Hacettepe University Children's Hospital between June 2007 and September 2019. Complete and incomplete KD patients were included in the study.
Results: A total of 129 patients, 79 boys (61.2%), with a median age 36 (IQR 19.5-57.0) months were included in the study. The median duration of fever was 7.0 (IQR 5-10) days. Complet KD was diagnosed in 87 patients (67.4%). The number of patients with IVIG resistance were 16 (12.4%). Coronary artery involvement was detected in 44 of 129 patients (34.1%). There were coronary artery dilatation (Z score 2 to <2.5) in 14 patients, small aneurysm (Z score ³2.5 to <5) in 18 patients, medium aneurysm (Z score ≥5 to <10, and absolute dimension <8 mm) in 7 patients, and giant aneurysm (Z score ≥10, or absolute dimension ≥8 mm) in 5 patients. Patients with extremity changes had more common coronary artery involvement (p=0.04). We observed a significant association with young age, male gender, high levels of white blood cell count, high lymphocyte count and high lymphocyte percentage. In univariate analysis, male gender, age under 1 year, changes in extremities, and high lymphocyte counts were associated with the coronary involvement (OR: 0.393; 95%CI: 0.176-0.879; p=0.023, OR: 3.873; 95%CI: 1.303-11.507; p=0.015, OR: 2.523; 95%CI: 1.008-6.313; p=0.048, and OR: 1.239; 95%CI: 1.046-1.467; p=0.013, respectively) while duration of fever, IVIG resistance, incomplet form of disease, white blood cell count, erythrocyte sedimentation rate, and C-reactive protein were not found as a risk factor. The multivariate analysis identified young age (<1 year of age) and high lymphocyte count as independent risk factors for coronary involvement (OR: 4.384; 95%CI: 1.192-16.128; p=0.026 and OR: 1.215; 95%CI: 1.017-1.452; p=0.032, respectively).
Conclusion: Children under 1 year of age and high lymphocyte counts were the risk factors of coronary involvement in KD. However, in order to accurately determine the risk of coronary artery involvement, there is a need to clarify the pathophysiology.
Disclosure of Interest: None declared

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KAWASAKI DISEASE IN INFANTS BELOW 6 MONTHS: CASE SERIES

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Introduction: Kawasaki Disease (KD), a medium vessel vasculitis having predilection for the coronaries is the commonest cause of myocardial infarction in children. Although infants tend to have incomplete forms of KD, they are at a greater risk for the development of coronary artery aneurysms.
Objectives: To describe our experience with KD in infants below 6 months of age.
Methods: Retrospective review of 4 infants below 6 months of age with KD who received treatment at the Amrita Institute of Medical Sciences, Kochi, India during the period from January 2019 to May 2020.
Results: We describe four infants below 6 months of age diagnosed with KD with coronary artery aneurysms (CAA). Cases 1, 2 and 4 were referred to our centre after diagnosis and primary treatment for the management of refractory KD.

Case	**1**	**2**	**3**	**4**
Age at onset	48 days	5 months	50 days	4 months
Complete/incomplete KD	Incomplete	Complete	Incomplete	Incomplete
Atypical features	Right lower motor neuron facial palsy	-	-	-
Time to diagnosis (from onset of fever)	16 days	16 days	13 days	6 days
Initial 2D ECHO	Normal	Multiple giant CAA	Medium sized aneurysms in LMCA and proximal LAD	Normal
Primary treatment	IVIG*, aspirin	IVIG*, aspirin	IVIG* aspirin, prednisolone	IVIG*, aspirin
Response to primary treatment	IVIG resistant (recrudescence of fever)	IVIG resistant (persistent fever)	Defervescence after IVIG	IVIG resistant (persistent fever)
Repeat 2D ECHO	Giant CAA (mid-LAD, RCA), mild pericardial effusion	Multiple giant CAA (LAD, RCA), LCx aneurysm, LMCA clot, pericardial effusion.	Smaller left coronaries compared to previous ECHO, medium proximal RCA aneurysm	Giant CAA (RCA, proximal LAD)
Further treatment	Second dose of IVIG and methylprednisolone pulse (prior to tranfer to our centre), prednisolone, infliximab (7 mg/kg), dual antiplatelet therapy, anticoagulation	Second dose of IVIG (prior to transfer), infliximab (7 mg/kg), prednisolone, dual antiplatelet therapy followed by abciximab, anticoagulation	Infliximab, dual antiplatelet therapy	Second dose of IVIG and methyl prednisolone pulse (prior to transfer), infliximab (6 mg/kg), prednisolone and dual anti-platelet therapy

* IVIG- 2 gm/kg
(Abbreviations- LMCA- left main coronary artery, LAD- Left anterior descending artery, LCx- left circumflex coronary artery, RCA- right coronary artery)

Cases 1 and 2 underwent myocardial perfusion scan which revealed myocardial infarction. This highlights the need for pre-emptive augmentation of primary therapy (with infliximab and/or steroids) in infants with KD.
Conclusion: Infants with KD often present with incomplete forms of the disease, resulting in delayed diagnosis and treatment, with catastrophic consequences. The clinical possibility of KD needs to be considered in infants below 6 months

of age presenting with unexplained fever for more than 5 days. Infants with KD are at a high risk for developing coronary artery aneurysms and should be considered for primary adjunctive therapy.
Disclosure of Interest: None declared

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THE SEVERITY OF SKIN SYMPTOMS IN PATIENTS WITH CHILDHOOD IGA VASCULITIS - FIVE TERTIARY CENTRES IN CROATIA EXPERIENCE

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Introduction: Henoch Schonlein purpura or IgA vasculitis (IgAV) is the most common childhood vasculitis which is characterized by nonthrombocytopenic purpura of the skin, gastrointestinal, renal and joint involvement. Skin symptoms can be localized on legs, affecting the glutes, or rarely presented atypically, affecting the head and neck area. In the most severe cases, ulcerations and necroses can be seen.
Objectives: To evaluate the prevalence and severity of skin involvement in patients with childhood IgAV, and its relationship with other clinical and biochemical characteristics.
Methods: In this retrospective study patients with IgAV referred to five tertiary teaching hospitals between 2009 and 2019 were included in the study. The severity and distribution of skin symptoms were classified into four categories: localized only to legs, extended to the gluteal region, generalized, and severe skin symptoms with ulcerations and necrosis.

Results: 611 patients, of which 320 boys and 291 girls with a median age of 6.42 (4.42 - 8.92) years were included in the study. All patients had skin involvements. In 205 (33.72%) patients, only legs were affected, in 207 (34.05%) the gluteal region was affected besides the legs, in 181 (29.77%) the rash was generalized, and 15 patients (2.47%) had the most severe skin symptoms which included ulcerations and necroses.
Patients with generalized (27.68%), and severe skin (28.57%) involvement had almost twice as much relapses compared to patients with legs (16.08%), legs and gluteal (16.1%) affection (p=0.011).
Patients with more severe skin symptoms had significantly more gastrointestinal symptoms (generalized: 53.59%, necroses and ulcerations: 66.67%, legs only: 36.1%, legs and glutes: 47.83%; p=0.002), joint involvements (generalized, necroses and ulcerations: 29.08%, legs only: 16.59%, legs and glutes: 21.27%, p=0.01), renal involvement (generalized: 28.18%, necroses and ulcerations: 46.67%, legs only: 21.46%, legs and glutes: 21.46%; p<0.001)
Regarding the treatment, patients with more severe skin involvement needed more corticosteroids (generalized: 52.78%, necroses and ulcerations: 93.33%, legs only: 21.11%, legs and glutes: 34.15%; p<0.001), and immunesuppressants (generalized: 2.22%, necroses and ulcerations: 20%, legs only: 1.97%, legs and glutes: 1.97%; p=0.017).
Conclusion: The prevalence of generalized skin symptoms, as well as the most severe forms in childhood IgAV is much less than the classical findings. However, the more severe the skin symptoms are, the more severe the course of the disease is, and aggressive treatment will be needed.
SUPPORT: Croatian Science Foundation project IP-2019-04-8822.

Disclosure of Interest: None declared

P300

VENOUS WALL THICKNESS IN BEHÇET'S DİSEASE: CAN IT BE A FINDING SUPPORTING OUR DIAGNOSIS?

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Introduction: Behçet's Disease (BD) is a systemic inflammatory disease that can involve both the arteries and veins. The lower extremity venous wall thickness (VWT) of patients who were followed with the diagnosis of Behçet's disease increased significantly compared to healthy controls in two studies conducted in adults.
Objectives: The aim of this prospective study was to investigate the lower extremity VWT in childhood Behçet's patients and in incomplete BD.
Methods: Pediatric patients classified according to the 2015 international pediatric BD criteria in Hacettepe University Department of Pediatric Rheumatology were included in the study. The control group was age and gender matched healthy children. VWT measurements of the lower extremity veins including common femoral vein (CFV), superficial femoral vein (FV), vena saphena magna (VSM), vena saphena parva (VSP) and popliteal vein (PV) were recorded.
Results: Venous wall thickness was measured in 20 patients (70% male) and 5 healthy controls (60% male). Eight of 20 patients fully met the criteria for the diagnosis of BD. The remaining 12 had incomplete BD. The median age was 18 (range 9,5-24) years in the BD group and 16 (range 12-17) in the control group. The median VWT values of BD patients were significantly higher than the control group in the right CFV, right superficial FV, right VSM, right PV, left CFV, left superficial FV and left PV (Table 1). Vascular involvement was present in 5 (25%) patients. Of those; sagittal vein thrombus was detected in two patients, thrombus in deep lower extremity veins in two patients and superficial thrombophlebitis in one patient. Venous wall thickness of the right CFV, right FV, left CFV and left FV in patients with vascular involvement were higher than those without vascular involvement. However, the difference was not statistically significant.
Table1. Behçet's patients (n=20) VWT values (median and IQR) vs healthy controls (n=5) VWT values (median and IQR) respectively.

Right Common Femoral Vein	0.77 (IQR 0.7-0.88)	0.57 (IQR 0.56-0.59)	**P=0.003**
Right Superficial Femoral Vein	0.67 (IQR 0.6-0.75)	0.54 (IQR 0.53-0.58)	**P=0.02**
Right Vena Saphena Magna	0.58 (IQR 0.46-0.62)	0.42 (IQR 0.40-0.42)	**P=0.038**
Right Vena Saphena Parva	0.45 (IQR 0.38-0.57)	0.40 (IQR 0.35-0.41)	P=0,31
Right Popliteal Vein	0.65 (IQR 0.56-0.74)	0.53 (IQR 0.51-0.52)	**P=0.025**
Left Common Femoral Vein	0.78 (IQR 0.6-0.86)	0.57 (IQR 0.55-0.58)	**P=0.025**
Left Superficial Femoral Vein	0.65 (IQR 0.55-0.75)	0.57 (IQR 0.46-0.53)	**P=0.035**
Left Vena Saphena Magna	0.50 (IQR 0.42-0.64)	0.40 (IQR 0.39-0.41)	P=0.057
Left Vena Saphena Parva	0.40 (IQR 0.33-0.58)	0.35 (IQR 0.31-0.37)	P=0.185
Left Popliteal Vein	0.66 (IQR 0.51-0.81)	0.47 (IQR 0.44-0.49)	**P=0.012**

Conclusion: The majority of pediatric patients do not meet the full criteria, and are followed with a diagnosis of incomplete Behçet's Disease. Increased venous wall thickness might serve as a biomarker supporting the diagnosis of Behçet's disease.

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Disclosure of Interest: None declared

P301

THE CHANGING EPIDEMIOLOGY OF KAWASAKI DISEASE IN EASTERN INDIA

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Introduction: Kawasaki disease(KD) is an emerging disease in India. Though there is an overall agreement that the disease is on the rise but there is no nation wide data. Publications from Northern India show an overall increase in disease incidence. Institute of Child Health Kolkata is a tertiary care pediatric hospital in eastern India with dedicated pediatric rheumatology services. In this study we have attempted to analyse data of KD patients from the Pediatric Rheumatology Unit of our hospital from April 2009 to April 2020.
Objectives: To evaluate the epidemiology of KD in Eastern India.
Methods: Medical records of 266 children admitted with KD during the study period was evaluated for annual incidence, complete and incomplete KD, incidence of coronary artery abnormalities and IVIg resistance.

Results: 1. A significant rise in the overall incidence of the disease was observed with number of cases doubling over the last 10 years; from 18 in 2009 to 35 in 2018 & 40 in 2019. In 2020, 13 cases have been diagnosed till April.
2. Majority (80%) of the children presented with complete form of KD.
3. Till 2017 the incidence of coronary artery aneurysms (CAA) was 12 to 15%. A rise in the CAA was observed over the last 2 years with 6 cases in 2018 (17%) & 13(32.5%) in 2019. It is interesting to note that majority of the 13 patients in 2019 was diagnosed and administered IVIg within 10 days of disease onset. In the current year, 3 of the 13 children had CAA at diagnosis.
4. There has been a significant increase in IVIG resistant KD. 12 patients with IVIg resistance were recorded from 2009 to 2017. However, in 2018 there were 7 cases (20%) and 8 (20%) in 2019.
5. 10 children over the last 4 years have developed giant aneurysms (z score> 10) inspite of timely initiation of IVIg. 4 of them had persistent ballooning even after Infliximab administration post IVIg.

Conclusion: 1. The number of patients diagnosed with KD has doubled over the last 10 years. Whether it is a true increase in incidence or because of increased detection remains speculative.
2. It seems that the disease is behaving more aggressively with higher incidence of coronary aneurysms and IVIg unresponsiveness inspite of timely IVIg administration.

Disclosure of Interest: None declared

P302

PREDICTIVE BIOMARKERS OF I IGA VASCULITIS WITH NEPHRITIS BY METABOLOMIC ANALYSIS

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Introduction: IgA vasculitis/ Henoch Schönlein Purpura (IgAV/HSP) is the most common vasculitis of childhood and renal involvement is the most serious long-term complication. A better understanding of the pathophysiology of the progression to kidney disease is required for better treatment to be achieved and current biomarkers of Ig A vasculitis with nephritis (IgAVN) lack the predictive value.

Objectives: In this study, an untargeted metabolomics approach was performed to reveal the underlying molecular mechanism of disease pathogenesis and to find potential biomarkers of plasma samples from patients with IgAV and IgAVN.

Methods: IgAV was diagnosed according to the Ankara criteria in 2008 (1). Forty-five patients, including 39 active IgAV patients (H), 6 IgAVN (N), and 6 age- and gender- matched healthy controls (C), were enrolled in the study. Plasma samples from subjects were collected on the same day of IgAV(HSP) diagnosis and before steroid or other immunosuppressive treatment initiated. This study has utilized liquid chromatography-mass spectrometry (LC-MS/ Q-TOF) to investigate the alterations in plasma metabolomic profiles. Three separate pools, health controls, active IgAV , and IgAVN were created. Peak picking, grouping, and comparison parts were performed (metabolite profiling) via XCMS (https://xcmsonline.scripps.edu/) software.

Results: Totally 2618 peaks were detected for group H, N and C. Among them 355 peaks were found to be statistically significant and reliable ($p<0.05$) and 155 of these peaks were found to be changed (fold change >1.5) between the groups C and H. On the other hand, 66 peaks were found to be changed (fold change >1.5) between the groups H and N. The number of the peaks on the intersection of the peaks found to be changed between the groups (C and H) and (H and N) was 39. Based on putative identification results, 15 peaks were matched with 11 metabolites. We found an up-regulated level of DHAP(18:0), prostaglandin D2/I2, 5-methyltetrahydrofolic acid, porphobilinogen and N-Acetyl-4-O-acetylneuraminic acid/N-Acetyl-7-O-acetylneuraminic acid, 5-Aminopentanamide /5-Aminopentanoic acid, Glycocholic acid, Saccharopine, N2-Succinyl-L-ornithine, gamma Tocopherol, and Galactosylsphingosine /Glucosylsphingosine in IgAV patients.

Conclusion: In conclusion, we have identified a number of metabolites that may be associated with the pathogenesis of IgAV. We also suggest that DHAP (18:0), prostaglandin D2/I2, porphobilinogen, 5-methyltetrahydrofolic acid and N-Acetyl-4-O-acetylneuraminic acid/N-Acetyl-7-O-acetylneuraminic acid may serve as biomarkers for predicting kidney disease since they were increased only in the patients who developed renal involvement at follow-up.

Grant Support: This work was supported by Hacettepe University Scientific Research Coordination Unit

Trial registration identifying number:
Disclosure of Interest: None declared

P303

SPATIAL ANALYSIS OF CHILDHOOD IGA-VASCULITIS IN CROATIA – A PILOT STUDY

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Introduction: Henoch-Schönlein purpura or IgA vasculitis (IgAV) is the most common childhood vasculitis. Although the etiology of IgAV is still unclear, however, it seems that a combination of genetic and environmental factors may contribute. Spatial analyses have previously been used in the analysis of infectious diseases spreading, and several researches showed promising applications in non-communicable diseases.

Objectives: To estimate the incidence and describe the spatial distribution of the incidence of IgAV in Croatia.

Methods: In this retrospective pilot study patient's data were collected over a six-year period between 2013 and 2019 in five tertiary hospitals in Croatia. The average annual incidence of IgAV was calculated with the population census data from 2011 as the denominator. To investigate the spatial distributions of IgAV, a choropleth map was created based on the raw and Bayesian adjusted incidence data.

Results: A total of 402 domestic patients were included in the study, of which 223 (55.47%) were male, and 179 (44.53%) were female, with a median age of 6.42 (4.5 to 9.08) years. The estimated average annual incidence was 8.4 with a 95% confidence interval between 6.51 to 10.66 per 100 000 children. As expected, the raw data showed that the highest number of cases was detected in administrative areas with a higher population. A statistically significant higher percentage of patients came from the continental (69.15%), when compared to the Mediterranean part (30.85%), $p<0.001$. Box maps and standard deviation maps showed with incidences higher (hot-spots) and lower (cold-spots) than the average annual incidence. However, when the standardized average annual incidence was plotted, the spatial distribution correlates with the location of higher incidence levels. Therefore, the spatial distribution pattern showed the existing of hot-spot clusters with higher incidences around large cities both in the continental, and Mediterranean part of Croatia.

Conclusion: This pilot study investigated the usefulness in expanding the epidemiological toolbox with applying spatial analyses. The results of this study suggested that the IgAV incidence might be clustered in space. However, for a more definitive conclusion, a geostatistical analytical approach is needed to evaluate the significance of observed clusters.

SUPPORT: Croatian Science Foundation project IP-2019-04-8822.

Disclosure of Interest: None declared

P304

ELEVEN CHILDREN WITH PRIMARY ANGIITIS OF THE CENTRAL NERVOUS SYSTEM: THE EXPERIENCE OF A SINGLE CENTER

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Introduction: Childhood primary angiitis of the central nervous system (cPACNS) is a rare condition, whose clinical presentation may embrace a large, but non-specific range of manifestations.
Objectives: To describe clinical presentation, treatment and outcome in our childhood PACNS cohort.
Methods: We retrospectively reviewed all cases of cPACNS followed at Anna Meyer Children Hospital from January 1st, 2010 through March 31st, 2020 analysing demographic, anamnestic, clinical, radiological, and laboratory data, type of treatment, and outcome.
Results: We included 11 patients, 2 females, median age at disease onset 6.8 years (range 0.9-15.8), median age at diagnosis 7.6 years (range 1.11-16.5). Motor deficits were the most frequent presenting symptoms (8/11), followed by consciousness impairment (5/11) and headache (5/11). All patients underwent magnetic resonance imaging (MRI) including magnetic resonance angiography (MRA) sequences in 10/11 cases. In 8/11 children digital subtraction angiography was also performed. Basal ganglia resulted the most frequently damaged area (6/11), and middle cerebral artery the most affected territory (8/11).
Two out of eleven patients remained stable during the follow-up.
Three out of eleven patients had new clinical manifestations, before starting mycophenolate mofetil (MMF): Pt #1 experienced a second stroke in a different cerebral vascular territory 1 month later the first one, Pt # 2 had a second stroke 8 months later, and Pt #3 had two consecutives strokes, one month a part each other, associated with MRA documented progressive radiological worsening at 6 and 12 months from the disease onset.
Six out of eleven children showed a radiological worsening without new clinical manifestations: 4/6 at the 3th month [of these 3/4 showed a new territory involvement and 1/4 a territory extension] while 2/6 had additional worsening with new territories involvement at the 6th month and at 12th month respectively.
All patients received MMF (650-1100 mg/m^2/day), after a median latency period of 6 months (range 2-32) from the disease onset.
MMF has been administered for a median period of 32 months (range 2-58). Five out of 11 patients were still receiving MMF at last follow-up. Five other children concluded the treatment due to the sustained clinical remission and stable/improved radiological findings. One child switched to Methotrexate plus Infliximab due to the progressive worsening despite MMF treatment. No MMF serious adverse events were registered.
All patients received a corticosteroid cycle during the acute phases.
At last follow-up (42 months, range 11-108), 10/11 patients showed radiological abnormalities, 5/11 patients had associated neurological symptoms or signs as motor deficits (5/11), cognitive dysfunction (2/11), concentration impairment (2/11), and behaviour changes (2/11).
Conclusion: Children with cPACNS may present clinical and/or radiological worsening few months after the disease onset. A strict MRI/MRA follow-up is recommended.
MMF has proven to be effective and safe in our cohort of children.
Disclosure of Interest: None declared

P305

INFLIXIMAB IN KAWASAKI DISEASE: SHARING AN EXPERIENCE OVER 4 YEARS

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Introduction: Tumor Necrosis Factor(TNF-α) blocker Infliximab (IFX) is emerging as an important drug in management of Kawasaki Disease (KD). This study was undertaken to evaluate the effectiveness of IFX in severe KD on 33 children over a period of 4 years (2015 to 2019).
Objectives: 1.Determine effectiveness of IFX in IVIg resistant KD.
2.Evaluate response on developing/ increasing coronary artery aneurysms (CAAs).

Methods: The study was carried out in the pediatric Rheumatology Unit of the Institute of Child Health Kolkata, India. 33 children aged between 6 weeks to 7 years with KD were included who received IFX after 1-2 doses of IVIg due to persistent fever/ increasing CAA or developing new CAA. Patients were analyzed for response in terms of achievement of defervescence in hours, normalization of CRP and improvement in echocardiographical findings specially CAAs. Children with severe CAAs were followed up by echocardiography weekly upto 6 weeks, monthly upto 3 months, and then 6 monthly.
Results: IFX was used in 1) IVIg resistant fever(23/33) and 2) increasing CAAs post IVIg (15/33). Overlapping indications ie. IVIg resistance with increasing CAAs were also present (7/33).IFX was administered at 5mg/kg and defervescence was achieved within 24 hours in all of the 23 resistant cases along with normalization/ drastic fall in CRP. 2 children whose fever persisted was later diagnosed as Systemic Arthritis and hence excluded from the study.

Diminution in size of aneurysm was seen in 80 % (12 out of 15) cases on follow up, giant aneurysms being converted to medium or small sized aneurysms over 6 to 18 months. Interestingly 50% reduction in the aneurysm size was noted in 60% (n=9) within first 6 months of administration.

Conclusion: 1.IFX showed remarkable success in rapidly lowering the inflammation (fever and CRP) in IVIg resistant patients. Superiority over 2nd dose IVIg cannot be commented though 2 patients were enrolled who had failed to respond to the 2nd dose IVIg.
2.Majority of patients with developing or increasing aneurysms receiving IFX post IVIg showed diminution in size on follow up.

Limitations:
1.The number of patients is relatively small and there was no control arm.

2.Coronary angiographic corroboration of the echocardiographic findings could be performed in only 2 of the patients.

Disclosure of Interest: None declared

P306

SYSTEMATIC REVIEW OF CHILDHOOD-ONSET POLYARTERITIS NODOSA AND DADA2

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Introduction: Polyarteritis nodosa (PAN) is a vasculitic disease characterized primarily by necrotizing vasculitis that may present with fever, weight loss, severe muscle and joint pains, and abdominal pain. Effective treatment is now available for PAN.[1]

Objectives: We aimed at assesing the characteristics of childhood-onset PAN in our center in the last ten years along with a systematic review.

Methods: We reviewed the charts of all pediatric PAN patients from 2010 onwards, in the Department of Pediatric Rheumatology in Hacettepe University, Ankara, Turkey. 47 pediatric patients who had fulfilled the Ankara 2008 for PAN, were included in the study.[2] The demographics, clinical findings and treatment were evaluated. A systematic literature review was conducted by using keywords 'Polyarteritis Nodosa' and 'childhood' in PubMed databases in the English literature.

Results: 12 children had cutaneous PAN, 18 patients had systemic PAN. After 2014, 17 patients who we had originally classified as PAN, were diagnosed as DADA2. Skin involvement (86%) was the most common feature of PAN, followed by abdominal pain (73%), arthralgia/arthritis, weight loss, renal and neurologic involvement. Cutaneous PAN patients were treated with corticosteroids. In systemic PAN both IV cyclophosphamide and mycophenolate mofetil were used for the induction phase. None of the patients died. All patients were ANCA negative. MEFV mutations were screened among 20 patients, 17 of them had mutations in at least one allele. Biopsy was performed in 21 patients and angiography was performed in 33 patients.

The literature review yielded 937 articles about PAN, 170 articles in childhood.

Conclusion: Early recognition and treatment accounts for a good prognosis in childhood PAN. A careful attention must be given to DADA2 in the differential diagnosis, since the DADA2 patients also meet both the Ankara 2008 and ACR criteria for PAN and have mimicking features.

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Disclosure of Interest: None declared

P307

PRES VASCULITIS WORKING PARTY ANNUAL REPORT FOR 2020 YEAR

M. Jelusic[1,*] on behalf of the PRES Vasulitis Working Party , D. Eleftheriou[2], T. Giani[3], E. D. Batu[4], N. Martin[5], M. Sestan[1]
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Introduction: The PRES Vasulitis Working Party is an international group of clinicians, scientists and trainees with about 50 members, and its main goal is to facilitate translational research in the field of vasculitis of the young. This encompasses basic science with potential to improve patient care, molecular genetics, clinical trials (investigator led and industry sponsored) and clinical guidelines.
Objectives: Current activities of this Working Party are divided into three areas: educational activities, activities for clinical care and activities in science and research.
The main educational activity includes endorsement of the First European Congress on Kawasaki Disease EURO – KiDs Congress from 14 to 16 January 2021 in Paris, France. A two-day main meeting aimed to update on clinical innovation, recommendations, basic science and sharing clinical experiences. We have applied for the PReS Educational Course "Vasculitis in paediatric age", which is planned to be held in Barcelona in March 2022.
Activities for clinical care include: implementation of existing diagnostic and treatment recommendations into clinical practice and development of new recommendations with translations to other languages; encouraging the application of clinical questionnaires in assessing the quality of life and disease activity; encouraging the issuance and use of brochures and educational materials for patients and their family members that will be available online; connection with organizations of patients to better understand their needs; developing web-based platform for healthcare professionals with virtual panels in order to discuss difficult cases in the field of vasculitis with the possibility of sharing medical imaging.
Currently there are three ongoing scientific projects.
The first project entitled "Comparison of pediatric criteria with adult classification criteria in granulomatosis with polyangiitis" is a multicentre study which will include at least 2 patients with granulomatosis with polyangiitis per center, and 2 controls (patients with other primary systemic vasculitis or mimicks such as sarcoidosis) per 1 granulomatosis with polyangiitis patient. For further information please contact principal investigator of the project, Prof. Seza Ozen (sezaozen@gmail.com).
The second project entitled "Multi-centre, randomised, open-label, blinded endpoint assessed, trial of corticosteroids plus intravenous immunoglobulin (IVIG) and aspirin, versus IVIG and aspirin for prevention of coronary artery aneurysms in Kawasaki disease" is a multicentre European study (funding already approved) to establish the efficacy and safety of added corticosteroids to IVIG and aspirin for treatment of Kawasaki disease. It aims to recruit 262 children over 30 months from around 40 centres in 12 countries. Chief investigators of the project are Dr. Despina Eleftheriou (d.eleftheriou@ucl.ac.uk) and Prof. Paul Brogan (p.brogan@ucl.ac.uk). The third project entitled "Histological predictors of outcome in patients with Henoch-Schonlein purpura and nephritis" is a multicenter, multinational study which aims to compare the International Study of Kidney Disease in Children, Haas, Oxford and modified semiquantitative classification for their ability to predict the clinical outcomes in Henoch-Schonlein purpura and to establish which variables of each histological classification most significantly predict renal outcome/have the strongest association with unfavorable outcome. The principal investigator of this project is Prof. Marija Jelusic (marija.jelusic.drazic@gmail.com).
Methods: *
Results: *
Conclusion: *
Disclosure of Interest: None declared

Publication only

AB001

A CASE OF MYOSITIS IN A PATIENT WITH POSSIBLE FAMILIAL MEDITERRANEAN FEVER,SUCCESSFULLY TREATED WITH COLCHICINE

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Introduction: Although Myalgia in FMF is quite common,reported cases of Myositis in FMF are rare.
Objectives: To report an unusual clinical presentation of possible FMF.
Methods: A 18 year old,male patient was admitted to the clinic,complaining of severe bilateral calf muscle pain. No edema or erythema was visible. No chest or abdominal pain was mentioned. Peripheral joints were not swollen,range of motion was preserved. His parents mentioned,that this was his second episode of calf muscle pain,but no documented evidence was present. Body temperature was 37,5ºC. On laboratory tests-CRP-50mg⁄L,ESR-30mm⁄h,transient mild proteinuria,Creatine phosphokinase 1995U⁄L. A number of viruses(AIDS,Hep.B,C, etc) was excluded. On EMG-definite pathological myopathy-like changes were visible.Muscle biopsy was not performed due to technical problems. Genetics-his uncle has definite diagnosis of FMF.MEFV gene mutation test revealed M694V⁄N genotype.
A possible diagnosis of FMF by Tel-hashomer criteria was made. Colchicine 1mg⁄day was prescribed.

Results: A total clinicolaboratory remission on Colchicine 1mg⁄daily was achieved.
Conclusion: Several types of Myalgia can occur in FMF patients. Exertional,spontaneous and protracted febrile myalgia syndrome are quite common. In all these cases CPK level and EMG are normal. So,we report an unusual case of Myositis in possible FMF,treated by Colchicine.
Disclosure of Interest: None declared

AB002

ABDOMINAL SYNDROME IN A MONOGENIC AUTOINFLAMMATORY DISEASE - NOT ONLY A FAMILIAL MEDITERRANEAN FEVER

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Introduction: Manifestations of the gastrointestinal tract (GIT) (abdominal pain, nausea, vomiting, diarrhea) are frequent symptoms of autoinflammatory diseases (AID). Acute abdominal pain occurs in 95% of patients with FMF and not rarely leads to unreasonable surgical interventions. This symptom is included in the diagnostic criteria for FMF. However, abdominal pain may be a serious symptom in patients with TRAPS, leading to occurrence of severe complications (peritonitis, peritoneal commissures, intestinal perforation) and emergency surgeries. The core targeted drug in the treatment of TRAPS is IL-1 inhibitor - Canakinumab, that prevents development of organ-lesions, including gastrointestinal disorders.
Objectives: to present a female patient with genetically confirmed TRAPS, suffering, in addition to standard manifestations (fever, rash, periorbital edema, arthritis, acute phase markers), from profound abdominalgia during seizures, formation of severe adhesive disease, which led to perforation of the intestine and an emergency surgical intervention.
Methods: Case report
Results: A female patient P., aged 13, for the first time was admitted to the Federal Rheumatology Center in March 2015 with complaints of intermittent episodes of fever, rash, periorbital edema, arthritis, and abdominal pain lasting for 10-20 days every 2-3 weeks. From the disease anamnesis: she has been sick almost from the birth, as episodes of a macular rash began to occur. From the age of 3 months, monthly fever up to 39.6-40.4°C, lasting for 10 days (sometimes even up to 20 days), accompanied by a confluent macular and annular rash, myalgia, arthralgia, conjunctivitis, periorbital erythema, a significant increase in acute phase markers (ESR, CRP). ANA,RF-negative. During the hospitalization period, 2 disease recurrences were noted, with febrile fever up to 40.4°C, erythematous rash, conjunctival hyperemia, periorbital erythema, myalgia, arthritis, profound abdominal pains. ESR: 43mm / h, leuk: 23.5, CRP: 211 mg / l (normal≤ 5). The use of pulse therapy of GS by a single intravenous administration interrupted the attack. The patient's condition between the attacks is relatively satisfactory. A molecular-genetic study was conducted: by the direct sequencing method a partial analysis of the TNFRSF1A gene was performed. In exon 3, a single nucleotide substitution c295T> C (pCys99Arg) in a heterozygous state was detected. The TRAPS diagnosis was confirmed. Canakinumab was prescribed in a dosage of 150 mg once every 4 weeks, which led to relief of the disease main manifestations and improvement of lab tests. An increase in the interval up to 8 weeks and interruptions in treatment resulted in acute exacerbations with fever, rash, increase CRP, ESR, diarrhea, nausea, vomiting, abdominal pains. In November 2018: an acute exacerbation, acute abdominal pains, increase in ESR level up to 82 mm/h, CRP up to 31 mg/dl (normal≤ 0.5),Hb – 8.7 g/dl. In December 2018, an emergency laparotomy was performed - perforation of the transverse colon, widespread serofibrinous peritonitis, massive adhesion process in the abdominal cavity were diagnosed. Treatment with Canakinumab re-initiation starting from January 2019 led to a complete relief of clinical manifestations, abdominal symptoms and normalization of ESR,CRP.
Conclusion: treating patients suffering from severe gastrointestinal manifestations during seizures, it is necessary to consider not only FMF, but also other autoinflammatory diseases, including TRAPS. Well-timed prescribed targeted therapy, strict adherence to the dosage and intervals between drug administrations, as well as a proper monitoring may help prevent severe gastrointestinal disorders and eliminate them in a prompt manner.
Disclosure of Interest: None declared

AB003

SEVERE GLOMERULONEPHRITIS COMPLICATING TRAPS SYNDROME

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Introduction: TRAPs is an autosommal dominant autoinflammatory disease. To date no severe inflammatory glomerular lesions leading to renal failure have been described associated to disease or its treatment. We present a case of severe glomerulonephritis in a TRAPs patient in treatment with IL-1 blocker canakinumab.
Objectives: To describe the clinical features, treatment and outcome of an acute renal failure due to glomerulonephritis in a 5 year old toddler who was under treatment with IL-a blocker canakinumab.
Methods: A retrospective chart review was conducted to extract clinical, laboratory, histology and evolutive data of the patient.
Results: A previously steady 5 year old male in chronic treatment with canakinumab 4 mg/Kg for a TRAPs due to an heterozygotic de novo mutation in TNFRSF1A p.(Cys43Tyr), presents in emergency room with a 12 hour macrohematuric oligoanuria and generalized oedema. He referred an auto limited febrile spike two weeks before, and a few days vomiting and nausea previous to consultation. Initial exams showed renal injury with urea 227mg/dl and creatinin 4.24mg/dl, hematuria, leucocituria and nephrotic range proteinuria (3.7 mg/Cr mg) with normal seric albumin, compatible with acute glomerulonephritis. Autoimmunity, lupus anticoagulant, and rheumatoid factor were negative, serology was normal apart from antistreptolysin O titres of 1663 UI/L. Levels of C4 were normal and C3 was low (10.7 mg/dL) with an ESR of 67 mm/h and a CRP of 0.95 mg/dL. First day after admission a drug refractory hypertension, metabolic acidosis and hyperpotasemia developed, requiring admission in intensive care unit for veno-venous continuous hemofiltration (HDFVVC). Metil prednisolone bolus (1g/1.73 m²) every 48 hours were initiated and a renal biopsy performed, showing generalized endocapilar proliferation with neutrophil infiltration and exclusive abundant mesangial pseudolineal deposits of C3 on immunofluorescence, no signs of amyloidosis. After five days of HDFVVC and two metilprednisolone bolus, oral prednisone (2mg/Kg) was initiated and a 10 day course of amoxiciline administered. Evolution was satisfactory thereafter, at two months follow-up visit only minimal hematuria (5-10 erytrocites/field) persisted, with normal renal function, complement levels, prednisone 2.5 mg every 48 hour and no hypertensive drugs required; canakinumab was reinitiated 8 weeks after renal failure, no further major events ocurred up to date.
Conclusion: We present a case of acute severe postinfectious glomerulonephritis in a TRAPs patient, presumably poststreptococal. This is to our best knowledge the first case reported and questions arise on the possible association of this severe event to TRAPs syndrome, ongoing treatment or just an unfortunate coincidence. Differential diagnosis was mandatory to discard a rapidly progressive glomerulonephritis and renal amyloidosis in this context. Mild and generally transient proteinuria and creatinine clearance reduction have been reported in association with canakinumab treatment but to no acute glomerulonephritis has been previously described.
Disclosure of Interest: None declared

AB004

CLINICAL CASE OF THE HYPERIMMUNOGLOBULINEMIA D WITH PERIODIC FEVER

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Introduction: In abstract presented clinical case of the hyperimmunoglobulinemia D syndrome, that usually characterized by earl onset and favorable course.
Objectives: Patient O., 27 years old, came to the center of the orphans diseases a year ago. Patient became sick at 10 months with the first episode of a fever occurred, with diarrhea, macular skin rush.
Methods: With a fever child was admitted to the infectious department, after the treatment with improved condition discharged home. In a 3 month, and than after 4 months the same episodes of a sudden fever and skin rush were observed, with nausea, vomiting, diarrhea. Child was excluded with common causes of prolonged infection disease. At the age of 1,6 together with fever and rush, episode of arthritis appeared. Child was admitted to the rheumatologist and confirmed with systemic JIA, treated with high dose of steroids. In a next 2 years involvement of both knee and ankle joints was observed, fever appeared at least once in 2-3 months and was treated with steroids. At the age of 5, child got long therapy with steroids, but frequency of fever episodes was high, followed by typical inflammatory signs in laboratory investigations, in periods between fever attacks – all laboratory and instrumental results were normal. At the age of 8 – 13 years, episodes of fever became rare, 2-3 times a year, and less severe. At the age of 13 treatment was added with metotrexate, as joint syndrome was still ongoing, steroids were stopped. Patients condition remain stable, with minimal arthritis of knee joint, fever was occurred once in a year, and at the age of 18 patient was transferred to adult rheumatologist. At the background of an argument between the patient and a doctor, he didn't come to his office for regular check-ups and discontinued treatment by himself. At the age of 20 new episodes of a fever started to appear, with rush, arthritis. Episodes of vomiting and diarrhea appeared as well. Patient by himself started to take steroids, but took them just during fever attacks. Patient started to suffer from muscle weakness and mother admitted that son became depressed, refused even from small walks. At the age of 24, during fever attack acute cerebrovascular accident happened. After the stroke, patient developed neurological symptoms that accompanied periodic fever, he got poor memorizing, difficulties with speech. Rheumatologist initiated systemic steroids, metotrexate, recommended pulse therapy with steroids. Patient refused from pulse therapy and didn't continue systematically treatment. At the age of 25,5 patient developed second acute cerobravascular accident during fever episode. This time patient was admitted to the ICU for long time, after the treatment discharged home with severe neurological complications. After the second stroke he got inversion of the day/night sleep, slept 18-20 hours a day, didn't recognize and communicate with no one, except mother and still had periodic fever and arthritis. Patient totally refused from the treatment and was deeply depressed.
Results: Ptient came to the center of orphan disease and was examined by genetic and pediatric rheumatologist, prescribed with additional investigations and mutation V377I was detected, as well high level of mevalonic acid in urine and decreased activity of mevolanatkinase. Patient was recommended to initiate treatment with anakinra and canakinumab. In a 4 months after the treatment was initiated, neurological symptoms normalized, disappeared fever and arthritis.
Conclusion: Adequate and in a timely manner diagnostic measures of the periodic fever syndrome with deficiency of mevalonatkinase allows initiate appropriate treatment, improve quality of patients life and avoid dozen complications. Estimation of the correct diagnose in case of our patient was late for 25 years.

Disclosure of Interest: None declared

AB005

HYPER - IMMUNOGLOBULIN D SYNDROME (HIDS)

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Introduction: HIDS is a rare genetic inflammatory disease (autosomal recessive), characterized by periodic episodes of fever accompanied by other symptoms such as joint pain, skin rash and abdominal pain. The fever episodes have a duration of 4-6 days, they begin from the first year of life and appear periodically throughout the whole life. The mutation in the case of HIDS leads to a decrease in the activity of mevalonate kinase, an enzyme important for cholesterol synthesis, and febrile episodes can further decrease this activity. Thus, during these episodes high levels of mevalonic acid can be found on blood serum and urine.

Objectives: Case presentation, a child with HIDS

Methods: A 12-year-old female patient, whose parents refer for recurrent episodes of fever (38-39.5ºC), that are accompanied with diffuse joint disease, skin rash, oral aphthous lesions and abdominal pain. The episodes had begun nearly at 18-months-old with a duration of 3-5 days up to 6-years-old. Then again at 11-years-old. The fever episodes did not improve with the use of antibiotics, NSAIDs, CS or antipyretics. The mother had a normal pregnancy, the child was born on term and the psycho-motor development was conform the age.

Results: In the examination performed during the febrile episodes the patient did have joint pain on pressure, non itchy skin rash in the abdomen and inferior limbs, appearing during the fever but that endure even outside the febrile episodes. Aphthous lesions can be seen on tongue and soft palate. Moreover, non painful, mobile nodules of 1-1.5 cm can be palpated in the cervical, axillary and inguinal area. Spleen at the level of iliac crest. In the laboratory evaluation: inflammatory anemia in the blood test and a mild leukocytosis, (WBC 14x103, RBC 3.12x106, HgB 9.7mg/dl, MCV 86 fl, ESR 40mm/h). The biochemical profile within range. In the blood and urine culture no pathogenic increases were found. Febrile infectious antigens were negative. Bone marrow examination was normal. Immunological evaluation: FR neg, AAN neg, ENA neg, ANCAp/c neg, C3-C4 within the range, PCR 9.6(<5UI/ml). Protein electrophoresis revealed an increase in ά1. Immunoelectrophoresis revealed an increase in IgD 350UI/ml(100UI/ml). Blood ferritin level was 60mg/dl (20-50mg/dl). Head MRI was normal. In the abdominal CT with contrast infusion, cervical, axillary and inguinal nodules of 1-2 cm can be seen, liver of 16cm without any visible lesions and homogenous spleen of 13.4cm. The data of lymphocyte immunophenotyping of peripheral and central blood within the range, no pathological lymphocytic populations were found. Nothing abnormal was found during nodule biopsy. HLA-B27 neg, HLA-B51neg. The level of mevalonic acid in urine resulted 130.8 mmol/ml (<69mmol/ml).

Discussion: For the case the diagnostic differentiation between several diseases was made, including lymphoproliferative disorders (the data of bone marrow examination, biopsy and lymphocyte immunophenotyping did not support the diagnosis), infectious diseases (the data of febrile antigens were negative and febrile episodes were not affected by use of antibiotics), JRA- Still's disease (blood ferritin slightly increased and recurrent febrile episodes that resolve by themselves), inflammatory connective tissue disease (FR, AAN, ENA, HLA-B27, HLA-B51 neg).

Conclusion: Since all other diseases were ruled out and both the level of IgD in blood and the level of mevalonic acid in urine were found to be elevated, besides the periodic febrile episodes and clinical symptoms, the patient was diagnosed with HIDS. In all patients with periodic febrile episodes the electrophoresis of immunoglobulins should be performed and also the evaluation of mevalonic acid both in blood and urine.

Disclosure of Interest: None declared

AB006

THE EVALUATION OF CALCIUM METABOLISM AND BONE MINERAL DENSITY IN PATIENS WITH CAPS

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Introduction: Cryopyrin-associated periodic syndrome (CAPS) includes a group of genetic conditions, caused by dominantly inherited mutations in the NLRP3 gene in Muckle-Wells syndrome (MWS) and familial cold autoinflammatory syndrome (FCAS), and de novo mutations in cases of chronic inflammatory neurologic cutaneous and articular syndrome (NOMID/CINCA).
Objectives: In this study, we aimed to investigate bone mineral density (BMD) and Ca metabolism in our patients with CAPS , mainly MWS.
Methods: Eight patients with MWS were included in the study. The clinical data were obtained from the file records of patients, retrospectively. Calcium (Ca), Phosphorus (P), Magnesium (Mg), Alkaline Phosphatase (ALP), 25 OH vitamin D, and bone mineral densitometry (BMD) tests were performed in all cases, but parathyroid hormone (PTH) levels were in 7 cases.
Results: The female to male ratio was 5/3 and their ages ranged from 13.5 to 70 years. Most patients had had a history of cold-induced urticaria (88.8%) and arthritis (100%) since . their early childhood. Hearing loss was detected in 3 out of 8 (55.5%). Alkaline Phosphatase levels ranged between 57-271 U / L, Ca 9-9.6 mg / dL, Mg 2-2.3 mg / dL, P 2.6-4.4 mg / dL, 25-OH Vitamin D 3.7- 20.2 µg / L and PTH 28.8-162.7 ng / L. Vitamin D level was low in 7 out of 8 cases (87,5%). The results of BMD tests showed that ; 2 cases were normal, 5 cases had osteopenia and 1 had osteoporosis. T scores of lumbar spine were between -2.4-0.5 in adult patients, the z score was -0.5 of the pediatric case. Six patients were treated with canakinumab and 2 patients with anakinra.
Conclusion: It is known that excessive production of IL-1β can cause inflammatory bone loss and abnormality. Vitamin D deficiency and osteopenia/ osteoporosis may cause additional musculoskeletal problems besides arthritis and joint destruction in CAPS. We think that Ca metabolism and bone mineral density measurements should be a part of routine controls in patients with CAPS.
Disclosure of Interest: None declared

AB007

CLINICAL AND GENETIC FEATURES OF PATIENTS WITH PERIODIC SYNDROME ASSOCIATED WITH MUTATION OF THE TUMOR NECROSIS FACTOR RECEPTOR GENE AND JUVENILE ARTHRITIS HAVING MUTATIONS IN TNFRSF1A GENE

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Introduction: The use of a new generation of sequencing allows us to evaluate the genetic characteristics of patients with JIA in the Russian Federation, as well as to optimize the treatment strategy for JIA and TRAPS.
Objectives: To reveal the clinical and genetic features of JIA and TRAPS in patients with a genetically confirmed nucleotide variant in the *TNFRSF1A* gene.
Methods: Retrospective analysis of 21 case histories of patients with JIA-12 and TRAPS-9 observed, of which 14 girls, median age-14.1, median debut age-4.7. All children underwent molecular genetic research by Next Generation Sequencing and revealed nucleotide variants of the *TNFRSF1A* gene.
Results: An analysis of clinical symptoms and laboratory activity in children with TRAPS was performed: in the onset of the disease, systemic manifestations were observed in 8/9: fever in 8/9, maculopapular rash in 5/9, hepatosplenomegaly occurred in 5/9, and lymphadenopathy in 4/9. High laboratory activity was recorded in 7/9. Active arthritis in 8/9, it was poly in 2, oligo in 6. When assessing the clinical symptoms and laboratory activity of patients with JIA, it was revealed that in the onset of the disease, systemic manifestations were observed in 8/12: fever in 8/12, rash in 4/12, hepatosplenomegaly in 5/12, pneumonitis in 2/12, carditis in 1/12 and lymphadenopathy in 5/12. High laboratory activity was recorded in 11/12. Active arthritis in 10/12, it was polys in 4, oligo in 6. In all 100% of patients, the nucleotide variants of the *TNFRSF1A* gene were identified in the study. 9/21 of patients were diagnosed with TRAPS. The most frequent heterozygous variant of *TNFRSF1A* gene with nucleotide substitution of *c.362G>A* was found in 7/9 of patients, in 1/9 of patients it was found homozygous variant with nucleotide substitution of *c.362G>A*, in 1/9 of children it was found heterozygous variant with deletion of *c.337_339del*. All of these variants are pathogenic. 12/21 of patients were diagnosed with JA: juvenile arthritis with a systemic onset was in 7/12, paucarticular arthritis was in 2/12, in 1/12 it was poly RF- and in 1/12 it was psoriatic arthritis. It is worth noting to note that in 6/12 a heterozygous version of the *TNFRSF1A* gene was detected with a nucleotide substitution *c.362G> A*, however, considering the absence of clinical manifestations of autoinflammatory disease and active articular syndrome in these patients, children were diagnosed with JA. In addition, in 2/12 a heterozygous variant with a nucleotide substitution *c.1110C> T* was detected, which is an undetermined value variant; in 2/12 a heterozygous variant with a nucleotide substitution c.43C>T was detected, in 1/12 heterozygous variant *c.374G>A* was detected, and 1/12 heterozygous variant *c.369C> T* was detected.
Conclusion: Systemic manifestations were more prevalent in patients with TRAPS - 91.6%, and active articular syndrome was approximately the same in patients with JIA and TRAPS. In patients with TRAPS, the most common was the heterozygous version of the *TNFRSF1A* gene with the nucleotide substitution *c.362G> A.* Despite the fact that in 57.1% of JIA patients, variants of *TNFRSF1A* gene were identified, it is not possible to establish a diagnosis of auto-inflammatory syndrome in such patients. It is necessary to correctly interpret the results of molecular genetic research in accordance with the severity of the course of the disease, clinical manifestations.
Disclosure of Interest: M. Shingarova: None declared, E. Alexeeva Speaker Bureau of: Novartis, Pfizer, Sanofi, MSD and Roche, T. Dvoryakovskaya: None declared, A. Mamutova Speaker Bureau of: Novartis, K. Isayeva: None declared, R. Denisova Speaker Bureau of: Novartis, MSD and Roche, A. Chomahidze: None declared, A. Fetisova: None declared, O. Lomakina: None declared, K. Chibisova: None declared, M. Gautier: None declared, D. Vankova: None declared, I. Kriulin: None declared, E. Krekhova: None declared, A. Pushkov: None declared, K. Savostyanov: None declared

AB008

DOES CORONA VIRUS CAUSE A SPECIFIC INFLAMMATORY TOE ABNORMALITY

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Introduction: During the recent coronavirus pandemic there was a description of inflammation of toes possibly related to Covid 19 infection. I have seen 4 patients present with inflamed toes.
Objectives: To ascertain if Covid-19 causes a specific toe inflammation or is this due to another problem
Methods: I reviewed the 3 patients who presented with toe inflammation doing a full rheumatological examination. They were all seen via Skype.
Results: None of the 4 patients had had any symptoms of Covid 19 and all had self isolated. Examination of the toes revealed chilblain type lesions and all 3 patients had evidence of Raynaud's syndrome with markedly delayed capillary refil times in the feet of around 10 seconds. 2 of the patients had had a previous diagnosis of Primary Raynaud's and the two were new patients both with Primary Raynauds and no underlying rheumatological disease. Hands were much less affected in the patients than feet with slight prolongation of CRT in hands compared to feet.
Conclusion: I think that although the weather was warm in the UK at the time of lockdown, indoor temperatures are significantly lower than outdoors. I think due to decreased exercise, lack of wearing socks and shoes indoors and cooler temperatures indoors these patients had suffered from acute Raynaud's syndrome with chilblains rather than immune mediated vasculitic type illness causing their toe problems. I question if 'Covid Toes' as it was described is actually a condition or a manifestation of lockdown and Raynaud's with chilblains. Once the patients wore socks and shoes and kept warm no further lesions occured.
Disclosure of Interest: None declared

AB009

COVID-19 AND RELAPSING KAWASAKI DISEASE: A CASE REPORT DURING THE PANDEMIA

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Introduction: The pandemia of COVID-19 remains a global health alarm with high incidence of lethality, especially in older age groups who suffer from underlying medical conditions. However, children are less likely to manifest severe conditions.
Objectives: COVID-19 was correlated to a higher incidence and a suspected increased risk of Kawasaki Disease (KD) in children.
Methods: We describe the case of a 2.2-year-old infant admitted for fever (>5 days; > 39°C), pharyngitis, cheilitis, arthralgia, feet oedema, rash, perineal and scrotal region erythema, bilateral lymphadenopathy of the neck, cough, rhinorrhea. He was extremely irritable. Heart rate: 140/min; capillary saturation 99 % in air. Laboratory tests showed: leukocytes 13.4 x 10^3/µl (neutrophils: 7.4 x 10^3/µl); platelets 502 x 10^3/µl; haemoglobin 11.1 g/dl; increased inflammatory markers, with C-reactive protein (CRP) of 14.7 mg/dl (n.v.: < 0.5); hyponatremia (133 mEq/l). The nasal swab for respiratory viruses, IgM and IgG anti-EBV, CMV, Parvovirus, Mycoplasma, Chlamydia were negative. Anamnestic records revealed a previous KD, without coronary artery lesions (CAL), 1 year before.
Results: He was treated with antibiotics, intravenous infusion of Immunoglobulins (IVIG) (2 gr/Kg), acetylsalicylic acid (ASA) (50 mg/Kg in 4 doses/day) and reached defervescence into 2 days. Echocardiography excluded CAL. The nasopharyngeal swab for SARS-CoV-2 was doubt. The second throat swab done the day after IVIG infusion, was negative; however, the third nasopharyngeal swab for SARS-CoV-2, done 4 days after IVIG infusion, was positive. Chest x-ray showed a significant lung interstitial thickening. IL-6 levels were < 6.25 pg/ml (n.v. < 6.25 pg/ml).
He continued treatment with antibiotics, ASA (5 mg/Kg/day), with the progressive resolution of the clinical symptoms and of the normalization of laboratory findings.
Conclusion: The peculiar outcome of the patient is the correlation of COVID-19 with KD, recently reported as associated. KD is considered as a multifactorial autoinflammatory disease, induced by a cytokine hypersecretion with a systemic vasculitis. COVID-19 is considered a cytokine storm syndrome, with a severe systemic vasculitis. SARS-CoV-2 infection could be the trigger that could lead to hyperinflammation of KD.
The IVIG infusion could explain the transient negative swab for SARS-CoV-2, with the successive positive relieve lasting 7 days, and the normal levels of IL-6, detected after IVIG infusion.
Relapsing KD is rare (1.7-3.5%); in our patient this event could be triggered by the documented SARS-CoV-2 infection.
Disclosure of Interest: None declared

AB010

MANAGEMENT OF CHILDREN WITH RHEUMATIC DISEASES IN COVID-19 OUTBREAK IN THE TERTIARY PEDIATRIC RHEUMATOLOGY CENTER IN IRAN

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Introduction: The COVID-19 disease identified and reported from Wuhan, Hubei, China. At the time being, the disease is a pandemic and has involved the entire world.
Objectives: The aim of this study is reporting the planning and actions after the COVID-19 epidemic for prevention of spread of the disease, supporting patients, and managing the disease at our center's outpatient clinic as a referral center for children suffering rheumatic diseases.
Methods: Since the first report of disease, we tried to reply to the patients' questions in a virtual social network. We were following lab data, radiograms, sonograms, CT scans, and MRI results in this network and provided solutions for the management of the children's problems without need to encountering.
Results: In cases that were controlled and their diseases were in remission, we invited one of the patient's parents to come and receive the prescriptions. We put some instructive short films about COVID-19 in the virtual network and in LED screens of our outpatient hospital clinic to provide useful information. About the turn rating system (queuing system) we omitted manual turn-taking stands to prevent virus transmission. In the peak of the epidemic, we stopped outpatient clinics for three weeks. After that, we started clinics with the least number of patients and the most standard protection measures for physicians, patients, and other staff. All people were triaged in the hospital yard before entering the waiting hall of the clinic by taking their temperature and screening questions. If they didn't have a fever and symptoms compatible with the disease, we let the patient and only one compeer enter the clinic hall with giving a free three-layer surgical mask to each of them. We requested the physicians to increase the time of their clinics to distance the appointments of the patients and to prevent overcrowding in the clinic. Each clinic was held with the presence of the attending physician and only one fellow physician. Gowns, protective glasses and face shields, surgical masks, and latex gloves were provided for secretaries and the other staff in the clinic. In the first eight weeks, daily disinfection was performed for all the surfaces of the clinic and after that, a disinfecting tunnel at the door of the clinic was added. With the screening of about 100 staff in the clinic, we found only one IgM positive person for COVID-19 during the first eight weeks who was one of the secretaries without any signs and symptoms and were quarantined at home. Among the physicians, 6 of them (8 percent) developed COVID-19 disease with laboratory confirmation. All of the involved physicians were working in the private section as well as a state-run system. From about 200 patients with different rheumatic diseases came to the clinic in eight weeks, 11 of them (5.5%) were in the relapse of their disease which in comparison to the same time in the last year, 26 from 760 patients (3%), a remarkable increase (almost double) is seen for which different causes can be considered. Most of the patients who came to the clinic in the COVID-19 outbreak were those who had to come due to the severity of their disease. In the patients who came before the epidemic, the most causes were musculoskeletal pains such as hypermobility and skeletal benign reasons and rheumatic diseases were in the next rank but in the epidemic outbreak, the prior group came in a lower number. Follow up on the patients after the epidemic will reveal this matter better.
Conclusion: Employing personal and patient protective equipments, patients' triage, postponement of face-to-face appointments, social distancing, telemedicine, and using the virtual social networks may be effective policies in outpatient clinics in the COVID-19 outbreak.
Disclosure of Interest: None declared

AB011

SEVERE CARDIAC INVOLVEMENT WITH MYOCARDIAL DYSFUNCTION AND ARRHYTHMIAS IN SARS-COV-2-RELATED KAWASAKI-LIKE DISEASE

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Introduction: During SARS-CoV-2 pandemic, different reports have been published regarding children who developed hyperinflammatory syndrome with certain or probable relationship with SARS-CoV-2. These patients presented incomplete or atypical manifestations of Kawasaki disease (KD), particularly abdominal pain, myocarditis and macrophage activation syndrome features.
Objectives: To report a case of SARS-CoV-2-related Kawasaki-like disease with severe cardiac involvement.
Methods: case report description.
Results: A 10-year-old previously healthy girl presented progressively worsening abdominal pain, high grade fever for 3 days and vomiting. Lab tests showed WBC 11680/mmc, N 9370/mmc, C-reactive protein (CRP) 329 mg/L, procalcitonin (PCT) 0,74 ug/L, PT-INR 1,35 and elevated D-dimer and fibrinogen levels (817 ug/L and 9,45 g/L respectively). Abdomen ultrasound revealed lymphadenopathies and hyperechogenic mesentery in the right lower quadrant, although the appendix was not visualized. She underwent laparoscopy showing moderate quantity of free fluid and appendectomy was performed. Thereafter she continued to complain of high-grade fever, abdominal pain and diarrhoea, despite broad-spectrum antibiotics. Blood, urine and stool cultures were negative. Bilateral non-exudative conjunctivitis was present. Moreover, the lab tests showed persistent marked elevation of CRP (370 mg/L), WBC 15590/mmc, N 14070/mmc, hypoalbuminemia (23 g/L), elevated ferritin and triglycerides (458 ug/L and 221 mg/dl). By taking into consideration the concomitant SARS-CoV-2 pandemic, nasopharyngeal and rectal swabs were taken with negative results. Conversely, serological test showed anti-SARS-CoV-2 IgG antibodies and absence of IgM. The family medical history showed that the mother had presented fever, cough, ageusia and anosmia one month before, preceded by a contact with a SARS-CoV-2 positive case, while the patient was asymptomatic at that time.
Suspecting a KD-like disease she was referred to our Paediatric Rheumatology Unit: cardiological assessment revealed negative T-waves in V4-V5-V6 on EKG while standard and advanced echocardiography showed mild mitral and tricuspid insufficiencies, mild dilatation of the left main coronary artery (LMCA, z score +2), normal global function (FEVS 2D 58%) but reduced longitudinal strain (GLS -16%). Lab tests confirmed myocardial injury with troponin (TnI) 100,1 ng/l and brain natriuretic peptide (P-BNP) 593 ng/L.
A single infusion of intravenous immunoglobulin 2 g/kg associated with methylprednisolone (1 mg/kg/day) led to a rapid clinical improvement with apyrexia and resolution of abdominal pain and conjunctivitis. Blood test confirmed gradual normalization of inflammatory markers, ferritin, troponin and BNP and EKG showed positive T-waves. Shortly after the discharge, while she was on prednisone 0.5 mg/kg/day and acetylsalicylic acid 100 mg/day, she referred some episodes of heart pounding, lasting about ten minutes with spontaneous resolution. Three weeks after onset, cardiac MRI was normal, however, speckle tracking echocardiography showed persistent dilatation of LMCA and reduction of global longitudinal strain (GLS -14%). 24-hour EKG-Holter detected episodes of supraventricular tachycardia and several ventricular and supraventricular extrasystoles. Thus, oral atenolol therapy was started.
Conclusion: In our patient SARS-CoV-2 induced a possible post-infectious antibody or immune-complex mediated reaction that led to KD-like disease with acute surgical abdomen presentation and persistent myocardial damage and arrythmias. Speckle tracking echocardiography appears more reliable than MRI in early detection of myocardial damage in patients with preserved left ventricular ejection fraction.
Disclosure of Interest: None declared

AB012

SPECTRUM OF SYSTEMIC INFLAMMATORY SYNDROME IN CHILDREN DURING COVID 19 PANDEMIC IN INDIA

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Introduction:
Recently reports from Europe and North America have described clusters of children and adolescents with a multisystem inflammatory condition with some features similar to those of incomplete Kawasaki disease. [1-3]

Objectives:
To unveil characteristics of systemic inflammatory syndrome (SIS) in children during COVID-19 pandemic in India

Methods:
This is a case series which included three such pediatric patients who were evaluated between April 2020 and May 2020 at five different hospitals from an Indian state of Gujarat. Our electronic data included demographics, clinical presentation, laboratory results and follow up.

Results:
Table 1 showed characteristics of SIS in children during COVID-19 pandemic in India

Age (years) / Sex (M/F)	3 / M	7.7 / M	7 / F
Fever (duration)	2 weeks	11 days	11 days
Containment Zone	**Yes**	No	**Yes**
Rash	**+**	+	+
Red eyes	+	+	(evanescent)
Red Tongue	--	+	--
Pharyngeal congestion	+	--	--
Distal edema	+	--	--
Skin exfoliation	--	+	--
Swollen lips	+	--	--
			--
Joint involvement	+	+	--
Serositis	+	--	--
Organomegaly	+	--	--
GI symptoms	+	+	--
Respiratory symptoms	+	--	--
Chest X-Ray findings	+	--	--
Shock or Hypotension	--	--	--
2d Echo findings	--	--	--
HB (11.5-14.5gm/dl)	7.2	9.1	9.6
TLC (4000-12,000/cumm)	7800	19,700	23,230
Platelets (1,50,000-4,50,000/ul)	46,000	5,20,000	5,57,000
Blood C/S	Negative	Negative	Negative
ESR (0-20 mm/hr)	**68**	**110**	**120**
CRP (0-6 mg/L)	**234**	44.7	**226**
Ferritin (7-140 ng/ml)	125.4	122	**6235**
Procalcitonin (<0.15 ng/ml)	**3.84**	Not done	**7.14**
Triglycerides (35-138mg/dl)	333	Not done	Not done

Fibrinogen (150-400 mg/dl) LDH (24-59 IU/L) PT, aPTT	209.5 663 Mild derangements	Not done Not done Not done	Not done Not done Not done
C0VID-19 RT PCR	Negative	Negative	Not done
Treatment	IV antibiotics Oral Azithromycin IV albumin[$]	IV Ig Oral aspirin	Oral naproxen Oral steroids
Last follow up	better	better	better

($ = IV albumin infusion was given in view of progressive generalized edema and hypoalbuminemia)

Conclusion:

Above three cases reemphasize the need for a high index of suspicion for COVID 19 (coronavirus) as a possible culprit in a child with unexplained multisystem inflammatory syndrome.

Trial registration identifying number:

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Disclosure of Interest: None declared

AB013

A CHILD WITH A SEVERE MULTI-SYSTEM INFLAMMATORY SYNDROME FOLLOWING COVID-19 INFECTION

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Introduction: Despite the mild clinical course during the acute phase of COVID-19 infection in children, latest ongoing researches are pointing the attention towards a hyperinflammatory shock in pediatric patients as a possible consequence to COVID-19 exposure.
Objectives: We report the case of a child with a severe systemic inflammatory syndrome following an asymptomatic COVID-19 infection.
Methods: A 9-year-old male was admitted to the Pediatric Emergency Unit due to fever and abdominal pain. Symptoms started 7 days before admission, with fever, vomiting and non-bloody-diarrhea. Family history revealed that the father had been admitted to a COVID-19 Sub-Intensive Unit with bilateral interstitial pneumonia until 7 days before the onset of symptoms in the child. On the basis of familial history and because of the presence of fever, patient entered the COVID-19 pathway and was isolated. He had no chronic underlying disease nor history of previous hospitalization. At admission, he appeared stable. Body temperature was 38.1°C, O2 saturation was 98% in ambient area, blood pressure was 106/60 mm Hg, heart rate was 140 bpm, respiratory rate was 21 breaths per minute. On examination he was alert, there were no cough, runny nose or other respiratory symptoms. No conjunctivitis, rash or peripheral edema was detected. He had mild hepatomegaly.
Results: The patient underwent blood and microbiological exams including blood specimens for cultures and nasopharyngeal swabs for SARS-CoV2 nucleic acid (by RT-PCR- assay). At baseline, leukocytosis with neutrophilia and relative lymphopenia were found. Hemoglobin was below the normal range, while platelets count was normal. Inflammatory markers were strongly elevated, particularly CRP(420.8 mg/L), ferritin(4488 ng/mL), D-dimer(5106 ng/mL). Several significantly altered parameters suggested liver function abnormality, with hypertransaminasemia, acute renal injury, with elevated blood urea nitrogen and serum creatinine, and myocardial injury, with elevated high sensitivity cardiac troponin (434 ng/L) and brain natriuretic peptide (825 pg/mL). Lymphocyte subsets were within the normal range, while NK cells were slightly reduced. Patient was also tested for respiratory syncytial virus (RSV) and for influenza viruses A and B, resulted all negative. Bacteria and fungi blood cultures were sterile, as well as urine and stool cultures. He was tested for COVID-19 antibodies which showed positivity of both IgG and IgM (qualitative test), confirmed by a quantitative analysis which showed a high level of IgG (5066 AU/ml) and a weak positivity of IgM (0.532 AU/mL). Echocardiography showed no ventricular dysfunction, no dilatated coronaries or pericoronary iperechogenicity. Chest CT on the 2nd day showed two small bilateral areas of atelectasis associated to minimal pleural effusion more evident on the right side.
The diagnosis of Hyperinflammatory syndrome COVID-19 related was made.
Conclusion: Because of the high levels of BNP and troponin, IV methylprednisolone (5 mg/kg/day) and subcutaneous heparin (100 U/kg/day) were started after 24 hours since admission.
Search for COVID-19 on nasopharyngeal swabs collected for 3 consecutive days resulted negative, The patient gradually recovered and fever disappeared after 48 hours. He presented no vomiting or diarrhea during the hospital stay, nor respiratory symptoms. Laboratory exams dramatically improved. According to his clinical and laboratoristic improvement, methylprednisolone was tapered to 3mg/kg/day and he started oral prednisone 1.25 mg/Kg/day four days after. He was discharged with steroid and heparin therapy and a close follow-up was planned.
Disclosure of Interest: None declared

AB014

CAMPATODACTLY-ARTHROPATHY –COXAVARA-PERICARDITIS (CACP) SYNDROME IN A LIBYAN FEMALE CHILD

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Introduction: Campatodactly-arthropathy –coxavara-pericarditis (CACP) syndrome is a rare autosomal recessive disorder caused by a mutation in the gene proteoglycan 4(PRG4) affecting lubricin production, which is an essential protein for joint function. We present this case of a female child to describe the clinical, laboratory and radiological findings of CACP syndrome that should help in differentiation of CACP syndrome from other childhood inflammatory arthritis.
Objectives: To increase the awareness of this familial condition to prevent confusion with other inflammatory conditions
Methods: A case report
Results: an 8-year-old female patient was referred to the Rheumatology clinic with complaints of joint deformities of her fingers namely campatodactly was noticed through the first year of life that treated surgically, while other joint involvement at age 3 was starting to have multiple joints swelling, she was the products of 3rd degree consanguineous marriage and other 2 siblings are healthy, she was referred as a case of poly juvenile idiopathic arthritis. She has normal intelligence with normal school performance, she's able to perform all daily activities except that she has difficulty in the traditional cross sitting.At the time of our assessment, articular findings revealed bilateral flexion deformity of proximal interphalangeal joints and limited flexion and extension of both wrist joints, additionally there was a thickened rubbery synovium, significant knee joints swelling with moderate to large effusion associated with it, significant limitation of hip joint movements mainly in the internal and external rotation as well as abduction, and she was unable to sit cross-legged , although she didn't have joint tenderness or hotness , she had sometimes a non-specific diffuse joint pain . Moreover , she had normal cardiac examination and echocardiography study , her ophthalmological assessment was normal , however ; her height was below 3rd percentile , there were no other associated systemic involvement. Her laboratory tests revealed that she had normal inflammatory marks (ESR, CRP) and the result of rheumatoid factor test was negative, she had low vitamin D and slightly elevated alkaline phosphatase level, her PTH, serum calcium and phosphate were within normal range. Regarding her radiological findings , her x ray showed that there were pictures of bilateral coxa vara with a short femoral neck and flat, irregular femoral head and intra-osseous cysts, increased joint space and abnormal modeling acetabulum with small iliac wings. Other joints (knees, ankle, elbow and wrist) showed soft tissue swelling consistent with thick cartilage. Her hand x-ray showed a soft tissue swelling around the interphalangeal and wrist joints , periarticular osteopenia and flexion deformities of the interphalangeal joints, affecting the 5 th joints bilaterally .A bilateral hip MRI showed effusion. Patient was treated at the referral hospital with a (NSIDs) and antirheumatic drugs , however ; they were ineffective.We treated her in the rheumatology clinic with vitamin D and calcium supplements as a treatment for osteopenia. We believe that synovial biopsy is not indicated in the correct clinical and radiological setting for atypical presentation, thus it is recommended if genetic testing is not affordable.
Conclusion: CACP syndrome should be considered in juvenile patients presenting with non-inflammatory arthropathy . We hope that this report will increase the awareness of this familial arthropathy condition and the clinical characteristics and the radiological findings well facilitate the differentiation from the common childhood rheumatic diseases.

Disclosure of Interest: None declared

AB015

RELATIONSHIP OF RAYNAUD'S PHENOMENON ON QUALITATIVE AND QUANTITATIVE VIDEOCAPILLAROSCOPY EVALUATION OF PEDIATRIC PATIENTS WITH RHEUMATIC DISEASES.

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Introduction: Capillaroscopy is a tool that helps to assess microcirculation (MC) by observing the shape, density, structure, and alterations in the capillaries of the nailfold. MC has an important association with rheumatic diseases (RD), which is why it has become an important tool in rheumatology, and is considered a low-cost, non-invasive method. Raynaud's phenomenon (RP), a clinical condition commonly found in patients with RD, requires capillaroscopic evaluation to differentiate primary RP from the secondary, and it also helps to monitor the activity of the disease, assess response to treatment and prognosis. To date, there are no standardized capillaroscopic patterns in pediatric populations.
Objectives: Describe qualitative and quantitative capillaroscopic differences between pediatric RD patients with RP and those without RP.
Methods: Patients from the pediatric rheumatology department of a tertiary center in Monterey, Nuevo León, Mexico from July 2017 to March 2020 were included. Eight fingers, excluding the thumb, taking for analysis the most representative 1 mm image of each finger with x200 videocapillaroscope (Optilia), all measurements were taken by the same observer. Demographic data captured to describe the diagnosis, age, and RP presence. Capillaroscopy data, qualitative data: pattern, density, abnormal shapes, microbleedings and edema; for quantitative characteristics length, width, inter capillary distance, afferent diameter and efferent diameter were obtained.
Results: Sixteen patients were included, of which 13 (81.2%) were female, the mean age was 12 years, RP was present in 12 (75%) patients. Regarding the diagnoses in the RP group, we found Systemic Lupus Erythematosus (5/12), Juvenile Idiopathic Arthritis (3/12), undifferentiated connective tissue disease (1/12), systemic sclerosis (1/12), IgA vasculitis (1/12) and primary RP (1/12); in the group without RP the diagnosis where psoriatic arthritis (1/4), psoriasis (1/4), localized scleroderma (1/4) and polymyositis (1/4). Among the quantitative characteristics, we found a greater length in R2, R4, R5, L4 and L5 of the patients with RP. Similarly, we observed a difference in the afferent diameter of R3, R4, R5, L2, L3, L4 and L5, being bigger in patients with RP. In L4 we found a difference in length, afferent and efferent diameter, being greater in those patients with RP, on the contrary, the width is usually smaller.

	Raynaud's phenomenon	R2	R3	R4	R5	L2	L3	L4	L5
Length (µm)	Yes	230.878	234.351	239.687	217.900	217.930	215.636	223.755	203.186
	No	253.036	281.273	180.926	200.546	275.238	268.120	192.640	194.445
Width (µm)	Yes	54.442	69.112	51.100	51.091	53.070	46.854	51.963	45.713
	No	57.696	54.518	45.658	48.696	52.281	60.571	53.029	42.710
Afferent diameter (µm)	Yes	18.511	21.858	20.718	18.033	18.106	17.241	18.143	17.149
	No	18.075	19.573	15.568	16.319	15.302	15.815	15.239	15.307
Efferent diameter (µm)	Yes	25.403	26.675	24.918	24.037	23.804	22.895	25.008	22.229
	No	26.493	27.900	22.088	22.763	30.990	22.396	20.148	18.834

Right hand finger No. 2 to No. 5 =R2, R3, R4, R5. Left hand finger No.2 to No. 5 = L2, L3, L4, L5.

Conclusion: We found both qualitative and quantitative differences in patients with RP versus those without RP, mainly in afferent diameter for all fingers, and in L4 we found a difference in most of the measurements. This study shows the quantitative data of the videocapilaroscopic analysis, and therefore it is proposed as a possible tool for the diagnosis and monitoring of RD in pediatric patients. Despite finding capillaroscopic alterations in both, the sample size in this cohort is small, so studies with a greater sample must be done, as well as studies with controls on healthy children, to make more conclusions.
Disclosure of Interest: None declared

AB016
IS SUBCLINICAL SYNOVITIS ASSESSED BY ULTRASOUND ABLE TO PREDICT FLARES IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS IN CLINICAL REMISSION ? A SYSTEMATIC REVIEW OF THE LITERATURE

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Introduction: Clinical examination may not detect mild degrees of synovitis that can be present in subjects deemed to be in clinical remission and with negative inflammatory markers. In adults, ultrasound (US) Power Doppler positivity in patients with RA in clinical remission has been suggested by some authors to have a predictive value for flare. In pediatrics there are less definite data, in relation to difficulties in practical application of US and physiological changes in growing joints. In asymptomatic JIA children with a normal joint examination the long term significance of subclinical arthritis detected by US is not clear.
Objectives: Aim of the present study is to review published articles related to the predictive value for flare of subclinical synovitis assessed by ultrasound in juvenile idiopathic arthritis (JIA) in clinical remission. This could have implications in the practical management both for adjustments in drug treatments and for the timing of clinical surveillance during follow-up.
Methods: Medline, Embase and Cochrane databases were searched from 1990 to 2020 by two authors, using PICO methodology to build the following strategy. Population: JIA patients, aged ≤ 16 years, in clinical remission. Interventions: Clinical assessment plus ultrasound. Comparison: Clinical assessment only. Outcome: Clinical flare. Reviews and case series < 10 patients were excluded. The study is built and reported according to PRISMA guidelines.
Results: The search found a total of 208 records. After removing duplicates, 168 articles were selected by title and abstract, and of those 163 were excluded since they did not meet the PICO inclusion criteria. Five articles were identified suitable for analysis. One of these, after reading the full text, lacked detailed data related to US findings at baseline and was therefore excluded. We considered four articles comprising a total of 202 patients with JIA in clinical remission from at least 3 months. Because of the small number of the articles and data heterogeneity meaningful statistical analysis could not be performed. Two of the articles found US subclinical signs of synovitis to be predictive for flare, with a five times higher risk (with Power Doppler signal as an important feature), while in the other two articles baseline US abnormalities could did not predict a clinical flare. The articles differed for protocols, definitions, and length of follow-up.
Conclusion: US has an expanding role in pediatric rheumatology. Although its usefulness in the early diagnostic phase may be questionable, a more interesting use could be applied during follow-up, for the possibility of identifying subclinical inflammatory signs predictive of a future flare. The small number of studies available, data heterogeneity, and conflicting results however do not allow yet any definite conclusions in this regard.
Disclosure of Interest: None declared

AB018

ETANERCEPT AND JUVENILE IDIOPATHIC ARTHRITIS, EXPERIENCE OF THE PEDIATRIC CENTER OF SÉTIF HOSPITAL

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Introduction: Etanercept (ETN) was the first anti-TNFα agent to obtain Marketing Authorization in 2000 for juvenile idiopathic arthritis (JIA) of polyarticular progression resistant to Methotrexate.
etanercept (ETN), a human IgG1 fusion molecule - soluble p75 receptor for human TNF alpha.
The indications of the ETN currently cover the JIA of polyarticular evolution, that is to say the polyarticular, extended oligoarticular forms and the systemic forms become polyarticular, the form associated with enthesopathies and psoriatic arthritis
Objectives: To analyze the effectiveness of Etanercept, as well as its tolerance in juvenile idiopathic arthritis (JIA).
Methods: We carried out a retrospective study of children diagnosed with JIA according to the ILAR classification criteria and treated with Etanercept at the pediatric center of Setif University Hospital since 2015.
15 children were included and judged at 3 months, 6 months, 1 year, 2 years, 3 years, 4 years on epidemiological criteria, efficacy criteria (Joint scores, uveitis, SV, CHAQ) and the occurrence of possible Side effects .
We defined the improvement of 30% (ACR 30), 50% (ACR 50), 70% (ACR 70), 90% (ACR 90), and 100% (ACR 100) as the improvement of minus 3 out of 6 criteria of 30%, 50%, 70%, 90%, 100%; patients must not have an aggravation of more than 30% from one of the 6 criteria.
Results: The epidemiological characteristics were as follows: 9 girls and 6 boys, 7 have a polyarticular form, 5 have an oligoarticular form, 2 cases with psoriatic arthritis, and only one case of arthritis-associated enthesitis (ARF).
ACR 30 is obtained in 75%, 84%, 88% of cases respectively at 3 months, 6 months, 1 year.
The most marked responses were obtained in the polyarticular, oligoarticular and and arthritis-related enthesitis.
for psoriatic arthritis = 72%.
Complete remission was maintained in the majority of the patients for varying durations depending on the outcomes.
Furthermore, no clinical or biological undesirable effects have been noted.
Conclusion: Etanercept has a spectacular efficacy in children suffering from juvenile idiopathic arthritis, particularly in polyarticular, oligoarticular forms and IBAs.
His overall tolerance is very good.
Disclosure of Interest: None declared

AB019

FIBROBLAST GROWTH FACTOR AND HEPATOCYTE GROWTH FACTOR IN ADOLESCENTS WITH JUVENILE IDIOPATHIC ARTHRITIS TREATED WITH METHOTREXATE

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Introduction: Risk of liver fibrosis development during juvenile idiopathic arthritis (JIA) treatment with methotrexate (MTX) in adolescents remains relevant.
Objectives: To study levels of basic fibroblast growth factor (BFGF) and hepatocyte growth factor (HGF) in adolescents with JIA treated with MTX
Methods: 68 children were observed, 25 boys (36.8%) and 43 girls (63.2%).The average age of the patients was 13.3 ± 0.3 years. Children were divided into four groups: those with JIA who didn't receive MTX yet (group 1); those who received MTX less than one gram during whole treatment (group 2); those who received MTX from 1 to 3 grams (group 3); children, received more than 3 grams of MTX (group 4).
Results: The autoimmune inflammatory process in JIA can cause formation of pathological changes in the liver, even before the start of treatment. It is confirmed by a statistically significant correlation of BFGF level in 1st group with liver steatosis according to ultrasound examination (r = 0.8) and the level of C-reactive protein (r = 0.7). This indicates a close relationship between the intensity of the inflammatory process and collagen synthesis activation, which can further provoke liver fibrosis. Alterative processes in the liver associated with autoimmune inflammation, as evidenced by the presence of a positive correlation between the level of ALT and BFGF (r = 0.5). Upon reaching MTX dose 1 gram and 3 grams, it is possible that compensatory processes in the liver are triggered, as evidenced by the negative correlation between the content of BFGF and HGF (r = -0.6).
Conclusion: The use of modern markers with routine laboratory and instrumental studies is appropriate for the timely determination of the risks of developing irreversible pathological changes in the liver during JIA treatment with MTX.
Disclosure of Interest: None declared

AB020

PREDICTORS OF THE EFFECTIVENESS OF INTRA-ARTICULAR GLUCOCORTICOID INJECTIONS IN JUVENILE HIP INVOLVEMENT

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Introduction: Juvenile idiopathic arthritis (JIA) is the most common chronic inflammatory arthritis in children. Intra-articular glucocorticoids (IAG) are recommended as the first-line therapy for oligoarticular JIA. The safety and the benefits of use of IAG in other subtypes should be more studied.
Objectives: The aim of our study is to evaluate the efficacy of (IAG) injections in hip in children with (JIA) and to assess the factors predicting the improvement of this management.
Methods: This is a retrospective study, between 2006 and 2009, including patients with JIA diagnosed according to the ILAR criteria. The socio-demographic data were collected as well as the parameters of the disease. The activity was evaluated by JADAS. The functional impact was assessed by the Lequesne score. The treatments taken have been specified as well as the infiltrations received. The improvement after infiltration was assessed by JADAS and Lequesne score.
Results: Fourteen patients were included, with mean age 17.21 +6.8 [6-33]. The mean age at the onset of symptoms was 11 +0.5 [3-15]. Subtypes of JIA according to The ILAR were: enthesitis-related arthritis in 7 cases, seropositive polyarticular JIA in 2 cases, seronegative polyarticular JIA in 2 cases, oligoarticular JIA in 2 cases and juvenile psoriatic arthritis in one case. All the patients had hip arthritis, inaugural in 90% of the cases. Of these, 92.8% had a flexion deformity and lower limb inequality. The average Lequesne index was 8.5 +4.6. The treatments taken were Methotrexate in 57.14% of the cases, Sulfasalazine in 14.28% of the cases, and the combination of the two in 21.4% of the cases. Eleven patients underwent hip infiltration, and three of them required more than one. Eighty one percent improved thereafter. The number of infiltrations was not statistically associated with the Lequesne index ($p = 0.069$). Improvement after infiltration was negatively associated with the prior existence of an inequality of the lower limbs ($p = 0.04$). The existence of a flexion deformity was not associated with good results after infiltration ($p = 0.476$, $r=-0,624$). Ten patients (90%) among those who had an infiltration did not have to resort to surgery.
Conclusion: IAG injection is an adjunct therapy in AJI with hip involvement offering a good results and delay surgery in the majority of cases. The presence of lower limb inequality is associated with less improvement of IAG.
Disclosure of Interest: None declared

AB021

RICE BODIES AT JUVENILE IDIOPATHIC ARTHRITIS ONSET.

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Introduction: Rice bodies are detached synovial fragments surrounded by fibrine concentric layers, giving them the aspect of a white oval rice grain. The pathologic mechanism is related to synovial hypertrofic growth and has been frecuently reported in rheumatoid ant tuberculous arthritis. This formations have been scarcely reported in juvenile idiopathic arthritis individual patients.

Objectives: To describe the difficulties and particularities of three cases Juvenile Idiopathic Arthritis in which rice bodies were present at onset.

Methods: Retrospective chart review, collection of clinical, radiological and microscopic images.

Results: CASE 1: A 3 years old girl presenting with five week history of right knee swelling. Two joint punctures with a 21 G needle were unable to completely drain the joint; with a 16 G needle the joint was finally drained and injected with triamcinolone acetonide. Synovial fluid had plenty of white oval shaped bodies. Culture of synovial fluid and mantoux were negative. Pathology showed to be compatible with synovial rice bodies. MRI and ultrasound images show an intense synovial hypertrophy.

CASE 2: A 3 years old girl presenting with an undetermined duration right knee effusion, recieved an steroid joint injection with good response. One month later she presents a left knee swelling; joint punture was performed with a 21 G needle obtaining synovial fluid with tiny oval white formations compatible with rice bodies. Culture of synovial fluid and mantoux were negative. Ultrasound images show intense synovial hypertrophy and positive synovial Doppler signal.

CASO 3: A 3 years old girl presenting with a nine week history of right knee swelling. Joint puncture was performed with a 21 G needle obtaining 10 ml of inflammatory fluid ank steroids injected in the joint. After two weeks a second procedure was performed with a 16G needle: giant white oval bodies were obtained but complete drenaige of the joint was not achieved. Finaly she underwent arthroscopic surgery for complete clearance of intraarticular loose bodies. Pathology showed synovial hypertrophy fragments surrounded by fibrine, compatible with rice bodies. Culture of synovial fluid and mantoux were both negative. MRI and ultrasound images show an intense sinovial hypertrophy with suprapatelar recess occupation and positive synovial Doppler signal.

CASE	**SEX**	**AGE**	**JOINT AFFECTED**	**DURATION OF ARTHRITIS**	**NUMBER OF PROCEDURES**	**DIAMETER NEEDED FOR EVACUATION**
1	FEMALE	3 Y	Knee	5 weeks	2	16 G
2	FEMALE	3 Y	Knee	Acute	1	21 G
3	FEMALE	3 Y	Knee	9 weeks	3	Arthroscopy

Conclusion: Synovial rice bodies are rarely described in juvenile idiopathic arthritis, even less at disease onset. Their presence has not been associated to a worse disease prognosis or joint outcome but awareness of the existence of this particular form of intraarticular loose bodies may encourage the clinician to use lower gauge needle during arthrocentesis procedure; this can prevent arthroscopy, as occurred in our case 1. Arthroscopy may be necessary in some cases to achieve full drainage of the joint. In our series the duration of arthritis correlated with the size of rice bodies and the number and agressiveness of procedures needed to evacuate them.

Disclosure of Interest: None declared

AB022

SPECTRUM OF JUVENILE IDIOPATHIC ARTHRITIS IN 27 PATIENTS FROM A SINGLE CENTER IN AN INDIAN STATE OF GUJARAT

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Introduction:

There is very limited information and awareness about juvenile idiopathic arthritis (JIA) amongst primary physicians in Gujarat and to make this matter even worse, we are not having a single exclusive pediatric rheumatology center for a population of around 60 million.[1-3]

Objectives:

To study characteristics of twenty seven JIA children managed at Dev Children's Hospital.

Methods:

I gathered a data of 27 pediatric patients with confirmed diagnosis of JIA who were seen at Dev Children's Hospital between January 2019 and January 2020. It included demographics, clinical presentation, laboratory results and treatment. All cases were re-classified according to preliminary PRINTO JIA classification.[4]

Results:

Table 1 showed characteristics of 27 JIA patients managed at Dev Children's Hospital.

Sub-types of JIA Total no of Cases 27	Early-onset ANA positive JIA 4 (15%)	**RF positive JIA 9 (33%)**	sJIA 7 (26%)	Enthesitis-spondylitis related arthritis (ESRA) 3 (11%)	Other and unclassified 4 (15%)
Average age of onset Sex predilection	3.7 years F > M	9.4 yrs All **females**	5.1 yrs F > M	12.9 All males	6.6 years M=F
Average number of joints affected	4.5	7	3	1.6	4
Most common affected joint	**Knee**	Wrist	Knee	Ankle	Knee
Eye involvement	None	None	None	**One patient**	None
Drugs used Naproxen Methotrexate Steroids Tocilizumab	 All All One None	 All All All One	 All Five All Two	 All All None None	 All All Two None
Alternative therapy **Anti-inflammatory diet** **Yoga[5]**	 **All** None	 All All	 All One	 All All	 All Two

Conclusion:

Most common JIA sub-type in our cohort is RF positive JIA. Knee is the most common affected joint irrespective of JIA sub-type. Only one patient showed eye involvement. Most of the patients have been given steroids at onset. One patient with RF positive JIA and two patients with systemic JIA have been given intravenous tocilizumab infusion. Anti-inflammatory diet and yoga were advised for almost all patients of more than 5 years of age.

Trial registration identifying number:

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The impact of yoga, anti inflammatory diet and self monitoring in children with rheumatic diseases
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Disclosure of Interest: None declared

AB023

RUXOLITINIB THERAPEUTIC TRIAL IN REFRACTORY CUTANEOUS JUVENILE DERMATOMYOSITIS(CASE REPORT)

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Introduction: Juvenile dermatomyositis(JDM) is the most recognizable paediatric-onset systemic autoimmune inflammatory myopathy .
Objectives: To confirm the significance of Type I interferon signature as a proven fascinating contributor in the pathogenesis of the disease that strongly correlates with disease measures in JDM.
Methods: An 8 years old female patient,2nd sibling of non consanginous marriage, presented at the age of seven with a two month history of high grade persistent fever, progressive proximal muscle weakness with evolving dysphonia , nasal tone, velopharyngeal dysfunction, dysphagia and severe dyspnea.
Results: On physical examination,patient was average built for age,conscious and alert . Systemic examination revealed evidence of heart failure, generalized muscle weakness more evident in the proximal groups(2 on Manual Muscle Testing Grading System), marked hypotonia and hyporeflexia with no affection of sensation , dermatologic manifestations showed only Gottron's papules on metacarpophalangeal joints of both hands and no organomegaly.Routine Laboratory evaluation showed a within normal CBC picture , ESR 11 mm/1st hr ,CRP 96 mg/dl, elevated ALT, AST, LDH and highly elevated CK (6000 U/L),non significant 24 hrs proteinuria level and negative viral markers.Immunological profile showed a within normal levels serum immunoglobulins assay, CD markers, negative immune markers (ANA , Anti-DNA , ANCA. Echo showed evidence of carditis and EF 38%, pelviabdomial US was free. Patient was diagnosed as a case of juvenile dermatomyositis(JDM) ,started on pulse steroid therapy (Methylprednisolone; 30mg/kg x 5 days)and IV cyclophosphamide (600 mg/m² planned monthly x6 doses),patient showed relative improvement and was maintained further on oral full dose steroids(FDS) and cardiac anti-failures.One month later, erythematous rash started on both elbows,regained weakness and dyspagia, CK (12000 U/L),24 hr proteinuria(500mg) so patient was given another pulse steroid therapy combined with IVIG(1 gm/kg) and an every 2 weeks course of Rituximab(375mg/m² x 4 doses) together with monthy cyclophosphamide.Patient went into clinical remission with a CK level 570 U/L. Four months later, patient developed full cutaneous manifestations (heliotrope rash, facial rash, nodular violaceous erythema and annular plaques on both elbows with periungual telangiectasia) and a CK rise to 790 U/L with fair general condition so a push on course of pulse steroids and IVIG were given and Mycophenolate Mofetil(MMF) was added to her FDS together as maintenance with Etanercept (0.8mg/kg/week SC) for three months where the patient entered into a complete clinical and laboratory remission(CK 56 U/L) except for a progressive non responsive cutaneous manifestations (V-sign ,Shawl sign, photosensitivity ,vasculopathic ear rash and starting upper eye lid calcinosis) adding to the previous ones.Considering the severity and progression of the cutaneous maifestations the dependence on FDS, partial failure of the previous therapies, low CD19 & CD20 follow up levels and assuming involvement of the type I IFN pathway led to initiating treatment with the JAK1/2 selective inhibitor ruxolitinib (5 mg twice a day, i.e. 0.5 mg/kg/day) with consecutive gradual tapering of oral steroids and maintenance on MMF(600mg/m²/12hr) . Patient's cutaneous manifestation went into a significant remission with good tolerance to ruxolitinib and no recorded disease activity or relapses for six months till now. Close follow up is done.
Conclusion: Refractory cutaneous dermatomyositis is a challenging situation.Steroid dependence, limited success of anti-TNF and difficult implementation of rituximab drove to applying JAK inhibitors. Ruxolitinib observed great efficacy emphasizes the importance of interferon in the cutaneous disease arm and provides a new therapeutic avenue.
Disclosure of Interest: None declared

AB024

AN UNIQUE CASE OF MULTIPLE AUTOIMMUNE SYNDROME COMBINED WITH GOUT IN A 16-YEARS BOY

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Introduction: Multiple autoimmune syndrome is a condition characterized by three or more autoimmune disorders in a same individual. About 25 percent of people with autoimmune diseases have a tendency to develop additional other autoimmune disorders.
Objectives: To describe a rare case of a boy with combination of juvenile idiopathic arthritis (JIA), RF and ACCP positive, Sjogren's syndrome, autoimmune thyroiditis and gout.
Methods: Case report.
Results: A 14 yo male patient with normal physical, psychosocial and cognitive development presented with polyarthralgia in October 2016 y, two months later he had acute onset arthritis in the right shoulder and right knee (intensive pain, swelling, hyperemia and local hyperthermia), which developed without potential triggering factors. The patient received short course of diclofenac i.m. with temporal positive effect. This episode was followed by stable swelling of metacarpophalangeal and proximal interphalangeal joints of 2-3 fingers on both hands with morning stiffness lasting up to 1 hour and multiple short episodes of acute arthritis in 1st metatarsophalangeal joint of the left foot, metacarpophalangeal joints of 2-5 fingers on both hands independently. The patient was hospitalized to local hospital in February 2019, lab findings were as follows: ESR 44 mm/h, CRP 36 mg/l, RF 24 U/ml, ANA screen neg, the serum level of uric acid was 653,0 µmol/L. Diagnosis JIA, RF+ polyarthritis was established, but NSAIDs (i/m and per os) and sulfasalazine therapy was ineffective followed by increasing number of flares and the persistence of high laboratory activity. He was first admitted to our hospital in April 2019 (at 16 yo) with active arthritis of metacarpophalangeal and proximal interphalangeal joints of 2-3 fingers on both hands, of right knee, 1st metatarsophalangeal joint of the left foot. Lab findings included ESR 36 mm/h, CRP 6.9 mg/l, RF 484 U/ml, ACCPhs 1000 U/ml, ANF Hep-2 1/640h+sp, a-TPO 1585.5 U/ml, a-TG 4028.9 U/ml, serum creatinine 122 µmol/L, urea 7.8 mMol/L, uric acid 577 µmol/L. Schwartz estimate glomerular filtration rate (GFR) was 110.9 ml/min, diurnal proteinuria 0.04 g/day. Chronic erosive arthritis of the hands and distal parts of the feet by ultrasound and X-ray imaging was confirmed. Crystals of sodium monurate were found in the synovial fluid from the right knee and 1st metatarsophalangeal joint of the left foot. Ultrasound finding of the thyroid gland revealed signs of autoimmune thyroiditis. Imaging modalities (US, sialography) identified visible changes of salivary glands characteristic for Sjogren's syndrome. Sialometry confirmed the presence of the sicca syndrome. Thus, JIA RF+ and ACCP+, secondary Sjogren's syndrome, autoimmune thyroiditis and gout were verified. Molecular-genetic testing didn't confirm the any genetic mutation. The patient was treated by methotrexate (15 mg per week), folic acid (1 mg/ 6 days a week), allopurinol with a titration of up to 300 mg per day, L-thyroxine 100 mg per day with gradual positive dynamics and good tolerance.
Conclusion: The presence of one autoimmune disease should be an indicator for the possibility of another one. Occurrence of multiple autoimmune phenomenon indicates the need for continued surveillance for the development of new autoimmune disease in predisposed patients. The simultaneous presence of several autoimmune conditions and gout, which is of autoinflammatory origin, seems to be unique, especially in pediatric patients.
Disclosure of Interest: None declared

AB025

RITUXIMAB FOR TREATMENT OF RESISTANT PAEDIATRIC MCTD

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Introduction: First described in 1972 by Sharp et al, Mixed Connective Tissue Disease (MCTD) is a rare entity in children. Diagnosis is made by clinical-immunological overlapping features of different Connective tissue diseases. Typical clinical features are Raynaud's phenomenon, myositis, arthritis, sclerodactyly along with positive anti RNP Antibody. There is a higher risk of interstitial lung disease and pulmonary hypertension. Treatment is tailored to the patient based on features present (1).
Objectives: We present a challenging case of Paediatric Mixed Connective Tissue Disease (MCTD) with Sjogren overlap resistant to standard treatment and requiring the addition of Rituximab to control recurrent debilitating parotitis.
Methods: We conducted a retrospective case review using electronic patient record.
Results: A 15 year old female, first presented at the age of 7 with Raynaud's phenomenon and a high ANA 1:5120 was referred from local hospital. Double stranded DNA was negative, ENA typing revealed anti U1-RNP positive. She then developed symptoms of Parotitis and arthritis when oral steroids were commenced. A lower lip biopsy revealed periductal lymphocytic infiltrate admixed with scattered plasma cells. USS of parotid glands showed bilateral chronic sialadenitis in submandibular and parotid glands. Increased vascularity in submandibular glands bilaterally may represent acute on chronic inflammation. She did not have dry mouth, pain with swallowing or dry eyes. Her capillary folds were abnormal. She was commenced on Hydroxychloroquine whilst awaiting Biopsy, which was consistent with Sjogren's syndrome. Methotrexate was added, which soon led to transaminitis and she also continued to have flares and Methotrexate was switched to Azathioprine. This helped with her symptoms but led to Neutropenia. Eventually decision was made to switch to Mycophenolate Mofetil (MMF). Initially MMF helped her with arthritis and energy levels improved but after a year of being on MMF her disease started to flare, requiring oral steroids, and leading to cushingoid facies. Her Lipase was elevated and Amylase was borderline elevated.
Due to ongoing disease activity with recurrent and painful parotitis, decision was made to use Rituximab. She gradually recovered from this. Since Rituximab infusion in January 2019 her disease has been continuously in remission and she has recently started to wean MMF down.
Conclusion: We report the successful use of rituximab in a difficult to treat patient with Sjogren-MCTD overlap (2). Rituximab was chosen due to the well-established role of B cell hyperactivity in the immunopathogenesis of primary Sjogren disease (3). Rituximab has mixed results in the management of primary Sjogren syndrome in adults. There is no evidence of the use of rituximab in paediatric Sjogren but it was successful at controlling paediatric Sjogren syndrome in our patient and allowed weaning of long-term DMARD.

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Disclosure of Interest: None declared

AB026
JUVENILE IDIOPATHIC ARTHRITIS
A MULTIFACETED APPROACH IS ESSENTIAL FOR ROBUST REHABILITATION
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Introduction: Introduction: The prognosis for JIA regarding joint destruction and disability has changed significantly during the last two decades due to the emergence of effective anti-inflammatory treatment regimens. However, approximately 50% of the patients will need ongoing medication far into adult life. The prospect of having a long lasting chronic disease requiring continuing medication, with possible side effects, frequent clinical controls and periods of pain can, by itself, for some patients lead to a passive and inactive lifestyle overshadowing the primary positive effect of the anti-inflammatory medication. In these cases, it can be difficult for the patient (child or adolescent) to resume a normal physically and mentally active lifestyle so important in childhood and youth and of great importance for general health in adulthood.
Recently a Danish version of the Juvenile Arthritis Multidimensional Assessment Report (JAMAR) was published, and we now have an internationally validated tool for assessment of our patients' life circumstances and their personal view of the burden of their disease. Using this tool, in combination with structured clarifying talks between nurse and/or physiotherapist and patient (and parents according to age of the patient) we aim to uncover unmet special needs that we may help to fulfil in the municipal system, in schools, in sports clubs or in other institutions. This structured approach may also by itself help the patient and the family to gain constructive insight in their life situation, with a chronically ill member, and find possible hitherto unknown resources.

Objectives: The purpose of this project is to investigate the effect of a structured multifaceted treatment of juvenile idiopathic arthritis, focusing on lifestyle and physical activity in parallel with anti-inflammatory medication.
We hypothesize that this strategy will help patients to obtain an early and robust rehabilitation and thus get the full benefits of the effective medicine currently available.

Methods: This is a prospective, non-randomized intervention project.
A pilot design is chosen with the purpose of early evaluation of practical circumstances.
Inclusion criteria:
- Danish speaking patients with JIA, followed in the outpatient clinic at the Pediatric Department at Slagelse Hospital
- having a low objective clinical disease activity and a high subjective burden of disease according to JAMAR

We aim to include 20 patients.
Intervention:
- structured clarifying talks between patient (and parents according to age of the patient) and the caregiving nurse or physiotherapist with the purpose of uncovering unmet needs
- special needs are sought fulfilled by individual agreements between patients/families and the municipal system, with schools, with sports clubs or with other institutions. The staff in the rheumatology clinic shall be drivers in this process.

Endpoints:
- Change in JAMAR score at 3 and 6 months after inclusion; the patient will serve as his/her own control.

Results: Pending
Delayed by the Corona Pandemic
Conclusion: Pending
Disclosure of Interest: None declared

AB027
AUTOIMMUNE HEPATITIS-SLE OVERLAP SYNDROME (LUPOID HEPATITIS)

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Introduction: Systemic lupus erythematosus (SLE) is a systemic autoimmune disease classically involving the skin, kidneys, and central nervous system. Several previous reports showed the manifestation of AIH in adult lupus patients; however, there are no reports of such an association between AIH and SLE in children. Both AIH and SLE have an autoimmune basis and hence can occur simultaneously or masquerading as presentations of each other. In this case report, we report AIH as the first manifestation of SLE in an 8-year-old girl.
Objectives: We described a case of liver involvement in SLE presenting with emphasis on the differential diagnosis with autoimmune hepatitis.
Methods: case report study
Results: : An 8-year-old female patient was referred to the Rheumatology clinic with complaints icteric sclera for 10 months anorexia, malaise, pain in the both knees, ankles joints and both wrists accompanied by swelling, and remarkable motion limitations. Laboratory revealed T bilirubin 4.9 mainly direct 3.9 with elevated liver enzymes GOT 401, GPT 189, ALKP 520, high Glutamyl transpeptidase 56U\L her WBC 7.4 HGB 10, PTL 317, except very high ESR 105ml\hr, CRP was positive 190mg\dl, viral screen (HCV, HBSAg, HIV) was normal, serology tests ANA was positive with high titer 1280, anti ds- DNA AB was positive 320, anti-Sm was negative, ANTI LKM1 antibodies negative, anti smooth muscle AB negative soluble liver antigen were negative, antimitohondrial AB(M1,M2,M3) .
ultrasound abdomen revealed mild enlarged spleen, abnormal diffused increased liver echogenicity with early stage of liver cirrhosis treated her by fresh frozen plasma 5 times, ViT k 10mg once\ day then was referred to rheumatology clinic regarding her serology tests & developed arthritis of her joints suspected PSLE! She was performed liver biopsy showed lesions necrotic inflammatory portal and lobular severe in eosinophilic polynuclear with cirrhosis evoking a syndrome of overlap associating a primary biliary cirrhosis and an autoimmune hepatitis. Laboratory data revealed liver dysfunction and liver biopsy Suggesting autoimmune hepatitis, and she underwent treatment for hepatitis (prednisolone with azathioprine), Urosdoxycholic acid with fat-soluble vitamins K, D&A, E. However, with the elimination of jaundice and decreased hepatic enzyme levels, the prednisolone dose was tapered within 2 months and stopped before they were referred to Rheumatology clinic. On her review of systems, she has malar rash, generalized fatigability. On physical examination, we found malar rash, levidoreticularis of her skin, swelling and limitation of movement in the knees, ankles, wrists joints. There was hepatosplenomegaly. Laboratory data revealed liver treatment for hepatitis, ANA still high titer 1:1280, Antids DAN positive with titer 307 IU\ml, antiSMA was negative .WBC 4.5, HGB 11.8, PLT 268, ESR 68ml\hr, Her ultrasound abdomen: revealed slightly heterogeneous liver with coarse echotexture without focal lesion with liver span 14 cm.These paraclinical results together with the clinical findings strongly suggested systemic lupus erythematosus (SLE) as the definitive diagnosis. Indeed, in this case, AIH was associated with SLE, prednisolone orally for 2 months, after that dose was tapered and continued, rapid clinical improvement in arthritis, malaise, and general condition. Azathioprine was continued. In addition, daily hydroxycholoquine sulfate

Conclusion: Overlapping of SLE and AIH should be suspected when AIH patients present with a malar or other skin rash. The prompt diagnosis and adjustment of further treatment plans can improve disease outcomes and prevent liver disease progression.
Disclosure of Interest: None declared

AB028

HEMATOLOGICAL PRESENTATION AS THE FIRST MANIFESTATION OF A POSITIVE TRIPLE MARKER ANTIPHOSPHOLIPID SYNDROME

CASE PRESENTATION AND LITERATURE REVIEW

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Introduction: Pediatric Antiphospholipid syndrome (p-AFS) is a rare autoimmune multisystemic syndrome, with a reported incidence around 3% in patients younger tan 15 years with a higher prevalence in female : male ratio of 1.2:1. Secondary p-AFS is associated with Systemic Erythematosus Lupus in 50% of the cases. The Sapporo criteria require al least 1 clinical criteria, one or more thrombosis events or comorbidities during pregnancy, associated with the finding of antiphospholipid antibodies, positive lupus anticoagulant, IgM or IgG anticardiolipin antibodies, IgM or IgG anti-b2-glycoproteins in two or more determinations separated by 12 weeks. In pediatric patients we take for consideration antiphospholipid antibodies and clinical manifestations, such as hematological (thrombocytopenia, anemia) and neurological (Chorea).
Objectives: To describe the clinical presentation of a 13 yo patient with positive triple marker for antiphospholipid syndrome (APS) secondary to Systemic Erythematosus Lupus (SLE), with hematologic manifestations.
Methods: Thirteen-year-old female patient under hematology department follow up due to pancytopenia, discarding an hematological malignancy. Presenting to our department complaining of anomalous uterine bleeding, clinically with a malar erythema. Routine labs were performed, reporting pancytopenia with Anemia (3.2), Thrombocytopenia (23, 000) and lymphopenia (850). Immunology test with hypocomplementemia (C3 56mg/dl and C4 2.9mg/dl), Positive Anti-DNA antibodies (410UI/ml), Positive Antinuclear antibodies with a speckled pattern (1:1280), positive lupus anticoagulant (1:8), IgG anticardiolipin)11.8U/ml), IgM anticardiolipin (37.7 U/ml), IgM anti.b2, glycoprotein (32 U/ml). With triple positive marker for APS and SLE, Initiating treatment with methylprednisolone bolus, hydroxychloroquine, acetyl salicylic acid and immunomodulation with Azathioprine. We performed a second determination 12 weeks after with positive IgG Anticardiolipin (10.9U/ml) IgM (56.8 U/l), Positive lupus anticoagulant (1.9), positive anti b2-glycoprotein (40.7U/ml). During follow up as an outpatient without thrombotic events.
Results: Our patient meets the 1997 ACR criteria for SLE and Sapporo criteria for APS. With APS positive triple marker. Clinically with anomalous uterine bleeding and hematological manifestations, persistent thrombocytopenia and lymphopenia, having discarded hematological malignancies.
Conclusion: Pediatric antiphospholipid syndrome is a rare condition, in most cases associated with Systemic Erythematosus Lupus. Triple positive marker increases the risk of thrombotic events significantly. Our patient, at presentation and during follow up, only hematological manifestations were presented as the only clinical symptom associated with pancytopenia, nevertheless the risk of thrombotic events is high during the natural course of APS.
Disclosure of Interest: None declared

AB029

JUVENILE SLE AND AUTISM: A CASE OF RARE COMBINATIONS AND DIAGNOSTIC DILEMMA

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Introduction: JUVENILE SLE AND AUTISM: A CASE OF RARE COMBINATIONS AND DIAGNOSTIC DILEMMA

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Objectives: Case

We present a case of a 7 yr old with severe Autism presenting with 2 week history of facial and bilateral neck swelling with bilateral cervical lymphadenopathy initially thought to be lymphoma but later diagnosed as systemic lupus with nephritis and neuro-lupus. Her initial course was stormy needing admission to intensive care unit and referral to oncology centre for work up of lymphoma.

This child had no significant hospitalisations in the past.

Methods: Her initial blood results and CT (Computerised tomography) chest suggestive of lymphoma with Tumor lysis. She was transferred to a local paediatric oncology centre for lymph node and bone marrow testing which showed no evidence of Leukemia or Lymphoma. She developed focal seizure secondary to hypertension and PRES (Posterior reversible encephalopathy), needing intubation and transferred to intensive care unit for 48 hours.

Magnetic resonance (MRI)imaging brain showed signs consisted with cerebral lupus. Autoimmune screen strongly positive for antibodies ANA (Antinuclear), dsDNA antibodies, Anti-Ro, Anti-Smith, RNP, RNP70, low C3(complement) and C4 in keeping with Juvenile SLE.

Renal biopsy was not performed as the child remained hypertensive despite being on antihypertensive medications and later due to parental refusal for Renal Biopsy. Echo showed evidence of mild Pericardial effusion, which was managed conservatively. She also had ascites and pleural effusion

Results: Course

She was managed with IV Pulse Methylprednisolone for 3 days, followed by oral prednisolone, and IV cyclophosphamide and later switched to Mycophenolate (MMF) therapy with which she made good recovery. She stayed in the hospital for 2 months for Nuro rehab with good neurological recovery back to her previous status.

At 3 months - She remains on immunosuppressive medication i.e. Mycophenolate therapy and small tapering dose of Oral Prednisolone and Hydroxychloroquine

Follow up MRI head shows significant improvement in comparison to her previous images, Echo showed complete resolution of the pericardial effusion and urine examination no evidence of proteinuria or haematuria.

At 1 yr follow up, she remains clinically stable with complete neurological recovery with no ongoing neurological, cardiac or Renal flare ups. She has been maintained on Oral Mycophenolate (MMF), and Hydroxychloroquine. Her inflammatory markers, complement profile, double stranded DNA levels remain normal and Urine shows no evidence of Haematuria or Proteinuria

Conclusion: Conclusion

Juvenile SLE with multi-system involvement in an Autistic child can be difficult to diagnose and manage. The case highlights that JSLE is a disease of thousand faces with varied clinical presentations and the need for high index of suspicion. This case also highlights the role of multidisciplinary teams in the management of such complex cases.

Trial registration identifying number: Autism and Juvenile SLE diagnostic dilemma- A case of rare combinations

Case

We present a case of a 7 yr old with severe Autism presenting with 2 week history of facial and bilateral neck swelling with bilateral cervical lymphadenopathy initially thought to be lymphoma but later diagnosed as systemic lupus with nephritis and neuro-lupus. Her initial course was stormy needing admission to intensive care unit and referral to oncology centre for work up of lymphoma.

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Renal biopsy was not performed as the child remained hypertensive despite being on antihypertensive medications and later due to parental refusal for Renal Biopsy. Echo showed evidence of mild Pericardial effusion, which was managed conservatively. She also had ascites and pleural effusion

Course
She was managed with IV Pulse Methylprednisolone for 3 days, followed by oral prednisolone, and IV cyclophosphamide and later switched to Mycophenolate (MMF) therapy with which she made good recovery. She stayed in the hospital for 2 months for Nuro rehab with good neurological recovery back to her previous status.
At 3 months - She remains on immunosuppressive medication i.e. Mycophenolate therapy and small tapering dose of Oral Prednisolone and Hydroxychloroquine
Follow up MRI head shows significant improvement in comparison to her previous images, Echo showed complete resolution of the pericardial effusion and urine examination no evidence of proteinuria or haematuria.
At 1 yr follow up, she remains clinically stable with complete neurological recovery with no ongoing neurological, cardiac or Renal flare ups. She has been maintained on Oral Mycophenolate (MMF), and Hydroxychloroquine. Her inflammatory markers, complement profile, double stranded DNA levels remain normal and Urine shows no evidence of Haematuria or Proteinuria
Conclusion
Juvenile SLE with multi-system involvement in an Autistic child can be difficult to diagnose and manage. The case highlights that JSLE is a disease of thousand faces with varied clinical presentations and the need for high index of suspicion. This case also highlights the role of multidisciplinary teams in the management of such complex cases.

Disclosure of Interest: None declared

AB030

JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS,EXPERIENCE OF THE PEDIATRIC CENTER

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Introduction: Juvenile systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by multi-visceral involvement with an unpredictable prognosis. The diagnosis is usually made in young women aged between 20 to 40years, however, it can affect people at any age and it is classified as a juvenile illness when it starts before the age of 16.
Objectives: We are reporting the epidemical, clinical, therapeutical and evolutional characteristics of a series done in the pediatric Pole in setif with 13 girls and 1 boy.
Methods: The average age of onset is 13 years. The average time limits of the diagnosis is 7 months. The clinical features is done with cutaneous, articular manifestations and fever respectively in 100% 71% and 57% of the cases ,followed by kidney damage in 42% of the cases , the cardiac, pulmonary and ophthalmological participations are reported with low percentage.
Haematological involvement was detected in 85% of the patients and the inflammatory syndrome was almost constant. A positive titer of anti-nuclear antibodies and anti-DNA is objectified, as well as a reduction in the complement rate. Antibodies anti GP 2 and anti cardiolopine are positive in 57% of cases. Kidney damage was diagnosed in 42% of the cases , and only one case of overlap syndrome with dermatomyosits was reported. Concerning the neurological form it was present in only one addolecent girl ,and only one case of familial lupus.

Results: The diagnosis is based on the classification of the American College of rheumatology (ACR) 1982 revised on 1997 and the new criteria SLICC"Systemic Lupus International Collaborating Clinics" .
The clinical characteristics of our series relies on global data of literature with the Predominance of Cutaneous and articular involvement. with however some specific characteristics which are individualized by a more advanced age of onset, 13 years on average in our study versus 10 years and 12 years, the rarity of familial forms (1 case), a lower percentage of kidney damage (42% versus 63% and 80%).
The therapeutic management was based on corticosteroid therapy and Hydroxychloroquine in the majority of cases, the use of immunosuppressants has been reserved for severe forms.

Conclusion: Lupus is an autoimmune disease with protean clinical manifestations, the prognosis of which is dominated by renal, neurological and thrombotic disorders. Cortisonic treatments and immunosuppressants have significantly improved the prognosis for life .
Trial registration identifying number: Lupus is an autoimmune disease with protean clinical manifestations, the prognosis of which is dominated by renal, neurological and thrombotic disorders. Cortisonic treatments and immunosuppressants have significantly improved the prognosis for life .
Disclosure of Interest: None declared

AB031

SYSTEMIC LUPUS ERYTHEMATOSUS WITH UNUSUAL PRESENTATION: A SINGLE CENTRE EXPERIENCE FROM NORTH INDIA

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Introduction: Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease. SLE mimics many clinical entities and diagnosis may become difficult at times,especially if presentation is atypical.

Objectives: To highlight unusual presentation of Pediatric SLE
Methods: Retrospective case review of all children diagnosed as SLE from July 2017–November 2018 at a single tertiary care hospital in north India was done. We here describe 4 children who presented with unusual manifestations.
CASE 1: 8 years,girl, presented with fever for 1 month and bilateral pleural effusion. She had fever, epistaxis , hepatosplenomegaly and bicytopenia and was managed as tropical infections initially.She was later on diagnosed to have SLE and managed for the same.
CASE 2: 11 years,boy, presented with arthritis in multiple small and large joints of body. On evaluation ANA and anti dsDNA was found to be positive . He was started on subcutaneous, weekly methotrexate and responded to treatment. However, he developed lupus nephritis during disease course after 6 months of diagnosis. Renal biopsy revealed ClassIII+V lupus nephritis. Intravenous Cyclophosphamide pulses were started for induction along with tapering doses of corticosteroids.
CASE 3: 8 years,girl, presented with early morning periorbital puffiness and abdominal distension with history of photosensitivity and Raynaud phenomenon. Urine routine examination revealed nephrotic range proteinuria with no hematuria. Clinical possibility of nephrotic syndrome secondary to SLE was kept.Renal biopsy revealed Class V Lupus nephritis.
CASE 4: 17 years old,girl,presented with high grade fever and pain in bilateral knee joints and malar rash. Investigation were suggestive of SLE with MAS(macrophage activation syndrome) .Child was started on iv antibiotics and iv immunoglobulins but died during the disease process.
ANA positivity , hypocomplimentimia and Anti ds DNA positivity were seen in all the 4 cases.

Results: out of 11 children diagnosed to have SLE, 4 presented with unusual manifestations as described above.

Conclusion: In this report we present unusual presentations as the predominant manifestation of SLE and emphasize the fact that early recognition and awareness of unusual presentation of SLE help institute timely initiation of appropriate treatment
Disclosure of Interest: None declared

AB032

RETROSPECTIVE ANALYSIS OF INTRAARTICULAR EFFECTIVENESS OF TRIAMCINOLONE ACETONIDE IN TREATMENT OF OLIGOARTICULAR JUVENILE ARTHRITIS IN CHILDREN

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Introduction: Despite significant advances in treatment and increased understanding of pediatric chronic disease the choice of first-line antirheumatic drugs of oligoarticular onset juvenile arthritis still remains relevant. Pediatric rheumatologists and to this day there are no consensus on the best modality for treatment.
Objectives: The aim of this study was to assessment of feasibility and efficacy of local steroid therapy oligoarticular onset JIA in children in the Russian Federation.
Methods: In a retrospective study 92 children (89% girls) aged median (IQR) 4,2 (1,6 – 7,6) years with oligoarticular onset JIA without extra-articular manifestations (oligo-JA) who did not received DMARDs were monitored. All children were met ILAR criteria. Ttriamcinolone acetonide (TA) was administered intra-articular at a dose of 20-40 mg with an injection interval of 3-6-12 months which was depended on the activity of the disease. The maximum allowable number of consecutive isolated intra-articular injections (is-IAI) was 3-4. A total of 218 active joints were injected with TA: knees – 156 injections, ankles – 62 injections. All children were divided into two groups: active / inactive arthritis based on the effectiveness of local corticosteroid treatment. The average follow-up was 48 [38; 62] months.
Results: 32 children (35%; all girls) were achieved remission oligo-JA after is-IAI of TA with mean of 2 [1,75; 2] injection per joint (inactive arthritis > 24 months). The mean interval between two consecutive is-IAI was 7 [5,25; 10] months. Other children did not achieve inactive oligo-JA after is-IAI of TA with mean of 3 [2; 4] injection per joint. The mean interval between first two consecutive injection was 5,5 [4,25; 7] months and other injections - 2 [2; 3] months. All children who did not achieve remission oligo-JA for is-IAI were treated by DMARDs. Statistical analyses were performed to determine the relationships between clinical, instrumental, laboratory signs and efficacy is-IAI of TA. Measures included the number of swollen or tender joints [active joint counts]; biological inflammatory markers [erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), serum and synovial fluid level of interleukin 6 (IL6) and tumor necrosis factor alfa (TNF-α)]; autoimmunity [titer of antinuclear factor (ANF)] and physicians' assessment of JIA disease activity [clinical Juvenile Arthritis Disease Activity Score including maximal 10 joints (cJADAS10)]. Efficacy is-IAI of TA was no associated significantly with number of active joint of onset oligo-JA, cJADAS10, serum level of CRP mg/ml, ESR mm/h, IL6 pg/ml and TNF-α pg/ml, titer of ANF. The mean inflamed synovial fluid of IL6 levels 2208 [710; 4564] / 3234 [1265; 16902] pg/ml and TNF-α levels 3,3 [2,5; 3,8] / 1,1 [0,6; 3,7] pg/ml at onset of inactive and active oligo-JA were not significantly differ. The analysis revealed a correlation between a short phase of beneficial effect after is-IAI of TA and risk of activity disease (with an inactive phase of arthritis less than 3 months, the risk activity was OR = 2.09, p <0.001; with an inactive phase less than 2 months - OR = 8.9, p <0.001).
Conclusion: Trimacinolone acetonide is an effective and safe treatment in children with oligoarticular juvenile arthritis. Research was revealed that about a third of children with oligo-JA achieved inactive arthritis of average after two intra-articular injections of triamcinolone acetonide. Despite the widespread use of biological treatment should not be neglected topic corticosteroid drugs as the first-line treatment in children with oligo-JIA.
Disclosure of Interest: None declared

AB033

THE USE OF OFF-LABEL BIOLOGICS IN CHILDREN WITH SYSTEMIC CONNECTIVE TISSUE DISEASES

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Introduction: Off-label prescribing often occurs in pediatric rheumatology. This is due to insufficient evidence base, the severity and unpredictability of the course of the disease.
Objectives: To analyze the cases of off-label use of biologicals among patients with rheumatic diseases.

Methods: Analysis of patient treatment was carried out using data from the registry of children's rheumatological patients: 38 systemic scleroderma (SSD), 47 systemic lupus erythematosus (SLE), 42 juvenile dermatomyositis (JDM), 19 systemic vasculitis (SV), 11 unspecified systemic involvement of connective tissue, 8 auto-inflammatory syndromes.
Results: The possibility of providing patients with systemic connective tissue diseases with expensive therapy in Ukraine is absent. Biologicals are prescribed only in cases of extremely severe courses of the diseases with the previous ineffectiveness of all other available methods of therapy CS and DMARDs. Biologicals were prescribed off-label 10 times in 8 patients. In case with SLE (SELENA-SLEDAI=60, ESR 30mm/h) rituximab (RTX) weas used after tocilizumab (TCZ). RTX was prescribed in another 4 patients (polyarteritis nodosa VDI=11, ESR 64mm/h; ANCA+SV VDI=12, ESR 56mm/h, CRP=18mg/l; JDM DAS 31, CMAS 4, CK 8000 IO/l; SLE SELENA-SLEDAI=59, ESR 45 mm/h). RTX was administered to patients who had received high-dose CS with 2–3 DMARDS; in all cases combined pulse therapy CS № 2–10 was preliminarily used. RTX 500 mg № 2 was applied after 6mo-2y from the debut of the disease. In all 5 cases, its use led to clinical improvement after 1-5 mo with normalization of laboratory activity indicators, in 4 cases a decrease in the level of B cells to 0-0.56 in µl was noted (3 with agammaglobulinemia). After 2 months 3 patients had severe infectious complications, 2 of them ended fatally. 2 another patients had a second stroke. The 1st patient survived, had a kidney allotransplantation, there is no disease activity. The 2nd patient, in connection with the development of the demyelinating process of CNS, attempted to continue therapy using golimumab with IVIG. It led to an increase in the infectious syndrome, therefore, we decided to refrain from continuing with iTNF as well. The patient died after 2 years from the administration of RTX due to the progression of neurological disorders. 2 cases with auto-inflammatory syndromes were: chronic infantile neurologic cutaneous and articular syndrome received TCZ; it was unsuccessful (hyperthermia and rash persisted, eye lesions progressed, there were no increase in height), later switched to anakinra. Family mediterranean fever, received adalimumab (ADA). The 1-year-course of ADA leaded to the disappearance of articular and abdominal syndrome while maintaining persistent increased levels of ESR and CRP and periodic fever. The use of TCZ in 2 patients with SSD was more successful. The first patient received it subcutaneously for 1 year, CS&DMARDs (3 were used) had already been canceled, lung and kidney lesions were contained, blood pressure normalized, EScSG-AI decreased from 7 to 1, MRSS decreased from 18 to 14. In the second case, the patient received TCZ for 6 months i/v, decrease of EScSG-AI 6.5 to 1, MRSS 33 to 21 were noted, the dose of CS was halved, he also continued treatment with cyclophosphamide.
Conclusion: The presented experience cannot be called completely positive; maybe this can be improved by earlier prescribing of medicines. An attempt to off-label use of biological cannot be rejected in pediatric rheumatology since sometimes this is the only chance for our patients to survive.
Disclosure of Interest: None declared

AB034

IATROGENIC CUSHING AFTER LOCAL INFILTRATION WITH TRIAMCINOLONE ACETATE. ABOUT TWO CASES

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Introduction:

Objectives: To describe two cases of Cushing's Syndrome secondary to local infiltration with triamcinolone acetate ,presented at our Hospital during 2019

Methods: CASE 1: 6-year-old girl referred, for asthenia, polyphagia, weight gain (4kg in 30 days) and progressive face and abdomen oedema, one month in evolution. It associates high TA (129/92mmHg) and frontal headache (without alarm data). The only antecedent: triamcinolone acetonide depot infiltration in ankle´s ganglion (equipotent x4:16mg/m2) one week before starting symptoms .No family history.**CASE 2:** 7-year-old gir ,father with psoriasis without joint involvement. Consultation in July 2019 to traumatology for right knee pain with functional impotence after trauma .In ultrasound and MRI, sinovial hypertrophy is visualized, with minimal joint effusion. Referred to Rheumatology, she was diagnosed by Polyarticular Juvenile Idiopathic Arthritis. In the analysis, hypochromic microcytic anaemia and PCR 3.6 mg/dl stand out. Haematology rules out haematological process and starts treatment with oral iron. She received corticosteroid treatment:Oral prednisolone(equipotential x5:supposes 31.5mg/m2 for 20 days and descending regimen) and intra-articular infiltration (knee and ankles) with Triamcinolone acetonide depot (equipotent x4: supposes 432.4mg/m2). Also, she receives treatment with methotrexate, folic acid, tocilizumab and abatacept. From the start of the corticosteroid treatment, she presented a Cushing phenotype and weight gain (7kg in 4.5 months). She did not have fatigue or any other symptom. It refers to paedriatic endocrine

Results: ***CASE 1 Complementary ambulatory tests***: leukocytosis (neutrophilia) and mild reticulocytosis, hypercholesterolemia 232mg/dl (HDL: 104mg/dl), ***Exploration:*** Age 6.59 years, height 122.3cm (0.5SDS), weight 27.2kg (0.76SDS), P/T 107.97%, BMI 18.19 (0.46SDS). TAS 121mmHg (p97)/TAD 81mmHg (p89).Cushing phenotype, prepubertal. ***Complementary tests:*** Ultrasound without pathological findings. ACTH and cortisol suppressed (ACTH <5pg/ml, cortisol<1µg/dl). Suspecting exogenous Cushing síndrome secondary to local infiltration with corticosteroid, The study was expanded with normal imaging tests (brain MRI, normal bonescan, total-body PET with normal F18-FDG PET/CT) and ACTH test with a suppressed response. In monthly controls, ACTH and suppressed cortisol persist up to five months after the infiltration that initiates analytical recovery of the adrenal axis. Clinically, phenotype persists. Continue to follow up. **CASE 2** ***Exploration:*** Age 8.12 years, TA 99/55mmHg, height 125.1cm (-0.73SDS), Weight 37.4kg (1.28SDS), P/T 138.9%, BMI 23.9 (2.14SDS). Good general condition, Cushing phenotype (full moonface, globular abdomen, few stretch marks in the inner thighs). Prepubertal. ***Complementary tests:*** ACTH plasma 17 pg/ml, Cortisol serum 10.9 µg/dl, Suppression test with normal dexamethasone. 24-hour cortisoluria decreased.

Conclusion: DISCUSSION: The use of intra-muscular or intra-synovial triamcinolone acetate is approved in children from 6 years. There are few cases described that develop a secondary Cushing syndrome. We found a systematic review describing 18 cases of Cushing after infiltrations and injuries in scars. Although there are no clear recommendations regarding its use in paediatrics, we must be cautious, use the lowest effective dose and adequately monitor these patients.

Disclosure of Interest: None declared

AB035

SUCCESSFUL HAPLO-IDENTICAL ALLOGENIC BONE MARROW TRANSPLANTATION IN A CHILD WITH REFRACTORY SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Some patients with systemic juvenile idiopathic arthritis (SJIA) and severe, refractory disease achieved remission through intensive immunosuppressive treatment followed by autologous hematopoietic stem cell transplantation (HSCT). However, disease relapsed in most cases. More recently selected SJIA patients received allogenic HSCT from a HLA-identical sibling or a HLA matched unrelated donor. While most transplanted patients achieved sustained SJIA remission off-treatment, the procedure-related morbidity was high.
Objectives: We try to demonstrate that haplo-identical allogenic HSCT in refractory SJIA can be an alternative treatment for refractory SJIA
Methods: We report the case of a child who was successfully treated with haplo-identical allogenic HSCT.
Results: A girl presented SJIA since the age of 15 months with a severe disease course. She was refractory to the combination of methotrexate and steroids to anti-interleukin(IL)-1, then anti-IL-6, tumor necrosis factor alpha inhibitors and thalidomide. Therefore allogenic HSCT was considered. In the absence of any possible HLA matched donor, a multidisciplinary team assessed carefully risks and benefits of an alternative graft. Given the high disease burden and treatment related toxicity the indication for a haploidentical HSCT from her mother was validated. The patient was. treated with intensive immunosuppression and received a T replete bone marrow graft at the age of 3.7 years. Conditioning contained Rituximab, Alemtuzumab, Busulfan, and Fludarabine, as well as Cyclophosphamide at D+3 and +4 post HSCT for GHVD prophylaxis, followed by Cyclosporine A and Mycophenolate Mofetil. Post HSCT complications included severe infections, grade 3 intestinal graft versus host disease, autoimmune thyroiditis, and immune thrombocytopenia. Three years after HSCT, the child was alive and well, notwithstanding persistent hypothyroidy requiring substitution. Immune thrombocytopenia had resolved. Most importantly, SJIA was in complete remission, off immunosuppressive drugs.
Conclusion: Allogenic HSCT may be a therapeutic option, even with a HLA haplo-identical donor, in patients with inflammatory diseases such as SJIA. Despite increased experience with this treatment, the risk of life-threatening complications restrains its indication to selected patients with severe, refractory diseases.
Disclosure of Interest: None declared

AB036

ANALYSIS OF PUBLISHED RANDOMIZED CONTROLLED TRIALS IN PEDIATRIC PATIENTS WITH RHEUMATIC INFLAMMATORY DISEASES TREATED WITH BIOLOGICS

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Introduction: The same biologic disease modifying antirheumatic drugs (bDMARDs) are prescribed in adult and pediatric rheumatology. Due to age-dependent changes, disease course, and pharmacokinetic (PK) processes pediatric patients with inflammatory rheumatic diseases (PiRD) differ from adult rheumatology patients.
Objectives: A systematic literature review was performed to assess current knowledge about bDMARDs use in PiRD patients by analyzing published randomized controlled trials (RCTs) in this pediatric population.
Methods: A systematic literature search for RCTs in PiRD with bDMARDs intervention such as rituximab, abatacept, anakinra, canakinumab, rilonacept, tocilizumab, ustekinumab, secukinumab, adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, belimumab, baricitinib, tofacitinib, upadacitinib was conducted on Medline, PubMed, EMBASE, the Cochrane Library, the US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov and the EU Clinical Trials Register in March 2020. Abstracts from conferences and relevant studies were added. RCTs were included if (i) patients were aged ≤ 20 years, (ii) patients had a previous defined pediatric rheumatic diagnosis and (iii) RCT met predefined outcomes. Studies were excluded in case of (i) observational or single arm study or (ii) sample size ≤ 5 patients. Study design, location, duration, treatment, population, sample size, age criteria, gender, concomitant treatments and primary outcome was extracted.
Results: Out of 550 screened references, 62 references reporting 35 unique RCTs in PiRD. All 35 RCTs reported efficacy while 34/35 RCTs provided safety outcomes and 15/35 RCTs provided PK data. Ten of 17 reviewed bDMARDs are approved for PiRDs by the Food and Drug Administration (FDA). Of these, seven had ≤ 2 RCTs. The most common intervention was TNF inhibitors (63%), IL-1 inhibitors (17%) and IL-6 inhibitors (8%). No RCTs with published results were identified for rituximab, secukinumab, certolizumab pegol, baricitinib, or upadacitinib. In patients with juvenile idiopathic arthritis (JIA) 26/35 RCTs were conducted. The remaining 9 RCTs were performed in non-JIA patients including plaque psoriasis, Kawasaki Disease (KD), systemic lupus erythematosus and idiopathic uveitis. In JIA-RCTs, the control arm was mainly placebo and the concomitant treatments were either methotrexate, NSAIDS or corticosteroids. Non-JIA patients received mostly NSAIDS. A majority of JIA-RCTs were global studies or otherwise conducted in Europe, the US, or Japan. The non-JIA RCTs took place in North America, Europe or globally and for KD mainly in Asia or the US. Currently three Phase III RCTs are investigating baricitinib and one Phase III global RCT investigating tofacitinib. Further, there are recruiting studies for secukinumab and certolizumab pegol in psoriasis, for adalimumab in JIA-associated uveitis, for abatacept and etanercept in JIA.
Conclusion: Despite the FDA Modernization Act and support of major pediatric rheumatology networks, such as the Pediatric Rheumatology Collaborative Study Group (PRCSG) and the Pediatric Rheumatology International Trials Organization (PRINTO), which resulted in bDMARDs approval for PiRD indications, there are limited RCTs in pediatric rheumatology. As bDMARDs therapy response is influenced by age-dependent changes, PK processes and disease course it is important to consider developmental changes in bDMARDs use in PiRD patients. As such it is critical to collaborate and conduct randomized clinical trials in PiRD patients with the goal to appropriately investigate PK, efficacy and safety in bDMARDs used in pediatric rheumatology.
Disclosure of Interest: None declared

AB037

EFFICACY AND SAFETY ON THE USE OF BISPHOSPHONATES FOR SECONDARY OSTEOPOROSIS IN PAEDIATRICS

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Introduction: The use of bisphosphonates has increased in paediatrics in the last twenty years.
Objectives: The study describes efficacy and safety of bisphosphonate therapy for secondary osteoporosis in children in Montpellier and Nimes University Hospitals, France.
Methods: In our retrospective study, all patients treated with bisphosphonates for secondary osteoporosis, between January 2012 and August 2018, were included, using medical files. The main endpoint was efficacy using fracture rate, bone mineral density (BMD) change, and bone pain frequency before and after treatment. Adverse effects were also analysed.
Results: 77 children, median age [IQR 25%>75%] of 14 years [11-15 years], with secondary osteoporosis: immobility (n=63), nutritional diseases (n=5), corticosteroids (n=7), sickle cell anaemia (n=1), growth hormone deficiency (n=1), were included. The median duration of treatment [IQR 25%>75%] was 9 months [1-25 months]: 25 using zoledronate, 52 using pamidronate. Fracture rate significantly decreased from 41.6% to 5.2% and bone pain frequency significantly decreased from 57% to 26% ($p<0.01$). Lumbar spine BMD Z-score significantly improved by 0.74 ($p<0.01$). Adverse events were reported for 79.2% of patients: flu-like symptoms (65%), hypocalcaemia (44.2%) and hypophosphatemia (27.3%). Only one serious hyponatremia occurred corresponding to a patient with renal failure before treatment.
Conclusion: Our results were similar to those previously published: bisphosphonates are effective and safe for secondary osteoporosis in children. The use of bisphosphonates beforehand requires dietary measures (vitamin D and calcium supplementation). Growth periods amplify bisphosphonates effects as we have shown with a maximum mean increase in the early years of life: this suggests a better time to start treatment in young people. Furthers systematic collection on efficacy and safety parameters for each bisphosphonates drug should confirm these data.
Disclosure of Interest: None declared

AB038

CUTANEOUS OR SYSTEMIC POLYARTERIITIS NODOSA?

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Introduction: Polyarteriitis nodosa (PAN) is a rare vasculitis of medium and small vessels. There is ongoing controversy about if systemic and cutaneous forms are different diseases or only a spectrum of symptoms
Objectives: Presenting a case of cutaneous polyarteritis nodosa and discussing the possibility evolving to a systemic disease
Methods: We introduce a 13-year-old girl patient who has been admitted to our clinic with suspicion of an erythema nodosum. She had painful subcutaneous nodules for 4 weeks, especially on the lower extremities and her face. Macroscopically, central necrotizing skin rashes could be seen. She had frank arthritis of both knee and ankle joints. The comprehensive serological diagnosis (including hepatitis serology and anti-streptolysin titer) were normal except for a slight increase in CRP 0,9 mg/dl and ESR 36 mm/h. The patient also complained of abdominal pain and bloody stools. Calprotectin was 3613 µg/g. A Gastro-coloscopy revealed a small mariske and a minimal inflammation of the Ileocecal valve, without signs of vasculitis or chronic bowel disease. A skin biopsy revealed leukocytoclastic vasculitis of the small arteries. Angiography of the intestinal arteries was rejected by the family. Initially we started a treatment with methylprednisolone pulses followed by oral prednisolone. The patient showed a very good response with quick resolution of the skin symptoms and abdominal pain. The medication could be quickly tapered and discontinued at full remission after one month
Results: PAN is classified as a cutaneous PAN (cPAN) when there are exclusive skin manifestations, besides arthralgia or arthritis. A systemic PAN must be diagnosed with the involvement of internal organs. However, cutaneous PAN may evolve into systemic PAN. In our patient, the skin and joints were primarily affected. If the existing gastrointestinal complaints are part of a systemic PAN or chronic bowel disease could not be cleared yet, due to refusal of further investigations.
Conclusion: cPAN must be considered as a suspected diagnosis in patients with necrotizing skin nodules. As transition of the cutaneous into the systemic form cannot be predicted regular monitoring is mandatory.
Disclosure of Interest: None declared

AB039

EFFICACY OF ANAKINRA IN REDUCING GIANT CORONARY ANEURYSMS IN REFRACTORY KAWASAKI DISEASE: A CASE REPORT

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Introduction: Coronary artery aneurysms (CAAs) are the most serious complication in Kawasaki Disease (KD). Treatment with intravenous immunoglobulin (IVIG) significantly reduces the risk of CAAs. However, up to 20% of cases are IVIG resistant with a higher risk of cardiovascular complications. Currently several second-line treatments are available for refractory KD. Nonetheless, the existing literature is still unable to identify which treatment is the most effective. Recent studies suggest that a IL-1 receptor antagonist (anakinra) may be an effective therapy in refractory KD.
Objectives: We report the case of a 3 year-old boy diagnosed with KD refractory to conventional treatment, who developed giant CAAs successfully treated with subcutaneous (sc) anakinra.
Methods: Case report.
Results: A 3 year-old boy was referred to our Pediatric Rheumatology Unit 18 days after the onset of a Typical refractory KD. He had been previously treated at a local hospital with two doses of IVIG (2 g/kg), infused respectively 8 and 11 days after the onset of the fever. Afterwards, given the persisting fever, doses of pulse intravenous (IV) methylprednisolone (MPDN 30 mg/kg/day) have been used for 3 days followed by oral prednisone (2 mg/kg/day). Treatment with Acetylsalicylic Acid (60 mg/Kg/day q8h) was also started. Following a transient defervescence the day after the first IV pulse MPDN, fever relapsed and the echocardiography showed CAAs of Left Main Coronary Artery (LMCA), Left Anterior Descending (LAD) and Right Coronary Artery (RCA) with z score 7.4, 11.7, 4.1 respectively. Laboratory tests showed a persistent elevation of inflammatory markers (WB 20810/mm3, PMNc 12860/mm3, CRP 50 mg/L). The patient was then transferred to our Unit. Therapy with sc anakinra (2 mg/kg/day) was started with rapid defervescence and reduction of CRP. Echocardiography was performed 5 days after and it showed a worsening of all coronary aneurisms, with evidence of giant CAAs (LMCA, LAD, RCA z score: 12.7, 15.1, 10.4). The anakinra dosage was increased to 4 mg/kg/day and anticoagulant therapy with warfarin was started. Echocardiography showed a significant reduction of CAAs (LMCA, LAD, RCA z score: 10.1, 12.29, 7.9) 6 days after, with complete resolution of giant CAA (LMCA, LAD, RCA z score 7.4, 9.4, 7.17) 13 days after. Therapy with sc Anakinra (4 mg/kg/day) was continued for a month, then it was gradually tapered down and completely stopped after 4 months. Follow up is still ongoing but serial echocardiographies confirmed a persistent positive remodelling of all CAAs.
Conclusion: It has been reported that therapy with Anakinra in refractory KD leads to a rapid and sustained improvement in clinical and biological inflammation. However, its effects on the size of CAAs are still unclear. In our patient with refractory KD, subcutaneous Anakinra was quickly effective in controlling the systemic and laboratory inflammatory aspects of the disease and, at a higher dose, led to a rapid and significant reduction of CAAs with complete resolution of giant aneurisms. No side effects were reported. Therefore Anakinra can represent a valuable and safe treatment approach in refractory KD patients, reducing cardiovascular damage. Further studies are needed to reach a standardized treatment protocol to better define the optimal dosage, duration and tapering of Anakinra therapy, facilitating improvement and uniformity of care.
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Disclosure of Interest: None declared

AB040

KAWASAKI DISEASE COMPLICATED BY ACUTE KIDNEY INJURY: A CASE REPORT

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Introduction: Kawasaki disease (KD) is a febrile vasculitis that affect young children < 5 years of age. Diagnosis of KD is a clinical challenge, given the wide variety of clinical presentations. There are few reports of acute kidney injury (AKI) in KD, defined as serum creatinine level elevation to more than 1.5 times of baseline level.
Objectives: To describe the case of Kawasaki Disease complicated by AKI
Methods: A 5-year-old female was admitted to our Rheumatology Unit with persistent fever (6 days), widespread polymorphous exanthema, change in lips and in oral mucosa. Family history was unremarkable. She had no chronic underlying disease nor history of previous hospitalization. At admission, she appeared stable. Body temperature was 38.9°C, O2 saturation was 96% in ambient area, blood pressure was 118/75 mm Hg, heart rate was 90 bpm, respiratory rate was 21 breaths per minute. On examination she presented widespread polymorphous exanthema, changes in lips and in oral mucosa, cervical lymphadenopathy and bilateral conjunctival injection.
Results: Exams revealed: white blood cells 11980/µl, Hb 10.4 g/dL, platelets 389.000/µl, albumin 2.5 g/dL, serum sodium 126 mEq/L, serum chloride 90 mEq/L. Transaminases were in normal range. creatinine was 1.5 mg/dL (nv 0.20-0.45). Inflammatory markers were strongly elevated (CRP 108 mg/L, ESR 45 mm/1h, ferritin 1421 ng/mL). Fluid balance evidenced oliguria. She underwent echocardiography that showed no dilatated coronaries or pericoronary hyperechogenicity. Abdomen ultrasound and Chest-RX were negative. Intravenous Immunoglobulin (IGIV) at the dose of 2 g/Kg and antinflammatory dosage of ASA were started at 7 days of fever. After the first dose of IVIG, fever, conjunctivitis and polymorphous rash disappeared. Blood tests revealed a reduction of inflammatory markers (CRP 89.9 mg/L, ESR 28 mm/1h) and creatinine (0.69 mg/dL). She presented also normalization of fluid balance.
Conclusion: Acute kidney injury (AKI) has rarely been reported in patients with Kawasaki disease (KD). The pathogenic mechanism underlying renal involvement in patients with KD and AKI is unknown. A recent review concluded that patients with KD and AKI had good outcomes. The reported patient presented rapid improvement of clinical and laboratory parameters after only one dose of IGIV.
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Trial registration identifying number: ·
Disclosure of Interest: None declared

AB041

PAEDIATRIC EXTRA-PULMONARY LARGE VESSEL ARTERITIS, A FORME FRUSTE OF PEDIATRIC BEHCET'S DISEASE?

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Introduction: Prevalence of Behcet's disease in children is not known, but is probably very low. Extra-pulmonary large vessel arteritis in these cases is even rarer as a presenting manifestation.
Objectives: To report two cases of paediatric extrapulmonary large vessel arteritis with a 'Behcet like disease'.
Methods: We present case reports of two cases who presented to paediatric rheumatology OPD to our department. Ms. F, a 16 year old girl was referred to us with history of short duration of fever, generalized lymphadenopathy, neutrophilic leucocytosis, thrombocytosis, hyperglobulinemia and high inflammatory markers. On detailed history and examination she was found to have a healed palatal ulcer and her maternal aunt was found to have a history of recurrent oral ulcer, genital ulcer and enthesitis. Patient's Montoux test was positive but the gene expert for MTB was negative. MD-CT showed a circumferential thickening of aorta, subclavian and bilateral renal artery with stenosis at origin of both renal arteries indicating a vasculitis. Few necrotic nodes were also noted in lungs. Lymph node biopsy suggested a reactive hyperplasia. Tissue typing showed presence of HLA B 44, B 51. She improved clinically with oral Prednisolone and Mycophenolate Mofetil and had no recurrence till her recent follow up visit. Second case, master FKN an 11 year old child was referred to us with a background of 2 week history of fever, non migratory arthritis, raised inflammatory markers and a symptomatic severe aortic regurgitation with pandiastolic flow reversal on 2D echo. His evaluation showed negative Montoux, normal IGG4 levels and HLA B35 B 51 on tissue typing. His aortic wall thickness resolved with 1 mg/kg oral Prednisolone and Mycofenolate mofetil.
Results: Both these cases have features similar to Behcet's disease. These cases do not fulfil ISG, ICBD 2014 or ICBD criteria for pediatric Behcet's disease. However, the aortitis and other clinical features responded well to the treatment in both cases.
Conclusion: Paediatric case with extra-pulmonary Large vessel arteritis that do not meet criteria for Behcet's disease but have specific clinical or laboratory features do respond well to immunosuppression. Therefore, after ruling out other causes of the large vessel vasculitis, a possibility of form fruste of Behcet's disease should be under consideration.
Disclosure of Interest: None declared