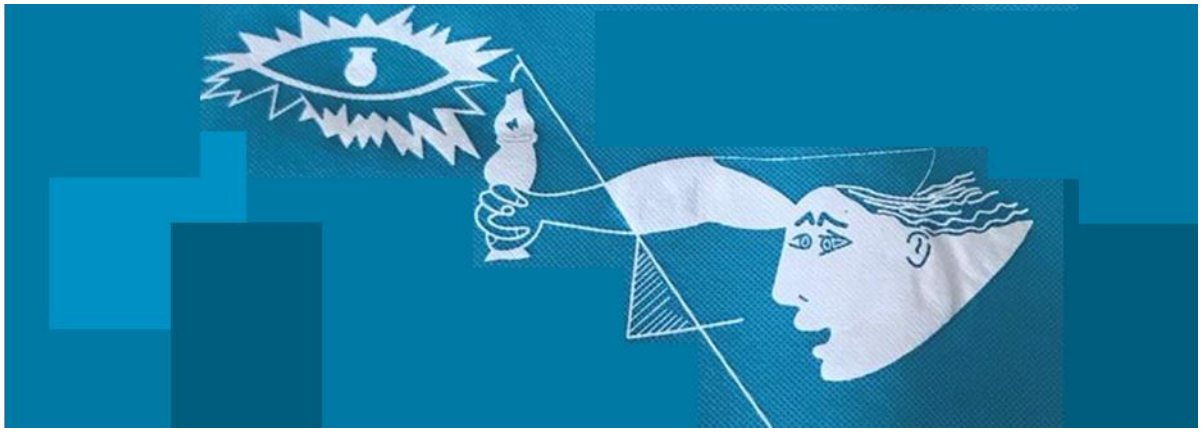


YOUNG INVESTIGATORS MEETING

YIM 2019 - MADRID

ABSTRACT BOOK

Contents

Oral Presentations

11.06.2019
SESSION-I 14:30-15:30

ALESSANDRA ALONGI

Clinica Pediatrica e Reumatologia, IRCCS Istituto Giannina Gaslini, PRINTO, Genoa, Italy

PAIN IS THE MAIN DETERMINANT OF WELL-BEING IN OLIGO- AND POLYARTICULAR JIA: DATA FROM THE PHARMACHILD REGISTRY

Background
Juvenile Idiopathic Arthritis (JIA) affects patients' Well-Being as the result of a complex interplay of multiple factors, including disease activity, symptoms, physical and emotional quality of life, and treatment burden. Little evidence exists about the relative contribution of these elements to disease impact.

Methods
In order to identify the determinants of Well-Being - as expressed by VAS-measured patient/parent global assessment of well being (PGW) - in Oligo- and Polyarthritis, we analyzed data on 1873 patients examined in 4464 prospective visits from the international JIA pharmacovigilance registry Pharmachild. We evaluated the direct and indirect effects across activity states of Physician Global Assessment, Erythrocyte Sedimentation Rate, Active Joint Count, Pain, Stiffness duration, Juvenile Arthritis Functional Score (JAFS), Physical (PhHS) and Psychosocial (PsHS) subscales of the Pediatric Rheumatology Quality of Life Scale, Juvenile Arthritis Damage Index (JADI) and Adverse Events (AE).

Results
Pain severity is the strongest direct determinant of PGW (b 0.521, p 0.000), followed by Psychosocial (b 0.191, p 0.000) and Physical Health (b 0.158, p 0.000). Stiffness (f2 0.047, p 0.000) and joint damage (f2 0.025, p 0.000) were also indirectly associated with the PGW, through their effects on function and PhHS. Patient-reported adverse events (AE) have a small effect on PGW (f2 0.025, p 0.000) through their impact on PsHS. Multi-group comparison between JADAS10 categories revealed that for subjects in Remission, pain has a lower impact on function and physical health compared to Low Disease Activity, while remaining the strongest predictor of PGW. Among visits with High Disease Activity, the direct effect of pain on Well-Being and the impact of physical health on psychosocial health is greater than in other categories.

Conclusion
Pain emerges as the main determinant of PGW in all disease activity states. PGW also captures other aspects of disease impact, reflecting physical limitations and psychosocial distress, and, in less extent, treatment burden. The impact of pain and physical functioning on psychic health and Well-Being differs with disease activity, contributing more in patients with higher activity levels.

VERONIKA RYPDAL

Department of Paediatrics, University hospital of North Norway, Norway

VALIDATION OF METHODS FOR PREDICTING LONG-TERM OUTCOME IN JUVENILE IDIOPATHIC ARTHRITIS: RESULTS FOR CANADIAN AND NORDIC MODELS IN THE NORDIC JIA COHORT

Background

Models predicting outcome in juvenile idiopathic arthritis (JIA) have recently been proposed by Guzman et al. and Rypdal et al. Guzman et al. constructed a model for predicting severe disease course derived from the ReACCh-Out study, and Rypdal et al. constructed models for prediction of non-remission from the Nordic cohort. The aim of the study was to validate methods for prediction of long-term outcome in JIA by testing the ability of Guzman's model and Rypdal's model to predict severe disease course (the ReACCh-Out outcome) in the Nordic cohort.

Methods

The Nordic cohort is a prospective longitudinal multicenter cohort from defined geographical areas of 4 Nordic countries. Children with a baseline and an 8-year study visit were included. Missing data was imputed using low rank matrix factorization, and a K-medoids algorithm was used to identify clusters corresponding to severe disease course in the ReACCh-Out study. With this outcome, the prediction model of Guzman et al. was tested with no re-estimation of parameters. A Receiver operating characteristic (ROC) curve and the corresponding area under the curve (AUC) were computed. For the same outcome, prediction models were built using the method proposed by Rypdal et al. on randomly sampled training sets, and tested on disjoint validation sets.

Results

In the Nordic cohort 98/440 (22%) patients were identified with a severe disease course. This ratio is similar to the 125/610 (20%) found in the ReACCh-Out study. Characteristics of groups of patients with severe and non-severe disease course are similar in the two cohorts. The model of Guzman et al. had an AUC of 0.85 for prediction of severe disease course and an AUC of 0.66 for predicting non-remission off medication. In repeated cross-validations, the model of Rypdal et al. had a median AUC of 0.90 (IQR 0.86-0.92) for prediction of severe disease course and 0.78 (IQR 0.72-0.82) for non-remission.

Conclusion

The Canadian model is stable, reproducible and have comparable performance to the Nordic prediction model in predicting severe disease course in the Nordic JIA cohort. The lower ability to predict non-remission in both cohorts suggest that model performance depends highly on the targeted outcome, underlining the need in prognostication for robust disease outcomes in JIA.

STEPHANIE SHOOP-WORRALL

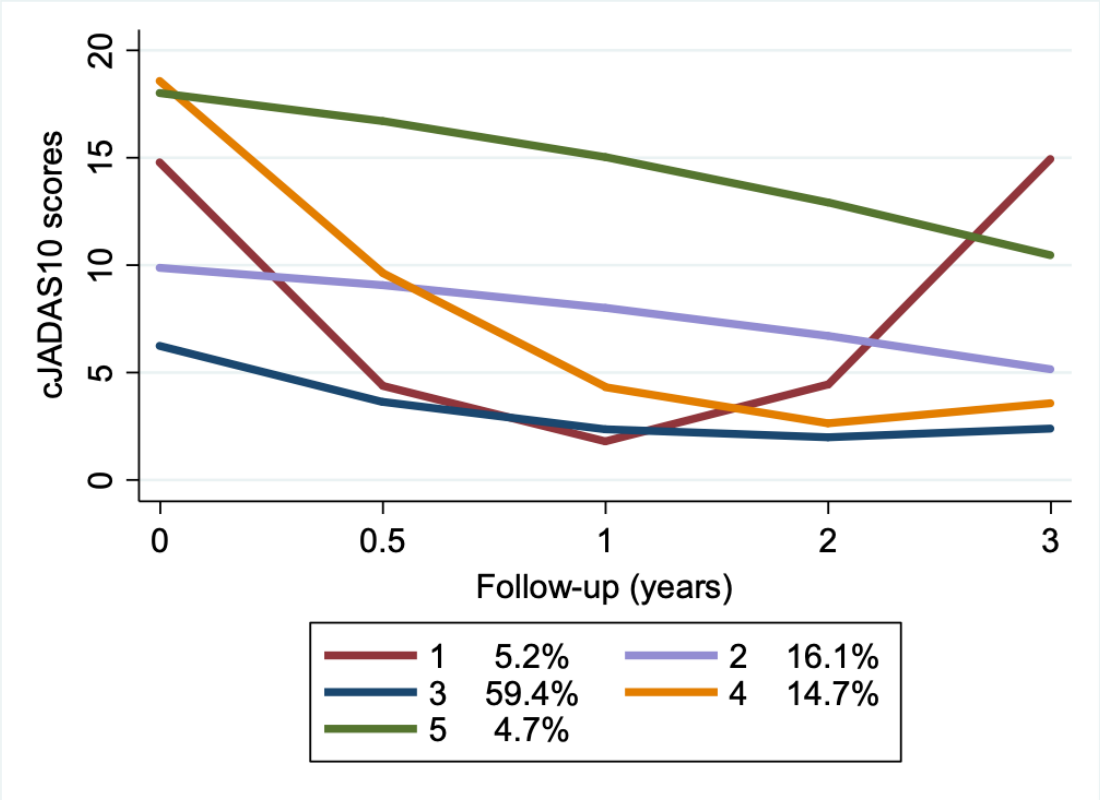
Centre for Health Informatics, The University of Manchester, Manchester, United Kingdom. Arthritis Research UK Centre for Epidemiology, The University of Manchester, Manchester, United Kingdom.

TRAJECTORIES OF DISEASE ACTIVITY OVER THE FIRST THREE YEARS FOLLOWING JUVENILE IDIOPATHIC ARTHRITIS DIAGNOSIS

Background
Biological therapies and early aggressive treatment strategies have drastically changed prognoses for children and young people (CYP) with juvenile idiopathic arthritis (JIA). Clinical trials and observational research have demonstrated improvements in disease for the majority, but not all, CYP over time. It is not currently known what the patterns of disease activity are in CYP with JIA and how these cluster over time. This study looked to explore latent patterns of clinical juvenile arthritis disease activity scores (cJADAS) following a diagnosis of JIA.

Methods
CYP with JIA were selected if enrolled in the Childhood Arthritis Prospective Study (CAPS), a UK multicentre inception cohort, before January 2015. cJADAS10 scores were calculated based on components (active joint count up to 10, physician global, patient/parent global) collected at diagnosis, six months, one year and then annually to three years. CYP were excluded if no cJADAS10 scores were available within this time frame. Group-based trajectory models were constructed to model latent groups of cJADAS10 scores. Linear, quadratic and cubic polynomials were tested, with one to six trajectories tested within each polynomial group. An optimal model within each polynomial group was selected using Bayesian Information Criteria. The final model was then selected from this shortlist based on model parsimony and clinical plausibility.

Results
Of 1183 CYP selected, the majority were female (65%) and of white ethnicity (90%) with oligoarticular JIA the most common JIA category (45%). The optimal model identified five cJADAS10 quadratic trajectories (Figure 1): Low-low (59%, initial cJADAS10 median: 6.1), moderate-low (16%, initial cJADAS10 median: 11.5) and three groups with high disease activity at initial presentation (initial median cJADAS10: 17.7 to 19.1). A high-low group experienced the greatest improvement (15%, median improvement 17.2 (IQR 13.7 to 20.1)), and a high-moderate group lesser improvement (5%, median improvement 7.3 (IQR 0.8 to 9.0)). A final high-low-high group experienced improvement to one year followed by disease relapse (5%).



Conclusion

Disease activity in CYP with JIA does not improve uniformly following initial presentation to paediatric rheumatology. Five latent trajectory groups have been identified. Identifying distinguishing characteristics for each group may facilitate personalised medicine in JIA.

JESSICA TIBALDI

Università degli Studi di Genova; IRCCS Istituto Giannina Gaslini, Genoa, Italy

DEVELOPMENT AND INITIAL VALIDATION OF THE SYSTEMIC JADAS, A NEW COMPOSITE DISEASE ACTIVITY SCORE FOR SJIA.

Background
Juvenile Arthritis Disease Activity Score (JADAS) has gained increasing popularity for the measurement of level of disease activity in patients with juvenile idiopathic arthritis (JIA); however, so far it's been validated only in children with non-systemic categories of JIA.

Methods
Systemic JADAS (sJADAS) is made up by adding a fifth item (Systemic Manifestation Score, SMS) to items included in the original tool in order to quantify the activity of systemic features. The validation sample included patients with sJIA with active systemic manifestations, assessed at baseline and then at a subsequent visit. Validation procedures included assessment of concurrent, construct and discriminant validity, internal consistency and responsiveness to clinical change.

Results
A total of 161 patients were enrolled in 57 centers in 10 countries from February 2017 to December 2018. Median age at disease onset was 5.0years (interquartile range, IQR 2.8 - 8) and median age at study entry was 6.9years (IQR 3.8 – 10.8). Median disease duration from onset to study entry was 0.2years (IQR 0.1 – 1.9). Median sJADAS at baseline visit was 28.2 (IQR 22.8 – 35.0). sJADAS correlated strongly with JADAS10 (r_s=0.98) and clinical JADAS10 (cJADAS10) (r_s=0.91); moderately with functional ability scales (JAFS and CHAQ) (r_s=0.69; r_s=0.62) and total score (r_s=0.57), physical (r_s=0.60) and psychosocial (r_s=0.40) subscale scores of health-related quality of life tool (PRQL) and with pain VAS (r_s=0.57); mildly with CRP (r_s=0.42). sJADAS discriminated well between patients with or without morning stiffness (p<0.0001), with different levels of disease activity defined by physician (p<0.0001) and with different degrees of pain (p<0.0001). **I**nternal consistency was good (Cronbach's alpha=0.639) and comparable to that of JADAS10 and cJADAS10 (Cronbach's alpha=0.595 and 0.629, respectively). Responsiveness to change, measured on all patients (SRM=2.23) and on patients classified as improved at second visit (SRM=2.41) was strong and superior to that of JADAS10 (SRM=1.92 and 2.14, respectively).

Conclusion
The sJADAS was found to be a valid instrument for assessment of disease activity in sJIA. It's feasible and easily applicable in standard clinical practice. The good responsiveness to clinical change indicates that the sJADAS is suitable to assess therapeutic response in sJIA clinical trials.

GEORGE ROBINSON

University College London, London, United Kingdom

METABOLOMICS IN JUVENILE-ONSET SLE: IDENTIFYING NEW BIOMARKERS TO PREDICT CARDIOVASCULAR RISK

Background
Juvenile-onset systemic lupus erythematosus (JSLE) is an autoimmune disorder characterised by immune dysregulation, chronic inflammation and increased cardiovascular risk (CVR). Cardiovascular disease is the leading cause of mortality in JSLE not attributable to lupus flare. Our findings in adult-onset SLE link immune cell dysregulation with dyslipidaemia but little is known about the immune profile or whether abnormal lipid metabolism contributes to disease pathogenesis in JSLE. The objective of this study was to investigate dyslipidaemia and CVR in a cohort of JSLE patients using in depth metabolomics and relate this to clinical profiles and to identify novel biomarkers to predict CVR in these patients.

Methods
Metabolic biomarker analysis (NMR) was performed on serum from a discovery cohort of 31 JSLE patients (median age 19). Data was analysed using cluster and receiver operating characteristic (ROC) analysis. Results were validated in a second cohort of 31 JSLE patients (median age 19).

Results
Patient stratification by metabolomic profile using unbiased hierarchical clustering revealed 3 groups that each had a unique lipoprotein profile and clinical presentation. Group-1 had decreased atheroprotective high density lipoproteins (HDL) and increased atherogenic very low and low density lipoproteins (VLDL/LDL) and Group-2 had elevated HDL but reduced VLDL/LDL indicating that these groups could be at high and low CVR respectively. Patients in Group-3 displayed an intermediate CVR. This hypothesis was validated by previously recognised markers of CVR including the atherogenic index of plasma, ApoB:A1 ratios and lipid biomarkers we previously identified to be associated with pre-clinical atherosclerotic plaque in adult SLE patients. This metabolomic patient stratification was validated in a separate JSLE cohort. Importantly ApoB:A1 ratio was identified as a highly predictive biomarker (ROC area under the curve>0.99) distinguishing between JSLE patients in Group-1 and 2, indicating high and low CVR respectively. Finally, longitudinal analysis revealed that the ApoB:A1 ratio biomarker remained stable over time.

Conclusion
ApoB:A1 ratio and metabolomic lipoprotein signatures could be new biomarkers to predict early CVR in JSLE patients. Patient stratification using these biomarkers could provide an opportunity for tailored disease treatments using lipid modification therapy and/or diet/lifestyle interventions.

EMILIANO MARASCO

Division of Rheumatology, Bambino Gesù Hospital, Rome, Italy

INTERFERON-Γ AMPLIFIES IMMUNE RESPONSE MEDIATED BY TYPE I INTERFERONS IN PAEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS AND CORRELATES WITH DISEASE ACTIVITY

Background
Paediatric systemic lupus erythematosus (pSLE) is an autoimmune disorder of childhood characterized by the production of autoantibodies against nuclear antigens. Several studies showed an up-regulation of genes induced by type I interferons (IFNα) in peripheral blood and tissues of pSLE patients. The expression of these genes correlates with disease activity. Recently, also the type II IFN (IFNγ) has been implicated in pSLE, but its role has not been clarified yet. In this study, we aim to investigate the potential role of IFNγ in the pathogenesis of pSLE.

Methods
Expression of IFNα-induced genes (IFI27, IFI44L, IFIT1, RSAD2, ISG15, SIGLEC1), IFNγ-induced genes (CXCL9, IDO1) and IFNγ itself were analysed by 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. Peripheral blood mononuclear cells (PBMCs) from 6 HDs were stimulated *in vitro* with recombinant human IFNγ and IFNα2b; gene expression was evaluated by qPCR. CXCL9 and CXCL10 in sera and supernatants from stimulated cells were measured by ELISA. Whole blood of pSLE patients and HDs was incubated with an anti-IFNγ neutralizing antibody and IFN signatures were assessed.

Results
Expression of IFNα-induced genes, IFNγ-induced genes and IFNγ were upregulated in pSLE patients with active disease (n = 21) compared to HDs and pSLE patients with inactive disease (n = 17). The type II IFN score correlated with the SLEDAI. As previously reported, also the type I IFN score correlated with SLEDAI. Serum CXCL9 and CXCL10 were increased in pSLE patients compared to HDs. We stimulated HD PBMCs with IFNα2b and IFNγ finding that IFNα2b up-regulated the IFNγ, CXCL9 and IDO1 expression. IFNγ induced the expression of the IFNα-related genes. IFNγ, but not IFNα2b, induced the release of CXCL9 in supernatants. Both IFNs induced the CXCL10 release. IFNγ also up-regulated the expression of both TLR7 and TLR9, two potent inducer of IFNα. Whole blood of pSLE was incubated with an anti-IFNγ neutralizing antibody: the type II signature was downregulated.

Conclusion
Our data suggest a potential role of IFNγ in the pathogenesis of pSLE.

SESSION III 17:10-18:00

HANNAH PECKHAM

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RELATIVE MONOCYTE SUBSET DIFFERENCES BETWEEN JUVENILE- AND ADULT- ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

Background

15-20% of patients with Systemic Lupus Erythematosus (SLE) develop the disease in childhood or adolescence (Juvenile-onset SLE, JSLE)(1). Whilst it is recognised that JSLE is often more severe than adult-onset SLE(2), there is a lack of knowledge related to differences in the disease pathogenesis. Peripheral blood CD14+ monocytes are thought to play a role in lupus development. CD16+ Non-classical and Intermediate monocyte subsets, producing inflammatory cytokines and contributing to T-cell activation and B-cell proliferation, are enriched in adults with SLE(3). Furthermore, CD16- Classical monocytes are important for phagocytosis of apoptotic cells - a process known to be aberrant in lupus- contributing to the generation of autoantibodies. Thus we hypothesised that monocyte subsets could be differentially dysregulated in SLE and JSLE and relate to the disparities seen in pathogenesis and clinical presentation.

Methods

Peripheral blood from female patients with SLE (n=17) and JSLE (n=23) was collected at the UCLH rheumatology clinics after obtaining informed consent. In depth phenotyping of peripheral blood mononuclear cells was performed using multiparameter flow cytometry. GraphPad Prism was used for Mann-Whitney U-tests and Spearman's Correlations, and 'R' for logistic regressions.

Results

Non-Classical CD14dimCD16++ (p=0.007) and Intermediate CD14highCD16+ (p=0.039) monocytes had significantly increased frequencies in SLE patients compared to those with JSLE while no significant differences were seen in Classical CD14highCD16- monocyte percentages between groups. Interestingly, non-classical monocytes correlated positively with age (p=0.006, rho=0.431), while classical monocytes negatively correlated with age (p=0.042, rho= -0.323), suggesting a relationship between age and increasing proinflammatory monocyte phenotype. No relationship was observed between dsDNA titre or C3 levels and monocyte subset frequencies in SLE or JSLE patients. Classical monocyte frequencies negatively correlated with ESR (p=0.027, rho= -0.323) in JSLE patients, but this correlation was lost when JSLE and SLE were grouped together, or when SLE was examined in isolation. Increased percentages of non-classical monocytes were associated with a higher odds of adult onset SLE relative to JSLE, after adjusting for the effects of disease activity (SLEDAI) (OR= 1.137, 95% CI= 1.021- 1.266, p= 0.018).

Conclusion

Pro-inflammatory CD16+ subset percentages were higher in adults and increased with age. Studies have shown a similar correlation in healthy adults(4), suggesting that age-related differences in baseline immune cells may underpin differing mechanisms of monocyte involvement in lupus pathogenesis.

RACHAEL WRIGHT

Department of Women's and Children's Health, Institute of Translational Medicine, University of Liverpool, Liverpool, United Kingdom.

MESANGIAL CELLS ARE KEY CONTRIBUTORS TO THE FIBROTIC DAMAGE SEEN IN THE LUPUS NEPHRITIS GLOMERULUS

Background
Lupus nephritis (LN) is a key clinical feature of systemic lupus erythematosus that affects up to 80% of paediatric patients (<18 years old). Mesangial cells (MCs) comprise a third of the glomerular cells and are key contributors to fibrotic damage within the kidney. This project aims to identify the roles of MCs in an in vitro model of LN.

Methods
Conditionally immortalised MCs were treated with pro-inflammatory cytokines (IL-1β, TNF-α, IFN-α and IFN-γ alone and in combination) to generate a model of LN or with sera from patients with active and inactive LN. The changes in mRNA for extracellular matrix (ECM) proteins and enzymes responsible for remodelling were assessed.

Results
MCs expressed significantly increased levels of mRNA for ECM proteins (COL1A1, COL1A2, COL4A1 and LAMB1) and matrix metalloproteinase enzymes (MMP9) as well as a concurrent decrease in tissue inhibitor of matrix metalloproteinase 1 (TIMP1) in response to treatment with pro-inflammatory cytokines in the model of LN. To confirm that this mimics that seen in LN, the cells were treated with sera from LN patients. When cells were treated with sera from patients with active LN (renal BILAG A/B) there was a significant increase in the mRNA for COL1A2 with a trend towards increased COL4A1 ($p=0.07$) as well as an increase in MMP9 mRNA suggesting that the sera was able to induce a similar, albeit milder phenotype. These increases in ECM protein mRNA were seen alongside an increase in the secretion of TGF-β1 by the MCs. Blocking the actions of TGF-β1 in the cytokine model using SB-431542 (ALK5 inhibitor) was able to attenuate these changes.

Conclusion
MCs contribute to the fibrotic changes occurring within the glomerulus in a model of LN by remodelling the ECM via protein deposition and enzymatic degradation. This occurs through TGF-β1 and thus this may represent a future therapeutic target for treatment of LN-associated fibrosis.

FRANZ KAPPLUSCH

University of Liverpool, EATC; Liverpool, United Kingdom

CAMP RESPONSE ELEMENT MODULATOR (CREM)A INDUCES DUAL SPECIFICITY PROTEIN PHOSPHATASE (DUSP)4 THROUGH EPIGENETIC REMODELING, PROMOTING IL-17A AND REDUCING IL-2 EXPRESSION IN T CELLS

Background
Tissue inflammation and organ damage in systemic lupus erythematosus (SLE) have been linked to effector T cells that are characterized by increased IL-17A and reduced IL-2 production (1). T cells from patients with SLE express increased levels of the transcription factor cAMP response element modulator (CREM)α that contributes to altered cytokine expression (1-3). However, the exact molecular events contributing to diametrically dysregulated IL-17A and IL-2 expression are incompletely understood.

Objectives: To investigate molecular events that contribute to effector T cell phenotypes in health and disease. The definition of molecular regulators of effector T cell generation and activity may deliver new biomarkers and potential therapeutic targets in disorders characterized by altered effector T cell function, including (but not limited to) SLE.

Methods
Using CRISPR/Cas9 genome editing and lentiviral transduction, we generated CREMα deficient (through bi-allelic deletion of one exon) and CREMα overexpressing cell lines. Gene expression profiles were assessed by qRT-PCR and mRNA probe based hybridization techniques. Gene regulation events were assessed using luciferase reporter assays (trans-activation) and ChIP (recruitment of CREMα and p300, histone acetylation). Protein-protein interactions between CREMα and the transcriptional co-activator p300 were assessed using proximity ligation assays and co-immunoprecipitation. Functional interactions were assessed through knock-down of p300 with siRNAs. Phosphorylation of the transcription factors STAT3 and STAT5 in genetically modified cells was tested using CyTOF mass spectrometry.

Results
We link increased CREMα production in effector CD4+ T cells with increased expression of dual specificity protein phosphatase (DUSP)4. Using genetically modified CREM-deficient and CREMα overexpressing CD4+ T cells, we demonstrate that CREMα induces DUSP4 expression not through trans-activation of the DUSP4 promoter, but co-recruitment of the transcriptional co-activator p300. Through its histone acetyltransferase function, p300 mediates epigenetic “opening” of the DUSP4 promoter and increased gene expression. Using DUSP4 transfection models and genetically modified CREM-deficient and CREMα over-expressing T cells, we support previous reports suggesting that DUSP4 induces IL-17A while limiting IL-2 expression likely through altered de-phosphorylation of STAT5. Furthermore, we demonstrate that CD4+ T cells from patients with juvenile-onset SLE share the phenotype with CREMα over-expressing CD4+ T cells with increased DUSP4 expression that contributes to imbalanced IL-17A and IL-2 production.

Conclusion
Collectively, our results deliver a new CREMα-mediated molecular mechanism promoting effector T cell phenotypes and support the central involvement of CREMα in the pathophysiology of SLE.

ANNA SURACE

Alder Hey Children's NHS Foundation Trust, Liverpool, UK. Department of Women's and Children's Health, University of Liverpool, Liverpool, United Kingdom

NUCLEOSOMES CAUSE NOT ONLY AUTOIMMUNE-LIKE, BUT ALSO INFLAMMATORY RESPONSES

Background

Juvenile-onset systemic lupus erythematosus (JSLE) is a multisystem autoimmune disease with autoantibodies potentially caused by increased neutrophil extracellular trap (NET) formation, which contain nucleosomes. The presence of NET autoantigens is considered to induce Interferon (IFN)· production by dendritic cells. As other effects of NETs on the immune system in JSLE remain poorly understood, potential therapeutic interventions may be missed.

Methods

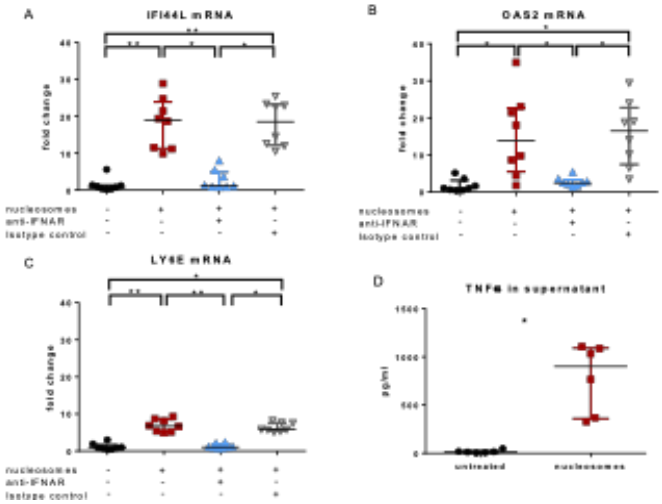
Healthy adult whole blood was stimulated for 5h +/-nucleosomes and +/-IFNα-receptor (IFNAR) antibody or isotype control. Neutrophils were stimulated with 1ng/ml TNFα for 45min (mRNA) and 1h (protein). mRNA expression was measured with qPCR for IFN-induced genes (OAS2, IFI44L and LY6E) and TLR2. S100A8/S100A9 and TNFα were measured by ELISA. TLR2 protein expression was analysed by flow cytometry.

Results

Nucleosomes caused significant upregulation of IFN-induced genes in whole blood (Figure 1A-C). IFNAR-inhibition abrogated up-regulation of IFN-induced genes showing that this increase in gene expression is a type-I IFN specific. Furthermore, two inflammatory markers, TNFα and S100A8/S100A9, were significantly ($p<0.05$) increased in culture supernatant in the presence of nucleosomes. Healthy paediatric neutrophils were stimulated with 1ng/ml TNFα in vitro, a concentration consistent with that measured following nucleosome stimulation (Figure 1D). This induced a significant increase of both mRNA and protein of TLR2.

Conclusion

Nucleosomes cause type-I IFN release in whole blood assays, in line with auto-immune features of IFN-high JSLE. Inflammatory proteins S100A8/S100A9 and TNFα were also released, which may contribute to inflammation observed in JSLE patients. Indeed, stimulation of neutrophils with the same concentration of TNFα found in the presence of nucleosomes increased TLR2 expression in line with our previous reports of JSLE patients with an IFN-low signature. This highlights a potential therapeutic option, targeted to a stratified subgroup of patients.



LUCY MARSHALL

JDCBS, Versus Arthritis, Myositis UK, University College London & Great Ormond Street Hospital, London, United Kingdom

INVESTIGATING INVESTIGATING THE ROLE OF COMPLEMENT ACTIVATION IN DRIVING THE TH1/17 IMBALANCE OBSERVED IN JUVENILE DERMATOMYOSITIS.

Background

A skewed Th17 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, SLE (systemic lupus erythematosus), and multiple sclerosis. This project aimed to investigate whether a Th1/17 imbalance can also be observed in patients with Juvenile Dermatomyositis (JDM) compared to age/sex-matched healthy controls.

Methods

PBMC from JDM (n=15) and age/sex-matched controls (CHC, n=6) were stimulated with PMA/Ionomycin in the presence of Brefeldin A for 4 hours with the Th1/17 phenotypes measured by intracellular staining for IFN-γ and IL-17 respectively. Using previously generated RNAseq data within the Wedderburn lab, immune pathways defined by hallmark gene sets, were analysed within peripheral blood CD4+ T cells from treatment-naïve patients and patients after approx. 12 months of standard treatment (n=10). To further investigate Th1 response and the role of complement an in vitro CD46-activation, assay was performed on JDM (n=6) and CHC (n=3). Read outs of the assay included IFN-γ and IL-10 secretion via cytokine bead array.

Results

Analysis of the ratio of CD4+IFN-γ+ to CD4+IL-17+ cells within peripheral blood demonstrated that the CD4+ T cell phenotype is significantly skewed towards Th17 cells in JDM (p=0.04) compared to CHC. Isolated CD4+ T cells included in RNAseq analysis revealed that the complement pathway was over-represented in pre-treatment JDM versus on-treatment JDM CD4+ T cells. Using an in vitro modelling assay to mimic intracellular complement activation in CD4+ T cells via anti-CD46 activation, a complement receptor known to induce Th1 responses, our preliminary analysis revealed that there is also low IFN-γ production in JDM compared to CHC under these conditions.

Conclusion

IFN-γ is reduced in CD4+ T cells from JDM patients compared to CHC leading to a Th17-skewed immunophenotype. Consistent with this observation, RNAseq analysis highlighted the complement pathway in CD4+ T cells from treatment naïve JDM patients compared to patients on treatment. Importantly, intracellular complement activation within CD4+ T cells has been shown to be critical for Th1 induction in healthy adults. To summarise, our initial results display a lack of Th1 response, via IFN-γ, in JDM patients compared to CHC. Future work aims to confirm these findings and investigate possible mechanisms involved.

12.06.2019
SESSION IV 08:35-09:25

LIANNE KEARSLEY-FLEET

Arthritis Research UK Centre for Epidemiology, The University of Manchester, Manchester, United Kingdom.

WHAT TO CHOOSE: A SECOND TNFI OR AN ALTERNATIVE CLASS OF BIOLOGIC FOR PATIENTS WITH JIA WHO HAVE FAILED THEIR FIRST TNFI

Background
Biologic therapies have revolutionised treatment pathways and outcomes for patients with juvenile idiopathic arthritis (JIA). Current NHS England guidelines recommend most patients to start a tumour necrosis factor inhibitor (TNFi), and switch to a second TNFi rather than change class after initial failure. The aim of this analysis was to compare the effectiveness of a second TNFi versus non-TNFi in patients with polyarticular JIA in routine clinical practice.

Methods
Analysis included patients with extended oligoarticular or polyarticular (RF+/RF-) JIA starting a second biologic following initial TNFi therapy in two UK cohort studies; BSPAR-ETN and BCRD. Within the studies, data were collected at start of biologic, 6 months, 1 year, then annually on patient characteristics and anti-rheumatic therapy. Patients with a history of uveitis at start of second biologic were excluded. Patient characteristics at start of second biologic were compared between patients starting a second TNFi versus non-TNFi. Kaplan-Meier drug survival was used to assess drug survival on second biologic. Stop reasons of second biologic were described. Change in core outcome variables, JADAS-71, ACR Paediatric 50% response (ACR Pedi 50), and Minimal Clinically Important Difference (MCID; ≤0.13 CHAQ reduction) from baseline to one year were compared. Multiple imputation and propensity scores were used.

Results
151 patients with polyarticular JIA starting a second biologic up to 13-Nov-2018 were included; 115 (76%) second TNFi, 36 (24%) non-TNFi. Patient characteristics at the start of second biologic were mostly similar. There was no difference in second biologic drug survival (p=0.8); ~60% remained on drug by one year. There was no difference between one year improvement in core outcome variables or JADAS-71 after start of second biologic, and no difference in the odds of achieving ACR Pedi 50 response (odds ratio [OR] 0.8; 95% confidence interval [CI] 0.3, 2.3; p=0.7) or MCID (OR 1.0; 95% CI 0.3, 3.1; p=0.9) between patients starting a second TNFi versus a non-TNFi.

Conclusion
In this real-world cohort of children and young people with JIA starting a second biologic, there appears to be no difference between drug survival and effectiveness outcomes in patients starting a second TNFi versus a non-TNFi.

ROLINE KROL

Wilhelmina Children's Hospital, Utrecht, The Netherlands

DEVELOPMENT OF INFLAMMATORY BOWEL DISEASE DURING TREATMENT WITH ETANERCEPT IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS.

Background
Inflammatory bowel disease (IBD) is an auto-immune disease that can develop in patients with juvenile idiopathic arthritis (JIA). The aim of this study was to describe characteristics of JIA patients who developed IBD and to evaluate a possible relationship between IBD onset and medication such as etanercept.

Methods
Pharmachild, the largest international JIA registry was used for this study. Patients were enrolled via members of the Paediatric Rheumatology INternational Trials Organisation (PRINTO). The registry contains both retrospective and prospective data. Inclusion criteria were children diagnosed with JIA who were treated with biologicals or synthetic disease modifying anti-rheumatic drugs (DMARDs). JIA was defined as proposed by the International League of Associations for Rheumatology (ILAR).

Results
A total of 8,309 patients were included in this study. 290 gastrointestinal disorders were reported in 260 patients. 50 cases in 47 patients were classified as IBD or suspected IBD. Age at JIA onset was significantly higher in patients who developed IBD (9.1 vs 7.1 years p=0.002), and female predominance was lower (48.9% versus 67.6% p=0.011). 40.4% of the JIA patients who developed IBD had enthesitis related arthritis (ERA). In 14 out of 47 patients more detailed information about IBD disease onset was available. Both methotrexate (MTX) and etanercept (ETN) were frequently used at disease onset or 3 months prior to disease onset. Information regarding quality of life was available for 2,752 patients of which 17 IBD patients. Quality of life, both physical and psychosocial, was significantly lower in patients who developed IBD.

Conclusion
In this study ERA patients were more at risk of developing IBD and 71.4% used etanercept while developing IBD. We did not find a protective role of MTX since 50.0% of patients with available data developed IBD while using MTX. Lastly, IBD has an important physical and psychosocial impact on quality of life.

DANIEL HORTON

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ORAL GLUCOCORTICOIDS AND INCIDENT DIABETES MELLITUS, HYPERTENSION, AND THROMBOSIS IN CHILDREN WITH CHRONIC DISEASES

Background
The cardiometabolic risks of oral glucocorticoids in pediatric populations are poorly understood. We quantified rates of new-onset diabetes mellitus, hypertension, and venous thromboembolism (VTE) associated with oral glucocorticoid exposure in children.

Methods
We studied >930,000 children ages 1-18 diagnosed with autoimmune diseases (inflammatory bowel disease, juvenile idiopathic arthritis, or psoriasis) or a non-immune comparator condition (attention-deficit/hyperactivity disorder) using Medicaid claims (2000-2010). We categorized time-varying oral glucocorticoid dose as low (<0.25 mg/kg/day), medium (0.25-0.99 mg/kg/day), or high (≥1 mg/kg/day) based on prescribed prednisone-equivalent dosage and age-/sex-imputed weights. Associations of glucocorticoid dose with incident treated diabetes, hypertension, and VTE were estimated using Cox regression and weighted cumulative exposure models.

Results
We found strong dose- and time-dependent relationships between glucocorticoids and rates of newly treated diabetes (aHR, current high dose: 5.9, 95% CI 3.9-8.9), hypertension (aHR, current high dose: 19.1, 95% CI 15.4-23.7), and VTE (aHR, current high dose: 16.2, 95% CI 8.9-29.2). These effects increased with longer durations of exposure and declined within 6 months after stopping. Sustained low-dose exposures (e.g., 0.1 mg/kg/day) appeared relatively safe (aHR<1.2), but risks increased even with brief high-dose exposures (2 mg/kg/day x7 days) (aHR 1.7-2.2). Numbers needed to harm were lowest for hypertension (2 mg/kg/day x7 days: 6,206-17,894) and highest for VTE (2 mg/kg/day x7 days: 54,886-612,350), with greater absolute risks with autoimmune diseases than with ADHD.

Conclusion
In children with various chronic conditions, current oral glucocorticoid use is strongly associated with newly treated diabetes, hypertension, and VTE in a dose- and duration-dependent fashion. Hypertension is a more common glucocorticoid-related complication than diabetes or VTE, but in absolute terms, all of these complications are uncommon in children.

ERDAL SAG

Department of Pediatric Rheumatology, Hacettepe University, Ankara, Turkey

OLIGOARTICULAR JUVENILE IDIOPATHIC ARTHRITIS DOES NOT SHOW SIGNS OF T -CELL EXHAUSTION, IN SPITE OF INCREASED EXPRESSION OF CO-INHIBITORY RECEPTORS

Background
Activated T cells are involved in the pathogenesis of the synovitis in oligoarticular Juvenile Idiopathic Arthritis (o-JIA). T cell activation is counter-balanced via co-inhibitory receptors (co-IRs) such CTLA-4, PD-1, LAG-3, and TIM-3. Here we identify the role of co-IRs in the pathogenesis of o-JIA.

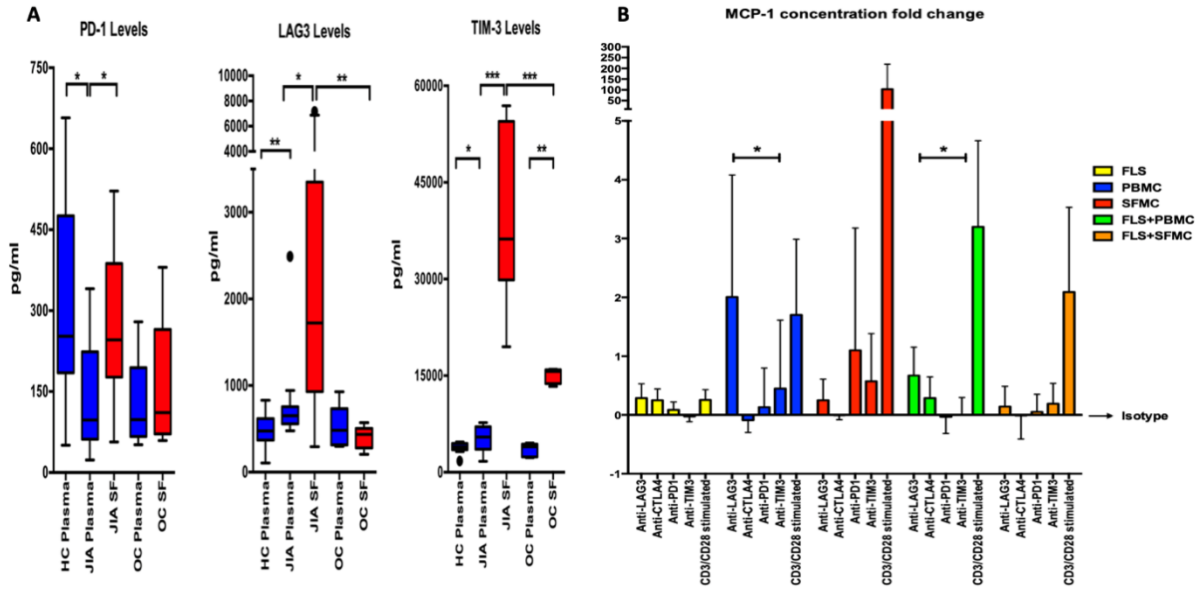
Methods
Paired synovial fluid (SF) and plasma, PBMCs and SFMCs, were obtained from o-JIA patients (n=14). Plasma from healthy controls (HC, n=14) and paired SF and plasma from 5 children requiring arthroscopy for non-inflammatory orthopedic problems (OC, n=5) served as controls. Soluble levels of co-IRs were measured by ELISA and their cellular expression by flow cytometry. Fibroblast like synoviocytes (FLS), co-cultured with autologous PBMCs/SFMCs were used as an ex-vivo disease models. Functional effects of co-IRs were evaluated via blocking them with checkpoint inhibitors in these ex-vivo disease models.

Results
o-JIA patients had increased soluble levels and CD3+CD4+CD45RO+ T cell surface expressions of sPD-1, sLAG-3, sTIM-3, but not sCTLA-4 in SF compared with plasma. Plasma and SF levels of sLAG-3 and TIM-3, but not sPD-1 levels were higher in o-JIA patients compared with controls. (Figure 1A) None of the soluble co-IR levels correlated with disease activity.

In the ex-vivo model, MHC class II expression was induced on FLS together with an increased Monocyte Chemoattractant Protein-1 (MCP-1) production. Only anti-LAG3 antibodies significantly increased the MCP-1 production in PBMC monocultures and FLS+PBMC co-cultures. (Figure 1B) PBMCs and SFMCs produced significantly higher levels of IFN-ɣ after CD3/CD28 activation ($p<0.001$), but they were not affected from addition of antibody towards the other checkpoint inhibitors.

Conclusion
This is the first report studying the effects of different co-IRs in o-JIA. Both the soluble levels and the surface expressions of co-IRs were higher at the site of inflammation in o-JIA. Thus SFMCs and PBMCs of o-JIA patients are not exhausted, based on their ability to respond to CD3/CD28 activation. This is opposite to what has been shown in adult inflammatory arthritis. Co-cultures of autologous FLSs and PBMCs/SFMCs may serve as an ex-vivo arthritis model to perform functional analysis. LAG-3 might play a role in o-JIA pathogenesis and maybe a potential therapeutic option.

Figure 1.


A
PD-1 Levels
LAG3 Levels
TIM-3 Levels
pg/ml
HC Plasma
JIA Plasma
JIA SF
OC Plasma
OC SF
B
MCP-1 concentration fold change
FLS
PBMC
SFMC
FLS+PBMC
FLS+SFMC
Isotype
Anti-LAG3
Anti-CTLA4
Anti-PD1
Anti-TIM3
CD3/CD28 stimulated

RENEE VAN DE WETERING

University Medical Center Utrecht & Wilhelmina Children's Hospital, Utrecht, The Netherlands

VITAMIN B3 (NAM) SUPPRESSES T CELL ACTIVATION IN AND PRODUCTION OF PRO-INFLAMMATORY CYTOKINES IN VITRO IN A DOSE DEPENDENT MANNER INDICATING THERAPEUTIC POTENTIAL FOR THE TREATMENT OF JIA

Background
Impaired immunological tolerance in Juvenile Idiopathic Arthritis (JIA) is the result of a disturbed balance between regulatory T-cells (Tregs) and effector T-cells (Teffs). Restoring this balance by either enhancing the suppressive function of Tregs or inhibiting activity of pro-inflammatory Teffs seems a promising therapeutic strategy. We have previously demonstrated that high concentrations of Vitamin B3 (VitB3), also known as nicotinamide (NAM), lead to an increase in FOXP3 positive cells in vitro, via suppression of the deacetylase SIRT1. However, while VitB3 has these promising effects on Tregs, the effect of VitB3 on Teff cells, the other side of the scale, is still unexplored.

Methods
T-cells were isolated from blood of healthy controls and JIA patients, as well as from the synovial fluid from JIA patients. Cells were stimulated with aCD3/aCD28 and cultured in the presence of increasing concentrations of VitB3 (0-9mM) for 1-4 days. Proliferation and expression of activation makers in primary T cells were determined using flow cytometry. Cytokine production was determined by qPCR, Luminex and flow cytometry. ERK phosphorylation was measured by flow cytometry and Western blot. ERK phosphorylation and GFP expression were also determined by flow cytometry using a murine NFAT-GFP reporter celline.

Results
In vitro VitB3 treatment of CD4+ Teff-cells significantly decreased the production of the pro-inflammatory cytokines IL-2 and IFNy measured both on mRNA and protein level. Correspondingly, surface activation markers were downregulated after VitB3 incubation, and ERK phosphorylation was decreased. Furthermore, proliferation of both CD4+ and CD8+ T-cells was inhibited with VitB3 treatment in a dose dependent manner. Murine reporter cells showed similar results.

Conclusion
In addition to the previously demonstrated increase of Treg numbers and functioning, this data demonstrates that VitB3 treatment also inhibits proliferation and activation of Teff cells in vitro. VitB3 treatment could therefore modulate the immunological balance by both increasing tolerance and suppressing immune activation. We envision that VitB3 treatment as an adjuvant therapy could thus benefit JIA patients and potentially patients with other autoimmune diseases.

SESSION VI 10:10-11:00

EZGI DENIZ BATU

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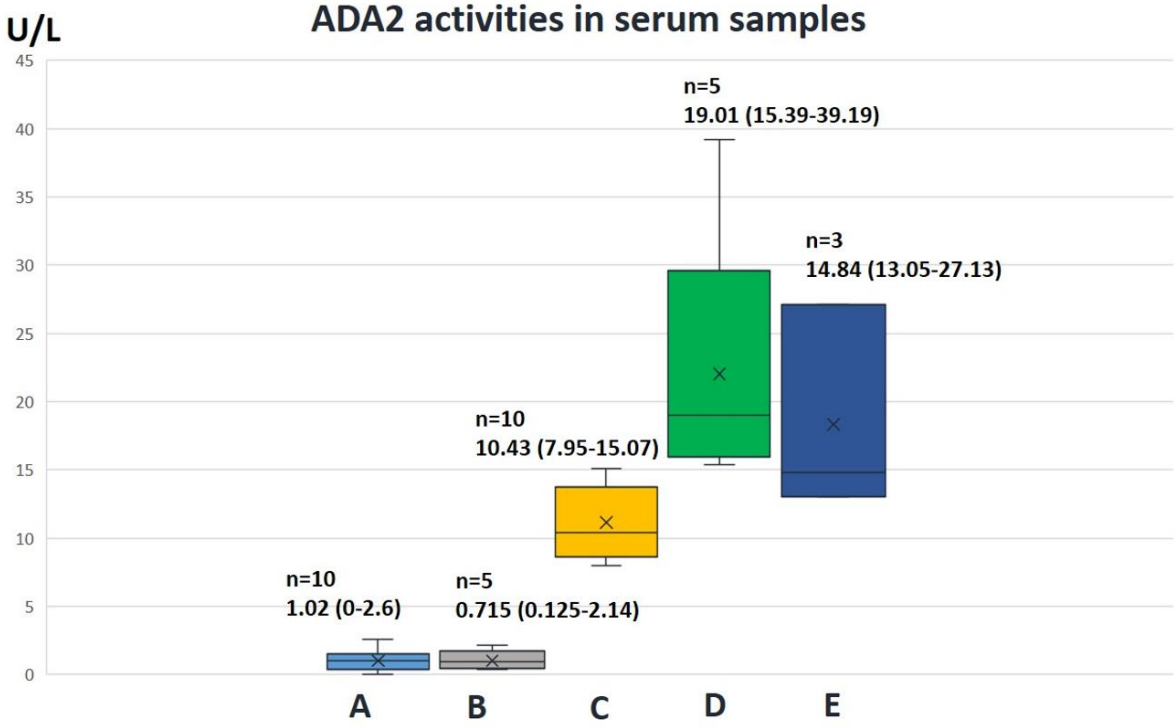
A MONOGENIC DISEASE WITH WIDE RANGE OF SYMPTOMS: DEFICIENCY OF ADENOSINE DEAMINASE 2

Background
Deficiency of adenosine deaminase 2 (DADA2) is an autosomal recessive autoinflammatory disorder caused by ADA2 mutations. We aimed to investigate the characteristics of DADA2 patients along with the ADA2 enzyme levels.

Methods
24 DADA2 patients who admitted to the Adult and Pediatric Rheumatology, Pediatric Haematology, and Pediatric Immunology Departments were included. All exons of the ADA2 gene were screened by Sanger sequencing in all DADA2 patients. Serum ADA2 enzyme activity was measured by modified spectrophotometric method.

Results
24 DADA2 patients were included; Group 1, 14 DADA2 patients with polyarteritis nodosa (PAN)-like phenotype; Group 2, 9 patients with Diamond-Blackfan anemia (DBA)-like features and one with immune deficiency. 14 PAN-like DADA2 patients did not have the typical thrombocytosis seen in classical PAN. Inflammatory attacks were evident in only Group 1 patients. Serum ADA2 was low in all DADA2 patients except one who was tested after hematopoietic stem cell transplantation. There was no significant difference in ADA2 levels between PAN-like and DBA-like DADA2 patients (Figure 1). ADA2 activities of heterozygote family members were about half the level of the control subjects. In heterozygote DADA2 patients, serum ADA2 levels were as low as the ones of homozygote DADA2 patients. ADA2 mutations were affecting the dimerization domain in Group 1 patients and in the catalytic domain in Group 2 patients.

Conclusion
We suggest that enzyme activity of ADA2 should be assessed along with genetic analysis since there are heterozygote patients with absent enzyme activity. Our data confirms a possible genotype phenotype correlation where dimerization domain mutations are associated with a PAN-like phenotype whereas catalytic domain mutations are associated with hematological manifestations.



A) DADA2 patients with PAN-like features
B) DADA2 patients with DBA-like features (prior to HSCT)
C) Family members of DADA2 patients (heterozygous for *ADA2* mutations)
D) DBA patients without *ADA2* mutations
E) PAN patients without *ADA2* mutations

CAMILLA CELANI

Ospedale Pediatrico Bambino Gesù, Rome, Italy

IDIOPATHIC RECURRENT PERICARDITIS: CLINICAL FINDINGS AND TREATMENT APPROACH

Background
Recurrent pericarditis affects 15-30% of patients with acute pericarditis. The etiology is poorly understood, being about 80% idiopathic. Several treatment options are available for recurrences, including NSAIDs, colchicine, glucocorticoides and IL-1 inhibitors (i.e. Anakinra). Standardized guidelines for the management of these patients are still lacking. To analyze clinical findings and treatment approach in a cohort of pediatric patients with recurrent pericarditis

Methods
Patients with at least two episodes of idiopathic pericarditis, followed at two Pediatric Rheumatology centers between 2006 and 2018, were included

Results
A total of 42 patients (18 males) were included. Mean age at disease onset was 11.8 years (range 4-17). Chest pain and fever were the presenting symptoms in all patients. In 47% pleural effusion was detected. Laboratory tests showed increased white blood cell count (mean 14.509/mm3), C-reactive protein (mean 18.01 mg/dl) and erythrocyte sedimentation rate (mean 39 mm/h) in all patients. The first episode was variably treated: 18/42 (43%) received NSAIDs alone, 5/42 (11.9%), colchicine alone or associated to NSAIDs and 3/42 patients (7%) received antibiotics alone. 16/42 (38%), not responsive to NSAIDs or colchicine, received glucocorticoides. Patients who received glucocorticoids at the first episode relapsed earlier (median time of 2.1 months range 10 days- 5 months), than patients treated with NSAIDs (6.6 months range 10 days -24 months) or with colchicine (5 months range 10 days-5 months) ($p<0.05$). In our study, initial treatment of the first episode did not affect the number of subsequent flares. To evaluate treatment strategy at relapses, we divided our study population in two groups: Group 1 (20 pts) in which recurrence was treated with NSAIDs, colchicine or glucocorticoid (alone or combined); group 2 (22 patients) in which anakinra was started. Among patients belonging group 2, 9 received anakinra at first relapse, 7 at the second, 2 at the third and 2 at the fourth. Anakinra treatment was followed by a prompt resolution of symptoms and inflammatory signs within 2 days. During daily treatment with full dose anakinra, no relapses were reported over a median of 13.3 months (range 5-24 months). In 13 out of 22 patients, anakinra was gradually tapered reducing the days of administration during the week. Four of these patients relapsed. The mean time from the start of anakinra to tapering was 17±4 months (range 14-23 months) in the 4 patients who experienced a relapse versus 14±4 months (range 7-21 months) in patients who did not flare, with no statistical difference. Among the 22 patients belonging to group 2 anakinra was finally discontinued in 11 after a mean time of 23.4 months (range 12-36). Among these, 8 relapsed after anakinra withdrawal (including 2 of the 4 patients already relapsed during tapering). Only 3 patients didn't present any relapse (up to 20.3 months of follow-up). All patients who relapsed responded quickly to the reintroduction of anakinra

Conclusion
Our study confirms the lack of a standardized treatment approach in patients with recurrent pericarditis. Patients treated with glucocorticoid at first episode relapse before than those treated with other drugs. Anakinra is an effective treatment; however, tapering/discontinuation of the drug

lead to relapses in several cases. Further experience on larger population is needed to define the best treatment duration and approach to withdrawal of IL-1 inhibitor

ÜMMÜŞEN KAYA AKCA

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COMORBIDITIES IN FMF

Background
Familial Mediterranean Fever (FMF) is a periodic fever syndrome, characterized by recurrent episodes of fever and serosal inflammation accompanied with high acute phase reactants.The analysis of possible comorbidities is important to understand the impact of these conditions on clinical care and whether they share a common etiological pathway. We aimed to evaluate the comorbidities associated with FMF patients in a large genetically diagnosed cohort.

Methods
We retrospectively evaluated the medical records of FMF patients who were followed up at Department of Pediatric Rheumatology in Hacettepe University between 2000 and 2015. This study was approved by the Research Ethics Committee and was conducted in accordance with the Declaration of Helsinki. The diagnosis of FMF was made according to Tel Hashomer diagnosis criteria for patients who applied prior to April 2009 and to the Turkish FMF pediatric diagnosis criteria after April 2009. The FMF patients who had homozygous or compound heterozygous mutations were included in the study. Comorbidities associated with FMF were divided into three groups; associated with increased inflammation, associated with FMF and incidental.

Results
A total of 1999 patients were enrolled in the study. Of all 1999 FMF patients, 636 were children (31.8 %), 1029 were males (51.4%), with a mean age of 31.60±16.01 years. The mean follow up time was 4.50±3.99 years (median:3.84 range from 0.21-29.4 years). 880 of 1999 (44%) FMF patients had homozygous MEFV gene mutation, the most common mutation was M694V homozygous. The remaining were compound heterozygous. 656 patients (32.8%) had one or more than one comorbidity associated with FMF. Ankylosing spondylitis was the most common comorbidity associated with increased inflammation while the most common comorbidity in FMF related comorbidities was renal amyloidosis. The frequency of ankylosing spondylitis, henoch schonlein purpura, juvenile idiopathic arthritis, polyarteritis nodosa (PAN), multiple sclerosis (MS) and Behçet's disease were increased in patients with FMF when compared to those in the literature. Systemic lupus erythematosus was observed less frequently in the patients with FMF than in the population. While the increase in the frequency of MS was 3.3 times, the frequency of PAN was increased 110 times.

Conclusion
This study shows that FMF is a hereditary disease associated with significant comorbidity. We also confirm thatinflamatory and rheumatic diseases are more common in FMF.

ELENA MORAITIS

Great Ormond Street Hospital NHS Foundation Trust, London, United Kingdom

AN INTERNATIONAL SURVEY ON APPROACHES TOWARDS IMMUNISATION IN CHILDREN WITH RHEUMATIC DISEASES: A REPORT OF THE PRES VACCINATIONS WORKING GROUP

Background
EULAR recommendations for vaccination in paediatric patients with rheumatic disease (RD) were published in 2011. The aim of the study was to ascertain the opinion and current practices of paediatric rheumatologists with regards to immunisation.

Methods
An online survey of practices and opinions towards immunisations was distributed to paediatric rheumatologists across the globe. Responses were collected via SurveyMonkey and descriptive analysis was performed.

Results
277 responses were received from 53 countries. 41% of respondents inform their practice on immunisation of patients with RD based exclusively on the EULAR recommendations, 37.5% based on national guidelines, 8.5% on local guidelines and 10% on combinations of the above. 48% of clinicians would postpone vaccinations in all cases if disease is active. In terms of immunisations with live vaccines of patients with JIA on immunosuppresive treatment, 41% of respondents would recommend the first dose of MMR or Varicella vaccines to patients with stable disease on Prednisolone < 1 mg/kg/day (maximum 20 mg) for less than 1 month or higher dose up to 2 mg/kg/day for less than 14 days, 14% would also recommend these vaccines if the above steroid dose was given in combination with Methotrexate (MTX) < 15mg/kg/week, 30% would recommend these vaccines if the patient was on MTX monotherapy. Comparable percentages reported confidence to also recommend booster doses of the two vaccines for the above drug combinations (45%, 15.7%, 37%, respectively), whilst up 10% of respondents would recommend them to patients on anti-TNF agent alone, and up to 7% for other biologics. For patients with SLE and quiescent disease on similar medications as above, 41%, 15%, 31%, respectively, of clinicians reported confidence to recommend MMR or Varicella booster doses. 48% of the respondents identified the reluctance of other health professionals involved in the process of immunisations as the main reason hampering the vaccination of paediatric patients with RD, whilst 22% indicated parental refusal or hesitancy.

Conclusion
There is variation in practice and opinions worldwide with regards to immunisations in paediatric patients with RD, and this likely reflects the discrepancies between national guidelines for immunisation of immunosuppressed child and also national policies. There is an increasing vote of confidence towards immunisation of patients on lower grade immunosuppression with MMR or varicella vaccines.

VERONICA MOSHE BERGONZO

Multicenter. Affiliations not listed. Israel

LIVE ATTENUATED VACCINES IN PEDIATRIC RHEUMATIC DISEASES ARE SAFE: MULTICENTER, RETROSPECTIVE DATA COLLECTION

Background
Common practice is to withhold vaccination with live-attenuated vaccines in patients with rheumatic diseases on high-dose DMARDs, glucocorticosteroids or biological agents, due to limited safety data, and the (theoretical) risk of introducing an infectious disease to the patient. Evidence for this approach is low. We collected data from pediatric rheumatologists who vaccinate these patients, to obtain additional safety data, which might update and revise this approach.

Methods
Data from 13 pediatric rheumatology centers in 10 countries were collected.

Results
234 patients were reported; mean age 5± 2.7, 70% girls. 206 had JIA;. 46% oligoarticular, 36% polyarticular, 8% systemic, 5% SPA types, 5% JIA and uveitis. 48% of JIA patients were in remission on medication. Disease activity was low in 38%, high in 2%, moderate in 7%; 11 patients had juvenile dermatomyositis, 3 systemic and 2 localized scleroderma, 4 isolated idiopathic uveitis, 1 CINCA syndrome, 1 MKD , and 1 FMF.

110 patients had MMR/V booster while on MTX; 3 reported mild side-effects of local skin reaction and pain, none had disease flare. 76 had booster while on MTX+ anti-TNF; 7 reported mild and transient adverse events of local skin reaction, fever and URTI. 39 had booster while on anti-TNF alone; 1 reported fever. 3 had booster while on tocilizumab, 7 on anakinra, and 5 on canakinumab. There was no relation between disease activity, type or duration, sex, age and outcome of vaccinations. No vaccine infection related to measles, rubella, mumps and varicella were reported.

Conclusion
This large, retrospective data collection demonstrates that live-attenuated booster vaccine is probably safe in children with rheumatic diseases, on immunosuppressive therapies. This strengthens the new PRES recommendation: “Vaccination of live-attenuated vaccines in patients on high-dose DMARD, high-dose glucocorticosteroids or biological agents can be considered on a case-by-case basis, weighing the risk of infections against the hypothetical risk of inducing infection through vaccination.” These data provide the basis for a large, prospective data collection study that is planned by the PReS vaccination study group. It will increase the current level of evidence for the safety of vaccinations in our pediatric rheumatology population.

Poster Presentations

11.06.2019

Poster Tour-I Group-1

ANTIA GARCIA FERNANDEZ

Rheumatology Department, Ramón y Cajal University Hospital, Madrid, Spain

DISEASE COURSE AND OUTCOMES OF PREGNANCY IN JUVENIL IDIOPHATIC ARTHRITIS: ANY DIFFERENCE AMONG DISEASE SUBSETS?

Background
To analyze the course of disease during pregnancy and pregnancy outcomes in patients with JIA according to disease subtype, with focus on the medication use.

Methods
A retrospective observational study of pregnant JIA patients followed between 2010 and 2018. Disease activity (DAS28-PCR3) was analyzed before conception, at each trimester and postpartum. Flare was defined as an increase in clinical activity leading to intensified therapy. Pregnancy outcome were also recorded.

Results
Sixteen patients and 22 pregnancies were included. Two pregnancies were voluntary interrupted. 10/22(45,5%) were pregnancies observed in Oligoarticular Extended (OLA-E), 6(27,3%) Polyarticular (PLA), 4(18,2%) Systemic (SYS), 1(4,5%) Oligoarticular (OLA) and 1(4,5%) Enthesitis related Arthritis (ERA) JIA patients. At conception 19(95%) pregnancies were on remission, 1(5%) OLA-E patient in low disease activity. Among the 20 pregnancies ended with a live birth, 1 OLA, 4 SYS and 1 ERA patients mantained sustained remission, without treatment, throughout pregnancy.There were 7 flares in 6 (31,8%) pregnancies, 5 (71,4%) of them among PLA patients and 2 (28,6%) among OLA-E patients. One pregnancy in a patient with PLA JIA (4,5%) was characterized by more that one flare. Most of flares occurred during 2^trimester. Eigth flares occurred in postpartum, also in 2 pregnancies after voluntary pregnancy interruption.Regarding treatment at conception; 8 (40%) pregnancies were on bDMARDs, treatment was stopped at positive pregnancy test in 6 pregnancies, 2 (33,3%) required restart of treatment due to a flare, and 3 flared in puerperium with restart of bDMARDs. Regarding pregnancy complications; one pregnancy was complicated with pre-term premature rupture of membranes, in a patient not taking prednisone. There were 5 (25%) pre-term deliveries.

Conclusion
Nearly one third of pregnant patients with JIA had a disease flare during pregnancy. Flares were observed only in 2 disease subsets (PLA; OLA-E) and associated with discontinuation of bDMARDs. The preconception counseling of patients with JIA should include the disease subset in the risk stratification and consequently the continuation of bDMARDs during pregnancy.

Table 1	Polyarticular	Oligoarticular	Oligoarticular extended	Systemic	Enthesitis related arthritis
Patients, n(%)	5(31.2)	1(6.25)	6 (37.5)	3 (18.8)	1 (6.25)
Pregnancies, n(%)	6 (27.3)	1 (4.5)	10 (45.5)*	4 (18.2)	1 (4.5)
Age at pregnancy (years) mean+SD, yrs	33 (5.51)	28 (0)	27.8 (5.63)*	24.5 (6.25)	26 (0)
Disease duration, months, mean+SD,	20.5 (2.6)	22 (0)	19.5 (6.2)*	19.5(6.5)	19 (0)
CCS before conception, n (%), daily dose, mg/day, mean+DS	4 (66.7) 6.6 (5.82)	0 (0) 0 (0)	3(33.3)* 4.5 (0.86)*	0 (0) 0 (0)	0 (0) 0 (0)
cDMARDs before conception None (%) Ciclosporin (%) Hydroxycloroquine (%) Methotrexate (%)	 5 (83.3) 1 (16.7) 0 0	 0 (100) 0 0 0	 6 (60)* 0 (0) 3 (30)* 1 (10)*	 0 (100) 0 0 0	 0 (100) 0 0 0
bDMARDs before conception None (%) ETANERCEPT (%) GOLIMUMAB (%) ABATACEPT (%)	 1 (16.7) 3 (50) 1 (16.7) 1 (16.7)	 0 (100) 0 0 0	 5 (50) 5 (50)* 0 0	 0 (100) 0 0 0	 0 (100) 0 0 0
Stop bDMARDS at positive pregnancy test, n (%)	4 (80)	0 (0)	4 (80)*	0 (0)	0 (0)
DAS28PCR, mean+DS **PC** **1T** **2T** **3T** **PP**	 1.69 (0.42) 2.47 (1.36) 3.11 (1.05) 2.84 (1.61) 2.66 (1.13)	 1.15 (0) 1.64 (0) 1.64 (0) 1.64 (0) Not available	 1.73 (0.45) 1.82 (0.47) 2.29 (0.53) 1.94 (0.29) 2.85 (0.71)	 1.27 (0.25) 1.53 (0.31) 1.56 (0.30) 1.71 (0.10) 1.59 (0.14)	 1.15 (0) 1.64 (0) 2.09 (0) 1.99 (0) 1.60 (0)
Flare, n (%) **1T** **2T** **3T** **PP**	 1/7 (14.3) 3/7 (43) 1/7 (14.3) 2/8 (25)*	 0/7 (0) 0/7 (0) 0/7 (0) Not available	 1/7 (14,3) 1/7 (14.3) 0/7 (0) 6/8 (75)*	 0/7 (0) 0/7 (0) 0/7 (0) 0/8 (0)	 0/7 (0) 0/7 (0) 0/7 (0) 0/8 (0)
Pregnancy outcome Live-births, n (%) Ongoing pregnancies, n (%) Spontaneus pregnancy loss n (%) VPI, n (%) P-PROM(%) Delivery week, median min-max Premature delivery, n (%)	 5 (83.3) 1(16.7) 0 (0) 0 (0) 1 (16.7) 36 (33-41) 2 (33.3)	 No available 	 7 (77.8)* 0 (0) 0 (0) 2 (22.2)* 0 (0) 38 (35-39) 3 (37.5)	 1 (100) 0 (0) 0 (0) 0 (0) 0 (0) 41 (38-41) 0 (0)	 1 (100) 0 (0) 0 (0) 0 (0) 0 (0) 41 (0) 0 (0)

cDMARDS conventional disease-modifying antirheumatic drug, bDMARDs biological disease-modifying antirheumatic drug, 1T, First trimester, 2T Second trimester, 3T Third trimester, PC preconception, PP postpartum, CCS corticosteroids, VPI voluntary pregnancy interruption, PROM premature rupture of membranes.
* Metothrexate exposure during 1^T at 8W and fetus malformation at 17W.
* Taking into account voluntary pregnancy interruption.

MARIO SESTAN

Department of Paediatrics, University Hospital Centre Zagreb, University of Zagreb School of Medicine, Zagreb, Croatia

QUALITY OF LIFE IN JUVENILE IDIOPATHIC ARTHRITIS-ASSOCIATED UVEITIS: DO WE NEED A NEW ASSESSMENT QUESTIONNAIRE?

Background
Although prognosis of uveitis within JIA (JIA-U) significantly improved, complications still cause severe impairment of visual function in 25-33% of children that certainly affects their psychophysical and psychosocial development and quality of life (QoL).

Methods
The study included 42 children with JIA divided into two groups. The first group consisted of 21 children with JIA-U and the second of 21 children with JIA and no uveitis. Both groups of patients and their parents filled the JAMAR questionnaire. The significance of differences between groups was verified by the independent-samples t-test. The Pearson correlation coefficient was used for measurement of the strength of the linear relationship between variables.

Results
There were no statistically significant differences in the JIA-U group and the control group in either of the examined variables. Although there is a tendency of higher scores in children with JIA-U, which indicates their worse functioning, higher pain intensity and worse current emotional state, these differences were not statistically significant. Two groups did not differ significantly in the assessment of their own overall functional ability, which was associated with experienced pain intensity. Stronger pain intensity was associated with dysfunction ($r = 0.642$, $p < 0.01$) while a lower level of QoL was associated with more intense pain ($r = 0.542$, $p < 0.01$) and poor current emotional state ($r = 0.401$, $p < 0.05$). The activity of the disease in children was not significantly related to any determinant of the QoL. In contrast to children, parents of children with JIA-U estimated current emotional state of their children significantly worse ($t = 2.05$, $p < 0.05$) and the overall level of functioning significantly lower than parents whose children did not have uveitis ($t = 2.03$, $p < 0.05$).

Conclusion
Since children with JIA evaluated the QoL equally well, whether they had uveitis or not, we can conclude that they are psychologically well adapted to their health status and cope well with different levels of pain. These results support a need for the development of new uveitis specific questionnaires that will enable us better identification of patient's requirements.

BRENDA DE JESÚS FORTUNA REYNA

Mexico (affiliations not listed)

LONG-TERM FOLLOW-UP OF PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS IN A MEXICAN CENTER.

Background
JIA comprises an heterogeneous group of diseases characterized by chronic arthritis, of unknown etiology, and onset age before 16. (1) Juvenile Idiopathic Arthritis(1) is the most common chronic rheumatic disease in children, being an important cause of disability, affecting quality of life (2). There are several subtypes of the disease, despite oligoarticular course has been described as the most frequently seen, up to 50% of JIA cases presented a polyarticular disease (4)(3). Data suggest that patients who receive early therapeutic intervention are more likely to reach clinical remission. In a systematic review, Wallace's criteria were used to determine drug remission and inactive disease. They reported 7% and 47% of patients reached remission at 1.5 and 10 years, respectively. Oligoarticular patients had a shorter time to remission, while polyarticular positive rheumatoid factor were the least likely to achieve it (5). Mexico belongs to a group of developing countries where there is limited information about incidence, prevalence, clinical features, age and time to diagnosis, treatment, and remission of JIA patients

Methods
The study design was observational with no intervention, ambispective, among patients with JIA, according to ILAR criteria of pediatric rheumatology clinic from University Hospital "Dr. José Eleuterio González" over a 2-year period (2016-2018). Medical records of patients were retrospectively reviewed and collected information as demographics, age at diagnosis, disease activity, joints involved, treatment, adverse events, clinical inactivity and remission. Statistical analysis was descriptive with measure of central tendency. For continuous variables, mean, median, interquartile range and standard deviation were used to present data.

Results
We enrolled 70 patients with JIA, 52 (74%) female, with a median age at diagnosis of 11.7 years. The most frequent subtype was polyarticular positive rheumatoid factor (25, 36%). Eighty adverse events were reported; 45 of special interest. The median time to remission observed was 61 months (95% CI 43.3-78.6); 33 (47%) patients reached inactive disease.

Conclusion
The rates of adverse events was low, demonstrating a good safety profile of the treatment, however time to remission is greater than reported in literature.

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DISCRIMINANT ABILITY OF THE PARENT VERSION OF THE JUVENILE ARTHRITIS DISEASE ACTIVITY SCORE IN A LARGE MULTINATIONAL COHORT OF PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS.

Background
In the management of children with juvenile idiopathic arthritis (JIA) most recent recommendations incorporate parents' and children's perception of the disease course and the therapeutic effectiveness. Therefore a new parent-centered disease activity tool, named parent Juvenile Arthritis Disease Activity Score (parJADAS) is currently under development (1).

Methods
The parJADAS includes 4 measures: 1) parent assessment of disease activity; 2) assessment of pain intensity; 3) proxy assessment of joint disease; 4) assessment of morning stiffness (MS). Disease activity and pain being assessed on a 21-numbered circle VAS (0 = best and 10 = worst), the active joint count on the total number of any swollen or painful joints, up to a maximum of 10, the MS duration on a Likert scale, ranging from no MS (0 points) to >2 hours of MS (10 points).
Validation was conducted on a dataset of 8,656 children with JIA from 49 countries, enrolled in the study of Epidemiology, treatment and Outcome of Childhood Arthritis (EPOCA). Discriminant ability was evaluated by comparing parJADAS levels (median, [IQR]) among patients with inactive disease (ID), with low, moderate or high disease activity (respectively LDA, MDA, HDA) according to the cJADAS10; among patients in remission, continued activity, or flare according to their physician and patients whose parents were satisfied or not satisfied with current disease state. To assess the possible influence of the articular and extra-articular damage on the parJADAS, the score levels were compared among ID patients with or without arthritic damage and with at least 2 years of disease (n=2,423).

Results
The levels of parJADAS in ID, LDA, MDA, and HDA patients were 0.0 [0.0, 1.0], 3.0 [1.0, 6.0], 6.0 [2.0, 11.5], and 14.5 [8.5, 21.0], respectively (Kruskal-Wallis test, $p<0.001$). Meanwhile in patients in remission, continued activity, or flare according to their physician were 0.5 [0.0, 3.5], 9.0 [3.5, 17.0], 12.0 [5.5, 20.0], respectively (Kruskal-Wallis test, $p<0.001$). Median parJADAS in patients whose parents were satisfied or not satisfied with disease state is 1.5 [0.0, 7.0] and 13.0 [6.6, 20.5], respectively (Mann-Whitney test $p<0.001$). ParJADAS was not different in JIA patients in remission with or without damage measured with the Juvenile Arthritis Damage Index(JADI), (Mann-Whitney test $p=0.08$).

Conclusion
The parJADAS showed excellent discriminant ability in a large multinational cohort and is not relevantly influenced by disease damage in JIA patients in remission.

(1)Consolaro A, van Dijkhuizen P, Januskeviciute G, Muratore V, Giancane G, Martini A, Ravelli A. "Development and Initial Validation of the Parent and Child Versions of the Juvenile Arthritis Disease Activity Score" [abstract]. Arthritis Rheumatol. 2016; 68 (suppl 10).

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HOME MONITORING OF CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS USING THE EQ-5D-5L-Y.

Background
In recent years, juvenile idiopathic arthritis (JIA) research has shifted towards treat-to-target therapy based on clinical assessments and patient-reported outcomes. A well-known generic measurement of quality of life is the EQ-5D-Y-5L. Herewith, we report preliminary results of using a mobile application (Reuma2Go) with the EQ-5D-Y-5L for remote monitoring of children with JIA.

Methods
The study was designed as a monocentric cohort study. Data from October 2017 to January 2019 were available for 70 patients with JIA. Correlations between EQ-5D-Y-5L dimensions and comparable questions of the Juvenile Arthritis Multidimensional Assessment Report (JAMAR) were assessed by Spearman's correlation. Diagnostic test characteristics were computed for external validity of the EQ-5D-Y-5L as potential instrument for monitoring disease activity, using an active joint count greater than zero as definition of active disease.

Results
Seventy patients with JIA completed 115 JAMAR and 113 EQ-5D-Y-5L questionnaires. Moderate to high correlations were found between EQ-5D-Y-5L dimensions and JAMAR questions. Individual dimensions of the EQ-5D-Y-5L and the EQ-VAS displayed comparable predictive value for active disease (accuracy 63.7%-76.1%). The unweighted sum of all EQ-5D-Y-5L dimensions demonstrated high sensitivity (82.9%) and negative predictive value (86.7%).

Conclusion
Initial results of a mobile application using the EQ-5D-Y-5L as monitoring instrument in patients with JIA are promising, indicated by high sensitivity and negative predictive values. Further research and prolonged data collection are necessary to investigate reliability and responsiveness of the EQ-5D-Y-5L. In the future, accurate assessment of HRQoL and disease activity in JIA patients at home could provide information to determine the frequency of clinical visits, assess efficacy of therapeutic interventions and guide treat-to-target strategies.

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CYTOKINE SIGNATURE DOES NOT CORRELATE WITH PAIN OR DISEASE ACTIVITY IN WELL CONTROLLED ERA

Background
Inflammation is a mediator and primary driver of joint damage in juvenile idiopathic arthritis (JIA). Musculoskeletal pain can be experienced in the presence or absence of inflammation. Enthesitis related arthritis (ERA) is a subtype of JIA characterised by inflammation of the spine, enthesis, and peripheral joints. Cytokines and numerous other regulatory molecules are implicated in pain and inflammation, yet, to date, no reliable biomarkers have been identified.

Methods
42 patients, with either a prior diagnosis of JIA or back pain, agreed to have a standard clinical MRI scan of lumbar spine, sacroiliac joints, and pelvis and to donate serum. Serum was also collected from 12 volunteer age matched healthy controls. Serum was analysed using a bead-based multiplex assay (Luminex) for the concentrations of the following analytes: IL-6, IL-12, IL-17, IL-23, IL-27, TNFα, IFNγ, MIF, OPG, SOST, GM-CSF, VEGF, DKK-1, S100A8, MMP-3 and CRP. To assess pain levels, patients indicated on a scale of 0-10 the amount of back pain experienced at night and separately the amount of back pain experienced at any time during the last week. They also completed a Bath Ankylosing Spondylitis Disease activity Index (BASDAI) questionnaire to assess disease activity. Cytokine concentrations in patients with ERA were compared with those of controls. The levels were also correlated with the two measures of back pain as well as individual questions from the BASDAI questionnaire.

Results
Of all 54 samples tested, 11 patients and 5 controls cross-reacted with the negative control for the assay and thus were excluded from analysis. Based on MRI scan results, 14 patients had ERA, 8 had biomechanical pain, 7 had other subtypes of JIA, and 2 had non-specific features of spinal inflammation. The median overall back pain and the total BASDAI scores for the ERA group were 2.4 (IQR=1.45-5.55) and 2.5 (IQR= 0.75-6.25) respectively, suggesting well controlled disease on treatment and minimal residual symptoms. There was no statistical difference between cytokine levels in the ERA group compared to controls when corrected for multiple testing, with the exception of IL-12 which was significantly higher in controls (p=0.003). No correlation was found between cytokines and pain scores (at night or overall during the last week) or with the overall BASDAI score or any of the sub-component questions of the BASDAI questionnaire.

Conclusions
Well-controlled ERA patients on treatment have similar cytokine profiles as healthy controls and they do not correlate with clinical pain scores or disease activity.

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THE PROJECT OF ESTABLISHING A RESEARCH AGENDA FOR JIA JOINTLY BY PATIENTS, CARERS AND CLINICIANS

Background

Research on Juvenile Idiopathic Arthritis (JIA) should have the primary goal to ultimately improve the lives of the affected patients, and help health professionals provide the best care for them. Therefore, these end users of research evidence – patients, carers (parents/caregivers) and clinicians – should be included in the process of identifying research priorities. Importantly, patients can use their unique experiential knowledge to give vital input to researchers in designing a study. Combining this input with the goal of research(ers) to make a true impact on patients' lives, will result in research that is more effective and meaningful, and thereby increases research value. To this end, we initiated the project of establishing a research agenda for JIA jointly by patients, carers and clinicians.

Methods

The method for research priority setting developed by the James Lind Alliance (JLA) is used. This method consists of several steps with the end goal of creating a top 10 list of research priorities. First, a steering group with equal representation of patients, parents and clinicians was assembled. We are now in the process of collecting research questions through an online survey. Focus groups are being held to ensure the inclusion of younger patients. Questions will be clustered and checked against the evidence. Next, the process of interim priority setting will follow, in which a shortlist of up to 30 questions will be assembled. During a final workshop, scheduled for the end of 2019, the top 10 research priorities will be established. A process evaluation is conducted to monitor ethical aspects in the decision-making process.

Results

The first step of collecting research questions is performed until the end of March 2019. We will be able to present preliminary results on the questions gathered from the online survey and focus groups by June 2019. Furthermore, we will discuss the effects of our efforts to be inclusive and representative of every party involved.

Conclusion

Through this project, patients, carers and clinicians are brought together to define the most important unanswered questions for JIA. Engaging patients and stakeholders in this crucial phase is the next step in performing more meaningful and effective research.

Poster Tour-I Group-2

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STUDY ON SERUM DNAASE1 ACTIVITY IN PEDIATRIC ONSET SYSTEMIC LUPUS ERYTHEMATOSUS FROM A TERTIARY CARE CENTRE IN NORTH WEST INDIA

Background

DNAase is an apoptotic endonuclease responsible for degradation of chromatin released by inappropriately cleared dead cells. DNAase1 activity in systemic lupus erythematosus (SLE) patients is lower than that in inactive disease in studies conducted in adult SLE patients from developed country. There is a paucity of data on DNAase1 activity in paediatric SLE from India.

Methods

A cross-sectional observational study was conducted over a period of 1 year. Thirty-three consecutive children with pediatric-onset SLE were enrolled and divided into active and inactive disease activity groups based on Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) score and compared the serum DNAase1 level between the two groups.

Results

Out of 33 children enrolled, 13 (39.3%) had active disease (SLEDAI score ≥ 3) and 20 (60.6%) had inactive disease activity. Mean age at diagnosis was 8.5 years and 10.2 years in active and inactive groups respectively. There is female preponderance (66.7%) in the enrolled patients. Anti nuclear antibody (ANA) was positive in 90.9% of patients. The most common pattern of ANA was diffuse pattern (48.4%). The patients in active disease activity group presented most commonly with nephritis (53.8%), rash (53.8%), arthralgia (38.5%), oral ulcer (30.8%) and central nervous system (CNS) involvement (38.4%) while patients in inactive disease activity group presented with nephritis (35%), arthralgia (35%), rash (25%) and CNS involvement (30%). Class III/ IV lupus nephritis was present in 25% in active disease activity group while it was present in 23.1% in inactive disease activity group. Anti-double stranded DNA (anti dsDNA) was elevated in 53.8% in active group and 50% in inactive group. Antiphospholipid antibody was present in 3 (23.1%) in active disease activity group and 5 (25%) in inactive disease activity group. The mean serum concentrations of DNAase1 were 15.394 ng/ml in active disease group and 15.205 ng/ml in inactive disease group. There was no statistically significant difference in the serum DNAase1 concentrations between the two groups (p=0.943). There was also no significant difference in the mean serum concentration of DNAase1 in patients with or without nephritis (p= 0.080).

Conclusion

The present study could not established any correlation between serum DNAase1 levels and disease activity in pediatric-onset SLE. There was no association between serum DNAase1 levels and organ involvement such as nephritis in the enrolled patients.

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DIAGNOSIS AND INITIAL MANAGEMENT OF JUVENILE-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS IN THE UK AND IRELAND

Background

The incidence of Juvenile-onset Systemic Lupus Erythematosus (JSLE) in the UK is not well described. Furthermore, we do not know how children and young people initially present and when and where they access care. Previous work has described significant variation in time to diagnosis for UK patients. The aim was to describe how patients with JSLE currently present, are diagnosed and managed across the UK.

Methods

Data was collected over 13 months on all children (aged <18 years) in the UK and Ireland with a new diagnosis of suspected JSLE (meeting either American College of Rheumatology classification criteria (ACR-1997) or Systemic Lupus International Collaborating Clinics classification criteria (SLICC-2012)). Anonymised data was collected from all UK/Ireland paediatricians every month using British Paediatric Surveillance Unit (BPSU) methodology and from relevant adult clinicians using a parallel reporting system. Patient consent was not required following Ethical and Confidentiality Advisory Group approval.

Results

102 cases were reported from Sept 2017–Oct 18. 65 cases were excluded (duplicate cases, diagnosis date outside study period, case definition not met, clinical data still pending) and 37 included. Of the 35 patients meeting ACR-1997, median age at diagnosis was 12.8 years with female:male gender of 4.8:1 respectively. 24/35 (69%) were non-Caucasian. Median time from symptom onset to diagnosis was 2 months (IQR 1 – 6 months). The longest delay was 106 months (patient initially diagnosed with Henoch Schnolein Purpura. The diagnosis was made by or in conjunction with paediatric rheumatology in 21/35 (60%) patients. 4/35 (11%) patients were diagnosed solely by paediatric nephrology, 2/35 (6%) by adult rheumatology, 7/35 (20%) by general paediatrics and 1/35 (3%) by paediatric infectious diseases. Of the twelve patients where diagnosis did not involve rheumatology ten were referred to either adult or paediatric rheumatology. Table 1 shows treatments used. No patients had died within one month of diagnosis.

Conclusion

Diagnosis of JSLE involved paediatric rheumatology in 60% of cases. Median time to diagnosis from symptom onset is two months but there is significant variation; future work will focus on factors influencing this. Analysis of final data (2 year incidence data) will facilitate estimation of current UK incidence rate.

Table 1: Treatments used within one month of diagnosis

Treatment	Patient number (%)
Oral/IV steroids	31 (89)
Hydroxychloroquine	33 (94)
Mycophenolate mofetil	17 (49)
Rituximab	8 (23)
Azathioprine	6 (17)
Methotrexate	5 (14)
Cyclophosphamide	3 (9)
Ofatumumab	1 (3)
IV immunoglobulin	1 (3)
Plasmapheresis	1 (3)

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LONGITUDINAL DISEASE- AND STEROID-RELATED DAMAGE AMONG ADULTS WITH CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

Background
Determine whether adults with childhood-onset systemic lupus erythematosus (cSLE) are at increased risk for disease- and steroid-related damage as compared to individuals with adult-onset SLE (aSLE), and whether they continue to accumulate disease damage in adulthood.

Methods
Data derive from the 2007-2015 cycles of the Lupus Outcomes Study, a longitudinal cohort of adults with confirmed SLE. The Brief Index of Lupus Damage (BILD), a validated, patient-reported measure, was used to assess SLE-associated damage. Participants with baseline BILD were included (N=1035). Diagnosis at age <18 years was defined as cSLE (N=113). Outcome variables included BILD score at baseline and follow-up, clinically significant change in BILD score over follow-up period, and presence of steroid-related damage (cataracts, osteoporosis-related fracture, avascular necrosis or diabetes mellitus).

Results
Mean time between baseline and follow up BILD assessment was 6.3±1.7 years. In adjusted analyses, participants with cSLE and aSLE had similar levels of disease-related damage, and accumulated damage at similar rates. Participants with cSLE were more likely to report steroid-related damage (OR 1.7, 95% CI 1.1-2.8) in the adjusted analysis as compared to those with aSLE. Likelihood of steroid-related damage increased with disease duration for both groups, but was consistently higher among cSLE participants.

Conclusion
In this longitudinal cohort of adults with SLE, participants continued to accumulate damage at similar rates over time, regardless of age at onset or disease duration. Childhood-onset predicted increased risk of steroid-related damage. Aggressive use of steroid-sparing treatment strategies during childhood may be important to prevent steroid-related damage in adulthood.

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GENETIC FACTORS IN JUVENILE-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS (JSLE): FUTURE GUIDES FOR INDIVIDUALIZED TREATMENT

Systemic Lupus Erythematosus (SLE) is an autoimmune and systemic inflammatory disease. Disease presentation, course and outcomes vary according patient age and/or ethnicity. For 15 to 20% of SLE patients the disease starts adolescence, they are classified as juvenile onset SLE (jSLE) and is known to be more aggressive than adult onset in particular with regards to kidney damage. Disease onset before 5 years of age are very uncommon and named early-onset SLE (eoSLE). The gender distribution varies between age groups with almost equal risk for boys and girls under 5 years, a 4 to 5-fold higher prevalence in girls under the age of 16, and a female to male ratio of 10:1 in the adult group. It is a multifactorial disease, not fully understood which explains the difficulty in determining the exact origin, although genetic factors are suspected. Indeed, family cluster, disease concordant in monozygotic twins (30%), and poor prognosis of individuals of African or Asian descent suggest a genetic involvement.

Our main hypothesis is that genetic causes may play a more pronounced role in jSLE. While in adult, it could be a consequence of genetic, environmental and hormonal factors.

This project will:

- Determe the occurrence of gene mutations and/or variants in a large cohort of jSLE patients from the United Kingdom (n=approximately 400) by using a based target enrichment approach on genes causing monogenic and/or previously reported genetic variants to be associated with SLE (from previous studies on adult).
- Associate variants with patient characteristic (symptoms, treatment, age at disease onset).
- Make comparison with MASTERPLANS (MAximizing Sle ThERapeutic PotentiaL by Application of Novel and Stratified approaches) project on adult SLE. The aim is to identify markers of systemic and renal inflammation and their potential as predictors of treatment responses (to Mycophenolate Mofetil, Belimumab and Rituximab). This will allow us to identify shared and unique genetic variants on disease courses, treatment response and outcomes in jSLE patients.

- Generate pilot data for future studies.

The aims will be:
To help in jSLE diagnosis because early detection is crucial in controlling the diseases before the occurrence of permanent damage.

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CLINICAL AND LABORATORY CHARACTERISTICS IN JUVENILE-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS (JSLE) ACROSS AGE GROUPS

Background
Systemic lupus erythematous (SLE) is a systemic autoimmune/inflammatory condition. Approximately 15-20% of patients are diagnosed before turning 18, and therefore have juvenile-onset SLE (JSLE). Gender distribution, clinical presentations, disease courses and outcomes vary between JSLE patients and individuals with adult-onset SLE. While frequently discussed and attributed to variable pathophysiology, differences between age groups within the paediatric cohort have not been systematically investigated.

Methods
The main aim was to identify and define age-specific clinical and/or serological differences in JSLE patients. Patient records from the UK JSLE cohort study were accessed and grouped based on the age of diagnosis: pre-pubertal (≤7), peri-pubertal (8-13) and adolescent (14-18). Disease activity (BILAG) and damage (SLICC) were analysed at diagnosis and during follow-up

Results
418 JSLE patients were included in this study: 43 patients were pre-pubertal (≤ 7); 240 were peri-pubertal (8-13) and 135 were adolescent (14-18) at the time of diagnosis. The adolescent group presented with more severe disease than peri-pubertal, and pre-pubertal patients (pBILAG2004 scores = median of 9[4-20], 7[3-14], and 7[3-13] respectively, p=0.015) with increased disease activity in the adolescent group in the following BILAG domains: mucocutaneous (p=0.025), musculoskeletal (p=0.029), renal (p=0.027) and cardiorespiratory (p=0.001). Adolescents exhibited higher frequency of ANA positivity (p=0.034) and higher anti-dsDNA titres (p=0.001). Pre-pubertal individuals less frequently presented with leukopenia (p=0.002), thrombocytopenia (p=0.004) or low complement (C3, C4) (p=0.002). There were no significant differences in pBILAG2004 defined disease activity between patient groups as disease progressed or in total SLICC and ACR at last follow-up visit (median followup in years: pre-pubescent 6[3-9]; peri-pubertal 4[2-6]; adolescent 2[1-4]).

Conclusion
Disease presentations and laboratory findings vary significantly between age groups within the UK JSLE cohort. Adolescent patients present with greater disease activity and “classic” autoantibody, immune cell and complement patterns. Conversely, prepubescent patients present with lower rates of autoantibody positivity, leukopenia and hypocomplementemia. No differences were seen at last follow-up. This supports that “earlyonset” JSLE cases (≤7) may develop from an initially primarily autoinflammatory pattern to a “classic” autoimmune pattern during disease. These results warrant further research, including investigation of genetic contributors, autoantibody titres and associated immunologic alterations.

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IS PEDIATRIC ONSET LUPUS MORE SEVERE IN BOYS? OUR EXPERIENCE AT A TERTIARY CARE CENTER IN NORTH-WEST INDIA

Background
There is diversity in clinical presentation of pediatric onset SLE (pSLE) and the manifestations are more severe as compared to adults. However, male patients with pSLE have been known to have a more severe disease course along with higher morbidity.

Methods
We analyzed the clinical and immunological profile and outcome of male patients diagnosed with SLE at less than 16 years of age. These children were followed-up in Pediatric Rheumatology Clinic, , Postgraduate Institute of Medical education and research, Chandigarh, India. Details on demographic data, clinical presentation, laboratory findings, immunological profile, treatment regimens and outcomes of these children were retrieved from clinic files.

Results
Forty-three boys were diagnosed to have SLE between January 1998 to December 2018. Mean age at presentation was 9.7 years (range: 9 months-12 years). Total patient years of follow up was 192 years. The most common clinical presentation was fever in 38 (88%) patients; rash in 27(63%); pallor in 21(49%); edema with urinary abnormalities in 17(40%) and photosensitivity in 16 (37%). A diagnosis of lupus nephritis was made in 25 (58%) patients out of which 17 (39.5%) had nephritis at presentation. Renal biopsies were performed in 18 patients; 11 had class IV disease, 2 had class 5 disease, 2 had class IV/V. Neuropsychiatric manifestations were seen in 11 (26%) patients. We also noted a family history of lupus like illness in 4 patients and 3 (6.9%) were found to have early complement deficiencies. Antiphospholipid antibodies (aPLA) were detected in 8 (18.6%)patients. Infections were seen in 16 (37%) patients during follow-up. All patients received steroids in gradually tapering doses along with hydroxychloroquine following a diagnosis of SLE. Cyclophosphamide was given for induction in 13 patients who had severe forms of lupus nephritis. Remission was maintained through azathioprine in 8 patients and 8 required Mycophenolate-mofetil. Ten patients (23%) had a relapse on therapy. Six fatalities (14%) were recorded during follow-up.

Conclusion
This is one of the largest series on boys with pediatric onset SLE from a developing country. It appears that while the severity of lupus nephritis in boys is no different from that in girls, neurological disease is more severe in the former. Further, boys appeared to have earlier onset of neuropsychiatric lupus as compared to girls. The incidence of complement deficiency lupus was also more in boys.

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THE PERFORMANCE OF A RENAL ACTIVITY INDEX IN LUPUS NEPHRITIS IN INDUCTION THERAPY

Background
Renal involvement in systemic lupus erythematosus (SLE) is associated with high morbidity and mortality. Current standard tools to monitor lupus nephritis (LN) are suboptimal compared to the invasive renal biopsy. The renal activity index in lupus (RAIL) was developed using 6 urinary biomarkers to reflect disease activity. In children this tool was 92% accurate in identifying active LN. We aim to study the changes in this score in relation to induction treatment in LN.

Methods
Urine samples were collected from active LN patients prior to induction treatment for LN and serially afterwards, coinciding with clinical visits. Luminex Bead Multiplex Assay was used for the analyses of urine biomarkers included in the RAIL score (neutrophil gelatinase-associated lipocalin, ceruloplasmin, monocyte chemoattractant protein-1, adiponectin, hemopexin, kidney injury molecule-1). RAIL scores were calculated per the defined algorithm for each urine sample. Data collected include LN histologic classification (International Society of Nephrology (ISN)/Renal Pathology Society (RPS) classification system), renal SLE disease activity index (rSLEDAI) score and type of therapy.

Results
At the time of the analysis, data from 6 active LN patients were collected longitudinally. Patients were all females and all had class IV LN per the ISN/RPS. Renal SLEDAI scores were on the higher end (M=11.3, SD=3.9). All patients were started on intravenous (IV) methylprednisolone and cyclophosphamide (CYC) therapy. All but one patient completed 6 doses of monthly CYC before switching to oral mycophenolate mofetil therapy. The RAIL scores for the 6 patients ranged between -1.8 and 3.29. All patients had reductions in their RAIL score at 2-3 months period at an average of 322% decline from baseline (Figure 1). At the end of induction treatment or at the 5-6 months interval, 5/6 samples were available for analysis and showed that 4/5 patients maintained a decline of RAIL scores below the baseline. Of note the patient with higher RAIL score at the end of treatment had only 3 monthly doses of CYC. All rSLEDAI scores decreased between baseline and the 6 months interval. However, one patient with known medication non-adherence had a flare of LN at the 6 months point leading to increased rSLEDAI.

Conclusion
RAIL scores show overall improvement from baseline with LN induction therapy. Lack of improvement was associated with flare of disease. Additional data points and a larger study sample are required to study the ability of the RAIL score to reflect clinical improvement of LN.

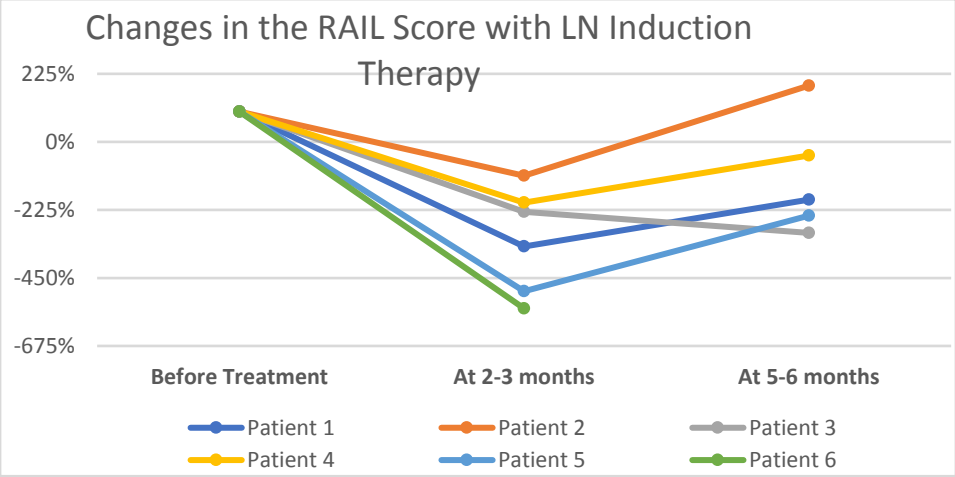

Figure 1. Changes in the RAIL score from baseline, at 2-3 months and at 5-6 months in 6 patients with LN. Baseline value is assigned 100%.

KELLY BUDGE

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STRUCTURAL PODOCYTE CHANGE IS ENCOURAGED BY S100A8/A9 IN THE INFLAMMATORY ENVIRONMENT OF LUPUS NEPHRITIS

Background
Systemic Lupus Erythematosus (SLE) is an autoimmune disease that presents clinical challenges in diagnosis and treatment due to its unique manifestation of symptoms. Renal inflammation as a result of SLE is termed lupus nephritis (LN), and damage to the kidney is the most important predictor of mortality in paediatric patients. In juvenile patients, 80% of SLE cases indicate kidney involvement, and 10-15% of these patients require dialysis or transplantation from end-stage renal failure. The post-mitotic podocyte cells are imperative for kidney function and are threatened in LN. Changes to podocyte structure from the inflammatory environment of LN directly impacts the cells' ability to maintain the glomerular filtration system. A recent correlation between a DAMP heterodimer and LN severity has been established. S100A8/A9 (Calprotectin) is released by granulocytes and monocytes to trigger continued inflammation, but its current role in LN is not well understood. It was therefore of interest to determine the effects of S100A8/A9 on resident renal cells, especially podocyte cellsng conditionally immortalized podocytes and glomerular endothelial cells, the effects of S100A8/A9 on these cell types were quantified in vitro. ELISA, qRT-PCR, Western Blot, phalloidin staining, flow cytometry, and a neutrophil adhesion assay were all employed in the analysis.

Methods
To determine the effects of S100A8/A9 on the structure and function of glomerular podocytes, a cytotoxicity assay, Western Blot, phalloidin staining, qRT-PCR, and ELISA protein assay were applied to a conditionally immortalized, human podocyte cell line.

Results
There was no observable change to the phenotype, genotype, or chemokine production of conditionally immortalized podocytes in the presence of recombinant S100A8/A9. When observing structural changes to the cell line, the addition of S100A8/A9 to podocyte medium led to a 165% increase in the percent area fraction and 168% increase in the integrated density of the podocyte cells.

Conclusion
This study indicates that S100A8/A9 causes a rearrangement of the F-actin cytoskeleton in conditionally immortalized podoctye cells. This suggests stress fibre formation in podocytes occurs in the presence of S100A8/A9 as potentially an adaptive response to the inflammatory environment of LN.

ANKITA SINGH

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LACC1 MUTATION IN THREE SIBLINGS WITH POLYARTHRITIS WITHOUT SYSTEMIC MANIFESTATIONS

Background
Juvenile idiopathic arthritis (JIA) is a complex group of disorders characterized by wide phenotypic diversity and genetic heterogeneity. It has multifactorial etiology varying among different subtypes. There are emerging reports on new gene locuses being identified especially in families with many affected members (1,2).

Methods
We reviewed case records of 3 siblings with infantile onset polyarthritis and performed whole exome sequencing on their DNA samples for LACC1, MMP2 and WISP genes.

Results
A non-consanguineous family from north-western part of India reported with 3 daughters having polyarticular joint disease. The chronology of symptoms was similar in all 3 children. Joint symptoms started in infancy around 9-10 month age with involvement of knee and ankle and rapidly progressed to involve small joints and cervical spine too (Figure 1). Over the next 2 years, multiple joint involvement, pain, deformities and contractures. The investigations at the time of first evaluation are tabulated in Table 1. Radiographs in all 3 sisters showed osteoporosis and erosion of vertebrae (Figure 2). We initially started them on non-steroidal anti-inflammatory drugs (naproxen). Later, in view of RF positivity in eldest sister we decided to give them trial of oral prednisolone (1 mg/kg) and subcutaneous methotrexate (10 mg/m2/week). She responded to it and thus other two sisters were also treated on the same lines. All three have been showing good response to immunosuppressants and physiotherapy and are currently ambulatory. However, all three are stunted with poor growth velocity. Subsequently whole-exome-sequencing in all three girls has revealed mutation in LACC1 gene [Exon 4; c.832G>C; p.(Ala278Pro), Homozygous, Autosomal recessive].

Conclusion
This case report further provides evidence to the emerging association of LACC1 mutation with familial aggregation of JIA (1,2). Long term follow-up of these patients may throw further highlight on the course of JIA in these subset of patients.

Poster Tour-I Group-3

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CLINICAL MANIFESTATIONS AND COMPARISON OF SUBTYPES OF JUVENILE IDIOPATHIC INFLAMMATORY MYOPATHIES: DATA FROM THE REMICAM REGISTRY

Background
Juvenile idiopathic inflammatory myopathies (JIIM) are a heterogeneous group of autoimmune diseases affecting children, characterized by symmetric muscular weakness, cutaneous rash and systemic organ involvement. Given its low incidence, there are few studies describing the characteristics of this disease and its subtypes in Spanish patients. Our objective is to describe de characteristics of patients with JIIM from the registry of inflammatory myopathies in Madrid community (REMICAM).

Methods
A multicentre retrospective study from the REMICAM registry was performed. Patients were selected if they were 18 years or younger at onset of JIIM and met definite or probable criteria for IIM by the modified Bohan and Peter criteria.

Results
86 patients were included, 12 classified as PM and 74 as JDM. 70% were women and 96% were Caucasian. Mean age at diagnosis was 11.8 years in PM group vs 7.2 years in JDM group. 44% presented arthritis and 93% presented muscular weakness. Gottron sign was present in 76% of the patients, and calcinosis was present in 31.4%. Cardiac and pulmonary manifestations were rare (<5%). There were no cases of neoplastic disease. Clinical features and complementary analysis are shown in table 1 and table 2.

Conclusion
JDM was the most frequent form of MIIJ in our study (86%). The most frequent manifestations were the muscular and dermatological ones, but an important group also presented arthritis and fever. There was no statistical difference between both groups, regardless, myalgias and dysphagia were more common in JDM group, and they had higher CPK and aldolase values. PM patients were older, had more fever and arthritis, also, cytopenia and ANA positivity were more common.

	Total (n=86)	PM (n=12)	JDM (n=74)	p-value
Fever	23 (29,1%)	6 (50,0%)	17 (25,4%)	0,084
Weight loss	12 (15,2%)	1 (8,3%)	11 (16,4%)	0,680
Arthralgia	38 (44,2%)	7 (58,3%)	31 (41,9%)	0,287

Arthritis	24 (28,4%)	6 (50%)	18 (24,7%)	0,071
Gottron sign	66 (76,7%)		65 (87,8%)	
Heliotrope erythema	46 (53,5%)		46 (62,2%)	
Mechanic hands	10 (12,3%)		10 (14,5%)	
Skin ulcers	3 (3,7%)		3 (4,3%)	
Raynaud	12 (13,9%)	3 (25,0%)	9 (12,2%)	0,362
Calcinosis	27 (31,4%)	2 (16,7%	25 (33,8%)	0,325
Muscular weakness	80 (93,0%)	11 (91,7%)	69 (93,2%)	1,000
Myalgia	68 (83,9%)	8 (66,7%)	60 (87,0%)	0,095
Myocarditis	2 (2,3%)		2 (2,7%)	
Arrythmia	3 (3,5%)	1 (8,3%)	2 (2,7%)	0,370
Heart failure	1 (1,2%)		1 (1,4%)	1,000
Interstitial lung disease	1 (1,2%)	1 (8,3%)		0,140
Dysphagia	19 (22,1%)	2 (16,7%)	17 (23,0%)	1,000
GI reflux	7 (8,1%)	1 (8,3%)	6 (8,1%)	1,000
GI hemorrhage	1 (1,2%)		1 (1,3%)	1,000

Table 1. Clinical features.

	Total (n=86)	**PM (n=12)**	**JDM (n=74)**	**p-value**
Anemia	13 (15,1%)	4 (33,3%)	9 (12,2%)	0,079
Leukopenia	4 (4,6%)	1 (8,3%)	3 (4,0%)	0,458
Thrombocytopenia	3 (3,5%)	2 (16,7%)	1 (1,3%)	0,050
ANA+	34 (40,5%)	7 (58,3%)	27 (37,5%)	0,173
Anti-Jo1	2 (2,6%)		2 (3,0%)	1,000
CPK	431 (97-3131)	206 (36-7428)	659 (104-3110)	0,730
Aldolase	12 (9-18)	9 (5-12)	12 (9-19)	0,230
CRP	0,35 (0-1,3)	0,12 (0-2,8)	0,42 (0-1,3)	0,817
ESR	19 (11-29)	25 (13-42)	19 (11-29)	0,450
Myopathic pattern	72 (92,3%)	12 (100%)	60 (90,1%)	0,508

Table 2. Complementary test.

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MEASUREMENT PERFORMANCE OF REDUCED VERSIONS OF MUSCLE STRENGTH TOOLS IN JUVENILE DERMATOMYOSITIS (JDM)

Background
Assessment of muscle strength is a fundamental component of the clinical evaluation of children with JDM. Regular measurement of muscle strength in daily care requires the availability of simple and quick assessment tools. Our aim was to investigate whether reduced versions of the MMT8 and CMAS are equally reliable as the original tools.

Methods
The following 4 reduced instruments were devised: 1) MMT4 (score 0-40), including 4 items of MMT8 (neck flexors, deltoid middle, gluteus maximus, and gluteus medius); 2) MMT6 (score 0-60), composed of the same items of MMT4 plus biceps brachii and quadriceps; 3) head lift time of CMAS (0-120 seconds or 0-5 points); 4) sum of CMAS head lift time in points and the 6 sit-ups maneuvers of CMAS (score 0-11). Validation was conducted according to OMERACT filter on 213 patients followed in standard clinical care at 13 pediatric rheumatology centers and evaluated at baseline and after a median of 5.9 months.

Results
All reduced instruments revealed strong correlations ($r > 0.7$) with muscle activity VAS and total DAS, moderate correlations ($r = 0.4$-0.7) with physician's global VAS, muscle DAS, skin activity VAS, pain VAS, parent's overall wellbeing VAS, and CK. Correlations with skin DAS and fatigue VAS were low ($r < 0.4$). Cronbach's alpha was excellent (0.92-0.95) for all reduced tools for which this property could be assessed. SRM was good-to-moderate (0.60-0.91) for all reduced instruments in patients judged as improved by the physician. All reduced tools discriminated strongly between patients classified in different disease activity states by the physician, and between patients whose parents were satisfied or not satisfied with their children's disease status. Overall, the metrologic performance of the reduced instruments was comparable to that of MMT8 and CMAS.

Conclusion
We found that reduced versions of the MMT8 and CMAS have good metrologic properties and perform similarly to the original tools in a population of patients followed in standard clinical care. Our results suggest that these simplified and shortened instruments could serve as surrogate for the complete measures in routine practice, particularly in a busy clinical setting.

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COMPARISON OF PAXGENE AND TEMPUS WHOLE BLOOD RNA COLLECTION AND ISOLATION SYSTEMS FOR THE QUANTIFICATION OF TYPE I INTERFERON-STIMULATED GENE EXPRESSION

Background

Type I interferons (IFN) have important roles in many pediatric and adult rheumatic diseases and are a new therapeutic target for which several "anti-interferon (anti-IFN)" treatments are currently in use or in development. Since the direct detection of these proteins in biological samples has proved challenging, indirect methods are often used to infer the presence of type I IFN. Most commonly this involves quantification of the relative expression of interferon-stimulated genes (ISGs) that are used to calculate an interferon score (IS). This score has been used for example to asses type I IFN activity in pediatric patients with type I interferonopathies, systemic lupus erythematosus, dermatomyositis and systemic juvenile idiopathic arthritis. Both qPCR and Nanostring technology have similar sensitivity and reproducibility for IS determination. The use of different whole blood RNA collection systems on the IS have not been evaluated however despite evidence of method-dependent changes in gene expression. The aim of the study was to compare expression of six common ISGs (IFI27, IFI44L, IFIT1, ISIG15, RSAD2, SIGLEC1) and the corresponding IS in RNA derived from two commonly used whole blood RNA collection systems (PAXgene and Tempus.

Methods

Whole blood was collected from ten healthy individuals (median age 25.5 years) in sodium heparin tubes and incubated without or with recombinant human interferon alpha 2b (rhIFNalpha, 2 IU/ml, 4 hrs, 37C°, 5% CO2). Next, samples were divided between PAXgene (PreAnalytiX, Becton Dickinson) and Tempus (Applied Biosystems) tubes and RNA was isolated according to the manufacturer's protocols. cDNA was synthesized (~500ng input RNA; qScript cDNA synthesis kit) and ISG expression measured on a QuantStudio 6 Real-Time PCR instrument using a TaqMan Fast Advanced Assay. For each ISG, expression was normalized against the geometric mean of two housekeeping genes (18s rRNA and HPRT1) and calculated using the formula 2-ΔCt. Relative gene expression is reported as the normalized expression of each ISG divided by the median of normalized expression of the same ISG in unstimulated samples. The median relative expression of all six ISGs was used to calculate the IFN score for each sample.

Results

There was no statistically significant difference in the normalized expression of any of the six ISGs in either the rhIFNalpha-stimulated or unstimulated samples derived from PAXgene or Tempus tubes. The greatest difference in mean normalized expression in both unstimulated and stimulated samples was observed for ISG15 (difference in mean normalized expression was 0.0034 and 0.11, respectively). Overall there was a strong correlation of the IFN score between PAXgene and Tempus tubes for both the unstimulated ($R2 = 0.9117$, $p<0.0001$) and and rhIFNalpha-stimulated samples ($R2 = 0.8529$, $p=0.0001$).

Conclusion

Despite reported differences in gene expression patterns associated with samples collected in PAXgene versus Tempus tubes, our results demonstrate that 6-gene interferon scores do not differ significantly between RNA samples obtained with these two systems. These results suggest that

health care and research centres can use either tubes for IFN score determination using these 6 ISGs and results can be directly compared irrelevant of the RNA collection system employed.

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SERUM S100A4 PROTEINS AS A BIOMARKER FOR DISEASE ACTIVITY IN JUVENILE LOCALISED SCLERODERMA.

Background
Juvenile localised scleroderma (JLS) is characterized by sclerosis typically limited to the skin, subcutis, and underlying bone and tissue without vascular or internal organ involvement. JLS causes significant morbidity and disfigurement in affected children. There is extreme variability in response to therapies used to treat JLS patients. There are also no serological markers to reliably help monitor disease activity, decide on treatment duration and determine risk of flare following treatment discontinuation. S100A4 is a member of calcium binding proteins that are important in cell homeostasis. S100A4 proteins are overexpressed in fibroblasts from adult patients with systemic sclerosis, in a TGF-β-dependent manner, suggesting a pro-fibrotic role and possible correlations with skin fibrosis during disease flare. Therefore, the objective of this study was to assess and evaluate serum S100A4 levels as a putative biomarker of disease activity in children with JLS.

Methods
Twenty-seven patients, median age 12 years (range 4 – 17 years), diagnosed with JLS (generalised/linear morphea and en coup de sabre subtypes) were studied. Serum levels of S100A4 and MRP8/14 (S100A8/A9) were measured using a commercial enzyme-linked immunosorbent sandwich assay (ELISA); other cytokines were measured using a commercial MSD U-PLEX immunoassay. Serum samples were also collected from healthy controls (N = 21). Disease activity was characterised using the localised scleroderma cutaneous assessment tool (LoSCAT). Results are expressed as median and range.

Results
S100A4 serum levels were significantly increased in patients with active JLS at 53.39 ng/ml (32.44–88.27) compared to healthy controls 39.65 ng/ml (22.06–87.28; P=0.003). MRP8/14, a previously described biomarker for JIA, was not significantly different between healthy controls and both JLS (active and inactive). Serum analyses for inflammatory cytokines (IL-6, IL-8, IL-10, IL-18 and IL-1β) were significantly elevated in both scleroderma groups compared with controls but no significant differences were found between the active and inactive groups.

Conclusion
S100A4 serum levels were significantly increased in patients with active scleroderma and may be associated with increased skin fibrosis in these patients. S100A4 serum analyses may therefore serve as a specific biomarker for JLS and enable monitoring of disease activity and assessment of therapeutic efficiency.

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CLINICAL PRESENTATION, GENETIC ANALYSIS AND IFN-SCORE IN PATIENTS WITH UNDEFINED INTERFERONOPATHIES

Background
A group of genetic disorders with a disturbance of the homeostatic control of IFN-mediated immune responses, have been identified (type I interferonopathies). An increased expression of type I IFN regulated genes, IFN signature (IS), is reported. The aim of the present study is to evaluate the correlation between clinical presentation, genetic analysis and IFN-score in 10 pts with undefined interpheronopathies

Methods
Patients with suspected interferonopathy based on the presence of typical clinical manifestations, laboratory parameters, instrumental abnormalities, were screened for the IFN-score. Defined IFN-mediated diseases were excluded. Patients with IFN-score above 10 underwent genetic screening by running a panel of 24 genes involved in interferonopathies

Results
10 pts followed in a pediatric rheumatology center were included. 7/10 presented with recurrent fever (table). Pts 2, 3 and 7 displayed neurological manifestation, respectively epilepsy, epilepsy and mental retardation and progressive hemiplegia. To note epilepsy in pts 2 might be due to a bilateral intraventricular hemorrhage presented at birth. In pts 1,4 gastrointestinal manifestation resembling inflammatory bowel diseases were described while pts 5,7 suffered from recurrent abdominal pain, diarrhea and patient 10 from hypertransaminasemia. Half of the patients complained arthromyalgia; arthritis developed in pts 2. Cutaneous involvement presented in pts 1,3,6 respectively with widespread panniculitis of trunk and limbs, aspecific vasculitis and Schonlein Henoch purpura. Other cutaneous manifestation were urticarial rash (pts2) and an erythematous, desquamative confluent eczema (pts 4). Autoimmunity was detected in 2 pts. Pts 4 8 had an immunological defect with recurrent infections. The genetic analysis resulted negative in pts 1 and 7 and is ongoing in patients 5,6 and 8. The other patients carried one mutation in at least one IFN correlated gene not confirming the diagnosis. All patients presented an increased IS ranging from 14 to 172

Conclusion
An elevated IFN-score represent a useful instrument in clinical practice to classify patients with suspected interferonopaties. It may be an important tool to select those to be genetically screened. The presence of a positive IFN-score, may guide clinicians in the management of genetically negative patients and may support therapeutic decisions

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10
Systemic symptoms	Fever		Fever			Fever	Fever	Fever	Fever	Fever, hemophagocytic lymphohistiocytosis
CNS involvement		Epilepsy (bilateral intraventricular hemorrhage at birth)	Epilepsy, mental retardation					Hemiplegia		
Gastrointestinal involvement	Epatosplenomegaly, aspecific IBD			Histological findings simil-RCU	Abdominal pain, diarrhoea		Abdominal pain			Hyper-transaminasemia
Skin/ osteoarticular involvement	Arthro-myalgia, panniculitis	Arthro-myalgia, arthritis, urticarial rash	Arthro-myalgia, vasculitis	Erythematous desquamative confluent eczema	Arthro-myalgia	erythema polymorphe, Shonlein Henoch purpura	Arthro-myalgia			
C3 (90-180 mg/dl)	144	127	81	133	53	137	96	203	97	83
C4 (10-40 mg/dl)	34	24	6	23	20	54	17	38	28	16
Immunodeficit/ Autoimmunity		ANA 1:2.560 Anti ds-DNA 1:640	ANA 1:10.240 Anti dsDNA 1:1280	Immunodeficit ANA neg					Immunodeficit	
WBC/ mmc^3	5,2	4,4	9,8	3,9	4,6	8,1	6,4	4,4	3,5	1,7
Hb g/dl	10,4	12	12,9	10,2	13	11,1	14,1	12,1	16,5	9,7
PLT/mmc^3	199	381	194	86	110	277	214	358	150	56
IFN signature	14,2	171,5	54,73	60,09	27,8	17,2	53,9	40,6	32,6	18,19
Genetic analysis	Negative	PSMB9: p.Arg60Cys OTULIN: p.Gln115His	CARD8: p.Leu426Phe	IFIH1: p.Arg374His			Negative		ACP5: p.Arg269Tr	DNASE2: p.Ala45Gly

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MYCOPHENOLATE MOFETIL (MMF) IN DEFINED AND UNDEFINED INTERFERONOPATHIES

Background
Type I interferonopathies are genetic disorders characterized by an up-regulation of type I interferon (IFN) activity. An increased expression of type I IFN regulated genes, IFN signature (IS), is described in these conditions. They are characterized by autoinflammation and varying degrees of autoimmunity or immunodeficiency. Some patients with a phenotype strongly suggestive for type I interferonopathy with a high IS, do not show any mutations in known type I interpheronopaties related genes, being classified as undefined. Aim of the study is to evaluate the effect of mycophenolate mofetil (MMF) in patients with defined and undefined type I interferonopathy

Methods
7 patients with type I interferonopathy followed at a Pediatric Rheumatology center, were included. Leucocyte (WBC) and platelet count, hemoglobin (Hb), CRP, ESR, serum amyloid A (SAA), autoantibodies, complement levels and IS, were assessed before and after 5-7 months of MMF treatment (600 mg/m2 BID). IS was determined by qPCR (high scores >1.42)

Results
Patient 1 and 2 presented respectively with SAVI and Aicardi-Goutieres syndrome. The others were classified as undefined. In patient 1(table), treated with JAK1/2 inhibitor, MMF was followed by decrease of inflammatory markers and resolution of lung involvement; in patient 2 to an increase in Hb and normalization of inflammatory markers. Among patients with an undefined phenotype the addition of MMF to low dose prednisone led to complete resolution of inflammation. A reduction of the antinuclear antibodies titre was observed in patients 2, 3 and 7 and a normalization of complement level in patients 3, 4 and 7. Patient 5 had normal inflammatory markers already before the beginning of MMF possibly due to previously administered immunosuppressive treatment. Despite all patients presented a significant improvement of clinical picture after 5 months of MMF treatment, the IS decreased only in 4/7 patients while it remain stable or increased in the others

Conclusion
Our data suggest that mycophenolate mofetil might be an effective therapy in patients with type I interferonopathy leading to improvement of clinical and laboratory features thus allowing a glucocorticoid sparing

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Disease	SAVI (lung and skin involvement, systemic inflammation)	Aicardi Goutieres (neurological involvement, rash, fever)	Undefined (epilepsy, arthritis,skin involvement)	Undefined (recurrent fever, hypertransaminasemia, HLH)	Undefined (hemiplegia)	Undefined (epilepsy, arthritis,skin involvement)	Undefined (recurrent fever, lymphadenopathy, hypogammaglobulinemia
Clinical improvement after MMF Resolution of:	Lung involvement	Fever and rash	Rash, arthritis, improvement of seizures	Fever, inflammation and hypertransaminasemia	Improvement of motility	Arthritis and skin involvement	Fever and limphadenopathy
Gender	F	F	M	M	M	F	M
Age at onset (yrs)	3 (days)	2	4	7	4	6	16
WBC/ mmc3*	16 /7,4	8,0/8,4	9,8/8,5	1,7/8,4	4,4/8,2	4,4/5,2	6,6/5,9
Hb g/dl *	7,7/8,9	8,5/12,3	12,9/12,8	9,7/13	12,1/10,7	12/12,9	11,5/15,1
PLT/mmc3*	950 /766	680/320	194/181	56/161	358/421	381/390	218/323
ESR (mm) *	44/40	49/9	38/10	7/6	2/5	24/6	3/3
CRP (mg/dl) *	1,22/0,73	3,13/0,06	5,55/0,32	<0,05/<0,05	<0,05/<0,05	1,15/<0,05	8,34/0,98
SAA (mg/dl)*	95,8/3,62	5,37/2,82	188/8,11	-/1,89	<0,84/-	4,19-0,78	/
C3(90-180mg/dl)*	154/134	122/108	81/92	83/118	203/170	127/108	53/133
C4(10-40 mg/dl)*	22/22	10/24	6/8	16/27	38/28	24/14	15/41
Antinuclear antibody*	Absent	1:2560/1:160	1:10.240/1:1280	Absent	Absent	1:2560/1:320	Absent
ENA*	pANCA 1:40/1:20	Absent	Anti dsDNA 1:1280/1:160	Absent	Absent	Anti dsDNA 1:320/1:40	Absent
IFN signature*	43,2/18,3	42,6/79,8	54,73/64,6	8,66/18,19	40,6/5,95	171,5/13,12	14,34/2,24

Table 1: * Lab value pre/post MMF therapy

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SJÖGREN'S SYNDROME IN CHILDREN: A CASE SERIES

Background
Symptoms of pediatric Sjögren's syndrome (SS) are different than in adults. There are currently no validated pediatric diagnostic criteria or treatment guidelines for SS. In most cases adult criteria are used, but they apply poorly to children. We aimed to present pediatric patients with primary SS who were treated at University Children's Hospital (UCH) Ljubljana in the past 10 years.

Methods
Eight children with primary SS were identified. Demographic data and clinical data were analysed by retrospective review of medical records at UCH Ljubljana.

Results
Six girls and 2 boys were evaluated. Mean age at disease onset was 12.3 years (range 6.5 – 17). Four patients presented with recurrent bilateral parotitis, two with rash, one with arthralgia and one with acute CNS vasculitis. During disease course arthritis and/or arthralgia was present in 5/8, parotitis in 4/8, oral symptoms in 4/8, rash in 4/8, fatigue in 3/8 and ocular symptoms in 2/8 patients. One patient developed calcinations on fingers. All patients had high titer of ANA, 7/8 were positive for anti-Ro and 5/8 for anti-La antibodies. 6/8 patients had elevated ESR and hypergammaglobulinemia. 4/8 patients had elevated serum amylase.

Biopsy of salivary glands was performed in 5 patients and all had foci of lymphocytic infiltration. Further two patients had salivary gland changes on MRI and/or US. Three patients had positive Schirmer test. One patient had CNS vasculitis and two decreased diffusing capacity of the lungs. Other patients showed no signs of internal organ involvement.

4/8 patients were treated with NSAIDs, 7/8 with hydroxychloroquine, 2/8 received corticosteroids and one patient MMF. At this point the patient with CNS vasculitis has stable changes on head MRI without clinical symptoms. Other patients have no signs of internal organ damage.

Conclusion
Most common symptoms in our cohort were arthritis and/or arthralgia, parotitis, oral symptoms and rash. One child developed calcinations on fingers, which have not yet been described in patients with SS. Pediatric SS differs from adult SS and specific pediatric diagnostic criteria would improve management of these patients.

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DESCRIPTIVE ANALYSIS OF PATIENTS WITH OSTEOGENESIS IMPERFECTA IN A TERTIARY HOSPITAL IN MADRID

Background

Osteogenesis imperfecta (OI) is an inherited connective tissue disorder with an incidence of 1 per 20000 births. It is also called brittle bone disease and is caused by mutations in genes encoding type I collagen. Clinical presentation is heterogeneous, varying from only premature osteoporosis to multiple atraumatic fractures. Bisphosphonates are usually used to try to prevent bone fragility, reducing the number of fractures in some patients. Our aim was to analyze both clinical and analytical characteristics of OI patients followed in our hospital and to evaluate the different treatments used in their management.

Methods

A retrospective study was conducted including all patients diagnosed with OI seen in the different departments of our hospital. A database was created and both clinical and epidemiological data were analyzed.

Results

25 patients with OI followed up in our hospital were included. 72% were female (18) with a mean age at diagnosis of 17 y (range: 1 month to 67 y). All of them had had fractures before the diagnosis. The number of fractures during follow-up varied according to the different types of OI, with an average of 6 fractures (range 3-24) per patient and at least 4.16 orthopedic surgeries. Only 3 patients had family background of OI. Phenotypically, 14/25 (56%) had short stature and 18/25 (72%) had blue sclerae. Only 4 patients suffered from dentinogenesis imperfecta (16%) and 3 suffered from otosclerosis (12%). Regarding analytical parameters, average uric acid in our OI cohort was 5.1 mg/dL ±1.74 and serum calcium was 9.34 mg/dL ±0.67. PTH levels were 44.94 pg/mL ±13.37 and vitamin D was 23.1 ng/mL ±11.33. Urinary calcium excretion rate was 114.41±72.39. 60% were on current treatment with calcium and 64% (16/25) with vitamin D supplements but only 15/25 received bisphosphonates (4 risedronate, 7 pamidronate, and 4 both zoledronic and pamidronate).

Conclusion

Although a rare disease, OI has an important morbimortality. Severe cases suffer multiple fractures and undergo several orthopedic surgeries during their lives. Treatment for this condition is not standardized and is generally reserved for type III OI patients. Bisphosphonates, calcium and vitamin D are usually used to try to prevent new fragility fractures but fracture rates remain high despite treatment.

12.06.2019
Poster Tour-II Group-1

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COMPARISON OF PAXGENE AND TEMPUS RNA COLLECTION TUBES IN JIA

Background
Heterogeneity in response to biological medication is a major challenge in the management of Juvenile Idiopathic Arthritis (JIA). Prediction of therapy efficacy prior to treatment initiation enables identification of responders to biological agents and lays the foundation of precision medicine. It was previously demonstrated that whole blood gene expression profiles can predict response to anti-TNF-α therapy in patients with JIA. These findings currently await validation in a multicenter prospective cohort study. An important challenge to biomarker research is variation in biological sample collection and processing, as it can irreversibly affect data quality at an early stage. In this study, we evaluated the comparability of gene expression profiles when whole blood from JIA patients is collected in different RNA collection tubes and processed accordingly. Next, we will investigate the predictive capacity for therapy response of RNA expression profiles from frozen PBMC of 63 JIA patients.

Methods
Peripheral blood from 11 children with non-systemic JIA with active disease was collected in PAXgene (PreAnalytiX) and Tempus (Applied Biosystems) tubes. RNA was isolated from PAXgene and Tempus blood according to the manufacturer's instructions. Gene expression of CSNK1D, C1D, ASAP2, SRRD, PPP1R3B, HLA-DQA1, PDZK1IP1 and MZB1 was determined with qPCR. For our next experiment, frozen PBMC derived from patients with non-systemic JIA will be used. Of the 63 patients, 28 (44.4%) children were diagnosed with oligo articular JIA, 19 (30.2%) with poly articular JIA, 9 (14.3%) with enthesitis-related JIA, 4 (6.3%) with psoriatic JIA and 3 (4.8%) with undifferentiated JIA. These samples will be run on a 96-analyte NanoString panel and associated with clinical response at 6 months after start of TNF-α blockade.

Results
Both RNA blood collection systems yielded high-quality RNA, with overall higher RNA concentrations for blood collected in Tempus tubes in comparison to PAXgene tubes. qPCR data showed that gene expression of all measured genes is affected by the method of blood collection and processing. However, the inter-individual variation was similar between both collection tubes, indicating that similar RNA profiles were observed.

Conclusion
Gene expression profiles derived from whole blood collected in PAXgene or Tempus tubes are comparable, but not interchangeable.

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PATIENTS' AND CAREGIVERS' ASSESSMENT OF A DEDICATED OUTPATIENT SERVICE FOR INTRAARTICULAR GLUCOCORTICOID INJECTIONS IN JUVENILE IDIOPATHIC ARTHRITIS

Background

Patients with juvenile idiopathic arthritis (JIA) may require several hospital admissions over the disease course, due to flares or persistently active arthritis, with a negative impact on the patients' and family's daily life. To provide timely intervention and support the patients' and families' quality of life, in 2018 an afternoon outpatient service for intraarticular glucocorticoid injections (IAGI) in JIA has been created at the study center.
The aim of the study is to evaluate the patients' and caregivers' assessment of the outpatient service for IAGI in JIA; to investigate demographic and clinical features of patients entering the service.

Methods

All consecutive JIA patients and their caregivers seen at the IAGI outpatient service from February 2018 to January 2019 completed a satisfactory questionnaire just after the IAGI procedure. The patient's part included: satisfaction on the overall service and on dedicated personnel (yes/no, why), procedure pain assessment (VAS 0-10, 0=none; 10 worst); whereas the caregiver's part: satisfaction on the overall service (yes/no, why), facilitation of family burden (yes/no, why). Demographic and clinical data of patients, including previous hospitalization for IAGI under general sedation or local anesthesia and geographical provenance, were registered during the questionnaire completion. Descriptive analysis was performed on data. Open answers were synthetized in items.

Results

All of the 46 JIA patients seen at the IAGI outpatient service and their caregivers completed the questionnaire. Patients were mostly females (78%) with early disease onset (median 4.8 years) and positive ANA status (61%). The majority (52%) had persistent oligo-JIA, followed by extended oligo-JIA (26%), RF-negative polyarthritis (17%), ERA and systemic JIA (2%, respectively). The median age at IAGI was 14.7 years (IQ 11.3-19.5). Forthy patients (87%) had previous hospitalization for IAGI, mostly under general sedation (64%). All patients, except a 12 year old girl (0.02%) with uncontrolled needle phobia and previous IAGI in general sedation, (99.98%) and all caregivers (100%) were satisfied with the IAGI outpatient service. In Table 1 reasons of satisfaction are detailed in items. Procedural pain was median rated 3 (IQ 2-6). Most of the families came from the city or province of the study center (76%); 17% from other provinces of the same geographical region; 7% from other regions.

Conclusion

The results outline the afternoon IAGI outpatient service foster the management of flares or persistently active arthritis in JIA patients, particularly at older ages, with high rate of satisfaction and lower impact on patients' and family burden compared to hospital admission and, of note, despite moderate pain rating and multiple site injections. This supports the development of Diagnostic Therapeutic Care Pathways for JIA patients, in the view of improving patients' quality of life and also towards resource optimization.

Table 1. Frequency of specific reasons of satisfaction on the IAGI outpatient service, synthesized in items, during the 56 procedures of the study.

Items	Patients, n (%)	Parents, n (%)
Time saving	45 (80)	30 (54)
Stress saving	5 (9)	-
Reduction of absence from school/work	27 (48)	23 (41)
Less negative impact on personal commitments	-	26 (46)
Improvement of family burden organization	-	54 (96)
High quality of dedicated Staff	55 (98)	19 (34)

Figure 1. Proportion of specific sites injected in the 46 JIA patients in the 56 procedures performed at the outpatient dedicated service during the study

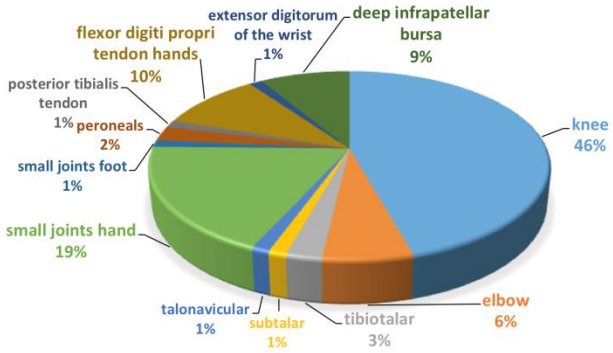
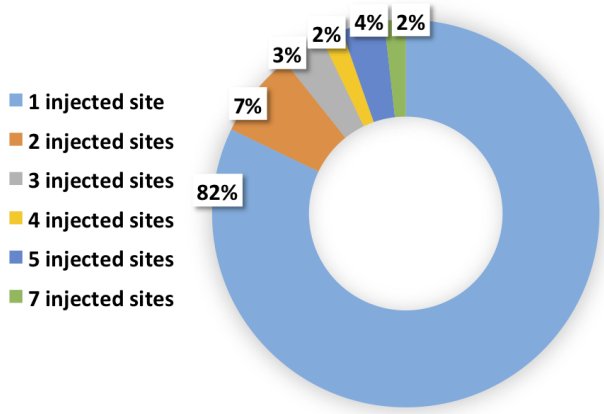


Figure 2. Proportion of procedures with one or multiple injected sites at the IAGI outpatient service during the study



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ASSOCIATIONS BETWEEN MARKERS OF BONE TURNOVER AND RADIOLOGICAL FINDINGS IN CHILDREN DIAGNOSED WITH JUVENILE IDIOPATHIC ARTHRITIS.

Background
Although many children attending pediatric rheumatology departments are diagnosed with low bone mineral density on the basis of clinical imaging, it is difficult to determine which patients have the higher risk of developing osteoporosis as the secondary disease.

Methods
Study involved 59 children previously diagnosed with JIA (mean age at diagnosis: 9.0±4.3 years, mean age at study baseline: 12.7±3.9 years). All patients underwent Dual X-Ray Absorptiometry (DXA) examinations in order to assess bone mineral density. Wrist radiographs were also taken for evaluation according to the Steinbrocker classification. The presence of abnormalities in these tests was chosen as the criterion to divide patients into subgroups to perform group comparisons for the serum levels of markers of bone turnover: bone alkaline phosphatase, osteoprotegerin and Beta-Crosslaps.

Results
According to the Steinbrocker classification, 10 (16.9%) patients were staged as class I or higher. These children had significantly lower serum levels of bone alkaline phosphatase (p=0.0333) than patients with no radiological changes on wrist radiographs. The non-zero Steinbrocker subgroup had also lower Total Body Less Head Z-Score results (p=0.010) than the remaining patients.

Bone alkaline phosphatase and osteoprotegerin were negatively correlated with DXA muscle mass (r=-0.359 p=0.040 for bone alkaline phosphatase, r=-0.372 p=0.0392 for osteoprotegerin).

Conclusion
Low serum concentration of bone alkaline phosphatase seems to be a risk factor for low bone mineral density and, by extension, for osteoporosis. Therefore it should be considered as an important laboratory test in JIA patients suspected of secondary osteoporosis.

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JIA TEAMWORK FOR IMPROVING PATIENTS' ACCEPTANCE OF INTRAARTICULAR GLUCOCORTICOID INJECTIONS IN LOCAL ANESTHESIA IN OUTPATIENT DEDICATED SERVICE

Background
The aim oft he study was to identify an appropriate approach for JIA patients' most critical issues related to intraarticular glucocorticoid injections (IAGI) in local anesthesia. To provide preliminary validation of the approach identified.

Methods
In the first part of the study the nurse of the IAGI outpatient service at the study center had conversation with all consecutive JIA patients and caregivers seen at the service, while preparing them to IAGI in local anesthesia and while on discharge. In agreement with the patient, the nurse synthetized in keywords and registered each patient's most relevant feelings with regard to the IAGI procedure. Patients and caregivers were also asked to suggest feasible tools for a better acceptance of the procedure. The results were discussed within the JIA team, who selected in a questionnaire the most frequently reported keywords and identified the most feasible among the proposed supportive tools. Secondly, all consecutive JIA patients seen at the service were asked to complete the feeling-status questionnaire after the IAGI. As the tools were available, the questionnaire was completed after IAGI procedures tool-supported. Statistics included descriptive analysis and Student's t-test for comparison between feelings rating by patients with and without supportive tools (significance: p-value<0.05).

Results
From the list of keywords obtained by the first 10 patients with the nurse, the most reported -stress, anxiety, fear, and anger- were included in a feeling questionnaire composed of a VAS 0-10 (0=none, 10=worst) for each keyword. Among the suggested supportive tools the JIA team identified as feasible: colored drawings/pictures in the procedure room and the availability of favourite songs/videoclips/cartoons on tablet just prior and during IAGI. Forthy-one patients completed the questionnaire in a mean time of 22 seconds. Among them, 24 (59%) were supported by the selected tools, been meantime available, during IAGI procedure.

Conclusion
Our preliminary results highlight that a setting for IAGI more comfortable for patients provide an improvement in the JIA patients' feelings rating undergoing injection procedures in local anesthesia. The nurse's attitude to patients and the teamwork were fundamental in collecting the patients' perspective and in adapting their suggestions to the IAGI outpatient service environment.

Table 1. Mean of response to the feeling-questionnaire by JIA patients seen at the IAGI outpatient service without (A) and with (B) supportive tools

	Patients n.17 (A)	Patients n.24 (B)	P-value
Female/Male	16 (94)/1 (6)	20 (83)/4 (17)	
Age at IAGI, years, median (IQ range)	15,1 (12,8-20,5)	13,5 (9,7-17,8)	
Age at disease onset, years, median (IQ range)	4,9 (1,7 -11,2)	4,1 (1,9 -7,1)	
Stress*, mean (SD)	9 (1)	4 (2)	<0.005
Anxiety*, mean (SD)	9 (1)	4 (2)	<0.005
Fear*, mean (SD)	7 (4)	2 (2)	<0.005
Anger*, mean (SD)	5 (3)	1 (2)	<0.005

*VAS 0-10, 0=none, 10=worst

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COMPARISON OF VARIOUS LYMPHOID CELLS IN PATIENTS WITH JUVENILE IDIOPATHIC AND REACTIVE ARTHRITIS SHOWED DIFFERENCES IN TREG CELLS SUBPOPULATION

Background
Juvenile idiopathic arthritis (JIA) is characterized by chronic joint inflammation lasting longer than six weeks, as opposed to the acute reaction in reactive arthritis (ReA) that develops in response to an infection, lasts shorter and ends with full resolution of symptoms. Nevertheless, those common forms of arthritis are often initially hard to differentiate on clinical and/or laboratory grounds. Therefore, the objective of this study was to examine the differences in occurrence of various subsets of lymphoid cells in JIA and ReA patients: regulatory T (Treg) and regulatory B (Breg) cells as immunosuppressors, type 3 innate lymphoid cells (ILC3) associated with a wide range of inflammatory disorders by an increase in IL-17 producing T cells and Th17 cells that exhibit plasticity and can be shifted to produce IFN-γ.

Methods
Treg cells, Breg cells, ILC3 and Th17 derived Th1 cells were analyzed in whole blood of ten JIA and six ReA patients by flow cytometry, using directly conjugated monoclonal antibodies. The blood samples were collected during the first visit to Pediatric Rheumatology Clinic in Sestre milosrdnice University Hospital Center in Zagreb, Croatia, while the final diagnosis of JIA or ReA was made three months after. At each visit, juvenile arthritis disease activity score (JADAS-CRP) for each patient was calculated. The median ages of the JIA and ReA patients were 6.41 and 7.22 respectively.

Results
In patients with JIA, the CD3+CD45+CD25+CD4+CD127-CD28- subpopulation of Treg cells was significantly abundant compared to ReA patients (*P=0.04*). No other significant differences in cell subpopulations among different patient groups were observed.

Conclusion
This proof-of-concept study has shown that patients with JIA have significantly higher levels of anergic Treg cells in peripheral blood than those with ReA, which could possibly result in the failure of their immunosuppressive effect and the development of a chronic disease.

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EXPLORING UVEITIS IN EARLY ONSET ANA POSITIVE JIA

Background
Juvenile idiopathic arthritis (JIA) is the most frequent childhood systemic disease affiliated with uveitis, where uveitis occurs in 10-13% of the patients, frequently causing long lasting consequences.

Methods
The retrospective study included 31 children treated for JIA and uveitis in the period 2009-2017 at UHC Zagreb. The SUN working group classification and grading system were used to evaluate ocular manifestations.

Results
81% of patients were female. Median age at JIA onset in girls was 2.5 (1-14) years and in boys 8.6 (1-14.5) years, while girls had median age 4.25 (1-14) years at first ocular manifestation and boys 8.25 (4 -13.5) years. All patients were RF negative. 61% were ANA positive, out of which 88% had onset of JIA before the age of 6 (all girls). Complete remission of uveitis was achieved in two patients treated with topical corticosteroids, non-steroid anti-inflammatory medication and methotrexate used in one of the patients. Inactive uveitis was most frequently achieved with a combined therapy which included biologics. A patient suffering from uveitis and JIA was found to be significantly more likely to suffer from oligoarthritic subtype ($p<0,001$). Positive ANA titer occurred statistically significantly more frequent in females ($p=0.001$). No significant statistical difference in ANA titer was found between groups of patients who were diagnosed with rheumatologic or ocular disease before and after the age of 6 ($p=0.6111$) nor between different subtypes of JIA. There was no difference in time passed between the occurrence of rheumatologic and ocular manifestations ($p=0,2597$), nor between ANA titer ($p=0,4775$) between groups with and without ocular complications. Patients who first presented with ocular manifestations did not have a greater likelihood to develop ocular complications ($p=0,175$).

Conclusion
We detected a group of ANA positive female patients suffering from RF negative JIA and uveitis, under the age of 6. Although having different subtypes of JIA, they are best described as “early onset ANA positive JIA”. The need for reclassification of JIA was concurred with findings of recurrent positive ANA titer in females with JIA and uveitis, and a more frequent occurrence of uveitis in oligoarthritis.

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PERIARTICULAR GLUCOCORTICOID INJECTIONS: DELINEATING THEIR USE IN JUVENILE IDIOPATHIC ARTHRITIS

Background
Glucocorticoid injections in periarticular sites (PAGI) such as tendons and bursae often complete the local treatment of active disease in juvenile idiopathic arthritis (JIA). However, the use of PAGI and their role in the achievement of disease remission has seldom been studied.

Methods
Records of JIA patients treated with PAGI were reviewed. Demographic and clinical features, including ongoing systemic treatment, sites of injection, type of glucocorticoid injected, remission and side-effects were recorded.

Results
In a total of 293 procedures 647 tendons and 26 bursae were injected in 191 patients. Most of the patients were females (74%), with ILAR oligoarticular JIA subtype (50% persistent, 23% extended) with a median age of 8.2 years (IQ 4.7-11.3) at the PAGI. Acetate methylprednisolone was used in 96 % of the procedures. In 255 procedures (87%) patients experienced remission in the injected sites after a median of 2.6 months (IQ 1.9-3.5). At the last follow up, after a median period of 29.4 months (IQ 15-45.48) from PAGI, patients experienced remission in 282 (96,2%) injected procedures. In 53 procedures with repeated injection(s) in the same site(s) (77%), patients were in remission at the last follow up. Concerning concomitant therapy, at the time of each PAGI 115 patients (39.2%) were not on treatment, 137 (46.7%) were on methotrexate, 29 (9.9%) on methotrexate and biologics, 8 (2.7%) on biologics and 4 (1.5%) received others. In 156 (53.2%) procedures, patients experienced remission and maintained the same treatment before or after the injection at the last follow up in a median period of 20.8 months (IQ 12.67- 39.35). Of notice, 81.4% of patients who experienced complete remission following the injection were not on concomitant treatment. In 24 injection procedures (8.2%) patients showed mild local side effects.

Conclusion
PAGI are a safe option. In our cohort, persistent oligoarticular JIA was the most injected subtype; acetate methylprednisolone was the most used glucocorticoid. In 96.2% procedures patients experienced remission at last follow up. Further evaluations are mandatory to assess the role of concomitant therapy in achieving/maintaining remission.

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PRESENCE OF ESCHERICHIA COLI (E COLI) SUBTYPES IN THE STOOL OF PATIENTS WITH REA AND JIA

Background
Painful join swelling is a symptom of many childhood diseases, most notably reactive arthritis (ReA) and juvenile idiopathic arthritis (JIA). Although the reaction to a known or unknown pathogen is involved in etiology of both conditions, ReA lasts for a short period of time with resolution of simptoms while JIA evolves into a chronic disease. While the reasons behind these opposite reactions are mostly speculative, the growing body of evidence suggests the gut microbiota could possibly be responsible for disease development. Therefore, the aim of this study was to assess the differences in the presence of Escherichia coli (E coli) subtypes in the stool of patients with ReA and JIA at the first occurrence of symptoms.

Methods
Stool samples of 14 patients with joint swelling where collected during their first visit to Pediatric Rheumatology Clinic in Sestre milosrdnice University Hospital Center in Zagreb, Croatia. Three months later, the diagnosis of JIA was made in seven patients while the other seven patients had been classified as ReA. The median age of patients was 7.14 and 7.11, respectively. All of the samples were analyzed by mass spectrometry on nanoLC-Synapt G2 Si instrument. To identify the most abundant E coli subtypes, specialized software named Protein Reader with implemented Dust algorithm have searched through NCBI nr database, that contains the records of more than 400 E coli subtypes.

Results
Various E coli subtypes (P0301867.1-10, O104:H4, O103:H25, O111:H11, KTE and K) were three times more abundant in patients with JIA, while in children with ReA, only the two times increased abundance of diarrheagenic E. coli (DEC) was detected.

Conclusion
This pilot study has shown differences in the subtypes of E coli present in the stool of children with ReA and JIA at the beginning of the disease. Since E coli is one of the paramount bacteria in gut microbiota with more than 600 recognized subtypes, it is reasonable to assume that differences described in this study can have a potential impact on the gut environment, with the contribution to the development of the chronic disease in JIA patients or the resolution of symptoms in children with ReA.

Poster Tour-II Group-2

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

Background
Macrophage Activation Syndrome (MAS) is a severe complication of rheumatic diseases, particularly of systemic Juvenile Idiopathic Arthritis (sJIA). A score that identifies sJIA patients at high risk to develop MAS would be useful in clinical practice.

Methods
To define a risk score able to predict the development of MAS in patients with active sJIA, based on routine laboratory parameters at disease onset. Laboratory parameters of disease activity and severity (WBC, N, PLT, Hb, ferritin, AST, ALT, gGT, LDH, TGL, fibrinogen, D-dimer and CRP), were retrospectively evaluated in 86 sJIA patients referred to our Division of Rheumatology from 1998 to 2017 with at least one year of follow-up. Laboratory parameters were collected during active sJIA, without MAS, at time of hospitalization (T1) and before treatment for sJIA was started (T2). Patients were divided in two groups: group 1 (without history of MAS), group 2 (at least one MAS episode during disease course). Laboratory parameters collected at T2 with a statistical significant difference between the two groups of patients were selected.

Results
33 patients, who fulfilled the 2016 classification criteria for MAS [1] at time of sampling, were excluded from the analysis. We analysed laboratory parameters of 53 patients, 33 in group 1 and 20 in group 2. Levels of ferritin, AST, LDH, gGT and TGL, collected at T2, were statistically significant higher in group 2 than in group 1. For each of these parameters an arbitrary cut-off was defined and an arbitrary rate was attributed. Sensitivity (Se), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV) were calculated and the scoring system with the best sensitivity was chosen. A MAS risk score >=3 identified 19 out of 20 sJIA patients in group 2 and 4 out of 33 in group 1. We also applied it on 53 patients from other paediatric Rheumatologic centres: 37 without history of MAS and 16 with at least one MAS episode. Sensitivity and specificity were 0.750 and 0.784 respectively.

Conclusion
We developed a MAS risk score based on routine laboratory parameters that can help clinicians to identify patients at higher risk to develop MAS. A validation on a larger population is necessary.

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A MULTINATIONAL STUDY OF THROMBOTIC MICROANGIOPATHY IN MACROPHAGE ACTIVATION SYNDROME: A DREADFUL CONDITION WHICH IS LIKELY UNDERRECOGNIZED

Background

Macrophage activation syndrome (MAS) is a severe complication of rheumatologic conditions, mainly systemic juvenile idiopathic arthritis (sJIA), and is classified among the secondary forms of hemophagocytic lymphohistiocytosis (HLH). Thrombotic microangiopathy (TMA) is a heterogeneous group of life-threating diseases characterized by microangiopathic hemolytic anemia, thrombocytopenia and organ injury. The association between TMA and HLH has been described only in single reports in adult renal transplant recipients and in two pediatric cases of virus-induced HLH. The aim of our study is to present the preliminary data from a multinational cohort of pediatric patients with MAS and TMA

Methods

The clinical charts of patients with MAS were retrospectively reviewed to identify the instances that were associated with TMA. Demographic, clinical and laboratory features at MAS and TMA onset, therapeutic interventions and outcome were collected

Results

A total of 24 patients, 58.3% females, with MAS and TMA were collected. An underlying rheumatologic disease was reported in 17/24 (13 sJIA or a sJIA-like illness, 2 systemic lupus erythematosus, 1 Kawasaki disease, 1 autoimmune hepatitis). The median age at MAS onset was 11.2 years. In 8 patients MAS and TMA occurred simultaneously, whereas in 4 TMA preceded and in 12 followed MAS. The main features at MAS and TMA onset are presented in Table 1. Low complement levels and reduced ADAMTS13 activity were observed in 64% and 50% of patients respectively. For MAS management, 91.7% of patients received high-dose corticosteroids and 70.8% cyclosporine; in 7 cases anakinra was added. TMA episodes were treated with plasma-exchange in 62.5% of patients; 13 patients were given biologics (4 rituximab and 9 eculizumab). Admission to the Intensive Care Unit was required in 90.9% of cases. Mortality rate was 12,5%.

Conclusion

The association of MAS and TMA is a dreadful complication, likely under-recognized. Clues to suspect TMA in a patient with MAS are the increase in LDH and decrease in platelet count out of proportion of other laboratory abnormalities, the drop in haptoglobin level, the finding of schistocytes in blood smear and the new onset of hematuria. Biologics, particularly rituximab and eculizumab, may offer an adjunctive therapeutic option for refractory cases.

	Features at MAS onset	Features at TMA onset	p
Fever, n (%)	24/24 (100)	20/24 (83.3)	0.10920
Hepatomegaly, n (%)	18/24 (75.0)	13/23 (56.5)	0.13130
Splenomegaly, n (%)	16/24 (69.6)	12/23 (52.2)	0.31150
CNS involvement, n (%)	17/24 (70.8)	21/24 (87.5)	0.15513
Kidney involvement, n (%)	13/24 (54.2)	22/24 (91.7)	**0.00346**
Median laboratory values			
Hemoglobin, g/dl	9.5	8.5	0.80258
Platelet count, x 10^9/l	114	36	**0.00208**
Aspartate aminotransferase, U/l	127	236	0.25848
Lactate dehydrogenase, U/l	1,315	1,914	0.19360
Fibrinogen, mg/dl	250	221	0.34722
Ferritin, ng/ml	7,949	7,650	0.92034
BUN, mg/dl	28	58	0.07346
Creatinine, mg/dl	1.0	1.4	0.40654
Hematuria	-	19/24 (79.2)	-
Schistocytes on blood smear	-	17/17 (100)	-
Low haptoglobin levels	-	11/13 (84.6)	-

Table 1.

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HYPERZINCAEMIA AND HYPERCALPROTECTINEMIA SYNDROME: MORE THAN JUST AUTOINFLAMMATION?

Background
Hyperzincaemia and hypercalprotectinemia (HandH) syndrome has been described as a new rare entity characterized by recurrent infections, dermatological involvement, increased inflammatory markers, hepatosplenomegaly and anemia. Little is known about its heterogeneous presentation, pathophysiology and treatment. Aim of the staudy is to describe 3 patients with HandH syndrome

Methods
Serum calprotectin (MRP8/14) was measured according to Buehlmann assay (ELISA) and plasmatic zinc by atomic absorption spectrometry

Results
Three patients were referred to our centre because an history characterized by recurrent episodes of skin rash, severe oral aphtosis and increased level of serum amyloid A (SAA). Patient 1 presented, since the age of ten recurrent episodes of fever and rash; skin biopsy was consistent with a lymphocytic lichenoid vasculitis resembling erythema multiforme. Patient 2 presented at birth, with hemolitic anemia and thrombocytopenia. At the age of 5 she was admitted to another hospital due to EBV related hemophagocytic limphohystiocytosis (HLH). At the age of 8, she was first seen at our center because of a persistent desquamant erythematous rash with recurrent abdominal pain and recurrent arthritis. Intestinal biopsy showed small intestine inflammation (erosions in the digiunum). Patient 3 presented with recurrent episodes of fever, rash, two episodes of transient hip synovitis and muscoloskeletal pain. A bone scintigraphy was performed resulting normal. Patients 1 and 2 suffered from recurrent infections (pneumonia, otitis, skin abscesses). Immunological studies revealed in patient 2 a reduction of memory B cells and a reduced response to Toll like receptor 9 agonist. Of note, all the patients presented in their medical history at least one episode of vasculitis: patients 1 and 3 suffered from Schonlein-Henoch purpura and patient 2 had an undefined vasculitis (evaluated elsewhere). All patients showed elevated inflammatory markers, zinchemia and serum calprotectin (table)

Conclusion
We report three patients with high serum levels of calprotectinemia and zinch presenting with a clinical phenotype consistent with previously reported cases. The presence of vasculitis in all of the patients suggests that it may represent the first symptom of this condition. Vasculitis could lead to an increase of serum calprotectin already proposed as a marker of vascular impairment. Moreover, considering the immunological defect detected in one of our patient, we speculate that recurrent infections described in this syndrome may underline an immune-dysregulation process in which the role of zinc metabolism needs to be assessed.

	Patient 1	Patient 2	Patient 3
Age at 1st evaluation (years)	14.3	7.8	4.9
Sex	F	F	M
Clinical features	Recurrent fever, recurrent infection, vasculitis, skin rash, musculoskeletal pain	Hemolitic anemia, thrombocytopenia, HLH, vasculitis, recurrent infections, recurrent fever, arthritis, skin rash, gastrointestinal involvement	Recurrent fever, skin rash, vasculitis, arthritis, musculoskeletal pain
SAA	13-23	27,5-76,4	20
Zinchemia (mcg/dl) (n.v. 80-125)	132-143	102-233	147
Serum MRP8/14 (ng/ml) (n.v. < 2900)	22431	10383	10363

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CLINICAL PICTURE OF 7 PAPA PATIENTS FOLLOWED IN A SINGLE PEDIATRIC RHEUMATOLOGIC CENTER

Background
Pyogenic sterile arthritis, pyoderma and acne (PAPA) syndrome is an autosomal dominant inflammatory disorder caused by mutations in the PSTPIP1 gene primarily affecting joints and skin. The E250K mutation cause the hyperzincaemia/hypercalprotectinemia syndrome termed PSTPIP1-associated-related proteinemia inflammatory (PAMI) syndrome in which a bone marrow involvement is reported. Aim of the study is to describe the clinical presentation of 7 PAPA patients followed in a single Centre

Methods
For each patient clinical and laboratory data were collected from medical charts. PSTPIP1 was sequenced through Sanger Sequencing or targeted resequencing using a customized panel and analyzed with the NextSeq® platform (Illumina)

Results
7 patients from 4 unrelated families with the E250K mutation in a mother and 2 siblings, the A230T variant in a father and his son and the R405C and D266N respectively in the last 2 unrelated patients were included. Disease onset occurred within the 7th year in all patients. Patients 3 and 4 (table) presented since 1 year recurrent episodes of fever without any cutaneous or articular symptoms. In both inflammatory markers were elevated during fever episodes but persistently negative during well-being not requiring any therapy. The variants described in these patients were not previously reported. However their pathogenic role is supported by the detection of markedly high serum calprotectin levels (>10.000 microg/ml). The predominant feature of patients 1 and 2 was articular involvement with recurrent arthritis and acne. Patient 1 was initially treated with prednisone with good clinical response but relapse of arthritis at discontinuation followed by the development of a sterile muscle abscess. An anti-TNF drug was started in both patients with complete clinical response. Patient 5 reported severe acne, psoriasis and recurrent episodes of arthritis. She presented a persistent elevation of acute phase reactants with severe anemia and leukopenia not resolving after splenectomy. His son (pts 6) had recurrent episodes of sterile arthritis, hepato-splenomegaly, anemia and neutropenia. Zinc and calprotectin serum levels resulted respectively 728 micromol/l and 2600 microg/ml. IL-1 inhibition determined a complete normalization of inflammatory parameters with no effects on anemia and neutropenia. In patient 6 zinchemia decreased to almost normal value after 4 months of therapy. Patient 7 presented at the age of 4 a sterile lymphnode abscess. She also presented with splenomegaly and neutropenia with persistent elevation of acute phase reactants. Anakinra was proposed but not administered for poor compliance

Conclusion
The clinical picture of patients carrying PSTPIP1 mutation may be heterogeneous. In our cohort TNF-inhibitors were successfully used in PAPA patients preventing new arthritis episodes and resolving cutaneous manifestation where present. In 2 patients the clinical picture was mild not requiring continuous treatment. One PAMI patient had a good response to IL-1 inhibition, which however, had no effect on hematological manifestations.

Pt	Mutation	Clinical features	Laboratory features	Therapy
1	A230T	Recurrent fever, acne, cutaneous absesses, arthritis	↑ CRP, ESR, SAA	Anti-TNF
2	A230T	Acne, arthritis	↑ CRP, ESR, SAA	Anti-TNF
3	R405C	Recurrent fever	↑ CRP, ESR, SAA, zincaemia	/
4	D266N	Recurrent fever	↑ CRP, ESR, SAA, zincaemia	/
5	E250K	Acne, psoriasis, arthritis, hepatosplenomegaly	↑ CRP, ESR, SAA, zincaemia calprotectinemia	/
6	E250K	arthritis, hepatosplenomegaly	↑ CRP, ESR, SAA, zincaemia calprotectinemia	Anti IL-1
7	E250K	Limphnode absess, hepatosplenomegaly	↑ CRP, ESR, SAA	/

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POTENTIAL ALLELIC BURDEN OF MULTIPLE VARIANTS IN A COMPLEX CASE OF UNDEFINED AUTOINFLAMMATORY SYNDROME

Background
Despite recent advances in diagnosis and understanding of many autoinflammatory diseases, there remains a significant number of patients with phenotypes that do not fit any clinically- and/or genetically-defined disorders. To achieve the best care for those patients, a detailed understanding of disease etiologies and mechanisms is imperative. The objective of this study was to improve mechanistic understanding of one such case of an undefined autoinflammatory syndrome.

Methods
Gene variants were identified using whole exome sequencing (WES) and confirmed by Sanger sequencing in the index patient, two siblings and parents. Serum cytokine mesurements were performed using mesoscale cytokine multiple assay. Type I Interferon-stimulated gene expression in whole blood was quantified using the RT-PCR.

Results
We describe a fourteen-year-old boy who presented at two and a half years of age with recurrent febrile episodes. Over the course of the disease, the episodes increased in frequency and severity, with new signs and symptoms continuing to appear; these included skin changes, splenomegaly and transaminitis. Partial control of the disease was achieved with colchicine and anti-IL-1 therapy. Extensive investigation showed immunological abnormalities, increased serum amyloid A and altered expression of several proinflammatory cytokines including Type I and Type II interferons. Exome sequence analysis identified multiple variants in genes associated with autoinflammatory disease and highlighted P369S and R480Q variants in the MEFV gene, and T260M and T320M variants in the NLRP12 gene as most likely to be causative.

Conclusion
Although none of this patient's rare variants met criteria to be regarded as pathogenic, we speculate that in aggregate they might confer an "allelic burden," such that their combination could create an autoinflammatory milieu consisting of increased proinflammatory cytokines. The operation of more than one underlying mechanism could also help to explain why the response to different treatment modalities, including complete blockade of IL-1, was variable with incomplete control of inflammation and persistence of some milder symptoms. Because patients like this present diagnostic and therapeutic challenges and collectively form a substantial part of every cohort of patients with autoinflammatory diseases, it is important to acquire their full genomic profile and present their cases to the broader audience.

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VACCINATION SAFETY AND COVERAGE IN AN ITALIAN COHORT OF AUTOINFLAMMATORY DISEASES

Background

Vaccine-preventable diseases are re-emerging after recent anti-vaccine campaign. In autoinflammatory diseases (AID), vaccine triggered-flares is a well known phenomenon for Hyper-IgD/Mevalonate-Kinase Deficiency (MKD). In CAPS, severe flares were reported after pneumococcus vaccine, while PFAPA patients did not achieve protective levels of antibodies.

Methods

An anamnestic questionnaire was administrated to AID patients refering to the AID Unit of Giannina Gaslini Institute from August 2017 to August 2018. Data about disease triggers in AID were obtained from the EUROFEVER registry for statistical reference.

Results

Triggers in AID Eurofever Registry: In august 2018 a total of 3783 patients were enrolled in the EUROFEVER registry. The mean age at disease onset was 7.04 +/- 9,48 SD yrs. The distribution among periodic hereditary fevers was: 28,75% FMF; 17,66% PFAPA; 9% Undefined inflammatory disease (UND); 7,85% CAPS; 7,16% TRAPS and 5,39% MKD. Vaccines triggered the disease in 70% of the MKD, while PFAPA, TRAPS and UND had a rate of reactions of 20%. This was also found in 12.34% of CAPS, whereas FMF and inflammatory bone disorders had a rate of 6% and 3%, respectively. Considering just vaccines as a cause of reactions, MKD presented a higher percentage of reactions (7,14%), while PFAPA and UND had 1% and CAPS, TRAPS, FMF and inflammatory bone disorders had less than 1%. Triggers in Gaslini cohort: 150 questionnaires were distributed with 70% rate of response. 105 patients were identified: PFAPA (n=26); CAPS (n=5); TRAPS (n=6); FMF (n=14); MKD (n=8); Inflammatory Bone Disorders (CRMO and PAPA, n=4) and UND (n=41). Rate of coverage was lower than 90% for Hib3 (83,11%) , MMR/MMRV (88,9%) and for Rota C (1,85%). For DTP3, Hep3, PCV3 and IPV the rate of coverage was higher than 90% for all vaccines. 11 moderate/severe reactions were observed; the general rate of severe reactions/shot was 6,36 for 1000 shots and no severe infection, death, persistent or significant disability or life-threatening condition was observed. One MKD patient had a severe disease flare requiring hospitalization following pneumococcal vaccine.

Conclusion

In AID patients vaccines may trigger disease flares. Specific recommendations for vaccination in AID are warranted as well as further investigations for immunologic protection.

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LONG TERM OUTCOMES AND TREATMENT EFFICACY IN PATIENTS WITH TNF RECEPTOR ASSOCIATED AUTOINFLAMMATORY SYNDROME (TRAPS): A SERIES OF 290 CASES FROM THE EUROFEVER/EUROTRAPS INTERNATIONAL REGISTRY

Background

Tumour necrosis factor (TNF) receptor-associated periodic syndrome (TRAPS) is one of the best known monogenic auto-inflammatory disorder resulting from an autosomal dominant variation in the TNF super family receptor 1A (TNFRSF1A) gene. To define best treatment approach in patients with TRAPS and effect on long-term outcomes.

Methods

We reviewed all data on patients with TNFRSF1A variants enrolled in the Eurofever/EUROTRAPS international registry.

Results

Data on 290 patients were available. Patients with R92Q, P46L or intronic variants (49%) displayed milder disease than 147 patients with mutations affecting other coding regions, with less frequent abdominal pain and skin rashes ($P<0.01$), higher efficacy rate of colchicine as maintenance treatment, and none developed AA amyloidosis. Almost 90% of patients with exon mutations required maintenance therapy. Anti-interleukin (IL) 1β drugs were the most frequently used (47 patients), with the highest efficacy rate (>90% complete response), while Etanercept was less effectively used and discontinued in 72% of patients. No patients on anti-IL1β treatment developed amyloidosis and 10 patients with amyloidosis have been successfully treated with anti IL-1 agents with preservation of native renal function in 7 and excellent long-term transplant function in 2. Nine women had a history of failure to conceive and seven had successful pregnancies without fertility treatment following complete disease control with anti-IL1β drugs. Long term safety profiles for anti IL-1 agents were excellent even in the presence of comorbidity.

Conclusion

Anti-IL1β drugs are the best maintenance treatment in TRAPS with potential to reverse the most serious disease complications of AA amyloidosis and infertility. The diagnosis of TRAPS should be considered very carefully in patients carrying R92Q, P46L or intronic TNFRSF1A variants

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EXTRA-OCULAR MANIFESTATIONS OF CHILDREN WITH SARCOID-LIKE UVEITIS

Background
Paediatric sarcoidosis represents a spectrum of disease. Both early(NOD2) & late onset presentations may lead to long term complications due to end-stage organ damage. Although similar disease manifestations can be seen in adults & children, some entities are essentially paediatric at onset, namely Blau syndrome & immunodeficiency associated granulomatous diseases.

Methods
Retrospectively case reviewed all children currently followed at GOSH with phenotype of ocular sarcoidosis & uveitis (ophthalmologist definition based on International Ocular Sarcoidosis Working Group Consensus, or a diagnosis of idiopathic uveitis with raised ACE at least once.)

Results
n= 52 patients with sarcoid like uveitis. 27/52 males. Median age at onset of uveitis4.20 years (1.41-15.16). Median ACE 73 & mean ACE 77 at presentation (0-90U/L normal). Median maximum ACE 79 & mean maximum ACE 88.2 (14-420). NOD2 (tested 12): 6+, 6-. (2/6 + patients had Blau phenotype). Ethnicity: black 13/52, asian 10/52, caucasian 13/52, unknown 16/52. 49/52 B/L uveitis. Uveitis anterior 17/52, intermediate 5/52, posterior 2/52, panuveitis 25/52, unknown 1/52. ANA + 15/47(32%).
Extra-ocular involvement n= 52:

1. Lymphadenopathy: 15 (29%)

2.Liver: 16 (31%) - transaminitis 9/16, ultrasound(hepatomegaly, calcification, increased echogenicity) 5/16 & both abnormal Ultrasound & blood tests 2/16

3. Arthritis: 15 (29%) knees, ankles & small joints of hands. Tenosynovitis 4 (7.7%)
4. Renal: 15 (29%) (ultrasound/tests – raised creatinine, raised urinary calcium creatinine ratio, raised urinary NAG/RBP) — 4/15 ultrasound & 9/15 tests, 2/15 on both ultrasound & tests.
5. Lungs: 7 (13.5%): 6 lung function test, 1 CXR, lung function & CT chest with severe ILD
6. Skin: 10 (19.2%), eczema-like
7. Parotid/glandular: 1 (1.9%)
8. Splenomegaly: 4 (7.7%)
9. SNHL: 2 (3.8%)

Medications: Methotrexate13 (25%), Methotrexate + Adalimumab 11 (21.2%), MMF 6 (11.5%), topical steroids 8 (15.4%), systemic steroids 2 (3.8%). 10 patients no medication.

Conclusion

Most of the sarcoid-like uveitis patients had at least 1 extra-ocular involvement. ACE not a sensitive biomarker. Some (19.2%) have mild phenotype & require no treatment. Our data demonstrates the importance of close monitoring for extra-ocular manifestations & highlight good clinical response to steroids, MTX, MMF & anti-TNF.

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EFFICACY AND SAFETY OF ETANERCEPT TREATMENT FOR REFRACTORY KAWASAKI DISEASE IN RUSSIAN CHILDREN

Background
Kawasaki disease (KD) is recognized in developed countries as a fundamental reason of acquired heart diseases in children nowadays. The main treatment is infusion of intravenous immunoglobulin (IVIG) at a dose of 2 g/kg. Until now there are no unified recommendations for treatment of such patients. As alternative therapy researchers empirically apply second infusion of IVIG (77%), high doses of glucocorticoids (18%), blockers of tumor necrosis factor α (3%) and interleukin-1, cyclosporine and other cytostatic drugs.

Methods
there were examined 152 patients (boys:girls – 2:1, median age Me = 21 months [10;36]) with KD (in compliance with AHA criteria), hospitalized in Morozovskaya Children's City Clinical Hospital in 2014-2018. The frequency of complete form of KD was 80,6%. All children had a standard therapy –IVIG. In case of ineffectiveness of therapy the second infusion of IVIG, pulse-therapy and inhibitor of TNF-alpha (Etanercept) were used.

Results
the resistance to standard IVIG therapy was revealed in 16 children (10,5%), mostly in boys (4,3:1) at the age of Me = 21,5 months [9,5; 34]. Complete form of KD was diagnosed in 11 patients (68,8%), incomplete form - in 5 children (31,2%). All children got a second IVIG infusion, 13 of those children (81,2%) had a positive effect:11 children with complete form of KD, 2 children with incomplete form of KD. For 3 children (18,7%) with incomplete form of KD and significant cardiovascular changes (pericarditis, giant aneurysm of coronary and peripheral arteries, thrombosis and thromboembolism) there was a need for additional therapy. As a second-line therapy the methylprednisolone pulse-therapy was used in 2 children (12,5%) at a dose of 10 mg/kg, without sufficient effect. For these patients (3) a third-line therapy was applied of Etanercept at a dose of 0,8 mg/kg/a week subcutaneousely. In all children normalization of body temperature, decrease of leukocytosis by factor of 1,5-3 and decrease of CRP by factor of 10-15 occurred after three injections of Etanercept. However, for 1 child there was a need for an additional fourth injection of Etanercept because of repeated fever, increased laboratory parameters, development of thrombosis of the left coronary artery after 2 weeks upon discharge.

Conclusion
the frequency of immunoglobulin-resistant forms was 10, 5%. The first-line therapy of resistance (second IVIG-infusion) was efficient in 13 children (81,2%). Methylprednisolone pulse therapy was ineffective. The use of 3 subcutaneous injections of Etanercept at a dose of 0,8 mg/kg/ a week resulted in decrease of intensity of inflammatory changes and in fever relief, but it did not prevent the development of relapse and thrombosis of coronary arteries. Our strategy for refractory Kawasaki disease was safe and effective

Poster Tour-II Group-3

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DEVELOPING AN ALLIED HEALTH CORE OUTCOME SET FOR PAEDIATRIC RHEUMATOLOGY MUSCULOSKELETAL CONDITIONS

Background
Musculoskeletal conditions are very prevalent within the general population. This is also true for children and young people (CYP), with a sufficient number seeking care for musculoskeletal pain. Allied Health Professionals (AHPs) are well placed to manage these patients but there is a wide variability in interventions, with no current standardisation in treatment, services or outcomes.

Methods
A modified Delphi study was undertaken with an expert panel of AHP's working in eight Tertiary Paediatric Rheumatology centres in the U. K. Literature search informed expert panel discussion with particular reference to: paediatric population specific, ease of clinical use, cost, general availability to clinicians, reliability, validity, length to administer/perform and previous research use. Expert panel discussion and ranking identified eight measures: Fatigue, muscle strength, hand function, school attendance, stamina, balance, sleep, quality of life and goal-setting. An anonymous survey was sent to twelve members of the expert panel asking participants to choose two strongest measures for each.

Results
Surveys were completed by 10 out of 12 members, representing a response rate of 83%. Consensus was achieved for 6/9 outcomes. Consensus could not be reached for hand function, sleep and goal-setting due to the large number of variation in use, lack of paediatric specific measures, length of time taken to administer or costs involved.

Conclusion
Standardising outcome measures across the Tertiary centres in the UK can help future collaboration, and quality improvement within musculoskeletal paediatric medicine. This would also be of wider interest to all paediatric AHP's working with a paediatric population. There was considerable consensus for outcome measures for AHP's working within paediatric rheumatology in clinical settings when time, space, money and ease of use is paramount although no consensus was achieved for assessment of sleep, goal setting and hand function. Psychological measures were not included within the scope of this work, but would be a valuable future addition to the set. Further work is underway to rectify this, and to seek opinions from CYP and parents regarding the feasibility and acceptability of the outcomes generated prior to their pilot later this year.

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CACP CASE REPORT

Background

Camptodactyly-Arthropathy-Coxa vara Pericarditis syndrome(CACP) is an uncommon autosomal recessive condition . We present a case of CACP from a tertiary care centre in Himachal-Pradesh, India, having a mutation not yet reported from India.

Methods

A 13 year, boy born of a non-consanguineous marriage presented with swelling and progressive restriction of movements of bilateral knee joints and elbow joints since 3 years of age and abdominal distention from last 6 months , with no history of fever, rash or shortness of breath. On examination, proportionate short stature with camptodactyly in hands and flexion deformity of bilateral elbow joints was noted. Investigations revealed normal haemoglobin, platelets and ESR. Liver function tests revealed hypoalbuminemia. Renal functions and urine examination were normal. Ascitic fluid analysis showed high SAAG (>1.1g/dl). Chest X-ray showed cardiomegaly and bilateral pleural effusion. 2-D echocardiography revealed constrictive pericarditis. X-ray of hip joints showed sclerosis and irregularity of acetabular margins with femoral neck shortening. With a clinical possibility of CACP in view of non-inflammatory arthropathy, genetic analysis for same was performed.

Results

Clinical exome sequencing showed homozygous 7 base pair deletion in exon 7 of PRG4 gene resulting in frameshift and premature truncation of the proteins at codon 1085 (p.Ser1085Ter;ENST00000445192.2). This, to the best of our knowledge, is a novel variant not reported from India till date.

Conclusion

CACP is an uncommon condition characterized by distinct radiological and histopathological features. Increased awareness of this familial condition will prevent confusion with other inflammatory musculoskeletal conditions seen during childhood, particularly juvenile idiopathic arthritis and SLE as management for these conditions is different. Treatment with antirheumatic drugs including biologic agents can be avoided if this condition is diagnosed early.

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RHEUMATOLOGICAL MANIFESTATIONS OF FIBRODISPLASIA OSSIFICANS PROGRESSIVA: LARGE EXPERIENCE OF THE SINGLE CENTER

Background

Fibrodisplasia ossificans progfessiva (FOP) – extremely rare (1:2000000) autosomal dominant disorder caused by mutation in the gene ACVR1 encoding a bone morphogenetic protein (BMP) type I receptor, results in uncontrolled osteogenesis. It seems to be a lot of similarities between rheumatic diseases, especially spondyloarthritis (SpA) and FOP in the pathophysiology, clinical manifestation and the therapy approach.

Methods

The aim is to present the single-center experience of the FOP patients and to identify similar symptoms in FOP and rheumatic disease. The analysis of the large series (n=28, 14 male and 14 female) of patients with FOP, who are under observation to pediatric rheumatological clinic.

Results

24 (85,7%) patients had common for FOP massive multiple heterotopic ossifications as a “second skeleton” manifestation. 3 of them had formed heterotopic ossification through the X-ray negative stage to visible changes. All patients have obvious typical FOP stigmas: great toe malformation in 26 (92,8%); thumbs malformation – 6 (21,4%); peripheral osteochondromas – 16 (59,3%); cervical spine abnormalities – 22 (81,4%). The similarities to RD were mentioned: ossifications/calcification in 85,7% cases; episodes of synovitis of major joints (knee and hip joints) in 5 patients; “classic” for spondyloarthritis type of changes - intervertebral and vertebral body fusion and X-ray/CT/MRI evidence of the sacroiliitis among most patients with active sacroiliitis by MRI stir regimen; 4 patients demonstrated gradually formation of great toe ankylosis during the follow-up observation; positive effect and FOP nodes involution were achieved by the using of prolonged course of NSAID and glucocorticoids.

Conclusion

In addition to typical FOP manifestation patients have clinical signs related to spondyloarthritis. Because of BMP receptor plays a significant role in other rheumatic process the detailed exploration of FOP could be regarded as a clinical model of new bone formation in spondyloarthritis.

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IMMUNOGLOBULIN G4 RELATED DISEASE IN A 10 YEAR-OLD-GIRL WITH MULTISYSTEM INVOLVEMENT

Background
IgG4-related disease is an immune-mediated fibroinflammatory condition characterized by the infiltration of IgG4-carrying plasma cells and storiform fibrosis in the tissues. Salivary gland is the most commonly affected organ with sialadenitis. Raised IgG4 concentrations in the serum and prominent infiltration of the lacrimal and salivary glands by IgG4 expressing plasmacytes have been confirmed.

Methods
We extracted patient's clinical, laboratory, and imaging data and reviewed literature to reveal different manifestations of the IgG4-RD.

Results
10 year-old-girl presented with lacrimal and salivary gland swelling with sicca symptoms, fatigue and abdominal pain. No family history of autoimmune or autoinflammatory conditions noted. Ultrasound scan(USS) neck revealed multiple small lymph nodes and enlarged submandibular glands. Salivary glands appeared bulky and heterogenous with multiple small hypoechoic focci. Appearances were most likely to represent sialoadenitis and there was no convincing evidence of malignancy. Full blood count, routine biochemistry and urinalysis were normal. Autoantibodies came back as negative(ANA, ANCA, Anti-Ro and Anti-La: Negative. Serum IgG level was elevated in repeated samples. IgG subgroups revealed highly elevated IgG4 levels (21.49, Normal range: 0-1.1) The biopsy of salivary gland showed chronic inflammation with IgG4 staining and was suggestive of IgG4 related disorder. Treatment was started with intravenous methylprednisolone followed by Anti-CD20(Rituximab) therapy and weaning of steroids. Mycophenolate mofetil was commenced for the maintenance therapy.

Conclusion
IgG4-RD is a rare condition which can cause multisystem involvement with infiltration of IgG4-bearing plasma cells in the tissues. We wanted to emphasize that this condition could also be seen in the pediatric population. Steroids are the cornerstone of the treatment, however Anti-CD20 medication and steroid sparing agents should be considered for the maintenance therapy.

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ORANGE BROWN CHROMONYCHIA IN KAWASAKI DISEASE: A CLINICAL SIGN THAT MERITS GREATER ATTENTION

Background
Peripheral signs in Kawasaki disease (KD) include erythematous swelling of hands and feet during acute phase, periungual desquamation and Beau's lines on nails in convalescent phase. Orange–brown discoloration of nails has, however, not been frequently described in KD.

Methods
Although chromonychia has been described by Pal et al way back in 2010, we had not been looking prospectively for this sign until very recently. We report 20 patients with KD and chromonychia that were seen during the period May 2017 to February 2019. We herin report children diagnosed with KD who developed orange brown chromonychia.

Results
Median age at diagnosis in these patients was 1.4 years (range:3 months-4 years). Seven patients were below 1 year. Eleven patients developed chromonychia in acute phase of KD, while in 9 this finding was identified in convalescent phase of disease. Associated atypical features that were seen in these patients included BCG reactivation in 2; macrophage activation syndrome in 2; uveitis in 1; peripheral gangrene in 1; bilateral parotidomegaly in 1; HIN1 pneumonia in 1. Ten (50%) children required second line therapy (infliximab in 6; second dose of IVIg in 1; methylprednisolone in 3). Coronary artery abnormalities were seen in 5 patients and 2 had giant aneurysms - one in left main coronary artery; another in left main, left anterior descending and left circumflex arteries.

Conclusion
Transverse orange brown chromonychia is a useful clinical sign in KD and may be seen in both acute and convalescent phases of the disease. This sign can be easily missed if not looked for carefully. It appears to be more common in infants and young children and may be a marker of more severe disease. Presence of this sign may help pediatricians in arriving at a diagnosis of KD, especially in situations where the presentation is incomplete.

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EFFICACY AND SAFETY OF BIOLOGICAL THERAPY WITH ETANERCEPT IN A CASE OF SEVERE POLIARTHRITIS ASSOCIATED TO HARLEQUIN ICHTIOSIS

Background

Harlequin Ichthiosis (HI) is a rare autosomical recessive congenital disease, due to mutations of gene ABCA12.The estimated incidence is approximately 1 in 300,000 births, and approximately 200 cases have been reported worldwide. Typical manifestations of the disease at birth are the presence of hyperkeratotic plates with erythematous fissures, ectropion (eversion of the lower eyelids) and eclabium (eversion of the lips), rudimentary ears and nasal hypoplasia, and articular contractures. Babies who survive into infancy tend to loose hyperkeratotic plaques in favour of generalized scaling and erythroderma. Mental retardation is present in about 2/3 of cases.The association between HI and inflammatory joint involvement has been reported only in few patients since now.

Methods

We report clinical and laboratory findings, treatment choices and outcomes of a kid with HI who developed polyarthritis.

Results

A 6 years old kid with HI (the genetic test showed homozigous mutation of ABCA12) came to our attention with an history of chronic arthritis. Since he was 4, he developed bilateral knee arthritis. In the following two years, he developed severe chronic poliarthtritis.At the first visit in our center, he showed the classical clinical feature of HI (severe ectropion, contracture and generalized erythroderma), and had history of multiple severe infections and sepsis. Arthritis affected both hips, knees, ankles, wrists, elbows , shoulders and all the feet joints. He lost the ability to walk since the onset of arthritis.Laboratorial features showed negative anti nuclear antibodies (ANA) and anti. extractable nuclear antigen antibodies (ENA), anti ciclic citrullinated peptide and rheumatoid factor. No signs of uveitis were present at ophtalmological evaluation.The patient was treated with intraarticular corticosteroid injections (IACI) into knees, wrists, elbows and ankles, and then oral methotrexate (MTX) was started.The clinical response was initially good, with partial recovery of deambulation in the 4 months following the intrarticular injection treatment. After 7 months ankles and wrists showed swelling and tenderness, and IACI were repeated, with clinical improvement.Nonetheless, two months later, due to the persisting arthitis activity, anti TNF therapy was started. Etanercept at the dose of 0,8 mcg/week was found to be effective and safe, allowing the patient to walk again. Since the therapy onset, no severe adverse reaction was observed.

Conclusion

This is the first case of a kid with HI and poliarthritis treated with IACI and anti-TNF agent in combination with MTX. This clinical case shows the efficacy of IACI as a safe and powerful mean, with fast clinical response, in the treatment of arthritis in those patients. Furthermore, we observate the efficacy and safety of anti-TNF agents as baseline therapy for arthritis in patients with HI.

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TRANSITION CLINIC PROGRAM FOR RHEUMATIC DISEASES, ONE YEAR OF EXPERIENCE IN MEXICO

Background

The purposeful, planned movement of adolescents and young adults with chronic physical and medical conditions from child-centered to adult-oriented health care systems is called transition (1). 30-70% of the patients with childhood rheumatic diseases have continuing disease activity in their adult life (2). This is the first model in Mexico of transition that includes skill training and support system development for adolescents with rheumatic diseases.

Methods

41 adolescents and young adults older than 15 years were systematically evaluated every 3 months over a year by a pediatric and adult rheumatologist, physiotherapist, nutritionist, psychiatrist, clinical psychologist, nurse and social worker. 11 phases were used to individually define the initial status of the transition skills of the patients and their family, establish priorities and prioritized goals.

Results

The median of age was 18 years (min15 - 21 max)**.** 75.6% were female, Juvenile Idiopathic Arthritis (JIA) in 60.9%, 61% attended deferent school levels, 22% reported not doing any activity related to school or employment.68.9% of the JIA patients reported high initial disese activity using JADAS10 score (mean 11.4) and 81% showed initial musculoskeletal alteration and showe a significant reduction ($p<0.05$) after the intervention through the transitional clinic (mean 6.4).

Conclusion

This is the first multidimensional and multidisciplinary model in Mexico for a transition policy in adolescents and young adults with rheumatic diseases. Our results shown a high prevalence of nutritional a disorders and high disease activity among adolescents with rheumatic diseases and a significant reduction of disease activity and other social and nutricional problems after the intervention of the clinic.

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OUTCOME OF TRANSITION OF CARE IN YOUNG ADULTS WITH JUVENILE ONSET CHRONIC RHEUMATIC DISEASES

Background
The transition process of adolescent care from a paediatric to an adult medical environment may affect the compliance with the management plan. Paediatric care is family oriented and relies on significant parental involvement in decision making. Contrarily, adult care is patient-specific and requires autonomy and independent skills. The aim of this study was to evaluate the transition of care at our centre.

Methods
All consecutive patients with juvenile onset of rheumatic chronic diseases followed in a young adult clinic were included. Disease activity was evaluated at the last appointment in the paediatric unit and up to 2 years after transition of care. Dropout was defined as not attending the clinic for 2 consecutive visits. Global assessment of the clinical appointments before and after transition of care was evaluated in a scale of 0 to 10. Variables were analysed as means, medians and frequencies as appropriate. Univariate analysis was performed with student t-test and Qui-square.

Results
126 patients were included. 77 (61.1%) had juvenile idiopathic arthritis (JIA), 78 (61%) were female with a mean age of 23.1±3.2 years and a mean disease duration of 12.7±5.3 years. During the transition of care, 92 (73%) patients were treated with conventional disease modifying antirheumatic drugs (DMARDs) and 35 (27.8%) with biologic therapy. 69 patients (54.7%) missed at least one clinical appointment with a dropout rate of 9%. This was associated with longer disease duration (15.9 vs 12.3 years, p=0.024). 11 patients (8.7%) had worsened clinical activity: 5 patients with polyarticular JIA with arthritis flare; 4 patients with oligoarticular JIA with new onset uveitis and 2 patients with juvenile systemic lupus erythematosus. 4 patients abandoned DMARDs. Regarding patient satisfaction questionnaire, paediatric rheumatology appointments had a median evaluation of 9 (7-10), adult rheumatology appointments of 8 (5-10) and the transition process had an evaluation of 8 (5-10). The longer appointment waiting time was the major negative aspect referred after transition.

Conclusion
Our centre registered a small percentage of dropping out from the clinic, which was associated with longer disease duration, a slight worsening of disease activity and a 10% decrease in patient satisfaction.