YO001

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

G. Armaroli[1,*], A. Klein[1], K. Minden[2], I. Foeldvari[3], A. Hospach [4], F. Weller-Heinemann[5], R. Trauzeddel[6], J. Kuemmerle-Deschner[7], G. Horneff[1]

[1]Centre of Paediatric Rheumatology, Department of Paediatrics, Asklepios Clinic Sankt Augustin, Sankt Augustin, [2]German Rheumatism Research Centre, Charité University Hospital, Berlin, [3]Centre of Paediatric Rheumatology, Hamburg, [4]Section of Rheumatology, Department of Paediatrics, Olgahospital, Stuttgart, [5]Division of Paediatric Rheumatology, Prof. Hess Children's Hospital, Bremen, [6]Department of Paediatrics, Helios Clinic Berlin-Buch, Berlin, [7]Department of Paediatrics, University of Tuebingen, Tuebingen, Germany

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

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YO002

SYNOVIAL TISSUE RESIDENT MEMORY T CELLS MEDIATE ARTHRITIS FLARES

M. H. Chang[1,*], A. Levescot[2], N. Nelson-Maney[2], R. B. Blaustein[2], K. D. Winden[3], A. Morris[2], S. Balu[2], A. Wactor[2], R. Grieshaber-Bouyer[2], K. Wei[2], L. A. Henderson[1], R. A. Clark[4], D. A. Rao[2], R. C. Fuhlbrigge[5], P. A. Nigrovic[1,2]
[1]Division of Immunology, Boston Children's Hospital, [2]Division of Rheumatology, Inflammation, and Immunity, Brigham and Women's Hospital, [3]Department of Neurology, Boston Children's Hospital, [4]Department of Dermatology, Brigham and Women's Hospital, Boston, [5]Section of Rheumatology, Children's Hospital Colorado, Denver, United States

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

YO003

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

S. L. N. Clarke[1,2,3,*], J. Zheng[1,2], R. C. Richmond[1,2], A. V. Ramanan[3,4], G. C. Sharp[1,2], C. L. Relton[1,2]
[1]MRC Integrative Epidemiology Unit, [2]School of Population Health Sciences, University of Bristol, [3]Department of Paediatric Rheumatology, Bristol Royal Hospital for Children, [4]School of Translation Health Sciences, University of Bristol, Bristol, United Kingdom

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

YO004

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

A. Alongi[1,2,*], M. Trachana[3], V. Stanevicha[4], L. M. Ailioaie[5], E. Tsitsami[6], A. Ravelli[7], A. Consolaro[7], N. Ruperto[7]
[1]IRCCS G. Gaslini, Genoa, [2]A.R.N.A.S. Civico, Palermo, Italy, [3]Hippokration General Hospital, Thessaloniki, Greece, [4]Children University Hospital, , Riga, Latvia, [5]Alexandru Ioan Cuza University of Iasi, Iasi, Romania, [6]Aghia Sophia Children's Hospital, Athens, Greece, [7]Clinica Pediatrica e Reumatologia, IRCCS G. Gaslini, Genoa, Italy

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

YO005

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

L. Farina[1,*], I. Caiello[1], L. Manni[2], M. Soligo[2], S. Coppola[3], F. De Benedetti[1,4], L. Bracci-Laudiero[1,2]
[1]Division of Immuno-Rheumatology Research Laboratories, IRCCS OSPEDALE PEDIATRICO BAMBINO GESÙ, [2]Institute of Translational Pharmacology , CNR , [3]National Center for Rare Diseases, Istituto Superiore di Sanità, [4]Division of Rheumatology, IRCCS OSPEDALE PEDIATRICO BAMBINO GESÙ, Rome, Italy

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

YO006

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

C. Trincianti[1,*], E. H. P. Van Dijkhuizen[2], S. Calandra[1], L. De Miglio[1], M. Mazzoni[1], F. Ridella[1], T. Herlin[3], M. Cattalini[4], H. Sanner[5], G. Susic[6], F. Sztajnbok[7], D. Maritsi[8], T. Constantin[9], N. Ruperto[10], A. Ravelli[1], A. Consolaro[1] on behalf of for PRINTO and the EPOCA study group

[1]Università degli studi di Genova, Genova, Italy, [2]Wilhelmina Children's Hospital, Utrecht, Netherlands, [3]Aarhus University Hospital, Aarhus, Denmark, [4]Spedali Civili, Brescia, Italy, [5]Oslo University Hospital, Oslo, Norway, [6]Institute of Rheumatology of Belgrade, Belgrade, Serbia, [7]Hospital Universitario Pedro Ernesto, Rio de Janeiro, Brazil, [8]National and Kapodistrian University of Athens (NKUA), Athens, Greece, [9]Semmelweis University, Budapest, Hungary, [10]Istituto Giannina Gaslini, Genova, Italy

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.

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YO007

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

S. Ozdemir Cicek[1,*], N. Şahin[1], A. Paç Kısaarslan[1], M. Kondolot[2], M. H. Poyrazoğlu[1], R. Düşünsel[1]
[1]Pediatric Rheumatology, [2]Social Pediatrics, Erciyes University Faculty of Medicine, Kayseri, Turkey

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)	12,95 (2-1000)	19,47 (2-1000) (±205,4)	26,1 (2-1000) (±180,97)	0,094

(median, range) (±SD)	(±140,53)	484 (0-5000) (±1426,1)	430 (0-5000) (±1460,81)	
Anti-VZV IgG titer(IU/L) (median, range) (±SD)	916,0 (0-5000) (±1294,8)			0,223
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

YO008

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

J. Poline[1,2,3,*], C. Ducrocq[1,3], B. Bueno[1], G. Dingulu[1,3], R. Wheeler[2], B. Postal[1], D. Berrebi[4], M. Roy[1], A. Ribeiro[5], J. P. Hugot[1,6], I. Gomperts Boneca[2], U. Meinzer[1,2,3]

[1]Center for Research on Inflammation , INSERM UMR1149, Université de Paris, [2]Biology and Genetics of Bacterial Cell Wall Unit, Pasteur Institute, [3]Department of General Pediatrics, Paediatric Internal Medicine, Rheumatology and Infectious Diseases, National Reference Centre for Rare Paediatric Inflammatory Rheumatisms and Systemic Auto-immune diseases RAISE, [4]Department of pathology, Robert Debré University Hospital, Assistance Publique-Hôpitaux de Paris, [5]Cordeliers research center, INSERM UMR1138, [6]Departemnt of gastroenterology, Robert Debré University Hospital, Assistance Publique-Hôpitaux de Paris, Paris, France

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

YO009

CLINICAL OUTCOMES OF JUVENILE ARTHRITIS IN ADULTHOOD: A SYSTEMATIC REVIEW

Y. Wang[1,*], W. J. Kim[2], K. Gu[2], S. H. L. Lim[3]
[1]Winnipeg, [2]College of Medicine, [3]Pediatrics, University of Manitoba, Winnipeg, Canada

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

YO010

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

J. W. van Straalen[1,*], G. Giancane[2], Y. Amazrhar[1], N. Tzaribachev[3], C. Lazar[3], Y. Uziel[3], A. Telcharova-Mihaylovska[3], C. A. Len[3], A. Miniaci[3], A. L. Boteanu[3], G. Filocamo[3], M. V. Mastri[3], T. Arkachaisri[3], M. G. Magnolia[3], E. Hoppenreijs[3], S. de Roock[1], N. M. Wulffraat[1], N. Ruperto[2], J. F. Swart[1]

[1]Department of Pediatric Immunology and Rheumatology, Wilhelmina Children's Hospital, Utrecht, Netherlands, [2]Clinica Pediatrica e Reumatologia, IRCCS Istituto Giannina Gaslini, [3]Paediatric Rheumatology International Trials Organisation (PRINTO), Genoa, Italy

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

YO011

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

M. N. Rossi[1,*], M. Pardeo[2], D. Pires Marafon[3], E. Sacco[2], C. Passarelli[4], C. Bracaglia[2], C. Perrone[4], A. Tulone[2], G. Prencipe[1], F. De Benedetti[1,2]
[1]Division of Immuno-Rheumatology Research Laboratories, [2]Division of Rheumatology, IRCCS, Bambino Gesù Children's Hospital, [3]Division of Rheumatology, IRCCS,Bambino Gesù Children's Hospital, [4]U.O.C. Laboratory of Medical Genetics, IRCCS, Bambino Gesù Children's Hospital, Rome, Italy

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

YO012

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

G. Giancane[1,*], R. Papa[1], S. Vastert[1], F. Bagnasco[1], J. Swart[1], E. Alexeeva[1], P. Quartier[1], I. Kone-Paut[1], J. Anton[1], S. Sawhney[1], F. Sztajnbok[1], S. Kamphuis[1], T. Herlin[1], V. Panaviene[1], R. Cuttica[1], W. M. Saad Suwairi[1], H. Sanner[1], C. Pallotti[1], K. Franck-Larsson[2], H. Malmström[2], S. Cederholm[2], N. Wulffraat[1], N. Ruperto[1]
[1]Clinica Pediatrica e Reumatologia - PRINTO, Istituto Giannina Gaslini, Genoa, Italy, [2]Sobi, Stockholm, Sweden

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.
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YO013

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

A. Briones Figueroa[1], A. Garcia Fernandez[1,*], L. Calvo Sanz[1], Á. Andreu Suárez[1], A. Boteanu[1]
[1]Rheumatology, Ramón y Cajal University Hospital, Madrid, Spain

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

YO014

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

R. M. Krol[1,*], J. W. van Straalen[1], S. Nielsen[2], S. Kamphuis[2], F. De Benedetti[2], L. Harel[2], S. Appenzeller[2], M. Maldonado[2], F. Zulian[2], P. Mesa-del-Castillo[2], E. Koskova[2], E. Gervais[2], A. Civino[2], N. M. Wulffraat[1], N. Ruperto[2], S. de Roock[1], J. F. Swart[1]

[1]Paediatric Rheumatology, Wilhelmina Children's Hospital, Utrecht, Netherlands, [2]Paediatric Rheumatology INternational Trials Organisation, CC at IRCCS Istituto Giannina Gaslini, Genoa, Italy

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

YO015

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

M. Bustaffa[1,*], I. Koné-Paut[1], S. Ozen[1], G. Amaryan[1], E. Papadopoulou-Alataki[1], R. Gallizzi[1], M. Carrabba[1], Y. Butbul Aviel[1], L. Cantarini[1], M. Alessio[1], J. Anton[1], L. Obici[1], F. Gok[1], E. D. Batu[1], E. Moreno[1], P. Brogan[1], M. Trachana[1], G. Simonini[1], D. Rigante[1], M. Gattorno[1], L. Rossi-Semerano [1]
[1]Eurofever Registry and the Paediatric Rheumatology International Trials Organisation (PRINTO), Genoa, Italy

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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YO016

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

E. Lovšin[1,2,*], J. Kovač[3], T. Tesovnik[3], N. Toplak[1,2], D. Perko[3], T. Rozmarič[4], M. Debeljak[2,3], T. Avčin[1,2]
[1]Unit of Allergology, Rheumatology and Clinical Immunology, University Medical Centre Ljubljana Division of Pediatrics, [2]Faculty of Medicine, University of Ljubljana, [3]Clinical Institute for Specialized Laboratory Diagnostics, University Medical Centre Ljubljana, Ljubljana, Slovenia, [4]Department of Pediatrics and Adolescent Medicine, Medical University of Vienna , Vienna, Austria

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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YO017

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

L. Lodi[1,2,*], I. Melki[1,3,4], V. Bondet[5,6], L. Seabra[1], G. I. Rice[7], E. Carter[8], A. Lepelley[1], M. J. Martin-Niclós[1], B. Al-Adba[9], B. Bader-Meunier[4], M. Barth[10], T. Blauwblomme[4], C. Bodemer[4], O. Boespflug-Tanguy[3], R. Dale[11], I. Desguerre[4], C. Ducrocq[3], F. Dulieu[12], C. Dumaine[3], P. Ellul[3], A. Hadchouel[4], V. Hentgen[13], M. Hié[14], M. Hully[4], E. Jeziorski[15], R. Lévy[4], F. Mochel[14], B. Neven[4], S. Orcesi[16], S. Passemard[3], M. Pouletty[3], P. Quartier[4], F. Renaldo[17], R. Seidl[18], S. Blanche[4], D. Duffy[5,6], Y. J. Crow[1,8], M.-L. Frémond[1]

[1]Laboratory of Neurogenetics and Neuroinflammation, Imagine Institute, Paris, France, [2]University of Florence - Meyer Children's University Hospital, Florence, Italy, [3]Robert-Debré Hospital, [4]Necker Hospital, [5]Immunobiology of Dendritic Cells, Institut Pasteur, [6]INSERM U1223, Paris, France, [7]Faculty of Biology, Medicine and Health, University of Manchester, Manchester Academic Health Science Centre, Manchester, [8]Centre for Genomic and Experimental Medicine, MRC Institute of Genetics and Molecular Medicine, Edinburgh, United Kingdom, [9]Hamad Medical Corporation, Qatar, Qatar, [10]MitoVasc Institute, University of Angers, Angers, France, [11]The Children's Hospital at Westmead, Westmead, Australia, [12]CHU LENVAL, Nice, [13]Versailles Hospital, Le Chesnay, [14]Pitié-Salpêtrière Hospital, Paris, [15]CHU de Montpellier, Montpellier, France, [16]Mondino National Neurological Institute, Pavia, Italy, [17]Trousseau Hospital, Paris, France, [18]Medical University of Vienna, Vienna, Austria

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.
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YO018

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

M. V. Ristori[1], M. Capponi[2,*], D. Pires Marafon[2], S. Gardini[3], S. Pane[4], A. Russo[1], V. Messia[2], M. Pardeo[2], F. De Benedetti[2], L. Putignani[1,4], A. Insalaco[2]
[1]Human Microbiome Unit, IRCCS Ospedale Pediatrico Bambino Gesù, [2]Division of Rheumatology, IRCCS Ospedale Pediatrico Bambino Gesù, [3]GENOMEUP S.R.L, [4]Parasitology Unit, IRCCS Ospedale Pediatrico Bambino Gesù, Rome, Italy

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

YO019

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

S. Torreggiani[1,2,*], A. Almeida de Jesus[1], S. Alehashemi[1], J. Mitchell[1], G. Souto Adeva[1], J. Wade[1], G. A. Montealegre Sanchez[1], B. Lin[1], R. Goldbach-Mansky[1] on behalf of SAVI Study Group
[1]TADS/NIAID, NIH, Bethesda, United States, [2]Università degli Studi di Milano, Milano, Italy

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

SAVI Study Group: AA Alrasheed, S Balci, R Berard, A Borzutzky, J Brunner, B Buehring, A Buthaina, J Carter, M Corbeto Lopez, H Do, G Duckers, LR Folio, RM Kisla Ekinci, M Miller, M Montes Cano, MP Morin, S Ozen, A Reinhardt, S Ramsey, D Rumsey, L Santiago, G Schulert, B Wright

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YO020

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

E. M. Smith[1,2,*], K. Tharmaratnam[3], A. Jorgensen[3], M. Beresford[1,4]
[1]Women and Children's Health, University of Liverpool, [2]Paediatric Rheuamtology, Alder Hey Children's Hospital, [3]Department of Biostatistics, [4]Paediatric Rheumatology, University of Liverpool, Liverpool, United Kingdom

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

YO021

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

E. Marasco[1,*], G. M. Moneta[1], C. Bracaglia[1], I. Caiello[1], C. Farroni[2], R. Carsetti[2], F. De Benedetti[1]
[1]Division of Rheumatology, [2]B Cell Physiopathology Unit, Immunology Research Area, OSPEDALE PEDIATRICO BAMBIN GESÙ, Roma, Italy

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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YO022

THE PERFORMANCES OF DIFFERENT CLASSIFICATION CRITERIA IN PEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS

E. D. Batu[1,*], U. Kaya Akca[1], A. Pac Kisaarslan[2], E. Sag[1], F. Demir[3], S. Demir[1], S. Ozdemir Cicek[2], H. Poyrazoglu[2], B. Sozeri[3], Y. Bilginer[1], S. Ozen[1]

[1]Department of Pediatrics, Division of Rheumatology, Hacettepe University Faculty of Medicine, Ankara, [2]Department of Pediatrics, Division of Rheumatology, Erciyes University Faculty of Medicine, Kayseri, [3]Department of Pediatrics, Division of Rheumatology, Umraniye Training and Research Center, University of Health Sciences, Istanbul, Turkey

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

YO023

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

G. A. Robinson[1,2,*], K. E. Waddington[1], A. Radziszewska[2], H. Peckham[2], D. A. Isenberg[1], Y. Ioannou[1], C. Ciurtin[2], I. Pineda-Torra[3], E. C. Jury[1]
[1]Rheumatology, [2]Centre for Adolescent Rheumatology Versus Arthritis, [3]Centre for Cardiometabolic and Vascular Science, UNIVERSITY COLLEGE LONDON, London, United Kingdom

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

YO024

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

E. A. Smitherman[1,*], R. A. Chahine[1], T. Beukelman[1], L. B. Lewandowski[2], A. F. Rahman[1], S. E. Wenderfer[3], J. R. Curtis[1], A. O. Hersh[4] on behalf of For the CARRA Registry Investigators
[1]University of Alabama at Birmingham, Birmingham, [2]National Institutes of Health, Bethesda, [3]Baylor College of Medicine, Houston, [4]University of Utah, Salt Lake City, United States

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

YO025

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

E. Sag[1,*], S. Demir[1], Y. Bilginer[1], B. Talim[2], G. Haliloglu[3], S. Ozen[1]
[1]Pediatric Rheumatology, [2]Pediatric Pathology Unit, [3]Pediatric Neurology, Hacettepe University, Ankara, Turkey

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

YO026

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

S. R. Veldkamp[1,*], J. Wienke[1], M. H.A. Jansen[2], S. J. Vastert[2], J. F. Swart[2], E. J. Schatorjé[3], E. P.A.H. Hoppenreijs[3], F. van Wijk[1], A. van Royen-Kerkhof[2]
[1]Center for Translational Immunology, [2]Pediatric Rheumatology & Immunology, UMC Utrecht, Utrecht, [3]Pediatric Rheumatology, Radboud UMC, Nijmegen, Netherlands

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

YO027

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

M. G. L. Wilkinson[1,2,*], E. C. Rosser[1,2], M. Orford[3], G. Otto[4], D. Kelberman[4], L. R. Wedderburn[1,2,5], S. Eaton[3], C. T. Deakin[1,2,5] on behalf of UK Juvenile Dermatomyositis Research Group and the Centre for Adolescent Rheumatology Versus Arthritis

[1]Centre for Adolescent Rheumatology versus arthritis, UCL, UCLH, GOSH, [2]Infection, Immunity and Inflammation Programme, [3]Developmental Biology and Cancer Programme, [4]Genetics and genomic medicine programme, UCL Great Ormond Street Institute of Child Health, [5]NIHR Biomedical Research Centre , GOSH, London, United Kingdom

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

YO028

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

B. Lerkvaleekul[1,2,*], S. Veldkamp[1], M. van der Wal[1], J. Wienke[1], E. P.A.H. Hoppenreijs[3], S. S.M. Kamphuis[4], J. M. van den Berg[5], P. C.E. Hissink Muller[6], W. Armbrust[7], A. van Royen-Kerkhof[8], F. van Wijk[1]

[1]Laboratory of translational immunology, University Medical Center Utrecht, Utrecht University, Utrecht, Netherlands, [2]Division of Rheumatology, Department of Pediatrics, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand, [3]Department of Paediatrics, Paediatric Rheumatology, Amalia Children's Hospital, Radboud University Medical Centre Nijmegen, Nijmegen, [4]Paediatric Rheumatology, Sophia Children's Hospital, Erasmus University Medical Centre, Rotterdam, [5]Department of Pediatric Immunology, Rheumatology and Infectious Diseases, Emma Children's Hospital, Amsterdam University Medical Center (AUMC), University of Amsterdam, Amsterdam, [6]Department of Paediatric Rheumatology, Leiden University Medical Centre, Leiden, [7]Department of Paediatric Rheumatology, Beatrix Children's Hospital, University Medical Centre Groningen, Groningen, [8]Pediatric rheumatology and immunology, University Medical Center Utrecht, Utrecht University, Utrecht, Netherlands

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

YO029

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

M. M. Nap-Van Der Vlist[1,*], J. H. Houtveen[1], G. W. Dalmeijer[2], M. A. Grootenhuis[3], C. K. van der Ent[1], M. van Grotel[3], J. F. Swart[1], J. M. van Montfrans[1], E. M. van de Putte[1], S. L. Nijhof[1]
[1]Wilhelmina Children's Hospital, University Medical Center Utrecht, Utrecht University, [2]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht University, [3]Princess Máxima Center for Pediatric Oncology, Utrecht, Netherlands

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

YO030

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

F. Dekaj[1,*], L. R. Wedderburn[1,2,3], Z. Wanstall[1], W. Thomson[4,5] on behalf of CLUSTER Consortium on behalf of CLUSTER Consortium Champions

[1]Infection, Immunity and Inflammation Research & Teaching Department, University College London, Great Ormond Street Institute of Child Health, [2]Centre for Adolescent Rheumatology Versus Arthritis, University College London, University College London Hospital, Great Ormond Street Hospital, [3]NIHR Great Ormond Street Hospital Biomedical Research Centre, London, [4]NIHR Manchester BRC, Manchester University NHS Foundation Trust, Manchester Academic Health Science Centre, [5]Centre for Genetics and Genomics Versus Arthritis, The University of Manchester, Manchester, United Kingdom

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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YO031

UTILIZATION OF ANTI-NUCLEAR ANTIBODY ANALYSIS IN TERTIARY PEDIATRIC CLINIC

N. Sahin[1,*], A. Pac Kisaarslan[2], S. Ozdemir Cicek[2], A. S. Pinarbasi[3], N. Gunay[3], S. Yel[3], I. Dursun[3], M. H. Poyrazoglu[4], H. Kilic[5], R. Dusunsel[4]

[1]Pediatric Rheumatology, Bursa City Hospital, Bursa, [2]Pediatric Rheumatology, [3]Pediatric Nephorolgy, [4]Pediatric Nephrology and Rheumatology, [5]Department of Microbiology, ERCIYES UNIVERSITY FACULTY OF MEDICINE, Kayseri, Turkey

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 Acute disseminated encephalomyelitis Chronic autoimmune urticaria Type 1 diabetes mellitus Tubulointerstitial nephritis	8 (0,9%) 4 (0,5%) 1 (0,1%) 6 (0,7%) 6 (0,7%) 0	2 (0,2%) 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*** Positive Negative ***≥1/1000 titer*** Positive Negative	**With autoimmune diseases n (%)** 345 (%10.4) 515 (%15.5) 208 (6.3%) 652 (19.6%)	**Without autoimmun diseases n (%)** 564 (%17) 1896 (%57.1) 270 (8.1%) 2190 (66%)	**Total (%)** 909 (%27.4) 2411 (%72.6) 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

YO032

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

F. García Rodríguez[1,*], B. D. J. Fortuna Reyna [2], I. Peláez Ballestas[3], E. Faugier Fuentes [4], S. Mendieta Zerón [5], G. Reyes Cordero[6], S. Jiménez Hernández[7], A. V. Villarreal Treviño[1], J. Guadarrama Orozco[8], S. Rosiles de la Garza[9], M. De la O Cavazos[9], N. Rubio Pérez[7]

[1]Pediatric Rheumatology, Hospital Universitario "Dr.José E. González", [2]Pediatric Rheumatology, Hospital Universitario "Dr. José E. González", Monterrey, [3]Rheumatology, Hospital General de México "Dr. Eduardo Liceaga", [4]Pediatric Rheumatology, Hospital Infantil de México Federico Gómez, CDMX, [5]Pediatrics, Hospital Regional de Toluca ISSEMyM, Toluca, [6]Rheumatology , Hospital Infantil de Especialidades de Chihuahua, Chihuahua, [7]Pediatric Rheumatology, Hospital Universitario "Dr. José E. González", Monterrey , [8]Palliative Care, Hospital Infantil de México Federico Gómez, CDMX, [9]Pediatrics, Hospital Universitario "Dr. José E. González", Monterrey, Mexico

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

YO033

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

M. J. Wahadat[1,2,*], M. Lourens[1], E. Huijser[1], C. van Helden-meeuwsen[1], S. Kamphuis[2], M. Versnel[1]
[1]Immunology, [2]Pediatric Rheumatology, Erasmus University Medical Centre, Rotterdam, Netherlands

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

YO034

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

M. H. Tedy[1,*], S. Fuehner[1], C. H. Hinze[1], M. Saers[1], D. Foell[1], C. Kessel[1]
[1]Pediatric Rheumatology & Immunology, University Children's Hospital, Muenster, Germany

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

YO035

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.

R. Caorsi[1,*], A. Insalaco[2], F. Bovis[3], G. Martini[4], M. Cattalini[5], M. Chinali[6], A. Rimini[7], C. Longo[8], S. Federici[2], C. Celani[2], G. Filocamo[9], R. Consolini[10], C. Maggio[11], G. Fadanelli[12], F. Licciardi[13], M. Romano[14], B. Teruzzi[15], A. Taddio[16], A. Miniaci[17], F. La Torre[18], A. De Fanti[19], G. Cavalli[20], B. Bigucci[21], R. Gallizzi[22], M. Chinello[23], A. Brucato[24], M. Imazio[25], R. Cimaz[26], F. De Benedetti[2], M. Gattorno[1]

[1]Center for autoinflammatory diseases and immunodeficiencies, Istituto Giannina Gaslini, Genova, [2]Division of Rheumatology, Ospedale pediatrico Bambino Gesù, Roma, [3]DISSAL , University of Genova, Genova, [4]Pediatric Rheumatology, Università di Padova, Padova, [5]Pediatrics clinic, University of Brescia, Brescia, [6]Pediatric Cardiology, Ospedale pediatrico Bambino Gesù, Roma, [7]Department of Cardiology, Istituto Giannina Gaslini, [8]Department of Paediatrics, University of Genova, Genova, [9]Pediatria a Media Intensità di Cure , Fondazione IRCCS Cà Granda, Milano, [10]Clinica pediatrica, Unoversity of Pisa, Pisa, [11]PROMISE “G. D’Alessandro” Department, University of Palermo, Palermo, [12]UOC di Pediatria, Ospedale Santa Chiara, Trento, [13]Immuno-reumatologia, Ospedale infantile Regina Margherita, Torino, [14]ASST G.Pini-CTO, [15]Pediatric Rheumatology, ASST GOM Niguarda , Milano, [16]IRCCS "Burlo Garofolo" , Trieste, [17]Unità di Pediatria, Policlinico S.Orsola-Malpighi , Bologna, [18]Pediatric Rheumatology Section, "Giovanni XXIII" Pediatric Hospital, Bari, [19]Reumatologia Pediatrica, Ospedale di Reggio Emilia, Reggio Emilia, [20]Reumatologia ed immunologia Clinica, Ospedale San Raffaele, Milano, [21]Unità di Pediatria, Ospedale di Rimini, Rimini, [22]Pediatric Rheumatology Center, University of Messina, Messina, [23]UOC Oncoematologia Pediatrica, Azienda Ospedaliera di Verona, Verona, [24]Dipartimento scienze cliniche e biomediche L. Sacco, Università di Milano, Milano, [25]Division of Cardiology, AOU Città della Salute e della Scienza di Torino, Torino, [26]Department of Clinical Sciences and Community Health and RECAP-RD, Università di Milano, Milano, Italy

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

YO036

COMPARISION OF IVIG RESISTANCE PREDICTIVE MODELS IN KAWASAKI DISEASE

U. Kaya Akca[1,*], O. Serin[2], E. Arslanoglu Aydin[2], E. Sag[1], S. Demir[1], E. Atalay[1], M. Kasap Cuceoglu[1], E. D. Batu[1], Y. Bilginer[1], S. Ozen[1]
[1]Division of Pediatric Rheumatology, Department of Pediatrics, [2]Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey

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

YO037

ISCHEMIC STROKE IN CHILDREN WITH SCLERODERMA EN COUPE DE SABRE.

M. S. Pavlova[1,*], M. K. Osminina[1], L. G. Khachatryan[1], N. S. Podchernyaeva[1], V. M. Trepilets[2], O. V. Shpitonkova [1], V. A. Seraya[2], S. V. Trepilets[3]
[1]N.F.Filatov Clinical Institute of Child Health, [2]Sechenov First Moscow State Medical University, [3]Burdenko National Medical Research Center of Neurosurgery, Moscow, Russian Federation

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

YO038

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

C. Anderson[1,*], C. Pain[2], V. Leone[3]
[1]Paediatric Rheumatology, Great Ormond Street Hospital, London, London, [2]Paediatric Rheumatology, Alderhey Children's Hospital, Liverpool, [3]Paediatric Rheumatology, Leed's Children's Hospital, Leeds, United Kingdom

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

YP001

EVALUATION OF THE NEW CLASSIFICATION CRITERIA FOR PFAPA SYNDROME

A. Fouriki[1,*], F. Crimi[1], A. Theodoropoulou[1], I. Kone-Paut[2], P. Dusser[2], S. Georgin-Lavialle[3], A. Fayand[3], P. Pillet [4], O. Richer [4], V. Hentgen [5], M. Hofer[1]

[1]DFME, CHUV, Lausanne, Switzerland, [2]Rhumatologie pédiatrique, Hôpital de Bicêtre, LE KREMLIN-BICÊTRE, [3]Rhumatologie pédiatrique, Hôpital Tenon, Paris, [4]Rhumatologie pédiatrique, CHU Bordeaux, Bordeaux, [5]Rhumatologie pédiatrique, Centre Hospitalier Versailles, Versailles, France

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

YP002

EVALUATION OF THE THYROID DISORDERS IN CHILDREN WITH FAMILIAL MEDITERRANEAN FEVER

H. Turan[1], M. Yıldız[2,*], O. Civan[3], A. D. Cakir[1], G. Tarcin[1], Y. Ozer[1], Z. Bayramli[4], M. Kucur[5], I. Adaletli[3], A. Adrovic[2], K. Barut[2], O. Ercan[1], O. Kasapcopur[2], S. O. Evliyaoglu [1]
[1]Department of Pediatric Endocrinology, [2]Department of Pediatric Rheumatology, [3]Department of Radiology, [4]Department of Pediatrics, [5]Department of Biochemistry, Istanbul University-Cerrahpasa, Istanbul, Turkey

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

YP003

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

E. D. Batu[1,*], E. Vezir[2], E. Öğüş[3], Ö. Özbaş[3], G. Akpınar[4], S. Demir[1], S. Özen[1]
[1]Department of Pediatrics, Division of Rheumatology, Hacettepe University Faculty of Medicine, [2]Department of Pediatrics, Division of Allergy and Immunology, [3]Department of Biochemistry, [4]Department of Pediatrics, University of Health Sciences, Ankara Health Research and Application Center, Ankara, Turkey

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

YP004

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

R. Gallizzi[1,*], M. Bustaffa[1], F. Mazza[1], D. Sutera[1], G. Fabio[1], L. Obici[1], M. Alessio[1], D. Rigante[1], L. Cantarini[1], A. Insalaco[1], M. Cattalini[1], M. C. Maggio[1], G. Simonini[1], A. N. Olivieri[1], S. Pastori[1], M. Lancieri[1], F. Calzantini[1], N. Ruperto[1], M. Gattorno[1]

[1]Eurofever Registry and the Paediatric Rheumatology International Trials Organisation (PRINTO), Genoa, Italy

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	20.7% of pts experience fatigue or chronic pain, 16.9% limitations in daily activities, and 16.9% have

life and patient-reported outcomes	lost school/work days.

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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YP005

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

R. Dagher[1,*], E. Sfeir[1], V. Modica[2], C. Djambas Khayat[3]
[1]Pediatric department, Notre Dame de Secours University Hospital, Byblos, [2]Holy Family University, Batroun, [3]Saint Joseph University, Beirut, Lebanon

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

YP006

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

H. Adiguzel Dundar[1,*], S. Turkucar[1], C. Acari[1], B. Makay[1], E. Unsal[1]
[1]Department of Pediatrics, Pediatric Rheumatology Unit, DOKUZ EYLUL UNIVERSITY FACULTY OF MEDICINE,, izmir, Turkey

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

YP007

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

D. O'leary[1,2,*], O. Killeen[1,2], G. Wilson[1]
[1]UCD Centre for Arthritis Research, Conway Institute , [2]National Centre for Paediatric Rheumatology, Children's Health Ireland at Crumlin, Dublin, Ireland

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

YP008

THE MUSCULOSKELETAL SYSTEM MANIFESTATIONS IN CHILDREN WITH FAMILIAL MEDITERRANEAN FEVER

F. Demir[1], G. L. Bolaç[2], T. Merter[2], S. Canbek[3], J. Yıldız[3], Ö. Akgün Doğan[3], Y. Kendir Demirkol[3], H. L. Doğanay[3], B. Sözeri[1,*]

[1]Department of Pediatric Rheumatology, [2]Department of Pediatrics, [3]Genetic Laboratory (GLAB), UMRANIYE TRAINING AND RESEARCH HOSPITAL, Istanbul, Turkey

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

YP009

AN ITALIAN COHORT OF PATIENTS WITH CHRONIC RECURRENT MULTIFOCAL OSTEOMYELITIS

M. Romano[1,*], T. Giani[2], G. Filocamo[3], F. Minoia[3], A. Marino[4], G. Ferrara[5], C. Chighizola[6], L. Gamalero[7], M. Gattinara[8], R. Cimaz[9] on behalf of Pediatric Rheumatology Group of the Milan Area
[1]Pediatric Rheumatology, ASST-G.Pini-CTO, Milan, Italy, Milan , [2]Pediatric Rheumatology, Anna Meyer Children University Hospital, Florence, [3]Pediatric Rheumatology, Fondazione IRCCS Cà Granda ospedale Maggiore Policlinico, Milan, [4]Department of Pediatrics, Desio Hospital, ASST Monza, Desio, Monza, [5]ASL Firenze Centro, Florence, [6]Allergology, Clinical Immunology & Rheumatology Unit, San Luca Hospital, IRCCS Istituto Auxologico Italiano, Milan , [7]Pediatric Rheumatology, University of Udine, Udine, [8]Pediatric Rheumatology, ASST-G.Pini-CTO, [9]Department of Clinical Sciences and Community Health, University of Milan, Milan , Italy

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

YP010

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

M. E. Pinto[1,*], M. L. Cagnato[1], D. Basso[2], S. Moz[2], A. Meneghel[1], F. Zulian[1], G. Martini[1]
[1]Pediatric Rheumatology Unit, [2]Department of Laboratory Medicine, University-Hospital of Padua, Padua, Italy

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

YP011

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

P. O. Avar-Aydin[1,*], Z. B. Ozcakar[1], F. Yalcinkaya[1], N. Cakar[1]
[1]Department of Pediatric Rheumatology, Ankara University School of Medicine, Ankara, Turkey

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

YP012

MOLECULAR AND CLINICAL FINDINGS IN CHILDREN WITH UNDIFFERENTIATED PERIODIC FEVER SYNDROMES

Z. Korobova[1,*], Y. Kuzina[1], A. Romanko[2], A. Tumakova[1], E. Suspitsin[1,2], M. Kostik[1,3]
[1]Saint Petersburg State Pediatric Medical University, [2]N.N. Petrov National Medical Research Center of Oncology, [3]Almazov National Medical Research Center, Saint-Petersburg, Russian Federation

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

YP013

BROADENING THE GENETIC AND CLINICAL SPECTRUM OF A20 HAPLOINSUFFICIENCY

A. Uva[1,*], C. Celani[2], G. Prencipe[2], C. Passarelli[3], I. Caiello[2], E. Piano Mortari[4], R. Carsetti[4], M. N. Rossi[2], S. Federici[2], S. Magni-Manzoni[2], F. De Benedetti[2], A. Insalaco[2]

[1]Dipartimento Materno-Infantile, Scienze Urologiche, Università Roma-Sapienza, [2]Division of Rheumatology, IRCCS Ospedale Pediatrico Bambino Gesù, [3]UOC Laboratory of Medical Genetics, IIRCCS Ospedale Pediatrico Bambino Gesù, [4]B Cell Pathophysiology Unit, Immunology Research Area, IRCCS Ospedale Pediatrico Bambino Gesù, Rome, Italy

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

YP014

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

M. Campisano[1], C. Celani[2,*], D. Pires Marafon[2], A. Franceschini[1], S. Federici[2], G. Brancaccio[1], F. De Benedetti[2], L. Galletti[1], A. Insalaco[2], M. Chinali[1]
[1]Division of Pediatric Cardiology, IRCSS Ospedale Pediatrico Bambino Gesù, [2]Division of Rheumatology, IRCSS Ospedale Pediatrico Bambino Gesù, Rome , Italy

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

YP015

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

V. Sgouropoulou[1,*], E. Farmaki[1], T. Papadopoulos[2], V. Tzimouli[1], P. Pratsidou-Gertsi[1], M. Trachana[1]
[1]Pediatric Immunology and Rheumatology Referral Centre, 1st Dept of Pediatrics, Aristotle University, Hippocration Hospital, Thessaloniki, Greece, Aristotle University, Thessaloniki, Greece, [2]Laboratory of Molecular Biology and Genetics, Karyo Center, Thessaloniki, Greece, Laboratory of Molecular Biology and Genetics, Karyo Center, Thessaloniki, Greece, Thessaloniki, Greece

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

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Disclosure of Interest: None declared

YP016

MRI AS A DIAGNOSTIC TOOL IN PROTRACTED FEBRILE MYALGIA

N. H. Aviran[1,*], G. Amarilyo[1], Y. Lakovsky[2], J. Garkaby[3], R. Haviv[4], L. Harel Liora[1], Y. Butbul[5]
[1]Rheumatology, [2]Radiology, Schneider Children's Medical Center of Israel, Petach Tikvah , [3]5Department of Pediatrics B, Ruth Rappaport Children's Hospital, Rambam Health Care Campus, Haifa, [4]8Pediatric Rheumatology Unit, Meir Medical Center, Kfar Saba, [5]Rheumatology, Ruth Rappaport Children's Hospital, Rambam Health Care Campus, Haifa, Israel

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

YP017

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

E. Roberts[1,2,*], I. Maccora[3], D. Chia[4], C. Suo[4,5], K. Armon[4,5], A. V. Ramanan[6,7], E. Sen[1,2]
[1]Department of Paediatric Rheumatology, Great North Children's Hospital, [2]Newcastle University, Newcastle-Upon-Tyne, United Kingdom, [3]Paediatric Rheumatology Unit, Anna Meyer Children's University Hospital, School of Human Health Science, Florence, Italy, [4]School of Clinical Medicine, University of Cambridge, [5]Department of Paediatric Rheumatology, Cambridge University Hospitals, Cambridge, [6]Department of Paediatric Rheumatology, Bristol Royal Hospital for Children, [7]Translational Health Sciences, University of Bristol, Bristol, United Kingdom

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

YP018

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

R. P. Khubchandani[1], N. Mohan Rao[1], P. Pimpale Chavan[1,*], A. Khan[1], D. Ramadoss[1], I. Aksentijevich[2]
[1]Section of Pediatric Rheumatology, NH SRCC Children's Hospital, Mumbai, India, [2]National Human Genome Research Institute, National Institutes of Health, Bethesda, Maryland, United States

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
Majed 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

YP019

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

F. E. Price-Kuehne[1,*], P. Bale[1,2], K. Armon[1,2]
[1]Cambridge University Hospitals NHS Foundation Trust, Cambridge, [2]Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich, United Kingdom

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

YP020

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

M. Capponi[1,*], D. Pires Marafon[1], F. Rivosecchi[2], Y. Zhao[3], M. Pardeo[1], V. Messia[1], L. Tanturri de Horatio[2], P. Tomà[2], F. De Benedetti[1], A. Insalaco[1]
[1]Division of Rheumatology, IRCCS, Ospedale Pediatrico Bambino Gesù, [2]Division of Radiology, IRCCS, Ospedale Pediatrico Bambino Gesù, Rome, Italy, [3]University of Washington, Seattle, United States

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

YP021

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

A. Glazyrina[1], Y. Petryaikina[1], A. Sologub[1,*], A. Rtishev[1], V. Yusupova[1], S. Kurbanova[1], M. Dzis[1], Y. Korobyanc[1], E. Kryshova[1], D. Ovsyannikov[2], A. Harkin[1]
[1]Rheumatology, MOROZOV CHILDREN'S CITY CLINICAL HOSPITAL OF THE MOSCOW CITY HEALTHCARE DEPARTMENT., [2]Rheumatology, People's Friendship University of Russia, Moscow, Russian Federation

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

YP022

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

C. C. Goetzke[1,*], F. Ebstein[2], A. Brehm[3], M. Schülke-Gerstenfeld[4], M.-F. Mashreghi[5], R. Goldbach-Mansky[6], T. Kallinich[7], E. Krüger[2]

[1]Department of Pediatrics, Division of Pulmonology, Immunology and Critical Care Medicine, Charité Universitätsmedizin Berlin, 13353 Berlin, [2]Institut für Medizinische Biochemie und Molekularbiologie , University of Greifswald, Greifswald, [3]Institute of Biochemistry, [4]Department of Neuropediatrics and Neurocure Clinicla Research Center, Charité Universitätsmedizin Berlin, [5] German Rheumatism Research Center, Berlin, Germany, [6]Translational Autoinflammatory Disease Studies Unit, National Institute of Allergy and Infectious Diseases, Bethesda, United States, [7]Department of Pediatrics, Division of Pulmonology, Immunology and Critical Care Medicine, Charité Universitätsmedizin Berlin, Berlin, Germany

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

YP023

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

M. Makhova[1,*], M. Kostik[1], A. Maletin[2], D. Kozlova[3], D. Vasilev[3], V. Khizha[3], A. Mushkin[2]
[1]Saint Petersburg Pediatric Medical University, [2]Saint-Petersburg Research Institute of Phtisiopulmonology, [3]"Scientific and Production Firm "Arbis+", Ltd, Saint-Petersburg, Russian Federation

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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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	70.8	3.3	0.95	0.00001	0.0000001	0.0000001	0.0000001

	(42.0; 51.3)	(65.3; 73.7)	(2.5; 7.7)	(0.7; 1.3)				
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

YP024

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

E. D. Batu[1,*], L. Lamot[2], E. Sag[1], S. Ozen[1], Y. Uziel[3] on behalf of on behalf of EMERGE group and Clinical Affairs Committee of the PReS council

[1]Department of Pediatrics, Division of Rheumatology, HACETTEPE UNIVERSITY FACULTY OF MEDICINE, DEPARTMENT OF PEDIATRICS, DIVISION OF RHEUMATOLOGY, Ankara, Turkey, [2]Division of Clinical Immunology and Rheumatology, Department of Pediatrics, Sestre Milosrdnice University Hospital Center, University of Zagreb School of Medicine, Zagreb, Croatia, [3]Pediatric Rheumatology Unit, Meir Medical Center, Kfar Saba, Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel

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

YP025

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

M. Pouletty[1], C. Borocco[2], N. Ouldali[1], M. Caseris[1], C. Beyler[1], S. Bonacorsi[1], G. Carcelain[1], I. Kone-Paut[3], B. Bader-Meunier[4], A. Faye[1], U. Meinzer[1], C. Galeotti[2], I. Melki[1,*] on behalf of Kawa-COVID Paris-Region Group
[1]APHP - ROBERT DEBRE - PARIS, Paris, [2]APHP- Bicetre Hospital, Kremlin-Bicetre, [3]APHP- Bicetre Hospital, [4]APHP-Necker hospital, Paris, France

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

YP026

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

M. Kasap Cuceoglu[1,*], E. D. Batu[1], S. Demir[1], E. Sag[1], U. Kaya Akca[1], E. Atalay[1], Y. Bilginer[1], S. Ozen[1]
[1]Pediatric Rheumatology, Hacettepe University, Ankara, Turkey

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

YP027

A META-ANALYSIS OF SEX BIAS IN COVID-19

H. Peckham[1,2,*], N. M. de Gruijter[1,2], C. Raine[2], A. Radziszewska[1,2], C. Ciurtin[1,2], L. R. Wedderburn[1,3,4], E. C. Rosser[1,2], C. T. Deakin[1,3,4], K. Webb[5,6]

[1]Centre for Adolescent Rheumatology Versus Arthritis at UCL, UCLH & GOSH, [2]Centre for Rheumatology Research, Division of Medicine, University College London, [3]Infection Immunity and Inflammation Research and Teaching Dept , UCL GOS Institute of Child Health, [4]NIHR Great Ormond Street Biomedical Research Centre, Great Ormond Street Hospital, London, United Kingdom, [5]Department of Paediatric Rheumatology, School of Child and Adolescent Health, Red Cross Children's Hospital , University of Cape Town, Cape Town, South Africa, [6]The Francis Crick Institute, Crick African Network, London, United Kingdom

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

YP028

KAWASAKI DISEASE DURING COVID-19 EPIDEMIC

F. Orlando[1,*], R. Naddei[2], G. Ranucci[1], M. Tardi[1], A. Mauro[1], A. Catzola[2], R. Borrelli[1], L. Martemucci[1], R. Sottile[1], M. Alessio[2]

[1]AORN SANTOBONO PAUSILIPON, [2]University of Naples Federico II, Naples, Italy

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

YP029

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

M. Wilkinson[1,2,*], W. Wu[1], K. O'Brien[1,2], C. T. Deakin[1,2,3], L. R. Wedderburn[1,2,3], P. Livermore[2,3] on behalf of UK Juvenile Dermatomyositis Research Group

[1]Centre for Adolescent Rheumatology versus arthritis, UCL, UCLH, GOSH, [2]Infection, Immunity and Inflammation Programme, UCL Great Ormond Street Institute of Child Health, [3]NIHR Biomedical Research Centre, GOSH, London, United Kingdom

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

YP030
ACRAL ERYTHEMATOUS/CYANOTIC LESIONS ASSOCIATED WITH VESSELS ARCHITECTURE DISTORTION DEFINE A NEW CLINICAL ENTITY DURING COVID19 PANDEMIC

A. Catzola[1,*], L. Pierri[1], F. Della Casa[2], A. Punziano[2], M. Vastarella[2], P. Nappa[2], E. Bruzzese[1], V. Discepolo[1], M. Alessio[1]
[1]Mother and Chid department, [2]Clinical Medicine and Surgery, University Hospital "Federico II", Naples, Italy

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

YP031

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

H. Chaudhary[1,*], R. Sharma[1], P. Patra[1], M. Sudhakar[1], A. Gummadi[1], D. Suri[1], A. Jindal[1], V. Pandiarajan[1], A. Gupta[1], S. Singh[1]
[1]Advanced pediatrics center, PGIMER, CHANDIGARH, INDIA, Chandigarh, India

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

YP032

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

J. Arroyo Palomo[1,*], P. Morán Álvarez[1], Á. Andreu[1], L. Villalobos Sánchez[1], A. Boteanu[1]
[1]Hospital Ramón y Cajal, Madrid, Spain

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

YP033

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

M. V. Mastrolia[1,*], R. Agostiniani[2], C. Azzari[1], R. Bernardini[2], U. Bottone[2], G. B. Calabri[1], F. Civitelli[2], R. Consolini[2], R. Danieli[2], R. Di Silvio[2], S. Falorni[2], L. Gagliardi[2], S. Grosso[2], M. Martini[2], G. Memmini[2], M. Pezzati[2], G. Suriano[2], L. Tafi[2], A. Vaccaro[2], P. L. Vasarri[2], G. Simonini[1]
[1]Meyer children's University Hospital, Firenze, [2]Pediatric Tuscany Network , Tuscany , Italy

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

YP034

ACRAL LESIONS IN A PEDIATRIC COHORT DURING COVID-19 EPIDEMIC

F. Orlando[1,*], A. Mauro[1], M. Tardi[1], R. Borrelli[1], E. Sammarco[1], G. Ruggiero[2], L. Martemucci[1], O. Ametrano[3], R. Sottile[1]
[1]Pediatric Rheumatology Unit, AORN SANTOBONO PAUSILIPON, [2]Italian Federation of General Pediatricians , [3]Pediatric Dermatology Unit, AORN SANTOBONO PAUSILIPON, Naples, Italy

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

YP035

TRANSITION READINESS ASSESSMENT FROM PEDIATRIC TO ADULT SERVICES IN RHEUMATIC DISEASES

S. Kittivisuit[1,2,*], B. Lerkvaleekul[1], S. Soponkanaporn[1], S. Vilaiyuk[1]
[1]Rheumatology Division, Pediatric Department, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, [2]Rheumatology Division, Pediatric Department, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand

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

YP036

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

J. J. C. Tan[1,*], G. Tiller[1], P. Gowdie[1], A. Cox[1], J. Munro[1], R. Allen[2], J. Akikusa[1]
[1]Royal Children's Hospital, Melbourne, [2]Royal Children's Hospital, Victoria, Australia

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

YP037

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

N. Vinšová[1,*], Š. Fingerhutová[1], D. Němcová[1], M. Schüller[2], J. Fráňová[2], H. Malcová[3], M. Svoboda[4], P. Doležalová[1]
[1]Centre for paediatric rheumatic and autoinflammatory diseases Department of Paediatrics and Adolescent Medicine, General University Hospital in Prague and 1st Faculty of Medicine, Charles University in Prague, Prague, [2]Paediatric Rheumatology Unit, Department of Paediatrics, Children´s Medical Center, Faculty of Medicine, Masaryk University Brno and Faculty Hospital Brno, Brno, [3]Department of rheumatology for children and adults, Motol University Hospital, Prague, [4]Institute of Biostatistics and Analyses Ltd (IBA), Brno, Czech Republic

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

YP038

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

N. M. de Gruijter[1,2,*], M. Naja[1], H. Peckham[1], A. Radziszewska[1], M. Kinsella[2], J. Glenister[2], E. C. Rosser[1,2], G. E. Butler[3], E. C. Jury[2], C. Ciurtin[1]

[1]Centre for Adolescent Rheumatology Versus Arthritis, Division of Medicine, [2]Centre for Rheumatology Research, Division of Medicine, [3]Department of Paediatric & Adolescent Medicine and Endocrinology, University College London, London, United Kingdom

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

YP039

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

S. Jiménez Hernández [1,*], A. C. Arana Guajardo[2], F. García Rodríguez [1], A. V. Villarreal Treviño[3], R. Negrete López [4], A. López Rangel[5], M. E. Corral Trujillo[4], P. Ancer Rodríguez[6], O. Salas Fraire [7], M. De la O Cavazos [8], D. Galarza Delgado[4], N. Rubio Pérez[1]

[1]Pediatric Rheumatology, Hospital Universitario "Dr. José E. González", [2]Internal Medicine Institute, Rheumatology Service, Escuela Nacional de Medicina Sistema Tec Salud, [3]Pediatric Rheumatology, Hospital Universitario "José Eleuterio González", [4]Rheumatology , [5]Psychiatry , [6]Nutrition, [7]Rehabilitation and Sport Medicine , [8]Pediatrics, Hospital Universitario "Dr. José E. González", Monterrey , Mexico

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

YP040

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

V. Mercer[1,2,*], N. Smith[1], S. Jandial[3,4], H. E. Foster[1,4]
[1]Translational and Clinical Research Institute, Newcastle University, Newcastle upon Tyne, [2]Children's Physiotherapy, South Tyneside and Sunderland NHS Foundation Trust, South Shields, [3]School of Medical Education, Newcastle University, [4]Paediatric Rheumatology, Great North Children's Hospital, Newcastle upon Tyne, United Kingdom

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

YP041

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

D. B. Pandya[1,*], C. Dave[2] on behalf of Dr Dhananjay Shah, Dr Yagnesh Popat, Dr Mehul Mitra,Dr Jay Dhirwani,Dr Rakesh Patel,Dr Yogesh Parikh and Dr Jhankhana Sanghvi.
[1]Paediatric Rheumatology & Immunology, [2]Paediatric Endocrinology, Dev Children's Hospital, Rajkot, India

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
1 Department of Paediatric Rheumatology, Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom
2 Department of Paediatric Rheumatology, Amrita Institute of Medical Sciences, Kochi, Kerala, India

Disclosure of Interest: None declared

YP042

DEVELOPMENT OF AN APP FOR THE MANAGEMENT OF AUTOINFLAMMATORY DISEASES USING AN INNOVATIVE PATIENTS-CLINICIANS CODESIGN APPROACH

S. Federici[1,*], C. Santu[2], M. De Munari[2], A. Insalaco[1], C. Celani[1], L. De Roberto[2], G. Ciniero[2], F. De Benedetti[1], R. Di Maulo[2]
[1]Rheumatology, Bambino Gesù Hospital, Rome, [2]Cloud-R s.r.l., Milan, Italy

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.

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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

YP043

SLCO1B1 RS4149056 VARIANT AS THE PREDICTOR OF METHOTREXATE – RELATED GASTROINTESTINAL TOXICITY IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

J. Roszkiewicz[1,*], D. Michałek[2], A. Ryk[2], Z. Swacha[3], B. Szmyd[4], E. Smolewska[1]
[1]Department of Pediatric Cardiology and Rheumatology, [2]Department of Biostatistics and Translational Medicine, Medical University of Lodz, Łódź, [3]Clinic of Dermatology, Military Medical Institute, Warsaw, [4]Department of Paediactrics, Oncology and Haematology, Medical University of Lodz, Łódź, Poland

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

YP044

CLINICAL AND MOLECULAR CHARACTERISTIC OF 13 PATIENTS WITH CACP SYNDROME

N. Garipova[1,*], M. Kostik[2], E. Suspitsin[2], G. Yanus[2], V. Kenis[3], A. Kozhevnikov[3], S. Salugina[4], Z. Gesheva[5], Y. Chasovskih[6], S. Ushakova[7], O. Khalidulina[7], E. Imyanitov[2], L. Sorokina[8], M. Gharabaghtsyan[9]
[1]Almazov National Medical Research Centre, Saint Petersburg, [2]St.-Petersburg Pediatric Medical University, Saint-Petersburg, [3]The Turner scientific research Institute for Children's Orthopedics, Saint Petersburg, [4]V.A. Nasonova Research Institute of Rheumatology, Moscow, [5]Medical Center "Mado" , Nalchic, [6]Siberian State Medical University, Tomsk, [7]Tyumen State Medical University, Tumen, [8]Leningrad's Regional Children Clinical Hospital, Saint Petersburg, Russian Federation, [9]Institute of Childand Adolescent Health with the Arabkir Medical Center, Yerevan, Armenia

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

YP045

COMPARISON OF CLINICAL AND ULTRASONOGRAPHIC EVALUATIONS IN JUVENILE IDIOPATHIC ARTHRITIS.

N. Bogdanova[1,*], I. Cīrule[1], I. Apine[1], L. Muižniece[1]
[1]Diagnostic Radiology department, Children's Clinical University Hospital, Riga, Latvia

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

YP046

A NEED TO TRAIN PAEDIATRIC RHEUMATOLOGISTS IN MUSCULOSKELETAL ULTRASOUND SCANNING. HOW DO WE MOVE FORWARD?

F. Jenabi[1,*], K. Mageean[2], A. Leahy[2], B. Davidson[3], H. de Graaf[2]
[1]Paediatrics, [2]Paediatrics rheumatology, [3] rheumatology, University hospital of Southampton, Southampton, United Kingdom

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

YP048

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

C. Matucci Cerinic[1,2,*], L. Oliveira Mendonça[3], P. Terranova[4], F. Casabona[2], F. Bovis[5], R. Caorsi[1,3], F. Fioredda[4], E. Palmisani[4], A. Grossi[6], D. Guardo[4], M. Bustaffa[3], S. Volpi[3], I. Ceccherini[6], A. Ravelli[1], C. Dufour[4], M. Gattorno[3], M. Miano[4]
[1]Clinica pediatrica e reumatologia, Istituto Giannina Gaslini, [2]DINOGMI, University of Genova, [3]Center for Autoinflammatory diseases and Immunodeficiencies, [4]Hematology Unit, Istituto Giannina Gaslini, [5]Department of Health Sciences (DISSAL), University of Genova, [6]Laboratory of Genetics and Genomics of Rare Diseases, Istituto Giannina Gaslini, Genova, Italy

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.

References:

1) Joao B. Oliveira et al. *Blood* 2010; 116 (14): e35–e40.
2) Lenardo MJ et al. *Immunity*. 2010;32(3):291–295.

CMC and LOM equally contributed to this work
Disclosure of Interest: None declared

YP049

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

G. Giancane[1,*], C. Campone[1], M. F. Gicchino[2], A. Alongi[1], C. Bava[1], S. Rosina[1], Y. Boyko[3], N. Martin[4], Y. El Miedany[5], M. Harjacek[6], S. Hashad[7], M. Ioseliani[8], R. Burgos-Vargas[9], R. Joos[10], C. Scott[11], M. Hofer[12], Z. M. Ayala[13], M. Ekelund[14], S. Al-Abrawi[15], M.-F. Aiche[16], X. Norambuena[17], J. A. Melo-Gomes[18], N. Ruperto[19], A. Consolaro[20], A. Ravelli[1]
[1]Pediatric Immunology and Rheumatology, IRCCS Gaslini, Genova, [2]Rheumatology Department, Second University of Naples, Naples, Italy, [3]Pediatrics, Western Ukrainian Specialized Children's Medical Centre, Lviv, Ukraine, [4]Rheumatology Department, The Royal Hospital for Children, Glasgow, United Kingdom, [5]Department of Rheumatology and Rehabilitation, Ain Shams University, Italian Hospital St Abbassia, Cairo, Egypt, [6]Department of Pediatrics, Division of Clinical Immunology and Rheumatology, Clinical Hospital Center Sestre Milosrdnice, Zagreb, Croatia, [7]Pediatrics, Tripoli Children's Hospital, Tripoli, Libya, [8]Rheumatology, M. Iashvili Children's Central Clinic, Tbilisi, Georgia, [9]Departamento de Reumatología, Hospital General de Mexico, Mexico City, Mexico, [10]Pediatric Rheumatology, Ghent University Hospital, Gent, Belgium, [11]Paediatric Rheumatology, Red Cross War Memorial Childrens Hospital, Cape Town, South Africa, [12]Unité Romande d'Immuno-Rhumatologie Pediatrique, CHUV, Geneva, Switzerland, [13]Reumatología Pediátrica, Cátedra y Servicio de Pediatría, Hospital de Clínicas, Facultad de Ciencias Médicas, Universidad Nacional de Asunción, San Lorenzo, Paraguay, [14]Futurum - the Academy for health and care, Ryhov County Hospital, Jonkoping, Sweden, [15]Department of Child Health and Pediatric Rheumatology, Royal Hospital, Muscat, Oman, [16]Departement of Rhumatology, Hospital of Douera, Alger, Algeria, [17]Servicio de Pediatria - Unidad de Inmuno- Reumatologia Pediatrica, Hospital Dr. Exequiel Gonzalez Cortes, Santiago, Chile, [18]Consulta de Reumatologia Infantil do Adolescente e do Adulto jovem, Instituto Português de Reumatologia, Lisbon, Portugal, [19]Pediatric Rheumatology and Immunology, IRCCS Gaslini, Genoa, [20]Pediatric Rheumatology and Immunology, IRCCS Gaslini, Genova, Italy

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.
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YP050

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

F. Dasoula[1,*], N. Alpert[2], B. Balažiová[3], M. Yildiz[4], A. Ziv[2] on behalf of Vaccination Working Party
[1]Second Department of Pediatrics, P. & A. Kyriakou Children's Hospital, National and Kapodistrian University of Athens, Athens, Greece, [2]Pediatric Rheumatology Unit, Meir Medical Center, Kfar Saba, Sackler School of Medicine, Tel Aviv, Israel, [3]Department of Pediatrics, Comenius University Medical School in Bratislava, National Institute of Children's Diseases, Bratislava, Slovakia, [4]Cerrahpasa Medical School, Istanbul University-Cerrahpasa, Instabul, Turkey

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

YP051
WHEN RHEUMATOLOGY AND GENETICS MEET: A CASE OF JUVENILE IDIOPATHIC ARTHRITIS IN A PATIENT CARRYING 18Q DELETION.

M. F. Gicchino[1,*], T. Giugliano[1], M. Cirillo[1], A. N. Olivieri[1], G. Cinalli[2], S. Perrotta[1], E. Miraglia del Giudice[1], G. Piluso[1], C. Santoro[1]
[1]University of the Study of Campania Luigi Vanvitelli, [2]Santobono-Pausilipon Children's Hospital, Naples, Italy

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

YP052

OBESITY IMPAIRS ACHIEVEMENT OF CLINICAL INACTIVE DISEASE (CID) IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA) TREATED WITH TNF INHIBITORS

F. Basta[1,2,3,*], D. Pires Marafon[1], A. Aquilani[1], M. I. Petrone[4], A. Uva[5], H. Jadoun[1], A. Puccacco[1], R. Nicolai[1], S. Magni Manzoni[1], F. De Benedetti[1]

[1]Division of Rheumatology, IRCCS Ospedale Pediatrico Bambino Gesù, Rome, Italy, [2]University Center of Autoimmunity, Johannes Gutenberg-University, Mainz, [3]Division of Rheumatology, Acura Rheumatology Center Rhineland Palatinate, Bad Kreuznach, Germany, [4]Dipartimento Pediatrico Universitario Ospedaliero, Tor Vergata University, [5]Dipartimento Materno-Infantile e Scienze Urologiche, La Sapienza University, Rome, Italy

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

YP053

CLINICAL SPECTRUM OF CHILDHOOD ARTHRITIS: EXPERIENCE FROM A SINGLE CENTRE IN SUB-HIMALAYAN REGION IN NORTH WEST INDIA

Y. Sharma[1,*], A. Sharma[1]
[1]Pediatrics, Dr Rajendra Prasad Government Medical College, kangra, India

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

YP054

DERMATOLOGIC ADVERSE EVENTS ASSOCIATED WITH JUVENILE IDIOPATHIC ARTHRITIS TREATMENT

J. Smorenburg[1,*], M. de Graaf[1], J. van Straalen[2], A. Consolaro[3], A. Belot[3], E. Alexeeva[3], V. Vargova[3], R. Consolini[3], M. C. Maggio[3], D. Rigante[3], R. Abdwani[3], A. L. Rodriguez Lozano[3], I. Orban[3], N. Ruperto[3], N. Wulffraat[2], S. de Roock[2], J. Swart[2]
[1]Department of Dermatology, University Medical Center Utrecht, [2]Department of Pediatric Immunology and Rheumatology, Wilhelmina Children's Hospital, Utrecht, Netherlands, [3]Paediatric Rheumatology INternational Trials Organisation, CC at IRCCS Istituto Giannina Gaslini, Genoa, Italy

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

YP055

ESTIMATION OF THE VITAMIN D STATUS AND ITS CORRELATION WITH CLINICAL ACTIVITY IN CHILDREN WITH JIA

Y. Vyzhga[1,*]
[1]National Pirogov Memorial Medical University, Vinnytsya, Vinnitsya, Ukraine

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

YP056

MUSCULOSKELETAL COMPLAINTS OF CHILDREN WITH PSORIASIS AND ULTRASONOGRAPHIC EVALUATION OF SUBCLINICAL ACHILLES ENTHESOPATHY

S. G. Karadağ[1], F. Çakmak[1], Z. Topkarcı[2], H. E. Sönmez[1], A. Tanatar[3], M. Kepekçi[4], E. Aldemir[5], N. Topal[5], M. Çakan[1], N. Aktay Ayaz[3,*]

[1]Pediatric Rheumatology, University of Health Science, Kanuni Sultan Süleyman Research and Education Hospital, [2]Dermatology, University of Health Sciences, Bakırköy Dr Sadi Konuk Research and Training Hospital, [3]Pediatric Rheumatology, Istanbul University, Faculty of Medicine, [4]Physical therapy and rehabilitation specialist, [5]Pediatrics, University of Health Science, Kanuni Sultan Süleyman Research and Education Hospital, İstanbul, Turkey

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

YP057

EARLY REGISTRATION OF MYOCARDIAL DISORDERS IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS USING THE 4TH GENERATION ELECTROCARDIOGRAPHY

A. Artsymovych[1,*], O. Oshlianska[1]
[1]pediatrics #1, Shupyk National Medical Academy of Postgraduate Education, Kyiv, Ukraine

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

YP058

A FAMILY HISTORY OF AUTOIMMUNITY IS A RISK FACTOR FOR CELIAC DISEASE AND JUVENILE IDIOPATHIC ARTHRITIS CO-OCCURRENCE

R. Naddei[1,*], S. Di Gennaro[1], R. Troncone[1], V. Discepolo[1], M. Alessio[1]
[1]Mother and Child Department, University of Naples Federico II, Naples, Italy

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

YP059

A LARGE PROPORTION OF PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS UNDERGO ANTIBIOTIC TREATMENT AND ARTHROTOMY AT THE ONSET OF DISEASE.

M. THOMAS[1,2,*], U. MEINZER[3]
[1]National Reference Center for Rare Pediatric Inflammatory Rheumatisms and Systemic Auto-immune diseases, Universitary Hospital Robert Debré, [2]University of Paris, [3]National Reference Center for Rare Pediatric Inflammatory Rheumatisms and Systemic Auto-immune Diseases (RAISE), Universitary Hospital Robert Debré, PARIS, France

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

YP060

VACCINATION COVERAGE IN A COHORT OF PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS: A SINGLE-CENTRE EXPERIENCE

R. Alfani[1], R. Naddei[1], A. Vincenzi[1], F. Viscogliosi[1], A. Paonessa[1], A. Catzola[1,*], M. Alessio[1]
[1]Pediatric Rheumatology Unit, Mother and Child Department, University of Naples Federico II, Naples, Italy

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

YP061

MINIMAL SEDATION/ANXIOLYSIS IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS UNDERGOING INTRARTICULAR INJECTION OF CORTICOSTEROIDS

S. M. Orsi[1,*], M. Gattinara[2], F. Baldo[1,3], S. Carbogno[1,3], A. Petaccia[1], C. Agostoni[1,3], G. Filocamo[1], R. Cimaz[2,4], S. Lanni[1] on behalf of on behalf of the Pediatric Rheumatology Group of the Milan Area (PRAGMA)
[1]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, [2]ASST G. Pini-CTO, [3]University of Milan, [4]Department of Clinical Sciences and Community Health, and RECAP-RD, University of Milan, Milano, Italy

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

YP062

ESTABLISHMENT OF A REGISTRY FOR JUVENILE IDIOPATHIC ARTHRITIS PATIENTS IN SOUTH AUSTRALIA: FOCUS ON PATIENT-REPORTED OUTCOME AND EXPERIENCE MEASURES (PROMS/PREMS)

M. Min[1,2,*], T. Crotti[2], C. Boros[1,3]
[1]University of Adelaide Discipline of Paediatrics, Women's and Children's Hospital, [2]Faculty of Health and Medical Sciences, University of Adelaide, [3]Women's and Children's Hospital Department of Rheumatology, Adelaide, Australia

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

YP063

POSSIBLE ROLE OF EARLY-LIFE EXPOSURES AND ENVIRONMENTAL RISK FACTORS IN JUVENILE IDIOPATHIC ARTHRITIS

O. Koker Turan[1,*], A. Aliyeva[2], M. Yildiz[2], A. Adrovic[2], S. Sahin[2], F. Haslak[2], K. Barut[2], R. Omeroglu[1], O. Kasapcopur[2]
[1]Pediatric Rheumatology, Istanbul Faculty of Medicine, Istanbul University, [2]Pediatric Rheumatology, Cerrahpasa Medical School, Istanbul University, Istanbul, Turkey

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

YP064

ADALIMUMAB TROUGH CONCENTRATIONS ARE ASSOCIATED WITH TREATMENT RESPONSE IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

M. Doeleman[1,*], S. De Roock[1], M. El Amrani[2], E. van Maarseveen[2], N. Wulffraat[1], J. Swart[1]
[1]Paediatric Immunology and Rheumatology, [2]Clinical Pharmacy, University Medical Centre Utrecht (UMCU), Utrecht, Netherlands

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

YP065

ECHOCARDIOGRAPHIC FINDINGS OF CHILDREN WITH JUVENILE SPONDYLOARTHROPATHIES

M. Yıldız[1,*], R. Dedeoglu[2], B. Akdeniz[1], A. Adrovic[1], F. Haslak[1], F. Karagozlu[2], O. Koker[1], S. Sahin[1], K. Barut[1], F. Oztunc[2], O. Kasapcopur[1]
[1]Department of Pediatric Rheumatology, [2]Department of Pediatric Cardiology, Istanbul University-Cerrahpasa , Istanbul, Turkey

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

YP066

SYNOVIAL FLUID NEUTROPHILS FROM PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS DISPLAY A HYPERACTIVATED PHENOTYPE

M. Metzemaekers[1,*], B. Malengier-Devlies[1], K. Yu[1], S. Vandendriessche[1], P. Matthys[1], L. De Somer[1,2], C. Wouters[2], P. Proost[1]
[1]KU Leuven, [2]UZ Leuven, Leuven, Belgium

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.
lien.desomer@uzleuven.b
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

YP067

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)

M. Ganeva[1,*], S. Fuehner[2], C. Kessel[2], C. Hinze[2], J. Klotsche[3], M. Niewerth[3], K. Minden[3], D. Foell[2]
[1]Department of Paediatric Rheumatology, Medical University Sofia, Sofia, Bulgaria, [2]Department of Paediatric Rheumatology and Immunology, University of Münster, Münster, [3]Department of Rheumatology and Clinical Immunology Charité, University Medicine Berlin, Berlin German Rheumatism Research Center, Leibniz Institute, Berlin, Germany

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

YP068

SCREENING FOR ANTITHYROID ANTIBODIES IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS: A SINGLE-CENTRE EXPERIENCE FROM SOUTHERN ITALY

R. Naddei[1,*], C. Esposito[1], F. Orlando[2], R. Alfani[1], V. Discepolo[1], M. Alessio[1]
[1]Pediatric Rheumatology Unit, Mother and Child Department, University of Naples Federico II, [2]Unit of Pediatrics 2, Santobono Pausilipon Children's Hospital, Naples, Italy

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

YP069

WHICH MUSCULOSKELETAL SITES INVOLVED CAN WE EXPECT AT JUVENILE IDIOPATHIC ARTHRITIS (JIA) ONSET?

G. Tarantino[1,*], A. Uva[2], D. Pires Marafon[3], H. Jadoun[3], A. Aquilani[3], R. Nicolai[3], F. De Benedetti[3], S. Magni Manzoni[3]
[1]Catholic University of Sacred Heart, [2]Sapienza-University , [3]Division of Rheumatology, IRCCS Ospedale Pediatrico Bambino Gesù, Rome, Italy

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

YP070

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

L. Baas[1,*], J. van Straalen [1], P. Quartier [2], V. Panaviene[2], J. Anton Lopez[2], I. Koné-Paut [2], S. Hashad[2], V. Keltsev[2], J. Brunner[2], F. Gok [2], G. Vega Cornejo[2], V. Chasnyk[2], S. de Roock [1], N. Wulffraat[1], J. Swart [1], N. Ruperto [2]
[1]Paediatric Rheumatology, Wilhelmina Children's Hospital, Utrecht, Netherlands, [2]Paediatric Rheumatology INternational Trials Organisation, CC at IRCCS Istituto Giannina Gaslini, Genoa, Italy

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

YP071

METHOTREXATE RESPONSE SUBGROUPS IDENTIFIED IN TWO UK JUVENILE IDIOPATHIC ARTHRITIS COHORTS

S. J. W. Shoop-Worrall[1,2,*], K. L. Hyrich[2,3], L. R. Wedderburn[4,5,6], W. Thomson[3,7], N. Geifman[1] on behalf of BSPAR-ETN Study, BCRD Study, CLUSTER

[1]Centre for Health Informatics, [2]Centre for Epidemiology Versus Arthritis, The University of Manchester, [3]NIHR Manchester BRC, Manchester University NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, [4]Centre for Adolescent Rheumatology Versus Arthritis , UCL, UCLH and GOSH, [5]Infection Inflammation and Rheumatology, UCL GOS Institute of Child Health, [6]NIHR Great Ormond Street Hospital Biomedical Research Centre, London, [7]Centre for Genetics and Genomics Versus Arthritis, The University of Manchester, Manchester, United Kingdom

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

YP072

RENAL OUTCOMES OF A COHORT OF PAEDIATRIC PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

M. F. Gicchino[1,*], A. Di Sessa[1], S. Guarino[1], E. Miraglia del Giudice[1], A. N. Olivieri[1], P. Marzuillo[1]
[1]University of the Study of Campania Luigi Vanvitelli, Naples, Italy

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

YP074

OVERLAP SYNDROME OF IDIOPATHIC INFLAMMATORY MYOPATHY WITH JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS PRESENTING WITH MACROPHAGE ACTIVATION SYNDROME

R. L. D. Bragança[1,*], R. P. Silva[2], J. F. Mendes[2], C. Rocha[2], J. L. Barreira[1], F. Aguiar[3], M. Rodrigues[3], I. Brito[3]
[1]Serviço de Pediatria, Centro Hospitalar Universitário de São João, Porto, [2]Serviço de Pediatria, Centro Hospitalar Entre Douro e Vouga, Feira, [3]Unidade de Reumatologia Pediátrica e Jovem Adulto , Centro Hospitalar Universitário de São João, Porto, Portugal

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

YP075

USE OF MYCOPHENOLATE MOFETIL IN INFLAMMATORY MYOPATHIES OF CHILDHOOD

G. C. Varnier[1,2,*], A. Consolaro[2,3], I. L. Cheng[4], A. Silva Riveiro[3], C. Pilkington[4], A. Ravelli[2,3,5] on behalf of Juvenile Dermatomyositis Research Group (JDRG)
[1]Paediatric Rheumatology, Royal Manchester Children's Hospital, Manchester, United Kingdom, [2]University of Genoa, [3]Paediatric Rheumatology, IRCCS G. Gaslini, Genoa, Italy, [4]Paediatric Rheumatology, Great Ormond Street Hospital, London, United Kingdom, [5]Sechenov First Moscow State Medical University, Moscow, Russian Federation

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

YP076

EVALUATION OF DISEASE ACTIVITY IN CHILDREN WITH JUVENILE DERMATOMYOSITIS: A COMPARISON BETWEEN ELECTROMYOGRAPHY AND WHOLE BODY-MAGNETIC RESONANCE IMAGING

S. Carbogno[1,2,*], M. Brusamolino[1], S. Lanni[2], A. Petaccia[2], C. Agostoni[1,2], R. Cimaz[3,4], G. Filocamo[2], F. Minoia[2], A. Cappellari[2] on behalf of on behalf of Pediatric Rheumatology Group of the Milan Area (PRAGMA)
[1]University of Milan, [2]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, [3]ASST G. Pini-CTO, [4]Department of Clinical Sciences and Community Health, and RECAP-RD, University of Milan, Milan, Italy

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

YP077

CLINICAL FEATURES, MUSCLE BIOPSY SCORES, MYOSITIS SPECIFIC ANTIBODY PROFILES AND OUTCOME OF JDM PATIENTS

E. Sag[1,*], S. Demir[1], Y. Bilginer[1], B. Talim[2], S. Ozen[1]
[1]Pediatric Rheumatology, [2]Pediatric Pathology Unit, Hacettepe University, Ankara, Turkey

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

YP078

INVESTIGATING NOVEL MECHANISMS OF T CELLS IN THE PATHOGENESIS OF JUVENILE DERMATOMYOSITIS

L. R. Marshall[1,*], C. T. Deakin[1,2,3], E. C. Rosser[1,3], D. Eleftheriou[1], L. R. Wedderburn[1,2,3] on behalf of the UK Juvenile Dermatomyositis Research Group
[1]III, UCL Great Ormond Street Institute of Child Health, [2]NIHR Biomedical Research Centre at GOSH, [3]Centre for Adolescent Rheumatology Versus Arthritis at UCL, UCLH and GOSH, London, United Kingdom

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

YP079

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

A. De Matteis[1,*], D. Pires Marafon[1], I. Caiello[1], M. Pardeo[1], G. Marucci[1], A. Arduini[1], E. Sacco[1], G. Prencipe[1], F. De Benedetti[1], C. Bracaglia[1]
[1]Division of Rheumatology, IRCCS, Ospedale Pediatrico Bambino Gesù, Rome, Italy

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

YP080

LIFE-THREATENING MACROPHAGE ACTIVATION SYNDROME WITH FULMINANT MYOCARDITIS SUCCESSFULLY RESCUED BY HIGH DOSE INTRAVENOUS ANAKINRA

A. Meneghel[1,*], G. Martini[1], A. Amigoni[2], A. Pettenazzo[2], M. Padalino[3], F. Zulian[1]
[1]Department for Women and Child Health-University Hospital of Padua, Pediatric Rheumatology Unit, [2]Department for Women and Child Health-University Hospital of Padua, Pediatric Intensive Care Unit, [3]Department of Cardiac, Thoracic and Vascular Sciences, 3Pediatric and Congenital Cardiac Surgery, Padua, Italy

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

YP081

ANKLE TENOSYNOVITIS IN PONCET'S DISEASE

L. R. Campos[1,*], K. L. Baptista[1], J. Caldas[2], V. Orenbuch [2], I. Gomes[3], C. A. A. Cardoso[3], C. Canella[4]
[1]Pediatric Rheumatology, Department of Pediatrics, [2]Hospital Universitário Antônio Pedro, Universidade Federal Fluminense, Niterói - Rio de Janeiro, Brazil, [3]Department of Maternal and Child, [4]Department of Radiology, Hospital Universitário Antônio Pedro, Universidade Federal Fluminense, Niterói - Rio de Janeiro, Brazil

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

YP082

CAMPTODACTYLY-ARTHROPATHY-COXA VARA-PERICARDITIS SYNDROME: A RARE AND MISDIAGNOSED CONDITION

L. R. Campos[1,*], K. L. Baptista[1], L. Ferreira[2], L. Lima[3], C. Canella[3], A. Serfaty[4]
[1]Pediatric Rheumatology, Department of Pediatrics, [2]Pediatrics, [3]Department of Radiology, Hospital Universitário Antônio Pedro, Universidade Federal Fluminense, Niterói - Rio de Janeiro, [4]Department of Radiology, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil

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

YP083

TREATING TWO FIBRODYSPLASIA OSSIFICANS PROGRESSIVA PATIENTS WITH INTERLEUKIN-1 INHIBITORS

R. Haviv[1,*], V. Moshe[2], F. De Benedetti[3], G. Prencipe[3], N. Rabinowicz[2], Y. Uziel[1]
[1]Pediatric Rheumatology Unit, Department of Pediatrics, Meir Medical Center, Sackler School of Medicine, Tel Aviv University, [2]Pediatric Rheumatology Unit, Department of Pediatrics, Meir Medical Center, Kfar Saba, Israel, [3]Division of Rheumatology, Bambino Gesù Children's Hospital IRCCS, Rome, Italy

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

YP084

GENETIC SYNDROMES MIMICKING RHEUMATOLOGIC DISEASES

U. Kaya Akca[1,*], P. O. Simsek Kiper[2], G. Urel Demir[2], E. Sag[1], E. Atalay[1], G. E. Utine[2], M. Alikasifoglu[3], K. Boduroglu[2], Y. Bilginer[1], S. Ozen[1]

[1]Department of Pediatric Rheumatology, [2]Department of Pediatric Genetics, [3]Department of Medical Genetics, Hacettepe University Faculty of Medicine, Ankara, Turkey

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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YP085

PEDIATRIC SJÖGREN SYNDROME: AN ITALIAN CASE SERIES

M. Romano[1,*], T. Giani[2], A. Marino[3], C. Gaggiano[4], G. Filocamo[5], I. Pontikaki[6], R. Cimaz[7] on behalf of Pediatric Rheumatology Group of the Milan Area
[1]Pediatric Rheumatology, ASST-G.Pini-CTO, Milan, Italy, Milan, [2]AOU Meyer, Florence, [3]Department of Pediatrics, Desio Hospital, ASST Monza , Desio, Monza, [4]Clinical Pediatrics, Department of Molecular Medicine and Development, University of Siena, Siena, [5]Pediatric Rheumatology, Fondazione IRCCS Cà Granda ospedale Maggiore Policlinico, Milan, Italy, [6]Pediatric Rheumatology, ASST-PINI-CTO, Milan, Italy, [7]Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy

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

YP086

SYSTEMIC JIA, KAWASAKI SYNDROME AND MACROPHAGE ACTIVATION, WHAT ELSE? NOT ONLY COVID-19.

R. Dagher[1,*], E. Sfeir[1], V. Modica[2]
[1]Pediatric department, Notre Dame de Secours University Hospital, Byblos, [2]Holy Family University, Batroun, Lebanon

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

YP087

THE MUSCULOSKELETAL MANIFESTATIONS OF SCURVY: A DIAGNOSTIC CHALLENGE FOR THE RHEUMATOLOGIST

T. Lastella[1], R. Naddei[1,*], F. Orlando[2], C. Porfito[1], F. Mozzillo[1], M. Amico[1], M. Alessio[1]
[1]Pediatric Rheumatology Unit, Mother and Child Department, University of Naples Federico II, [2]Rheumatology Unit, Department of Pediatrics, Santobono-Pausilipon Children's Hospital, Naples, Italy

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

YP088

INFLAMMATORY ARTHRITIS COMPLICATING GALACTOSIALIDOSIS : A CASE REPORT AND REVIEW OF THE LITERATURE

F. Verkuil[1,2,*], A. M. Bosch[3], P. A. Struijs[4], R. Hemke[2], J. M. van den Berg[1]
[1]Pediatric Immunology, Rheumatology and Infectious Diseases, [2]Radiology and Nuclear Medicine, [3]Pediatric Metabolic Diseases, [4]Orthopedic Surgery, Amsterdam UMC, location AMC, Amsterdam, Netherlands

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

YP089

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

M. C. Marques[1,*], N. Tennermann[1], S. Angevare[2], R. Sinha[3], J. Tousseau[4], P. Readon[3], S. Lapidus[5], G. Schulert[6], K. Durrant*[4], F. Dedeoglu*[1] on behalf of *Contributed Equally
[1]Boston Children`s Hospital, Boston, United States, [2]Autoinflammatory org, KAISZ/VAISZ, ENCA, National Organizations, Netherlands, [3]SJIA Foundation, [4]Autoinflammatory Alliance, National Organization, [5]Joseph M. Sanzari Children's Hospital, Hackensack, [6]University of Cincinnati College of Medicine, Cincinnati, United States

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.
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YP090

CAN ARTIFICAL INTELLIGENCE HELP WITH DIAGNOSING GROWING PAIN?

E. D. Batu[1,2,*], F. Akal[3], S. G. Karadağ[4], F. Demir[5], N. Aktay Ayaz[4], B. Sözeri[5]
[1]Department of Pediatrics, Division of Rheumatology, Hacettepe University Faculty of Medicine, [2]Department of Pediatrics, Division of Rheumatology, Ankara Training and Research Hospital, University of Health Sciences, [3]Department of Computer Engineering, Hacettepe University, Ankara, [4]Department of Pediatrics, Division of Rheumatology, Kanuni Sultan Suleyman Training and Research Hospital, University of Health Sciences, [5]Department of Pediatrics, Division of Rheumatology, Umraniye Training and Research Hospital, University of Health Sciences, Istanbul, Turkey

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

YP091

STRUCTURAL AND FUNCTIONAL STATUS OF THE BONE TISSUE IN CHILDREN DURING GROWTH SPURT

N. Osman[1,*], T. Frolova[1], N. Stenkova[1], I. Siniaieva[1]
[1]Kharkiv National Medical University, Kharkiv, Ukraine

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

YP092

A NOVEL MULTIDIMENSIONAL ASSESSMENT TOOL FOR CLINICAL CARE OF PATIENTS WITH JUVENILE FIBROMYALGIA SYNDROME

E. Drago[1,*], M. Mazzoni[1], M. Macciò[2], C. Lavarello[1], M. Sansone[3], R. Russo[4], E. Pescio[4], A. Ronchetti[5], A. Ravelli[1], C. Malattia[1]

[1]Clinica Pediatrica e Reumatologia, IRCSS Giannina Gaslini, [2]Università degli studi di Genova, [3]Child Neuropsychiatry Unit, IRCSS Giannina Gaslini, [4]Clinical Psicology Unit, AMRI Onlus, [5]UOC Medicina Fisica e Riabilitazione , IRCSS Giannina Gaslini, Genova, Italy

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

YP093

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

A. Y. Spivakovskaya[1,*], Y. M. Spivakovskiy[1], Y. V. Chernenkov[1]
[1]Depertment of Hospitality Pediatrics, SARATOV STATE MEDICAL UNIVERSITY, Saratov, Russian Federation

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

YP094

PSYCHOLOGICAL INVOLVEMENT IN YOUNG PEOPLE WITH CHRONIC RHEUMATOLOGICAL DISEASE: WHAT INPUT DO PATIENTS NEED?

O. Ogundiran[1,2,*], A. Leahy [1,2], E. Lee[3], A. Griffin [3], S. Hartfree[2], S. Small[2], B. Davidson[2], A. De Schutter[3], H. De Graaf[2]
[1]Faculty of Medicine, University of Southampton, [2]Paediatric Rheumatology, [3]University Hospital Southampton, Southampton, United Kingdom

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

YP095
DESCRIPTION OF THE CHARACTERISTICS OF THE NAILFOLD CAPILLARY STRUCTURE IN HEALTHY CHILDREN:
A PILOT STUDY

H. Adiguzel Dundar[1,*], A. Adrovic[2], S. Demir[3], F. Demir[4], F. Cakmak[5], N. Aktay Ayaz[5], B. Sozeri[4], Y. Bilginer[3], O. Kasapcopur[2], E. Unsal[1]
[1]Department of Pediatrics, Pediatric Rheumatology Unit, DOKUZ EYLUL UNIVERSITY FACULTY OF MEDICINE,, izmir, [2]Department of Pediatrics, Pediatric Rheumatology Unit, Istanbul University-Cerrahpaşa, Cerrahpaşa Medical Faculty, Istanbul, [3]Department of Pediatrics, Pediatric Rheumatology Unit, Hacettepe University Faculty of Medicine, Ankara, [4]Department of Pediatrics, Pediatric Rheumatology Unit, Health Sciences University, Ümraniye Training and Research Hospital, [5]Department of Pediatrics, Pediatric Rheumatology Unit, Istanbul University Çapa Medical Faculty, Istanbul, Turkey

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

YP096

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

S. Papailiou[1,*], F. Dasoula[2], M. N. Tsolia[1], D. N. Maritsi[1]
[1]Second Department of Paediatrics, 'P.&A. Kyriakou' Children's Hospital, [2]Second Department of Paediatrics, 'P&A. Kyriakou' Children's Hospital, National and Kapodistrian University of Athens, Athens, Greece

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

YP097

THE COMPARISON OF THE HLA-B27-POSITIVE AND HLA-B27-NEGATIVE PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS IN THE SINGLE CENTER

R. Raupov[1,*], L. Sorokina[2], M. Gharabaghtsyan[3], N. Garipova[4], I. Avrusin[1], L. Snegireva[1], M. Dubko[1], A. Santimov[1], E. Gaidar[1], V. Masalova[1], E. Isupova[1], I. Chikova[1], T. Likhacheva[1], F. Vinokurova [5], M. Kostik[1]
[1]Saint Petersburg State Pediatric Medical University, [2]Leningrad's Regional Children's Clinical Hospital, Saint Petersburg, Russian Federation, [3]Institute of Child and Adolescent Health with the Arabkir Medical Center,, Yerevan, Armenia, [4]Almazov National Medical Research Centre, Saint Petersburg, [5]Yakut Science Centre of complex medical problems, Yakutsk, Russian Federation

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

YP098

CROSS-SECTIONAL STUDY OF FECAL CALPROTECTIN IN CHILDREN WITH VARIOUS FORMS OF ARTHRITIS AND NON-INFLAMMATORY MUSCULOSKELETAL DISORDERS: A SINGLE CENTRE EXPERIENCE

L. Lamot[1,2,*], A. Kovacevic[1], M. Miler[3], M. Lamot[1], N. Nikolac Gabaj[3], M. Vidović[1], M. Harjaček[1,2]
[1]Pediatrics, Sestre milosrdnice University Hospital Center, [2]Pediatrics, University of Zagreb School of Medicine, [3]Clinical Chemistry, Sestre milosrdnice University Hospital Center, Zagreb, Croatia

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

YP099

ACHIEVING INACTIVE DISEASE IN ERA WITH SECUKINUMAB FOLLOWING TNF INHIBITOR FAILURE; A REAL-LIFE, DUAL-CENTER EXPERIENCE

S. Papailiou[1,*], M. Onoufriou[2], F. Dasoula[1], M. N. Tsolia[1], D. N. Maritsi[1,3]
[1]Second Department of Paediatrics, 'P. & A. Kyriakou' Children's Hospital, National and Kapodistrian University of Athens, Athens, Greece, [2]Rheumatology Unit, Department of Paediatrics, 'Makarios III' Children's Hospital, Nicosia, [3]Rheumatology Unit, Department of Paediatrics, 'Makarios III' Children's Hospital , Nicosia, Cyprus

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

YP100

COXARTHROSIS RISK FACTORS IN SYSTEMIC AND NON-SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS.

L. Sorokina[1,*], I. Avrusin[2], R. Raupov[2], N. Garipova[3], M. Gharabaghtsyan[4], S. Khrypov[5], E. Isupova[2], E. Gaidar[2], A. Santimov[2], I. Chikova[2], M. Dubko[2], V. Masalova[2], T. Likhacheva[2], L. Snegireva[2], M. Kostik[2]
[1]Leningrad's Regional Children's Clinical Hospital, Saint-Petersburg, Russia, [2]Saint-Petersburg State Pediatric Medical University, [3]Almazov National Medical Research Centre, Saint Petersburg, Russian Federation, [4]Institute of Child and Adolescent Health with the Arabkir Medical Center, Yerevan, Armenia, [5]Saint-Petersburg clinical research-practical center for specialized healthcare (oncology), Saint Petersburg, Russian Federation

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

YP101

EFFECT OF DOSE AND DURATION OF GLUCOCORTICOID TREATMENT ON PROGNOSIS OF SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

A. Paç Kısaarslan[1], S. Ozdemir Cicek[1,*], N. Şahin[1], M. Basol[2], S. Doğantan[1], S. N. Taşkın[1], M. H. Poyrazoğlu[1]
[1]Pediatric Rheumatology, Erciyes University Faculty of Medicine, Kayseri, [2]Biostatistics,, Abant İzzet Baysal University Faculty of Medicine, Bolu, Turkey

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)			
Rash	23	0,644 (0,223-1,864)	0,149		
Joint involvement	33	0,440 (0,189-1,026)			
Morning stiffness	38	1,603 (0,653-3,936)	0,417		
Lymphadenopathy	89	2,099 (0,963-4,574)			
Hepatosplenomegaly	96	1,108 (0,578-2,125)	0,057		
Macrophage activating syndrome	10	0,846 (0,648-1,105)			
Patient/parent VAS	14	1,002 (0,777-1,293)	0,303		
PGA	42		0,062		
	42		0,757		
	42		0,219		
			0,987		
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)			
PLT (/µL)	42	0,998 (0,997-1,000)	0,407	0,997 (0,995-0,999)	**0,008**
ESR (mm/h)	42	1,000 (0,991-1,008)			

CRP (mg/L) 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 4 2 2 4 1 7 2 7 1 7	1,000 (0,995-1,006) 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)	**0,028** 0,925 0,892 0,474 0,134 0,694 0,802 0,662 0,711 0,924 0,999		
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)	0,099 0,724 0,464 0,159 **0,018** **0,007**	**-** 0,837 (0,754-0,929)	**-** **0,001**
*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

YP102

PERFORMANCE OF THE "MS-SCORE" AND "HSCORE" IN THE DIAGNOSIS OF MAS IN SYSTEMIC JIA PATIENTS

E. Sag[1,*], A. Keskin[1], S. Demir[1], M. K. Cuceoglu[1], E. Atalay[1], U. K. Akca[1], E. D. Batu[1], Y. Bilginer[1], S. Ozen[1]
[1]Pediatric Rheumatology, Hacettepe University, Ankara, Turkey

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

YP103

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

E. M. Smith[1,2,*], S. Gorst[3], M. Beresford[1,2], B. Young[4]
[1]Women and Children's Health, University of Liverpool, [2]Paediatric Rheumatology, Alder Hey Children's Hospital, [3]Department of Biostatistics, [4]Institute of Population Health Sciences, University of Liverpool, Liverpool, United Kingdom

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

YP104

CHILDHOOD SYSTEMIC LUPUS ERYTHEMATOSUS: EXPERIENCE FROM SUB -HIMALAYAN REGION OF NORTH WEST INDIA

Y. Sharma[1,*], A. Sharma[1]
[1]Pediatrics, Dr Rajendra Prasad Government Medical College, kangra, India

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

YP105

A RARE CASE OF MIXED TYPE AUTOIMMUNE HEMOLYTIC ANEMIA IN A 15-YEARS OLD ADOLESCENT– DON'T ALWAYS BLAME LUPUS

C. D. A. S. Faria[1], J. A. Guimarães[1], L. R. Campos[2,*], K. L. Baptista[2], F. P. L. F. Veiga[3], T. G. Noronha[1], D. P. Bulkool[1], R. D. C. Villalba[1], A. C. F. Bassani[1], C. Pinheiro[4], T. R. D. Souza[4], B. Cohen[4]
[1]Pediatrics, [2]Pediatric Rheumatology, Department of Pediatrics, [3]Pediatric Nephrology, Hospital Universitário Antônio Pedro, Universidade Federal Fluminense, Niterói - Rio de Janeiro, [4]Hematologistas Associados, Rio de Janeiro, Brazil

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

YP106

BICKERSTAFF ENCEPHALITIS WITH OVERLAPPING GUILLAIN-BARRÉ SYNDROME AS A FIRST MANIFESTATION OF JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS: A CASE REPORT

A. Koryllou[1,*], M. Mejbri[1], S. Garcia-Tarodo[2], P. Parvex[3], E. Gonzalez Nguyen Tang[3], C. M. Korff[2], M. Hofer[1]
[1]Pediatric Immuno-Rheumatology Unit, Lausanne University Hospital (CHUV), Lausanne, [2]Pediatric Neurology Unit, [3]Pediatric Nephrology Unit, University Hospitals of Geneva, Geneva, Switzerland

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

YP107

SPECTRUM OF CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS AND ITS CLINICAL COURSE

P. Morán Álvarez[1,*], A. Boteanu[2], M. Vázquez Díaz[2]
[1]Rheumatology, [2]Hospital Ramón y Cajal, Madrid, Spain

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

YP108

THE USE OF 'THE LUPUS CHECKLIST' IN CONSULTATIONS WITH PAEDIATRIC PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN IMPROVING PATIENT MONITORING OUTCOMES

K. A. Alexander[1,*], C. Scott[2], L. B. Lewandowski[3]
[1]Western General Hospital, Edinburgh, United Kingdom, [2]Department of Paediatric Rheumatology, Red Cross War Memorial Childrens Hospital and University of Cape Town, Cape Town, South Africa, [3]National Institute of Arthritis, Musculoskeletal and Skin Diseases, Bethesda, United States

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

YP109

NEUROLOGICAL MANIFESTATIONS OF PEDIATRIC SYSTEMIC LUPUS ERYTHEMTOSUS

Y. Gazar[1,*], S. Y. Mostafa[2], H. M. Emam[2], S. S. Rashed[2]
[1]Rheumatology, [2]neurology, Al-Azhar university, cairo, Egypt

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

YP110

LUPUS MANIFESTATIONS IN CHILDREN WITH PRIMARY IMMUNODEFICIENCY DISEASES: PHENOTYPIC AND GENETIC FEATURES AND OUTCOME

S. M. Al-Mayouf[1,2], H. Alreefi[3,*], T. Alsinan[3], G. AlSalmi[4], A. AlRowais[5], W. Al-Herz[6], A. Alsonbul[4], H. Al-Mousa[4]
[1]Pediatric Rheumarology, King Faisal Specialist Hospital and Research Center, [2]Pediatric Rheumarology, [3]Alfaisal University, [4]King Faisal Specialist Hospital , [5]Prince Sultan Military Medical City, Riyadh, Saudi Arabia, [6]Al-Sabah Hospital, Kuwait, Kuwait

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

YP111

OFATUMUMAB USE IN JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS: A SINGLE CENTRE EXPERIENCE

O. Kul Cinar[1,*], M. Marlais[2], M. Al-Obaidi[1], F. I. Cheng[3], K. Tullus[2], P. Brogan[1,4], E. Moraitis[1]
[1]Paediatric Rheumatology, [2]Paediatric Nephrology, [3]Pharmacy, Great Ormond Street Hospital for Children NHS Trust, [4]Infection, Immunity and Rheumatology Section, UCL Great Ormond Street Institute of Child Health, London, United Kingdom

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	Lupus nephritis, ISN/RPS Class III Serositis (pleural and pericardial effusions) Haemat	Haematological (ITP, anaemia) Arthritis

	Class III) Haematological		ological 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

YP112

HOW DO NOT TO MISS THE SYSTEMIC LUPUS ERYTHEMATOSUS IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS: PRELIMINARY RESULTS OF A RETROSPECTIVE STUDY.

A. Kupreeva[1,*], E. Kuchinskaya[2], L. Sorokina[3], M. Dubko [1], A. Mazing[4], O. Tkachenko[4], S. Lapin [4], M. Kostik[1,2]
[1]Saint-Petersburg State Pediatric Medical University, [2]Almazov National Medical Research Centre, [3]Leningrad's Regional Children's Clinical Hospital, [4]Pavlov First Saint Petersburg State Medical University, Saint Petersburg, Russian Federation

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

YP113

RELIABLE DETECTION OF SUBTYPES OF NAILFOLD CAPILLARY HAEMORRHAGES IN CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

S. C. Bergkamp[1,*], D. Schonenberg-Meinema[1] on behalf of EULAR study group on Microcirculation in Rheumatic Diseases, A. Nassar-Sheikh Rashid[1], K. Melsens[2,3] on behalf of EULAR study group on Microcirculation in Rheumatic Diseases, A. Vanhaecke[2,3] on behalf of EULAR study group on Microcirculation in Rheumatic Diseases, M. J. Boumans[4], P. C. Hissink Muller[5], T. W. Kuijpers[1], J. M. van den Berg[1], V. Smith[2,3,6] on behalf of EULAR Study Group on Microcirculation in Rheumatic Diseases

[1]Department of Pediatric Immunology, Rheumatology and Infectious diseases, Amsterdam University Medical Centers , Amsterdam, Netherlands, [2]Department of Rheumatology, Ghent University Hospital, [3]Faculty of Internal Medicine, Ghent University, Ghent, Belgium, [4]Department of Rheumatology, Maxima Medical Centre, Eindhoven, [5]Department of Pediatric Rheumatology, Leiden University Medical Center , Leiden, Netherlands, [6]Unit for Molecular Immunology and Inflammation, VIB Inflammation Research Center (IRC), Ghent, Belgium

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

YP114

VALIDATION OF THE 2019 ACR/EULAR CLASSIFICATION CRITERIA OF SYSTEMIC LUPUS ERYTHEMATOSUS IN A MEXICAN PEDIATRIC POPULATION

R. E. Loor[1,*], E. Faugier[1]
[1]Reumatología Pediátrica, HOSPITAL INFANTIL DE MÉXICO FEDERICO GÓMEZ, México, Mexico

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

YP115

EVALUATION OF FLARE RATE AND TAPERING STRATEGIES IN JUVENILE IDIOPATHIC ARTHRITIS

A. García Fernández[1,*], A. Briones Figueroa[1], L. Calvo Sanz[1], Á. Andreu Suárez[1], A. Boteanu[1]
[1]Rheumatology, Ramón y Cajal University Hospital, Madrid, Spain

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

YP116

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

S. Rodríguez Aguayo[1,*], J. F. Gaytan Morales[2], I. Castorena Villa[2], D. C. Cortes Flores[2], E. Faugier Fuentes[3]
[1]Pediatric rheumatology, [2]Bone marrow transplant, Hospital Infantil de México Federico Gómez, [3]Pediatric rheumatology, Hospital Infantil de México , Ciudad de México, Mexico

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

YP117
HYPERSENSITIVITY REACTIONS WITH DMARDS
M. Kasap Cuceoglu[1,*], E. Sag[1], S. Demir[1], U. Kaya Akca[1], E. Atalay[1], Ö. Uysal Soyer[2], E. D. Batu[1], Y. Bilginer[1], S. Ozen[1]
[1]Pediatric Rheumatology, [2]Pediatric Allergy, Hacettepe University, Ankara, Turkey

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

YP118

THE RANGE OF BIOLOGICAL DRUGS USED IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS, SARATOV REGION EXAMPLE.

Y. M. Spivakovskiy[1], A. Y. Spivakovskaya[1,*], Y. V. Chernenkov[1]
[1]Depertment of Hospitality Pediatrics, SARATOV STATE MEDICAL UNIVERSITY, Saratov, Russian Federation

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

YP120

BIOLOGICAL THERAPIES IN JUVENILE IDIOPATHIC ARTHRITIS: ARE THERE ANY DIFFERENCES BETWEEN CATEGORIES?

L. Calvo Sanz[1], A. García Fernández[1,*], A. Briones Figueroa[1], Á. Andreu Suárez[1], A. Boteanu[1]
[1]Rheumatology, Ramón y Cajal University Hospital, Madrid, Spain

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

YP121

ANTI-ADALIMUMAB ANTIBODIES DETECTION USING A NOVEL PEPTIDE-BASED ASSAY IN A COHORT OF PEDIATRIC PATIENTS WITH CHRONIC RHEUMATIC DISORDERS : A PILOT STUDY

E. Marrani[1,*], H. Rusche[2], F. Terzani[3], E. Peroni[2], F. Real-Fernandez[4], O. Monasson[2], R. Ponti[5], G. Simonini[6], A. M. Papini[3], P. Rovero[4]

[1]Rheumatology Unit, Anna Meyer Children Hospital, Firenze, Italy, [2]Peptlab@CY and Laboratory of Chemical Biology, Cergy-Paris University, Cergy-Pontoise, France, [3]PeptLab, Dep. Chemistry, University of Florence, sesto fiorentino, [4]PeptLab, Dep. NEUROFARBA, University of Florence, firenze, [5]Pediatric Department, University of Udine, Udine, [6]Rheumatology Unit, AOU Meyer, NEUROFARBA, University of Florence, firenze, Italy

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

YP122

SAFETY ON THE USE OF BISPHOSPHONATES IN PAEDIATRICS

S. Odorico[1], E. Jeziorski[2], F. Rivier[3], T.-A. Tran[1,*]
[1]Pediatrics, Nîmes University Hospital, Nîmes, [2]Pediatrics, [3]Pediatric Neurology, Montpellier University Hospital, Montpellier, France

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

YP123

A REAL-LIFE STUDY OF EFFECTIVENESS AND TOLERABILITY OF ADALIMUMAB BIOSIMILAR IN JIA-A SINGLE CENTRE EXPERIENCE

V. Choida[1,2,*], S.-A. Yeoh[2], C. Fisher[1,2], M. Leandro[1,2], D. Sen[1,2], C. Ciurtin[1,2]
[1]Centre for Adolescent Rheumatology Versus Arthritis, University College London, [2]Rheumatology, University College London Hospitals, London, United Kingdom

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

YP124

METHOTREXATE INTOLERANCE: CHILDREN VS ADULTS

U. Kaya Akca[1,*], B. Farisogullari[2], G. K. Yardimci[2], S. Demir[1], E. Sag[1], E. Atalay[1], M. Kasap Cuceoglu[1], L. Kilic[2], S. Ozen[1], Y. Bilginer[1]
[1]Division of Pediatric Rheumatology, Department of Pediatrics, [2]Division of Rheumatology, Department of Internal Medicine, Hacettepe University Faculty of Medicine, Ankara, Turkey

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

YP125

RATES OF PSORIASIS DE-NOVO IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS PRECEDING ANTI-TNF THERAPY: A SINGLE-CENTER OBSERVATIONAL STUDY

N. Tsurikova[1,*], E. Ligostaeva[1], V. Avdeenko[1], N. Kobzeva[1], I. Tsiganok[1]
[1]Rostov Regional Children Hospital, Rostov-on-don, Russian Federation

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

YP126

THE POSSIBILITY OF INCREASING THE INTERVALS BETWEEN INJECTIONS OF TNF-ALFA INHIBITORS IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS: A SINGLE-CENTER OBSERVATIONAL STUDY

N. Tsurikova[1,1,*], E. Ligostaeva[1], V. Avdeenko[1], N. Kobzeva[1], I. Tsiganok[1]
[1]Rostov Regional Children Hospital, Rostov-on-don, Russian Federation

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

YP127

NEUTRALIZING ANTI-RITUXIMAB ANTIBODIES IN CHILDREN WITH IMMUNE MEDIATED DISEASES

I. Oomen[1,*], A. Nassar-Sheikh Rashid[1], A. H. Bouts[2], S. C. Gouw[3], T. W. Kuijpers[1], T. Rispens[4], A. de Vries[4], G. Wolbink[4], J. M. van den Berg[1], D. Schonenberg-Meinema[1]
[1]Department of Pediatric Immunology, Rheumatology and Infectious diseases, [2]Department of Pediatric Nephrology, [3]Department of Pediatric Hematology, Amsterdam University Medical Centers, [4]Department of Immunopathology, Sanquin Research and Landsteiner Laboratory, Amsterdam, Netherlands

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

YP128

SWITCHING FROM REFERENCE TO BIOSIMILARS DOES NOT REDUCE EFFICACY AND SAFETY IN JUVENILE IDIOPATHIC ARTHRITIS

I. Maccora[1,*], G. Simonini[1], A. Bettiol[2], I. Pagnini[3], N. Lombardi[4], V. Maniscalco[1], G. Crescioli[4], E. Marrani[1], R. Bonaiuti[4], M. V. Mastrolia[1], C. Ravaldi[5], A. Vannacci[4]

[1]Rheumatology Unit, Anna Meyer Children's Hospital and Department of Neurosciences, Psychology, Drug Research and Child Health, Section of Paediatric, , University of Florence, [2]Department of Neurosciences, Psychology, Drug Research and Child Health, Section of Pharmacology and Toxicology,University of Florence, [3]Rheumatology Unit, Anna Meyer Children's Hospital and Department of Neurosciences, Psychology, Drug Research and Child Health, Section of Paediatric, University of Florence, [4]Department of Neurosciences, Psychology, Drug Research and Child Health, Section of Pharmacology and Toxicology, University of Florence, [5]Department of Health Sciences, University of Florence, Florence, Italy

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

YP129

SUCCESSFUL HAPLO-IDENTICAL ALLOGENIC BONE MARROW TRANSPLANTATION IN A CHILD WITH REFRACTORY SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

G. Morelle[1,*], D. Moshous[1], P. Quartier[1]
[1]Paediatric Hematology-Immunology and Rheumatology Department,, Hôpital Necker-Enfants Malades, Paris, France

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

YP130

EFFICACY AND SAFETY ON THE USE OF BISPHOSPHONATES FOR SECONDARY OSTEOPOROSIS IN PAEDIATRICS

S. Odorico[1], E. Jeziorski[2], F. Rivier[3], T.-A. Tran[1,*]
[1]Pediatrics, Nîmes University Hospital, Nîmes, [2]Pediatrics, [3]Pediatric Neurology, Montpellier University Hospital, Montpellier, France

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

YP131

TO TAPER OR NOT TO TAPER IN JUVENILE IDIOPATHIC ARTHRITIS: IS THERE A RISK OF DEVELOPMENT OF UVEITIS FLARES?

M. A. TERAN[1,*], A. BOTEANU[1], C. GUILLEN[1], C. PIJOAN[1]
[1]REUMATOLOGIA, HOSPITAL RAMON Y CAJAL, MADRID, Spain

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

YP132

THE CLINICAL FEATURES OF UVEITIS DE-NOVO IN JUVENILE IDIOPATHIC ARTHRITIS PATIENTS DEVELOPED ON BIOLOGIC TREATMENT

M. Chakhalian[1,*], E. Gaidar[1], E. Isupova[1], I. Chikova[1], M. Dubko[1], V. Masalova [1], T. Likhacheva[1], A. Santimov[1], T. Nikitina[1], L. Snegireva[1], M. Kostik[1]
[1]Saint Petersburg State Pediatric Medical University, Saint-Petersburg, Russian Federation

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

YP133

CHANGING EVIDENCE OVER TIME: UPDATED META-ANALYSIS REGARDING ANTI-TNF EFFICACY IN CHILDHOOD CHRONIC UVEITIS

I. Maccora[1,*], E. Fusco[2], E. Marrani[2], A. V. Ramanan[3], G. Simonini[4]
[1]Rheumatology Unit, Anna Meyer Children's Hospital, School of Human Health Science, , [2]Rheumatology Unit, Anna Meyer Children's Hospital, School of Human Health Science, University of Florence, Florence, Italy, [3]Bristol Royal Hospital for Children, UK & University of Bristol, Bristol, United Kingdom, [4]Rheumatology Unit, Anna Meyer Children's Hospital, NEUROFARBA Department, University of Florence, Florence, Italy

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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MORBIDITY OF JIA-ASSOCIATED UVEITIS: HALF OF PATIENTS DESPITE SYSTEMIC TREATMENT STILL SHOW OCULAR DAMAGE DURING A LONG-TERM FOLLOW-UP

G. B. Beretta[1,*], L. Marelli[2], V. Casotto[1], M. Romano[3], E. Miserocchi[3], C. Mapelli[1], A. Petaccia[1], S. Lanni[1], I. Pontikaki[3], F. Minoia[1], R. Cimaz[3] on behalf of on behalf of the Pediatric Rheumatology Associated Group of Milan Area
[1]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, [2]San Giuseppe Hospital, IRCCS Multimedica, [3]ASST Gaetano Pini-CTO Institute, Milan, Italy

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

YP135

ASSESSING S100 PROTEINS AND CYTOKINES IN TEARS AS POTENTIAL BIOMARKERS FOR UVEITIS DIAGNOSIS AND ACTIVITY IN JIA PATIENTS

J. Rodriguez-Smith[1,*], V. Miraldi Utz [2], S. Thornton[1], G. Schulert [1], A. Sproles[1], N. Mwase[1], T. Hennard[1], A. A. Grom[1], M. Altaye[3], S. T. Angeles-Han[1]
[1]Rheumatology, [2]Ophthalmology, Cincinnati Children's Hospital Medical Center, [3]Biostatistics and Epidemiology, University of Cincinnati, Cincinnati, United States

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

YP136

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

M. Held[1], M. Sestan[1,*], M. Coric[1], S. Bulimbasic[1], T. Giani[2], N. Martin[3], N. Kifer[1], S. Srsen[4], A. Gudelj Gracanin[5], D. Kifer[6], M. Heshin[7], A. Ravelli[8], R. Cimaz[9], S. Ozen[10], A. Gagro[11], M. Frkovic[1], M. Jelusic[1] on behalf of the PReS Vasculitis Working Party

[1]University Hospital Centre Zagreb, University of Zagreb School of Medicine, Zagreb, Croatia, [2]Anna Meyer Children's Hospital, Florence, Italy, [3]Royal Hospital for Children, Glasgow, United Kingdom, [4]University Hospital Centre Splt, University of Split School of Medicine, Split, [5]University Hospital Dubrava, University of Zagreb School of Medicine, Zagreb, Croatia, [6]Faculty of Pharmacy and Biochemistry, Zagreb, Croatia, [7]Dana Dwek Children's Hospital, Tel Aviv, Israel, [8]Division of Rheumatology, Giannina Gaslini Institute, Genoa, [9]Division of Clinical Rheumatology, Research Center for Adult and Pediatric Rheumatic Diseases, Università degli Studi di Milano, Milan, Italy, [10]Department of Pediatric Rheumatology, Hacettepe University, Ankara, Turkey, [11]Children's Hospital Zagreb, Josip Juraj Strossmayer University of Osijek, Medical Faculty Osijek, Zagreb, Croatia

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.

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Disclosure of Interest: None declared

YP137

A PILOT PROTEOMIC ANALYSIS OF PLASMA BIOMARKERS IN IGA VASCULITIS

S. DEMIR[1,*], M. SARDAN[2], I. YET[3], E. SAG[1], Y. BILGINER[1], O. ÇELIKBICAK[4], S. OZEN[1]
[1]Depatrment of Pediatric Rheumatology, Hacettepe University Medical Faculty, [2]Hunitek Research Center, Hacettepe University, [3]Department of Bioinformatics, Hacettepe University Medical Faculty, [4]Department of Chemistry, Hacettepe University , Ankara, Turkey

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).

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Disclosure of Interest: None declared

YP138

KAWASAKI DISEASE COMPLICATED BY MACROPHAGE ACTIVATION SYNDROME AND PARVOVIRUS B19 INFECTION: WHICH RELATIONSHIP?

M. G. Magnolia[1], S. Martelossi[2], C. Stefani[3], L. Da Dalt[4], G. Martini[5,*]
[1]Pediatric and Neonatologic Unit, “Santa Maria della Stella” Hospital, Orvieto, [2]Pediatric Unit, "Ca' Foncello Hospital", [3]Pediatric Unit, "Ca' Foncello" Hospital, Treviso, [4]Pediatric Emergency Unit, [5]Pediatric Rheumatology Unit, Department of Woman and Child Health, Padova, Italy

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

YP139

SPECTRUM OF VASCULITIS IN 27 CHILDREN FROM A SINGLE CENTER IN AN INDIAN STATE OF GUJARAT

D. B. Pandya[1,*] on behalf of Dr Haresh Dobariya , Dr Hitesh Bhambhani, Dr Jay Dhirwani , Dr Rakesh Patel , Dr Nayan Kalawadia,Dr Sudhir Rughani and Dr Savan Vamja.
[1]Pediatric Rheumatology & Immunology, Dev Children's Hospital, Rajkot, India

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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AkhilaKavirayani1, SumaBalan2
1 Department of Paediatric Rheumatology, Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom
2 Department of Paediatric Rheumatology, Amrita Institute of Medical Sciences, Kochi, Kerala, India

Disclosure of Interest: None declared

YP140

GASTROINTESTINAL MANIFESTATIONS AND THEIR ASSOCIATION WITH THE RISK FOR RENAL DISEASE IN PATIENTS WITH HENOCH-SCHÖNLEIN'S PURPURA

M. Sestan[1,*], N. Kifer[1], S. Srsen[2], A. Ovuka[3], M. Batnozic Varga[4], M. Sapina[5], M. Held[1], M. Ban[1], A. Kozmar[1], M. Coric[1], S. Bulimbasic[1], K. Crkvenac[1], D. Milosevic[1], M. Frkovic[1], A. Gagro[6], M. Jelusic[1]
[1]University Hospital Centre Zagreb, University of Zagreb School of Medicine, Zagreb, [2]University Hospital Centre Split, University of Split School of Medicine, Split, [3]University Hospital Centre Rijeka, University of Rijeka School of Medicine, Rijeka, [4]University Hospital Centre Osijek, Josip Juraj Strossmayer University of Osijek, Medical Faculty Osijek, [5]University Hospital Centre Osijek, Josip Juraj Strossmayer University of Osijek, Medical Faculty Osijek, Faculty of Dental Medicine and Health, Osijek, [6]Children's Hospital Zagreb, Josip Juraj Strossmayer University of Osijek, Medical Faculty Osijek , Zagreb, Croatia

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

YP141

LONG TERM OUTCOME OF POST-VARICELLA ARTERIOPATHY IN CHILDREN

S. Signa[1,*], M. Bertamino[2], M. Veneruso[3], G. Prato[3], R. Caorsi[1], M. Di Rocco[4], G. Losurdo[5], G. Amico[6], A. Zanetti[2], D. Tortora[7], S. Volpi[1], A. Rossi[7], P. Moretti[2], A. Ravelli[8], M. Gattorno[1], M. Severino[7]
[1]UOSD Centro Malattie Autoinfiammatorie e Immunodeficienze, [2]UOC Medicina Fisica e Riabilitazione, [3]UOC Neuropsichiatria Infantile, [4]UOSD Malattie Rare, [5]UOC Malattie Infettive, [6]UOC Genetica Medica, [7]UOC Neuroradiologia, [8]UOC Clinica Pediatrica e Reumatologia, IRCCS Istituto Giannina Gaslini, Genoa, Italy

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

YP142

CAN WE PREDICT CORONARY ARTERY INVOLVEMENT IN KAWASAKI DISEASE?

U. Kaya Akca[1,*], O. Serin[2], E. Arslanoglu Aydin[2], E. Sag[1], S. Demir[1], E. Atalay[1], M. Kasap Cuceoglu[1], E. D. Batu[1], Y. Bilginer[1], S. Ozen[1]
[1]Division of Pediatric Rheumatology, Department of Pediatrics, [2]Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey

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

YP143

PREDICTIVE BIOMARKERS OF I IGA VASCULITIS WITH NEPHRITIS BY METABOLOMIC ANALYSIS

S. Demir[1,*], M. CELEBİER[2], O. KAPLAN[3], E. SAG[4], Y. BILGINER[1], I. LAY[5], S. OZEN[1]
[1]Department of Pediatric Rheumatology, [2] Department of Analytical Chemistry, [3]Department of Analytical Chemistry, [4]Depatrment of Pediatric Rheumatology, [5]Department of Biochemistry, Hacettepe University Medical Faculty, Ankara, Turkey

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.

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Trial registration identifying number:
Disclosure of Interest: None declared

YP144

SPATIAL ANALYSIS OF CHILDHOOD IGA-VASCULITIS IN CROATIA – A PILOT STUDY

M. Sapina[1], M. Frkovic[2], M. Sestan[2,*], S. Srsen[3], A. Ovuka[4], M. Batnozic Varga[5], N. Kifer[2], K. Kramaric[6], D. Brdaric[7], K. Milas[5], A. Gagro[8], M. Jelusic[2]

[1]University Hospital Centre Osijek, Josip Juraj Strossmayer University of Osijek, Medical Faculty Osijek, Faculty of Dental Medicine and Health, Osijek, [2]University Hospital Centre Zagreb, University of Zagreb School of Medicine, Zagreb, [3]University Hospital Centre Split, University of Split School of Medicine, Split, [4]University Hospital Centre Rijeka, University of Rijeka School of Medicine, Rijeka, [5]University Hospital Centre Osijek, Josip Juraj Strossmayer University of Osijek, Medical Faculty, [6]University Hospital Centre Osijek, Josip Juraj Strossmayer University of Osijek, Faculty of Dental Medicine and Health Osijek, [7]Josip Juraj Strossmayer University of Osijek, Faculty of Dental Medicine and Health, Institute of Public Health for the Osijek-Baranja County, Osijek, [8]Children's Hospital Zagreb, Josip Juraj Strossmayer University of Osijek, Medical Faculty Osijek, Zagreb, Croatia

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.
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SYSTEMATIC REVIEW OF CHILDHOOD-ONSET POLYARTERITIS NODOSA AND DADA2

M. Kasap Cuceoglu[1,*], S. Demir[1], E. Sag[1], U. Kaya Akca[1], E. Atalay[1], E. D. Batu[1], Y. Bilginer[1], S. Ozen[1]
[1]Pediatric Rheumatology, Hacettepe University, Ankara, Turkey

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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