Proceedings of the 21st European Pediatric Rheumatology (PReS) Congress

Belgrade, Serbia. 17-21 September 2014

Published: 17 September 2014

These abstracts are available online at http://www.ped-rheum.com/supplements/12/S1

INVITED SPEAKER PRESENTATIONS

I1
A year in review: basic science
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Pediatric Rheumatology 2014, 12(Suppl 1):i1

The year of September 2013 - 2014 has seen some seminal discoveries in the field of human autoimmunity and immunology : work in Paediatric Rheumatology has led the way in several of these. In this session we will review together some of the exciting and important new developments in basic understanding of disease pathogenesis. We will also hear of the application of high throughput techniques and large datasets to our understandings of mechanism and to our translational goals towards improving lives of our patients.

However one small note of caution - it is never possible to review everything of high importance and relevance, so apologies in advance if some studies cannot be squeezed in.

Disclosure of interest: None declared.

I2
JIA pathogenesis - genetics
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Pediatric Rheumatology 2014, 12(Suppl 1):i2

Juvenile Idiopathic Arthritis is a heterogeneous disease with significant variability in long-term outcome and treatment response; this occurs both between and within JIA subtypes, as defined by the current International League Against Rheumatism (ILAR) classification. There are currently no robust clinical or biological predictors of outcome or treatment response in JIA. Given that JIA is a complex genetic disorder, genetic studies provide an opportunity to address this issue, and whilst previous studies have often been limited by statistical power to identify the likely modest effect sizes, the recent establishment of a number of international consortia for JIA genetics has allowed this issue to be resolved. This presentation will summarize the current understanding of the genetic basis of JIA susceptibility, prognosis and treatment response and will describe how these genetic associations may further our understanding of the molecular mechanisms and immunological pathways involved in this disease. In addition it will provide insights into how we might utilise this data to progress towards the ultimate goals of predicting long-term disease outcomes at onset, predicting drug response, and move towards more targeted treatment options for children with JIA.

Disclosure of interest: None declared.

I3
Juvenile idiopathic arthritis classification
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Pediatric Rheumatology 2014, 12(Suppl 1):i3

Juvenile idiopathic arthritis (JIA) is not a disease, but an exclusion diagnosis that encompasses all forms of arthritis that begin before the age of 16 years, persist for more than 6 weeks, and are of unknown origin. This heterogeneous group of chronic arthritides has been classified on clinical and laboratory grounds to try to identify homogeneous, mutually exclusives categories suitable for etiopathogenic studies. During the last years evidence has accumulated suggesting that while some JIA categories identify quite definite disease entities, others represent heterogeneous conditions and in particular that a homogeneous disease entity (ANA positive, early onset oligoarthritis) is included in several different JIA categories. These and other findings suggest the need to reconsider some aspects of the current International League of Associations for Rheumatology (ILAR) JIA classification and nomenclature.

Disclosure of interest: None declared.

I4
Uveitis: basic concepts and differential diagnosis
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Pediatric Rheumatology 2014, 12(Suppl 1):i4

Uveitis describes a variety of patterns of intraocular inflammation that may be linked with other localised ocular and orbital inflammations as well as extraocular disease. Experimental models of autimmune uveitis fail to reflect not only the clinical variety of ocular inflammatory disease but also the marked differences in pathology of human multi-system diseases that often result in very similar ocular disease.

There are marked differences in the epidemiology of paediatric ocular inflammatory diseases, compared to adults, and their rarity has needed a specific approach to both diagnosis and the evaluation of treatment. The age -related differences in epidemiology partly relate to the earlier presentation of genetically driven inflammatory disorders as well as differences in clinical presentation of more commonly adult-onset inflammatory disorders. The recent advances in genetics require novel diagnostic pathways for ocular inflammatory disease as well as the revision of longstanding clinical descriptors.

Children’s eyes react differently to inflammation, usually for the worse. Presentation is often late with established damage. This leads to a need for child-specific disease damage evaluation and clear separation of the complications subsequent to late presentation and those amenable to amelioration with effective immunosuppression. Reported outcomes need
clear identification of the cohort characteristics. The limitations of existing outcome modelling is discussed as well as their relevance for cost-effective analysis of biologics in childhood uveitis.

Disclosure of interest: None declared.

15 Uveitis outcome and complication
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Pediatric Rheumatology 2014, 12(Suppl 1):15

Anterior uveitis is a well-known threatening comorbid condition of JIA and affects around 10 to 20% of the patients depending on JIA subtype. A large proportion of children with JIA develop uveitis in the first year of disease and 73 to 90% do so after four years of the arthritis onset. Uveitis can progress into the adulthood and usually occur as “white uveitis” which is not associated with symptoms like redness and pain as opposed to JIA related to the enthesitis subtype that is symptomatic. Factors associated to lower uveitis remission rate are: JIA diagnosis, findings of 1+ or more vitreous cells at presentation and initial visual acuity of 20/200 or worse. The Standardization of Uveitis Nomenclature (SUN) Group took the first step to define outcome measures for uveitis, but it was established just for adults. The Multinational Interdisciplinary Working Group for Uveitis in Childhood (MIWUGC) proposed outcome measures for JIA associated uveitis incorporating the Standardization of Uveitis Nomenclature (SUN) criteria in 2011.

Disclosure of interest: None declared.

16 Systematic review on treatment of juvenile idiopathic arthritis – associated uveitis
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Pediatric Rheumatology 2014, 12(Suppl 1):6

Background: Juvenile idiopathic arthritis (JIA) is commonly complicated by chronic uveitis that frequently leads to visual loss.

Methods: Review of the current literature on the treatment of JIA - associated uveitis.

Results: Therapy of JIA-associated uveitis is guided by the severity of inflammation and complications. Topical corticosteroids are generally used as the initial treatment. Severe uveitis is commonly treated with immunosuppressive drugs. Methotrexate is presently the first-choice agent. If uveitis is not responding, another immunosuppressive agent or biological is applied. Currently, adalimumab is the preferred TNF-inhibitor. In refractory disease, other biologics are used (e.g., rituximab, tocilizumab or abatacept). Ocular corticosteroid injections / - implantsation are considered as ‘rescue therapy’.

Conclusions: Controlled studies are warranted to offer most effective and safe therapy for children with JIA - associated uveitis. Better knowledge of the basic mechanisms underlying the disease and of the molecules that are important for regulating inflammation may help to create new and more specific treatment approaches, and to improve disease monitoring.

Disclosure of interest: None declared.

17 The pathogenesis of macrophage activation syndrome
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Pediatric Rheumatology 2014, 12(Suppl 1):7

The term macrophage activation syndrome (MAS) identifies a severe and potentially fatal complication of s-JIA, and, more rarely, of other rheumatic diseases. MAS share similarities in clinical features and laboratory abnormalities with primary and secondary hemophagocytic lymphohistiocytosis (HLH). Indeed, it is currently classified among secondary HLH and the term rheuma-HLH has been used to indicate this condition. The clinical and laboratory similarities with primary genetic- caused HLH led to the hypothesis that pathogenic mechanisms leading to the typical features of MAS/rheuma-HLH are similar to those involved in primary HLH. We will review the evidence supporting this hypothesis; particularly the role of hyper-responses to TLR activation, of subclinical variants of genes involved in the cytotoxic pathways, and of the transient NK cytotoxicity defect induced by inflammatory cytokines. We will also present evidence on the role of IL-6, IL-1 and IFN-g in this syndrome and discuss the potential benefits of therapies targeted to these cytokines.

Disclosure of interest: F. De Benedetti Grant / Research Support from: Sobi, Novimmune, Novartis, Roche, Pfizer, Abbvie

18 Treatment of MAS and HLH
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Pediatric Rheumatology 2014, 12(Suppl 1):8

Macrophage activation syndrome (MAS) is a life-threatening complication of inflammatory disease, occurring secondary to a complex interplay of genetic factors, drugs, infectious agents and immunological anomalies. Early identification and aggressive treatment are mandatory to prevent fatal evolution. Precipitating factors should be looked for and eventually removed such as infections (leishmania, EBV, Parvo B19...) or drug exposure. Epstein Barr Virus (EBV) is a major cause of MAS and anti-EBV therapies can be helpful to control MAS. First line therapies usually include high-dose steroids associated to cyclosporine. In the context of primary hemophagocytic lymphohistiocytosis (HLH), bone marrow transplantation is the only treatment able to cure the disease. In inflammatory disease with secondary HLH, a few case reports indicate an efficacy of anti-cytokine treatment (anti-IL-1, anti-IL6, anti-TNFα). However, a role of these cytokines in MAS development remains unproven. To investigate whether the IL-1 pathway might contribute to MAS, we compared IL-1RA-/- to wild type mice after stimulation with CpG, a TLR9 activator. TLR9-induced MAS was similar in the two groups, suggesting that IL-1 excess is not a major inducer of MAS. More interestingly, recent data implicate IFNγ as a crucial factor in MAS onset. Thus, the inhibition of secreted IFNγ might represent an interesting therapeutic avenue worthy of further investigation.

Disclosure of interest: None declared.

19 Current evidence for the medical treatments of systemic juvenile idiopathic arthritis
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Pediatric Rheumatology 2014, 12(Suppl 1):9

Systemic juvenile idiopathic arthritis (JIA) is the most severe category within the group of arthritis which are classified under the umbrella term of JIA. Systemic JIA has been considered a therapeutic orphan until few years ago when the disease was treated primarily with corticosteroids with the known side effect especially on child growth. More recently the availability of new treatment modalities with biologic agents such as anti L6 and anti IL1 therapies have greatly advanced the possibilities for these children to be adequately treated. This lecture will describe the current status of the treatment for systemic JIA and the future perspectives.

Disclosure of interest: N. Ruperto Grant / Research Support from: The Gaslini Hospital, which is the public Hospital where I work as full time public employee, has received contributions from the following industries: Abbott, BMS, “Francesco Angelini”, GlaxoSmithKline (GSK), Hoffman-La Roche, Italfarmaco, Janssen, Novartis, Pfizer, Sanofi Aventis, Schwarz Biosciences, Sobi, Xoma, Wyeth, Speakers Bureau of: Abbott/AbbVie, Astellas, Alter, AstraZeneca, Boehringer, BMS, CD-Pharma, Celgene, Crescendo Bio, EMD Serono, Hoffman-La Roche, Italfarmaco, Janssen, MedImmune, Medac, Novartis, Novo Nordisk, Pfizer, Sanofi Aventis, Vertex Pharmaceuticals, Servier.
The evolution of cellular and molecular immunology has made available high-throughput discovery tools which can provide an entirely new, comprehensive and multi-dimensional picture of the immune system. A combination of different approaches, such as deep phenotyping by mass and flow cytometry, multiplex gene expression and functional assays, have been applied to identify immunological and epigenetic signatures leading to the prediction of responsiveness to anti-TNF therapy in autoimmune arthritis. These signatures are originated at the microenvironmental interface between the immune system and the target organ and can then be found in the periphery. We will present novel data demonstrating this concept in the context of human autoimmune arthritis.

Disclosure of interest: None declared.

I10
Immunophenotype
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Pediatric Rheumatology 2014, 12(Suppl 1):110

Juvenile idiopathic arthritis (JIA) is a chronic inflammatory disease which commonly shows a remitting-relapsing course. Monitoring disease activity and adaptation of immune-suppressive therapy is still a challenge in clinical practice. In previous work our group has shown that members of the S100-protein family are reliable biomarkers for monitoring arthritis in JIA patients on medication and that these proteins may even predict risk of relapses in these patients. In my talk I will present novel data regarding the local release mechanism of these proteins during joint inflammation, use of serum concentrations of these S100-proteins for monitoring JIA as well as novel molecular imaging methods based on local S100-protein expression in preclinical models of inflammation and arthritis.

Disclosure of interest: None declared.

I11
Monitoring local inflammation in JIA
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Pediatric Rheumatology 2014, 12(Suppl 1):111

Micro(mi)RNAs are small non-coding RNAs that play critical roles in physiological networks by regulating genetic programs. They are conserved from worms to mammals and function as physiological networks by regulating genetic programs. They are conserved from worms to mammals and function as regulatory elements called epigenics includes acetylation, methylation, phosphorylation, sumoylation and non-coding RNAs (ncRNA), such as miRNA and lncRNAs. Our laboratory is addressing over the past decade inflammatory rheumatic diseases [2], like rheumatoid arthritis (RA), AS, SSC and pulmonary hypertension and thereby searching for the regulation of pro-inflammatory cytokines [3,4], novel diagnostic signatures and new therapeutic targets. In this regard, DNA demethylation of RA synovial cells can be modulated by targeting specific enzymes [5]. Also, miRNA signatures for new response markers are in development [6].

Disclosure of interest: None declared.

I12
Epigenetics in rheumatic diseases
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Pediatric Rheumatology 2014, 12(Suppl 1):112


Comparison of epidemiological studies of JIA is challenging due to many influencing factors, mainly differences in classification criteria or study designs (e.g. population-based, hospital-based, questionnaires, registry data). Recently, longitudinal cohort studies have provided important contributions to the understanding of the disease course of JIA in the long run. Latest advances in research of incidence and prevalence of JIA will be highlighted and discussed to facilitate understanding the consequences of epidemiological knowledge of the disease.

References

I13
Sensitivity and resistance to glucocorticoids
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Pediatric Rheumatology 2014, 12(Suppl 1):113

In humans, glucocorticoids regulate a broad spectrum of physiologic functions essential for life and play an important role in the maintenance of basal and stress-related homeostasis. Approximately 20% of the genes expressed in human leukocytes are regulated positively or negatively by glucocorticoids. These steroids are involved in almost every cellular, molecular and physiologic network of the organism and play a pivotal role in critical biologic processes, such as growth, reproduction, intermediary metabolism, immune and inflammatory reactions, as well as central nervous system and cardiovascular functions. Physiologic amounts of glucocorticoids are also essential for normal renal tubular function and thus for water and electrolyte homeostasis. Furthermore, glucocorticoids represent one of the most widely used therapeutic compounds often employed in the treatment of inflammatory, autoimmune and lymphoproliferative disorders. Both excess and deficiency of glucocorticoids are respectively associated with disease, i.e. Cushing syndrome or Addison disease. Hence, target tissue resistance or hypersensitivity to these hormones is also expected to be associated respectively with glucocorticoid deficiency or excess manifestations.

Disclosure of interest: None declared.

I14
Micromas in autoinflammation and autoimmunity
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Pediatric Rheumatology 2014, 12(Suppl 1):114

Micro(mi)RNAs are small non-coding RNAs that play critical roles in physiological networks by regulating genetic programs. They are conserved from worms to mammals and function as negative regulators of protein-encoding gene expression. Research on the role of miRNAs in pathophysiological conditions is very active since 10 years and several works evidenced that miRNAs play a key role in the regulation of immunological functions and the prevention of autoimmunity. I will discuss the involvement of miRNAs in the regulation of innate and adaptive immune functions and in the development of autoimmune disease. Focusing on the role of few miRNAs, I will emphasize the intertwined relationships between tissue homeostasis and immunity, and on how studying miRNAs in autoimmunity and immune-mediated inflammatory disorders will shed light on pathological processes and help identifying novel drug candidates and biomarkers.

Disclosure of interest: None declared.

I15
Epidemiology of JIA
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Pediatric Rheumatology 2014, 12(Suppl 1):115

Comparison of epidemiological studies of JIA is challenging due to many influencing factors, mainly differences in classification criteria or study designs (e.g. population-based, hospital-based, questionnaires, registry data). Recently, longitudinal cohort studies have provided important contributions to the understanding of the disease course of JIA in the long run. Latest advances in research of incidence and prevalence of JIA will be highlighted and discussed to facilitate understanding the consequences of epidemiological knowledge of the disease.
Disclosure of interest: P. Lahdenne Speakers Bureau of: Consultancy and speaker's fees from Pfizer, Abbvie, Roche, Novartis

116 The clinical picture and outcome in adults
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Pediatric Rheumatology 2014, 12(Suppl 1):i16

The field of spondyloarthritis (SpA) has undergone substantial changes in the past decade. Increasing emphasis has been made on early diagnosis. Thus, MRI imaging has permitted new imaging modalities to detect early signs of inflammation in the axial skeleton. Additionally, much new data have emerged on the link between spinal inflammation and bone new formation, another hallmark of SpA. Classification of disease has evolved as well by focusing on the main clinical presentation (axial versus peripheral disease) and permitted to classify early forms of SpA. Early recognition facilitated early treatment regimens which showed markedly better responses in early disease and in patients with objective signs of inflammation (MRI positivity/ elevated CRP). Furthermore, there is increasing evidence that extra-articular manifestations of disease, particular gut involvement have marked impact on disease severity and long term outcome in SpA. It can be foreseen that extensive patient phenotyping will become critically important in the near future when new treatment modalities become available with differential efficacy on the various clinical features of SpA.

Disclosure of interest: None declared.

117 Spondyloarthritis - the clinical picture in children
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Pediatric Rheumatology 2014, 12(Suppl 1):i17

A group of clinical conditions with the spectrum of adult onset Spondyloarthritis (SpA) characterized at presentation by the inflammatory involvement of the lower limb joints and entheses and in some cases, particularly those with HLA-B27, sacroiliac and spinal joint involvement. Enthesitis Related Arthritis (ERA) and Psoriatic Arthritis (PsA), both categories of Juvenile Idiopathic Arthritis correspond to juvenile-onset SpA at some extent. With the advent of new classification criteria for axial SpA (axSpA) and peripheral SpA (pSpA) proposed by the Assessment of SpondyloArthritis international Society (ASAS) to identify patients with ankylosing spondylitis in the earliest pre-radiographic stage of the disease to treat them with Tumor Necrosis Factor (TNF) alpha blockers and halter disease progression, there is a tendency to search for early sacroiliac involvement with Magnetic Resonance Imaging (MRI) and peripheral disease with Ultrasound Imaging (US) studies in children. There is a clearly risk in trying to resemble the objective and procedures developed for the adult patient in the pediatric population.

In the first place, the most frequent and often severe inflammatory and structural changes in children and adolescents with SpA occur at peripheral sites five to 10 years before the onset of axial disease. Peripheral involvement might be so severe that TNF blockers may be indicated years before sacroiliitis and spondylitis. It is therefore obvious that searching for early axial disease with MRI may be useless. Both anatomy and biomechanics of peripheral sites and axial skeleton change throughout childhood and adolescence. In consequence, it is important to understand basic aspects of the sacroiliac and spinal joints before developing plans to search such sites to detect inflammation and prescribe TNF blockers.

Disclosure of interest: None declared.

118 JDM update September 2014
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Pediatric Rheumatology 2014, 12(Suppl 1):i18

Aim: To review work in the field of JDM over the last 10 years, and to give an update on the progress of work that is being undertaken in 2014.

Introduction: JDM is the commonest inflammatory myopathy of childhood and has a wide variation in disease severity and disease course. Collaborative work has moved forward the understanding and the management of JDM in the last 10-15 years.

Review of international collaborative work: International groups have developed tools for the assessment of muscles, as well as the assessment of disease activity and disease damage. This has allowed physicians to standardise their patient assessments. Core outcome variables for JDM have been proposed (IMACS and PRINTO) as well as definitions of disease flare and remission. Work is going on to agree definitions of improvement to help future treatment trials.

Diagnostic criteria continue to be based on those of Bohan and Peter, but an international survey in 2006 proposed additional items such as MRI and capillaroscopy. An IMACS collaboration has produced a proposed new Classification Criteria which should allow more accurate delineation of cases for future research.

This international work has enabled the first international RCT in treatment-resistant DM and JDM to be undertaken, and for PRINTO to conduct a trial of treatment in new onset cases of JDM. National collaborative efforts have led to setting up registries and cohort studies, allowing better understanding of variation in disease and variation in disease management.

Consensus work has also produced a muscle biopsy score, treatment guidelines to allow comparison of patients within normal clinical practice and whilst the SHARE project will produce a European consensus on treatment advice. Work is being undertaken to produce an MRI scoring system; as well as work to agree the minimum data that needs to be collected by physicians caring for JDM (i.e. minimum standards of care).

Laboratory research on myositis specific autoantibodies in JDM is beginning to define different subgroups of JDM patients. This may lead to a better stratification of disease severity and prognosis. This would enable physicians to tailor their patient’s treatment, hopefully improving long-term outcomes.

Disclosure of interest: None declared.

119 SLE and APS
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Pediatric Rheumatology 2014, 12(Suppl 1):i19

Childhood-onset systemic lupus erythematosus (cSLE) represents 15-20% of all SLE cases and is in general associated with a more aggressive disease course and more rapid damage accrual than adult-onset SLE. Disease expression varies according to ethnicity, with more severe disease course in non-Caucasian ethnic groups. The majority of patients with cSLE develop damage within 5-10 years of disease onset, most frequently involving the musculoskeletal, ocular, renal and central nervous systems. Premature atherosclerosis and osteoporosis have become increasingly prevalent comorbidities in cSLE patients.

Treatment of cSLE is challenging and is further complicated by an unpredictable disease course, adolescent noncompliance and long requirement for therapy. New therapeutic regimens combining immunosuppressive agents and targeted B-cell depletion often provide improved disease control and follow the oncologic model of remission induction and maintenance therapy. Management of children with SLE must include also prevention of medication side effects on growth, delayed puberty, development and fertility. Optimal management of an adolescent with SLE should take into account also patient’s quality of life, psychosocial development and organization of successful transition from pediatric to adult care.

The antiphospholipid antibody syndrome (APS) is a multisystemic autoimmune disease characterized by thromboembolic events, pregnancy morbidity, hematologic, dermato logic, neurological and other manifestations in the presence of elevated titers of antiphospholipid antibodies (aPL). APS may occur as an isolated clinical entity (primary APS) or in association with autoimmune diseases, infections and malignancies. Multiple pathogenic mechanisms have been proposed by which aPL may predispose to thrombosis including interaction between aPL and endothelial cells, platelets, monocytes, activation of the complement system, and interaction with the proteins involved in the regulation of the coagulation cascade.

Management in all patients with APS include avoidance of additional risk factors for thrombosis. Patients with persistently positive aPL in particular...
those with lupus anticoagulants (LA), have a high risk for recurrent thrombosis and should receive long-term anticoagulation with warfarin. The standard treatment in APS patients with venous or non-cerebral arterial thromboembolism consists of oral anticoagulation at a target INR of 2.0-3.0. However, it is essential to individualize treatment according to the presence of additional thrombophilic risk factors and the aPL profile (multiple aPL antibodies, high titer of aCL and/or anti-IIgG, presence of LA). An improved understanding of the pathogenic mechanisms by which aPL induce thrombosis has suggested some innovative treatments such as new anticoagulant and antiplatelet drugs, hydroxychloroquine, statins, complement inhibitors, rituximab and other targeted therapies.

Disclosure of interest: None declared.

I20
Vasculitis
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Pediatric Rheumatology 2014, 12(Suppl 1):I20

Primary systemic vasculitides (PSV) in children belong to the most challenging conditions in paediatric rheumatology practice. The spectrum of vasculitides affecting children as well as their clinical presentations differ from that of adults. Apart from relatively common Henoch-Schönlein purpura and Kawasaki disease, chronic PSV are extremely rare in childhood. They include mainly childhood polyarteritis nodosa (cPAN), Takayasu arteritis (cTA) and granulomatosis with polyangiitis (cGPA, formerly Wegener’s granulomatosis). From organ-specific diseases, primary CNS angiitis (PACNS) has been increasingly recognised in children over the recent years. Differential diagnosis of vasculitis covers wide spectrum of systemic diseases of inflammatory and neoplastic origin as well as etiologically heterogeneous group of non-inflammatory conditions referred to as “pseudovasculitises”. In general, diagnostic confirmation of vasculitis requires histopathological or angiographic evidence of vascular involvement. Main diagnostic and treatment principles and classification criteria for the main vasculitides will be reviewed. Principles of vasculitis assessment have been formulated by the OMERACT (Outcome Measures in Rheumatology) Vasculitis Working Group. Reversible features of acute morbidity directly related to the underlying inflammation are captured by the disease activity domain while irreversible consequences of previous active disease or long-term sequelae of treatment adverse effects form the basis of the disease damage domain. Physical function in terms of the degree of disability as well as psychosocial functioning including educational and vocational aspects are additional important components of patient-reported outcomes covered by the damage domain. Ongoing health-related quality of life (HRQoL). Paediatric-specific tools for vasculitis disease activity and damage assessment have been derived from adult instruments. Principles of Paediatric Vasculitis Activity Score (PVAS) and Paediatric Vasculitis Damage Index (PVDI) will be explained. Availability of childhood vasculitis classification and disease assessment tools has enabled initiation of the first paediatric vasculitis clinical trials. Ongoing international activities in the field of vasculitis include prospective disease registries that would allow update of disease classification and development of diagnostic criteria as well as improvement and validation of disease assessment tools. Disclosure of interest: P Dolezalova Grant / Research Support from: Novartis, Roche, Abbvie, Pfizer, Consultant for: Roche.

I21
Lessons and challenges from RA
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Pediatric Rheumatology 2014, 12(Suppl 1):I21

The application of modern imaging modalities such as magnetic resonance imaging (MRI) and ultrasonography (US) to rheumatoid arthritis (RA) has led to important advances in understanding of disease phenotypes that are now impacting on diagnosis, monitoring and even therapy delivery. This presentation overviews the concepts derived from modern RA imaging, to underpin discussions of their relevance to juvenile idiopathic arthritis. Obviously there are particular issues for the application of MRI in children. Modern imaging first demonstrated increased sensitivity for detection of both activity and damage measures above standard clinical examination and conventional radiography (CR). Both MRI and US have increased sensitivity for synovitis detection and in particular can distinguish synovitis and tenosynovitis. For erosions, both modalities have increased sensitivity above CR. MRI has better sensitivity in anatomical sites where US has a poor acoustic window, such as in the mid-carpus. The pathologies identified by both modalities have been validated against histology and other relevant techniques including CT. Uniquely MRI has demonstrated bone marrow oedema lesions, characterised histologically as osteitis. This lesion is highly predictive of subsequent erosion development. The increased sensitivity of MRI and US have provided evidence for a direct relationship between inflammation, its persistence and subsequent damage.

The next important message from modern imaging relates to what has been termed sub-clinical (perhaps better termed ‘non-clinically detected’) synovitis. A study in patients with low disease activity on clinician evaluation were studied with MRI and US of a single hand. About half the patients were in clinical remission criteria, but over 80% had synovitis in the studied hand on sensitive imaging. Follow up demonstrated this synovitis was important, in that it did result in erosions progressing for 3 years. Another study using US in oligoarticular arthritis found a large percentage of patients were re-classified as polyarticular when US criteria were employed. This has obvious implications for diagnosis and for pediatric disease.

Validity and reliability for assessment of pathologies with these modalities is now well evidenced. The sensitivity of these tools means they are well placed to objectively monitor therapeutic response. There has been a growing trial literature over the decade using both modalities, starting with smaller proof of concept studies that demonstrated that MRI and US could both demonstrate responses in keeping with large clinical trials, but in very small patient cohorts. There have been many advances in developing quantification for clinical trials, with responsiveness of the tools now established. Clearly there are strengths and weaknesses for each modality: for example MRI can give excellent synovitis and bone information, while US can evaluate more joints and is more patient-friendly. Challenges remain, especially about the optimal number of joints to assess. The use of these tools in clinical practice has been restricted by access and training issues, with US being widely utilised now by adult rheumatologists across Europe, based on its immediacy in clinic, patient tolerance, ability to scan multiple joints and ability to guide intra-articular therapy. However cost-effective clinical algorithms are required for widespread use.


I22
Musculoskeletal ultrasound imaging
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Pediatric Rheumatology 2014, 12(Suppl 1):I22

Both MSUS and MR imaging are two suitable methods used in the investigation of immature skeleton of paediatric patients. It is important to keep in mind that these methods are complementary instead of exclusive, acting in a synergistic way when are properly combined. MSUS is a bedside method for evaluating children at all ages because of anaesthesiological support is not needed.

From a paediatric rheumatologic perspective, the principal indication of MSUS is direct visualization of synovitis in peripheral joints and tendon sheaths in few minutes, even when clinical examination does not evidence abnormalities. But, MSUS imaging should never replace or precede clinical evaluation. An additional advantage of MSUS over MRI is its easy repeatability and capability to evaluate a large number of joints during a single session. The latter is of paramount importance for current ILAR classification of JIA based on the number of affected joints and the presence of particular extra-articular manifestations. Unlike MRI, MSUS is unable to display the temporomandibular joint properly.
So, far, much of the ongoing development in paediatric USUS field has been driven by a search for solutions to clinical problems. MSUS is usually used for a child with articular pain, swelling, or mechanical symptoms, without definitive diagnosis on clinical examination, in order to elucidate the diagnosis at peripheral joints. MSUS is also used to guide needle injection. Table 1 lists the main detectable musculoskeletal diseases by ultrasound in daily practice. Currently the principal applications for using MSUS in patients with JIA include: detection of synovitis, tenosynovitis, enthesitis and cartilage and bone abnormalities. To date, the role of MSUS in therapy monitoring has not been fully established.

The challenge to assess synovitis has been minimized thank to technology for MSUS equipments has evolved considerably. Nevertheless, real time (or dynamic) examination is the most reliable method to distinguish quick and early between synovitis and joint cartilage leading to immediate improvement of the diagnosis and initial therapy decision of articular disorders. The MSUS appearance of tenosynovitis and enthesitis on B-mode is the same in all patients with inflammatory disease irrespective of age. As the ossification centre could show a smooth surface or irregular surface, the presence of other pathologic features along with erosion avoids misdiagnosis. MRI has proven earlier detection of bone abnormalities than MSUS. To date, the role of Doppler technique has not been entirely established yet.

Future topics for study include: establishing international definitions for joint components in healthy children and for MSUS findings in JIA patients, consensus on scanning protocols and scoring systems, evaluation of the role of MSUS with power Doppler in the assessment of the real state of disease (activity /remission) and developing a specific training programme for paediatric rheumatologists performing US in patients with JIA.

Disclosure of interest: None declared.

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**I23** Magnetic resonance imaging

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*Pediatric Rheumatology* 2014, 12(Suppl 1):e23

MR imaging is encountering an expanding application in the assessment of patients with paediatric chronic rheumatic diseases. By providing multiplanar tomographic imaging with unparalleled soft tissue contrast, MRI allows the simultaneous evaluation of all joint structures involved in inflammatory arthritis and it is regarded as one of the most attractive imaging modalities for the investigation of juvenile idiopathic arthritis (JIA). MRI provides additional and more sensitive information over clinical examination and other imaging modalities and holds great promise in supporting diagnosis of JIA, assessing its severity and prognosis, monitoring disease course and treatment efficacy. The use of MRI in the assessment of the musculoskeletal system in children has important differences from its adult counterpart. Growing joints change anatomically over time making imaging in JIA a real challenge without the availability of normative data. A sound knowledge of growth-related changes, in fact, is of foremost value to establish whether joint surface changes reflect a real damage or are actually part of normal development.

Main indications for musculoskeletal MRI in paediatric rheumatology, technical issues and diagnostic accuracy, pitfalls in image analysis and newer MRI and scanner techniques (ie whole-body MRI) will be discussed thus providing an overview of the recent advances and challenging in imaging children with rheumatic disorders.

Disclosure of interest: None declared.

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**I24** Auto-inflammatory diseases

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*Pediatric Rheumatology* 2014, 12(Suppl 1):e24

Auto-inflammatory diseases are a rapidly moving field, where the description of new entities, the understanding of the pathogenesis and the treatment has shown important progress in the past years. This group of conditions include monogenic auto-inflammatory diseases, like FMF, CAPS, TRAPS and MKD, and non-monogenic auto-inflammatory diseases, like PFAPA, SoJIA, CRMO, and Behçet. The most common clinical feature is recurrent fever and a pro-inflammatory cytokine, IL-1, is a key molecule involved in the pathogenesis of these diseases. The treatment aims to control chronic inflammation and blocking agents of IL-1 have shown a great efficacy in most of these diseases.

The aim of the presentation is to make an update on the diagnosis and the treatment and review the recent recommendations elaborated by experts’ consensus through the SHARE project.

Disclosure of interest: None declared.

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**I25** An update of the management of hypermobility in children

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*Pediatric Rheumatology* 2014, 12(Suppl 1):e25

The management of symptoms potentially related to hypermobility frequently require a Biopsychosocial model of management. This intervention may be provided by a variety of professionals depending upon the individual service provision; however the principals encourage an approach that promotes independent self-management. It is becoming increasingly understood that the degree of flexibility is not as important in predicting symptoms and outcomes as the degree of muscle strength and stamina as well as psychosocial factors such as levels of anxiety and low mood. It is not clear how many children with hypermobility are affected by symptoms, however musculoskeletal pain is common in young people.

The principals of the physical treatments should be based around ensuring correct biomechanics are maintained with individual strengthening programmes which are then supported by paced integration into sport and physical activity. Fulltime School should be the goal for all young people with hypermobility as well as inclusion into most activities. The use of aids and adaptations including wheelchairs and crutches should be avoided as this actually promotes muscle weakness and a long term increase in symptoms. It is important that a good sleeping pattern should be restored and then maintained and the use of Active Relaxation Techniques are very effective.

Teaching the young person and their family about pain and its non-pharmaceutical management is very helpful in empowering them to manage independently and not to fear pain but to be in control and therefore not limited by it.

Hypermobility should be a condition that is self-managed by the young person and their family but the professionals are extremely important in ensuring this approach is understood and effective and it is their responsibility to ensure unnecessary drugs, surgeries or treatments are given to each child. The majority of young people with symptoms related to their hypermobility respond extremely well with this approach.

Disclosure of interest: None declared.

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**I26** JIA rehabilitation in 2014 and beyond: - a collaborative effort between child, family and health professional

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*Pediatric Rheumatology* 2014, 12(Suppl 1):e26

With the introduction of biologics in pediatric rheumatology the options for effective treatment have increased considerably. Consequently the majority of children with JIA reach a remission in earlier stages of their disease and the impact on joint health, ambulation and functional ability of JIA have changed accordingly. This brings new perspectives for the (allied) health professional in the field of pediatric rheumatology. “Creation”, family centered care, even family integrated care models are currently explored in this field. Multi-level; composed outcome measures (Process-outcomes, patient-rated outcomes measures (PROM,s) are increasingly used in research and outcomes research, emphasis on family centered approaches deliver new measures such as the Family Needs
Pediatric osteoporosis
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Pediatric Osteoporosis (PO) is rarely due to bone primary genetic diseases, more frequently a consequence of chronic illness and/or medical treatments. Considering dual X-ray absorptiometry (DXA) the gold standard, the exact relationship between Bone Mineral Density (BMD) and risk of fracture in children is unknown. Furthermore, BMD measurements in children are affected by body size, since the bone density value produced is an areal bone density (aBMD), failing to provide a true volumetric BMD. Diagnosis should therefore be made on the basis of a low BMD in addition to the presence of a clinically significant fracture history. Newer diagnostic techniques such as bone ultrasound and pQCT seem very promising. Peak bone mass is a major determinant of bone mass later in life, as a consequence it is critical to maximize during childhood and adolescence the potential of reaching its optimal value through management of factors contributing to bone loss. Secondary forms of low bone mass include systemic inflammatory diseases which affect bone metabolism due to proinflammatory cytokines and glucocorticoid use. Failure to develop adequate bone mineralization is common in JIA. Methotrexate has been shown to be toxic for bone, but this effect was not confirmed in studies that evaluated its in vivo effect on bone when used for the treatment of JIA. TNF-inhibitors have also been shown not to interfere with bone density, likely because they are very effective in decreasing the underlying disease activity. Regarding other paediatric rheumatic diseases, many data have shown that also patients with juvenile SLE are prone to suffer from decreased BMD. Similar findings could be expected for dermatomyositis, in which according to the mechanostat theory muscle disease has an additional negative effect on bone strength. Since the cause of bone loss is frequently multifactorial and the exact pathogenic mechanism of PO has not been clearly established in many conditions, it is difficult to proceed with rational treatments and prevention. The armamentarium of drugs to treat bone fragility in children is limited and most have never been established as safe or effective in randomized controlled trials. Furthermore, while the guidelines for the treatment of osteoporosis in adults are widely accepted, the paucity of data for children and adolescents with PO makes it harder to set clear guidelines for the pediatric population. If there is evidence of vitamin D deficiency and/or poor dietary calcium intake it is appropriate to replace such deficits, but routine calcium and vitamin D supplementation is not recommended. Physical activity in childhood is one of the most powerful preventive strategies in the fight against osteoporosis, especially during the peripubertal years; physical activities shown to have the greatest osteogenic effects on the growing skeleton are those characterized by a considerable loading magnitude applied at a rapid rate. Finally, bisphosphonates are effectively used as a principal treatment of bone fragility in some genetic forms, such as osteogenesis imperfecta. The same beneficial effect has been shown in children and adolescents with connective tissue diseases. However, their use still raises some concern for possible unknown long-term side effects and for their theoretical teratogenic potential. Therefore the routine use of bisphosphonates in childhood is not recommended. The D hormone [1α,25(OH)2D], regulated in endocrine, autocrine and paracrine manner, must be bound to the specific nuclear vitamin D receptor (VDR) to exert epigenetic and genetic effects influencing more than 2000 genes in all tissues and immune cells, essential for proliferation, differentiation and immunoregulation. VDR agonists inhibit in myeloid DCs, but not in plasmacytoid DCs, expression of surface co-stimulatory molecules such as MHC class II, CD40, CD80 and CD86. In T cells, 1,25(OH)2D decreases the production of IL-2, IL-17 and interferon-γ (IFNγ) and attenuates the cytotoxic activity and proliferation of CD4+ and CD8+ T cells, and promote the development of FoxP3+ regulatory T (Treg) cells and IL-10-producing T regulatory type 1 cells. In contrast to glucocorticoids which are non-selective immunosuppressive compounds, 1α,25(OH)2D induces monocyte proliferation and the expression of interleukin-1 (IL-1) and cathelicidin (an antimicrobial peptide) by macrophages, thereby contributing to innate immune responses to some bacteria. Additionally it was shown that 1α,25(OH)2D can override steroid resistance and antagonize its negative bone turnover influence.

The discovery of the immunomodulatory and anti-tumor properties of D-hormone prompted researchers to investigate possibility of its use as a preventive and therapeutic agent for different autoimmune and malignant diseases. Several publications in last years have found a high prevalence of vitamin D deficiency in JIA, SLE and other chronic inflammatory diseases in childhood, with the mean values of 25(OH)D levels at the lower end of ‘acceptable’ range. Measurement of 25(OH)D level (as the only standardized test to estimate vitamin D status) is actually only the reflection of the balance between food and/or supplement vitamin D diet intake and its utilization in the local tissues into the active D hormone (especially immune cells in the state of chronic inflammation). Recent recommendations and clinical guidelines have suggested vitamin D supplementation of up to 2000 IU/d to be safe and well tolerated in children with chronic diseases. New recommendations and guidelines for vitamin D supplementation, as adjunct treatment option in JIA and other chronic inflammatory rheumatic diseases, is an appealing need due to its pleiotropic effects. It can both minimize bone fragility and contribute improvement of immunomodulatory properties in children, especially those with necessity for long term steroid treatment.

Disclosure of interest: None declared.

Autoimmune encephalitis
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It is now accepted that there are antibody-mediated diseases of both the peripheral and central nervous systems. Myasthenia gravis remains the prototype autoimmune disease of the neuromuscular junction, but subsequent studies have revealed antibodies to other peripheral and autonomic targets. In the 1990s, antibodies to voltage-gated potassium channel complexes were identified in acquired neuromyotonia, a condition caused by peripheral nerve hyperexcitability that leads to muscle fasciculations, muscle cramps and pain. Somewhat surprisingly, the same antibodies were identified in relatively acute-onset central nervous system disorders such as Morvan’s syndrome and limbic encephalitis. It turned out that the potassium channel antibodies were mainly directed at other proteins that are complexed with the channels in situ, such as LGI1 and CASPR2. These proteins help localise (CASPR2) and modify (LG1) potassium channel function, and the antibodies bind to extracellular epitopes and are pathogenic in vitro. Tumours can be found in a proportion of each of these conditions, but the proportion varies from <10% to around 50%. Thymomas are the most common. In 2007, antibodies to NMDA receptors (NR1 principally) were identified and subsequently found quite commonly in younger patients, often women and small children. They have a very complicated form of encephalitis that results in psychiatric and movement disorders. Ovarian teratomas are common in the adult females but rare in children. Other antibodies have now been discovered, each one directed at a specific receptor or ion-channel related associated protein, although so far the associated diseases are fairly rare. Antibodies to glycine receptors were associated with a form of stiff person plus, usually termed progressive encephalomyelitis with rigidity and myoclonus (PERM), a condition which is well described in the literature and can be life
threatening. Now it is recognised in more patients with a greater breadth of clinical symptoms. Each of these diseases shows a very good response to immunotherapies such as steroids, plasma exchange, intravenous immunoglobulins. If the response is poor, second line therapies such as rituximab and/or cyclophosphamide are tried. Some require longer term immunosuppression with azathioprine or mycophenolate. Altogether there is a growing field of immunotherapy-responsive neurological diseases which need to be recognised by the clinicians and treated appropriately. There are now many neurological presentations in which the possibility of an autoimmune disease needs to be considered, and this is beginning to apply to those that are less clearly “organic”.

Disclosure of interest: None declared.

I30
Treatment of septic arthritis and acute osteomyelitis
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Pediatric Rheumatology 2014, 12(Suppl 1):I30

Acute hematogenous bone and joint infections, septic arthritis, and osteomyelitis with or without adjacent septic arthritis, are rare among children in a standard Western setting, but still potentially devastating diseases, as even deaths have been reported recently. For this reason, and in part due to historical reasons, the treatment has comprised of months-long courses of antibiotics, started intravenously for at least a week, and aggressive surgery. Recent prospective and randomized trials have shown that a 2–4-day parenteral course, completed orally to a total duration of 10–14 days for septic arthritis and of 3 weeks for osteomyelitis, heals the great majority of cases, provided large-enough doses of a well-absorbing antibiotic, and a four-times-daily (qid) regimen is used. *Staphylococcus aureus* - the most common causative agent in ostearticular infections - is the primary target for treatment. For methicillin-susceptible strains, first-generation cephalosporins, clindamycin, and staphylococcal penicillins are first-line antibiotics of which clindamycin has retained activity even for most cases due to methicillin-resistant *S. aureus*. This said, instead of clindamycin, beta-lactam antibiotics are effective also against *Kingella kingae*. The role of surgery in uncomplicated cases is minor, even in cases of shoulder or hip arthritis, as most children recover uneventfully with no greater intervention than diagnostic bone or joint aspiration. Routine arthroscopy seems unnecessary even in hip or shoulder arthritis. However, each patient needs an individual approach, and a deviation from the general treatment lines should be executed when the conditions so dictate.

Disclosure of interest: None declared.

I31
Familial arthropathies
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Pediatric Rheumatology 2014, 12(Suppl 1):I31

Familial arthropathy is a descriptive term, comprises a heterogeneous group of disorders. It can be either an inflammatory or a non-inflammatory condition, syndromic or non-syndromic disorder. Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in children. However, the underlying genetic background remains poorly understood. Though familial aggregation of JIA is rare, it suggests that JIA is influenced by shared genetic factors. Inheritance patterns and phenotypes probably help to clarify if familial JIA is a distinctive subtype of JIA. Using our JIA cohort, we have identified siblings with JIA characterized by autosomal recessive transmission. Patients with familial JIA probably are different with respect to clinical and laboratory variables from sporadic JIA patients. We used linkage, homoygosity mapping and whole exome sequencing to identify the disease associated gene and underlying mutation. It is important to remember that some patients with skeletal dysplasia and certain syndromes may present with musculoskeletal manifestations mimicking inflammatory arthrits and because of their mild phenotypes may be misdiagnosed as JIA. Careful evaluation of a child presenting with an arthropathy, particularly in a population where consanguniy is common, is required for timely and accurate diagnosis. This presentation will give an overview of the clinical and genetic aspects of autosomal recessive JIA patients and discuss the main inherited musculoskeletal disorders including camptodactyly-arthropathy-coxa-vara-pericarditis (CACP) syndrome seen in our practice.

Disclosure of interest: None declared.

I32
Eurofever - lessons from last year
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Pediatric Rheumatology 2014, 12(Suppl 1):I32

Autoinflammatory diseases are rare disorders secondary to mutation of genes involved in the regulation of innate immunity. The main limitation to a better knowledge of Autoinflammatory diseases is related to the extreme fragmentation of the diagnosed cases that are spread over different centers and countries. The general aim of the Eurofever Project was to build an international registry on Autoinflammatory diseases. A web-based registry collecting baseline and cross-sectional clinical information on Autoinflammatory diseases is available in the member area of the PRINTO web-site (www.printo.it). The registry is open to all pediatric and adult Centers with a specific interest in Autoinflammatory diseases. The following monogenic autoinflammatory diseases were considered: Familiar Mediterranean fever (FMF), Cryopyrin-associated periodic syndrome (CAPS), TNF-receptor-associated periodic syndrome (TRAPS), mevalonate kinase deficiency (MKD), Blau syndrome, pyogenic arthritis, pioderma and acne (PAPA) syndrome, deficiency of IL-1 receptor antagonist (DIRA), NLRP12-mediated periodic fever. Information on CRMO, Behçet’s disease, PFAPA and undefined periodic fevers were also collected.

2916 patients, from 95 centers in 53 countries, have been enrolled in the registry during the first 36 months. Baseline demographic data (country of residence, disease onset, disease duration, mutations, family history etc) from all patients are now available. In 2275 (81%) complete information on clinical manifestations and responses to treatments is also available. The disease distribution of enrolled patients is: FMF 787 (621 with complete clinical data); TRAPS 237 (211 with complete clinical data); CAPS 207 (186 with complete clinical data); MKD 153 (133 with complete clinical data); Blau syndrome 62 (21 with complete clinical data); PAPA 19 (18 with complete clinical data); NLRP12-mediated periodic fever 8 (6 with complete clinical data); DIRA and Majeed 3 and 2 patients, respectively (all with complete clinical data).

Among multifactorial autoinflammatory diseases: PFAPA 564 (402 with complete clinical data); CRMO 392 (370 with complete clinical data); pediatric Behçet disease 84 (68 with complete clinical data) and 205 patients with undefined periodic fever (174 with complete clinical data).

So far 8 papers involving 56 different authors and 32 centers have been published in high-rank international journals and other papers are in preparation. A large registry of patients with Autoinflammatory diseases is available and, despite the expiring of the initial grant, the enrolment is still ongoing with an increasing number of centers involved. Eurofever represents a good example of how a disease-oriented registry can provide relevant scientific answers to many unknown clinical aspects of ultra-rare diseases. This aspects was the main reason of the relevant success of the enrolment we have observed.

Disclosure of interest: None declared.

I33
FMF: an update
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Pediatric Rheumatology 2014, 12(Suppl 1):I33

Familial Mediterranean fever (FMF) is the most common autoinflammatory disease over the world. This autosomal recessively inherited disease is due to mutations in the gene coding for pyrin. Disease causing mutations in the gene are associated with elevated levels of IL-1. The clinical symptoms of inflammation are mainly in the form of fever and serositis along with laboratory evidence of persistently raised acute phase reactants, including serum amyloid A levels. Untreated patients suffer the consequences of chronic inflammation.

Patients who display inflammatory symptoms but who carry one mutation only should be carefully evaluated for the need of therapy. Colchicine is the main treatment of FMF. Management of the patients includes following clinical activity of the disease and acute phase reactants on a regular basis.

Disclosure of interest: None declared.
and checking for drug compliance, and monitoring side effects of the drug. If patients are intolerant to or unresponsive to colchicine anti IL1 treatment should be considered.

Disclosure of interest: None declared.

### I34

**Autoinflammation and immunodeficiency**

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**Methods:**

Autoinflammatory diseases are characterized by more or less spontaneous inflammation without inciting infection or autoimmunity. There can be either acquired or genetically determined. The latter – hereditary – autoinflammatory syndromes have been classified by some as primary immunodeficiencies: defects affecting the control of the innate arm of the immune system. Immunodeficiency syndromes, however, have generally been considered to be defects in host defense, rendering the patient susceptible to infectious diseases.

Every year, immunodeficiency syndromes and autoinflammation as separate entities, situations do occur where patients suffer both non-specific sterile inflammation and increased susceptibility to infection. This may occur in prototypic autoinflammatory diseases as well as in well recognized primary immunodeficiencies. In addition, there are intermediate disorders that are both autoinflammatory and immunodeficient by nature (table 1).

**Table 1(abstract I34)**

<table>
<thead>
<tr>
<th>Autoinflammatory disease</th>
<th>Mixed disorder</th>
<th>Innate immunodeficiency</th>
<th>Adaptive immunodeficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>example</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mevalonate kinase deficiency</td>
<td>HOIL1-deficiency</td>
<td>Chronic granulomatous disease</td>
<td>Common Variable immunodeficiency</td>
</tr>
<tr>
<td>Serious bacterial infections</td>
<td>Recurrent fever and</td>
<td>Sterile granulomatoma</td>
<td>RAG1 deficiency</td>
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<td></td>
<td>humoral immunodeficiency</td>
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</tbody>
</table>

**Diagnosis of infection in autoinflammatory diseases is challenging, as both autoinflammatory and immunodeficient by nature (table 1).** Conversely, ruling out infection is a prerequisite for diagnosing autoinflammation in patients with MAS. This distinction is relevant for patient management, since some autoinflammatory patients may benefit from antimicrobial prophylaxis, whereas sterile inflammation in immunodeficiency may benefit from approaches like interleukin-1 blockade.

Disclosure of interest: J Frenkel Consultant for: Novartis Pharma.

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### ORAL PRESENTATIONS

**O2**

**Interferon gamma (IFNg) production is associated to disease parameters in TLR9-induced secondary hemophagocytic lymphohistiocytosis (sHLH) in mice**

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**Introduction:**

Macrophage activation syndrome (MAS) is a potentially fatal complication of systemic juvenile idiopathic arthritis (sJIA), whose prompt recognition and treatment are critical. However, early diagnosis of MAS is often challenging and none of the current diagnostic criteria is satisfactory. An international project aimed to develop a new set of classification criteria for MAS was recently started.

**Objectives:**

To present the results of the consensus conference that led to the development of the new classification criteria for MAS complicating sJIA.

**Methods:**

28 pediatric specialists (20 rheumatologists and 8 hematologists) with expertise in MAS reviewed 428 profiles of patients with sJIA-associated MAS or with a confusable condition (active sJIA or systemic infection). The expert panel classified each patient as having or not having MAS based on clinical and laboratory features at disease onset. Using the experts’ consensus as “gold standard”, a statistician tested 982 candidate definitions, derived from both literature and statistical analyses. Definitions with a kappa level of agreement ≥ 0.85 were included in the expert voting process during the consensus conference. In a secondary analysis, experts were asked to declare whether the change in laboratory parameters over time was consistent or not with MAS and to rank laboratory tests in order of the importance of their change in the diagnosis of MAS.

**Results:**

After 5 rounds, experts achieved consensus on approximately 90% (391/428) of the profiles submitted. Statistical analyses led to select 45 definitions with kappa ≥ 0.85. During the consensus conference, 7 voting sessions were made. Finally consensus (82%) was reached on the following definition: “A febrile patient with known or suspected sJIA is classified as having MAS if the patient has: ferritin >684 ng/mL and at least 2 of the following 4 laboratory abnormalities: platelets ≤ 181 x 10^9/L, aspartate aminotransferase (AST) > 48 U/L, triglycerides > 156 mg/dL, and fibrinogen ≤ 360 mg/dL”. In the evaluation of change, falling platelet count, hyperferritinaemia and increased AST received the highest scores.

**Conclusion:**

A new set of classification criteria for MAS complicating sJIA was agreed upon in a multinational consensus conference, which gathered the leading experts in the field. The new criteria deserve validation in a new cohort of patients with MAS seen prospectively.

Disclosure of interest: None declared.
C57BL/6 mice received i.p. injections of CpG on days 0, 2, 4, 7 & 9. Neutralizing IL-10R, mAb 181.3A at 200 μg/mouse (days 0, 2, 4, 6), and anti-mouse IFNγ, mAb XMG1.2 at 100 mg/kg (days 1, 3, 6) were administered iv. Results: In murine sHLH, the neutralization of IFNγ caused a reduction in body weight loss and spleenomegaly, normalized white blood cell counts and hyperferritinemia, and corrected anemia. Blockade of IFNγ in mice with fulminant sHLH improved key disease features by decreasing the body weight loss by 20%, reduced splenomegaly by 23%, improved anemic parameters by 13%, reversed cytopenia by 30% and normalized sHLH-associated cytokine storm as evidenced by a 60% decrease in circulating levels of TNFα. Circulating levels of IFNγ reached steady state at 250 ng/ml. In the murine models (sHLH and fulminant sHLH), expression of IFNγ-induced inflammatory genes demonstrated that spleen and liver are major sites of IFNγ production. Conclusion: Neutralization of IFNγ appears to effectively improve the clinical and laboratory features in the CpG-induced models of sHLH, including fulminant sHLH. These data offer a rationale for the neutralization of IFNγ as a potential targeted therapeutic approach in patients with severe form of sHLH.

Disclosure of interest: None declared.

03 Interferon-gamma (IFNγ) in macrophage activation syndrome (MAS) associated with systemic juvenile idiopathic arthritis (sJIA). High levels in patients and a role in a murine mas model
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Pediatric Rheumatology 2014, 12(Suppl 1):O3

Introduction: IFNγ is the pivotal mediator in murine models of primary HLH. Objectives: Given the similarities between primary and secondary (sHLH), including MAS, we analyzed IFNγ levels in patients with sJIA and MAS and evaluated the pathogenic role of IFNγ in a murine mas model. Methods: We measured levels of IFNγ, IFNγ-related chemokines (CXCL9, CXCL10, CXCL11), and IL-6 in patients with sHLH (n=14), and in patients with sJIA (n=54) of whom 20 had MAS at sampling using the Luminox multiplexing assay and evaluated their relation to disease activity. The effect of the anti-IFNγ antibody XMG1.2 was assessed in IL-6 transgenic (IL6TG) mice in which a MAS-like syndrome leading to death is triggered by TLR ligands (Strippoli, Arthritis Rheum 2012). An LPS LS05 (5 μg/g body weight) was used, as a trigger for MAS, followed 10 hours later by administration of 100 μg/g of XMG1.2.

Results: Levels of IFNγ and of IFNγ-related chemokines [median pg/ml (IQR)] were markedly elevated in active MAS and active sHLH, with no significant differences between active sHLH [IFNγ: 34.7 (23.9-170.1); CXCL9 564.8 (197.5-1007)] and active sJIA [IFNγ: 33598 (3083-127687); CXCL9 1612(424.8-4309); CXCL10 4420 (799.7-8226); CXCL11 1327 (189-2000)]. Levels in active sJIA without MAS [IFNγ: 1545.1 (52-56); CXCL9 13392 (2163-35452); CXCL10 1612 (248.8-4509); CXCL11 5648 (197.5-1007)]. Levels in active sJIA without MAS and in active sJIA with uveitis (19.2 U/ml) than in the non-uveitis group (10.3 U/ml) (p=0.002). Conclusion: AHA-IF was analyzed twice >3 months apart in local laboratories. Serum samples taken early after disease onset were analyzed for AHA IgG/IgM in an enzyme immunoassay (Varelixa BIA Pharmacia Diagnostics) for the Danish and Swedish cohort. No serum samples were available in the Finnish cohort, and antihistone analyses in the Norwegian cohort has previously been published.

Disclosure of interest: None declared.

04 Histone antibodies as a biomarker of uveitis in JIA
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Pediatric Rheumatology 2014, 12(Suppl 1):O4

Introduction: Uveitis is the most common extraarticular manifestation of juvenile idiopathic arthritis (JIA). The nature of JIA-associated uveitis is often insidious and asymptomatic, and baseline predictors can aid early diagnosis of eye disease for prompt and adequate treatment. Antihistone antibodies (AHA) are among subtypes of antimicrobial antibodies (ANA) identified in children with JIA. An association between early-onset JIA, oligoarthritis and uveitis is shown in some studies, and we have previously shown that AHA is a significant predictor of chronic uveitis in a Norwegian JIA cohort. New interest for histones has emerged because epigenetic alterations of these DNA-binding molecules may be involved in the pathological processes of autoimmunity.

Objectives: The aim of the study was to analyze presence of AHA in children with JIA with and without uveitis. We also wanted to compare AHA to previously described predictors of uveitis, such as early-onset arthritis, presence of ANA, oligoarticular ILAR category, and female gender.

Methods: Consecutive cases of JIA from defined geographical areas of Denmark, Finland, Norway and Sweden with disease onset in 1997 to 2000 were included and followed for >7 years in a multi-center cohort study. Clinical information on joint and eye disease was prospectively collected in this longitudinal study aimed to be as close to population-based as possible. ANA-IF was analyzed twice >3 months apart in local laboratories. Serum samples taken early after disease onset were analyzed for AHA IgG/IgM in an enzyme immunoassay (Varelixa BIA Pharmacia Diagnostics) for the Danish and Swedish cohort. No serum samples were available in the Finnish cohort, and antihistone analyses in the Norwegian cohort has previously been published.

Results: Uveitis occurred in 21.7 % of the 424 children with regular ophthalmologic follow-up, among the total cohort of 500 children. In the Danish and Swedish sub-cohort of 189 children, 132 had available serum samples. Significant predictors of chronic uveitis were onset of arthritis ≤7 years (OR 2.6 (1.5-4.7)), presence of antihistone antibodies (AHA ELISA IgM/IgG >15 U/ml) (OR 4.3 (1.5-12.3)), and presence of both ANA and AHA (OR 9.1 (2.5-32.9)). Gender and oligoarticular onset category did not reach significance as predictors of uveitis. Mean AHA ELISA IgM/IgG was significantly higher in the children with uveitis (19.2 U/ml) than in the non-uveitis group (10.3 U/ml) (p=0.002).

Conclusion: AHA, ANA and early-onset arthritis were significant predictors of chronic uveitis in the Nordic JIA cohort study. The strongest predictor was presence of both ANA and AHA. The present results in the Swedish and Danish sub-cohorts confirm previous findings in the Norwegian sub-cohort.

Disclosure of interest: None declared.

05 Effectiveness of adalimumab in the treatment of juvenile idiopathic arthritis associated with uveitis
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Pediatric Rheumatology 2014, 12(Suppl 1):O5

Introduction: Juvenile idiopathic arthritis (JIA) is a chronic autoimmune disease of children and adolescents with primary joints involvement and various manifestations. Uveitis is of extra-articular signs characterized by eye
inflammation. Standard antirheumatic drugs in combination with local therapy are effective in 60%. When these drugs are ineffective, genetically engineered drugs are used in JIA with rheumatoid uveitis.

**Objectives:** This prospective observation was aimed to assessing effectiveness and safety of adalimumab (ADA) in the treatment of juvenile idiopathic arthritis associated with uveitis in patients with severe JIA, prolonged disease and resistance to standard antirheumatic therapy.

**Methods:** Among 27 patients with JIA and eye involvement included in the study, 13 children had oligoarticular JIA, 8 children - polyarticular, 6 patients had systemic disease. Study group included 20 girls and 7 boys. Mean age was 7.0 years, age of disease onset was 3.5 ± 2.07 years; mean disease duration before ADA administration was 5 ± 3.6. Disease onset with initial joint damage was observed in 22 children, with eye involvement - in 5 children. Prior to ADA administration most children had high (III) disease activity. Number of active joints was 10.8 ± 3.2, mean ESR was 27.0 ± 13.37 mm/h, CRP – 2.25 ± 1.1 mg/dl (ref. <0.8 mg/dl). All 27 patients had active uveitis at the moment of ADA administration. Twenty-four (89%) patients had bilateral ocular involvement, 3 patients (11%) - unilateral. Clinical Global Impression - Disease Activity (VAS) score was 76.2 ± 14.0, parent/patient score was 65.9 ± 17.1. Mean functional disability in patients before ADA administration was 20.4 ± 0.57. Prior to ADA administration all children received immunosuppressive drugs: 26 children (96%) methotrexate (MTX), 10 children - MTX plus 2mg/kg Sandimmune Neoral per week, 10 children (37%) were treated with TNF inhibitors, 23 children - with inhibitors of B cell activity. Mean duration of continued treatment in 11/39 (28.2%) children maintained a complete remission over a median period of 18 months. At 49 months of follow-up, 6/8 children with IdCU (75%) compared to 5/31 children with JIA (16.1%) were still in remission without treatment (p<0.003). A higher probability of maintaining uveitis remission after discontinuing treatment was shown in IdCU compared to JIA group (Mantel-Cox c2 7.62, p<0.006). ANA positivity was associated with a higher probability of flare in overall population (Mantel-Cox c2 6.68, p<0.01), in ICU, but not in sub-analysis limited to JIA (Mantel-Cox c2 0.78, p=0.37) and IdCU (Mantel-Cox c2 1.18, p=0.27). None clinical variable, including time on remission therapy, total length of treatment, and type of treatment, resulted significant predictors of long-lasting remission without therapy.

**Conclusion:** When JIA is refractory to antirheumatic treatment, combination therapy with adalimumab and methotrexate is effective in the vast majority of patients with chronic juvenile idiopathic arthritis and uveitis with high clinical and laboratory activity, and resistance to standard antirheumatic therapy.

**Disclosure of interest:** None declared.

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**O6 Predictors of relapse after discontinuing systemic treatment in autoimmune chronic uveitis**

Gabella S, Sciacca G, Crucia BR, Rizzuto G, Diana V, Stroppiana D, Marcello A, Maria Elena Verzaro G, Rolando Cimaz

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**Pediatric Rheumatology 2014, 12(Suppl 1):O6**

**Introduction:** Non infectious uveitis in childhood is a relatively uncommon severe disease, with potential significant long-term complications such as cataract, glaucoma and eventually blindness. For these reasons refractory uveitis usually requires early and aggressive immunosuppressive treatment in order to preserve visual acuity and to prevent the significant morbidity of chronic steroid administration. However, the lack of evidence from head-to-head randomized controlled trials (RCT) limits our understanding about the best treatment choices, as well as time of instituting therapy and its duration. Once a child with active uveitis has achieved remission on treatment, there are no evidence-based guidelines with respect to the duration of continued treatment in autoimmune chronic uveitis.

**Objectives:** Aim of our study was to assess the time on remission after discontinuing systemic therapy in a retrospective, comparative, multicentre, cohort study of childhood non-infectious chronic uveitis.

**Methods:** 39 patients (29 F, 10 M; median age: 11.6 years, 31 JIA, 8 Idiopathic Chronic Uveitis (IdCU)) from 4 different paediatric rheumatology centres, with previously refractory, vision threatening, non-infectious inactive uveitis, which discontinued all related treatments for at least 3 months were enrolled. 23 children previously received Methotrexate, 16 TNF inhibitors. Primary outcome was to assess, once remission was achieved, the time on remission up to the first relapse after discontinuing treatment. Time to remission once systemic non-stereoid treatment was started, was time to steroid discontinuation, number of relapses before achieving remission and time on remission therapy before discontinuing all treatments were also considered.

**Results:** Median follow-up on remission therapy was 5 months. At last available follow-up 20 children (51%) received immunosuppressive drugs: 18 children (46%) methotrexate (MTX), 10 children - MTX plus 2mg/kg Sandimmune Neoral as monotherapy or in combination with methotrexate, 10 children (37%) received oral corticosteroids (CS), 27 children (100%) received active topical treatment of uveitis.

**Conclusion:** Median follow-up on remission therapy was 5 months. At last available follow-up 20 children (51%) received immunosuppressive drugs: 18 children (46%) methotrexate (MTX), 10 children - MTX plus 2mg/kg Sandimmune Neoral as monotherapy or in combination with methotrexate, 10 children (37%) received oral corticosteroids (CS), 27 children (100%) received active topical treatment of uveitis.

**Disclosure of interest:** None declared.

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**O7 SHARE – workshop package 5: development of best practices of diagnosis and treatment for paediatric rheumatic diseases throughout Europe**

Sebastian Vaster, Ana Maria Gallo, Cristina Brescianini, Denise Pires Marafon, Annet van Royen, Nico Wulffraat, Sebastiaan van Asperen, Anogeelis Arnel, Eric Pannen, Stefania Battaglia, Gabriella Borghi, Anna Meyer, Raphaël Baran, Sebastiaan Vastert, Caliandra Cattalin, Andrea Taddio, Alice Brabilla, Cinzia de Libero, Denise Pires Marafon, Roberto Caputo, Rolando Cimaz

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**Pediatric Rheumatology 2014, 12(Suppl 1):O7**

**Introduction:** Paediatric rheumatic diseases (PRD) form a group of rare diseases that can lead to significant morbidity, to which morbidity and treatment guidelines are sparse and treatment regimens differ throughout Europe. In 2012, a European initiative called SHARE (Single Hub and Access point for pediatric Rheumatology in Europe) was granted by the European Agency for Health and Consumers (project number 2011 1202) to optimize and disseminate diagnostic and management regimens in Europe for children with PRD.

**Objectives:** Workshop package 5 (WPS) aims to develop best practices of diagnosis and treatment for PRD.
Methods: Evidence based recommendations were developed using the European League Against Rheumatism (EULAR) standard operating procedure [1]. Expert committees were formed, consisting of paediatric rheumatologists and experts in the 4 core PRD: Juvenile Idiopathic arthritis (JIA), Juvenile Dermatomyositis (JDM), Systemic Lupus Erythematosus (SLE, including antiphospholipid syndrome and vasculitis) and Juvenile Scleroderma (Jsc, localized and systemic). The periodic fivers were incorporated in a later phase of the project and will be discussed separately. The expert committees defined domains and search terms for systematic literature reviews, which were executed in July 2013 in Medline, Embase and Cochrane databases. Subsequently, all available abstracts were checked for inclusion (published after 1970, English, no case reports, case series only when including at least 3 paediatric patients). All relevant papers were subsequently scored for validity and level of evidence (LOE) by 2 independent experts. In case of disagreement, a 3rd independent expert confirmed the validity and LOE. Papers and scores were used to develop recommendations that were evaluated by all experts via an online survey as a 1st step. Those with > 80% agreement in the survey were reformulated. Finally, recommendations were discussed at a consensus meeting with all experts present, using the nominal group technique [2]. Recommendations were accepted if > 80% agreement was reached.

Results: Table 1 shows the number of scored papers after the standardised literature search and the number of recommendations on diagnosis and treatment for each PRD.

Conclusion: Based upon standardised literature searches, WPS of SHARE developed evidence based recommendations for diagnosis and treatment of PRD. These recommendations were discussed and agreed upon in a 1st consensus meeting and will serve as input for the ultimate goal: development of best practices for care and management of PRD throughout Europe. These best practices will be finalized in a 2nd consensus meeting in March 2015 and presented to all stakeholders including paediatric rheumatology units throughout Europe, patient/parent organisations and health authorities.


References

**O8**

A multinational study of the epidemiology, treatment and outcome of childhood arthritis (epoca study): preliminary data from 6,940 patients

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Introduction: The epidemiology of juvenile idiopathic arthritis (JIA) is known to be variable worldwide and the therapeutic approach to JIA is not standardized. Moreover, the availability of the novel and costly biologic medications is not uniform throughout the world, with possible significant impact on disease prognosis.

Table 1(abstract O7)

<table>
<thead>
<tr>
<th>Paediatric Rheumatic Disease</th>
<th>Nr of scored papers</th>
<th>Nr of recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>JIA</td>
<td>174</td>
<td>46</td>
</tr>
<tr>
<td>JDM</td>
<td>108</td>
<td>29</td>
</tr>
<tr>
<td>SLE/APS</td>
<td>143</td>
<td>36</td>
</tr>
<tr>
<td>Scleroderma</td>
<td>89</td>
<td>26</td>
</tr>
</tbody>
</table>

Objectives: Accurate description of the risk and nature of flares will help counsel families when JIA is controlled and when considering discontinuing treatment.

Introduction: Accurate description of the risk and nature of flares will help counsel families when JIA is controlled and when considering discontinuing treatment.

Objectives: To describe the probability and characteristics of flares across JIA categories in an inception cohort of Canadian children treated with a contemporary approach.

Methods: We studied children diagnosed with JIA between 2005 and 2010 who had at least one visit with inactive disease while being prospectively followed in the Research in Arthritis in Canadian Children emphasizing Outcomes (ReACCh-Out) cohort. They received usual pediatric rheumatology care at 16 Canadian centres. Flare was defined as any recurrence of disease manifestations after attaining inactive disease (no active joints, no extraarticular manifestations and a physician global assessment <10mm). Flares were considered major if they required re-initiation or intensification (a new drug was started) of anti-rheumatic treatment. Risk of flare was calculated with Kaplan-Meier survival methods starting at the time of attainment of inactive disease, and at the time of discontinuing all treatment.

Results: Of 1492 children recruited in ReACCh-Out, 1128 had at least one visit with inactive disease. Median follow-up was 24 months (IQR 12, 39) after attaining inactive disease. A total of 1,179 flares were observed in 532 patients; 55% of all flares were major flares. The cumulative probability of flare was 25%, 42% and 60% within 6, 12 and 24 months after attaining inactive disease, respectively. By 24 months the risk varied from 49% for systemic JIA to 72% for RF-positive polyarthritis. 625 patients discontinued all treatment. The probability of flares after stopping treatment is shown in the Table (except for RF-positive polyarthritis because only 4 subjects discontinued treatment) Table 1.

Conclusion: Flares after attaining inactive disease were common in this JIA cohort, and the risk was lowest for systemic JIA and highest for RF-positive polyarthritis. Flares after stopping treatment were uncommon in systemic JIA, but occurred in up to 45% of children within one year in other JIA categories. About half the flares required intensification or re-initiation of treatment.

Disclosure of interest: None declared.
Table 1(abstract O8)  

<table>
<thead>
<tr>
<th>JIA category</th>
<th>Subjects stopping treatment / total</th>
<th>Risk within 6 months (%)</th>
<th>Risk within 12 months (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Any flare</td>
<td>Major flare</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systemic arthritis</td>
<td>37 / 66</td>
<td>11</td>
<td>3</td>
</tr>
<tr>
<td>Psoriatic arthritis</td>
<td>44 / 75</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Oligoarthritis</td>
<td>318 / 481</td>
<td>15</td>
<td>12</td>
</tr>
<tr>
<td>Undifferentiated arthritis</td>
<td>60/111</td>
<td>24</td>
<td>13</td>
</tr>
<tr>
<td>Enthesitis-related arthritis</td>
<td>77 / 152</td>
<td>29</td>
<td>21</td>
</tr>
<tr>
<td>RF-negative polyarthritis</td>
<td>85 / 209</td>
<td>25</td>
<td>20</td>
</tr>
<tr>
<td>RF-positive polyarthritis</td>
<td>4 / 34</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

O10  
Classification of juvenile spondyloarthropathies according to asas criteria  
Maria M Katsicas, Ricardo A Russo  
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Pediatric Rheumatology 2014, 12(Suppl 1):O10  

Introduction: The juvenile spondyloarthropathies (JSpA) are a group of related seronegative rheumatic diseases characterized by involvement of the axial joints, peripheral large joints and entheses. JSpA and adult SpA are probably parts of the same disease continuum. JSpA are represented by enthesitis related arthritis (ERA), juvenile spondarthritis (JPsA) and probably undifferentiated arthritis (UA) in the ILAR criteria. Sets of classification criteria have been developed in adult patients with SpA. The ASAS classification criteria for axial and peripheral SpA have not been validated in pediatric populations.  

Objectives: To assess the sensitivity and specificity of the ASAS criteria for identification of patients with JSpA (ERA, JPsA and UA) among the different Juvenile idiopathic arthritis (JIA) categories. To compare the performance of the ASAS criteria with that of ESSG classification criteria in JIA patients. To identify associations between criteria fulfillment and disease features.  

Methods: Consecutive patients with JSpA followed in our center with complete records were included. Clinical charts and databases were retrospectively reviewed. Randomly selected patients with oligoarthritis, polyarthritis RF negative and systemic arthritis from our cohort served as controls. Demographic and clinical characteristics as well as disease duration at first visit and follow up time were recorded. Items corresponding to the ASAS, ESSG, Amor, seronegative enthesopathy and arthropathy (SEA) syndrome and Modified New York (NY) criteria were obtained from first visit and during disease course. Descriptive , summary statistics (sensitivity [sen], specificity [sp], positive predictive value [PPV] and negative predictive value [NPV]) and Wilcoxon rank sum test were used.  

Results: 106 patients with JSpA (103 ERA, 2JPsA, 1UA) were included (M:92), age at onset: 10 (1-15) years, disease duration at first visit 10 (1-15) months, follow-up time 4 (1-12) years. Controls: 65 patients with other JIA (24 oligoarthritis, 21 polyarthritis RF negative, 20 systemic) (M: 27). At first visit cases showed: 103 (97%) arthritis, 87 (82%) asymmetrical oligoarthritis, 67 (63%) elevated CRP, 52 (49%) limitation of lumbar spine motion, 51 (48%) HLA-B27, 45 (42%) enthesitis, 39 (37%) low back pain, 32 (30%) good response to NSAIDS, 26 (25%) positive family history, 20 (19%) radiographic bilateral sacroiliitis grade 2-4, 13 (12%) dactylitis, 8 (8%) uveitis, 7 (7%) unilateral sacroiliitis grade 3-4, 7 (7%) diarrhea, 5 (5%) previous infectious disease, 2 (2%) urethritis, 2 (2%) inflammatory bowel disease, 2 (2%) buttocck pain, 1 (1%) psoriasis. At first visit (106 patients): 79 (75%) patients fulfilled ASAS criteria, 78 (74%) peripheral ASAS, 78 (74%) ESSG, 69 (65%) Amor (58 definite, 11 probable), 32 (30%) SEA, 25 (24%) NY (22 definite, 3 probable), 24 (23%) axial ASAS. During disease course (102 patients): 100 (98%) patients fulfilled ESSG criteria, 97 (95%) ASAS, 97 (95%) peripheral ASAS, 94 (92%) Amor (82 definite, 12 probable), 75 (74%) NY (63 definite, 12 probable), 42 (41%) SEA, 41 (40%) axial ASAS. ASAS sen 95%, sp 83%, PPV 90%, NPV92%. ESSG sen 98% sp 89% PPV 93%, NPV 97%. Unilateral and bilateral sacroiliitis were associated only with axial ASAS (p=0.0066 and 0.04 respectively).  

Conclusion: In our cohort ASAS criteria performed similarly to ESSG criteria in the classification of JSpA. Both sets of criteria allow the inclusion of JSpA patients under one unified category to facilitate research and communication. Peripheral ASAS criteria allow the classification of all patients with JSpA who meet axial ASAS criteria.  

Disclosure of interest: None declared.

O11  
Serious infections in JIA patients upon MTX, TNF inhibitors and combinations  
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Pediatric Rheumatology 2014, 12(Suppl 1):O11  

Introduction: Serious infections are a major concern in JIA patients treated with immunosuppressants and biologics. Effect of TNF inhibitors on the risk for serious infections and further factors are studied here.
Table 1(abstract O11) Inactive Disease - Multivariate logistic regression analysis on 12-week data

<table>
<thead>
<tr>
<th>Variable</th>
<th>univariate</th>
<th>HR (CI)</th>
<th>multivariate</th>
<th>HR (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP at Day 15 (elevated vs normal)</td>
<td>0.20 (0.07, 0.55)</td>
<td>0.14 (0.04, 0.41)</td>
<td>0.26 (0.10, 0.66)</td>
<td>0.31 (0.12, 0.82)</td>
</tr>
<tr>
<td>Number of active joints (11-20 vs. ≤10)</td>
<td>0.22 (0.03, 1.66)</td>
<td>0.55 (0.09, 3.41)</td>
<td>0.17 (0.03, 0.97)</td>
<td>0.37 (0.06, 2.10)</td>
</tr>
<tr>
<td>Number of active joints (&gt;20 vs. ≤20)</td>
<td>2.56 (0.12, 55.39)</td>
<td>1.53 (0.06, 37.44)</td>
<td>0.01 (≤0.4, 0.4)</td>
<td>16.10 (1.00, 258.12)</td>
</tr>
<tr>
<td>Prior NSAID treatment (no vs. yes)</td>
<td>2.01 (0.71, 5.71)</td>
<td>9.33 (2.44, 35.68)</td>
<td>3.10 (1.03, 9.31)</td>
<td>5.31 (1.66, 17.05)</td>
</tr>
<tr>
<td>Prior anti-TNFa treatment (no vs. yes)</td>
<td>5.48 (0.97, 31.01)</td>
<td>8.89 (1.26, 62.64)</td>
<td>2.98 (0.51, 17.46)</td>
<td>11.16 (1.72, 72.34)</td>
</tr>
<tr>
<td>Steroid Level (&gt;0.4 mg/kg/day)</td>
<td>0.32 (0.08, 1.29)</td>
<td>0.41 (0.09, 1.82)</td>
<td>0.81 (0.25, 2.60)</td>
<td>0.13 (0.03, 0.57)</td>
</tr>
<tr>
<td>Steroid Level (&lt;0.4 vs. &gt;0.4 mg/kg/day)</td>
<td>1.94 (0.75, 5.00)</td>
<td>2.78 (0.93, 8.33)</td>
<td>2.79 (1.04, 7.51)</td>
<td>1.71 (0.65, 4.83)</td>
</tr>
</tbody>
</table>

Values in bold are significant; *Significant in at least one time point

Methods: Pts exposed to Etanercept (ETA), Adalimumab (ADA) and Methotrexate (MTX) but no biologics and serious infections were identified in the BIKER registry. Descriptive statistics, infection rates, Cox-regression, Hazard ratios (HR) were calculated. Potential risk factors were analysed.

Results: A total of 3350 pts. with 5929 exposure years were identified in the German BIKER registry data base. First biologic was ETA in 1720 and ADA in 177 cases. 1333 patients were not exposed to biologics. 28 serious infections have been reported (4.7/1000 pt-years). MTX patients had 5 events, Etanercept patients 21 and patients with Adalimumab therapy 2 events. The serious infections were of bacterial origin in 16, viral in 10 and unknown in 2. Total infection incidence per 1000 person years was 4.72 (CI 3.6 – 6.84). The highest rate was found under ADA (9.73, CI 2.43-38.91) followed by ETA (8.08, CI 5.27 – 12.40) and the lowest rate of 1.6 (CI 0.67 – 3.84) with MTX. Univariate Cox regression revealed a number of significant risks for infection, besides therapy (p=0.004) also JADAS10 at start of therapy, mean JADAS level during therapy, corticosteroids as pre- or concomitant medication as well as MTX and DMARDs as preamedication were relevant. In multivariate Cox regression only presence of JADAS10 at start of therapy and mean JADAS during observation time remained significant. Both ETA (HR=4.88) and ADA (HR=10.06) showed an increased risk compared to MTX, whereas ADA and ETA differed not significantly. Risk for infection was significantly increased by an elevated mean JADAS10 level (HR=1.12). Gender, JIA category, age at start of disease, disease duration, ANA status were not significant. Kaplan Meier analysis confirmed the influence of disease activity as demonstrated by the JADAS10. Table 1. Conclusion: ETA and ADA treatment as well as higher disease activity contribute to serious infections.

Disclosure of interest: None declared.

Table 1(abstract O12) Inactive Disease - Multivariate logistic regression analysis on 12-week data

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio (95% CI) Day 15</th>
<th>Odds Ratio (95% CI) Day 29</th>
<th>Odds Ratio (95% CI) Day 57</th>
<th>Odds Ratio (95% CI) Day 85</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP at Day 15 (elevated vs normal)</td>
<td>0.20 (0.07, 0.55)</td>
<td>0.14 (0.04, 0.41)</td>
<td>0.26 (0.10, 0.66)</td>
<td>0.31 (0.12, 0.82)</td>
</tr>
<tr>
<td>Number of active joints (11-20 vs. ≤10)</td>
<td>0.22 (0.03, 1.66)</td>
<td>0.55 (0.09, 3.41)</td>
<td>0.17 (0.03, 0.97)</td>
<td>0.37 (0.06, 2.10)</td>
</tr>
<tr>
<td>Number of active joints (&gt;20 vs. ≤10)</td>
<td>2.56 (0.12, 55.39)</td>
<td>1.53 (0.06, 37.44)</td>
<td>0.01 (&lt;0.4, 0.4)</td>
<td>16.10 (1.00, 258.12)</td>
</tr>
<tr>
<td>Prior NSAID treatment (no vs. yes)</td>
<td>2.01 (0.71, 5.71)</td>
<td>9.33 (2.44, 35.68)</td>
<td>3.10 (1.03, 9.31)</td>
<td>5.31 (1.66, 17.05)</td>
</tr>
<tr>
<td>Prior anti-TNF treatment (no vs. yes)</td>
<td>5.48 (0.97, 31.01)</td>
<td>8.89 (1.26, 62.64)</td>
<td>2.98 (0.51, 17.46)</td>
<td>11.16 (1.72, 72.34)</td>
</tr>
<tr>
<td>Steroid Level (0 vs. &gt;0.4 mg/kg/day)</td>
<td>0.32 (0.08, 1.29)</td>
<td>0.41 (0.09, 1.82)</td>
<td>0.81 (0.25, 2.60)</td>
<td>0.13 (0.03, 0.57)</td>
</tr>
<tr>
<td>Steroid Level (&gt;0.4 vs. &gt;0.4 mg/kg/day)</td>
<td>1.94 (0.75, 5.00)</td>
<td>2.78 (0.93, 8.33)</td>
<td>2.79 (1.04, 7.51)</td>
<td>1.71 (0.65, 4.83)</td>
</tr>
</tbody>
</table>

Introduction: Canakinumab (CAN), a selective, human, anti- interleukin-1β monoclonal antibody, has been shown to be efficacious in the treatment of SJIA (Ruperto et al. N Engl J Med 2012).

Objectives: To explore baseline demographics and clinical characteristics that are most predictive of response to CAN in CAN-naive SJIA patients during the initial 12 weeks of therapy.

Methods: Data from 3 trials were pooled for this analysis. CAN-naive patients (pts.; n=178) aged 2–19 years with active SJIA were enrolled and received sc CAN 4 mg/kg/month; Predictors of response (according to aACR 30, 70, and Inactive Disease (ID)) at Days (D) 15, 29, 57 and 85 were explored using univariate and multivariate logistic regression analyses. The candidate predictors (categorical variables) of CAN-response considered were: Age group; Gender; Prior NSAIDS (no/yes); Prior MTX(no/yes). Steroids (≤0.4 vs. >0.4 mg/kg/day), Number of Active Joints (≤10 vs. >10, >20 vs. >20) and Joints with Limitation of Motion (≤10, 11–≤20, >20) and CRP (elevated/normal) at baseline and at D15. All candidate predictors with p<0.1 in univariate analyses were included in the multivariate analysis. *ACR response plus absence of fever.

Results: By week 2 there was substantial clinical benefit with 102 pts (57%) and 36 pts (20%) achieving aACR70 and ID, respectively; by week 12, 108 pts (61%) had aACR70 and 50 pts (28%) ID. The multivariate analysis indicated that normal CRP at D15 is the only predictor significant (all p<0.05) for ID at all time points (Table 1).

Conclusion: This exploratory analysis suggests that CAN-naive patients with normal CRP (i.e. ≤0.4 mg/l) at Day 15, lower baseline steroid doses, low number of active joints, no prior anti-TNF or prior NSAID use are those most likely to achieve inactive disease up to 12 weeks.

AbbVie, Cellgene, Chugai, B. Magnusson: None declared., S. Ozen Consultant for: Novartis (Turkey), Speaker Bureau of: Speaker's fee from SOBI, F. Szatnjobok Grant / Research Support from: Institutional grant (UERI) for participating in the canakinumab trial., Speaker Bureau of: Novartis-Brasil, J. Anton Consultant for: Novartis, Speaker Bureau of: Novartis, J. Barash Grant / Research Support from: Investigator in the Canakinumab study sponsored by Novartis, F. Corona: None declared., K. Lheritier Shareholder of: Novartis, Employee of: Novartis Pharma AG, C. Gaillez Employee of: Novartis Pharma AG, A. Martini Grant / Research Support from: Bristol Myers and Sibbld, Centocor Research & Development, Glaxo Smith & Kline, Novartis, Pfizer Inc, Roche, Sanofi Aventis, Schwarz Biosciences GmbH, I declare that the Gaslini Hospital which is the public Hospital where I work as full time employee has received contributions to support the PRINTO research activities from the industries above mentioned. ODL: Francesco Angelini S.P.A., Janssen Biotech Inc, Abbott, Consultant for: Bristol Myers and Squibb, Centocor Research & Development, Glaxo Smith & Kline, Novartis, Pfizer Inc, Roche, Sanofi Aventis, Schwarz Biosciences GmbH, I declare that the Gaslini Hospital which is the public Hospital where I work as full time employee has received contributions to support the PRINTO research activities from the industries above mentioned., Speaker Bureau of: Abbott, Bristol Myers Squibb, Astellas, Boehringer, Italfarmaco, Medimmun, Novartis, Novo Nordisk, Pfizer, Sanofi, Roche, Servier, D. Lovell Grant / Research Support from: National Institutes of Health- NIAAMS, Consultant for: Astra Zeneca, Centocor, Amgen, Bristol Meyers Squibb, Abbott, Pfizer, Regeneron, Roche, Novartis, UCB, Westborn Research Institute, Horizon, Johnson & Johnson, Speaker Bureau of: Novartis, Roche.

**O13**

**Tapering and withdrawal of tocilizumab in patients with systemic juvenile idiopathic arthritis in inactive disease: results from an alternative dosing regimen in the TENDER study**

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**Pediatric Rheumatology 2014, 12(Suppl 1):O13**

**Introduction:** The TENDER clinical trial is a 3-part, 5-year, phase 3 study of tocilizumab (TCZ) in patients with active systemic juvenile idiopathic arthritis (sJIA). After 2 years of treatment, sJIA patients who have maintained clinically inactive disease (CID) for 3 months are given the option to participate in an alternative TCZ dosing regimen aimed at spacing the infusions and eventually withdrawing TCZ.

**Objectives:** To describe the patients registered to participate in the optional alternative dosing schedule in the TENDER study.

**Methods:** To qualify for the optional alternative dosing schedule, patients had to be in the study for a minimum of 2 years and had to achieve American College of Rheumatology JIA CID status. Among the 112 patients enrolled, 39 (35%) entered the optional alternative dosing regimen. This entailed a staged prolongation of the time interval between TCZ infusions from 2 weeks (standard interval) to 3 weeks, then every 3 weeks in 3 patients and every 4 weeks in 9 patients; 7 patients were able to discontinue TCZ (range of time since discontinuation: 13.7-20.8 months). During the April 2013 data review, 9 patients were able to discontinue TCZ. During the May 2014 data review, 7 patients maintained CID status and remained off TCZ, and 2 patients returned to the 2-week dosing interval.

**Conclusion:** A proportion of patients with sJIA who maintain clinically inactive disease status can progressively space TCZ infusions. Of the 35% who entered the optional alternative dosing regimen, approximately half were able to maintain inactive disease over an extended period of time.

**Trial registration identifying number:** TENDER, NCT00642460

**Disclosure of interest:** F. De Benedetti Grant / Research Support from: Abbott, Pfizer, BMS, Roche, Novimmune, Novartis, SOBI, N. Ruperto Grant / Research Support from: Abbott, AstraZeneca, BMS, Centocor, Eli Lilly, Francesco Angelini s.p.a., GlaxoSmithKline, Italfarmaco, Merck Serono, Novartis, Pfizer, Regeneron, Roche, Sanofi Aventis, Schwarz Biosciences, Xoma, Wyeth, Consultant for: Abbott, AstraZeneca, BMS, Centocor, Eli Lilly, Francesco Angelini s.p.a., GlaxoSmithKline, Italfarmaco, Merck Serono, Roche, Sanofi Aventis, Schwarz Biosciences, Xoma, Wyeth, Consultant for: Abbott, AstraZeneca, BMS, Centocor, Eli Lilly, Francesco Angelini s.p.a., GlaxoSmithKline, Italfarmaco, Merck Serono, Novartis, Pfizer, Regeneron, Roche, Sanofi Aventis, Schwarz Biosciences, Xoma, Wyeth, D. Lovell Consultant for: AstraZeneca, Centocor, Roche, Consultant for: Novartis, Roche, Pfizer, AbbVie, Consultant for: Novartis, Roche, Pfizer, M. Henrickson: None declared., R. Jerath: None declared., Y. Kimura: None declared., A. Kadva Employee of: Genentech, a member of the Roche group, J. Wang: None declared., A. Martini Grant / Research Support from: Abbott, AstraZeneca, BMS, Centocor, Eli Lilly, Francesco Angelini s.p.a., GlaxoSmithKline, Italfarmaco, Merck Serono, Novartis, Pfizer, Regeneron, Roche, Sanofi Aventis, Schwarz Biosciences, Xoma, Wyeth, Consultant for: Abbott, AstraZeneca, BMS, Centocor, Eli Lilly, Francesco Angelini s.p.a., GlaxoSmithKline, Italfarmaco, Merck Serono, Novartis, Pfizer, Regeneron, Roche, Sanofi Aventis, Schwarz Biosciences, Xoma, Wyeth, Consultant for: Abbott, AstraZeneca, BMS, Centocor, Eli Lilly, Francesco Angelini s.p.a., GlaxoSmithKline, Italfarmaco, Merck Serono, Novartis, Pfizer, Regeneron, Roche, Sanofi Aventis, Schwarz Biosciences, Xoma, Wyeth, D. Lovell Consultant for: AstraZeneca, Centocor, Roche, Wyeth, Amgen, BMS, Abbott, Pfizer, Regeneron, Hoffmann La Roche, Novartis, Genentech, Speaker Bureau of: Genentech, Roche.

was maintained in 26 of 39 patients (67%), whereas during the May 2014 data review inactive disease status was maintained in 19 of the 39 patients (49%) entering the optional alternative dosing schedule. Dosing intervals were every 3 weeks in 3 patients and every 4 weeks in 9 patients; 7 patients were able to discontinue TCZ (range of time since discontinuation: 13.7-20.8 months). During the April 2013 data review, 9 patients were able to discontinue TCZ. During the May 2014 data review, 7 patients maintained CID status and remained off TCZ, and 2 patients returned to the 2-week dosing interval.

**Conclusion:** A proportion of patients with sJIA who maintain clinically inactive disease status can progressively space TCZ infusions. Of the 35% who entered the optional alternative dosing regimen, approximately half were able to maintain inactive disease over an extended period of time.

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**O15**

**Musculoskeletal ultrasound versus magnetic resonance in supporting clinical management of juvenile idiopathic arthritis**

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**Pediatric Rheumatology 2014, 12(Suppl 1):O15**

**Introduction:** Over the last decade the use of musculoskeletal ultrasound (US) for the assessment of juvenile idiopathic arthritis (JIA) has increased considerably. However, little is known about the potential of US in supporting the clinical management of JIA, when compared to magnetic resonance (MR).

**Objectives:** To evaluate whether US is able to equate MR in providing the information desired by the clinician in practice situations of patients with JIA.

**Methods:** Fifty-nine consecutive children with JIA who performed a joint MR were scanned at the same day also with US. Overall, 23 patients were assessed by imaging in the wrist, 13 in the hips, 12 in the ankle, 4 in the temporomandibular joints (TMs), 5 in the knee, and 2 in the shoulder. The clinician was requested to specify the clinical indication for which the MR was prescribed. MR and US pathological findings were defined according to OMERACT definitions. Concordance between MR and US results was tested using Cohen's kappa coefficient.

**Results:** MR was requested for: 1) confirming disease remission, 2) assessing disease activity, 3) evaluating presence of structural damage. Twenty-five
patients were in clinical remission; both MR and MSUS confirmed remission in 10/25 (40%) patients, whereas both imaging modalities revealed active disease in other 10/25 (40%) patients. In the remaining 5 (20%) patients, remission was confirmed only by MR or MSUS in 1 and 4 patients, respectively. Concordance between MR and MSUS for evaluating disease remission was good (k=0.61). In the 34 patients with clinically active JIA, both imaging modalities confirmed active disease in 23/34 (68%) patients. Ten/34 (29%) patients had no signs of active disease on MSUS, but only 4 (40%) of them showed inactivity on MR. Concordance between MR and MSUS for evaluating disease activity was moderate (k=0.42). MR and MSUS agreed on the presence of structural damage in 7 out of 9 patients whose MR was requested also for evaluating joint damage. In 1 patient damage was revealed only by MSUS, and in the remaining patient no damage was depicted by both imaging modalities. Irrespective of the clinical question, the percentages of agreement between MR and MSUS for each joint were: 100% for knee and shoulder, 85% for hips, 83% for ankle, 74% for wrist, and 50% for TMJs.

Conclusion: MSUS is able to equate MR in assessing patients in clinical remission. The two imaging modalities show a moderate concordance in evaluating disease activity. Unexpectedly, MSUS seems as useful as MR in demonstrating structural damage. MR is more suitable than MSUS for the assessment of TMJs and wrist.

Disclosure of interest: None declared.

O16 Virtual 3D/4D vascular sonobiopsy of the knee joint: validation of the method in the JIA patients treated with IA infliximab or triamcinolone hexacetonide
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Pediatric Rheumatology 2014, 12(Suppl 1):O16

Introduction: In the past few years the use of musculoskeletal ultrasound (MSUS) in pediatric rheumatology has proven to be better than clinical examination in detecting synovitis. Beside standard power doppler ultrasound (PDUS), vascularization of the tissues can be assessed using 3D/4D PD sonography. Using this technique, we can now assess a virtually reconstructed vascular tree within a volume of interest and can ‘objectively’ determine its vascularization by calculating indices using the specially designed VOCAL™ software (Virtual Organ Computer-aided Analysis). 3D/4D US is a well established method for determination of accurate vascularity and blood flow in the field of obstetrics and gynecology, but limited data is available in rheumatology patients.

Objectives: To describe and investigate the ability of 3D/4D PD sonography in accurately predicting vascular and clinical response to IA infliximab (INF) or triamcinolone hexacetonide (TCH) in knee joints of JIA patients.

Methods: JIA patients (n=15) with clinically active knee synovitis underwent IA injection of either IFX (50 mg/kg; 13 joints in 9 patients) or TCH (1 mg/kg; 8 joints in 6 patients). All patients were treated with first and second line therapy (NSAID, DMARD, corticosteroids). The 3D/4D virtual vascular sonobiopsy was performed by experienced rheumatologists. Patients were examined with the Medison Samsung Accuvix V10 US using a 3D/4D linear probe with 6.2 MHz PD frequency (PRF 1 kHz, gain 45). The VOCAL™ software was utilized to calculate volume of pre-determined spheres in the five standardized positions adjusted for the IA size using a specially designed grid. Subsequently, the software automatically displayed sphere volume and three 3D indices: vascularization index (VI), flow index (FI) and vascularization and flow index (VFI). The indices are assumed to reflect the number of vessels within the volume of interest (VI), intensity of flow at the time of 3D sweep (FI), and both blood flow and vascularization (VFI), respectively.

Clinical (JADAS) and sonographic (3D/4D US) examination was performed before and after therapy. To compare indices and analyze correlations, paired samples t-test and Pearson’s test were used.

Results: In total, 21 joints in 15 patients were analyzed using VOCAL software. At the time of IA injections with INF, 13 joints of 9 patients showed grade 3 synovitis in B mode with increased PD signal (2-3/3), while 8 joints of 6 patients treated with TCH showed grade 1-2 synovitis in B mode and increased PD signal (1-2/3). The mean time for follow up was 6.5 months (range 3-11) for IFX, and 2.8 months (range 1.5-6) for TCH treated patients, respectively. The VI index was expressed as percentage, and both FI and VFI as values of 1-100/cm3. There were significant differences in mean value of VI (p=0.03) and FI/SW (p=0.02) in patients treated with IFX, as well as in JADAS value (p<0.01) in both groups of treated patients. Statistical analysis also showed significant correlations among used indices.

Conclusion: 3D/4D US appears a valid, sensitive-to-change and feasible method for evaluating knee joint inflammation/vascularization, and possible outcome measure in children with mono/oligoarticular JIA treated with IA TCH, or in selected patients with IA IFX. Further multicenter studies including larger number of patients, other joints and intra and interobserver variability are warranted, before 3D/4D US may be applied as a valid measurement tool suitable for daily clinical practice.

Disclosure of interest: None declared.

O18 Sub-phenotyping of juvenile dermatomyositis: can it assist clinical decisions?
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Pediatric Rheumatology 2014, 12(Suppl 1):O18

Introduction: Juvenile Dermatomyositis (JDM) is a rare serious disease (affecting 2-3 million children/year) presenting with rash and proximal muscle weakness. Serious complications can include calcinosis, GI ulceration, interstitial lung disease (ILD) and even death. It is becoming clear that JDM is a heterogeneous condition. Dividing JDM into sub-phenotypes would allow better prediction of disease severity and more targeted treatments. We have identified novel auto-antibodies in subtypes of JDM that may correlate with specific phenotypes.

Objectives: To define clinical & pathological phenotypes of patients with JDM who have antibodies to Melanoma Differentiation-Associated protein 5 (MDA-5).

Methods: Patients: Patients were included from the Juvenile Dermatomyositis Cohort and Biomarker Study, a multi-centre study including 13 centres from across the UK. The study collects longitudinal clinical and serological data from patients with idiopathic inflammatory myopathies (IM) of which 85% are diagnosed with JDM or JDM overlap features (currently n=446 patients). Clinical data collected included presence of clinical features, treatment, physicians global assessment and muscle strength assessments including the Childhood Muscle Assessment Score (CMAS).

Autoantibodies: Plasma or serum, available for 285 patients, were screened for the presence of autoantibodies by immunoprecipitation and confirmed by ELISA using recombinant MDA-5 protein.

Muscle biopsies: Muscle biopsies were stained and scored using the JDM Muscle biopsy score tool as described (1,2). The validated muscle biopsy score tool measures severity of muscle pathology across 4 domains and with a separate visual assessment score (0-10).

Results: Autoantibody screening identified the presence of MDA-5 antibodies in 7.4% of patients (21/285 cases); MDA-5 positive patients had significantly increased incidence of ulceration (p=0.03), arthritis (p<0.01) and lung disease, yet had less severe muscle involvement, measured by CMAS score (p=0.03), than MDA-5 negative patients. In addition, median muscle biopsy scores for the MDA-5+ve patients were significantly lower than the MDA-5-ve patients (p<0.005) suggesting a less severe muscle pathology.
JDM is a heterogeneous condition with sub-phenotypes defined by autoantibody status, clinical features and muscle pathology. Identification and classification of sub-phenotypes could be used to predict disease course and severity. In the future, JDM specific autoantibodies could be used as biomarkers allowing for stratified approaches to treatment.

Disclosure of interest: None declared.

O20
Safety and efficacy of varicella vaccination in children with JIA treated with biologic therapy
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Pediatric Rheumatology 2014, 12(Suppl 1):O20

Introduction: Varicella infection is a highly contagious disease which can have a complicated course especially in immunocompromised children and children receiving immunomodulatory therapy.

Objectives: To evaluate safety and efficacy of varicella vaccination in children with JIA treated also with biologic therapy.

Methods: We designed a prospective study on a long term follow up. Five patients with JIA (median age 5, range 3.5-7 years), treated also with biologic therapy (2 etanercept, 2 tocilizumab, 1 infliximab), received 2 doses of varicella vaccine. One patient treated with etanercept received the first dose before starting etanercept, others received both doses on biologic therapy. Before vaccination JIA was stable on therapy and lymphocytic inflammation was present in all vaccinated children. All had negative varicella serology. Parents were asked for written informed consent before vaccination. After vaccination children were followed for disease activity, infections and protective antibodies (pAb) against varicella virus on a long term.

Results: There were no serious side effects after vaccination and no clinical varicella infection in a period of 3 months after vaccination. One patient had mild local reaction after the first dose. One patient treated with etanercept got adenovirus infection 3 days after the second dose of vaccine. Disease activity remained stable in all patients in a period of three months after the second dose. Four patients (75%) had pAb against varicella virus 6 weeks after the second dose. One patient treated with infliximab and methotrexate didn’t develop pAb after the second dose. Two patients treated with etanercept developed low levels of pAb after the second dose. Two patients treated with tocilizumab developed low levels of pAb even after the first dose and very high levels of pAb after the second dose. One patient treated with etanercept got varicella infection 4 months after the second dose despite the protective, however, low levels of pAb. Varicella infection was mild. The other patient treated with etanercept lost his pAb 22 months after the second dose. One patient treated with tocilizumab still has low pAb 27 months after the second dose and one patient treated with tocilizumab has very high pAb 3 month after the second dose.

Conclusion: Varicella vaccination appears to be safe in JIA patients treated also with biologic therapy. However, it is possible that protection is only short term and does not always protect against infection. Follow up of pAb is recommended and the need for revaccination should probably be carefully considered in cases with high risk of varicella infection. Larger cohort studies are needed to obtain more reliable data on varicella vaccination in JIA patient treated with biologic therapy.

Disclosure of interest: None declared.

O21
TRNT1 missense mutations define an autoinflammatory disease characterized by recurrent fever, severe anemia, and B-cell immunodeficiency
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Pediatric Rheumatology 2014, 12(Suppl 1):O21

Introduction: We observed a syndrome characterized by recurrent fever, severe anemia, gastrointestinal symptoms, and a spectrum of immunologic and neurologic symptoms in five children from four unrelated families. Neurologic manifestations ranged from mild developmental delay to nystagmus, spasticity, optic nerve atrophy, and sensorineural hearing loss. Sideroblastic anemia was identified by bone marrow biopsies in two of the children.

Objectives: We suspected a genetic cause because of early onset symptoms.

Methods: We performed whole-exome sequencing in three unrelated families and candidate gene sequencing in one patient with a similar phenotype. Cytokine profiling, flow cytometry, mitochondria-function and ribosomal assembly related experiments were performed on samples from patients. We used morpholino-mediated knockdowns in zebrafish to study protein function.

Results: After filtering for novel and rare variants (allele frequency <1:1000) and homozygous recessive inheritance in one consanguineous family, we observed that three patients carried missense mutations in TRNT1, encoding tRNA nucleotide transferase, CCA-adding 1. By additional exome and Sanger sequencing we found two other patients with mutations in TRNT1. All disease-associated mutations affect highly conserved amino acid residues and are predicted to be damaging to the protein function. The first family from Saudi Arabia had two affected daughters, both homozygous for the p.H215R mutation; the second family of mixed Czech and British background had one affected son, carrying a compound heterozygous p.I223T/p.D163V mutation; two families of mixed European ancestry from the US each had one affected daughter, both compound heterozygous for a p.R99W/p.D163V mutation. Two out of five patients died. The p.H215R mutation was not found in any public database or in 1061 Arabian control DNA samples. The three Caucasian mutations are either novel, or found at a very low allele frequency, consistent with recessive inheritance. Cytokine profiling revealed increased IL-6 serum levels in 2 patients suggesting that their inflammation may be driven by the IL-6 cytokine. Preliminary analysis of two patients who presented with severe B-cell immunodeficiency suggests that the paucity of B-cells is caused by the abnormal proliferation and maturation of B-cells. Knockdown of the zebrafish TRNT1 homologue caused hydrocephaly, defects in tail development, anemia and a reduction in the number of hair cells present in the lateral line, which subserves functions of the inner ear in zebrafish.

Conclusion: Missense mutations in TRNT1 are associated with an autoinflammatory disease manifesting with fevers, transfusion dependent anemia, gastrointestinal symptoms, immunologic, and neurologic symptoms. The TRNT1 enzyme catalyzes the addition of the CCA terminus to the 3-prime end of tRNA precursors and is essential for protein biosynthesis. This phenotype is distinct from other autoinflammatory disorders for the reason that the mutated protein have a profound effect on multiple cells and organs. This likely explains a broad spectrum of features in these patients that are consistent with mitochondrial phenotypes.

Disclosure of interest: None declared.

O22
Identification of a novel monogenic autoinflammatory disease due to mutation in a mitochondrial chaperone protein in a single kindred, and cure with allogeneic haematopoietic stem cell transplantation
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Pediatric Rheumatology 2014, 12(Suppl 1):O22

Introduction: The monogenic autoinflammatory syndromes are characterized by seemingly unprovoked inflammation which derives from a disruption of innate immunity. Novel as yet undefined autosomal recessive
syndromes are increasingly recognised in consanguineous families. This type of family is ideal for genetic mapping.

**Objectives:** To conduct genetic mapping and sequencing to identify the causal variant(s) in a single consanguineous family with a severe unclassified autoinflammatory disease; and confirm pathogenicity with functional studies of novel genetic mutation(s).

**Methods:** Three affected children in a Pakistani family suffered from a severe and unusual autoinflammatory syndrome, presenting in the first year of life with recurrent fevers, erythema nodosum-like rash, severe otorhinocutaneous ulceration, systemic inflammation, and massively elevated serum IgD, without mutation in MKN. One of the affected children also suffered from multifocal sterile osteomyelitis with bony lytic lesions and died at age 12 months from bronchopneumonia, and acute cervical myelopathy from cervical vertebral collapse. The two older children were resistant to treatment with corticosteroids, colchicine, several different DMARDs, anakinra and infliximab. Both were cured by allogeneic haematopoietic stem cell transplantation (HSCT) in their teenage years and remain well and off all treatment approximately 5 years later. DNA from the three patients, two unaffected siblings and their parents were genotyped on Illumina 610 SNP arrays and this data was used for homozygosity mapping and parametric multipoint linkage analysis. A 5Mb region was identified from this mapping. Candidate genes were chosen by members of an expert panel and the exons of these genes were Sanger sequenced. DNA from the entire homozygous region linked to the disease locus (5Mb) was captured using a custom designed 385k capture array from Nimblegen and then resequenced using the Illumina Genome Analyser II, revealing over 50 coding change variants. These entered a filtering process involving: the selection of rare variants and screening of extended family members, ethnically matched controls from the Jat Kalyal tribe, and the exclusion of unlikely candidates. siRNA knockdown was conducted in THP1 monocytes derived to macrophages with measurement of cytokine and reactive oxygen species (ROS) production measured by flow cytometry and electron spin resonance (ESR).

**Results:** A missense variant of interest in a mitochondrial chaperone-like protein was discovered that fully segregated with disease in the family. Knockdown of this protein in THP1-derived macrophages caused an enhanced production of mitochondrial superoxide detectable by ESR and mitoSOX fluorescence, and increased production of TNF-alpha.

**Conclusion:** We describe a novel monogenic autoinflammatory disease driven by mitochondrial ROS production, leading to enhanced inflammatory responses. Increased leukocyte ROS have previously been implicated in other autoinflammatory diseases (TRAPS, FMF, CAPS and FCAS2); we suggest that this was the cause of the severe, recalcitrant and novel autoinflammatory syndrome in the family described herein, ultimately cured by HSCT.

**Disclosure of interest:** None declared.

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**O23 Development and validation of juvenile autoinflammatory disease multi-dimension assessment report (JAIMAR)**

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**Pediatric Rheumatology 2014, 12(Suppl 1):O23**

**Introduction:** There are lots of effects of auto-inflammatory diseases (e.g. pain, fatigue, fear of attack, lifelong drug use, being nervous and angry, problems at school) and those are quite important to patients but have not been measured with the outcome instruments currently included in clinical trials of auto-inflammatory diseases.

**Objectives:** The aim of this study is to develop and validate a new multidimensional questionnaire for assessment of children with auto-inflammatory disorder (AID) in standard clinical practice.

**Methods:** JAIMAR includes 16 parent or patient-centered measures and four dimensions that assess functional status, pain, therapeutic compliance and health-related quality of life (physical, social, school, emotional status) with disease outcome. The JAIMAR is proposed for use as both a proxy-report and a patient self-report, with the suggested age range of 8-18 years for use as a self-report. The study was conducted both with children with FMF and their parents in seven different paediatric rheumatology centers from Turkey. To validate the JAIMAR, the Outcome Measures in Rheumatology Clinical Trials (OMERACT) filter for outcome measures in rheumatology was applied.

**Results:** The analysis data set was collected between December 2012 - April 2013 from the parents of 250 children with FMF in 351 visits and from 179 children in 187 visits. The median age of the children was 10.64 ± 4.38. The JAIMAR was found to be feasible and to possess face, content, criterion and construct validity. Completing and scoring of the JAIMAR is quick and can be finished approximately in 15 minutes. The Cronbach's alpha coefficient for internal consistency for the JAIMAR dimensions was between 0.507-0.998. Between the test-retest scale scores, there is a significant and a positive correlation from medium level to high level (0.607-0.966). For construct validity all the factor loadings are above 0.30. When the criterion validity is considered, we would say that the correlation level between the subscale and the related scale spanned from medium (r = 0.329, p < 0.0001) to large (r = 0.894, p < 0.0001). Parents' proxy-reported and children's self-reported data were outstandingly concordant. Cronbach's alpha values were between 0.770-0.989.

**Conclusion:** The development of the JAIMAR introduces a new and a multi-dimensional approach in pediatric rheumatology practice. It is a valid tool for children with autoinflammatory disease and will help enhance the quality of care of in this group of patients.

**Disclosure of interest:** None declared.

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**O24 IL-18 production upon s100 stimulation is reduced in active sJIA patients compared to sJIA patients in remission and healthy controls**

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**Introduction:** Systemic onset Juvenile Idiopathic Arthritis (sJIA) is considered to be an autoinflammatory disease. The S100-proteins S100A8, S100A9, and S100A12 in serum and interleukin (IL)-18 in plasma are extremely elevated in sJIA patients and have been proposed to be useful biomarkers for diagnosis, disease activity and response to therapy. Moreover, sJIA patients seem to have a defective IL-18 NK cell axis as NK cell lytic function is impaired in spite of high IL-18 levels. However, it is still unknown how the inflammatory S100 proteins and IL-18 relate to each other, and to the defective NK cell lytic function.

**Objectives:** Our aim is to study the relation between S100 proteins and IL-18 in sJIA.

**Methods:** sJIA patients are prospectively followed and sampled during active disease, during treatment and in remission. Peripheral blood mononuclear cells (PBMCs) from sJIA patients during active disease and during remission and PBMCs from healthy controls (HCs) were stimulated with S100A8, S100A9, S100A12 and LPS for four hours. As a second signal for NLRP3 inflammasome activation, ATP was added during the last 30 minutes. To investigate signalling pathways of the S100 proteins, TLR4 and RAGE were blocked by adding CLI-095 and anti-RAGE antibody, respectively. Cytokine levels in supernatant were measured by Luminec; cell frequencies and TLR-expression were analyzed by flow cytometry. Caspase 1-activity was measured with a colorimetric assay (RnD). Further, mRNA levels of NLRP3, IL-1b and IL-18 after S100 stimulation were measured by qPCR.

**Results:** Stimulation of PBMC with S100A8, S100A9 and S100A12 resulted in cytokine production of IL-1b, IL-18 as well as IL-6 and TNF-a. The addition of ATP during the last 30 minutes of stimulation further enhanced IL-1b and IL-18 levels. Blocking TLR4 by adding CLI-095 decreased cytokine production of IL-1b, IL-18 as well as IL-6 and TNF-a. The addition of ATP during the last 30 minutes of stimulation further enhanced IL-1b and IL-18 levels. Blocking TLR4 by adding CLI-095 decreased cytokine production to near normal levels, while blocking RAGE did not have an effect on cytokine production. When compared to healthy controls, PBMCs from sJIA patients produced less IL-18 upon S100 stimulation. The addition of ATP enhanced this differential effect. Four paired samples of active disease and remission were analyzed; PBMCs from active patients were less responsive to S100 stimulation and S100A9 stimulation decreased IL-18 production. Blocking IL-18R decreased the production of IL-18. None declared.
stimulation compared to PBMCs from the same patient while in remission. There were no significant differences in cell subset frequencies, viability of the cells or TLR4 expression in these patients.

Conclusion: S100A8, S100A9 and S100A12 serve as a first signal to establish mutation in a candidate gene. Inclusion criteria were oligoarticular JIA by ILAR criteria, age < 3 year-old Caucasian male born at 31 weeks.

Disclosure of interest: None declared.

**POSTER PRESENTATION**

### P1

**A controlled trial of intra-articular corticosteroids with or without methotrexate in oligoarticular juvenile idiopathic arthritis**


**Pediatric Rheumatology 2014, 12(Suppl 1):P1**

Introduction: Intra-articular corticosteroid (IAC) injection is the therapy of first choice for oligoarthritis in many pediatric rheumatology centers. However, although IAC injections are usually highly efficacious, relapses of synovitis are common and sometimes occur only a few months after the procedure. It is still unclear whether concomitant administration of methotrexate (MTX) may increase and prolong the effectiveness of IAC injections.

Objectives: To compare the efficacy of IAC injection administered as monotherapy or in association with MTX in children with oligoarticular JIA in a phase II, randomized, actively controlled, multicenter trial.

Methods: Inclusion criteria were oligoarticular JIA by ILAR criteria, age < 18 years, and parent informed consent. Patients who were previously treated with synthetic or biologic DMARDs, had undergone an IAC injection < 3 months, were newly injected only in 1 knee, or had active uveitis were excluded. Patients enrolled were randomized 1:1 to receive either IAC therapy alone (Arm 1) or IAC therapy plus MTX (Arm 2). MTX was given orally at 15 mg/m2/week (maximum 20 mg/week). All patients were followed for 12 months and were assessed at 3, 6 and 12 months.

The primary outcome was synovitis flare, defined as recurrence, persistence or new onset of synovitis in 1 or more injected or un.injected (i.e. previously unaffected) joints. Flare rate/probability was compared by chi-square and Kaplan-Meier methods.

Results: A total of 207 patients (50 boys and 157 girls) were enrolled, 102 in Arm 1 and 105 in Arm 2. Fifteen patients lost to follow-up <6 months were included only in the intention-to-treat (ITT) cohort. Patients in arms 1 and 2 were comparable for demographic features and median number of injected joints (2 vs. 2). In the ITT cohort (n=207) flare of synovitis occurred in 133 patients (64.2%), 69 (67.6%) in Arm 1 and 64 (60.9%) in Arm 2 (p=0.31), whereas in the as-observed (AO) cohort (n=192) flare of synovitis occurred in 118 patients (61.4%), 64 (66%) in Arm 1 and 54 (56.8%) in Arm 2 (p=0.19). By Kaplan-Meier analysis, the probability of synovitis flare in the 2 treatment arms was comparable in both ITT and AO cohorts (log-Rank test: p=0.18 and 0.07, respectively). However, among the 118 patients who flared in the AO cohort, flare in injected joints occurred more frequently in Arm 1 than in Arm 2 (46/64, 71.9% vs. 29/54, 53.7%; p= 0.04).

Conclusion: The association of oral MTX did not increase the overall effectiveness of IAC therapy. However, flare of synovitis in injected joints occurred less frequently in patients who received concomitant MTX.

Trial registration identifying number: FARM7279L. AIFA, Italy.

Disclosure of interest: None declared.
**P2**

Joint inflammation assessed by physical examination and MRI of the knee in juvenile idiopathic arthritis: low predictive value for synovitis

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Pediatric Rheumatology 2014, 12(Suppl 1):P2

**Introduction:** The presence of joint inflammation in juvenile idiopathic arthritis (JIA) patients can be made by physical examination and confirmed by imaging. The discrepancy between physical examination and MRI for evaluation of synovitis in a target joint is possibly explained by the fact that clinical measures mostly reflect overall disease activity instead of measures specific for the joint imaged by MRI.

**Objectives:** To compare clinical disease activity of the major target joint upon physical examination with a validated MRI score for the knee in JIA.

**Methods:** MRI datasets and corresponding clinical parameters of disease activity of the knee were analyzed in 167 JIA patients (61.7% female, mean age 12.8 years, SD 3.4 years). Local physical examination of the knee included absence or presence of swelling, warmth, pain or limitation-of-motion (LOM) as assessed by experienced pediatric rheumatologists. A blinded radiologist (6 years of experience in MRI in JIA) analyzed synovial hypertrophy (SH) on a scale from 0-12 on all MRI datasets following the validated Juvenile Arthritis MRI Scoring system (JAMRIS). SH was ‘present’ when the total JAMRIS score was >2. Diagnostic accuracy of the local physical examination parameters for detection of arthritis was determined with MRI as reference standard.

**Results:** Sensitivity and specificity of the parameters scored by local physical examination compared with MRI varied from 39-71%. The overall positive predictive value for synovitis was very low (21-28%), while the negative predictive value was relatively good (71-74%). Median time between the clinical assessment and the MRI was 38 days (IQR 28-53 days). Subgroup analysis on 51 patients with <31 days (median 25 days) between clinical assessment and MRI did not improve the diagnostic accuracy.

**Conclusion:** The presence of swelling, warmth, pain or LOM on physical examination did not predict the presence of synovitis upon MRI. The time between clinical assessment and MRI appeared to have no influence on the diagnostic accuracy of the physical examination inflammation parameters. While the discrepancy between physical examination and MRI persists, follow-up studies are warranted to unravel the difficulties in assessment of disease activity.

**Disclosure of interest:** None declared.

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**P3**

Prognostic factors for the disease course and 8-year outcome in Nordic children with oligoarticular-onset juvenile idiopathic arthritis

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Pediatric Rheumatology 2014, 12(Suppl 1):P3

**Introduction:** Juvenile idiopathic arthritis (JIA) refers to chronic childhood arthritides of unknown aetiology with onset before the age of 16 and persisting for more than 6 weeks. According to ILAR criteria patients are divided into 7 categories of which oligoarthritis is the most common one in western countries. It is further distinguished into persistent and extended oligoarthritis depending on whether the disease is confined to four or fewer joints or it extends to more than four joints after the first 6 months of the illness. Earlier studies have proposed factors that could predict the severity in oligoarticular-onset JIA such as high initial erythrocyte sedimentation rate (ESR) and involvement of upper limb. However, more studies are needed for better and earlier identification of high-risk patients to prevent possible permanent damages.

**Objectives:** The aim of the study was to find out prognostic factors that would predict disease course i.e. who of oligoarticular JIA patients will have a persistent disease course and who will develop the extended form. Another target was to determine whether the main features vary between the two oligoarticular categories and to see if the outcome is different between the two groups at 8 years after disease onset.

**Methods:** This study is a multicentre population-based follow-up study in the Nordic countries based on consecutive patients with a new diagnosis of JIA according to ILAR criteria. They were enrolled between 1997 and 2000 from 14 geographically defined areas in Finland, Sweden, Norway and Denmark. Information regarding clinical data, serology, and disease activity was registered at clinical visits for 8 years.

**Results:** 212 of the 440 JIA patients included in the 8-year study had oligoarthritis (48.2%). 134 of them had persistent and 78 extended form. Females constituted 65.7 and 76.9% of the groups, respectively. Mean age at onset was 5.7 for persistent and 5.3 for extended oligoarthritis. During the 8 years’ follow-up period 18.7% of patients with persistent and 20.5% with extended oligoarthritis developed uveitis. The percentage of positive antinuclear antibodies (ANA) was 42.5% in the persistent and 48.7% in the extended group. At 8 years the percentage of patients with active disease was 29.1% for persistent and 60.3% for extended oligoarthritis. When analyzing the data, both small joint arthritis and inflammation of joints in upper extremities independently correlated strongly to a higher number of cumulative joints ($p<0.001$). Neither gender, ANA positivity, age at onset, family history of rheumatic diseases, nor high ESR in the initial period of the illness correlated to the number of affected joints in a statistically significant way.

**Conclusion:** The most striking finding was the poor prognosis of the extended oligoarthritis category compared to the persistent one; 60% did not reach remission vs. 29%. Upper limb involvement was a predictor of disease severity, which is in agreement with previous studies. Furthermore, arthritis of small joints predicted development to extended oligoarthritis with a high likelihood.

**Disclosure of interest:** None declared.

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**P5**

The Swedish paediatric JIA-registry

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Pediatric Rheumatology 2014, 12(Suppl 1):P5

**Introduction:** The Swedish JIA-registry started in 2009 with the primary goal to follow all children on biologics, cytokine modulators, but later expanded to all patients with or without antirheumatic drugs. It offers care givers a tool for overview on patient level in clinical settings and involves patients and parents as partners in the process. Patient reports are given through e-tablets and summaries will be provided as feed backs. Diagrams on treatment between regions can be followed on line and data can be extracted to promote quality work in the local interprofessional team. National data can be analyzed together with official registries with the aim to follow future morbidity and process of care given to patients with the aim for equal care for all patients. Eye examinations and uveitis is integrated in the registry.
Objectives:  
1. Description of the registry  
2. Registration rates and coverage  
3. Patterns of medical treatment 

Methods: Use of web-based national registry with reports from care givers, patients and medical records. JADAS, CHAQ, Disabkidd includes the arthritis specific questions are followed together with growth. 

Results: After 5 years there are 1700 patients included and data enough to make analyzes possible. Coverage is almost complete but registration rates differ between regions. The total registration rate is above 60 % for all JIA and above 90 % for patients on cytokine modulators. The figures are calculated from prevalence date in cohort studies done together with data from the official patient registry of care given in Sweden for JIA and data from register for over the counter sell of cytokine modulators. The use of cytokine modulators differs from 15 up to 35 patients / 100 000 between different care givers. Some of the drugs are not approved for use in children and are given in schedules not recommended. Guidelines for treatment are>}'

Conclusion: Registration rates and number of included patients are high enough to make it possible to start analyzing data from the registry. There are differences between regions in all aspects of treatment but so far no data showing differences of outcome or health which cannot be explained by differences in reporting data or differences in registration rates. The registry is a tool for care givers in partnership with patients and gives data for local quality work. There is a need for treatment goals, key ratios and to treat to target definitions in different subgroups of JIA. 

Disclosure of interest: None declared.

Evaluation of PPD response in patients with idiopathic arthritis who are on biological drug therapy

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Pediatric Rheumatology 2014, 12(Suppl 1):P6

Introduction: Juvenile idiopathic arthritis (JIA) is a disease most commonly presenting as peripheral arthritis, and increased inflammatory response due to endogenous and exogenous antigens plays a role in its pathogenesis. Tuberculin skin test (TST) is used to determine whether a person is infected with Mycobacterium tuberculosis. In studies, delayed type hypersensitivity response was found to be suppressed in vitro among JIA patients. TST in JIA patients was studied for the first time by our group. In that study, PPD response was found not to be affected by the distribution of subgroups of the disease, the activity of the disease or treatment (methotrexate, prednisolone). None of the enrolled children in that study were using biological drugs. 

Objectives: The aim of our study was to investigate the effect of biological drugs on PPD reaction mediated by Th1 immune response in a group of JIA patients who were not involved in our previous study. 

Methods: The study group consisted of 234 patients with the diagnosis of JIA according to ILAR diagnostic criteria and who were using biological drugs, and 45 healthy controls. PPD of the patients which was routinely done during the follow up was obtained from the patient files. BCG vaccination status of the patients and controls was similar. PPD values ≥ 10 mm were considered positive. Subjects with a PPD ≥ 10 mm were evaluated with the suspicion of tuberculosis infection and those with the final diagnosis of tuberculosis infection were given anti-tuberculosis drug therapy. 

Results: Of the 234 JIA patients on biological drug therapy, 102 (43.6%) were male and 132 (56.4%) were female. Age distribution was 3.25-19.8 years, mean age was 12.8 ± 4.7 years. Disease duration ranged between 3 months and 17 years and mean duration of disease was 5.9 ± 4.11 years. Mean diameter of PPD indurations was 4.996± 6.8494 mm (diameter: 0- 40 mm) in JIA patients and 7.83 ± 3.47 mm (diameter 0–16 mm ) in controls (p = 0.0056). PPD positivity was found in 96 (4%1) and 38 (6%4.4) of the subjects in JIA and control groups, respectively (p<0.0001). PPDx10 mm was detected in 59 (25%2) and 19 (4%2) subjects of the JIA and control groups, respectively (p=0.03). PPD was negative in 125 (55.4) and 31 (6.6) of the subjects in JIA and control groups, respectively (p< 0.0001). When PPD induration was reported with respect to the biological drugs that were used; PPD was 4.632 ±3.4900 mm in 185 (79.1%) of the subjects using etanercept (p=0.01), 4.957±9.1873 mm in 23 (9.8%) of the subjects using adalimumab (p=0.06), 8.3917±7.7386 mm in 23 (9.8%) of the subjects using infliximab (p=0.6) and 1.667 ± 2.8868 mm in 3 (1.3%) of the subjects using anakinra. There was no difference in PPD response between patients using etanercept and adalimumab. PPD induration was larger in subjects using infliximab. 

Conclusion: In patients with JIA who had infantile BCG vaccination and who were currently on biological drugs, PPD induration was significantly lower compared to the control group. There was no difference in PPD response between patients who were on biological drugs or who were not using drugs according to our two major studies. Prospective studies evaluating measurements of PPD reaction in patients on biological drug therapy would provide further information on this issue. 

Disclosure of interest: None declared.

Pharmacovigilance in juvenile idiopathic arthritis patients (Pharmacahlid) treated with biologic agents and/or methotrexate. Consolidated baseline characteristics from Pharmacahlid and other national registries

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Pediatric Rheumatology 2014, 12(Suppl 1):P7

Introduction: The availability of methotrexate (MTX) and biological agents has provided a major change in the treatment of children with juvenile idiopathic arthritis (JIA). An international registry named Pharmachild (European Union grant 260353) has been set up by the Pediatric Rheumatology International Trials Organisation (PRINTO)/Pediatric Rheumatology European Society (PRES). In parallel several national registries with the same p

Methods: We merged into a unified database the baseline demographic data of JIA patients treated with MTX or biologicals coming from the Pharmacahlid registry and from the national registries of Germany, United Kingdom and Portugal. Data are presented as frequencies (%) or medians with 1st and 3rd quartiles. 

Results: About 63% of the patients has been treated with biologicals alone or in combination with MTX, and 29% only with MTX. The events of special interest (ESI) range from 4.5 to 15.0% and the other moderate/severe/adverse events (AE) from 13.1% to 69.9%. 

Conclusion: Combination of information from different data sources is a recommended task and will provide a powerful tool for the future analysis of safety events coming from different registries. 

Disclosure of interest: None declared.
### Introduction

The nuclear oncoprotein DEK is a biochemically distinct, pro-inflammatory protein that is a chemoattractant for neutrophils and T-cells. High levels of DEK autoantibodies have been found in several autoimmune diseases including juvenile idiopathic arthritis (JIA), but their role in disease pathogenesis is unclear. Objectives: Since DEK and DEK autoantibodies can contribute to the development of immune complexes and joint inflammation, we suggest that DEK antibody levels may correlate with flare within the first 14 months after stopping anti-TNF therapy. This study suggests that DEK antibody levels might predict the outcome of discontinuation of anti-TNF therapy.

Conclusion: In children with polyarticular JIA on anti-TNF therapy that maintain CID for at least 6 months while on therapy, high DEK antibody levels may correlate with flare within the first 14 months after stopping therapy. This study suggests that DEK antibody levels might predict the outcome of discontinuation of anti-TNF therapy.


### Methods

In 16 pediatric rheumatology centers, sera samples were collected from 137 children with polyarticular JIA on anti-TNF therapy. Therapy was stopped after 6 months for patients with clinically inactive disease (CID). Disease activity was then monitored for 14 months or until disease flare. Each patient that maintained their CID at least 6 months while on therapy, high DEK antibody levels may correlate with flare within the first 14 months after stopping therapy. This study suggests that DEK antibody levels might predict the outcome of discontinuation of anti-TNF therapy.


### Results

103 female and 34 male patients with polyarticular JIA were enrolled, mean age 11.3 years and disease duration of 5.0 years (77% were on etanercept, 18% adalimumab, 5% infliximab, and 40% concurrent methotrexate). 31 patients discontinued the study for various reasons, including loss of CID during therapy. 39 patients flared within 14 months of stopping therapy, but 67 subjects had no flare within those 14 months. In 89 patients’ samples collected at the end of the study or at time of flare, DEK antibody levels compared to healthy controls ranged from -0.69 to 0.83, mean difference of 0.068 (Q1-Q3 of -0.25-0.28 and 0.025 (SD, 0.39). High levels of DEK antibodies, mean and SD of 0.164 ± 0.39, with 95% confidence interval of (0.02, 0.31), were detected in 30 of the patients that flared within 14 months as compared to lower levels of DEK antibodies (-0.05 ± 0.39, 95% confidence interval of (-0.15, 0.05)) measured in 59 of the patients with no disease flare for 14 months (Student-T, P=0.016). Thus, patients that experience flare within 14 months of stopping anti-TNF therapy have significantly increased levels of DEK antibodies compared to patients that maintained their CID till the end of the study.

Conclusion: In children with polyarticular JIA on anti-TNF therapy that maintain CID for at least 6 months while on therapy, high DEK antibody levels may correlate with flare within the first 14 months after stopping therapy. This study suggests that DEK antibody levels might predict the outcome of discontinuation of anti-TNF therapy.


### Treatment to target of minimal disease activity and normal function in polyarticular juvenile idiopathic arthritis with adalimumab: analysis from a phase 3 clinical trial

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Pediatric Rheumatology 2014, 12(Suppl 1)P9

### Introduction

The Juvenile Arthritis Disease Activity Score (JADAS) [1] is becoming widely accepted in juvenile idiopathic arthritis (JIA) for defining a treat to target strategy. Objectives: To evaluate patients (pts) treated with adalimumab (ADA) (methotrexate [MTX]) that achieved minimal disease activity (MDA) and both MDA and normalization of function.

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<td><strong>Pharamchild</strong> (N=5571)</td>
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<td><strong>Age at onset</strong></td>
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<td><strong>Nr. patients with ESI or AE</strong></td>
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Table 1 (abstract P9)

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<th>n (%)</th>
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<td>ADA Continuation</td>
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<td>+MTX</td>
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<td>Week 16</td>
<td>28 (37.3)</td>
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<td>Week 48</td>
<td>19 (76.0)</td>
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<td>Week 88</td>
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Minimal Disease Activity with Normal Function

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<td>Week 16</td>
<td>21 (28.0)</td>
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<td>Week 48</td>
<td>17 (68.0)</td>
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<td>Week 88</td>
<td>24 (77.4)</td>
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Methods: This post hoc analysis assessed pts aged 4-17 with polyarticular JIA enrolled in a phase 3 clinical trial (DE038)[2], which consisted of a 16 week (wk) open-label (OL) phase with ADA+MTX, 32wk double-blind (DB) phase with ADA or placebo (PBO) at week 48 (wk48), and OL extension (OLS) with ADA+MTX up to 346wks. Outcomes were assessed by 27-joint JADAS (JADAS27), based on C-reactive protein, and Childhood Health Assessment Questionnaire Disability Index (CHAQ-DI). MDA was defined as JADAS27<3.8 and normal function as CHAQ-DI<0.5. Pts who entered the DB phase were included; data were stratified by MTX treatment (tx) at entry.

Results: At baseline, 75 pts on MTX had a mean JADAS27 of 21.2 and CHAQ-DI of 0.9, and 58 pts who were MTX naive or had withdrawn from MTX had a mean JADAS27 of 23.8 and CHAQ-DI of 1.2. After 16wks of OL ADA, the mean JADAS27 was 6.1 and 6.7 and CHAQ-DI was 0.4 and 0.5 for ADA+MTX and ADA-MTX, respectively. Clinical improvements were seen at wk48 and wk88, and the mean JADAS27 at wk88 was 2.6, 3.0, 4.3, and 5.0 for ADA+MTX, ADA-MTX, PBO+MTX, and PBO-MTX, respectively. No pts had MDA or normal function at baseline; however, a good proportion achieved MDA and normal function during OL ADA. Fewer pts achieved MDA and normal function in the PBO tx compared with ADA continuation at both wk48 and wk88. Table 1.

P-value based on Cochran-Mantel-Haenszel statistics to test if there was a difference between ADA continuation vs. PBO.

Conclusion: ADA+MTX resulted in a high percentage of pts achieving MDA and normal function during OL ADA. Fewer pts achieved MDA and normal function at baseline; however, a good proportion achieved MDA or normal function at baseline; therefore, a proportion achieved MDA and normal function during OL ADA. Fewer pts achieved MDA and normal function in the PBO tx compared with ADA continuation at both wk48 and wk88.


References

P10
5-aminimidazol-4-carboxamide ribonucleotide-transformylase and inosine-triphosphate-pyrophosphatase genes variants predict remission rate during methotrexate therapy in patients with juvenile idiopathic arthritis

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Introduction: For children with Juvenile Idiopathic Arthritis (JIA) who fail to respond to methotrexate, the delay in identifying the optimal treatment at an early stage of disease can lead to long-term joint damage. Recent studies indicate that relevant variants to predict methotrexate response in JIA are those in 5-aminimidazol-4-carboxamide ribonucleotide-transformylase (ATIC), inosine-triphosphate-pyrophosphatase (ITPA) and solute-liquid-carrier-19A1 (SLC19A1) genes.

Objectives: The purpose of the study was to explore the role of these candidate genetic factors on methotrexate response in an Italian cohort of children with JIA.

Methods: Clinical response to methotrexate was evaluated clinical remission stable for a 6-months period, as ACRPed score and as change in JADAS score. The most relevant SNPs for each gene considered were assayed on patients’ DNA. ITPA activity was measured in patients’ erythrocytes.

Results: 69 patients with JIA were analyzed: 52.2% responded to therapy (ACRPed>70 score), while 37.7% reached clinical remission stable for 6 months. ATIC rs2372536 GG genotype was associated with improved clinical remission (adjusted p-value = 0.0090). For ITPA, rs1127354 A variant was associated with reduced clinical remission: (adjusted p-value = 0.028); this association was present even for patients with wild-type ITPA and low ITPA activity.

Conclusion: Genotyping of ATIC rs2372536 and ITPA rs1127354 variants or measuring ITPA activity could be useful to predict methotrexate response in children with JIA after validation by further prospective studies on a large patient cohort.

Disclosure of interest: None declared.

P11
Transition care: the link between pediatric rheumatology and adult rheumatology

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Pediatric Rheumatology 2014, 12(Suppl 1)p11

Introduction: Transition from childhood to adolescence is particularly difficult in patients with chronic rheumatic diseases. Moving from pediatric to adult assistance, is not an administrative procedure; it involves a change from “child-centered” to an “adult-oriented” system, in a delicate phase of life in which emotional stability has not been achieved yet. A structure addressing medical, psycho-social and educational adolescents needs is therefore necessary, representing a link between adult and pediatric rheumatology, in order to maintain the benefits of treatment administered during in childhood.

Objectives: We report the experience of Young Adults Rheumatology Outpatient of Florence taking charge of the patients in this phase.

Methods: From January 2000 to May 2014, 754 patients were visited at the Transition Outpatient: 41% with JIA; 16% arthralgia; 9% Raynaud’s phenomenon; 6% SLE; 3% scleroderma; 2% connective tissue; 2% idiopathic arthritis, in order to maintain the benefits of treatment administered during in childhood.

References
Results: 147 patients, all with JIA, were evaluated for the involvement of the temporomandibular joint that was noted in 73/147; of these, 29/73 are affected by oligoarticular JIA, 18/73 polyarticular, 15/73 ERA, 7/73 psoriatic and 4/73 systemic onset. 66/311 (21.2%) patients with JIA are treated with biologics: 32/66 etanercept, 27/66 adalimumab, 3 abatacept, 3 tocilizumab and 1 golimumab. The prevalence of female gender is observed among patients with Raynaud’s (76%) and SLE (91%). Of the 25 patients with scoliosis, 22 (88%) had localized form, 3 (12%) the systemic one. Out of the 13 patients with ARF (9M, 4F), 9 (69%) had cardiac involvement. Among the 134 patients defined as “others”: 7 have Kawasaki Disease, 3 Takayasu and 3 PAN.

Conclusion: Our experience shows that over than 60% of JIA patients had active disease despite biological therapy; all SLE patients had active disease in varying degrees and require therapy. Osteopenia/osteoporosis, chronic ulcers, alterations in the TMJ required ongoing specialty care. Contraception and pregnancy should be handled with special care, in particular in SLE. It is crucial to work closely with other specialists, considering in our center. It is necessary to assiduously support, understand and care of these young patients to prevent therapy suspension, as they frequently want to achieve independence from drugs and become equal to healthy peers. It would desirable: 1) to achieve a better collaboration between pediatricians and adult rheumatologists for a gradual transition between the two types of assistance; 2) to organize Transition Outpatients Clinics to make this transition less dramatic and maintain adherence to therapy and disease control.

Disclosure of interest: None declared.

P12 Intra-articular corticosteroid injections in juvenile idiopathic arthritis

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Childhood Arthritis Prospective Study CAPS

Introduction: Intra-articular corticosteroid injections (IACI) are a standard treatment in juvenile idiopathic arthritis (JIA). This study aims to assess the use and response to IACI in a large prospective cohort of children and young people (CYP) recruited at initiation of treatment for JIA.

Objectives: This study aims to assess the use and response to IACI in a large prospective cohort of children and young people (CYP) recruited at initiation of treatment for JIA.

Methods: Participants were in the Childhood Arthritis Prospective Study (CAPS), an ongoing prospective inception cohort study in 7 UK paediatric rheumatology centres. The aim of CAPS is to provide long-term outcome data on CYP with new-onset inflammatory arthritis receiving specialist care. CAPS recruits CYP <16 years with new inflammatory arthritis persisting for ≥2 weeks. Demographics, disease features, joint count, treatment details, Childhood Health Assessment Questionnaire (CHAQ), physician’s global assessment (PGA), parent’s general evaluation of well-being (PGE), ESR are collected at first presentation, 6 months, then yearly.

Results: Of the 1477 CYP recruited to CAPS 759 have completed 3 years follow-up. 603 (79.5%) were treated with intra-articular corticosteroid injections. 185 (24.4%) patients required IACI alone (with a single episode of injection as the only treatment in 100, (13% of the total cohort) usually in conjunction with other therapies. Approximately one quarter of patients required monotherapy with IACI alone. 13 of all patients and 25% of oligo-articular course patients were managed with a single injection alone. Higher measures of disease activity were significantly associated with the need for DMARD therapy in addition to IACI.

Disclosure of interest: None declared.
Table 1 (abstract P13)

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N (1066)</strong></td>
<td>285</td>
<td>265</td>
<td>306</td>
<td>210</td>
<td>–</td>
</tr>
<tr>
<td>Time between symptom onset and 1st PRh, weeks</td>
<td>22.7 (11.9, 40.1)</td>
<td>23.5 (12.1, 52.7)</td>
<td>24.7 (12, 58.2)</td>
<td>23.1 (13.2, 50.1)</td>
<td>0.28</td>
</tr>
<tr>
<td>% seen within 10 weeks</td>
<td>20.5%</td>
<td>21%</td>
<td>20%</td>
<td>19%</td>
<td>0.66</td>
</tr>
<tr>
<td>Time from referral to 1st PRh appointment, weeks</td>
<td>3.4 (1.2, 7.9)</td>
<td>4 (14, 7.3)</td>
<td>4.7 (14, 8)</td>
<td>4.3 (14, 8.7)</td>
<td>0.03</td>
</tr>
<tr>
<td>% seen within 4 weeks</td>
<td>58%</td>
<td>55%</td>
<td>49%</td>
<td>50%</td>
<td>0.02</td>
</tr>
</tbody>
</table>

**Methods:**

Objectives: To describe the appearance of the healthy knee on MRI after IV contrast and to compare the enhancing synovium in asymptomatic children to juvenile idiopathic arthritis patients.

A significant difference (p<0.007) in the total SH score was observed between controls and JIA children. SH score could differentiate controls from the clinically active JIA subgroup (p=0.002) but not from the clinically inactive JIA subgroup (p=0.303). Findings only observed in the asymptomatic group consisted of an diffuse ‘contrast-outfading’ pattern in 28% of the controls and ‘pseudo-enhancement’ of the cartilage at the posterior condyles only, that could be mistaken for true synovial inflammation.

**Conclusion:** In asymptomatic children only very mild synoval enhancement was detected as well as two as yet undescribed findings representing potential pitfalls in the assessment of disease activity upon MRI of the knee. The existing, very reliable JAMRIS system for assessment of enhancing synovium can differentiate JIA patients from asymptomatic controls but only at group-level. For individual differentiation improved MRI scoring needs to be developed avoiding the measurement of synoval thickness scoring to further establish MRI as more accurate monitoring tool for JIA disease activity.

**Disclosure of interest:** None declared.

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**P14**

Contrast-enhanced MRI of the knee in asymptomatic pediatric controls compared to juvenile idiopathic arthritis patients to validate synovitis scores

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Pediatric Rheumatology 2014, 12(Suppl 1):P14

Introduction: The primary target of disease in juvenile idiopathic arthritis (JIA) is inflamed synovium, i.e. synovitis, which can be best visualized with magnetic resonance imaging (MRI) upon administration of intravenous (IV) contrast. Adequate differentiation between pathologic from physiologic extent of synovial enhancement has important implications for (dis) continuation of therapy.

Objectives: To describe the appearance of the healthy knee on MRI after IV contrast and to compare the enhancing synovium in asymptomatic children to JIA patients.

Methods: An axial fat-saturated T1-weighted MRI sequence of the knee of 25 asymptomatic controls and 25 JIA patients was collected, blinded and randomized. The asymptomatic controls were children who underwent MR enterography with IV contrast for unrelated diseases, had no (history of) joint complaints or signs of joint inflammation and gave permission for an additional sequence of the knee. JIA patients were age/sex-matched and divided in three clinical subgroups: ne

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**P15**

The transcription factor crem-alpha regulates inflammatory T cell subsets in juvenile idiopathic arthritis

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Pediatric Rheumatology 2014, 12(Suppl 1):P15

Introduction: The cAMP response element (CRE) module (CREM) binds to promoters of genes with CREs and regulates transcription via a chromatin-dependent mechanism. CREMs is important for the T cell pathophysiology of SLE by suppression of IL-2 and CD3, but enhancement of IL-17 transcription. Juvenile idiopathic arthritis (JIA) is an autoimmune disease of unknown origin. Th17 cells have a pathogenic role in arthritis and are not controlled by local FoxP3+ regulatory T cells (Tregs). Pathogenic T cells in the inflamed joints of JIA patients have enhanced expression of IL-17, IFN-γ and CD161. CD161+ CD4+ cells also contain FoxP3+ cells that produce proinflammatory cytokines. A higher frequency of CD161 Tregs appears to associate with more severe disease in JIA, a fact which might contribute to the failure by Treg to suppress ongoing inflammation.

Objectives: The aim of this study was to evaluate the role of CREM-expressing T cells in juvenile idiopathic arthritis.

Methods: T cells and peripheral blood mononuclear cells (PBMCs) from healthy donors and JIA patients as well as synovial fluid mononuclear cells (SFMCs) from JIA patients were stimulated in vitro with anti-CD3/CD28 antibodies. PBMCs from healthy donors were incubated in the presence of synovial fluid from JIA patients. CREMs was knocked down in PBMCs and SFMCs by transfection with CREM siRNA. Flow cytometry was used to measure CREM protein, CD161, Helios and Foxp3 expression as well as secretion of cytokines. RNA was quantified by quantitative Real-time PCR.
We observed enhanced expression of CREM in synovial fluid T cells from JIA patients. Enhanced expression of CREM was also induced after ex vivo culture of PBMCs from healthy donors with synovial fluid from JIA patients. We furthermore found enhanced expression of CREM in CD4+CD161+ and in CD4+FoxP3+CD161+ cells, which are known producers of inflammatory cytokines, compared to CD4+CD161+ and CD4+FoxP3+CD161+ cells. We next asked what drives enhanced expression of CREM in synovial fluid stimulated T cells and if pharmacologic inhibition of these factors might reduce occurrence of inflammatory Tregs and effector T cells. Interestingly in in vitro assays both Anakinra as well as Enbrel, which antagonize IL-1 respectively TNF-a signaling downregulated expression of inflammatory cytokines in T cells and both downregulated CREM expression as well. We then aimed to directly block CREM activating by inhibiting Calcium/calmodulin-dependent kinase type IV (CaMKIV). We have shown before that SLE serum IgG activates CaMKIV and identified CaMKIV as being responsible for the increased expression of CREM in SLE T cells. Inhibition of CaMKIV in PBMCs markedly downregulated CREM expression and reduced numbers of IL-17 and Foxp3+ T cells.

Conclusion: We thus suggest that the overexpression of CREM in T cells contributes to T cell pathophysiology in JIA by regulating percentages of inflammatory CD4+IL-17 producing cells, as well as inflammatory CD161+Foxp3+ cells.

Disclosure of interest: None declared.

P17 Bone health assessment of patients with juvenile idiopathic arthritis: a comparison between DXA and BoneXpert

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Pediatric Rheumatology 2014, 12(Suppl 1)P17

Introduction: Juvenile idiopathic arthritis (JIA) affects bone mineral density (BMD) due to chronic inflammation, glucocorticoid treatment and immobilization. Dual-energy X-ray absorptiometry (DXA) is most widely used to determine BMD. BoneXpert is a new, feasible and reproducible method for automatic determination of cortical BMD on hand radiographs. Moreover radiation exposure is low and in low-risk peripheral areas.

Objectives: The aim of this study is to compare BoneXpert and DXA in the assessment of BMD in JIA patients.

Methods: Thirty-five JIA patients with available DXA and hand radiograph within the same time period were included from a tertiary hospital of the Dutch Arthritis and Biologicals in Children register. Outcome measures for BMD were Bone Health Index (BHI) from BoneXpert and BMD total body, BMD lumbar spine and Bone Mineral Apparent Density (BMDA) from DXA.

For all outcome measures Z-scores were calculated. Correlations between BMD measurements by DXA and BoneXpert were assessed with Pearson correlation coefficients.

Results: The patients in this study had significantly lower mean BMD compared to the healthy population on all BMD measures (p<0.05). The pearson correlation coefficient for the absolute scores of DXA BMD and BHI varied between 0.568-0.770 (p=0.000). The correlation coefficient for the Z-scores of DXA and BoneXpert (0.127-0.322) was not significant.

Conclusion: BHI measured by BoneXpert is correlated to measurements of BMD by DXA. The correlation of Z-scores of BMD measured by the two methods is weaker. Longitudinal studies and assessment of the association of the BMD measurements with outcome (for instance atrumatic fractures) are necessary to determine the value of BoneXpert in clinical use.

Disclosure of interest: None declared.

P18 Advanced bone age in the affected side predicts worse radiographic progression in patients with juvenile idiopathic arthritis and unilateral wrist disease

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Pediatric Rheumatology 2014, 12(Suppl 1)P18

Introduction: Previous anecdotal observations have suggested that patients with juvenile idiopathic arthritis (JIA) and unilateral wrist synovitis often have an advanced bone age in the affected side and that advancement in skeletal maturation may be associated with development of long-term structural joint damage. However, it is unclear whether the risk of damage in the affected wrist is greater than that of JIA patients with bilateral wrist disease.

Objectives: To compare the amount of radiographic damage in the wrists between patients with unilateral and bilateral wrist synovitis.
Table 1 (abstract P18)

<table>
<thead>
<tr>
<th>Bone-chronological age lag (years)</th>
<th>Baseline Poznanski score</th>
<th>Follow-up Poznanski score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unilateral-affected side</td>
<td>1.03</td>
<td>-1.94</td>
</tr>
<tr>
<td>Unilateral-unaffected side</td>
<td>0.63</td>
<td>-0.47</td>
</tr>
<tr>
<td>Bilateral-average L/R wrist</td>
<td>0.23</td>
<td>-0.83</td>
</tr>
</tbody>
</table>

p=0.03; *p=0.002; †p=0.02

Methods: 21 patients with unilateral wrist synovitis and 21 patients with bilateral wrist synovitis who underwent longitudinal bilateral hand/wrist radiographs were evaluated. Bone age in each wrist was assessed on radiograph made at first examination by two experienced pediatric endocrinologists according to Greulich & Pyle atlas. Endocrinologist assessments were then averaged and the time lag between chronological age and bone age was calculated. Radiographic damage was assessed at baseline and last follow-up visit by measuring carpo-metacarpal ratio (Poznanski score). The Poznanski score was evaluated separately in patients with unilateral wrist disease, whereas in patients with bilateral wrist disease the score of the two wrists was averaged. The demographic and clinical characteristics, including disease duration at first and last radiographic assessments, were comparable between patients with unilateral and bilateral wrist disease. However, patients with unilateral wrist disease had more frequently oligoarthritis (52.3%), whereas patients with bilateral wrist disease had more frequently systemic arthritis (52.3%).

Results: Bone age was advanced by > 6 months in the affected side in 12/21 patients (57.1%) with unilateral wrist disease and in the right and left side in 8/21 (38.1%) and 7/21 (33.3%) patients with bilateral wrist disease. Comparison of chronological-bone age and radiographic damage on baseline and follow-up films in patients with unilateral and bilateral wrist disease is shown in table 1.

Conclusion: Our results show that JIA patients with unilateral wrist disease often have advanced skeletal maturation in the affected side and that this is associated by a greater destructive course. This indicates that these patients deserve a careful radiographic follow-up and an early aggressive therapy aimed at suppressing joint inflammation in the wrist to prevent progression of joint damage.

Disclosure of interest: None declared.

P19

Potential value of cartilage and soluble biomarkers in evaluating joint damage in juvenile idiopathic arthritis
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Pediatric Rheumatology 2014, 12(Suppl 1):P19

Introduction: Serum biomarkers of bone and cartilage turnover were found to predict structural damage progression in Rheumatoid Arthritis (RA). Their potential value in Juvenile Idiopathic Arthritis (JIA) has never been explored.

Objectives: 1) To examine associations between soluble biomarkers of bone (CTX-I) and cartilage degradation (C1, C2C, C2C) and joint damage as assessed by Conventional Radiography (CR) and Magnetic Resonance Imaging (MRI) in patients with JIA. 2) To investigate whether these biomarkers can predict structural damage progression.

Methods: The clinically more affected wrist of 88 JIA patients was studied compared between patients with and without structural damage progression according to JSN (joint space narrowing)-SHS score compared to patients without progression (C1, C2: 240 ng/ml vs 125 ng/ml, P= 0.01; C2C: 133.7 ng/ml vs 65.7 ng/ml, P= 0.001). Unlike RA, patients with radiographic progression showed significantly lower levels of CTX-I (1.03 ng/ml) compared patients without structural damage progression (1.53 ng/ml; P=0.03). Patients, who required either initiation of methotrexate or addition of a biologic agent at the 6 months follow-up visit, had significantly higher levels of C1,2C (P=0.027) and C2C (P=0.034) compared to patients who did not require treatment changes.

Conclusion: Our results suggest an inhibition of bone and cartilage turnover in patients with JIA. Biomarkers of cartilage degradation are promising as potential predictors of structural damage progression and severity of disease course.

Disclosure of interest: None declared.

P20

Administration of routine preventative vaccinations in children with polyarticular juvenile idiopathic arthritis receiving adalimumab
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Pediatric Rheumatology 2014, 12(Suppl 1):P20

Introduction: Adalimumab (ADA) has been shown to be safe and effective in polyarticular juvenile idiopathic arthritis (pJIA), and is approved for use in moderate to severe pJIA patients (pts) ≥4 years (yrs) in the US, Australia, and Japan, and in the EU for pts ≥2 yrs.

Objectives: This post hoc report describes the observed use of vaccines in pJIA pts receiving ADA in 3 clinical trials and one registry.

Methods: Pts with active pJIA were enrolled in one of the following trials: M10-444 (ages 2 to <4 or ≥5 yrs), DE038 (ages 4-17 in Japan), DE038 (ages 4-17 in US, EU) or the STRIVE (P10-262) registry (ages 4-17 in US, EU, and Australia). Pts received ADA±methotrexate. Vaccinations were administered based on the judgment of the study investigator or the treating physician. Descriptive statistics were used to summarize all vaccinations. Adverse events (AEs) related to active influenza virus infection events occurring within 270 days after influenza vaccination were collected by a predefined MedDRA query 15.1 [Lack of efficacy/Effect Influenza (Vaccination Product Specific)].

Results: The influenza vaccine was the most frequently administered: 55, 63, 10 and 22 influenza vaccines were administered in DE038, M10-240, M10-444 and P10-262, respectively. In addition, pneumococcal, human papilloma virus, diphtheria, tetanus and/or pertussis, hepatitis A and B, and polio vaccines were administered. 2 pts each received >5 vaccinations in DE038 and M10-240, while 3 pts each in M10-444 and P10-262 received >1 but ≤5 vaccinations. The influenza vaccine was administered to 32/171 (19%), 20/25 (80%), 6/32 (19%) and 21/533 (4%) of pts during the course of the study in DE038, M10-240, M10-444 and P10-262 respectively, and the mean (SD) time to 1st influenza vaccination while pts were on ADA was high: 675 (615), 189 (80), 93 (90) and 443 (396) days. The rates of influenza-related AEs reported for pts who received influenza vaccinations and those who did not were: 13% vs 9% for DE038, 15% vs 20% for M10-240, 0% vs 12% for M10-444, and 5% vs 0.4% for P10-262. Table 1.

Conclusion: These data support the idea that pJIA pts treated with ADA can be immunized with routine, inactive, preventative vaccines. Not all of the eligible pts were vaccinated on time according to the Centers of Disease Control (CDC) recommendations, and many pts were not vaccinated at all,
Further investigation of vaccination

Table 1(abstract P20)

<table>
<thead>
<tr>
<th>Vaccination</th>
<th>DE038</th>
<th>M10-240</th>
<th>M10-444</th>
<th>P10-262</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total patients vaccinated, n/N</td>
<td>38/171</td>
<td>20/25</td>
<td>6/32</td>
<td>22/533</td>
</tr>
<tr>
<td>Mean age, yrs (SD)</td>
<td>11.8 (3.6)</td>
<td>13.6 (3.3)</td>
<td>3.0 (0.7)</td>
<td>12.7 (4.0)</td>
</tr>
<tr>
<td>Total vaccinations, n</td>
<td>77</td>
<td>64</td>
<td>10</td>
<td>25</td>
</tr>
<tr>
<td>Patients with &gt;1 type of vaccination, n</td>
<td>11</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Different types of vaccinations, n</td>
<td>9</td>
<td>2</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Mean time to 1st vaccination*, days</td>
<td>688</td>
<td>189</td>
<td>93</td>
<td>448</td>
</tr>
<tr>
<td>Mean age at 1st vaccination*, yrs</td>
<td>12.9</td>
<td>14.0</td>
<td>3.6</td>
<td>12.0</td>
</tr>
</tbody>
</table>

*while on ADA

suggesting that physicians may be reluctant to use vaccines in children receiving antirheumatic therapies. Further investigation of vaccination practices for pts with JIA is warranted.

Trial registration identifying numbers: NCT00774537, NCT00690573, NCT00048542 and NCT00783510


P21

Comparison of bone mass and quality determinants in adolescents and young adults with juvenile systemic lupus erythematosus (JSLE) and juvenile idiopathic arthritis (JIA).

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1Department of BioMedicine, Section of Rheumatology, Transition Clinic, University of Florence, Italy; 2Department of Internal Medicine, Endocrinology Unit, University of Florence, Italy; 3Health Sciences Department, Anna Meyer Children’s University Hospital, University of Florence, Florence, Italy. Pediatric Rheumatology 2014, 12(Suppl 1):P21

Introduction: Few prospective data have been published on the comparison of bone density and quality in homogeneous groups of patients with juvenile systemic lupus erythematosus (JSLE) and juvenile idiopathic arthritis (JIA).

Objectives: To perform a longitudinal evaluation of the prevalence and the characteristics of bone mass and quality in JSLE patients and to evaluate the differences on the bone biochemical parameters, using DXA, pQCT, and QUS, in respect to two homogeneous for age- and sex-groups of JIA patients and healthy controls.

Methods: Forty-three JSLE patients (35 females, 8 males, median age 18.8 years, range 14.0 – 31.4 years) have been cross-sectionally studied with DXA, pQCT, and QUS scans and compared with 138 JIA patients (112 females, 26 males, median age 18.9 years, range 13.4 - 33.2 years: 89 oligoarticular, 26 poly, 8 systemic, 15 enthesis-arthritids (ERA), and 79 healthy subjects (59 females, 20 males; median age 19.3 years, range 13.5 to 36.5 years). Of these, 39 patients (32 females and 7 males, median age 20.3 years, range 16.6 - 36.8 years) with JSLE were followed longitudinally and compared with 131 patients (108 females, 23 males median age 20.7, range 15.8 - 37.1 years) with JIA and 63 healthy subjects (48 females, 15 males; median age 21.9 years, range 15.5 to 38.3 years).

Results: JSLE patients have a higher bone cortical density (CrtBMD) than controls, with JIA patients (p < 0.005), except the systemic subgroup (p < 0.0001), showing a lesser CrTBMD than controls and JSLE group. However, JSLE and JIA patients, except for ERA onset, have a significantly reduced bone trabecular density (TbBMD) compared to controls (p < 0.0001), with no differences between JSLE and JIA. In addition, JIA patients show a significantly reduced muscle area (muscle CSA) compared to JSLE and controls (p < 0.0001). Conversely, fat area (fat CSA) is significantly increased in both JIA and JSLE patients when compared to controls (p < 0.0001), with no differences between JSLE and JIA groups. Analogous results are observed in the polar resistance to stress (SSp).

Conclusion: The evaluation of the main parameters that define bone density and structure in adolescents and young adults with JIA and JSLE highlights significant differences among the two groups and subgroups, and among JIA or JSLE patients and controls. These data might indicate a different pathogenesis of bone damage in the two entities, and suggest a different diagnostic and therapeutic approach to improve the peak bone mass.

Disclosure of interest: None declared.

P22

Monitoring the efficacy of intraarticular infliximab by musculoskeletal ultrasound and juvenile arthritis disease activity score (JADAS) in JIA patients – single center experience

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Introduction: Pediatric rheumatologists use musculoskeletal ultrasound (MSUS) in everyday practice as a simple, painless and inexpensive tool for detecting synovitis. Along with MSUS, Juvenile Arthritis Disease Activity Score (JADAS) was proven to be valid for clinical assessment. In JIA patients with mono- or oligoarthritis who are inadequately responding to conventional therapy, but do not meet criteria for biological therapy, intraarticular infliximab could be therapy of choice. Since this therapeutic option is not routinely used, there is a need for a continuous follow-up, in which MSUS and JADAS could have great value.

Objectives: To assess the efficacy of intraarticular infliximab injections in patients with juvenile idiopathic arthritis (JIA) using MSUS and juvenile arthritis disease activity score (JADAS).

Methods: IA infliximab was administered in 22 joints of 14 patients diagnosed with JIA according to ILAR classification criteria. All patients received first and second line therapy (NSAID, DMDAR, corticosteroids systemic and IA). None of the patients fulfilled criteria for treatment with biologic therapeutics, but were resistant to DMDAR’s. Intraarticular infliximab (25 mg or 50 mg per joint) was administered.

The patients were monitored by monthly assessment using JADAS (number of active joints, pain assessed by patient/parent or physician (VAS), ESR) and MSUS. The MSUS assessment included Omeract semiquantitative grades (0–3 grades) for both B-mode and Power-Doppler (PD) and 12 patients were examined using 3D/4D US. We used paired samples T-test for comparing JADAS before and after the treatment.

Results: At the point of IA injections all 22 joints showed grade 2-3 synovitis in B mode and increased PD signal (2.3/3). The mean value of JADAS was 17.31 (± 2.78). At the end of the follow-up period (mean time 7.07 months, range 6-10 months) the mean value of JADAS was 5.66 (± 3.52). There was also improvement in MSUS with 0-1 grade synovitis without effusion in B mode and PD signal decreased to 0-1.3. The deference in JADAS was statistically significant (p < 0.001). However, 3/14 patients subsequently flared (mean time 6-8 months) and fulfilled criteria for systemic biologic therapy. Two of those three patients received lower IA dose of infliximab (25 mg per joint).

Conclusion: IA infliximab should still be considered as a therapy option in selected children with therapy resistant, isolated mono/oligoarticular JIA. The effect of IA therapy could be easily monitored both by MSUS and JADAS.

Disclosure of interest: None declared.
### P23

**Treatment prescribing patterns in a cohort of patients with juvenile idiopathic arthritis (JIA): Data from the childhood arthritis prospective study (CAPS)**

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**Introduction:** Juvenile idiopathic arthritis (JIA) is a heterogeneous disease, classified according to the International League of Associations for Rheumatology (ILAR). Initial treatment is based largely on disease severity; intra-articular injections for oligoarthritis, methotrexate (MTX) for polyarthritis and systemic presentations. The recent licensing of biologic therapies for use in JIA has revolutionised treatment of the disease. It is not currently known what proportion of children who present with polyarthritis will require biologic therapy. Although not studied formally, it is recognised a proportion of children with oligoarthritis will also require systemic therapy to control symptoms.

**Objectives:** To describe prescribing patterns in JIA over the first 3 years on presentation to rheumatology.

**Methods:** Children with at least 3 years of follow-up within the Childhood Arthritis Prospective Study (CAPS), a prospective observational inception study of inflammatory arthritis, were included. For analysis, children were placed into one of 4 groups based on physician-assigned ILAR category and number of active joints at first presentation (baseline): oligoarthritis, polyarthritis, systemic (sJIA) and enthesitis-related arthritis (ERA). All treatment exposures were categorised into NSAID, intra-articular steroids, disease modifying anti-rheumatic drug (DMARD) including MTX and sulphasalazine (SSZ) and biologics including adalimumab (ADA), etanercept (ETN), infliximab (INF), and tocilizumab (TCZ).

**Results:** 790 children were included originally (406 oligoarthritis, 221 polyarthritis, 42 sJIA and 43 ERA). Of these, 78 had missing ILAR and were excluded, leaving 712 children. Over a 3 year period, almost 100% of children with polyarticular presentation and 50% with oligoarthritis went on to receive a DMARD. 44% with polyarthritis and 17% with oligoarthritis presentation also received a biologic (Table). The most recent ILAR category among children with oligoarticular onset who received a biologic comprised 39% extended, 19% polyarthritis, 4% ERA, 11% other subtypes; 27% had persistent oligoarthritis. All 52 sJIA patients were treated with DMARDs with 36% having biologics. 63% of ERA patients receive a DMARD with 26% going on to receive a biologic. Table 1.

**Conclusion:** Over a three year period almost all patients with polyarthritis received treatment with MTX and almost 50% also received a biologic therapy. A high proportion of children presenting with oligoarthritis also went on to receive DMARDs and biologics, many children for persistent oligoarthritis. This is despite the lack of clinical trial evidence for effectiveness in this subtype. Further studies on the efficacy/effectiveness in this subtype should be undertaken to ensure appropriate use of advanced therapies in this population.

**Disclosure of interest:** None declared.

### Table 1 (abstract P23)

<table>
<thead>
<tr>
<th>Arthritis pattern at presentation</th>
<th>N</th>
<th>Ever had a DMARD, n (%)</th>
<th>Ever had a biologic, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oligoarthritis</td>
<td>406</td>
<td>204 (50)</td>
<td>70 (17)</td>
</tr>
<tr>
<td>Polyarthritis</td>
<td>221</td>
<td>217 (98)</td>
<td>98 (44)</td>
</tr>
<tr>
<td>Systemic arthritis</td>
<td>42</td>
<td>42 (100)</td>
<td>15 (36)</td>
</tr>
<tr>
<td>Enthesitis-related arthritis</td>
<td>43</td>
<td>27 (63)</td>
<td>11 (26)</td>
</tr>
</tbody>
</table>

### P24

**HLA II class alleles in juvenile idiopathic arthritis patients with temporomandibular joint involvement**

Zane Davidson¹, Elena Egger², Sarmite Dzelzite³, Anna Lazareva⁴, Ruta Santere⁵, Dace Berzina⁵, Valda Stanevicha⁵, ¹Paediatric Department, Riga Stradins University, Riga, Latvia; ²Laboratory of Clinical Immunology and Immunogenetics, Riga Stradins University, Riga, Latvia; ³Radiology Department, Children University Hospital, Riga, Latvia; ⁴Rheumatology Department, Children University Hospital, Riga, Latvia

**Introduction:** Temporomandibular joint (TMJ) involvement is seen very often (17-87%) in children with juvenile idiopathic arthritis that can lead to compromised craniomandibular function, dentofacial aesthetics and morphology. Contrast enhanced MRI is the golden standard for diagnosis of TMJ arthritis (Argyropoulou, 2009). Previous studies show that HLA II class alleles may have protective or risk importance in JIA subtypes (Hollenbach, 2010).

**Objectives:** To identify HLA II class alleles of risk and protection in JIA patients with TMJ involvement.

**Methods:** 53 JIA patients were evaluated treated at Children University Hospital in whom MRI for TMJ from 2010-2014 was performed. Patients were genotyped for HLA-DRB1; DQB1; DQA1- using RT-PCR with sequence-specific primers. Associations of DRB1; DQB1; DQA1 alleles in patients were examined individually using the χ² test. P-value and odds ratio were calculated using EPI INFO 6.0 software with 95% confidence intervals and Fisher correction for small numbers.

**Results:** 53 JIA patients with mean age of 14.67 ±1.15 years (range 1.15 – 17.9 yr); 39 (73.6%) girls and 14 (26.4%) boys. The mean duration of the disease from the time of diagnosis till performing TMJ MRI was 3.96 ±2.22 years (range 0.2 – 10.2 yr). JIA subtype were as follows: seronegative polyarticular 29 (54.7%), seropositive polyarthritis 6 (11.3%), oligoarthritis extended 4 (7.5%), arthritis with enthesis 9 (17%), undifferentiated 2 (4.7%) and 2 (4.7%) for systemic arthritis, 2 groups where separated after TMJ MRI: 1st with ≥2 signs of active inflammation or any structural damage; 2nd with no pathologic signs or with slight contrast enhancement. In the 1st group alleles DRB1 *16:01 (OR 0.90, p=0.0001), *13:01 (OR 0.63, p=0.01); DQB1 *02:01-02:02 (OR 3.3, p=0.001); DQA1 *05:01 (OR 6.39, p=0.041) were observed. In the 2nd group DRB1 *11:01 (OR 0.40, p=0.001), *13:01 (OR 0.63, p=0.01); DQB1 *03:01 (OR 0.3, p=0.005), *05:01 (OR 0.4, p=0.026); DQA1 *05:01 (OR 0.22, p=0.001) were found more often.

**Conclusion:** 1) JIA patients with alleles DRB1 *16:01, *13:01; DQB1 *02:01-02:02 and DQA1 *05:01 may have higher risk for TMJ involvement with 2 or more signs of active joint inflammation or any structural damage. 2) DRB1*11:01; DQB1 *03:01, *05:01 and DQA1 *05:01 alleles are probably protective for TMJ involvement.

**Disclosure of interest:** None declared.

### P25

**Genetic association with articular damage in patients with juvenile idiopathic arthritis (JIA)**

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**Introduction:** Bone loss in inflammatory arthritis such as rheumatoid arthritis is partly due to aberrant expression of cytokines and bone homeostasis regulatory molecules, leading to excess bone resorption.

**Objectives:** To investigate if genetic factors affect the degree of cartilage and bone loss in JIA, irrespective of disease duration and treatment.

**Methods:** DNA was extracted from saliva samples from 80 JIA patients from Great Ormond Street Hospital, UK, 98 from Hôpital Necker, France, and 54 from Istituto Giannina Gaslini, Italy. Genetic variation was investigated using the tagging single nucleotide polymorphisms (tSNPs) approach. 17 candidate genes were selected for analysis: RANK, RANKL, osteoprotegerin (OPG), osteopontin, DKK-1, IL-1α, IL-1β, IL-1R1, IL-1R2, IL-6, IL-17A, IL-17F, IL-17F, TNF-α, TNF-β, TNF-βR, FGF-2, FGF-2, and FGF-2. Association analyses were performed using the Eggers test for small sample size, and Fisher correction was used for small sample size. The results were calculated using EPI INFO 6.0 software with 95% confidence intervals and Fisher correction for small numbers.

**Results:** The mean duration of the disease was 14.67 ±1.15 years (range 1.15 – 17.9 yr). A high proportion of children presenting with oligoarthritis also went on to receive a biologic. A high proportion of children presenting with oligoarthritis also went on to receive a biologic. A high proportion of children presenting with oligoarthritis also went on to receive a biologic.
Table 1 (abstract P25)

<table>
<thead>
<tr>
<th>Gene</th>
<th>JADI</th>
<th>MRI</th>
<th>Gene</th>
<th>MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>(associated with damage)</td>
<td></td>
<td>Followup</td>
<td>(associated with improvement)</td>
</tr>
<tr>
<td>n=110 vs n=119</td>
<td>upstream RANKL</td>
<td>0.0004</td>
<td>1.98</td>
<td>RANKL promoter</td>
</tr>
<tr>
<td>n=109 vs n=24</td>
<td>upstream RANKL</td>
<td>0.0036</td>
<td>0.57</td>
<td></td>
</tr>
<tr>
<td>n=55 vs n=118</td>
<td>upstream OPG</td>
<td>0.0094</td>
<td>1.68</td>
<td></td>
</tr>
<tr>
<td>Followup</td>
<td>(associated with no change)</td>
<td></td>
<td>Followup</td>
<td>(associated with no change)</td>
</tr>
<tr>
<td>n=101 vs n=17</td>
<td>IL1R2 intronic</td>
<td>0.0024</td>
<td>0.48</td>
<td>RANKL promoter</td>
</tr>
<tr>
<td>n=25 vs n=29</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=55 vs n=17</td>
<td>IL1R2 promoter</td>
<td>0.0043</td>
<td>2.05</td>
<td>IL19 intron</td>
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<td>n=10 vs 19</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=24</td>
<td>upstream IL1R2</td>
<td>0.0050</td>
<td>0.50</td>
<td>between IL1R2 and IL1R1</td>
</tr>
<tr>
<td>RANKL intronic</td>
<td></td>
<td>0.0090</td>
<td>9.21</td>
<td></td>
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<tr>
<td>n=34 vs 20</td>
<td>RANKL promoter</td>
<td>0.0009</td>
<td>1.91</td>
<td>IL6 promoter</td>
</tr>
<tr>
<td>n=17</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=23</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=17</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>n=34</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

IL-1RN, IL-1RAP, IL-6, TGFβ1, IL-10, IL-19, IL-20, IL-24. 391 tSNPs were genotyped using the illumina GoldenGate assay genotyping platform and KBioscience, UK. JADI-A scores, wrist MRI bone erosion scores, and X-ray Poznanski scores were taken at presentation (baseline) and after 1 year followup.

Results: At baseline patients were divided into those with no damage (JADI or MRI score of 0) or with damage (any score>0). At 1 year followup patients were divided into those who had improved, unchanged, or worsened. Significant tSNPs from genetic association analysis using PLINK are presented below. Table 1. We observed weak correlations between JADI-A and MRI scores (Spearman’s r = 0.298, p<0.0001), JADI-A and Poznanski scores (Spearman’s r = -0.288, p=0.012), and Poznanski and MRI scores (Spearman’s r = -0.381, p=0.001). Disease duration, activity, and treatment were varied and were not significantly associated with the damage parameters in this cohort.

Conclusion: Our findings suggest that polymorphisms in cytokine and bone remodeling genes such as RANKL or OPG may be associated with the degree of articular damage in JIA. Given the weak correlations we found between JADI-A and MRI scores, it is not surprising that different tSNPs were found to associate with MRI damage than with JADI-A damage. Further studies including a larger cohort of patients are needed to validate these findings.

Disclosure of interest: None declared.

P26
Genetic determinants of methotrexate treatment efficacy in patients with juvenile idiopathic arthritis

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Pediatric Rheumatology 2014, 12(Suppl 1):P26

Introduction: Single nucleotide polymorphisms (SNPs) are common (1%) variations in DNA sequence, which can be the reason for individual variability in drug efficacy and drug safety.

Objectives: To investigate the effect of single nucleotide polymorphisms in the genes for methotrexate (MTX) uptake and efflux mechanisms and in the genes of the adenosine pathway on response to therapy in JIA.

Methods: The data of 116 consecutive patients with JIA treated with MTX at the University Children’s Hospital Ljubljana from June 2011 to May 2014 have been retrospectively reviewed. The disease activity was measured by JADAS 71. score 3 and 6 months after the beginning of treatment with MTX and at the last follow up visit. All adverse events were noted separately for different organ systems. Genotyping of single nucleotide polymorphisms (SNP) in the genes of MTX transporters and in the adenosine pathway was performed using real time PCR methods. The following SNPs were analyzed: ABCB1 3435C>T (rs1045642), ABC2 24C>T (rs717620), ABC2 1019A>G (rs2804402), ABC2 1249G>A (rs2273697), ABC2 3465C>A (rs2231137), ABC2 421C>A (rs2231142), SLC19A1 174Ala>Val (rs4149056), SLC19A1 388 A>G (rs2306293), SLC19A1 int13 T>C (rs11045879), SLC19A1 (RFC1) 80G>A (rs1051266), ATIC (347C>G), AMPD (343C>T) and ITPA (94A>C). Kaplan Meier estimator and penalized Cox regression model were used for statistical analysis.

Results: The study group included 88 (76%) girls and 28 (24%) boys with JIA. 10 (9%) patients had systemic arthritis, 43 (37%) patients had polyarthritis (5 out of these were RF positive), 25 (22%) patients had persistent oligoarthritis, 22 (19%) extended oligoarthritis, 10 (9%) patients had juvenile psoriatic arthritis and 2 (2%) patients suffered from enthesitis related arthritis. Mean follow up time was 80 months. 75 (65%) patients were switched to higher dosage of methotrexate to achieve inactive disease. In total 52 (45%) patients had to be switched to biologic therapy due to treatment inefficacy or severe adverse events. Mean treatment duration until switching to biologic therapy was 17,5 months. Adverse events developed in 70 (60%) patients, 14 (12%) patients had severe adverse events and 10 (9%) patients discontinued MTX treatment because of adverse events. 16 (14%) patients were in remission without therapy at the last follow up visit. Using Kaplan Meier estimator ABCB1 3435C>T (rs1045642) and ABC2 1249G>A (rs2273697) were associated with probability of starting biologic treatment (P=0.1 and P=0.11). Using a penalized Cox regression model, ABCB2 1249G>A (rs2273697) was confirmed to be found associated to probability of starting biologic treatment (HR=1.09 vs wt).

Conclusion: ABCB2 1249G>A could be a useful early predictor for MTX treatment inefficacy. SNPs in MTX transporter genes and in the adenosine pathway could be factors to predict treatment outcome, but more studies need to be done.

Disclosure of interest: None declared.

P27
Risk factors for juvenile idiopathic arthritis: exposure to tobacco and environmental factors during and before pregnancy

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Pediatric Rheumatology 2014, 12(Suppl 1):P27

Introduction: Juvenile idiopathic arthritis (JIA) is a heterogeneous group of chronic arthritis that occurs in susceptible subjects and may be related to environmental triggers. In this regard, air pollution could be a potential
To evaluate the influence of exposures to inhaled environmental factors at the same time during pregnancy and one year before pregnancy on JIA diagnosis in residents of a large city.

Methods: A case-control study comprising 21 JIA and 40 controls matched by age and gender, residents in the metropolitan region of São Paulo. A structured and reliable questionnaire (kappa index for test-retest of 0.81) assessed demographic data and environmental inhalation exposure during pregnancy (occupational exposure to demolition, chalk, construction and/orerry dust, paints, varnish, gasoline vapor and/or battery fluids; the presence of industrial activities or gas station near the mother’s home/work, maternal tobacco exposure and exposure to tropospheric pollutants). Daily concentrations of inhaled particulate matter (PM10), sulphur dioxide (SO2), nitrogen dioxide (NO2), ozone (O3), and carbon monoxide (CO) were evaluated throughout one year in the pre-gestational and gestational period.

Results: The mean current age was similar in JIA and controls (11.5±3.78 vs 11.6±3.20 years, p=0.93). “Fetal smoking” (mother’s second and smoke exposure and/or smoking mothers at home) one year before pregnancy was significantly higher in JIA patients versus controls (52% vs. 20%, p=0.002) as was the presence of industrial activities or gas station at mother’s work place > 200 meters was significantly lower in JIA group (14% vs. 52%, p=0.003). In univariate analysis for one year before pregnancy, “fetal smoking” was significantly associated with JIA (OR4.4 CI95%1.4-14.0, p=0.012, respectively), while the presence of industrial activities or gas station at mother’s work > 200 meters had a significantly negative association with JIA (OR0.14 CI95%0.4-0.6, p=0.006). Regarding tropospheric pollutants no positive association was evidenced (p>0.05). In multivariate analysis for one year before pregnancy, “fetal smoking” remained risk factor for JIA (OR3.69 CI95%1.06-12.8, p=0.04) and the presence of industrial activities or gas station at mother’s work > 200 meters was protective factor for JIA (OR0.16 CI95%0.4-0.7, p=0.01). Regarding pregnancy, “fetal smoking” was significantly higher in JIA group (52% vs. 20%, p=0.01), whereas maternal occupational exposure, the presence of industrial activities or gas station at mother’s work place > 200 meters and the presence of industrial activities or gas station at mother’s home > 200 meters were significantly higher in controls (9% vs. 12%, p=0.016; 19% vs. 50%, p=0.02; 52% vs. 85%, p=0.008, respectively). In multivariate analysis during pregnancy, only the presence of industrial activities or gas station at > 200 meters had a significantly association with JIA (OR13 CI95%0.3-0.7, p=0.02).

Conclusion: Mother’s exposure to tobacco smoking may contribute to JIA onset, while exposure to long distance industrial activities or gas station could be a protective factor for this inflammatory chronic disease.

Disclosure of interest: None declared.

P29

TH17-phenotypes of juvenile idiopathic arthritis

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Pediatric Rheumatology 2014, 12(Suppl 1) p29

Introduction: Juvenile idiopathic arthritis (JIA) is a chronic disorder with unknown etiology and characterized by autoimmunity, infiltration of synovium by activated proinflammatory cells, synovial hyperplasia and progressive destruction of cartilage and bone. IL-17A is a proinflammatory cytokine that is expressed in the inflamed synovium. Th17 cells have been identified as main producers of this cytokine. IL-17A is a potent inducer of various cytokines and chemokines. In addition, this cytokine has been shown to have additive or even synergistic effects with TNFα and IL-1β on cytokine induction and tissue destruction.

Objectives: To characterize Th17 pathway in children with different subtypes of JIA as a mechanism for determining the nature of the clinical course and outcome of the disease.

Methods: PB samples were obtained from 100 patients with different subtypes of JIA and 20 PB samples from healthy control. The bases of quantitative evaluation of Th17 cells were taken directly determination of IL-17A. IL-17A and TNFα were determined in serum samples of the patients by ELISA.

Results: Highest level of Th17 cells, IL-17A, IL-1β and IL-6 were detected in PB in children with active HLA B27-associated arthritis (p=0,001, p=0,001, p=0,007 and p=0,05, respectively) and systemic onset of JIA (p=0,002, p=0,021, p=0,04 and p=0,03, respectively) in compare with oligo-, polyarticular and pauciarticular where level of these cytokines was significantly different from healthy control. Statistically significant differences in level of TNFα in serum in all subtypes of JIA were not obtained. Level of IL-17A>1.04 pg/ml and Th17 memory cells>3,2% were associated with high risk of active disease (OR=3,727, p=0,003) and level of IL-17A>1.04 pg/ml and IL-6>10,1 pg/ml were associated with the risk of osteoporosis (OR=2,905, p=0,008).

Conclusion: The improvement in HRQoL after start of etanercept was sustained after 8.5 years. Disability was low. On many aspects of daily life, patients functioned comparably to or better than the general population. The need for surgery for 14% of patients stresses the importance of early treatment of JIA. Chronic pain - also when the disease is inactive - remains an important issue that should not be overlooked.

In order to identify phenotypes of JIA hierarchical cluster analysis followed by discriminant analysis were used. Thus, can be distinguished at least Th17-dependant and Th17-independent phenotypes. Th17-dependant phenotype includes children with different subtypes of JIA with high disease activity and high risk of bone and cartilage destruction. Key inflammatory mediator of this phenotype is IL-17A. Th17-independent phenotype characterized by lower disease activity and lower risk of bone and cartilage destruction.

Conclusion: Our data suggest that Th17 cells and their cytokines play a crucial role in pathogenesis of HLA B27-associated arthritis and systemic onset of JA. This research allows determining the level of Th17 cells and IL-17A as markers of high risk of persistence of «active» disease, while low level of Th17 cells and IL-17A increase the chance of a favorable disease outcome.

Disclosure of interest: None declared.

P30
Clinical and radiological features of down’s arthropathy
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National Centre for Paediatric Rheumatology (NCPR), Dublin, Ireland
Pediatric Rheumatology 2014, 12(Suppl 1):P30

Introduction: The ‘arthropathy of Down syndrome’ was first described in 1984. Three decades on we still have limited literature on the clinical and radiological features of this arthritis, despite the fact that it is thought to be 3-6 times more common than JIA in the general paediatric population. Down’s Arthropath (DA) is rarely recognised at onset, and remains under-diagnosed and largely under-reported in this population group. Ireland has one of the highest Trisomy 21 birth rates in Europe (1/547), & therefore provides an ideal setting for such a study. Research Q’s - 1. What are the clinical & radiological features of DA? 2. Is DA missed, leading to a delay in dx?

Objectives: To perform a musculoskeletal examination on children with T21, aged 0-18 years & document - 1. Features of presence to suggest old and/or present arthritis. 2. Radiological findings.

Methods: From May 2013 to September 2014, Children with T21 (aged 0-18 years) will be invited to attend a screening clinic. Screening involves completion of a health questionnaire & musculoskeletal examination. Suspected cases of DA will be invited to attend the NCPR for dx, Rx & F/U as per normal clinical practice.

Results: To date, 370 children with Trisomy 21 have enrolled in the study, 56% Male. 17 new cases of DA have been detected, only three (17.6%) of which were referred with suspected arthritis. In total, 28 children with DA now attend the NCPR for management of their arthritis, the largest cohort ever reported in the literature. We estimate the Point Prevalence of DA in Ireland to be 17-18/1000. For comparison, the UK Prevalence of JIA is 1-2/1000.

Conclusion: Children with T21 are at increased risk of developing arthritis, however there is often a delay in diagnosis. Reasons for this are multifactorial. Early Dx & Rx of DA is key to preventing irreversible joint destruction & long-term functional impairment. MTX nasea is a significant barrier to successful treatment of DA with this DMARD. However, a good response to steroid joint injections has been observed. We advocate that children with T21 have an annual musculoskeletal assessment as part of their Health Screening Programme.

Disclosure of interest: None declared.

Table 1(abstract P30) Comparison of study characteristic by diagnosis

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>DA (n=28)</th>
<th>JIA (n=21)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small Joint Involvement</td>
<td>Mean (sd)</td>
<td>4.46 (1.95)</td>
<td>3.05 (2.29)</td>
</tr>
<tr>
<td>Time to Diagnosis</td>
<td>Mean (sd)</td>
<td>1.71 (1.47)</td>
<td>0.74 (0.36)</td>
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P31
Single nucleotide polymorphism of NLRP3 (Q705K) in juvenile spondyloarthritides and oligo/ polyarticular juvenile idiopathic arthritis
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Pediatric Rheumatology 2014, 12(Suppl 1):P31

Introduction: The NLRP3 inflammasome is a key component of the innate immune system serving as an intracellular sensor of microbial components and cell injury. Gain-of-function mutations of the NLRP3 gene, such as single nucleotide polymorphism (SNP) Q705K, lead to autoproteolytic activation of caspase 1, resulting in excessive and uncontrolled production of proinflammatory cytokines. This may represent the mechanism by which an inflammatory loop is triggered leading to a long-term uncontrolled inflammatory phenotype.

Objectives: Our objective was to compare the frequency of SNP Q705K of NLRP3 among patients with juvenile spondyloarthritides (JSpA) and juvenile idiopathic arthritis (JIA).

Methods: DNA was extracted from blood samples of 37 JSpA patients and patients with oligoarticular or polyarticular JIA, diagnosed according to ILAR criteria. Polymorphism of the NLRP3 (Q705K) was determined using real time and multiplex PCR.

Results: Among 37 genotyped patients, 24 patients with JSpA (92.31%) and 9 patients (81.82%) with JIA were carriers of the wild type allele. Only 2 patients in each group were heterozygous for NLRP3 (Q705K) polymorphism (7.69% in JSpA and 18.18% in JIA group). Although the observed frequency among groups was not statistically significant (Pearson Chi-square 0.8820724, p=0.64337), the frequency of allele polymorphism observed among our study population was higher (10.81%) than previously described in the general population (6.5%).

Conclusion: The frequency of SNP Q705K of the NLRP3 gene did not differ among JSpA and JIA patients. There was also no evidence that variant of NLRP3 is a major risk factor for JSpA or JIA, however, lack of susceptibility should be confirmed in a larger group of patients.

Disclosure of interest: None declared.

P32
Complement analysis reveals new biomarkers in patients with juvenile idiopathic arthritis
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Pediatric Rheumatology 2014, 12(Suppl 1):P32

Introduction: The juvenile idiopathic arthritis is a well researched disease in the group of autoimmunopathies. Beside the deregulation of T-cells and cytokines also the complement system is involved in the pathogenesis of this group of diseases.

Objectives: This prospective longitudinal study investigated the contribution of the complement system in patients with juvenile idiopathic arthritis, using practicable ELISA techniques (Wieslab® screening kit; SC5b9 soluble terminal complement complex ELISA).

Methods: Serum and plasma of the peripheral blood and the synovial fluid were investigated for the activity of the three complement pathways - classical (CP), mannose binding lectin (MBL), and the alternative pathway (AP) and total complement activity by measuring SC5b9. Results where compared to published reference controls and 18 children without activation of inflammation as an age matched control group.
In total 57 samples of peripheral blood (PB) and 8 samples from synovial fluid (SF) from 28 children with JIA were investigated in a longitudinal observation during acute phase and remission.

**Results:** The screening of complement system showed debasement of the AP (8 of 10) and CP (7 of 10) in patients during acute phase (7 of 10). The SC5b9 measurement showed a significant (p<0.0002) higher amount in plasma (3.6AU/ml in median) and serum (31.4AU/ml) during acute phase compared to the control group (serum – 7.72AU/ml and plasma –1.25AU/ml in median).

**Conclusion:** In conclusion the study confirmed, that the AP and CP of the complement system are main contributors in the pathogenesis of JIA. Because of significant elevation of SC5b9 in acute phase of JIA, complement blockade with Anti-CS may be a therapeutically option in the future.

**Disclosure of interest:** None declared.

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**P33**

**Ankle arthritis predicts worse outcome in children with juvenile idiopathic arthritis**

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**Introduction:** The ankle joint is commonly involved in children with Juvenile Idiopathic Arthritis (JIA) and ankle arthritis predicts a more severe disease according to earlier studies. These studies have mainly been cross-sectional and the results are problematic to generalize to broader populations.

**Objectives:** To evaluate the presence of ankle arthritis in children with JIA in a population-based cohort, to describe clinical characteristics in children with ankle arthritis and to evaluate the relation between ankle arthritis and remission status eight years after disease onset.

**Methods:** In total 440 children with JIA were included prospectively in a 2014, Volume 12 Suppl 1:

**Results:** Of the 440 children with JIA, 251 (57%) experienced ankle arthritis. Remission was defined according to the preliminary criteria of ILAR. The odds ratio was evaluated considering the presence of at least one single joint involvement as predictor. P values less than 0.05 were considered significant.

**Conclusion:** Ankle joint involvement in children with JIA is associated with failure to achieve remission.

**Disclosure of interest:** None declared.

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**P34**

**The role of cannabinoid receptor 2 in oligo/poly-articular juvenile idiopathic arthritis**

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**Introduction:** Juvenile Idiopathic Arthritis (JIA) is an inflammatory chronic disease concerning joints and others structures. According to International League of Association for Rheumatology (ILAR) seven subtypes of arthritis can be defined in relation with the number of joints and the extra-articular involvement occurring in the first six months of disease. Although JIA pathogenesis is not completely clear is known that T-cell activation is a feature of oligoarticular and polyarticular JIA. The endocannabinoid system is involved in immune regulation by reducing cells activation, modulating Th1 and Th2 balance, inhibiting proinflammatory cytokine production, T-cell and other cellular components of immune system express cannabinoid receptor 1 and 2 (CB1-CB2).

**Objectives:** It has been demonstrated that a CB2 common variant, glutamine-arginine substitution Q63R, differently modulated the EC-induced inhibition of T-cells proliferation. T lymphocytes from RR homozygotes had a two fold reduction of EC-induced inhibition of proliferation compared to those from QQ homozygotes, suggesting this CB2 variation as a risk factor for autoimmune diseases. The aim of this study is to investigate whether the functional variant Q63R of CB2 is associated with the susceptibility to oligo/polyarticular JIA and with its clinical features.

**Methods:** This study includes 171 children suffering from JIA (124 females; 47 males) genotyped for the CNR2 rs35761398 variant causing the substitution Q63R. JIA diagnosis was made according to ILAR criteria and treatment was assigned with recommendations of the American College of Rheumatology. For each patient we evaluated number of affected joints, age of onset, comorbidities, presence of autoimmune diseases associated and relapses. The presence of uveitis was considered a comorbidity. Celiac disease, thyroiditis and diabetes mellitus were considered autoimmune disease associated. According to Wallace criteria any symptom appearing after six months from remission was considered as relapse of arthritis. 600 healthy children previously genotyped for the CB2 Q63R functional variant were used as controls. P values less than 0.05 were considered significant.

**Results:** We genotyped 105 oligoarticular and 66 polyarticular JIA affected children for the CNR2 rs35761398 variant causing the substitution Q63R. JIA diagnosis was made according to ILAR criteria. For each patient we evaluated number of affected joints, age of onset, comorbidities, presence of autoimmune diseases associated and relapses. The presence of uveitis was considered a comorbidity. Celiac disease, thyroiditis and diabetes mellitus were considered autoimmune disease associated. According to Wallace criteria any symptom appearing after six months from remission was considered as relapse of arthritis. 600 healthy children previously genotyped for the CB2 Q63R functional variant were used as controls. P values less than 0.05 were considered significant.

**Conclusion:** None declared.

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**P35**

**The local and systemic cytokine signatures of juvenile idiopathic arthritis are attributable to TCR-independent activation of two novel subsets of prematurely senescent t cells found in synovial fluid**

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**Introduction:** The screening of complement system showed debasement of the AP (8 of 10) and CP (7 of 10) in patients during acute phase (7 of 10). The SC5b9 measurement showed a significant (p<0.0002) higher amount in plasma (3.6AU/ml in median) and serum (31.4AU/ml) during acute phase compared to the control group (serum – 7.72AU/ml and plasma –1.25AU/ml in median).

**Conclusion:** In conclusion the study confirmed, that the AP and CP of the complement system are main contributors in the pathogenesis of JIA. Because of significant elevation of SC5b9 in acute phase of JIA, complement blockade with Anti-CS may be a therapeutically option in the future.

**Disclosure of interest:** None declared.
Introduction: Cytokine upregulation is considered a hallmark of the autoimmune and inflammatory manifestations in Juvenile Idiopathic Arthritis (JIA). Whilst T cells are thought to contribute to cytokine dyscrasia, the underlying mechanism(s) is poorly understood.

Objectives: We have reported recently that JIA patients carry high numbers of unusual senescent CD8 T cells bearing CD31, a molecule known mediate leukocyte diapedesis into sites of injury. In the present work, we re-surveyed the T cell populations of patients for other CD31+ senescent T cell subsets. We hypothesized that CD31 signaling in these senescent cells is a self-perpetuating mechanism for the upregulation of inflammatory cytokines in JIA.

Methods: Blood and/or synovial fluid (SF) were collected from children with oligoarticular (Oligo) or polyarticular (Poly) JIA. Blood was also collected from age-matched healthy children. By multiplex analysis, cytokine profiles of plasma and SF were determined. By multicolor flow cytometry, abT cell phenotypes in blood and SF were examined. Based on results of the multiplex assay, receptor crosslinking bioassays for cytokine production, and proteomic screening for signaling substrates were performed using primary SF T cells, and transfomed T cells expressing CD31.

Results: The cytokine signature of JIA is characterized by the dominance of IL-6, IL-10 and TNFα in both blood and SF. In addition to CD28 CD31+ CD8 abT cells, we found a novel subset of DN abT cells that were CD4+ CD8 CD28−, but were CD31+. CD31 receptor cross-linking of fresh SF T cell enriched for these abT cell subsets showed specific induction of IL-6, IL-10, IL-17, TNFα, and IFNγ. These responses were accompanied by phosphorylation of several signaling substrates including ZAP70 and RelA.

Specificity of TCRαβ-independent, CD31-driven activation was verified by similar bioassays using somatic T cell line mutants expressing CD31, but deficient in TCR or CD3. Pharmacologic inhibitors of signaling substrates abrogated protein phosphorylation as well as cytokine production, indicating that CD31 ligation sufficiently and effectively bypass conventional TCR-mediated route of T cell activation.

Conclusion: Blood and SF cytokine profile of JIA is dominated by five cytokines. Such profiles are recapitulated by CD31-driven activation of senescent CD8 and DN abT cell subsets. TCR-independent CD31 l-driven cellular activation indicates maladaptive T cell function in JIA. Further investigation on the CD31 signaling cascade may pave way to innovations in cell-targeted therapy in JIA.

Disclosure of interest: None declared.

P36

Is it worth including subtalar joint in ultrasound ankle assessment of patients with juvenile idiopathic arthritis?

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Pediatric Rheumatology 2014, 12(Suppl 1):P36

Introduction: The ankle is a complex anatomical structure owing to the multiple joint recesses and surrounding tendons. The involvement of subtalar joint (STJ) can be difficult to discern clinically from tibiotalar, tarsal or adjacent tendon disease. To date, only a few efforts have been centred around ultrasound (US)-detectable assessment of STJ in juvenile idiopathic arthritis (JIA).

Objectives: 1) To assess the frequency of US-detectable involvement of STJ, 2) To compare clinical versus US assessment in STJ detection, 3) To determine the most informative scanning approach to STJ.

Methods: Fifty consecutive JIA patients, followed at the study center, with clinically-detected ankle involvement were enrolled. If both the ankles were involved, only the most affected side was selected for US. All clinical and US examinations were performed by experienced physicians and ultrasonographers, respectively, blinded to each other evaluations. US findings were collected using a lateral, medial and posterior STJ scanning approach. US synovitis was considered when both or either of joint effusion and synovial hypertrophy, with or without power Doppler signal, were visualized. Inter-observer reliability of US STJ involvement was tested using Cohen’s kappa coefficient in a subgroup of 24 patients. A control group of 10 healthy subjects was recruited.

Results: None of the controls showed US STJ synovitis. US detected synovitis in 27 (54%) STJs of patients. Agreement between clinical and US assessment for presence and absence of STJ involvement was found in 17 (34%) and 16 (32%) ankles, respectively. In 10 (20%) STJs not considered to be clinically affected, synovitis was found on US. In 7 (14%) ankles labelled as having STJ involvement on clinical examination US was negative for STJ, but showed the involvement of different anatomical sites (midfoot, tibiotalar joint, tendons). Overall, the concordance between clinical and US evaluation was poor (k=0.32). The Cohen-kappa value for inter-observer reliability of STJ involvement on US was high (k= 0.92). All patients having US findings in the medial and/or posterior side of STJ presented also with US findings using the lateral scanning approach, but the reverse was not true.

Conclusion: US is more sensitive than clinical evaluation in the assessment of STJ in ankles with active disease. The high frequency of its involvement may suggest to include the assessment of STJ in US scanning protocols. In this perspective, the lateral approach to the joint seems to be more appropriate for US evaluation of STJ involvement.

Disclosure of interest: None declared.

P37

Musculoskeletal ultrasound findings of articular manifestations on juvenile primary Sjögren’s syndrome

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Pediatric Rheumatology 2014, 12(Suppl 1):P37

Introduction: Articular manifestations (joint swelling, joint tenderness) are common extra-glandular manifestations of primary Sjögren’s syndrome (SJ). In past studies those have been reported that anti-cyclic citrullinated peptide antibody (ACPA) is associated with arthritis in adult SJ’s and that there is no clear method to distinguish arthritis of primary SJ from early rheumatoid arthritis, but there is no report on children. Musculoskeletal ultrasound (USUS) can clearly evaluate arthritis or enthesis which are difficult to assess in detail by only physical examination.

Objectives: To investigate USUS findings in juvenile primary SJ having articular manifestations with or without ACPA.

Methods: Subject patients are 8 children who were diagnosed as juvenile primary SJ’s with articular manifestations between February 2013 and March 2014. We retrospectively evaluated sex, age of disease onset, disease duration, physical findings, blood examination data (rheumatoid factor and autoantibody) and USUS findings from clinical records. All patients underwent salivary gland biopsy and satisfied 2012 American College of Rheumatology classification for Sjögren’s syndrome. Joints (shoulder, sternoclavicular, elbow, wrist, metacarpophalangeal, proximal interphalangeal, hip, knee, ankle, metatarsophalangeal) and 5 entheseal sites of the lower limbs were scanned by a trained physician.

Results: In 8 patients (7 females and 1 male), mean age of disease onset was 10.9 ± 3.3 years old. Mean disease duration was 0.9 ± 1.2 years. Six patients were positive for rheumatoid factor and 3 patients were positive for ACPA. 2 patients were positive for anti-SS-A antibody and 3 patients were positive for anti-SS-B antibody. The total times of USUS were 19 times, and 560 joints/128 entheseal sites were scanned. In 6 patients, USUS revealed abnormal findings to 42 of 560 joints (35/286 joints of ACPA positive patients vs. 7/274 joints of ACPA negative patients, P<0.001). Power Doppler (PD) signal was found at 28 joints in 3 patients with ACPA, while no PD signal was detected in 5 patients without ACPA. One patient developed arthritis with PD signal in the course of illness. Tenosynovitis was detected at 15 joints in 5 patients. Active enthesitis with PD signal and bursitis were found at Achilles tendons in 2 patients with ACPA. By MSUS, subclinical arthritis was found in some joints (to 23 in 286 joints of ACPA positive patients vs. to 4 in 274 of ACPA negative patients, P=0.001). On the other hand, there found no abnormality in 67 swelling and/or painful joints by MSUS (31/286 joints of ACPA positive patients vs. 36/274 joints of ACPA negative patients, P=0.40). Bone erosion was not detected in our cases. From this study, we also did not found calcifications nor entheseophytes even on joints with PD signal positive arthritis or enthesis. This result is comparable to past report that arthritis with SJ are usually non-erosive. However, it is capable that this result is just because of being in early phase.
or we started treatment promptly, we have to observe their course deliberately.

Conclusion: We suggest that juvenile primary SJ patients with ACPA have

**Disclosure of interest:** None declared.

### P38
Decrease health-related quality of life in pediatric leprosy patients with musculoskeletal manifestations

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**Introduction:** Leprosy, also known as Hansen’s disease, is caused by the *Mycobacterium leprae*. The clinical features of pediatric leprosy include several skin lesions, numbness of the skin, damage of peripheral nerves, arthralgia and arthritis. In this regard, we recently reported that musculoskeletal manifestations were associated with severe leprosy in children and adolescents, especially in patients presenting nerve function impairment and neuropathy. Furthermore, adult leprosy patients could present a decrease in health-related quality of life (HRQL), particularly in physical capacity and social participation domains. To our knowledge, HRQL was rarely reported in pediatric leprosy, and the impact of musculoskeletal manifestations on HRQL was not previously investigated.

**Objectives:** To evaluate the HRQL in pediatric leprosy patients.

**Methods:** A cross-sectional study included 47 leprosy patients and 45 healthy subjects. The HRQL was measured by Pediatric Quality of Life Inventory 4.0 (PedsQL 4.0), and evaluated physical, emotional, social and school domains. The leprosy patients were classified by Ridley and Jopling classification criteria and assessed according to clinical musculoskeletal manifestations, laboratory and radiographic examinations.

**Results:** The median of current age was similar in leprosy patients and

controls [12 (6-18) vs. 15 (5-18) years, p=0.384], likewise the frequencies of female gender (p=0.835) and middle/lower Brazilian socio-economic classes (p=1.0). The domain school activities, among the child-self report was significantly lower in leprosy patients compared to controls in the age group of 13-18 years (75 (45-100) vs. 90 (45-100), p=0.021). The other domains were alike in both groups (p=0.05). At least one musculoskeletal manifestation (arthralgia, arthritis and/or myalgia) was observed in 15% of leprosy patients and none in controls (p=0.012). Further comparison between all leprosy patients showed that the median of the physical capacity domain [91.25 (50-100) vs. 98.44 (50-100), p=0.036] and school activities domain by child-child report [60 (50-85) vs. 90 (45-100), p=0.042] were significantly lower in patients with musculoskeletal manifestations compared to patients without these manifestations. No differences were evidenced between the other HRQL parameters in both groups, reported by patients and parents (p=0.05).

**Conclusion:** A reduced HRQL was observed in pediatric leprosy patients with musculoskeletal manifestations. Specific interventions in physical and school activities are required to improve HRQL in this high-risk population.

**Disclosure of interest:** None declared.

### P40
Molecular dissection of human b-cell tolerance - insights from primary immunodeficiencies

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**Introduction:** Autoimmune diseases result from the failure of self-tolerance mechanisms and the ability of regulatory T cells to maintain the balance between self-reactive and self-tolerant T cells. In contrast to the many insights that have been obtained from animal models and studies of human autoimmune diseases, little is known about the mechanisms that regulate B-cell tolerance in humans. CD19 is a co-receptor expressed on B cells and regulates B-cell tolerance in humans. CD19 has been shown to play an important role in the suppression of autoimmunity. Proper CD19 expression may normally prevent autoimmunity.

**Objectives:** To investigate if CD19 expression can prevent autoimmunity in humans.

**Methods:** To test the function of the central B-cell tolerance checkpoint in humans, we analyzed ELISA and immunofluorescence tests the reactivity of recombinant antibodies cloned from single transitional B cells from individuals carrying CD19 mutations. Additionally, we analyzed alterations in
TLR and BCR signaling pathways in CD19-deficient human B cells using flow cytometry and immunoblotting.

Results: We found that individuals carrying CD19 mutations displayed defective central B-cell tolerance checkpoints. In addition, CD19-deficient transitional B cells were enriched in anti-nuclear clones, a feature previously observed in IRAK4- and MYD88-deficient patients in which TLR7/9 sensing nucleic acids cannot signal. Therefore, we investigated the functions of these TLRs in B cells in the absence of CD19 expression. CD19-deficient human B cells displayed defective up-regulation of activation markers after TLR7/9 triggering and failed to induce BTK, AKT but not p38 MAPK or IκB-α phosphorylation after TLR7/9 stimulation. Additionally, inhibitors blocking BTK, AKT and PI3K function as well as mutations in BTK impaired CD19-dependent TLR7/9 responses in healthy donor’s B cells.

Conclusion: Thus, CD19 and its PI3K/BTK/AKT signaling pathway is essential for B-cell activation and the establishment of central human B-cell tolerance by mediating the function of both BCRs and TLRs that recognize self-antigens during early B-cell development.

Disclosure of interest: None declared.

P42

PRKDC mutations associated with immunodeficiency, granuloma and aie-dependent autoimmunity

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Pediatric Rheumatology 2014, 12(Suppl 1):P42

Introduction: PRKDC encodes for DNA-dependent protein kinase catalytic subunit (DNA-PKcs), a kinase that forms part of a complex (DNA-PK) crucial for DNA double-strand break (DSB) repair and V(DJ) recombination. In mice, DNA-PK also interacts with the transcription factor AIRE (autoimmune regulator) to promote central T cell tolerance.

Objectives: We sought to understand the causes of an inflammatory disease with granuloma and autoimmunity, associated to decreasing T and B cell counts over time diagnosed in two unrelated patients.

Methods: Genetic, molecular, and functional analyses were performed to characterize an inflammatory disease evocative of a combined immunodeficiency.

Results: We identified PRKDC mutations in both patients. These patients exhibited a defect in DNA DSB repair and V(DJ) recombination. Circulating T cells had a skewed cytokine response typical of Th1 and Th2 profiles. Moreover, mutated DNA-PKcs failed to promote AIRE-dependent transcription of peripheral tissue antigens in vitro. The latter defect correlated in vivo, with the production of anti-Calcium Sensing Receptor (anti-CaSR) autoantibodies, which are usually found in AIRE-deficient patients.

Conclusion: Deficiency of DNA-PKcs, a key AIRE partner, can present as an inflammatory disease with organ-specific autoantibodies and these findings highlight the essential role of DNA-PKcs in regulating autoimmune responses and maintaining AIRE-dependent tolerance in human.

Disclosure of interest: None declared.

P43

High Treg development in the first year of life gives insight into immune regulation

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Pediatric Rheumatology 2014, 12(Suppl 1):P43

Introduction: Juvenile Idiopathic Arthritis (JIA) pathology is characterized by a disregulated adaptive immune system. This fact is exemplified by reduced regulatory T cell (Treg) functionality and increased T helper (Th17) cell activity.

Objectives: In order to further understand the relation between Treg and Th17 development, we investigated the induction of these cells from naive T cells in early human life.

Methods: For this, we compared cells from umbilical cord blood (CB) with cells from adult volunteers, as well as cells from schisiss patients who...
We show that upon activation, CB cells easily adopt a Treg phenotype, whereas Th17 cells cannot be induced. Although production of inflammatory cytokines is dramatically lower in CB cells, addition of Th17 inducing cytokines IL-1β or IL-6 did not influence this phenomenon. Instead, an increased programmed death (PD-1) signaling and decreased Th17 defining transcription factor RORC activation underlie the prevention of inflammatory T cell activity. The propensity for Treg development is a phenomenon which we still observed in samples from 12 month old children, whereas we found Th17 cell development as early as three months after birth. This development in the first year of life is likely related to prevention of aberrant T cell responses towards self and the developing microbiome.

Conclusion: These data give more insight into the development of the immune system and inflammation and can lead to novel targets in JIA therapy, aiming at the balance between Treg and Th17 cells.

Disclosure of interest: None declared.

The new proposal classification criteria for juvenile spondyloarthropathies
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Pediatric Rheumatology 2014, 12(Suppl 1):p45

Potential biomarkers and therapeutic targets in juvenile spondyloarthropathies
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Pediatric Rheumatology 2014, 12(Suppl 1):p44

Introduction: To understand disease mechanism and close the gap between genotype and phenotype, majority of studies today use the high-throughput methods that allow us to study genes on a global scale. One of these methods is expression profiling which generates a "snapshot" of cellular activity at the time of analysis, telling us exactly what processes are occurring. By comparing disease and control samples it is possible to elucidate the processes contributing to disease and how they are altered. To date a number of disparate expression profiling studies in patients diagnosed with spondyloarthropathy (SpA) have been undertaken, but results of these studies were often inconsistent. To the best of our knowledge, there has been no expression profiling study with RNA isolated from whole blood in a cohort of patients diagnosed with juvenile spondyloarthropathies (JSpA) using ILAR criteria for enthesitis related arthritis (ERA), with known HLA genotype and calculated odds ratio (OR) for disease development. Further on, there was no study in which expression of selected genes was independently confirmed in new cohorts of unselected and treated patients diagnosed with JSpA, as well as with other forms of juvenile idiopathic arthritis (JIA).

Objectives: The aim of the present study was to identify and confirm gene signatures and novel biomarkers in various cohorts of untreated and treated patients diagnosed with JSpA and other forms of JIA.

Methods: Total RNA was isolated from whole blood of 45 children with known HLA genotype, calculated odds ratio for disease development and diagnosis of JSpA according to ILAR criteria, 11 children with oligo- and polyarticular forms of JIA, as well as 12 age and sex matched control participants without diagnosis of chronic inflammatory disease. DNA microarray gene expression with Affymetrix GeneChip was performed in 11 patients with JSpA and in four healthy controls, along with bioinformatics analysis of retrieved data (DAVID, GSEA, IPA). Carefully selected differentially expressed genes (TLR4, NLRP3, PTPRN2, CXCR4, DUSP6, TNFSF4, MAP2K2, MAPKBP1, MYST3, PTPN12) where analyzed by qRT-PCR in all study participants.

Results: Microarray results and bioinformatics analysis revealed 745 differentially expressed genes involved in processes such as antigen recognition and activation of immunological response, migration of inflammatory cells and regulation of the immune system. qRT-PCR analysis of selected genes confirmed data universality and specificity of expression profiles in JSpA patients.

Conclusion: The present study has identified differences in the expression of genes related to various processes responsible for JSpA development.

Among these, the genes of highest importance, which showed consistent expression in study patients diagnosed with JSpA, were TLR-4 and NLRP3, which can lead to the development of systemic autoimmunity, as well as CXCR4 and PTPN12, which can drive other processes important for pathophysiology of JSpA. We strongly believe that our results represent an important step toward a better understanding of the molecular mechanisms and complex pathophysiology of JSpA, while highlighted genes and their products could have a prognostic value and potential therapeutic use.

Disclosure of interest: None declared.

P45

P46
The demographic and clinical characteristics of a turkish enthesis-related arthritis cohort: a single center experience

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Pediatric Rheumatology 2014, 12(Supp 1):P46

Introduction: Enthesitis-related arthritis is a subgroup of JIA, which is encountered more frequently in Turkish patients than the European populations. Our knowledge about the difference of disease characteristics between Turkish ERA patients and other populations are limited.

Objectives: To evaluate the demographic and clinical characteristics of a Turkish ERA cohort and to identify the distinguishing features of patients who required anti-TNF α treatment compared to the patients who did not.

Methods: The hospital charts of patients who were diagnosed as ERA in our department between 2000-2013 according to the ILAR criterion were retrospectively evaluated. The demographic and clinical characteristics of patients were recorded. The characteristics of patients in whom anti-TNF α treatments were indicated were compared with the other patients on conventional therapies.

Results: A total of 100 patients were included. Eighty five percent were males. The mean age at onset of disease was 11.7 ± 2.9 years, age at diagnosis was 13.2 ± 2.8 years and delay time for diagnosis was 1.5 ± 1.8 years. There was a negative correlation between the age at disease onset and delay time for diagnosis (r=-0.382, p=0.000). The family history for ankylosing spondylitis was present in 63% patient. HLA B27 was available in 87 patients and positive in 60% of them. Erythrocyte sedimentation rate (ESR) was high in 69 patients and normal in 31 at the time of diagnosis. Enthesitis was positive in 65 patients, the most common site being the Achilles followed by plantar fascial insertion at calcaneus. Fifty patients had radiologically proven sacroilitis (14 unilateral, 36 bilateral). Thirty six patients had hip involvement (19 unilateral, 17 bilateral). Fifty seven patients had ankle and/or knee involvement. Tarctitis was present in 22 patients. Only 7 patients had anterior uveitis. The treatments used were as follows: systemic corticosteroid use, intraarticular steroid injection, methotrexate (n=21), sulfasalazine (n=97). Anti-TNF α treatments were used in 21 patients (etanercept 13, adalimumab 8). High ESR, tarctitis, sacroilitis, hip involvement and systemic corticosteroid use were found associated with anti-TNF α requirement. There was not a significant association between the delay time for diagnosis and anti-TNF α use.

Conclusion: The presented Turkish cohort displayed some remarkable differences from other series reported in the literature:

- Lower frequency of HLA B27 positivity
- Lower frequency of anterior uveitis

The patients who had the mentioned characteristics at the time of diagnosis were seen to have more severe disease that required anti-TNF α treatment:

- High ESR
- Tarctitis
- Sacroilitis
- Hip involvement
- Systemic corticosteroid use

Disclosure of interest: None declared.

P47
The intestinal microbiota in enthesis-related arthritis

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Pediatric Rheumatology 2014, 12(Supp 1):P47

Introduction: There are no official published recommendations how and when to stop treatment with biologics when remission achieved.

Objectives: Primary objective of this study was to evaluate influence of JIA subtype and duration of metotrextate (MTX) and steroids treatment on time to achieve and ability to maintain remission in JIA patients on biologic treatment.

The second aim was to establish if there is contribution of tumor necrosis factor α (TNFα–308) promoter and FokI vitamin D receptor (VDR) polymorphism on clinical outcome and possibility to discontinue treatment in JIA patients treated with biologics.

Methods: 68 JIA patients treated with etanercept from Serbian biologic registry were included and retrospective data analysis performed. Genomic DNA was extracted from blood samples and TNFα–308 promoter and FokI VDR polymorphism was evaluated using the PCR-RFLP method. Disease subtypes, activity and treatment efficacy were collected during six years following period in intervals after commencing etanercept treatment: 6 months, 1 year and annually thereafter. Disease remission, as a condition to stop biologic treatment, was defined using Wallace and all criteria [1].

Results: At enrolment JIA patients mean age were 183.34±60,58 months, disease duration 70.29±44,57 months, average dose of MTX 13.85±4.47 mg/m2/week. Eanesthesia treatment could be stopped after 42.66±21.64 months with sustained remission during the next 30.33±21.04 months.
Therapy resistant patients required higher doses of MTX for a longer period, with statistically significant in systemic JIA (15.97±5.6 vs. 13.15±4.55, p=0.016). Remission in this patients was shorter and they needed retreatment with biologics (16.31±18.55 vs. 35.8±19.5, p=0.001) due to disease worsening. Treatment inefficacy was present in systemic JIA with the longest etanercept treatment 5.9±5.97 and shortest remission 17.67%±9.82, while etanercept therapy was the most effective in RF–JIA patients. There was no statistically significant difference in cumulative dose of steroids in different JIA subtypes. The distribution of TNFα–308 (GG, GA, AA) and FokI VDR genotypes (FF, Ff, ff) was not significantly different among JIA subtypes. After six years follow up period 37% (54.5%) patients were in remission (20 patients with FF–GA and 17 patients with FF–GA polymorphism). Associate presence of FF–GA genotype was present more frequently in patients who needed longer treatment and have had shorter remission time.

Conclusion: JIA patients needing higher MTX doses to control disease and have associated presence of GA–FF polymorphisms (for TNFα–308 promoter and FokI VDR, respectively) have less chance to achieve and sustain remission off biologics, especially in systemic JIA. 

Disclosure of interest: None declared.

Reference

P49
Update on the juvenile systemic sclerosis inception cohort www.
juvenile-sclerodema.com
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Pediatric Rheumatology 2014;12(Suppl 1):P49

Introduction: Juvenile systemic sclerosis (JSSc) is an orphan autoimmune disease. Currently only retrospective data is existing regarding the organ involvement and evolvement of the disease. Our project is the first project, where in a prospective manner and with a protocol regarding standardized assessment of the organ systems and quality of life in early JSSc patients are assessed.

Objectives: to learn about the evolvement of juvenile systemic sclerosis

Methods: Patients with less than 18 months of disease duration, after the prospective evaluation of this project are prospectively assessed, using a standardized protocol.

Results: We report the patient characteristics at time point 0, 6 and 12 months of their follow up. We present data on 25 patients. The mean follow up of the patients in the cohort are 3.5 years. No patient died during the follow up. Eighteen of the 25 patients were female. The mean age of the onset of Raynaud symptomats was 10.4 years, the youngest patient was 2.0 years of age. The mean age at the onset of the non-Raynaud symptomats were 11.0 years. 19 of the 25 have diffuse subtype, 6 of them have an overlap symptomatic, two of them associated with diffuse subtype. ANA positive were 20, and 8 of them were anti-Scl 70 positive. None of them were antinuclear positive The mean modified Rodnan Skin Score was at timepoint 0, 6 and 12 month 18.1, 15.1 (n=21) and 15.1 (n=17).

Raynaud’s Phenomen occurred in 22/25 at time point 0 and 16 of 21 at time point 6 months and 12 of 17 at 12 months. 18 of 25 of them had capillary changes already at time point 0. 7 of them had ulceraations at time point zero, 9 of 21 at month 6 and 4 of 17 at months 12. 15 of them had cardiopulmonary involvement, at time point zero already, 9 of them had interstitial lung disease. 6 of 21 had cardiopulmonary involvement at month 6 and 7 of 17 at month 12 of follow up. Two of them have renal involvement at time point 0 and 3 at time point 6 and 12 months. 9 of 25 had gastrointestinal involvement, and 5 of them oesophageal involvement at time point zero, 3 from 21 at month 6 and 5 of 17 at 12 months. 22 of 25 have musculoskeletal involvement 19 of at month 6 and 16 of 17 at 12 months.

Conclusion: We present the data on the first 25 prospectively assessed patients with JSSc. The current recruitment data confirms that pediatric patients are different from the adult patients. There is a striking majority of diffuse patients with 76% and overlap features in 24% of the patients. None of the patients were antinuclear positive. Unfortunately despite the prospective data collection, we miss some data. The collection of patients and data is ongoing (www.juvenile-sclerodema.com).

Disclosure of interest: None declared.

P50
First results of the uveitis outcome study of the multinational interdisciplinary working group for uveitis in childhood (MIWGC)
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Pediatric Rheumatology 2014; 12(Suppl 1):P50

Introduction: Juvenile idiopathic arthritis (JIA) associated uveitis is one of the most severe comorbidities of JIA and it occurs in about to 20 % of JIA patients. There are currently no specific established outcome measures for this specific uveitis. The Standardization of Uveitis Nomenclature SUN* group made the first attempt to establish outcome measures for uveitis in adults (1). We adapted part of it and developed and proposed outcome measures over a consensus process specific for JIA associated uveitis (2). Here we present the first results of the prospective evaluation of this outcome measures.

Objectives: To validate the proposed outcome measures for JIA associated uveitis

Methods: Patients were enrolled, at a start of the treatment with a nonbiologic or biologic disease modifying agents due to the severity of the uveitis and were followed with the proposed parameters to asses changes of the uveitis. The parameters evaluated at each visit included: demographics, rheumatologic assessment (JIA type, activity of arthritis, JIA-related disability), ophthalmologic assessment (duration of uveitis, activity of uveitis,visual acuity, ocular complications, topical and systemic medications, surgical procedure, uveitis-related disability). Quality of life questionnaire for patients and children were also assessed throughout the study.

Results: At present 33 patients completed the first 3 months of the follow-up. 61% of them were female. Mean age at inclusion into the study was 8 years. 97% of the patients were Caucasian. The JIA subset distribution was 68% oligoarticular, 16% extended oligoarticular, 12% RF negative polyarticular and 4% enthesis-related. At enrolment mean disease duration of JIA was 53 months and the uveitis 33 months. On a VAS-score(0-100) the uveitis related disability was 20 and the JIA related disability 30. Insidious anterior uveitis was found at 95% of the patients at baseline , had, the left eye was involved more frequently ( 97 %) compared to 79% the right eye, in some patients both eyes were involved. Number of patients with more then 6 cells in the anterior chamber dropped from around 60% at baseline to 13% at months 3. A flare faint or more severe was observed in 75% of the eyes at baseline and in 30% at months 3. The anterior chamber flare grade according to the MIWGC group responded quite well, at time point 0 over 80% had a flare and after 3 months only around 30%.

Conclusion: These preliminary results of the standardized assessment of the JIA associated uveitis are promising. Further evaluation of these items will probably help to establish standardized measures to assess the activity of uveitis and the efficacy of a drug involved in the treatment.

Disclosure of interest: None declared.
PS1

Prognostic factors for chronic arthritis in children with acute joint swelling
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Pediatric Rheumatology 2014, 12(Suppl 1):PS1

Introduction: Acute inflammatory arthritis is frequent clinical sign in children with variable outcomes. Often post infectious or viral arthritis progress to chronic joint disease

Objectives: Our aim is to determine prognostic factors that predict the course of chronic arthritis in children.

Methods: 116 consecutive children with acute arthritis with symptoms duration < 6 weeks included in prospective study. A standardize rheumatologic evaluation was performed on newly referred patients. Possible diagnostic variables collected at the first visit: active joints count, symptoms duration, time of morning stiffness, erythrocyte sedimentation rate (ESR), C reactive protein (CRP), antinuclear antibodies (ANA), HLA B27, myeloid-related protein 8/14 (MRP8/14) and IL-6. Arthritis outcome was defined at 1 and 2 years follow-up. We considered the clinical outcomes - chronic arthritis and inactive disease. Multiple linear regression with forward stepwise was used to determine the prognostic variables.

Results: 109/116 patients completed follow-up period. Of all patients 36.7% had clinically active (or chronic) arthritis after 1 year, and 30% - after 2 year follow-up periods, and had been treated with appropriate therapy after establishing initial diagnosis (JIA, arthritis related to infections and self-limited undiagnosed arthritis). The mean serum level of MRP8/14 at baseline measured in patients with arthritis related to infection was 1123.74 ng/ml, and 7836.05 ng/ml in JIA patients, compared with self-limiting arthritis 4832.19 ng/ml (p<0.001). Predominantly very high MRP8/14 concentrations were measured in patients who developed chronic disease.

Logistic regression analysis showed that significant predictors of chronic disease presence were morning stiffness (OR 8.7 [2.15-35.04]), arthritis in ≥ 5 joints (OR 6.3 [2.19-9.1]) and MRP8/14 concentration >5785 ng/ml (OR 4.4 [1.59-12.01]) at baseline.

Conclusion: The early presence of morning stiffness, polyarthritic joint involvement and high MRP8/14 concentration in a child with acute arthritis indicates the likelihood of chronic disease after 1 and 2 years follow-up.

Disclosure of interest: None declared.

PS2

Gastrointestinal involvement in juvenile systemic sclerosis: development of recommendations for screening and investigation
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Pediatric Rheumatology 2014, 12(Suppl 1):PS2

Introduction: There are currently no agreed recommendations on how to investigate children for gastrointestinal (GI) involvement in juvenile Systemic Sclerosis (JSSC). The aim of screening is to detect disease early to facilitate early aggressive therapy and improve outcomes. GI involvement at diagnosis incurs a worse outcome [1]. Most deaths occur early in the disease course [1, 2].

Objectives: To develop recommendations for investigation of GI involvement in JSSC, based on paediatric evidence and where this was lacking, consensus expert agreement.

Methods: Members of the PRES Scleroderma Working Group were invited to participate; additionally a paediatric gastroenterologist was invited. A nominal group technique was used. 75% consensus was defined as agreement.

Results: Table 1 shows the recommendations for screening for GI involvement at baseline and at defined time points from diagnosis. Other recommendations agreed by the group which are relevant at any stage in the disease course are as follows:

<table>
<thead>
<tr>
<th>Clinical</th>
<th>Laboratory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening guidelines are based on asymptomatic patients. However, children may need more frequent monitoring depending on clinical status and abnormalities detected on previous investigation.</td>
<td>Upper GI endoscopy Barium swallow 24 hours pH monitoring</td>
</tr>
</tbody>
</table>

P53

Mutations of familial hemophagocytic lymphohistiocytosis (FHL) related genes and abnormalities of cytotoxicity function tests in patients with macrophage activation syndrome (MAS) occurring in systemic juvenile idiopathic arthritis (sJIA)
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Pediatric Rheumatology 2014, 12(Suppl 1):P53

Introduction: MA is a severe complication of rheumatic diseases, mostly sJIA. Clinical and laboratory features are similar to those of FHL resulting from mutations in selected genes involved in the cytotoxicity pathway.

Objectives: We investigated the presence of mutations of FHL-related genes and of abnormalities in degranulation and perforin expression, in patients with MAS occurring in the context of sJIA.

Methods: From the HLH Italian National Registry, we selected patients with MAS defined according to the HLH 2004 criteria and with confirmed diagnosis of sJIA based on ILAR criteria. Mutation analysis was performed by Sanger sequencing of FHL-related genes. Perforin expression and degranulation were analyzed using flow-cytometry.

Results: We identified 31 patients (17 females; 25 Southern European, 6 Indian) with MAS and sJIA. Eleven patients (35.5%) had 14 monoallelic mutations in PRF1 (n=7), UNC13D (n=1), STX11 (n=1), STXBP2 (n=4), and Rab27a (n=1). Three patients had mutations in 2 genes. Both degranulation and perforin expression were evaluated in 18 patients. At least one test was defective in 11 patients (61%). The clinical and laboratory features of patients with monoallelic mutation and/or with abnormalities in at least one functional test, were not different from those of the remaining patients.

Table 1 (abstract P52)

<table>
<thead>
<tr>
<th>Gastrointestinal</th>
<th>Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients should have a barium swallow to assess for dysmotility or stricture and 24 hour pH monitoring for GORD and progress to upper GI endoscopy if any abnormality detected</td>
<td></td>
</tr>
</tbody>
</table>

Follow-up

<table>
<thead>
<tr>
<th>Upper GI endoscopy Barium swallow 24 hours pH monitoring</th>
<th>Lower GI symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Every 3 years or sooner if worsening lung involvement and/or worsening GI symptoms</td>
<td></td>
</tr>
</tbody>
</table>
However, re-occurrence of MAS tended to be more frequent in patients carrying mutations (mutated 27% versus non-mutated 10%) and in patients showing abnormalities in at least 1 functional test (abnormal 18% versus 0%). One patient died of MAS: she carried the N252S PRF1 variant and showed reduced perforin expression.

Conclusion: Monoallelic mutations in FHL-related genes and partial defect in either perforin expression or degranulation capacity are frequently observed in patients with SJIA who develop MAS. Additional genetic studies are warranted to identify additional genes potentially linked to MAS development.

Disclosure of interest: None declared.

**P54**

Dissecting the heterogeneity of macrophage activation syndrome


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**Introduction:** Macrophage activation syndrome (MAS) is an acute, potentially fatal complication of systemic juvenile idiopathic arthritis (sJIA). Changes in therapies, including biologics, have been associated with the onset of MAS. Interleukin-6 (IL-6) plays a major pathogenic role in SJIA; in animals suggest that high IL-6 levels contribute to the triggering of MAS [1]. Treatment with the IL-6 receptor inhibitor tocilizumab (TCZ) is highly effective in patients with SJIA [2].

**Objectives:** To investigate the rates and features of MAS occurring during TCZ treatment in patients with SJIA.

**Methods:** Data were collected from patients with SJIA treated with TCZ in the international phase 3 trial (TENDER), 4 clinical trials in Japan, and the Japanese postmarketing surveillance (JPMS) program. Reported MAS events or disease flares associated with alanine aminotransferase/aspartate aminotransferase (ALT/AST) elevations were collected. Worksheets with event information were assessed by an independent panel (2 pediatric rheumatologists, 1 pediatric hematologist with MAS expertise) overseen by the TENDER lead investigator. Cases were adjudicated as definite MAS, potential MAS, not MAS, or insufficient data.

**Results:** The data set included 112 patients from TENDER (403.0 patient-years [PY] exposure to TCZ), 149 patients from the Japanese trials (326 PY), and 366 patients from the JPMS program (523.9 PY). Of 31 cases reviewed, 22 events were adjudicated as definite or potential MAS: 5 from TENDER (3 definite, 2 potential), 6 from the Japanese trials (3 definite, 3 potential), and 11 from the JPMS program (5 definite, 6 potential). The rates/100 PY of definite/potential MAS were 1.24 (95% CI, 0.4-2.90) in TENDER, 1.84 (95% CI, 0.58-4.00) in the Japanese trials, and 2.10 (95% CI, 1.05-3.76) in the JPMS program. Laboratory and clinical features most commonly contributing to the adjudication of the 11 definite MAS events were elevated ALT/AST in 11 (100%), thrombocytopenia in 10 (91%), elevated ferritin in 8 (73%), leukopenia in 7 (64%), neutropenia in 6 (55%), and fever in 6 (55%). All 11 events adjudicated as definite MAS met the preliminary MAS diagnostic guidelines [3]. All definite and potential MAS resolved, with the exception of MAS in a patient from the Japanese phase 3 study who died after respiratory/cardiac arrest.

**Conclusion:** The use of TCZ does not appear to be associated with increased risk for MAS in SJIA. No unusual clinical or laboratory features were observed in these MAS cases.


**References**
P56
Inhibition of natural killer (NK) cell cytotoxicity by interleukin-6: implications for the pathogenesis of macrophage activation syndrome

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Pediatric Rheumatology 2014, 12(Suppl 1):P56

Introduction: MAS occurs frequently in patients with active SJIA and because of the similarities with HLH is classified as secondary HLH. Systemic juvenile idiopathic arthritis (s-JIA) is characterized by high levels of interleukin-6 (IL-6). Impairment of natural killer (NK) cell function and decrease perforin expression have also been reported in s-JIA.

Objectives: Aim of this study was to evaluate the effect of IL-6 on NK cell cytotoxic function.

Methods: Following in vivo treatment with poly(I:C), splenic NK cell cytotoxic activity from wild type (WT) or IL-6 transgenic (IL-6TG) mice was evaluated using the chromium51 release assay. NK cell number, perforin, GranzymeB, CD69 and CD107a expression were evaluated by flow cytometric analysis. Human polyclonal NK cells were expanded from peripheral blood mononuclear cells (PBMCs) in co-cultures with the feeder cell line RPMI8866 in the presence of tocilizumab, an IL-6 receptor blocker, or isotype control. IL-6 production in the supernatants of human polyclonal NK cells was measured by ELISA. PBMCs from healthy donors were treated with IL-6. IL-6 NK cell cytotoxic activity, Perforin and CD107a expression were evaluated as above.

Results: Following poly(I:C) administration, in vivo generation of splenic NK cell cytotoxic activity was markedly reduced in IL-6TG compared to WT mice. In IL6TG mice number of NK cells, number of CD69+ NK cells and degranulation were comparable to WT mice. Defective expression of both perforin and GranzymeB were found in NK cells from IL-6TG mice. High levels of IL-6 were found in the supernatants of human polyclonal NK cells. Neutralizing IL-6 with tocilizumab in co-cultures of human PBMCs increased human NK cell cytotoxicity and perforin expression. Addition of IL-6 to human PBMCs decreased perforin expression in NK cells.

Conclusion: Both in vivo in mice and in vitro in humans, IL-6 inhibits NK cytotoxicity down-regulating perforin expression. In patients with prominent inflammatory response, such as JIA, high levels of IL-6 may contribute to the induction of MAS also by inhibiting cytotoxicity inducing a defect similar to that of primary HLH.

Disclosure of interest: None declared.

P57
Cytokine active disulfide-HMG18 increased during severe macrophage activation syndrome

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Pediatric Rheumatology 2014, 12(Suppl 1):P57

Introduction: Macrophage activation syndrome (MAS) is a life-threatening complication of childhood systemic inflammatory disorders. HMG18 is a nuclear protein that extracellularly orchestrates key events in inflammation. Recent data revealed that different redox states of three cysteines within HMG18 render it with mutually exclusive activities: reduced all-thiol-HMG18 exerts chemotactic activity, disulfide-HMG18 cytokine-inducing effects, and terminally oxidized sulfonly-HMG18 without inflammatory activity.

Objectives: This study was set to assess the kinetics of HMG18 in four patients with severe MAS, on the basis of S0A(4) (n=3) or SLE (n=1), and to identify which HMG18 redox isoforms appear during different disease stages.

Methods: Serial serum samples were analyzed with ELISA for detection of HMG18, IL-1b, IL-1a, IL-18, IFN-g and MCP-1. Isoforms of HMG18 were identified and quantified by high-resolution and sensitive proteomic mass spectrometry (MS).

Results: At onset of MAS three patients had ongoing biologic therapy: two with tocilizumab; one with combination anakinra and CsA. All patients were intensive care treated, three with severe CNS involvement, and all were steroid-resistant. Mass spectrometric characterization revealed early increased levels of predominantly cytokine-inducing disulfide-HMG18 during severe disease activity. Inflammatory control was achieved in all patients with etoposide, given 50-100mg/m²/week. After initiation of treatment and resolving inflammation the HMG18 levels declined and changed to the non-inflammatory isoform. IFN-g and ferritin appeared concomitant with HMG18, whereas IL-18 and MCP-1 levels peaked later. As opposed to other studies in MAS, IL-13 could not be detected in any of the patients.

Conclusion: This work provides new insights in HMG18 biology suggesting different roles of HMG18 during the course of the highly inflammatory condition MAS, indicating that the observed elevated HMG18 levels are not just a product of the inflammation but rather contribute to the development of the cytokine storm seen in MAS patients.

Disclosure of interest: None declared.

P58
The efficacy and cost effectiveness of a multidisciplinary intervention strategy for the treatment of benign joint hypermobility syndrome (BjHS) in childhood: a randomised, single centre parallel group trial.

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Pediatric Rheumatology 2014, 12(Suppl 1):P58

Introduction: Joint hypermobility is common in childhood and can be associated with musculoskeletal pain and dysfunction. Current management is delivered by a multidisciplinary team but evidence of efficacy is limited.

Objectives: This clinical trial aimed to determine whether a structured multidisciplinary intervention resulted in improved clinical outcomes compared with standard care.

Methods: A prospective randomised, single centre parallel group trial comparing an 8-week individualised multidisciplinary intervention programme with current standard management (advice and a physiotherapy appointment). Children and young people (CYP) were assessed for pain, function, coordination and strength at baseline, 3 and 12 months.

Results: 119 CYP, aged 5 to 16 years, with symptomatic hypermobility were randomised to receive targeted multidisciplinary intervention (I) (n=59) or standard management (S) (n=60). Of these, 105 were followed to 12-months. There was a significant improvement in child and parent reported pain, coordination and strength. However, no added benefit could be shown from the intervention (Table 1). The number of CYP showing significant pain reduction (≥40%) was 27 (50.0%) (I) vs 21 (41.1%) (S). Those pain free at 12 months were 29 (56.9%) (I) vs 20 (40.0%) (S). The response was independent of the degree of hypermobility.

Conclusion: This is the first RCT to compare a structured multidisciplinary intervention with standard care in symptomatic childhood hypermobility. The study demonstrates significant improvement among subjects but no additional benefit from targeted intervention. The findings emphasise the benefit of information and physiotherapy, but highlight the difficulty in demonstrating subtle benefit from specific interventions without better tools for case definition and outcomes assessment.

Trial registration identifying number: UKCRN Portfolio 9366.

Disclosure of interest: None declared.

P59
Differential monocyte micromRNA expression profiles in children with active systemic juvenile idiopathic arthritis

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Pediatric Rheumatology 2014, 12(Suppl 1):P59

Introduction: Systemic juvenile idiopathic arthritis (SJIA) is an autoimmune disease of childhood, and the predominant effector cells are mononuclear phagocytes rather than lymphocytes as in autoimmune...
diseases such as RA. Previous gene expression data has shown that monocytes in SJIA have a novel phenotype with clear proinflammatory activation as well as features of alternative activation. This aberrant phenotype may contribute to the potential of these children to develop macrophage activation syndrome (MAS). What controls monocyte/macrophage differentiation in SJIA is unknown. MicroRNA are small, non-coding RNA that serve as transcriptional negative regulators to fine-tune gene expression programs involved in cell differentiation, metabolism and immunity. There is growing evidence that miRNA contribute to the pathogenesis of human disease, including adult rheumatoid arthritis (RA). These regulators have also been implicated in controlling differentiation of monocytes and macrophages. However, miRNA expression in SJIA has not been examined.

Objectives: Here, we examine miRNA expression profiles in peripheral blood monocytes from children with SJIA.

Methods: We enrolled children with active SJIA, defined as presence of active arthritis or systemic features, as well as those with clinically inactive disease (CID). CD14+ cells were isolated by magnetic beads separations, and used to generate RNA which in turn was used to quantitate the expression of 384 miRNA and controls on the TaqMan™ MicroRNA Array A (Life technologies).

Results: We found several specific miRNA that have been implicated in monocyte/macrophage differentiation with increased expression in monocytes from children with active SJIA, including miR-27a, miR-125a-5p and miR 142-3p. We also found increased expression of several other miRNA that have been associated with pathogenesis of RA, including miR-223 which has been implicated in regulation of the NALP3 inflammasome, miR-26a, and miR-132. Interestingly, while monocyte expression of miR-146a has been correlated with disease activity in RA, we found no difference in expression between monocytes from patients with active SJIA and those with CID.

Conclusion: These results provide the first report of miRNA expression profiles in children with SJIA. Taken together, these data suggest that differential miRNA expression contributes to the phenotype of monocyte/macrophages in SJIA, and may have implications for disease pathogenesis and development of MAS. Further work will correlate miRNA expression with clinical features and gene expression profiles, as well as examine impact of miRNA expression on monocyte function and differentiation.

Disclosure of interest: G. Schuler: None declared, N. Fall: None declared, N. Shen: None declared, A. Grom Grant / Research Support from: Novartis, Novimmune, Consultant for: Novartis, Roche.

Table 1 (abstract P58)

<table>
<thead>
<tr>
<th>Outcome variable</th>
<th>Baseline score (SD)</th>
<th>Rate of change over 12 months (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child pain assessment (0-5, zero is the best), n=103</td>
<td>2.31 (1.55)</td>
<td>-1.42 (-1.78 to -1.06)</td>
</tr>
<tr>
<td>Parent observed pain assessment (0-100 VAS, zero is the best) n=105</td>
<td>35.90 (26.46)</td>
<td>-6.09 (12.90 to 0.73)</td>
</tr>
<tr>
<td>Child health assessment questionnaire (CHAQ) (0-3, zero is the best), n=104</td>
<td>0.82 (0.63)</td>
<td>+0.02 (-0.12 to 0.16)</td>
</tr>
<tr>
<td>Child health 9 dimensional utility (CHU9D) (0-1, zero is the worst), n=104</td>
<td>0.85 (0.11)</td>
<td>+0.02 (-0.01 to 0.04)</td>
</tr>
<tr>
<td>Movement assessment battery for children (M-ABC) (0-100, zero is the worst), n=104</td>
<td>34.56 (28.61)</td>
<td>+2.60 (-2.92 to 8.11)</td>
</tr>
<tr>
<td>Grip Strength (Dynamometer), n=104</td>
<td>57.29 (28.30)</td>
<td>+4.55 (0.16 to 8.94)</td>
</tr>
</tbody>
</table>

P60
Arthritis as presenting manifestation of acute lymphoblastic leukemia in children

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Pediatric Rheumatology 2014, 12(Suppl 1):P60

Introduction: At disease onset children with acute lymphoblastic leukemia (ALL) may present with arthralgia (join pain) or even signs of arthritis with joint swelling, redness, and restriction of motion. This might cause misdiagnosis and thereby lead to prolonged diagnostic delay. The present study aimed to identify ALL children with joint involvement and to compare their characteristics and outcome with ALL children without joint involvement.

Objectives: Case records of 286 children diagnosed with ALL between 1992 and 2013 were reviewed and analyzed in this retrospective, descriptive study.

Methods: Data analysis was mainly descriptive and selected differences in frequencies were tested for statistical significance using Fisher’s exact test with two-sided tests and 5% level of significance. The overall and event free survival were determined using Kaplan-Meier plotting.

Results: Eighteen percent of the children with ALL presented with localized joint pain and half (9%) had objective signs of arthritis. The mean number of joints involved was 2.5, most frequently presenting as asymmetric oligoarthritis. The suspected misdiagnosis were reactive arthritis: 19/53, osteomyelitis: 9/53 and juvenile idiopathic arthritis: 8/53. Children with joint involvement had less objective signs of leukemia: Cytopenia was absent in 24% (vs. 8%, p=0.001), 50% had less than two cell lines affected (vs. 21%, p=0.0005), 44% had no organomegaly (vs. 29%, p=0.05). Median diagnostic delay was 4 weeks vs 2 weeks. The 5-year event-free survival was better for children with joint involvement compared to those without (94% vs. 87%, p=0.049), as well as the 5-year overall survival (96% vs. 83%, p=0.044).

Conclusion: Acute lymphoblastic leukemia with joint involvement is a frequent finding (18%). At presentation cytopenia and hepatosplenomegaly are rarely seen in ALL with joint involvement. The risk of an initial rheumatic misdiagnosis was significant. The overall and event-free survival were superior compared to the children without joint involvement.

Disclosure of interest: None declared.

P61
The correlations of serum interleukin-6 (IL-6) levels and serum soluble IL-6 receptor levels with disease activity in systemic juvenile idiopathic arthritis patients with and without tocilizumab treatment

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Pediatric Rheumatology 2014, 12(Suppl 1):P61

Introduction: Interleukin-6 (IL-6) and soluble IL-6 receptor (sIL-6R) have been demonstrated to play a significant role as inflammatory mediators in systemic juvenile idiopathic arthritis (SJIA). Tocilizumab, a humanized anti-IL-6 receptor antibody, becomes a new biologic treatment for SJIA nowadays but the correlation of serum IL-6 levels and serum sIL-6R levels with disease activity in SJIA with and without tocilizumab treatment are still unclear.

Objectives: To determine the correlations of serum IL-6 levels and serum sIL-6R levels with disease activity in SJIA patients with and without tocilizumab treatment

Methods: SJIA patients in pediatric rheumatology clinic, Ramathibodi hospital between September 2011 and June 2013 were enrolled in this study. Patients were followed up three times in 2-3 months interval. Fifteen healthy children were included as normal controls. Demographic...
data was collected. During the visit, patients were evaluated according to Juvenile Arthritis Disease Activity Score-71 (JADAS-71) and blood samplings were collected for complete blood count, erythrocyte sedimentation rate, IL-6 levels, and sIL-6R levels, then patients were categorized into 4 groups: 1) active disease with systemic features and arthritis 2) active disease with only arthritis 3) remission on medication 4) remission off medication

Results: Forty-two SJIA patients, 131 blood samplings were included in this study. Seventeen patients (40%) were treated with tocilizumab during the study. Serum IL-6 levels in patients without tocilizumab treatment significantly elevated in active disease with systemic features and arthritis [median (IQR) = 101.8 (303.2) pg/mL] when compared to active disease with only arthritis [median (IQR) = 4.5 (23) pg/mL], and remission on medication [median (IQR) = 1.5 (0.55) pg/mL], whereas serum IL-6 levels in patients with tocilizumab treatment were not different between groups but there were statistically different when compared to healthy children (p < 0.05). In addition, the correlation between serum IL-6 levels and JADAS in patients without tocilizumab treatment (r = 0.71, p < 0.001) was stronger than patients with tocilizumab treatment (r = 0.42, p = 0.01). Serum sIL-6R levels in SJIA patients with and without tocilizumab treatment were significantly higher when compared to healthy children (p < 0.05). Interestingly, in patients with treatment, serum sIL-6R levels were extremely higher [median (IQR) = 1.110.3 (840.2) ng/mL] than patients without tocilizumab treatment [median (IQR) = 94.2 (82.7) ng/mL].

Conclusion: The correlation between serum IL-6 levels and disease activity in patients without tocilizumab treatment was stronger than patients with tocilizumab treatment. In addition, serum sIL-6R levels in patients with tocilizumab treatment were extremely higher than patients without tocilizumab treatment.

Disclosure of interest: None declared.

P62

Effects of antihemotropic treatment with tocilizumab on longitudinal growth in children with juvenile idiopathic arthritis

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Pediatric Rheumatology 2014, 12(Suppl 1)P62

Introduction: Inflammation and glucocorticoid therapy are major factors in the growth retardation seen in children with severe forms of juvenile idiopathic arthritis (JIA).

Objectives: The objective of the this study was to evaluate effects of antihemotropic treatment with recombiant humanised monoclonal antibody that acts as IL-6R antagonist (tocilizumab) on longitudinal growth.

Methods: Nineteen patients with systemic JIA were included into the study (8 boys and 11 girls). The mean age at first visit was 6.8 ± 2.4 years, and disease duration 4 (2.2;6) years. All patients had stage 1 of sexual development by Tanner scale and before therapy with tocilizumab had standard antihemotropic therapy. Anthropometric parameters were estimated one year before tocilizumab treatment, at the day of first infusion and in one year after tocilizumab treatment was started. SDS for height and height velocity calculated according to the growth curves for European population (Auxology, Pfizer, Version 1.0).

Tocilizumab was administered intravenously once every 2 weeks at a dose of 8-12 mg/kg of body weight. In all patients who received corticosteroids before tocilizumab treatment dose of prednisolone was reduced from 0.5 (0.4; 0.6) to 0.1 (0.02; 0.2), but not in one case it was completely abolished. Treatment efficacy was assessed according to criteria ACR pedi scale.

Results: Clinical response to the treatment was obtained in all patients included in this study. The ACR Pedi 50, 70 and 90 improvement were achieved by 3, 3, and 1 patients at Week 52, inactive disease was achieved by 11 patients at week 52. The mean height SDS one year before treatment was -2.38 ±1.43 and -2.64±1.94 by the day of 1st tocilizumab infusion (p < 0.001). Height velocity SDS was -4.24 ±1.18 and -4.55 ±1.49 respectively (p < 0.001). After one year of treatment the mean height SDS was -2.27 ±1.85 and height velocity SDS 2.51 ±1.98 (p < 0.001).

Conclusion: An intensified antihemotropic treatment with tocilizumab has a beneficial effect on growth in children with JIA. This effect might be related to the inhibitory effect of proinflammatory cytokines, especially IL-6, on the synthesis of IGF-1 and IGF-BP-3.

Disclosure of interest: None declared.

P63

Use of the JADAS criteria to assess efficacy of canakinumab in patients with SJIA – an analysis of 12-week pooled data

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3Necker-Enfant Malades Hospital, Paris, France, 4UMC Utrecht, Utrecht, Netherlands, 5Novartis Pharma AG, Basel, Switzerland

Pediatric Rheumatology 2014, 12(Suppl 1)P63

Introduction: The composite score JADAS1, 2 27-CRP (J27), 10-CRP (J10), and cut-off values for inactive (ID), low (LDA), moderate (MDA) and high disease activity (HDA) were designed to monitor the level of disease activity in all JIA subtypes. The efficacy of canakinumab (CAN), a selective, human, anti-IL-1β monoclonal antibody, was previously demonstrated in SJIA in phase III trials using aCR-JIA response criteria.

Objectives: To assess the level of disease activity in CAN-treated SJIA patients, using J10 and J27 in a 12-week pooled (phase III studies) data set.

Methods: Patients; 2–19 years of age, with active SJIA were enrolled and received sc CAN 4 mg/kg. This post-hoc analysis focuses on a 12-week pooled dataset (from 3 phase III studies) in a total of 178 CAN-naïve patients, assessing the J10 and J27 scores at Days (D) 15, 29, 57, 85, and applies the appropriate cut-off values for ID, LDA, MDA and HDA.

Results: At baseline, the median [Q1,Q3] J10 for complete patients (i.e. patients who complete 12 weeks treatment) was 29.1 [23.1,33.2], and the median change [J10] from baseline at D15 and D85 was -19.4 [-25.7,13.4] and -21.2 [-27.7,16.7], respectively. Results for J27 were very similar. The disease status at all time points for J10 and J27 are reported in Table 1. Median change from baseline at each time point was consistent between the completers and the full analysis dataset for J10 and J27.

Conclusion: In the pooled 12-week dataset, there was a dramatic reduction in disease activity from baseline to D85, with much of the reduction taking place by D15 onwards in both completers and in the full analysis set. An increasing proportion of CAN patients achieved ID or LDA according to J10 and J27 - in the first 12 weeks of treatment, despite corticosteroid tapering, a finding consistent with that using the previous ID definition from the phase III trials. These data confirm the early onset of effect as well as the short-term and sustained efficacy over 12 weeks of canakinumab, and suggest that JADAS may represent a useful tool to monitor treatment response.

Disclosure of interest: A. Ravelli Grant / Research Support from: Pfizer, Consultant for: Abbvie, Bristol Myers Squibb, Novartis, Pfizer, Roche and Johnson & Johnson, Speaker Bureau of: Abbvie, Bristol Myers Squibb, Novartis, Pfizer, Roche and Johnson & Johnson, H. Brunner Consultant for:

Table 1 (abstract P63) J10 and J27-related disease criteria on all patients

<table>
<thead>
<tr>
<th>Disease State*</th>
<th>Baseline</th>
<th>D15</th>
<th>D29</th>
<th>D57</th>
<th>D85</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=178</td>
<td>N=172</td>
<td>N=157</td>
<td>N=131</td>
<td>N=125</td>
</tr>
<tr>
<td>J10 ID</td>
<td>0.0</td>
<td>18.0</td>
<td>26.8</td>
<td>34.4</td>
<td>33.6</td>
</tr>
<tr>
<td>LDA</td>
<td>0.0</td>
<td>14.0</td>
<td>11.5</td>
<td>16.8</td>
<td>24.8</td>
</tr>
<tr>
<td>MDA</td>
<td>0.6</td>
<td>19.2</td>
<td>19.7</td>
<td>206.6</td>
<td>16.8</td>
</tr>
<tr>
<td>HDA</td>
<td>99.4</td>
<td>48.8</td>
<td>42.0</td>
<td>282.2</td>
<td>24.8</td>
</tr>
<tr>
<td>J27 ID</td>
<td>0.0</td>
<td>18.0</td>
<td>26.8</td>
<td>34.4</td>
<td>33.6</td>
</tr>
<tr>
<td>LDA</td>
<td>0.0</td>
<td>14.0</td>
<td>11.5</td>
<td>16.8</td>
<td>25.6</td>
</tr>
<tr>
<td>MDA</td>
<td>0.6</td>
<td>15.1</td>
<td>16.6</td>
<td>17.6</td>
<td>12.8</td>
</tr>
<tr>
<td>HDA</td>
<td>99.4</td>
<td>52.9</td>
<td>45.2</td>
<td>31.3</td>
<td>28.0</td>
</tr>
</tbody>
</table>

*Cut-off values for ID, LDA, MDA and HDA, respectively for J10: ≤1, >1–3, >3–8, >8.5, and for J27: ≤1, >1–3, >3–8, >8.5 and >8.5.
Use and lower overall well being scores. Joint damage on imaging was reported more often in those with younger age at diagnosis (p = 0.0003). 308 had at least one follow up visit, 259 of whom had visits occurring at least 3 mos from enrollment. Trends towards improvement in disease activity measures were found in these 259 patients. Of 234 children with no systemic features at baseline, 91 had active arthritis (median active joints = 4). In this subset of children with persistent arthritis, there were no differences in age at onset, time to diagnosis or disease duration, but differences in medication use at baseline enrollment were noted (increased current IL-6 inhibitor, corticosteroid, and NSAID use and increased past use of all biologics).

Conclusion: This study describes characteristics and medication usage of the largest sJIA cohort reported to date. Significant changes occurred in sJIA medication usage from 2010-2013, but corticosteroids are still frequently used (29.2% at enrollment). AA children have more severe disease, as do children diagnosed at a younger age. A significant proportion of children have persistent arthritis despite the use of new treatments. Further study is needed to identify predictors of persistent arthritis in order to improve treatment and outcomes in this subgroup of patients.


P65

Course, outcome and complications in a single centre cohort of 53 Indian children with systemic onset juvenile idiopathic arthritis with a minimum follow up of 3 years

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Pediatric Rheumatology 2014, 12(Suppl 1):P65

Introduction: Systemic-onset Juvenile Idiopathic Arthritis (SOJIA) is not rare in India, where biotherapies are unaffordable. Data on its course, outcome and complications are scarce.

Objectives: We describe this data in a monocentric cohort of 53 patients, followed up for at least 3 years.

Methods: A pre-biologic era Italian study where one of the authors (RC) had participated, formed a template and comparator. After ethics committee approvals and consents, a cohort of 53 consecutive patients diagnosed with SOJIA before 10-2009 using the ILAR criteria were followed up until 09-2012. At each visit, general (including growth parameters) and articular examination, laboratory parameters (CBC, ESR, liver enzymes) and ongoing treatment were entered in a customized database. Course was classified as mononcytic (single episode) polycytic (multiple episodes with remissions in between) and persistent (continuous articular/systemic disease activity). At last visit, outcome was studied with respect to remission (Wallace criteria) and Steinbrocker functional classification.

Juvenile Arthritis Damage Index (JADI) measured on 20/53 patients.

Results: In the 53 patients studied (35M,18F), 21 constituted an inceptional cohort and 32 were referred to our center with prior diagnosis / treatment. Mean age at diagnosis was 6.3 years (range 4m-14y), mean follow up period was 5.5 years (range 3-10 years) and mean time from onset of symptoms to diagnosis was 8.5 months (range 2wks-7 years). Forty four patients received NSAIDs, 52 oral corticosteroids and 34 required pulses of methylprednisolone with intra-articular triamcinolone acetonide being used in 14. Methotrexate was used in 50 patients, other DMARDs in 25, including 2 patients treated with infliximab. Nineteen patients used biologics (etanercept-2, tocilizumab-3). 44 had a monocyctic, 31 intermittent and 13 persistent course. At last visit, 9/9 patients of the monocyctic group, 17/31 in the intermittent group and 3/13 in the persistent group were in remission. Patients diagnosed within 6 months from disease onset were more likely to have a monocyctic / intermittent than a persistent course, compared to those diagnosed later. 33/53 suffered from complications of the disease and/or drug. MAS was observed in 5 and death occurred in 1, due to hepatic encephalopathy complicating viral hepatitis A. Three required orthopedic surgeries for residual deformities. All children in the monocyctic group belonged to Steinbrocker class 1 at last visit. Of 31 in
Efficacy of canakinumab in biologic-naïve versus previously biologic-exposed SJIA patients: A 12 week pooled post-hoc analysis

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Introduction: Canakinumab (CAN), a selective, human anti-IL-1β monoclonal antibody is approved for SJIA in over 30 countries. Efficacy and safety of CAN over 12 weeks have been demonstrated in 2 phase III trials [1]. Out of these trials >60% of the pts received a previous biologic and were switched to CAN due to lack of efficacy or for safety reasons, and may be more refractory to another biologic therapy.

Objectives: To present a post-hoc evaluation of CAN efficacy in biologic-naïve (BN) pts and those previously exposed to biologics (BE) during the first 12-weeks.

Methods: Pooled data from CAN naïve pts, enrolled in two phase III trials and an extension phase (up to interim data lock 10 August 2012) were considered. Pts (2–19 yrs) with active SJIA were enrolled and received CAN 4 mg/kg or placebo sc every 4 weeks for 12 weeks. CAN naïve pts who entered the trials and received at least one dose of CAN were included in this analysis (N=178 CAN naïve pts). Descriptive efficacy analyses of adapted ACR-JIA responses at Week 12 are provided for the BN and BE pts groups.

Results: At baseline, there were 66 (37%) BN pts whereas anakinra (ANA), tocilizumab (TCZ), etanercept (ETN) and adalimumab (ADA), were the biologics used by 78 (44%), 10 (6%) and 58 (33%) and 9 (5%) pts, respectively. The main reasons for discontinuation of biologics in BE group (n=112) was lack of efficacy (ANA, n=32; TCZ, n=77; ETN, n=56; ADA, n=9) or safety/tolerability (ANA, n=20; TCZ, n=14; ETN, n=90). At Week 12, the BN and BE groups were similar in aACR-JIA 30 and 90 response rates (Week 2: aACR-JIA 30: 80% vs 80%; aACR-JIA 50: 76% vs 67%; Week 12: aACR-JIA 30: 76% vs 67%; aACR-JIA 50: 74% vs 65%). Numerically higher aACR-JIA 70 and 90 response rates were achieved in BN vs BE pts (Week 2: aACR-JIA 70: 67% vs 52%; aACR-JIA 90: 36% vs 37%; Week 12: aACR-JIA 70: 70% vs 55%; aACR-JIA 90: 61% vs 42%). aACR-JIA 70 and 90 response rates were similar in pts previously exposed to ANA vs those not exposed to ANA at 12 weeks (aACR-JIA70: 58% vs 63%; aACR-JIA90:47% vs 50%). Compared to pts who discontinued ANA due to lack of efficacy, there was a trend towards higher aACR-JIA 70 and 90 response rates at Week 12 in pts who stopped ANA for other reasons (aACR-JIA70: 34% vs 74%; aACR-JIA90: 25% vs. 63%). A higher aACR-JIA 30, 50, 70 and 90 response rates were observed in TCZ naïve pts vs those pts exposed to TCZ (n=10) (aACR- JIA30: 71% vs 50%; aACR-JIA50: 70% vs 50%; aACR-JIA70: 61% vs 50%; aACR-JIA90: 48% vs 40%). Higher aACR-JIA 70 and 90 response rates were observed for ETN pts vs those exposed to ETN (aACR-JIA70: 67% vs 48%; aACR-JIA90: 58% vs 31%); while ADA naïve pts had similar responses to CAN as ADA-exposed pt (aACR-JIA 70: 61% vs 56%) and they had higher aACR-JIA 90 response (aACR-JIA90: 50% vs. 22%).

Conclusion: In general, pts previously exposed to biologics achieved aACR-JIA 50,70 and 90 responses to CAN quickly in the first 2 weeks, and maintained their response up to Week 12; albeit at a numerically lower level than biologic-naïve pts. These data support the consistent efficacy of CAN across different subgroups of pts.

Disclosure of interest: None declared.


Tocilizumab therapy in systemic juvenile idiopathic arthritis – lessons of real clinical practice

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Introduction: Clinical trials of tocilizumab(TCZ) have verified its efficacy and safety in systemic juvenile idiopathic arthritis (sJIA), but there are many outstanding issues, relevant to the real clinical practice.

Objectives: to investigate TCZ in pts with sJIA depending on the age of disease onset;duration of disease, the number of active joints, the number of systemic features and previous biologic(s).

Methods: In prospective study were included 45 pts(19b/26g) with sJIA refractory to conventional treatment, who was treated by TCZ from 9 months to 54 months. At baseline mean age of 6.25(2.0-17.8)years; mean disease duration of 4.5(0.3-15.9)years. TCZ used as the 1st in 28 pts, 2nd – in 12, 3rd – in 5. 37.8%pts previously received TNF- inhibitors-17, abatacept-2, rituximab-3. 41 pts(91.1%) had arthritis at the baseline. Systemic features were observed in 40(88.9%)pts. Mean number of systemic manifestations(NSM) was 2.82 (1.5-6). 2 pts had MAS before of TCZ initiation. Retrospectively all pts were separated into the groups depending on the age of manifestation of disease (before 3 yrs/older 3 yrs -22/3), duration of disease (less than 3 yrs/more – 20/5), the number of active joints (less than 10/more-22/3), the number of active systemic features (NSM 0 – 13) and previous biologic(s) (Bi-naive/previous B-28/17). Efficacy of TCZ therapy was evaluated in accordance to ACRpedi criteria in 1, 3, 6, 9, 12 and every 6 months of treatment later.

Results: 36 pts continue the treatment, mean duration 27.4 months(9.5). In 9 pts TCZ was cancelled due to serious adverse effects(5), another reasons(4). All pts achieved more than 30-50% improvement by ACRpedi
criteria. We found no significant differences in efficacy parameters at the response to therapy depending on the investigated factors. However, pts who had early manifestation of disease, long disease duration, large NSM achieved good response on articular status more slowly. Also we observed some increasing of disease activity in all groups between 30-36 months of therapy. Steady improvement allowed to decrease prednisolone (PR) dose in all pts, to cancel PR in 19.4% pts, to cancel NSAIDs in 14% pts. 9 pts achieved inactive disease status. Adverse events were observed independently of investigated factors and included postinfusion reactions (vomiting-1, headache-2, sore throat-4, chestpain-4, blood pressure increasing-1, eczema-2), infections (upper respiratory infection-16, bronchitis-1), pneumonia-2, gastroenteritis-1, ear infections-3, periodontitis-2), temporary laboratory abnormalities (neutropenia-2, thrombocytopenia-8, IgG decreasing -10, hyperbilirubinemia-3, elevated transaminases-7). We have observed some SAE: infusion reaction (5); severe infections – varicella (2), atypical pneumonia (1), tuberculosis(1).

MAS observed in 4 pts (1-after respiratory infection, 1-after elective surgery, 1-after increase interval between infusion more than 4 weeks, 1-unknown reason), in all case of MAS TCZ was continued.

Conclusion: TCZ is the best choice among B at SJIA in Pts independently on the age of manifestation of disease, duration of disease, the number of active joints, the number of active systemic features, previous B. Careful monitoring provided an acceptable safety profile of TCZ in the pts with SJIA. TCZ was well tolerated, and the majority of AE were mild or moderate, reversible, and not treatment limiting.

Disclosure of interest: None declared.

P68 Canakinumab treatment shows maintained efficacy in systemic juvenile idiopathic arthritis patients

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Pediatric Rheumatology 2014; 12(Suppl 1)P68

Introduction: Systemic juvenile idiopathic arthritis (SJIA), an interleukin-1β (IL-1β)-mediated autoinflammatory disease, is characterized by recurrent flares of active disease. Treatment with canakinumab (CAN), a selective, human, anti-IL-1β monoclonal antibody allows for successful steroid dose reduction/discontinuation and reduces risk to experience a flare in patients with SJIA [1]. CAN is approved for SJIA patients (≥ 2 years old) by over 30 countries including USA, EU, Russia and Canada.

Objectives: To evaluate the maintenance of efficacy with continued CAN treatment in SJIA patients during the blinded randomized treatment withdrawal part of a large phase III trial.

Methods: Patients 2–19 yrs of age with active SJIA who had responded to open-label CAN treatment 4mg/kg/4wks sc, maintained a minimum adapted ACR Pediatric criteria [aACR] 30 for up to 32 weeks, and were steroid-free or had successfully reduced systemic steroids to a minimum dose, were randomized to either continue CAN or receive placebo until 37 flare events occurred [1]. Patients were considered to have completed the study if they entered clinical remission on medication (CRM), i.e. achieved 24 consecutive weeks of clinical inactive disease (CID) [2]. A survival analysis of the time to worsening in aACR level, after randomization for the CAN and placebo groups was performed. Time to worsening is the time to fail to maintain at least the same level of aACR response seen at randomization. The change in the proportion in each group of those with CID was also evaluated.

Results: 100 pts were randomized to a CAN (n=50) or a placebo (n=50) group, of whom 26 (53%) and 27 (54%), respectively, had CID at the start of the randomization part. In the first 2 months, probability of maintaining aACR response was similar for both treatment groups. Thereafter, the probability of maintaining aACR response was greater in the CAN vs placebo groups. The median time to worsening in aACR level for patients in the placebo group was 141 days (95% CI 85, 281), and could not be calculated for CAN as <50% of CAN group had a worsening in their aACR level by the end of this phase. The median duration of exposure for the CAN group was 221.5 days (range: 8-617 days). There was a statistically significant relative risk reduction of 51% for the CAN vs placebo group to experience a worsening in aACR level (HR= 0.49; 95% CI: 0.27, 0.90; p=0.0131). CID was achieved by 31(62.0%) vs 17 (34.0%) patients in CAN vs placebo at their last visit (HR= 3.4; 95% CI 1.5, 8.0; p=0.0020) and CRM was reached by 20 (40%) CAN and 2 (4%) placebo patients by the end of the study.

Conclusion: A greater proportion of SJIA patients who continued CAN treatment maintained/improved their aACR response, achieved CID and CRM than patients who discontinued CAN by being switched to placebo, demonstrating maintenance of efficacy with continued CAN treatment even in flare events.

Disclosure of interest: N. Wulffraat Grant / Research Support from: Abbvie, Roche, Consultant for: Novartis, Pfizer, Roche, N. Rupperto Grant / Research Support from: To Gaslini Hospital: Abbott, Astrazeneca, BMS, Centocor Research & Development, Eli Lilly and Company, “Francesco Angelini”, Glaxo Smith & Kline, Iftalmaco, Novartis, Pfizer Inc., Roche, Sanofi Aventis, Schwarz Biosciences GmbH, Xoma, Wyeth Pharmaceuticals Inc., Speaker Bureau of: Astrazeneca, Bristol Myers and Squibb, Janssen Biologics B.V, Roche, Wyeth, Pfizer, H. Brunner Consultant for: Novartis, Genentech, Pfizer, UCB, AstraZeneca, Biogen, Boehringer-Ingehelm, Regeneron, Paid Instructor for: Novartis, Speaker Bureau of: Novartis, Genentech, S. Oliveira Grant / Research Support from: Novartis, Roche, Y. Uziel Speaker Bureau of: Fee for few talks at medical meeting- Novartis, Neopharm, Roche, K. Nistala: None declared., R. Cimaz: None declared, M. Ferrandiz Grant / Research Support from: Principal investigator’s fee by Novartis, B. Flato Grant / Research Support from: Coinvestigator in the initial study on efficacy by canakinumab treatment in systemic juvenile idiopathic arthritis patients. Expenses for personnel covered by Novartis, M. Gamir: None Declared., L. Kone-Paut Grant / Research Support from: SOBI, Chugai, Consultant for: Pfizer, SOBI, Novartis, Chugui, C. Gaillez Employee of: Novartis Pharma AG, K. Lheritier Shareholder of: Novartis, Employee of: Novartis Pharma AG, K. Abrams Shareholder of: Novartis, Employee of: Novartis Pharmaceuticals corporation, A. Martini Grant / Research Support from: Bristol Myers and Squibb, Centocor Research & Development,Glaxo Smith & Kline, Novartis, Pfizer Inc, Roche, Sanofi Aventis, Schwarz Biosciences GmbH, I declare that the Gaslini Hospital which is the public Hospital where I work as full time employee has received contributions to support the PRINTO research activities from the industries above mentioned. OLD: Francesco Angelini S.P.A., Janssen Biotech Inc, Abbott, Consultant for: Bristol Myers and Squibb, Centocor Research & Development,Glaxo Smith & Kline, Novartis, Pfizer Inc, Roche, Sanofi Aventis, Schwarz Biosciences GmbH, I declare that the Gaslini Hospital which is the public Hospital where I work as full time employee has received contributions to support the PRINTO research activities from the industries above mentioned, Speaker Bureau of: Abbott, Bristol Myers Squibb, Astellas, Boehringer, Iftalmaco, Medimmune, Novartis, NovoNordisk, Pfizer, Sanofi, Roche, Service, D. Lovell Grant / Research Support from: National Institutes of Health- NIHAMS, Consultant for: Astra-Zeneca, Centocor, Amgen, Bristol Meyers Squibb, Abbott, Pfizer, Regeneron, Roche, Novartis, UCB, Forest Research Institute, Horizon, Johnson & Johnson, Speaker Bureau of: Novartis, Roche.

References
Objectives: To evaluate the maintenance of efficacy at the level of the individual patient from Week 2 to 12, using the adapted ACR-JIA response criteria (aACR) as well as J10 and J27 on the 12-week pooled data set (3 phase III studies).

Methods: For this post-hoc analysis of the CAN Phase III program in SJIA, the change in disease states between Day(D)15 and D85 of a total of 178 CAN-naïve patients was assessed. Subjects were 2–19 years of age and had active SJIA at enrollment. This shift analysis considered the aACR response and certain disease activity states as defined using J10 and J27: Inactive Disease (ID), Low Disease Activity (LDA), Moderate Disease Activity (MDA), High Disease Activity (HDA).

Results: J10 changes during the study period are provided in Table 1. Results for the J27 were very similar to the J10 observations.

The D15-D85 aACR shift analyses, including only patients who had a D15 and D85 value, likewise indicated that the majority of patients maintained or improved their response: NR (n=32): 12.5% of patients improved; aACR0 (n=14): 0.0% were maintained/78.6% improved; aACR50 (n=21): 33.3% were maintained/42.9% improved; aACR70 (n=36): 25.0% were maintained/58.3% improved; aACR90 (n=26): 30.8% were maintained/57.7% improved; aACR100 (n=34): 82.4% were maintained.

Conclusion: The great majority of CAN patients either maintained or improved their JADAS status or aACR response level from week 2 to 12. These data confirm the consistent maintenance of efficacy of CAN at the individual level in the first 3 months, irrespective of the measure of response, i.e. aACR criteria or JADAS-derived criteria, and extend previous findings at the study group level.

Disclosure of interest: A. Ravelli Grant / Research Support from: Pfizer, Consultant for: Abbvie, Bristol Myers Squibb, Novartis, Pfizer, Roche and Johnson & Johnson, Speaker Bureau of: Abbvie, Bristol Myers Squibb, Novartis, Pfizer, Roche and Johnson & Johnson, H. Brunner Consultant for: Novartis, Genentech, Pfizer, UCB, AstraZeneca, Biogen, Boehringer-Ingelheim, Regeneron, Paid Instructor for: Novartis, Speaker Bureau of: Novartis, Genentech, N. Ruperto Grant / Research Support from: To Gaslini Hospital: Abbott, Astrazeneca, BMS, Centoroc Research & Development, Eli Lilly and Company, "Francesco Angelini", Glaxo Smith Kline, Italfarmaco, Novartis, Pfizer Inc., Roche, Sanofi Aventis, Schwarz Biosciences GmbH, Xoma, Wyeth Pharmaceuticals Inc., , Speaker Bureau of: AstraZeneca, Bristol Myers and Squibb, Janssen Biologics B.V.,Roche, Wyeth/Pfizer, P. Quartier Grant / Research Support from: Abbvie, BMS, Chugai-Roche, Novartis, Pfizer, SOBI, Consultant for: Abbvie, Chugai-Roche, Novartis, Pfizer, Servier and SOBI, Speaker Bureau of: Chugai-Roche, MEDIMMUNE, Novartis, Pfizer, A. Consolaro Consultant for: Novartis, N. Wulfraat Grant / Research Support from: Abbvie, Roche, Consultant for: Novartis, Pfizer, Roche, K. Heritier Shareholder of: Novartis, C. Gaillez Shareholder of: Novartis, E. Gonzalez-Roca, Shareholder of: Novartis, A. Martini Grant / Research Support from: The Gaslini Hospital, which is the public Hospital where I work as full time employee, has received contributions to support the PRINTO research activities from the following companies: Bristol Myers and Squibb, Centoroc Research & Development, GlaxoSmithKline,Novaltis,Farset, Roche, Sanofi Aventis, Schwarz Biosciences GmbH, Speaker Bureau of: Abbott, Bristol MyersSquibb, Astellas, Behringer, Italfarmaco, MedImmune, Novartis, NovoNordisk, Pfizer,Sanofi,Roche, Servier, D. Lovell Grant / Research Support from: National Institutes of Health- NIAAMS, Consultant for: Astra-Zeneca, Centocor, Amgen, Bristol Meyers Squibb, Abbvie, Pfizer, Regeneron, Roche, Novartis, UBC, Forest Research Institute, Horizon, Johnson & Johnson, Speaker Bureau of: Novartis, Roche.

References

Table 1(abstract P69) J10 shift analysis table from D15 to D85*

<table>
<thead>
<tr>
<th>N (%)</th>
<th>Disease State at Day 15*</th>
<th>Disease state at Day 85*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ID</td>
<td>LDA</td>
</tr>
<tr>
<td></td>
<td>ID</td>
<td></td>
</tr>
<tr>
<td>28 (100)</td>
<td>24 (85.7)</td>
<td>1 (3.6)</td>
</tr>
<tr>
<td>LDA</td>
<td>20 (100)</td>
<td>10 (50.0)</td>
</tr>
<tr>
<td>MDA</td>
<td>30 (100)</td>
<td>5 (16.7)</td>
</tr>
<tr>
<td>HDA</td>
<td>44 (100)</td>
<td>2 (4.5)</td>
</tr>
</tbody>
</table>

*Only patients with both a Day 15 and a Day 85 value are included
Clinical presentation and cytokine production abnormalities in a cohort of patients carrying NLRP12 gene variants

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Introduction: The NLRP12 related autoinflammatory disorder (NLRP12-RD) is a rare autosomal dominant disease, caused by mutations in the NLRP12 gene. Clinical manifestations are extremely heterogeneous. At present only few cases have been described. Patients occasionally required treatment with steroids and NSAIDS for short periods. Treatment with Anakinra induced an initial good response; that appears to decrease over time.

Objectives: To describe clinical features and inflammatory response of a cohort of five carriers of different NLRP12 variants, some of which not yet described as being associated with NLRP12-RD.

Methods: Twelve caucasian patients (6 males) carrying NLRP12 variants were identified. Blood samples obtained from 9/12 NLRP12 patients and from 7 active Juvenile idiopathic arthritis (JIA) patients were stimulated ex vivo with 1 mg/ml of Zymosan for 22h. Whole blood RNA analysis was also performed, using a human immune array (TaqMan Human Immune Array from Applied Biosystems), containing 92 genes typically involved in the immune response.

Results: The median age at symptoms onset was 11.4 months (IQR 4.6–35.2) and the median disease duration was 6.8 years (IQR 4.1–11). Sequencing of NLRP12 gene in the 12 patients revealed 5 heterozygous mutations: F402L(n=6), G448A(n=1), H304Y(n=1), R1030G(n=1) and G39V (n=1). Two patients were homozygous for NLRP12 variants: F402L and G39V. In 12/12 variants of NLRP3 were also found: Q703K(n=4) and V198M(n=2). All patients had symptoms consistent with a recurrent inflammatory syndrome: 11/12 presented recurrent episodes of skin lesions, 11/12 arthralgia, 10/12 recurrent fever episodes, 8/12 arthritis, 10/12 headache, 11/12 fatigue, 5/12 conjunctivitis, 7/12 recurrent abdominal pain and lymphadenopathy, 5/12 oral aphthosis, 4/12 thoracic pain and 2/12 sensorineural deafness. During the attacks 5/12 patients showed increased acute phase reactants. In 5/12 patients anakinra was administered because of the severity of phenotype and the persistence of elevated acute phase reactants. In 2 of these 5 patients lack of efficacy led withdrawal of anakinra and introduction of tocilizumab with good response. In vitro cytokine release studies, performed in 9 patients, showed that the production of IL-6 and TNF-α was significantly higher in patients carrying the NLRP12 variants compared to patients with JIA (IL-6: 2841±1682 ng/ml and 1496±982.4 ng/ml respectively; p=0.0002 and p=0.0007) and even higher in homozygous patients; no significant difference in IL-1β production was found (2134±1026 ng/ml versus 1527±930.3 ng/ml; p=0.39). Whole blood RNA samples collected from 5 NLRP12 patients were compared to whole blood RNA samples collected from healthy controls for expression of 92 genes evaluated.

Conclusion: Our data in vitro and in vivo suggest that these NLRP12 variants are pathogenic. The role played by the concomitant presence of the NLRP3 variants remains to be clarified, though an effect in modifying the disease phenotype cannot be excluded. Our data also confirm the clinical and functional heterogeneity of NLRP12 related disorder, a condition often misunderstood. Furthermore, although the small number of patients treated, our data suggest that inhibition of IL-6 may be effective in NLRP12-related disorder.

Disclosure of interest: None declared.

Evidence based recommendations for diagnosis and management of mevalonate kinase deficiency (MKD)

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**P74**

**A functional inflammasome activation assay discriminates between genetically proven caps patients and patients with low penetration NLR3 variants**

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**Introduction:** The cryopyrin-associated periodic syndromes (CAPS) are characterized by recurrent episodes of systemic inflammation. CAPS is caused by mutations in the NLRP3 gene encoding cryopyrin, an important component of the NLRP3 inflammasome that activates caspase-1 resulting in inflammation by excessive production of IL-1β and other cytokines. A diagnostic dilemma is often encountered in patients with unspecific inflammatory symptoms like fatigue, muscle pain, arthralgia or slight hearing loss and low penetrance variants in NLRP3 / CASP1 with an inconsistent clinical phenotype. The analysis of IL-1β in the serum did not prove to be a valid diagnostic test in these individuals. **Objectives:** In this study we sought to investigate, if a functional inflammasome activation assay discriminates between genetically proven CAPS patients, patients with low penetrance NLR3 variants and healthy controls. **Methods:** The study population consisted of 16 patients with genetically proven Muckle-Wells syndrome, 9 patients with low penetrance NLRP3 variants (V198M, Q703K and E627G) and 14 healthy controls. **Results:** After 4h of LPS stimulation, secretion of NLRP3 inflammasome products (IL-1β, IL-1α, IL-18) and Caspase-1 were potently increased in MWS patients, whereas there was no increase in low penetrance NLRP3 variants and healthy controls (for IL-1β < 0.001 and for < 0.001, respectively). Minor differences were still detected at later timepoints and for LPS + ATP stimulation. **Conclusion:** Our functional inflammasome activation assay discriminates between genetically proven CAPS patients and patients with low penetrance NLRP3 variants. This assay might add to the decision, which individuals presumably benefit from an anti-IL-1 therapy. **Disclosure of interest:** N. Rieber Grant / Research Support from: Novartis Research Grant; A. Gavrilov: None declared, T. Endres: None declared, D. Hartl: None declared, J. Kümmerele-Deschner Grant / Research Support from: Novartis Research Grant.

**P75**

**Diagnostic value of urinary mevalonic acid excretion in mevalonate kinase deficiency (MKD)**

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**Introduction:** Mevalonate kinase deficiency (MKD) is a rare hereditary autoinflammatory syndrome, characterized by recurrent fever episodes with gastrointestinal complaints, rash and arthralgia. The deficient mevalonate kinase activity leads to elevated mevalonic acid, which is excreted in the urine. Therefore, an elevated mevalonic acid excretion is suggestive of MKD. However, the diagnostic value of this analysis has not been investigated yet and remains unclear. **Objectives:** To investigate the diagnostic value of urinary mevalonic acid excretion in patients with suspected MKD.
Methods: In this single center study, we retrospectively analyzed the results of all patients in whom both measurement of urinary mevalonic acid excretion and genetic analysis of the MVK-gene had been performed in the preceding 17 years. Mevalonic acid excretion was analyzed by using gas chromatography - mass spectrometry (GC-MS) and was expressed as mmol/mol creatinine and compared with age dependent reference values. The presence of two MVK mutations was considered as gold standard for the diagnosis of MKD. 

Results: The study included 63 patients (33 male, 30 female, aged: 0-36 year) with clinical features suggestive of MKD. Twenty-one patients had more than one assessment of mevalonic acid excretion. 

Thirteen patients harboured two MVK mutations. These 13 MKD patients suffered predominantly from recurrent fever episodes (n=13), diarrhoea (n=13), abdominal pain (n=13), arthralgia (n=12), myalgia (n=10), stomatitis (n=10) and rash (n=9). Further, arthritits (n=6), seizures (n=3), mild mental retardation (n=2), dysarthria (n=1) and retinitis pigmentosa (n=1) were reported. The disease started within the first year of life in all MKD patients. Two out of 13 had at least one negative mevalonic acid excretion. In one patient, this measurement was performed during a febrile episode. Another patient had one normal mevalonic acid excretion alongside five elevated assessments. 

Six patients had an elevated mevalonic acid excretion, but harboured no MVK mutations. At least two of these assessments were performed during a fever episode. Multiple urinary analyses were performed: all of the six patients had discrepancies between the urine analyses. Urinary mevalonic acid excretion was elevated twice in two patients, while four patients had only one elevated assessment. Main symptoms were recurrent fever episodes (n=5), abdominal pain (n=2), neutropenia (n=1), hypotonia (n=1), dysmorphic features (n=1), mild mental retardation and mild ataxia (n=1). None of the remaining 44 patients with a normal mevalonic acid excretion had an MVK mutation. 

This resulted in a sensitivity of 92%, a specificity of 88%, a positive predictive value of 67% and a negative predictive value of 98%. 

Conclusion: MKD seems very unlikely in patients with a normal mevalonic acid excretion, but it cannot be excluded completely. Therefore, detection of urinary mevalonic acid should not be mandatory before genetic testing. Nonetheless, a positive urinary mevalonic acid excretion requires MVK analysis to confirm the diagnosis MKD. 

Disclosure of interest: None declared.

References

P76

The IL-1 receptor antagonist anakinra (kineret®) stabilizes the NLRP3 mutation-specific risk for hearing loss in patients with severe cryopyrin-associated periodic syndromes (CAPS)

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Introduction: CAPS is a rare monogenic autoinflammatory syndrome consisting of a spectrum of three conditions: Familial cold autoinflammatory syndrome (PCAS), Muckle-Wells syndrome (MWS), and the most severe form, NOMID/CINCA. Progressive hearing loss is a characteristic of severe CAPS [1]. Previous analyses showed that long-term anakinra treatment stabilized the progression of hearing loss [2,3]. CAPS patients with different NLRP3 mutations have distinctly different trajectories of hearing loss, suggesting a mutation-specific risk that should be considered when making treatment decisions [4].

Objectives: To characterize the correlation between different NLRP3 mutations and hearing loss in severe CAPS patients and to evaluate whether long-term anakinra treatment stabilizes the progression of hearing loss.

Methods: A prospective open-label study with long-term extension including patients with severe CAPS was conducted at the National Institutes of Health [1,2]. The patients were treated with anakinra for up to 5 years. The patients who presented with NLRP3 mutations at baseline were further classified based on the gene location (D303N versus other locations). Hearing was monitored with audiogram which was evaluated with four frequency (0.5/1/2/4 kHz) pure tone average (4F-PTA), based on both air and bone conduction in the ear with best and worst hearing. The longitudinal changes in 4F-PTA were estimated with a mixed model for repeated measures (MRRM).

Results: Altogether 22 patients provided pre and post treatment audiogram data. NLRP3 mutation was identified in 18 (82%) patients, 7 (32%) presented with D303N and 11 (50%) with other locations (2 x T348M, G569R, L264F, A374N, F443L, G326E, L632F, Q600P, V262A, V351L). In a multivariate analysis, the baseline 4F-PTA (ear with best hearing, air conduction) correlated with both age (p=0.032) and location of NLRP3 mutation (p=0.049) so that older patients and patients with mutations outside of D303N presented with more hearing loss. Following the initiation of the anakinra treatment, no significant changes were seen in mean 4F-PTA at any time point up to 5 years in either patients with D303N or patients with other NLRP3 mutations in the MRRM analysis adjusting for age; thus, hearing remained stable. Comparable findings were seen in the worst ear based on air conduction and for best/worst ear based on bone conduction assessments.

Conclusion: Mutation-specific risk for hearing loss which is independent of age was seen based on the baseline audiogram data. Anakinra treatment for up to 5 years stabilized the progression of hearing loss regardless of the mutation.

Trial registration identifying number: NCT00069329


References
Evidence based recommendations for diagnosis and treatment of cryopyrin-associated periodic syndromes (CAPS)

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Objective: Cryopyrin-associated periodic syndromes (CAPS) is a group of rare monogenetic autoinflammatory disorders. Evidence-based guidelines are lacking and management is mostly based on physician’s experience. Consequently, treatment regimes differ throughout Europe. In 2012, a European initiative called SHARE (Single Hub and Access point for Autoinflammatory Disorders) was launched to optimize and disseminate diagnosis and management regimes in Europe for children and young adults with rheumatic diseases.

Method: Evidence based recommendations were developed using the European League Against Rheumatism (EULAR) standard operating procedure. An expert committee was instituted, consisting of pediatric and adult rheumatologists. The expert committee defined search terms for the systematic literature review. Two independent experts scored articles for validity and level of evidence. Recommendations derived from the literature were evaluated by an online survey. Those with less than 80% agreement on the online survey or with relevant comments of the experts were reformulated. Subsequently, all recommendations were discussed at a consensus meeting using Nominal Group Technique. Recommendations were accepted if more than 80% agreement was reached.

Result: The literature search yielded 1698 articles, of which 25 papers on treatment were considered relevant and therefore scored for validity and level of evidence. Seventeen were scored valid and used in the formulation of the recommendations. Fifteen recommendations were suggested in the online survey and discussed during the consensus meeting. Six general recommendations on management, five for monitoring and four for treatment were accepted with more than 80% agreement. Topics covered are the following: the multidisciplinary team, treatment goals, adjunctive therapies, psychosocial support and vaccinations [general recommendations], monitoring frequency, minimal assessments in all CAPS patients and monitoring of severe phenotypes [monitoring] and IL-1 blockade, NSAIDs and/or glucocorticoids during attacks and DMARDs/biologics other than IL-1 blockade [treatment].

Conclusion: The SHARE initiative provides recommendations for the management of CAPS and thereby facilitates improvement and uniformity of care throughout Europe.


Generalized pustular psoriasis in infant with heterozygous mutation in the IL36RN gene successfully treated with infliximab

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Objective: Homozygous missense mutation in the IL36RN gene resulting in deficiency of interleukin-36-receptor antagonist (DITRA) is phenotypically presented as severe generalized pustular psoriasis starting in early childhood. Compound heterozygous cases have been described with the same DITRA phenotype, but to our knowledge heterozygous IL36RN mutation related to severe generalized pustular psoriasis in early childhood has not been described.

Method: Case report

Result: First child of non-consanguineous caucasian (Danish) parents prenatally diagnosed with tetralogy of Fallot. Array CGH revealed normal karyotype. Pregnancy and delivery was uneventful. Mother had hemorhagic proctitis and psoriasis. The girl presented at 3 months of age with what appeared as infectious dermatitis and S. aureus cultured from skin lesions spreading to extremities and trunk. Blood tests including acute phase reactants were normal. She started on intravenous antibiotics and topical corticosteroids. During the following week the dermal changes presented with scaly sharply demarcated psoriasisform plaques. Infection was cleared and topical betamethasone gave a partial improvement. Cardiac surgery was performed at the age of 4 months. Procedures were uncomplicated but a precipitous flare of numerous pustules was then observed. Methotrexate treatment was initiated. On suspicion for DIRA or DITRA testing for IL1RN and IL36RN gene mutations was initiated. The girl was found to be heterozygous for a mutation in the IL36RN gene (exon 3, c.338C>T p Ser113Leu) whereas the IL1RN gene (mutated in DIRA patients) was normal. Additionally, a heterozygous mutation in the NLRP3 gene was also found (exon 3, c.2107C>T, p.Gln703Lys) via whole exome sequencing. Treatment with anakinra (4 mg/kg/day) had a marked positive effect, but did not result in total remission. MTX was increased to 15 mg/m²/week given subcutaneously. After 8 weeks and optimized doses 8 mg/kg/day of anakinra without sufficient remission the treatment was shifted to...
infliximab 6.5 mg/kg/dose on Day 0, 14, 28, hereafter every 4 weeks with excellent effect within few days on skin, general condition and thrive. Conclusion: To the best of our knowledge we report the first detailed description of an infant with heterozygous S113L IL6Ra mutation along with heterozygous Q705K NLRP3 mutation, phenotypically expressed as DITRA with severe generalized pustular psoriasis. Reduction of the IL36Ra function will lead to excessive activity of cytokines belonging to the IL-1 family, furthermore the gain-of-function mutation in NLRP3 will lead to excessive IL-1b and IL-18 production. Collectively, it makes conceivable that anti-IL-1 treatment would exert an effect on the disease. Accordingly anakinra has previously been reported with a successful result for the treatment of DITRA (11). Also in our patient anakinra showed a marked effect on general condition, reduced the eruptions of pustular lesions, but the erythodermal changes were preserved and therefore only a partial response of the skin lesions could be registered. However, we demonstrate in this infantile DITRA patient that TNF-alpha inhibition with infliximab dramatically improved the dermal changes and could normalize the skin within few weeks. Disclosure of interest: None declared.

P80 Evidence based recommendations for diagnosis and treatment of tumor necrosis factor receptor-1 associated periodic syndrome (TRAPS)

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Introduction: Tumor necrosis factor receptor-1 associated periodic syndrome (TRAPS) is a rare hereditary autoinflammatory syndrome that can lead to significant morbidity. Evidence-based guidelines are lacking and management is mostly based on physician’s experience. Consequently, treatment regimens differ throughout Europe. In 2012, a European initiative called SHARE (Single Hub and Access point for pediatric Rheumatology in Europe) was launched to optimize and disseminate diagnostic and management regimens in Europe for children and young adults with rheumatic diseases. Objectives: One of the aims of SHARE was to provide evidence based recommendations for diagnosis and treatment of TRAPS.

Methods: Evidence based recommendations were developed using the European League Against Rheumatism (EULAR) standard operating procedure. An expert committee was instituted, consisting of pediatric and adult rheumatologists. The expert committee defined search terms for the systematic literature review. Two independent experts scored articles for validity and level of evidence. Recommendations derived from the literature were evaluated by an online survey. Those with less than 80% agreement on the online survey or with relevant comments of the experts were reformulated. Subsequently, all recommendations were discussed at a consensus meeting using the nominal group technique. Recommendations were accepted if improved more than 80% agreement was reached.

Results: The literature search yielded 523 articles, of which 22 were considered relevant and therefore scored for validity. Seventeen were scored valid and used in the formulation of the recommendations. Seventeen recommendations were suggested in the online survey and discussed during the consensus meeting. Five general recommendations on management, two recommendations for diagnosis, seven for monitoring and eight for treatment were accepted with more than 80% agreement. Topics covered are the following: use of the multidisciplinary team, treatment goals and vaccinations [general recommendations], TNFRSF1A screening, interpretation of R92Q and P46L variants [diagnosis], monitoring frequency and minimal assessments, the use of AIDAI score in clinical studies and the risk of amyloidosis [monitoring], NSAIDS and/or glucocorticoids during attacks, IL-1 blockade, anti-TNF monoclonal antibodies, switching between biologicals [treatment].

Conclusion: The SHARE initiative provides recommendations for diagnosis and treatment for TRAPS and thereby facilitates improvement and uniformity of care throughout Europe.


P81 MEFV and NLRP3 gene variants in children with pfapa syndrome in slovenia

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Introduction: PFAPA syndrome is the most common autoinflammatory fever disorder in childhood, characterized by recurrent fever, aphthous stomatitis, pharyngitis and adenitis. Mutations in the MEFV and NLRP3 genes are known to cause syndromes with PFAPA overlapping symptoms (Familial Mediterranean Fever and Cryopyrin-Associated Periodic Syndrome), which are rarely reported in patients from Slovenia.

Objectives: The aim of the study was to assess the frequency of MEFV and NLRP3 gene variants in pediatric patients with PFAPA syndrome from Slovenia in order to determine whether genes involved in other autoinflammatory diseases, might play a role in PFAPA pathogenesis.
Methods: We collected clinical and laboratory data of PFAPA patients under the age of 5, who were followed at the University Children’s Hospital Ljubljana. All 10 exons of MEFV gene and 9 exons of NLRP3 gene, including intron/exon regions of both genes were directly sequenced.

Results: In total, 30 PFAPA patients were tested for MEFV and NLRP3 gene variants. Mean age at the syndrome onset was 2.1±1.3 and at diagnosis 4.2±1.8 years. 19(63%) patients were male and 11(37%) were female. Mean duration of episode was 3.5 days, mean interval between the episodes was 3.5 weeks. Most common symptoms beside fever were pharyngitis and cervical adenitis in 90% and aphthosis (always or sometimes) in 63%. Overall, 10 patients (33%) were found to have 11 variants, all in heterozygous state. 6 patients have Q703K variant in NLRP3, one E148Q in MEFV and one combination of I591T in NLRP3 and Q703K in NLRP3. Novel variant in NLRP3, P200T, was identified in one patient. One girl was found to have known variant in NLRP3 gene, S726G, which is associated with CINCA syndrome. This girl has had typical PFAPA symptoms, but she also has epilepsy and mild developmental delay.

Conclusion: Five different MEFV and NLRP3 gene variants were identified in 10 of 30 PFAPA patients with MEFV variants found in 2 patients and NLRP3 variants in 9. Our results indicate genetic heterogeneity of PFAPA population and possible overlap with other periodic fever syndromes.

Disclosure of interest: None declared.

Table 1(abstract P82)

<table>
<thead>
<tr>
<th>Gene</th>
<th>Sensitivity (Best Accuracy cut-off)</th>
<th>Specificity (Best Accuracy cut-off)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FMF</td>
<td>MKD</td>
</tr>
<tr>
<td>Genetically confirmed (Group A)</td>
<td>85%</td>
<td>92%</td>
</tr>
<tr>
<td>Not genetically confirmed (Group B)</td>
<td>58%</td>
<td>67%</td>
</tr>
</tbody>
</table>

P83
Genetic profiling of auto-inflammatory disorders in patients with periodic fever: a prospective study

Carlo De Pieni 1, Josef Vych 1, Anna Monica Bianco 1, Francesca Barbieri 1, Serena Pastore 1, Luca Ronfani 1, Sergio Crovella 1, Andrea Taddio 1, Giovanni Maria Severini 1, Alberto Tommasini 1, Institute For Maternal And Child Health Ircs Burlo Garofolo, Trieste, Italy; 1Department Of Medicine And Surgery And Health, University Of Trieste, Trieste, Italy; 1Institute For Maternal And Child Health Ircs Burlo Garofolo, Trieste, Italy; 1Department Of Medicine And Surgery And Health, University Of Trieste, Trieste, Italy; 1Pediatric Rheumatology 2014, 12(Suppl 1):P83

Introduction: Hereditary periodic fevers (HPF) are an emerging group of auto-inflammatory disorders. Although this group includes five well defined disorders, overlap of phenotypes can be often observed making the diagnosis more difficult. Although genetic diagnostics is currently available for different periodic fevers, many patients will require subsequent analyses for different genes. The selection of patients for genetic analysis is also not easy, despite scoring systems to assist the choice have been developed (Gaslinski score).

Objectives: We tested if a novel approach based on the simultaneous sequencing of HPF-related genes, can improve the diagnostics in this field.

Methods: Patients consecutively referred to the unit of pediatric rheumatology of the IRCCS Burlo Garofolo from March 2012 to April 2013 for unexplained periodic fever since 1 year or more, still active at the time of recruitment. In particular we considered the following three groups: 1) patients already studied for a single candidate gene with negative results; 2) atypical pharyngitis, adenitis and aphthae (PFAPA) syndrome based on absent response to steroids or relapse after tonsillectomy; 3) other patients with periodic fever with multi-systemic involvement.

Structured chart was used to collect personal data and information about episode duration and clinical features, including symptoms, laboratory and imaging investigations results, response to treatments (steroids, colchicine).
Results: A total of 43 patients were included in the study: 8 were previously evaluated for single genes (7 MVK, 2 NLRP3, 1 MEFV); 11 had atypical PFPAA (no response to the glucocorticoids of tionsellcotoxicy); 23 had periodic fever with multisystemic symptoms suggestive of no specific HPF. According to the international consensus for the interpretation of genetic results, we could find: definitly causative mutations (V377I/V377I mutation in MEFV H304Y in NLRP12); low penetrance mutation (2 R92Q in TNFRSF1A heterozygous high penetrance mutations (2 E148Q mutation in MEFV, 1 complex allele P369S-R408Q in MEFV, 1 V377I in MVK); single or multiple variants of unclear significance (overall 17, of which, 8 F402L variant in NLRP12, 5 Q703K variant in NLRP3). No variant in the five gene was found in 18 subjects.

Statistical analysis showed that the failure of glucocorticoids was significantly more frequent in subjects with any positive results to genetic analysis compared with subjects with negative genetic results.

Conclusion: Simultaneous sequencing of multiple HPF-related genes can help diagnosing in few cases. In most cases a wide range of genetic abnormalities is observed, ranging from low penetrance mutations to complex genotypes with multiple variants in different genes.

Disclosure of interest: None declared.

**P84**

Somatic mosaicism of CIAS1/NLRP3 gene in two patients with chronic infantile neurologic, cutaneous, articular syndrome

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Introduction: CINCA syndrome (chronic, infantile, neurological, cutaneous, articular syndrome) also known as neonatal-onset multisystem inflammatory disease (NOMID) represents the most severe form of cryopyrin-associated periodic syndrome (CAPS). This condition was found to be associated with missense mutations in the CIAS1/NALP3/PYPAF gene, which encodes cryopyrin. Cryopyrin is a member of the cytoplasmatic protein family CATERILLER, which is involved in inflammasome molecular platform assembly, leading to inflammatory immune response and apoptosis regulation. It has been hypothesized that mutant cryopyrin spontaneously oligomerizes and induces the inflammasome activation with elevated IL-1β production and autoinflammatory phenotype. Causative CIAS1 mutations have been detected in only half of the patients with CINCA and the genetic cause of the disease in patients who tested negative remains unclear.

Objectives: We describe two patients with severe CINCA syndrome who exhibited somatic CIAS1 mutations, with different percentage of mosaicism.

Methods: Case 1: female with urticarial skin rash since the first days of life, fever spikes since age of six months responsive only to steroids, knee arthritis from age 2 to 5 years. During the follow up she developed papilloma, persistent headache with mild cerebral atrophy at magnetic resonance, patella overgrowth and at age of 8 years perceptive deafness. Laboratory data always showed increased acute phase reactants. She was dependent on glucocorticoids to control her fever but no other symptoms until the age of 17, when she could be treated with anakinra and afterwards canakinumab with good clinical and laboratory response. Only perceptive deafness remains stable in spite of anti-IL1 therapy.

Case 2: female with widespread urticarial rash at birth who progressively developed spleen, liver, lymphnodes enlargement, recurrent coxalgia, a large lytic proximal tibial lesion histologically diagnosed as benign chondroid dysostosis; at age of 7 years a mild intellectual damage emerged; cerebral magnetic resonance was normal. Laboratory data were always abnormal with increased acute phase reactants. She reached complete remission after anti IL1 therapy (anakinra, followed by canakinumab).

Results: Conventional mutation analysis of all exons of CIAS1 failed to evidence any mutation in the two patients. A new mutation analysis was performed by dr. Arostegui (department of immunology, Hospital Clinic, Barcelona, Spain) to detect the allelic frequency of possible somatic mutations in exon 3 of CIAS1. The 1688 A>G mutation was found with a 6.5% allelic frequency in patient 1 and the c1298 C>T mutation was found with a 3.2% allelic frequency in patient 2.

Conclusion: In conclusion, we described two patients with typical CINCA syndrome or atypical genetic mosaicism of CIAS1. Such somatic mosaicism could be easily missed with the traditional sequencing of CIAS1. Notably, gain of function cryopyrin mutations are able to provoke a strong inflammatory phenotype even when presents in mosaicism only in a small percentage of immune cells.

Disclosure of interest: None declared.
on the transition process from pediatric care to adult care in patients with chronic inflammatory rheumatic diseases with childhood-onset.


### P86

**Title:** Regulatory B cell IL-10 production is diminished in juvenile dermatomyositis

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**Disclosures:** Christopher Piper: None declared., David Bendig: None declared., Hemlata Varsani: None declared., Katie Arnold: None declared., Lucy Wedderburn: None declared., Claudia Maun: None declared., Kiran Nistala: None declared.

**Introduction:** Juvenile dermatomyositis (JDM) is a childhood autoimmune disease characterised by proximal muscle weakness and cutaneous manifestations. Previous studies have identified an increase in circulating B cells in JDM patients, but their provenance and functional characteristics have not been examined. In this study we investigated whether an immature B cell subset (CD24hiCD38hi) known to be enriched for interleukin (IL)-10 producing regulatory B cells (Breg), accounted for the expansion of circulating B cells seen in JDM. The aryl hydrocarbon receptor (AhR) is a ligand based transcription factor, which induces IL-10 expression in T cells. We investigated the effects of modulating the AhR pathway on IL-10 expression in B cells.

**Objectives:**
- To characterise the peripheral blood B cell compartment in JDM patients with active disease and in disease remission (according to the PRINTO criteria).
- To test if the capacity of B cells from JDM patients to produce IL-10 and the AhR pathway alters B cell IL-10.

**Methods:** 54 patients were recruited through the UK JDM Cohort and Biomarker Study. B cell subpopulations from peripheral blood mononuclear cells (PBMC) isolated from healthy controls (HC) and JDM patients were analysed by flow cytometry using the surface markers CD19, CD24, CD38 and CD27. To detect B cell IL-10, PBMC were stimulated for 72 hours with CD40 ligand (CD40L) transfectected CHO cells or the toll like receptor 9 agonist CpG (ODN 2006) +/- Ahr antagonist (CHC-223191), together with PMA and ionomycin for the last 5 hours in the presence of Brefeldin A. Cells were then stained for CD19 and intra-cellular IL-10, which was detected by flow cytometry.

**Results:** PBMC from JDM patients with active disease had a significantly lower frequency of CD24hiCD38hi Breg when compared to inactive JDM patients (median of 7.6% vs 12.9% respectively, p=0.0109). Active patients had a lower frequency of IL-10 producing B cells compared to inactive patients (median of 3.5% vs 4.3% respectively, but this was only observed following stimulation with CD40L and not CpG. Inhibition of AhR following CD40L stimulation augmented IL-10 production in JDM B cells, restoring it to normal levels. Blocking AhR had no effects on CpG induced B cell IL-10.

**Conclusion:** These data identify a reduction in Breg in JDM patients with active disease that was associated with defective CD40L induced IL-10, when compared to child controls. This defect was reversed following blockade of AhR. These results suggest that over-activity of the AhR pathway may contribute to the pathophysiology of JDM, by attenuating Breg function.

**Disclosure of interest:** None declared.

### P78

**Title:** How do tissue infiltrating B cells and plasma cells correlate with other inflammatory features in muscle tissue from patients with JDM?

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**Affiliations:** UK Juvenile Dermatomyositis Research Group

**Disclosures:** Erdal Sag: None declared., Sheena A. Yasmin: None declared., Katie Arnold: None declared., Janice L. Holton: None declared., Tom S. Jacobs: None declared., Lucy R. Wedderburn: None declared.

**Introduction:** The International Juvenile Dermatomyositis (JDM) Biopsy Consensus Group has previously published and validated a scoring tool for assessment of the severity of pathological change in biopsy specimens from patients with suspected or proven JDM. This tool assesses histological features characteristic of JDM, organised into four domains (inflammatory, vascular, muscle fibre and connective tissue). The score tool includes the assessment of CD3+ and CD68+ inflammatory cells. Given that JDM is a disease characterised by production of autoantibodies and some patients respond to anti-B cell therapy we hypothesise that B cells play an important role in the pathogenesis of the disease.

**Objectives:** We aimed to define the extent and patterns of B cell and plasma cell infiltration in JDM muscle biopsy tissue and compare these features with inflammatory domain scores of the validated score tool.

**Methods:** Muscle biopsies from the UK Juvenile Dermatomyositis Cohort and Biomarker Study taken at the time of disease presentation were analysed. All children had definite or probable JDM according to the Bohan and Peter criteria, disease duration of <12 months before biopsy and had their biopsy sample taken before use of steroids or disease-modifying agents such as methotrexate or other immunosuppressive agents. Each biopsy was stained for cells expressing CD20 (B cells), CD138 (plasma cells), CD3 (T cells), and CD68 (macrophages). For each of endomysial, perimysial and perivascular distributions, scoring was performed for CD3+, CD68+, CD20+ and CD138+ infiltrating cells using the criteria of the score tool. Spearman’s rank correlation coefficient was used to assess correlation between score data elements. SPSS 21.0 was used for statistical analysis.

**Results:** Twenty-six patients with JDM (14 male, 12 female) were included in this study. 73% of biopsies (n=19) contained CD20+ B cells while only 26% of biopsies (n=7) contained CD138+ plasma cells. The score for CD20+ cells was strongly correlated with the score for CD3+ cells (r=0.81; p<0.0001) and the inflammatory domain score (r=0.87; p<0.0001). Among those biopsies that contained CD138+ plasma cells, the CD138+ score was correlated with the score for CD20+ cells (r=0.89; p=0.026), the score for CD3+ infiltrating cells (r=1.0; p<0.0001) and the inflammatory domain score (r=0.84; p=0.015). In most cases, B cells were co-localised with T cells especially at perivascular and endomyosal regions but in some cases they were diffusely scattered. No specific patterns were observed for plasma cells which were found as individual scattered cells mainly in the perimysium.

**Conclusion:** Both B cells and plasma cells are present in the inflamed tissue of some muscle biopsies of JDM patients. In this cohort of JDM patients, B cell and plasma cell infiltration was correlated with CD3+ and the inflammatory domain scores of the published score tool. The distinct patterns of B and plasma cell infiltration and how these correlate with autoantibody production and clinical features, warrant further investigation.

**Disclosure of interest:** None declared.

### P88

**Title:** Clinically inactive disease in juvenile dermatomyositis – a proposed revision to the printo criteria

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**Affiliations:** Juvenile Dermatomyositis Research Group (JDRG)

**Disclosures:** Beverley Almeida: None declared., Katie Arnold: None declared., Raquel Campanilho-Marques: None declared., Lucy Wedderburn: None declared., Clarissa Pilkington: None declared., Kiran Nistala: None declared.

**Introduction:** Chronic inflammatory rheumatic diseases with childhood-onset.

**Objectives:** How do tissue infiltrating B cells and plasma cells correlate with other inflammatory features in muscle tissue from patients with JDM?

**Methods:** Muscle biopsies from the UK Juvenile Dermatomyositis Cohort and Biomarker Study taken at the time of disease presentation were analysed. All children had definite or probable JDM according to the Bohan and Peter criteria, disease duration of <12 months before biopsy and had their biopsy sample taken before use of steroids or disease-modifying agents such as methotrexate or other immunosuppressive agents. Each biopsy was stained for cells expressing CD20 (B cells), CD138 (plasma cells), CD3 (T cells), and CD68 (macrophages). For each of endomysial, perimysial and perivascular distributions, scoring was performed for CD3+, CD68+, CD20+ and CD138+ infiltrating cells using the criteria of the score tool. Spearman’s rank correlation coefficient was used to assess correlation between score data elements. SPSS 21.0 was used for statistical analysis.

**Results:** Twenty-six patients with JDM (14 male, 12 female) were included in this study. 73% of biopsies (n=19) contained CD20+ B cells while only 26% of biopsies (n=7) contained CD138+ plasma cells. The score for CD20+ cells was strongly correlated with the score for CD3+ cells (r=0.81; p<0.0001) and the inflammatory domain score (r=0.87; p<0.0001). Among those biopsies that contained CD138+ plasma cells, the CD138+ score was correlated with the score for CD20+ cells (r=0.89; p=0.026), the score for CD3+ infiltrating cells (r=1.0; p<0.0001) and the inflammatory domain score (r=0.84; p=0.015). In most cases, B cells were co-localised with T cells especially at perivascular and endomyosal regions but in some cases they were diffusely scattered. No specific patterns were observed for plasma cells which were found as individual scattered cells mainly in the perimysium.

**Conclusion:** Both B cells and plasma cells are present in the inflamed tissue of some muscle biopsies of JDM patients. In this cohort of JDM patients, B cell and plasma cell infiltration was correlated with CD3+ and the inflammatory domain scores of the published score tool. The distinct patterns of B and plasma cell infiltration and how these correlate with autoantibody production and clinical features, warrant further investigation.

**Disclosure of interest:** None declared.
Introduction: Juvenile dermatomyositis (JDM) affects 3 children/million/year with myositis and skin disease being the typical features. PRINTO have recently established criteria to classify JDM patients who are clinically inactive by meeting at least 3 out of the following 4 conditions – CK ≤150, CMAS ≥48, MMTB ≥78 and physician global VAS (PGA) ≤0.2. CK, CMAS and MMTB all measure muscle involvement, only PGA includes skin or other organ involvement. The hypothesis that these criteria may fail to detect patients who have active skin disease but normal muscle parameters was tested.

Objectives: To demonstrate the prevalence of clinically inactive disease in the UK JDM Cohort and Biomarker Study and to identify whether skin disease is still present in these patients on the basis of the PRINTO criteria.

Methods: Data were analysed from children who were recruited and met Bohan-Peter criteria. Data from patient episodes (either a clinic visit or hospital admission) were assessed using the PRINTO criteria. Using the PRINTO rules stipulating 3 of 4 criteria are required, all data entries were divided into 2 groups based on the criterion that was omitted. Each case was analysed to determine whether skin disease was present or absent. Results: 682 data entries (DE) from 321 patients were identified as clinically inactive. 255 (37.4%) of these DE (119 patients) met all 4 criteria. 21.2% of DE had skin rash and 10.5% had nailfold changes (Table 1) at the time of assessment. 427 of the total DE (202 patients) met 3 of the 4 criteria. Of these, 320 (74.9%) had clinically inactive based on the 3 muscle criteria (PGA was not met). 61.6% of this group had ongoing skin rash present. Among the 107 remaining DE, which were clinically inactive by 3 criteria of which one was PGA, the frequency of skin changes was lower. The differences between the 3 groups were statistically significant in terms of rash (χ² 111.5, p<0.0001), nailfold changes (χ² 65.5, p<0.0001) and calcinosis (χ² 22.07, p<0.0001).

Conclusion: This study is one of the first to test the PRINTO criteria in a large independent cohort of JDM patients. When clinically inactive disease is defined by "muscle-based" criteria, without PGA, there is a greater frequency of skin disease. As a revision, we propose that PGA should be included as an essential criterion together with 2 of the 3 muscle criteria. This would prevent skin disease being overlooked in the clinical assessment which is important since it is often recalcitrant to treatment and may be associated with poor long-term disease outcomes. A revision of the criteria would need testing in independent cohorts.

Disclosure of interest: None declared.

**P90**

Correlation between muscular edema on magnetic resonance imaging versus major histocompatibility complex type II overexpression on muscle biopsy at diagnosis on juvenile dermatomyositis patients

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Introduction: Juvenile Dermatomyositis (JDM) is the most common idiopathic inflammatory myopathy in childhood. Magnetic resonance imaging (MRI) is a non invasive tool to assess muscular edema. Its ability to distinguish between active JDM patients and inactive and healthy children is well described in the literature. However muscle biopsy still
remains the gold standard in JDM diagnosis. Major Histocompatibility Complex (MHC) type I is overexpressed on sarcolemma of inflammatory myopathies and it could be detectable before inflammatory infiltrate appears on conventional techniques and remains there in spite of treatment.

Objectives: To assess clinical characteristics, muscular MRI pattern and MHC type I overexpression on sarcolemma and sarcoplasm on muscle biopsy at diagnosis of our JDM patients among 2000 and 2013.

Methods: We made a retrospective chart, including MRI and muscle biopsies. Muscular edema, fascia involvement and soft tissue edema were assessed by a Pediatric Radiologist on paravertebral and scapular and pelvic girdle muscles and scored as present or not and defined as patchy or diffuse. Muscle biopsies were evaluated with conventional techniques (hematoxilin-eosine and trichromique) and MHC type I immunohistochemical study. We evaluated perifascicular atrophy, regenerated and necrotic fibers and inflammatory infiltrated, being pathological the presence of one of the aforementioned. We study the MHC type I overexpression on sarcolemma and sarcoplasm scored as mild=1, moderate=2 and severe=3, describing as well the percentage of affected muscle fibers. The results were assessed by a neuropathologist.

Results: 23 patients were included. Demographic and clinical characteristics are summarized on table 1. MRI: 16 patients had MRI at diagnosis being pathological in 15. Thigh muscles were the most frequently affected (93% vs 86% and 79% of arm and paravertebral muscles respectively) and diffuse pattern more common than patchy one. 5 patients had soft tissue edema, 4 of these with fascia edema too. Muscle biopsy: 18 patients had muscle biopsy at diagnosis. All biopsied muscles except one were pathological on simultaneously MRI. Histological study show muscle affectation in 14 out of 18 patients but all patients overexpressed MHC type I on sarcolemma and sarcoplasm with 100% of fibres affected and a range of 50-100% and 15-100% on sarcolemma and sarcoplasm respectively. Median intensity scored on sarcolemma and sarcoplasm was 3 [1-3] and 1.5 [1-2].

Conclusion: MRI is an important non invasive tool to evaluate muscular edema in JDM patients but MHC type I overexpression on muscle biopsy seems to be the most sensitive technique for diagnosis at this moment. All our patients overexpressed MHC type I on sarcolemma and sarcoplasm, despite some of them had normal history.

Disclosure of interest: None declared.

P91 Tubuloreticular inclusions in juvenile dermatomyositis: a diagnostically useful marker?
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Pediatric Rheumatology 2014, 12(Suppl 1):P91

Introduction: Juvenile Dermatomyositis (JDM) is a rare life threatening disease affecting children. Symptoms include severe proximal muscle weakness and characteristic skin rashes. Vascular pathology is often a key finding in JDM including typical features of capillary drop out and abnormal blood vessel endothelial cells. We have observed that another common finding in JDM biopsies is the presence of tubuloreticular inclusions (TRI) detected by electron microscopy (EM) in blood vessel endothelial cells in muscle and the overlying skin. These are tubule-like structures within cisternae of endoplasmic reticulum.

Objectives: The aim of this study was to determine the frequency and specificity of TRIs in JDM biopsies compared to muscle biopsies investigated for other pathologies.

Methods: The UK JDM Biomarker and Cohort Study (JDBCS) provides access to a large JDM cohort, with linked samples and biopsies, (n=446, biopsies =135). We examined pathology by EM of 41 JDM biopsies and recorded reports of TRIs in blood vessel endothelial cells.

Results: Tubuloreticular inclusions were demonstrated in blood vessel endothelial cells in 80% of JDM muscle biopsies (33/41) and in the overlying clinically unaffected skin in 78% of cases (26/33) where this tissue was available. In contrast no TRIs in vessel endothelial cells had previously been reported in muscle biopsies investigated for other pathologies in children (n=500).

Conclusion: The high number of JDM muscle biopsies with identified TRIs compared to control biopsies investigated for other diseases suggests that TRI’s are a specific marker of JDM pathology. TRIs have also been found in other diseases such as glomerulonephritis (GN), lupus nephritis (LN), HIV and Degas disease and are suggested to be a biomarker of type I interferon (IFN) exposure. Type I IFN gene and chemokine signature is thought to be associated with JDM pathology and clinical features. The high specificity of TRIs in vessel endothelium in JDM biopsies compared to non-JDM biopsies suggests that their detection is useful in supporting a diagnosis of JDM in patients.

Disclosure of interest: None declared.

P92 Juvenile overlap myositis: retrospective study about 20 cases
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Pediatric Rheumatology 2014, 12(Suppl 1):P92

Introduction: Inflammatory myopathies during childhood are clinically, biologically and pathologically heterogeneous.

Objectives: The objective of this study is to collect cases of pediatric-onset overlap myositis to improve description and classification.

Methods: Retrospective study of patients followed in Necker-Enfants Malades Hospital (Pediatric Rheumatology, Pediatric Dermatology) from January 2002 to march 2014, with overlap myositis defined by the association of inflammatory myositis and clinic features and/or biological signs of other connective tissue diseases (clinical features among polyarthritis, Raynaud syndrome, sclerodactyly, morphea, lupus skin rash, esophageal dyskinésia, pulmonary, intestinal, renal involvement and/or presence of overlap autoantibodies). For every patient we collected at diagnosis clinical features, biological profile, histological and radiological (MRI) data, treatments and evolution.

Results: Twenty patients were included, 3 boys and 17 girls. The median age was 9 years 5 months (age between 3 years 9 months and 14 years 1 month). Every patient had myositis at diagnosis associated with polyarthritis (7 patients), Raynaud syndrome (4 patients), esophageal dyskinésia (2 patients), lung damage (interstitial lung disease or DLCO< 70%, 5 patients). Two patients had sclerodactyly, 5 had morphea. One patient had typical dermatomyositis at diagnosis and developed pulmonary involvement and cutaneous sclerosis during evolution. Serum creatine kinase level was elevated for thirteen patients at diagnosis. Eighteen patients had autoantibodies at diagnosis or during evolution (ANA=17/20, anti-RNP=6/19, anti-cardiolipin=6/14, anti-DNA=2/20, anti-Ku=2/12, anti-synthetase=1/15, anti Pm Scl=1/7). Muscular MRI was performed on 12 patients (myositis=5/12, subcutaneous involvement=7, bone edema=6). Muscular biopsy was done on 16 patients (inflammation=8, capillary loss=6, CMH I expression=14, perifascicular atrophy=6). The first-line treatment included corticosteroid therapy (18 patients), alone (11 patients) or associated with hydroxychloroquine (8 patients), methotrexate (5 patients), intravenous immunoglobulins (2 patients), mycophenolate mofeti (2 patients), azathiorpine (1 patient) and plasmatic exchange (1 patient). The median duration of follow up is 20 months (from 7 months to 5 years): no patient died. Ten patients are in complete remission on the muscular plan. Nevertheless a majority develops a reactivation of the disease. Corticosteroid therapy is required for a long period of time.

Conclusion: This study is the first study emphasizes juvenile overlap myositis. Juvenile overlap myositis is a heterogeneous diseases and differ from adult myositis. A specific pediatric classification is warranted to improve characterization and to adapt treatments. MRI and histological datas appear to be relevant, nevertheless it is essential to evaluate their reliability prospectively so that we can use them to improve classification and determination of prognostic factors.

Disclosure of interest: None declared.
Between 2012 and 2014, 67 JDM patients were assessed. 59.7% of the cohort were included. Each patient was evaluated using classifications for disease activity (CMAS and MMT8), disease damage, Disease Activity Score (DAS) and Myositis Intention to Treat Activity Index (MITAX), either with skin components, with all skin assessed to measure skin disease in JDM; however the optimal tool is unknown.

Objectives: To compare three tools for assessment of skin disease in JDM and correlate them with the physician's 10cm visual analogue scale (physician's skin VAS) to define which tool best assesses skin disease.

Methods: Patients recruited to the UK JDM Cohort & Biomarker Study who fulfil Bohan-Peter criteria for JDM were included. Each patient was assessed for skin disease using the CAT, DAS, MITAX and an overall physician's skin VAS. Markers of muscle disease (CMAS, MMT8, CK U/L), inflammatory markers (CRP mg/L and ESR mm/hr) and overall physician’s global score were also recorded. Spearman's correlations (r_s) were used to correlate categorical and continuous variables and a relationship >0.75 was considered strong. A p-value <0.05 was considered significant.

Results: Between 2012 and 2014, 67 JDM patients were assessed. 59.7% were female. The mean (±SD) age of the patients was 9.86 ±3.37 years, with mean age at diagnosis 6.59 ±3.42 years and mean disease duration of 3.26 ±3.08 years. The skin section of the DAS had the strongest correlation with the physician’s skin VAS (Table 1). The skin section of the MITAX and the CAT activity scores were significantly correlated with the physician's skin VAS. DAS skin, MITAX skin and CAT Activity scores were all negatively correlated with CMAS and MMT8 scores; no significant correlations were noted with the CK. DAS skin scores were significantly correlated with both the CRP and ESR, while the MITAX skin was significantly correlated only with the ESR, and CAT Activity only with the CRP.

Conclusion: These data demonstrate the potential application of using a skin assessment tool to evaluate and monitor skin involvement in JDM patients. It also demonstrates that the DAS skin section appears to be the best of the three tools for physician's skin VAS as the gold standard. The DAS skin tool was concise, quick to use and easy to score.

Disclosure of interest: None declared.

Table 1 (abstract P93) Spearman’s correlation between items shown as r_s and corresponding p value

<table>
<thead>
<tr>
<th></th>
<th>Physician’s skin VAS</th>
<th>CMAS</th>
<th>MMT8</th>
<th>CK</th>
<th>CRP</th>
<th>ESR</th>
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<tr>
<td>n=67</td>
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<td>n=52</td>
<td>n=55</td>
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</tr>
<tr>
<td>DAS</td>
<td>r_s 0.795</td>
<td>-0.443</td>
<td>-0.424</td>
<td>0.176</td>
<td>0.280</td>
<td>0.311</td>
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<td></td>
<td>p&lt;0.001</td>
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<td>p&lt;0.001</td>
<td>p&lt;0.012</td>
<td>p&lt;0.039</td>
<td>p&lt;0.022</td>
</tr>
<tr>
<td>MITAX</td>
<td>r_s 0.594</td>
<td>-0.404</td>
<td>-0.453</td>
<td>0.177</td>
<td>0.208</td>
<td>0.281</td>
</tr>
<tr>
<td></td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
<td>p&lt;0.020</td>
<td>p&lt;0.017</td>
<td>p&lt;0.040</td>
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<tr>
<td>CAT</td>
<td>r_s 0.623</td>
<td>-0.471</td>
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<td>0.157</td>
<td>0.300</td>
<td>0.164</td>
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<td>p&lt;0.001</td>
<td>p&lt;0.027</td>
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P94

Progress report on development of classification criteria for adult and juvenile idiopathic inflammatory myopathies

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Introduction: Classification criteria are needed to aid recruitment of appropriate patients into research studies. The International Myositis Classification Criteria Project (IMCCP) was set up with support from ACR and EULAR.

Objectives: To develop and validate new classification criteria for adult and juvenile IIM.

Methods: Candidate criteria variables were taken from published criteria and inclusion criteria from clinical trials of myositis. Comparator groups for IIM were defined. Clinical and laboratory data from IIM and comparator patients were collected from 47 rheumatology, dermatology, neurology and pediatrics clinics worldwide from 2008-2011. Pair-wise associations among all items and between each item and clinicians’ diagnoses were assessed. Three approaches for derivation of classification criteria were explored: Traditional, Probability score and Classification tree. Internal validation using bootstrap methods and external validation using data from the Euromyositis register and the Juvenile Dermatomyositis cohort biomarker study and repository UK and Ireland was performed.

Results: 976 IIM (74% adults; 26% children) and 624 comparators (81% adults; 19% children) were obtained. The new criteria comprise clinical items on muscles, skin, and laboratory measures. Muscle biopsy features can be included. Each item has an assigned score, the total score corresponds to the probability of having IIM. Each probability has specific sensitivity/specificity measures making it possible to use individual inclusion criteria for clinical studies. If no skin rash is present a muscle biopsy is mandatory. High probability of IIM is considered if the score > 7.5 (or > 8.7 if no skin rash), with minimum probability cutoff of 50% (score 5.3 or 6.5). Table 1.

External validation using data on 592 adult or 332 juvenile IIM patients yielded 100% sensitivity.

Conclusion: The new classification criteria for IIM have easy-to-access items and show generally superior performance compared to existing criteria. Approval for these will be sought from ACR/EULAR.

Disclosure of interest: None declared.

P96

Safety and efficacy of creatine supplementation in juvenile dermatomyositis: a randomized double-blind placebo-controlled cross-over trial

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Pediatric Rheumatology 2014, 12(Suppl 1) P96
Juvenile dermatomyositis patients may experience persistent weakness, loss of bone mass, and skeletal muscle atrophy as a long-term result of drug treatment and/or disease itself. In this regard, efforts to develop new therapeutic strategies able to attenuate these adverse outcomes have been considered of clinical relevance. It has been suggested that creatine supplementation could be safe, effective and inexpensive for treating idiopathic inflammatory myopathies, but no pediatric study has been conducted so far.

Objectives: To examine the safety and efficacy of creatine supplementation in JDM patients

Methods: JDM patients received placebo or creatine supplementation (0.1 g/kg/d) in a randomized, crossover, double-blind, repeated-measures design. Subjects were assessed at baseline and at 12 weeks, with 8-week washout period. Primary outcome was muscle function. Secondary outcomes included body composition, bone mineral density, biochemical markers of bone remodeling, inflammatory cytokines, aerobic conditioning, health-related quality of life, and disease-related parameters, dietary intake and muscle phosphorylcreatine (PCR) content. Safety was assessed by laboratory parameters and kidney function

Results: Intramuscular PCR content was not significantly different between creatine and placebo before or after the intervention (Creatine - Pre: 21.4 ± 5.3, Post: 20.6 ± 2.7, delta score = -0.3 ± 3.5 mmol/kg wet muscle, ES = -0.15; Placebo - Pre: 20.4 ± 3.7, Post: 20.7 ± 3.6, delta score = -0.1 ± 4.2 mmol/kg wet muscle, ES = -0.15; 95% CI for delta score = -2.8 ± 2.4, p = 0.45 for interaction between creatine and placebo). No significant changes between placebo and creatine for muscle function and aerobic conditioning, body composition, bone mineral density, and quality of life were seen, probably due to the lack of change in intramuscular PCR content. Kidney function was not changed after creatine supplementation and no side effects were noticed.

Conclusion: A 12-week creative supplementation protocol is well tolerable and free of adverse effects but did not affect intramuscular PCR, muscle function, body composition, bone mineral density or quality of life in JDM patients.

Disclosure of interest: None declared.

Table 1(abstract P94) Performance of new and existing classification / diagnostic criteria for idiopathic inflammatory myopathies

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<td>Without muscle biopsy data</td>
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<td>94</td>
<td>98</td>
<td>96</td>
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<td>6</td>
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<tr>
<td>With muscle biopsy data</td>
<td>82</td>
<td>85</td>
<td>55</td>
<td>31</td>
<td>88</td>
<td>99</td>
</tr>
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a Cut point for probability: 55%

Introduction: Subclinical pulmonary abnormalities in juvenile dermatomyositis

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Pediatric Rheumatology 2014, 12(Suppl 1)P97

Introduction: Subclinical pulmonary abnormalities in juvenile dermatomyositis (JDM) is frequent and associated with poor outcome. However, a systematic assessment of pulmonary function and high-resolution computed tomography (HRCT) was rarely reported in this population.

Objectives: To assess pulmonary function and HRCT in JDM patients and to evaluate possible associations between pulmonary abnormalities and disease activity, cumulative damage and health-related quality of life (HRQL) scores.

Methods: A cross-sectional study was performed in 20 JDM patients. Pulmonary function test included spirometry, body plethysmography and diffusion capacity for carbon monoxide (DLCO). They were also carried out six-minute walk test (6MWT) and HRCT scan. Disease activity score (DAS), childhood myositis assessment scale (CMAS), myositis damage index (MDI) and HRQL (Pediatric Quality of Life Inventory - PedsQL) data were also assessed.

Results: The mean age was 11.6 years (6-18). Subclinical mild/moderate obstruction according to American Thoracic Society criteria was observed in 35% and DLCO was reduced in 20% of JDM patients. Spirometric and/or DLCO abnormalities were observed in 45% of patients. In plethysmography, reduced total lung capacity (TLC) and conductance were observed in 25% and 50% of JDM patients, respectively. In contrast, increased resistance and residual volume (RV)/TLC were evidenced in 10% and 35% of JDM patients, respectively. Thirteen patients underwent HRCT and 8 had alterations: interstitial lung disease in 6 and a mixed pattern in two. A positive correlation was observed between DAS and ratio between forced expiratory volume in one second and vital capacity (VEF1/CV) (r=+0.50, p=0.003), conductance (r=+0.46, p=0.045) and HRCT score (r=+0.60, p=0.003). A positive correlation was observed between CMAS and VEF1/CV (r=+0.47, p=0.042), DLCO (r=+0.67, p=0.002) and 6MWT (r=+0.54, p=0.048), and negative correlation between DAS and HRCT score (r=-0.63, p=0.021). Correlations were identified between MDI and conductance (r=+0.72, p=0.0004), DLCO (r=-0.46, p=0.042) and HRCT score (r=+0.81, p=0.0008); and between PedsQL and VEF1/CV (r=-0.45, p=0.046), conductance (r=+0.60, p=0.006) and HRCT score (r=+0.62, p=0.024). Correlations were also observed between HRCT score and VEF1/CV (r=-0.64, p=0.017), forced expiratory flow between 25 and 75% of vital capacity (FEF25%-75%) (r=-0.59, p=0.035) and conductance (r=-0.78, p=0.0018).

Conclusion: Subclinical pulmonary abnormalities were frequent in this rare idiopathic inflammatory myopathy. Importantly, these findings may be related to disease severity and activity, and may influence HRQL of these patients.

Disclosure of interest: None declared.

P98

New criteria for diagnosis of benign joint hypermobility in children

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Pediatric Rheumatology 2014, 12(Suppl 1)P98

Introduction: Benign joint hypermobility (BJH) is a clinical condition characterized by an increased ability of joints during passive and dynamic movements.

Objectives: To our knowledge, current criteria’s for BJH are on the basis of all age groups. These criteria are not specified for pediatrics yet. Therefore, we decided to determine new diagnostic criteria for benign hypermobility in children and compared it with the most popular, Beighton Criteria.

Methods: Clinical study which enrolled 108 cases, from 3 to 16 years of age who was diagnosed as BJH previously by Beighton Criteria. The
A survey of knowledge attitudes and practices relating to musculoskeletal examination amongst pediatricians in maharashtra, India

Introduction: Musculoskeletal examination(MSKe) is a neglected clinical skill in paediatric practice and this could contribute to delayed or missed rheumatological diagnosis in children. paediatric Gait Arms Legs Spine (pGALS), a simple format of MSKe, targeted at non specialists has been shown to be acceptable and valid. Its potential as a clinical tool in populations underserved by paediatric rheumatologists, such as India, has yet to be explored. This information could be used to design curricula and teaching methods to students and practitioners in such areas.

Objectives: To assess the Knowledge, Attitude and Practices relating to MSKe in Paediatricians in one state of India.

Methods: An internet based survey between March and April 2014 based on a published UK study of self reported confidence in MSKe in children (Jandal). A questionnaire was emailed to all paediatricians on a professional database from Maharashtra state (capital-Mumbai).The questions (with Likert scale) related to profiling respondents qualifications / experience, clinical practice, MSKe training (in adults / children), confidence in MSKe compared to other systems, awareness / use of pGALS and free text comments regarding preferred technique of MSKe teaching. Responses were anonymous and reminders were sent. This was deemed an audit of clinical practice without need for ethical approval.

Results: The response rate was 223/1523 (14.6%). Most respondents, (180/223,80.72%) reported training in MSKe either in children (36.77%) or adults (6.28%) or both (37.67%). Despite this training 120/223, (53.81%) were confident in ‘some aspects’ and a lesser number (80/223,35.87%) in ‘most aspects’ of MSKe; notably respondents were less confident in MSKe compared to other systems. Respondents reported that physical exam comprised 1/3 of routine paediatric consultation, but MSKe was included in a minority (70/223, 31.39%) of routine consultations; many respondents (115/223, 51.57%) deemed MSKe integral to routine physical exam (albeit of these 62/115 ie 55.3% were not confident in their ability to perform MSKe) and the rest, performed MSKe only in the presence of overt MSK complaints. Notably of those who had been taught MSKe 58/180 (32.2%) actually performed this as a part of their routine consultation; of these respondents, 43.8% claimed to be confident in ‘most’ aspects. Most respondents (158/223,70.85%) were unaware of pGALS, although almost all (99%) expressed the need to include MSKe teaching in medical schools and 64% stated a need for training in both undergraduate and post graduate curricula. Of those unaware of pGALS, most (85%) expressed a desire to learn it and from a list of multiple options for format of resources, preferred ‘hands on’ workshops (50%), a CD demonstration (49.47%), or written materials (36.7%).

Conclusion: This survey shows that at least for one state in India many paediatricians are not confident in MSKe and are less confident about it compared to other systems included in medical training. There is need for greater training and awareness about the importance of MSKe to those already in practice which should translate to its routine use with increased confidence. There is also a definite need to emphasize MSKe training in medical schools. Lastly as a simple validated skill, there is considerable potential to increase awareness about pGALS amongst paediatricians using easy methods and thereby improve performance of MSKe in clinical practice.

Disclosure of interest: None declared.

Factors associated with pain in children with hypermobility – a pilot study

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Great Ormond Street Hospital, London, UK

Objective: To explore the relationships between the degree of musculoskeletal pain, pain associated with disability and quality of life are affected by having hypermobile joints.

Methods: Young people aged between 8-14 were recruited from the rheumatology based Non-Inflammatory Musculoskeletal Pain Clinic at Great Ormond Street Hospital over a 12 month period. They were assessed using biomechanical measures (muscle strength and degree of hypermobility), sensory processing using Quantitative Sensory Testing and psychological measures of anxiety, depression and pain coping styles using validated questions. Full Ethics approval was granted.

Results: 30 children were recruited (18 female: 12 male); mean age 11.08 with 77% being Caucasian. The mean Beighton score was 6.79/9. All patients reported pain mainly affecting lower limbs with an average score of 49/100 VAS. Degree of hypermobility did not have any impact. Reduced muscle strength was associated with increased pain and reduced quality of life. Other measures were compared to the norms for healthy children. Children with hypermobility appeared to demonstrate increased depression, negative mood, anhedonia and increased anxiety. They demonstrated reduced quality of life specifically with school, emotional well being, physical health and psychosocially. The subjects also had reduced sensitivity to touch including hot and cold.

Conclusion: The pain experienced by children with hypermobile joints is complex and includes biomechanical, sensory, psychological and social factors. This pilot study is planned to be expanded into a multi-centred project depending upon funding.

Disclosure of interest: None declared.

Autoantibodies frequency in children with visceral leishmaniasis

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Introduction: The visceral leishmaniasis (VL), or Calazar, is a chronic severe systemic disease, potentially fatal to humans. Currently, VL is the prototype of a specific immune dysfunction resulting from parasitism of leishmania donovani in macrophages, producing a broad spectrum of clinical and immunological reversible only with specific treatment. Serum Analysis from infected adult patients demonstrated the presence of autoantibodies against cellular and humoral components, and circulating immune complexes.

Objectives: To identify the profile of autoantibodies in pediatric patients with VL and its correlation with clinical outcome.

Methods: Through a transversal study, was investigated the occurrence of autoantibodies (antinuclear antibodies (ANA), anti-ODA, anti-SM, anti-RNP, anti-SSb, anti-SSa, lupus anticoagulant, IgG and IgM anticardiolipin (aCL) antibodies) in 34 patients (under 18 years) with diagnosis of VL, at the beginning and shortly after treatment, in the period October 2010 to March 2011.

Results: The incidence of autoantibodies present at the beginning in patients with VL was 64,7% (10 with ANA positive (29,4%), 7 with lupus anticoagulant antibodies positive (20,58%), 8 with IgM aCL antibodies positive (23,5%) and 5 with IgG aCL antibody positive (14,7%) and 1 with Anti-RNP (2,9%). Sex, age, visceralomegal, nutritional status, treatment, use of corticosteroids, infections, hemophagocytic syndrome, febrile neutropenia,
hemoglobin level and platelet count parameters were correlated with the presence of antibodies (table 1). It was found associated anemia (p<0.05) with the antibody presence, but more studies are needed to evaluate the presence of hemolytic anemia associated. Infections: sepsis, pneumonia and urinary tract infection in 71.42% of total patients, but not correlated with antibodies. Autoimmunity was greatly reduced after treatment; the statistical significance remained after stratification in ANA.

**Conclusion:** Visceral leishmaniasis appears to correlate positively with the presence of ANA. Lupus anticoagulant, IgG ang IgM aCL, in children, as in adults possibly by triggering a systemic humoral response of Th2. We found association statistically significant with lower hemoglobin level in these patients. Further studies are needed to evaluate the antibodies pattern in these infections.

**Disclosure of interest:** None declared.

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**P102**

**Clinical and psychological status of patients with different types of juvenile arthritis**

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Pediatric Rheumatology 2014, 12(Suppl 1):P102

**Introduction:** Juvenile arthritis (JIA) is chronic potentially disabling disease, which may form certain psychological features in children. **Objectives:** The purpose is to reveal difference in psychological status of children depending on the clinical type of JIA. **Methods:** Clinical interview; Lüscher 8-color test; Spielberger-Khanin test; CMAS (A. Prikhozhan adaptation); family drawing test; non-existent animal test, house tree man test; pathodiagnostic test.

**Results:** A tendency for higher level of personal anxiety is found in patients with oJA (33.3%), to a lesser extent in patients with pJA (20.7%) and sJA (17.6%). The patients have low social adaptation (16.7%; 11.3%; 5.9% correspondingly) and signs of stress disorder (11.1% with oJA; 5.7% with pJA; 0% with sJA); Cognitive disorders (23.5% with sJA; 11.1% with oJA; 7.5% with pJA) and aggression (11.8% with sJA; 7.5% with pJA; 0% with oJA) are more frequent in patients with JA. Communicative disorders are equally usual in patients with sJA (35.3%) and pJA (32%) and found in 22.2% of patients with oJA. Dissatisfaction with appearance is more frequent in patients with sJA (11.8%) and oJA (11.1%) than in patients with pJA (7.5%). Chronic low mood slightly prevails in patients with pJA (13.2%) over sJA (11.8%) and occurs in 5.5% of patients with oJA. Different neurotic fears are found with virtually the same frequency in patients with pJA (28.3%) and sJA (27.8%) and also in 5.9% of patients with sJA. Domestic stress is equally felt by patients with all JA types (44.4% with oJA; 41.5% with pJA; 35.3% with sJA). Hospital adaptation is harder for patients with oJA (5.5%) and pJA (3.8%) than for patients with sJA (0%).

**Conclusion:** Children with different types of JIA have been found to have certain differences in psychological status. Chronic low mood is more frequent in patients with pJA than in case of other types of the disease. Cognitive disorders and aggression are more frequent in patients with sJA. Patients with oJA are characterized by more frequent symptoms of personal anxiety, low social adaptation and school stress. Domestic stress indicators can be noted in patients with all types of JA. Clinical psychological status of patients with JIA needs further study with larger material to reveal stable tendencies and develop psychocorrective programs.

**Disclosure of interest:** None declared.

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**P103**

**Pain perception in turkish adolescents with fmf and their mothers: a preliminary report**

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Pediatric Rheumatology 2014, 12(Suppl 1):P103

**Introduction:** Familial Mediterranean fever (FMF) is the most common inherited autoinflammatory disease in the world and the patients suffer from recurrent self-limiting episodes of fever and painful polyserositis, particularly peritonitis, pleuritis and arthritis. **Objectives:** To determine whether there is a difference in pain perception between adolescents with FMF and their mothers'. **Methods:** Adolescents age 13-18 with a certain diagnosis of FMF and their mothers were invited to participate in the study. Demographic and clinical characteristics of the patients were obtained from hospital records and family interview. Pain perception was measured in rest and in activity with Visual Analog Scale 0-100 mm form.

**Results:** Fourteen children (10 Female) and their mothers were included in the study so far. The mean age was 15.21±1.37 years (min-max: 13-17 years), the mean duration of disease was 78.32±66.00 months (max-min: 2.5-180 months), the mean time since diagnosis was 53.36±63.40 months (min-max: 1-174 months). Mothers’ mean age was 39.93±5.38 years. The mean pain perception in rest was evaluated as 35.00±27.69 mm and 46.64±35.26 mm in adolescents and mothers, respectively (p=0.34). The mean pain perception in activity was determined as 63.29±32.11 mm and 67.93±38.86 mm (p=0.70) in adolescents and mothers, respectively.

**Conclusion:** According to our primary findings even though mothers have slightly greater pain perception for their children there is no statistically significant difference in pain perception between Turkish adolescents with FMF and their mothers. However, it should be kept in mind these are the preliminary results. Further studies including fathers and other relatives needed make permanent decision about pain perception of different family members.

**Disclosure of interest:** None declared.

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**P104**

**Psychosocial profile of children and adolescents followed in a pediatric musculoskeletal pain clinic**

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Pediatric Rheumatology 2014, 12(Suppl 1):P104

**Introduction:** Amplified pain syndrome preferentially affects girls between the ages of 10-17 years. It is a disease with multiple causes that could be associated with major psychosocial disorders of patients and caregivers, affecting their quality of life. These psychosocial aspects can interfere intensifying the pain. **Objectives:** This is a transversal study with the objective of evaluating the quality of life of patients seen in a pediatric musculoskeletal pain clinic, using a panorama of the educational, social, and psychological aspects.

**Methods:** 25 patients from our Pediatric Musculoskeletal Pain Clinic were consecutively selected. The patients and their caregivers responded to the following questionnaires: Children’s Depression Inventory (CDI), PedsQL™ (Pediatric Quality of Life Inventory™) 4.0, PedsQL Multidimensional Fatigue Scale, family APGAR score, and SF-36 Health Survey.

**Results:** We included 25 patients between the ages of 8 and 17, with an average of 12.6 years, 68% girls. In relation to the CDI, 95% were below the cutoff point, average=5.72. The highest score was 18 points. In the Family APGAR, the average was 13.4. In the PedsQL 4.0 the score of the patients were between 20.8 and 95.1 with an average=62.6 and SD=19.8. The score from the point of views of patients were between 25.15 and 90.1, with an average=59.5 and SD=18.6. Regarding the PedsQL-Fatigue, the variation was between 20.8 and 91.7, with an average=60.9 and SD=17.4, and the caretakers varied between 18.0 and 93.0 with an average=60.6 and SD=22.3. In the SF-36 the patients obtained averages (SD) of 57.7(29.14); 43.2(47.14); 46.5(21.87); 47.4(20.88); 52.2(19.16); 54.4(28.46); 56.3(35.36), and 61.9(24.30) for the domains: Functional capacity, limitation from physical aspects, pain, general health, vitality, social aspects, emotional and mental health aspects, respectively.

**Conclusion:** The patients did not present high rates of depression. However, we observed problems in family relationship and social life. Psychological problems could establish a causal relationship in some cases or reinforce the sensation of pain.

**Disclosure of interest:** None declared.
**P105**

**Rheumatic illness: transition from pediatric to adult care, patient satisfaction before and after the transition**

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*Pediatric Rheumatology* 2014, 12(Suppl 1)P105

**Introduction:** There is increasing focus on the problems involved in the transition and transfer of young adult patients, from paediatric to adult rheumatic units, because transition is a critical process in the life of patients.

**Objectives:** To assess patient satisfaction and quality of life from the "patients perspective", before and after the transition from paediatric to adult care.

**Methods:** Patients: Participants included 50 patients (M=12, F=38), matched for social class were asked to answer questionnaires for satisfaction end to fill PGWB1 test. This observational study had two phases. Prior to transfer pediatric patients to adult care, the subjects were asked to fill out a closed-question questionnaire addressing patients' satisfaction and PGWB1 to assess their quality of life. During the second period, the patients answered the same questionnaire when they were involved in their adult care. The psychological status of patients was assessed by the psychological general well-being (PGWB1). The PGWB1 is a 22-item questionnaire which produces self-representations of intra-personal affective or emotional states reflecting a sense of subjective well-being or distress, expressed by a summary score. The instrument measures components of psychological well-being such as anxiety, depressed mood, sense of positive well-being, self-control, general health and vitality. The closed-questionnaire is a short list of items aimed at investigating the sense of security felt by patients against the pediatrician rather than the adult clinician.

**Results:** See Table 1.

**Conclusion:** Transition from paediatric to adult care for chronic diseases causes a little increase in anxiety but an improvement of self control and of general health. Patients report a fair amount of dissatisfaction, but the results of PGWB do not confirm their dissatisfaction. Even the results of the questionnaire on patient satisfaction show that patients feel secure with doctor, both before and after the transition.

**Disclosure of interest:** None declared.

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**P106**

**Cyberbullying in adolescents: the next transition frontier**

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*Pediatric Rheumatology* 2014, 12(Suppl 1)P106

**Introduction:** Cyberbullying, particularly among adolescents, is an emerging issue within our society. Cyberbullying shares similar characteristics with traditional bullying such as repetition, power imbalance and intention. However, it differs in the fact that it is anonymous and rapid, with its victims unable to escape. The effects of cyberbullying on young people may have serious negative affects on their confidence, self-esteem, and emotional and mental wellbeing.

**Objectives:** To assess the incidence, experience, knowledge and beliefs on cyberbullying.

**Methods:** A convenience sample of 14 patients completed an on-line questionnaire. All participants attend the National Centre for Paediatric Rheumatology, Dublin.

**Results:** 14 participants: 6 Male, 8 Female. Median age = 14 years (13-18). 100% have daily access to the internet (average daily use, 3.8 hours). 100% have a profile page on 1 or more social networking sites (SNS). 45% do not have their SNS protected i.e. maximum privacy settings. 100% were familiar with the term "cyberbullying”. 83 % believed that social networking sites were the most common forum used to bully. Participants were asked if they had heard of the following categories of cyberbullying (Table 1).

67% of participants believed harassment was the most common type of cyberbullying followed by flaming (17%), cyber threats (8%) and cyber stalking (8%).

When asked if they had ever been a victim of cyberbullying, 33% admitted that they had. Of these 100% stated they had been harassed while 1 reported they were victims of flaming with 1 subjected to outing. All those who admitted to have been bullied in the past stated they did nothing about it.

2 respondents admitted to bullying other people online previously. When asked why, both stated it was in response to being threatened / harassed first. 88% stated they had been contacted by a stranger via the internet. Of these 29% reported that the stranger did try to arrange to meet them in person. 1 participant provided the stranger with false information about themselves and 1 gave their mobile phone number.

56% believed that health care professionals play an important role in preventing cyberbullying. 100% reported that if they were being bullied online that they would report it to a doctor or a nurse.

**Conclusion:** Awareness of health care professionals on the challenges associated with internet use is required in order to promote the safety and health of adolescents in cyberspace.

**Disclosure of interest:** None declared.

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**P107**

**MicroRNA’s role as biomarkers of lupus nephritis in children**

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*Pediatric Rheumatology* 2014, 12(Suppl 1)P107

**Introduction:** There is a dire need of non-invasive biomarkers of lupus nephritis (LN) activity. MicroRNAs (miRNAs) are endogenous, non-coding, single-stranded RNAs involved in the regulation of host genome expression at the post-transcriptional level. Previous microRNA expression profiling studies have generated some unique miRNA signatures (including miR-125a, miR-127, miR-146a, miR-150,miR-155) that are associated with systemic lupus erythematosus (SLE), but their role as biomarkers of LN has not been well examined.

**Objectives:** To determine levels of candidate miRNA biomarkers in blood and urine to the assess the differences in children with active LN vs. extrarenal SLE vs. controls. Also to assess potential associations with the LN-Panel [NGAL, MCP1, transferrin (Tf), Cystatin C, Beta-trace protein] of novel urinary biomarkers and traditional LN biomarkers (GFR, protein: creatinine ratio); and to explore combinations of biomarkers to predict LN activity using stepwise regression modeling.

**Methods:** In this ongoing research study, miRNA was measured using qPCR in the urine pellet (UP) and supernatant (sup) as well as blood in

**Table 1(abstract P105)**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before transition</th>
<th>After transition</th>
</tr>
</thead>
<tbody>
<tr>
<td>PGWB anxiety subscale</td>
<td>13,09±6,61</td>
<td>12,45±5,22</td>
</tr>
<tr>
<td>PGWB depressed mood subscale</td>
<td>10,91±3,42</td>
<td>10,64±2,54</td>
</tr>
<tr>
<td>PGWB positive well-being subscale</td>
<td>8,45±3,56</td>
<td>7,82±3,19</td>
</tr>
<tr>
<td>PGWB self-control subscale</td>
<td>9,64±3,26</td>
<td>10,64±3,47</td>
</tr>
<tr>
<td>PGWB general health subscale</td>
<td>9,00±3,10</td>
<td>10,55±3,21</td>
</tr>
<tr>
<td>PGWB vitality subscale</td>
<td>11,91±3,94</td>
<td>11,00±4,40</td>
</tr>
<tr>
<td>PGWB overall score</td>
<td>64,50±17,52</td>
<td>63,45±17,04</td>
</tr>
</tbody>
</table>
Table 1 (abstract P106)

<table>
<thead>
<tr>
<th>Activity</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flaming (online fights)</td>
<td>83%</td>
</tr>
<tr>
<td>Harassment (Repeated, malicious messages)</td>
<td>100%</td>
</tr>
<tr>
<td>Denigration (Posting rumours)</td>
<td>58%</td>
</tr>
<tr>
<td>Masquerading (The bully pretends to be the target)</td>
<td>42%</td>
</tr>
<tr>
<td>Outing (Sharing someone’s secrets)</td>
<td>58%</td>
</tr>
<tr>
<td>Trickery (Talking someone into revealing secrets, then sharing it online)</td>
<td>58%</td>
</tr>
<tr>
<td>Exclusion (Intentionally excluding someone from an online group)</td>
<td>42%</td>
</tr>
</tbody>
</table>

patients with JIA and fibromyalgia serving as disease controls and 14 patients with active LN and 10 with extraarrenal SLE every 6 months. Disease activity was measured by the SLEDAI. Urine samples were assayed for the LN-Panel and traditional biomarkers were recorded.

Results: LN activity measured by the SLEDAI was strongly positively correlated with sup levels of miR-125a (r > 0.7), moderately with miR-127, miR-150, miR-155 (r = 0.5), and moderately with miR-146a in blood cells. In the sup, miRNA-125a was significantly higher in active vs. not active LN (WSS test; p = 0.018) and was moderately associated with all LN-Panel markers (r = 0.53 – 0.66). Exploratory regression modeling suggests that NGAL, MCP-1, TF and miR-125a in the sup are relevant combinatorial LN biomarkers (all standardized beta coefficients > |0.3| and p < 0.01) to predict LN activity (renal SLEDAI) at high accuracy (R-square = 87%).

Similar results were found when the renal BILAG or SLICC Renal Activity Score were used to measure LN activity instead of the renal SLEDAI.

Conclusion: The miRNAs miR-125a, miR-127, miR-146a,miR-150,miR-155 are differentially excreted in the urine with active LN. Based on initial evaluations these miRNAs complement newer LN biomarkers (NGAL, MCP, TF) in their ability to assess concurrent LN activity.

Disclosure of interest: None declared.

P108 Urinary VCAM-1 as a biomarker of lupus nephritis disease activity

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Pediatric Rheumatology 2014, 12(Suppl 1):P108

Introduction: Up to 80% of children with Juvenile Systemic Lupus Erythematosus (JSLE) develop lupus nephritis (LN) (1), with the 5-year renal survival rate varying between 44-94% (2-4). Conventional markers of JSLE disease activity fail to adequately predict impending LN flares (5), with significant renal involvement (class III, IV or V LN) known to occur with low level proteinuria (6). Cross-sectional adult SLE studies have shown urinary vascular cell adhesion molecule-1 (VCAM-1) to be significantly higher in active LN than inactive LN or healthy controls, correlating with traditional markers of LN disease activity (7, 8).

Objectives: To investigate the role of VCAM-1 as a urinary biomarker in JSLE.

Methods: Urinary VCAM-1 concentrations were measured by ELISA (R&D Systems Ltd). The assay demonstrated 108-122% linearity of dilution, and 90-106% recovery using spike and retrieval techniques. Samples were diluted 1 in 80, and re-run at different dilutions where necessary. JSLE patients were classified as ‘JSLE active renal’ or ‘JSLE non-active renal’ based on the renal domain of the British Isles Lupus Assessment Group score (BILAG) (BILAG A/B vs. D/E). Healthy children (HC), attending for non-inflammatory surgery were recruited as controls. Demographic, clinical and biomarker data were not normally distributed, and expressed as median values and interquartile ranges (IQR). Mann-Whitney U test was used when comparing between groups, and correlations utilized the Spearman rank test.

Results: Sixty-seven patients participated in the study (50 JSLE patients and 17 healthy controls). JSLE patients had a median age of 16.5 years (range 10.07-21.91), and 36/50 (72%) were female. All JSLE patients had a median of 5 ACR classification criteria (IQR 4-7), with a median length of disease of 4.66 years (IQR 3.2-7.5). 23 (46%) JSLE patients were classed as JSLE active renal disease and 27 (54%) were JSLE non-active renal. Eleven (22%) JSLE patients had previously undergone a renal biopsy. Class IV LN (n=3), Class III (n=6) and Class II (n=6). The healthy controls had a median age of 12 years (range 4.0-16.0), with 5 being female (29%).

Urinary VCAM-1 levels were significantly higher in JSLE active renal patients (16.65 ng/mgCr [IQR 2.58-51.78]), versus non-active renal patients (2.3ng/mgCr [IQR 0.61-10.01], p=0.002) and HC’s (2.4ng/mgCr [0.54-4.50], p=0.003). A statistically significant correlation was seen between VCAM-1 levels, C3 (r = -0.38, p=0.009) and urinary albumin-to-creatinine (UAUC) ratio (r=0.49, p=0.001).

Conclusion: We have shown for the first time in children, that urinary VCAM-1 is able to identify patients with active renal lupus. Further assessment is required in prospective longitudinal studies.

Disclosure of interest: None declared.

P109 SHARE – workshop 5 : evidence based recommendations for diagnosis and treatment of childhood-onset systemic lupus erythematosus

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Pediatric Rheumatology 2014, 12(Suppl 1):P109

Introduction: Childhood-onset systemic lupus erythematosus (cSLE) is a rare multisystem autoimmune disease that often leads to significant morbidity. Evidence-based guidelines are sparse and management is mostly based on physician’s experience. Consequently, treatment regimens differ throughout Europe. In 2012, a European initiative called SHARE (Single Hub and Access point for paediatric Rheumatology in Europe) was launched to optimize and disseminate diagnostic and management regimens in Europe for children and young adults with rheumatic diseases such as cSLE.

Objectives: To develop evidence-based recommendations for diagnosis and treatment of cSLE.

Methods: Evidence based recommendations were developed using the European League Against Rheumatism (EULAR) standard operating procedure. An expert committee, consisting of paediatric rheumatologists from across Europe with expertise in cSLE, defined search terms for the systematic literature review. Two independent experts scored articles for validity and level of evidence. Through an online survey, experts evaluated recommendations derived from the literature. The recommendations were discussed at a consensus meeting using the nominal group technique 1.

Recommendations were accepted if more than 80% agreement was reached.

Results: The literature search yielded 9341 articles, of which 128 (75 for diagnosis; 53 for treatment) were selected for validity and level of evidence. Only sixteen articles (4 for diagnosis; 12 for treatment) were deemed valid; a larger number of articles were scored moderately valid (62 for diagnosis, 25 for treatment). Both were used in the formulation of the recommendations. Eighteen recommendations for diagnosis and 24 for treatment were suggested in the online survey. Thirteen recommendations for diagnosis and 14 for treatment were accepted with more than 80% agreement during the consensus meeting.

Table 1 summarizes the categories of recommendations.
Table 1 (abstract P109)

<table>
<thead>
<tr>
<th>Recommendations regarding:</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis:</td>
<td></td>
</tr>
<tr>
<td>Classification</td>
<td>3</td>
</tr>
<tr>
<td>Laboratory features</td>
<td>2</td>
</tr>
<tr>
<td>Access to other specialties</td>
<td>2</td>
</tr>
<tr>
<td>Comorbidities (growth/MAS/ hereditary conditions)</td>
<td>3</td>
</tr>
<tr>
<td>NP-SLE</td>
<td>3</td>
</tr>
<tr>
<td>Acknowledgement of necessary research</td>
<td>2</td>
</tr>
<tr>
<td>Treatment</td>
<td>1</td>
</tr>
<tr>
<td>General</td>
<td>2</td>
</tr>
<tr>
<td>Haematological involvement</td>
<td>1</td>
</tr>
<tr>
<td>Lupus Nephritis (Class III/IV/V)</td>
<td>8</td>
</tr>
<tr>
<td>Compliance</td>
<td>1</td>
</tr>
<tr>
<td>NP-SLE</td>
<td>2</td>
</tr>
</tbody>
</table>

Conclusion: The SHARE initiative provides recommendations for diagnosis and treatment for cSLE and thereby facilitates improvement and uniformity of care throughout Europe. Currently, a similar process is going on to add further guidelines including those on treatment and holistic care for PRD patients. As a final result, SHARE will provide standards of minimal care for different PRDs, including cSLE.

Disclosure of interest: None declared.

P110
Neutrophil extracellular trap-mediated activation of endosomal toll-like receptors induce immune activation in juvenile-onset systemic lupus erythematosus
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Pediatric Rheumatology 2014, 12(Suppl 1):P110

Introduction: Juvenile-onset Systemic Lupus Erythematosus (JSLE) is a multisystem autoimmune disorder characterized by the overproduction of autoantibodies against nuclear self-antigens. Activated neutrophils may undergo cell death by NETosis, forming mesh-like structures termed Neutrophil extracellular traps (NETs). Comprising of DNA, histones and antimicrobial proteins, increasing evidence implicates NETs in many pathological conditions, including SLE. Toll-like receptors (TLRs) are pattern recognition receptors capable of mediating immune responses. Endosomally localised TLR 7 and 9, endocytosed during NET formation, are TLRs that activate endosomal TLRs. NETs may be an important source of auto antigens in JSLE that are being detected through TLR 7/9 leading to the activation of these receptors. Furthermore, inhibition of TLR7/9 signalling reduced NET mediated activation of these receptors. Further studies are warranted of this important pathway in JSLE in order to identity potential therapeutic targets.

Disclosure of interest: None declared.

P111
SHARE – workpackage 5: evidence based recommendations for diagnosis and treatment of the antiphospholipid syndrome
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1Alder Hey Children’s Hospital, Liverpool, UK; 2Erasmus MC-Sophia, Rotterdam, Netherlands; 3University Medical Centre Utrecht, Utrecht, Netherlands; 4University Medical Centre, Ljubljana, Slovenia; 5Necker Hospital, Paris, France; 6Great Ormond Street Hospital, London, UK; 7General University Hospital, Prague, Czech Republic; 8 Sick Kids Hospital, Toronto, Canada; 9CHU de Béjere, Paris, France; 10Children’s Hospital of Helsinki and Uusimaa, Helsinki, Finland; 11Gazi University Hospital, Ankara, Turkey
Pediatric Rheumatology 2014, 12(Suppl 1):P111

Introduction: Antiphospholipid syndrome (APS), either primary or secondary to other paediatric rheumatic diseases, is rare in children, but it can lead to significant morbidity. Evidence-based guidelines are sparse and management is mostly based on physician’s experience. Consequently, treatment regimens differ throughout Europe. In 2012, a European initiative called SHARE (Single Hub and Access point for paediatric Rheumatology in Europe) was launched to optimize and disseminate diagnostic and management regimens in Europe for children and young adults with rheumatic diseases such as APS.

Objectives: To provide evidence based recommendations for diagnosis and treatment of APS. NETs may be an important source of auto antigens in JSLE that are being detected through TLR 7/9 leading to the activation of these receptors. Furthermore, inhibition of TLR7/9 signalling reduced NET mediated activation of these receptors. Further studies are warranted of this important pathway in JSLE in order to identify potential therapeutic targets.

Disclosure of interest: None declared.

Methods: Evidence based recommendations were developed using the European League Against Rheumatism (EULAR) standard operating procedure. An expert committee was instituted, consisting of paediatric rheumatologists from across Europe with expertise in APS. The expert committee defined search terms for the systematic literature review, which was performed in summer 2013. Two independent experts scored articles for validity and level of evidence. Recommendations derived from the literature were evaluated by an online survey. Those with less than 80% agreement during the online survey were reformulated. Subsequently, all recommendations were discussed at a consensus meeting using the nominal group technique (1). Recommendations were accepted if more than 80% agreement was reached.

Results: The literature search yielded 1463 articles, of which 15 (all relating to diagnosis only, none were relevant for treatment) were considered relevant and therefore scored for validity and level of evidence. Only 8 articles were deemed valid and were used in the formulation of the recommendations. In view of paucity of paediatric-specific data, the majority of proposed recommendations were developed based on adult-derived literature or expert opinion. Four recommendations for diagnosis and 2 for treatment were suggested in the online survey. During the consensus meeting, recommendations based on expert opinion were added. Three recommendations for diagnosis and 6 for treatment were accepted with more than 80% agreement after the consensus meeting. Table 1 summarizes the categories of recommendations.

Conclusion: The SHARE initiative provides recommendations for diagnosis and treatment for APS and thereby facilitates improvement and
uniformity of care throughout Europe. Currently, a similar process is going on to add additional guidelines including those on holistic care for PRD patients. As a final result, SHARE will provide standards of minimal care for different PRDs, including APS.

Disclosure of interest: None declared.

P112

B cell activating factor in juvenile onset systemic lupus erythematosus, looking beyond the B cell

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Pediatric Rheumatology 2014, 12(Suppl 1):P112

Introduction: Increased B cell activating factor (BAFF) in the serum of juvenile-onset systemic lupus erythematosus (JSLE) patients is thought to be key to the survival of auto-reactive B cells. BAFF signals through three receptors, BAFF-R, BCMA and TACI, activating the NF-kB pathway. Belimumab is a human monoclonal antibody against BAFF that has recently become the first drug licensed for the treatment of SLE in 50 years. In order to investigate the potential effect of BAFF inhibition on the wider immune system, receptor expression was investigated in another SLE pathogenic cell, the T lymphocyte.

Objectives: To determine T cell expression of the BAFF-R and BCMA receptors and the effect of BAFF on cell survival in JSLE patients compared to healthy paediatric controls.

Methods: Lymphocytes were isolated from JSLE patients and healthy paediatric controls. Cells were dual immunostained with fluorochrome conjugated monoclonal antibodies for BAFF receptors, BAFF-R or BCMA (FITC labelled) as well as the T cell marker CD3 (PECy5 labelled) allowing detection of T cells expressing the receptor to be identified by flow cytometry (n=8). Survival of T cells was assessed by quantifying the degree of apoptosis taking place using an Annexin V stain after 4 hours incubation with recombinant human BAFF (rhBAFF); receptor expression was analysed as stated previously (n=5). Results expressed as: mean+/-SEM. Statistical significance was taken when p values were <0.05.

Results: The total lymphocyte population was found to express both BAFF-R and BCMA receptors similarly in JSLE patients (BAFF-R 14.8% +/- 3.15; BCMA 4.98% +/- 0.86) and controls (BAFF-R 8.2% +/- 1.6; BCMA 6.07% +/- 0.87). T cells also displayed similar expression (JSLE: BAFF-R 3.37% +/- 0.42; BCMA: 1.91% +/- 0.31; Controls: BAFF-R, 3.27% +/- 0.82; BCMA, 2.34 +/- 0.96) with BAFF-R receptor expression more frequently than BCMA in both cohorts. Importantly, incubation with rhBAFF led to an increase in the survival of T cells when analysing both JSLE patients and controls together (n=9 pre treatment 29% +/- 3.1; rhBAFF treated, 19.7 +/- 2.7; p=0.008), and separately (JSLE: pre treatment, 31.04% +/- 2.34; rhBAFF treated, 25.03% +/- 1.13; p=0.043; Control: pre-treatment, 17.59% +/- 4.27; rhBAFF treated, 12.99% +/- 4.24, p=0.068). rhBAFF also significantly down-regulated BAFF-R expression in lymphocytes of both groups (n=9). Pre-treated; 11.51% +/- 2.00; rhBAFF treated: 5.02% +/- 0.907) Finally a positive correlation with the disease activity score SLEDAI was observed with JSLE patient BCMA receptor expression on both lymphocytes (correlation coefficient r=0.6 p=0.024) and T cells (r=0.67 p=0.013).

Conclusion: This study has demonstrated that T cells from paediatric patients express BAFF receptors as previously noted in adults. Interestingly both BAFF-R and BCMA receptors were detected. Whether by direct signalling or an indirect mechanism, BAFF has been shown to reduce apoptosis of T cells in both JSLE patients and healthy controls. This observation challenges the notion that T cells exclusively express BAFF-R highlighting that BCMA expression on T cells could be unique to the immature immune system. Importantly, these data indicate that this ‘B cell survival factor’ is also capable of influencing the survival of T cells in vitro. Aberrant T cell homeostasis is a pathogenic feature of SLE. To understand how increased T cell survival may affect the disease, it is important to understand receptor expression on different T cell subsets, including the inflammatory Th17 and anti-inflammatory Tregs. Allowing a clearer picture of how BAFF inhibition may affect the wider immune system.

Disclosure of interest: None declared.

P113

The effect of juvenile systemic lupus erythematosus serum activated macrophages on a lupus nephritis model

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Pediatric Rheumatology 2014, 12(Suppl 1):P113

Introduction: Podocytes are kidney cells residing in the Bowman’s capsule wrapping around the capillaries of the glomeruli; they form a seal, which contracts greatly to the glomerular filtration barrier (GBF). Their function is highly linked to their morphology, alterations result in loss of integrity of the podocyte seal which can allow the diffusion of proteins from the circulation resulting in proteinuria. A human podocyte cell-line with human-monocyte derived macrophages can be used to create an in vitro model of lupus nephritis (LN). Using this model, it is known that the chemokine monocyte chemoattractant protein 1 (MCP-1) may be released, which has also been identified as a biomarker of the active disease. MCP-1 causes recruitment of pro-inflammatory cells to the kidney. Incubation of this model with JSLE serum may mediate an inflammatory response representing a biologically relevant environment and subsequently provide a clearer understanding into the development of LN.

Objectives: To determine the effect of JSLE serum on the regulation of MCP-1 produced in a LN in vitro model.

Methods: Human monocytes were differentiated into macrophages using media containing monocyte colony stimulating factor. The macrophages were then either unstimulated (inactive cells) or incubated with IFNγ (1ng/ml) or 5% JSLE serum. After 48 hours the supernatant from the macrophages were removed and added to mature podocytes. MCP-1 concentration (meansSEM) was measured using ELISA. Images were taken using a light microscope to allow any morphological changes in the podocytes to be observed.

Results: Previously we have shown IFNγ activated macrophages to produce MCP-1 which in turn increases the concentration of MCP-1 produced by podocytes, while unstimulated macrophages show no difference. Importantly when JSLE serum (n=6) is added to unstimulated macrophages, it activates them in a similar manner to IFNγ alone. Incubated with JSLE serum elicited a significant increase in MCP-1 concentration produced by the macrophages (1357±84ng/ml) compared with unstimulated (252±162ng/ml; p=0.0001). There was no significant difference in MCP-1 concentration compared to IFNγ activated macrophages (1396±349ng/ml; p=0.477). When JSLE serum stimulated macrophages are co-cultured with podocytes, MCP-1 concentration is again found to be significantly higher than unstimulated macrophages (2567±87ng/ml; p=0.0002) with no significant difference with IFNγ activated macrophages (3030±289ng/ml; p=0.099). Podocytes incubated with JSLE serum activated macrophages also result in dramatic changes to the podocyte morphology which was again similar to that seen with IFNγ activated macrophages.

Conclusion: JSLE serum stimulated the macrophages in an analogous way to IFNγ, resulting in increased MCP-1 production by both the macrophages and podocytes, suggesting that macrophage activation by IFNγ is similar to that observed in LN. However, the concentration of MCP-1 does not exceed that which is produced by the co-culturing of podocytes with IFNγ activated macrophages. Therefore serum factors directly acting on the podocytes need to be identified. The importance of IFNγ in JSLE pathogenesis is widely accepted however the role of the IFN subtypes in the development of the disease is unclear. This study provides evidence to suggest that factors in JSLE serum such as IFNγ may play a prominent role in the activity and progression of the disease particularly when there is kidney involvement.

Disclosure of interest: None declared.
Introduction: Neuropsychiatric manifestations are considered to be a serious complication in childhood-onset systemic lupus erythematosus (cSLE). The pathogenesis of neuropsychiatric manifestations has been attributed to autoantibody-mediated neural dysfunction.

Objectives: To investigate the prevalence and associations of neuropsychiatric manifestations with antinuclear P protein antibodies, S100P, subunit of high molecular weight neurofilament (NF-H), antiphospholipid (aCL) and lupus anticoagulant (LA), anti-dsDNA and anti-Smith.

Methods: We included consecutive cSLE followed at the pediatric rheumatology unit of the State University of Campinas. Neurological manifestations were analyzed according to the ACR classification criteria. Cognitive evaluation was performed in all participants using Wechsler Intelligence Scale for children (WISC-III) and Wechsler Intelligence Scale for adults (WAIS), according to age and validated in Portuguese. Mood disorders were determined through Beck Depression and Anxiety Inventory in all participants. SLE patients were further assessed for clinical and laboratory SLE manifestations, disease activity (SLE Disease Activity Index (SLEDAI)), damage (Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI)) and current drug exposures. Antiribosomal P protein antibodies, S100P and NF-H were tested by ELISA using commercial kits. The levels of dsDNA antibodies were determined by indirect immunofluorescence using Crithidia luciliae as a substrate and were considered positive if they were higher than 110. The levels of precipitating antibodies to extractable nuclear antigens (ENA), including Sm, were detected using a standardized enzyme-linked immunosorbent assay (ELISA) method and were considered positive if higher than 180. The levels of IgG and IgM antinuclear antibodies (aCL) were measured by ELISA. Lupus anticoagulant (LA) activity was detected by coagulation assays in platelet-free plasma obtained by double centrifugation following the recommendations of the Scientific and Standardization Committee of the International Society of Thrombosis and Hemostasis and Homeostasis subcommittee on LA Antiphospholipid (aCL and LA); anti-dsDNA and anti-Smith were obtained of the medical charts. Data were compared by non-parametric tests.

Results: We included 77 cSLE patients (69 women; mean age 17.64±4.64 years). The mean disease duration was 4.35±3.39 years. At time of study entry, 33 (42.85%) cSLE patients had active disease (mean SLEDAI scores 3.5±0.97; range 0-14). Eighteen (23.7%) cSLE had cumulative damage (mean SDI scores 0.35±0.67; range 1-3). We observed neuropsychiatric manifestations in 49 (63.63%) cSLE. The most frequent manifestations observed in our cohort were cognitive impairment (46.93%), depression (36.73%) and seizure (24.48%). Mean NF-H protein levels were 101.80±89.40 pg/mL and mean serum S100P (36.73%) and seizure (24.48%). Mean NF-H protein levels were 101.80±89.40 pg/mL and mean serum S100P (36.73%) and seizure (24.48%). Mean NF-H protein levels were 101.80±89.40 pg/mL and mean serum S100P (36.73%) and seizure (24.48%). Mean NF-H protein levels were 101.80±89.40 pg/mL and mean serum S100P (36.73%) and seizure (24.48%). Mean NF-H protein levels were 101.80±89.40 pg/mL and mean serum S100P (36.73%) and seizure (24.48%). Mean NF-H protein levels were 101.80±89.40 pg/mL and mean serum S100P (36.73%) and seizure (24.48%). Mean NF-H protein levels were 101.80±89.40 pg/mL and mean serum S100P (36.73%) and seizure (24.48%). Mean NF-H protein levels were 101.80±89.40 pg/mL and mean serum S100P (36.73%) and seizure (24.48%). Mean NF-H protein levels were 101.80±89.40 pg/mL and mean serum S100P (36.73%) and seizure (24.48%). Mean NF-H protein levels were 101.80±89.40 pg/mL and mean serum S100P (36.73%) and seizure (24.48%). Mean NF-H protein levels were 101.80±89.40 pg/mL and mean serum S100P (36.73%) and seizure (24.48%).
The aim of this study was to identify the cause of presumably recessively inherited form of SLE and/or lupus-like syndrome (LLS) in a consanguineous family from Turkey.

Methods: We studied 2 pairs of young female siblings (4 patients), who presented with Lupus-like syndrome but with a significant phenotypic variability and differences in the disease severity. They shared a history of episodes of malar and/or generalized rash and ANA positivity, while anti-dsDNA were negative in all four. Renal involvement was prominent in one of the siblings and one patient developed CNS manifestations including convulsion.

DNA samples from the affected patients, their unaffected parents and siblings were isolated from whole blood. We performed whole-exome sequencing in 9 samples from this family and Sanger sequencing in other family members.

Results: We identified a homozygous frameshift mutation in the CR1 gene (NM_001733.4;c.1331delT; p.Pro445Leufs*11), encoding complement 1r subunit, in all 4 affected siblings. The homozygous p.Pro445Leufs*11 mutation was validated with Sanger sequencing in all four patients while their unaffected parents and siblings were either heterozygous carriers or non-carriers. One 9y old sibling was identified as homozygous for the mutation but is yet unaffected. Despite the same genotype the affected patients have variable phenotypes concerning disease features, severity, disease outcome, thus suggesting a role for other modifying alleles or epigenetic factors.

Conclusion: Our findings show the second molecular evidence that loss-of-function mutations in CR1 are the cause of SLE or lupus-like syndrome. We report a novel genetic defect in the C1r complement protein leading to a recessive form of familial SLE/LLS in the Turkish population. This mutation is likely present in the general population and it should be included in diagnostic evaluation of Turkish patients with early onset SLE. We plan extensive biochemical, immunologic, and functional assays to assess the impact of this pathogenic mutation on complement function, apoptosis, neutrophil and B cell biology.

Disclosure of interest: None declared.

P117

SHARE – workpackage 5: evidence based recommendations for diagnosis and treatment of juvenile localized scleroderma and juvenile systemic sclerosis

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4Pediatric Rheumatology 2014, 12(Suppl 1):P117

Introduction: Juvenile Localized Scleroderma (JLS) and Juvenile Systemic Sclerosis (JSSc) form a group of rare pediatric diseases that can lead to significant morbidity. Evidence-based guidelines are sparse and management is mostly based on physician’s experience. Consequently, treatment regimens differ throughout Europe. In 2012, a European initiative called SHARE (Single Hub and Access point for pediatric Rheumatology in Europe) was launched to optimize and disseminate diagnostic and management regimens in Europe for children and young adults with rheumatic diseases.

Objectives: One of the aims of SHARE was to provide evidence based recommendations for diagnosis and treatment of Juvenile Scleroderma.

Methods: Evidence based recommendations were developed using the European League Against Rheumatism (EULAR) standard operating procedure. An expert committee was instituted, consisting of pediatric rheumatologists and experts in Juvenile Scleroderma. The expert committee defined search terms for the systematic literature review. Two independent experts scored articles for validity and level of evidence. Recommendations derived from the literature were evaluated by an online survey. Those with less than 80% agreement during the online survey were reformulated. Subsequently, all recommendations were discussed at a consensus meeting using the nominal group technique [Delbecq AL. A group process model for problem identification and program planning. The Journal of Applied Behavioral Science July 1971 7: 466-492]. Recommendations were accepted if more than 80% agreement was reached.

Results: The literature search yielded 1550 articles for JLS and 8562 for JSSc, of which 52 and 37, respectively (25 for diagnosis and 27 for treatment of JLS, 21 for diagnosis and 16 for treatment of JSSc) were considered relevant and therefore scored for validity and level of evidence. 42 articles (15 for diagnosis and 14 for treatment of JLS, 6 for diagnosis and 7 for treatment of JSSc) were scored valid and used in the formulation of the recommendations. 11 recommendations for diagnosis and 7 for treatment were suggested in the online survey on JLS. Ten recommendations for diagnosis and 6 for treatment were accepted with more than 80% agreement after the consensus meeting. Six recommendations for diagnosis and 5 for treatment were suggested in the online survey on JSSc. 6 recommendations for diagnosis and 4 for treatment were accepted with more than 80% agreement after the consensus meeting. Topics covered for diagnosis and for treatment were, for JLS, disease activity assessment and response to therapy, disease severity and damage assessment, extra-cutaneous involvement (articular, musculoskeletal, neurological, ophthalmological, dental, maxillo-facial), topical treatments (medium-dose UVa1 phototherapy, imiquimod) and systemic treatment (corticosteroids, metotrexate, mychophenolate mofetil); for JSSc disease severity and damage assessment, diagnosis of skin involvement, lung involvement and Raynaud’s phenomenon, treatment of skin, lung and vascular involvement and autologous stem-cell transplantation.

Conclusion: The SHARE initiative provides recommendations for diagnosis and treatment for Juvenile Scleroderma and thereby facilitates improvement and uniformity of care throughout Europe.

Disclosure of interest: None declared.

P118

Juvenile systemic sclerosis: review of 15 patients

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Pediatric Rheumatology 2014, 12(Suppl 1):P118

Introduction: Systemic sclerosis, a rare disease in childhood, is characterized by skin fibrosis, internal organ involvement, and vasculopathy. Juvenile systemic sclerosis (JSSc) represents less than 10% of all scleroderma patients.

Objectives: To describe the clinical characteristics and disease progression of children with JSSc followed in Portuguese pediatric rheumatology centers.

Methods: Clinical and laboratory features as well as medication and outcome of children who met classification criteria for JSSc were reviewed.

Results: Fifteen patients were identified and included in the analysis, 3 of them were overlap syndromes. Eleven girls (73%), 89% Caucasians, with a mean age at diagnosis of 11.1±3.0 (3-15) years and a mean disease duration of 7.2±4.2 years (8 months-17 years). In 14 (93%) cases, the first symptom attributable to JSSc was Raynaud’s phenomenon, followed by arthritis and/or puffy hands (9 patients, 60%). At disease diagnosis 12 (80%) patients presented periungual capillaropathy and in 8 patients, pulmonary involvement was documented, despite the absence of respiratory complaints. Cumulative disease manifestations as well as complications developed during follow-up are shown in table 1.
Conclusions: Diffuse cutaneous disease was the subtype of JIA most prevalent identified in pediatric rheumatology centers. Raynaud’s phenomenon as well as capillaroscopic abnormalities are almost universal at disease presentation. Internal organ involvement is common and occurs early during disease course, although clinically silent in several cases.

Disclosure of interest: None declared.

Table 1 (abstract P118) Cumulative manifestations and complications observed during the follow-up

<table>
<thead>
<tr>
<th>Diffuse cutaneous disease</th>
<th>Digital ulcers</th>
<th>Calcinosi</th>
<th>Musculoskeletal involvement</th>
<th>Interstitial lung disease</th>
<th>Cardiac disease</th>
<th>Gastrointestinal disease</th>
<th>Renal disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 (100%)</td>
<td>11 (73%)</td>
<td>3 (20%)</td>
<td>13 (87%)</td>
<td>8 (53%)</td>
<td>2 (13%)</td>
<td>7 (47%)</td>
<td>1 (7%)</td>
</tr>
</tbody>
</table>

All but one child were ANA positive (93%), 7 tested positive for anti-ScI70, 2 positive for anti-RNP and 1 for anti-fibrilairin antibodies. There were no cases of anti-centromere antibodies.

Immunosuppressants (93%), proton pump inhibitors (80%), calcium channel blockers (33%) and corticosteroids (60%) were the most common therapeutic options. Five and four children were treated with protacyclin analogues and ET-1 receptor antagonist, respectively. One child needed autologus bone marrow transplant due to severe refractory disease.

An improvement of skin thickening and stabilization of pulmonary involvement was documented in most cases. No deaths were registered in this cohort. Tab. 1.

Conclusion: Conclusions: Diffuse cutaneous disease was the subtype of JSSc more prevalent identified in pediatric rheumatology centers. Raynaud’s phenomenon as well as capillaroscopic abnormalities are almost universal at disease presentation. Internal organ involvement is common and occurs early during disease course, although clinically silent in several cases.

Disclosure of interest: None declared.

P119
First episode of chronic anterior uveitis in patients with juvenile idiopathic arthritis and relationship with administrated treatments

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Pediatric Rheumatology 2014, 12(Suppl 1) P119

Introduction: Chronic anterior uveitis is one of the most serious complications of juvenile idiopathic arthritis (JIA), showing an increased incidence in patients with early-onset disease, oligoarticular, ANA (+). Biologic therapy used in the treatment of JIA has greatly improved the articular prognosis, however their effectiveness in JIA associated uveitis is still not well established, having reported new cases of uveitis during treatment with anti-TNF, especially during treatment with etanercept.

Objectives: The objective of this work is to report the incidence of new cases of chronic anterior uveitis in patients who were treated with Methotrexate (MTX), Adalimumab (ADM) or Etanercept (ETN) for JIA.

Methods: We performed a retrospective observational study of 70 patients with diagnosis of early-onset JIA with high risk of developing chronic anterior uveitis. There were recorded the new episodes of uveitis per patient. Incidence was calculated as the number of new episodes per 100 patients per year of follow-up according to the ILAR category and treatment and based exclusively on the treatment. Comparisons were made using T Student test.

Results: Fifty-six (80.0%) patients were female and 14 (20.0%) males. The categories ILAR were: 42 (60.0%) oligoarticular, 10 (14.3%) extended oligoarticular, 15 (21.4%) polyarticular and 3 (4.3%) associated with psoriasis. The average age at diagnosis was 3.5 SD 1.6 years (median 3 years). ANA positive were found in 41 (58.6%) patients. The mean follow-up of patients was 4.44 SD 3.65 years. There were 5 new cases of uveitis during treatment (3 MTX, 2 MTX-ETN or ETN and 6 with ADM) and 10 cases presented to debut or before starting DMARDs or biologic therapy. The incidence was 0.15 and 0.11 cases per 100 patient / year, respectively (p > 0.05, t Student test). The accompanying table describes the distribution of new cases according to the ILAR category and administered treatment during the follow up period.

Conclusion: The incidence of occurrence of uveitis in our series of JIA patients at high risk of uveitis is comparable to that described in the literature (22.8%) and similar between patients who received MTX as monotherapy and those who received MTX and ETN or ETN. We reported no new cases of uveitis in patients treated with ADM, although in 85% of cases ADA was recomended in patients diagnosed with uveitis, with studies that have shown that it is more effective than treating this complication with ETN. The number of cases that occurred during treatment with ETN in our series of cases is too small to infer a causal relationship, the stratification by Immunological profile, sick time, age or baseline severity of the symptoms could influence the development of this complication. Prospective comparative studies of biological and non-biological DMARDs are needed to assess the increase or decrease in the risk of uveitis associated with JIA.

Disclosure of interest: None declared.

P120
Non-anti TNF biologic modifier drugs in non-infectious refractory chronic uveitis: the current evidence from a systematic review of the literature

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Pediatric Rheumatology 2014, 12(Suppl 1) P120

Introduction: Non-infectious chronic uveitis is a serious and disabling sight-threatening disease accounting for up to 10% of pathologies leading to blindness. Currently, a step-by-step escalating immunosuppressive therapy is generally used, in children as well as adults, and anti-TNFα biologic therapies have markedly increased the treatment options for sight-threatening uveitis refractory to conventional immune-modulatory therapy (DMARD) in addition to topical and/or systemic corticosteroids. However, a subset of patients fails to respond to TNFa blockers or is unable to tolerate these therapies and may therefore benefit from switching to another drug. In this clinical setting, the large availability of several different molecules, mostly off-label, poses the clinical question if it can be useful and safe to administer another class of biologic drugs, such as Abatacept or Rituximab, for patients with refractory auto-immune uveitis.

Objectives: To summarize the evidence regarding the effectiveness and the safety of switching to a Non anti-TNF biologic modifier immunosuppressant treatment (NTT) currently available in clinical practice.

Methods: A comprehensive systematic review was undertaken involving a literature search between January 2000 and April 2013 was conducted using EMBASE, Ovid MEDLINE, Evidence Based Medicine Reviews-ACP Journal Club, Cochrane libraries, and EBM Reviews. Studies investigating the efficacy of NTT as biologic modifier immunosuppressant medication for autoimmune chronic uveitis, refractory to topical and/or systemic steroid therapy, were eligible for inclusion. The primary outcome measure was the improvement of intraocular inflammation, as defined by the SUN working group criteria. We determined a combined estimate of the proportion of subjects responding to NTT.

Results: We initially identified 526 articles, of which 89 were potentially eligible. From the selection process, a total of 10 retrospective chart reviews and 1 randomized single-blind controlled study, providing a total of 12 children and 34 adults, were deemed eligible. The studies were related to Rituximab (n=3), Abatacept (n=3), Tocilizumab (n=3) and single studies on Alemtuzumab and Anakinra. Before the NTT treatment, all the eligible subjects received several combinations of one or more DMARD and at least one anti-TNF therapy. Considering the observational studies, thus excluding 7 adults enrolled in the RCT, 8 children out of 12, and 18 adults out of 27 responded to NTT treatment. 0.66 was the combined estimate of the proportion of subjects improving on NTT treatment for children (95% CI: 0.58-0.81) and adults (95% CI: 0.64-0.79). Further statistical comparison between different NTT strategies was not possible.
due to the small sample size. The only RCT reported a success rate of 2 out of 7 adult Behcet’s disease patients with a 6-month exposure to Rituximab.

Conclusion: Although randomized controlled trials are needed, the available evidence suggests that a NTT strategy may be useful in selected categories of autoimmune chronic uveitis in adults as well in childhood, refractory to a previous course of immunosuppressive treatment, both with DMARDs and anti-TNFa.

Disclosure of interest: None declared.

P121
SHARE – workpackage 5: evidence-based recommendations for diagnosis and treatment of rare paediatric vasculitides

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Pediatric Rheumatology 2014, 12(Suppl 1):P121

Introduction: Polyarteritis Nodosa (PAN), Granulomatosis with Polyangiitis (GPA), Microscopic Polyangiitis (MPA), Eosinophilic Granulomatosis with Polyangiitis (EGPA) and Takayasu Arteritis (TA) are rare paediatric vasculitides that can lead to significant morbidity. Evidence-based guidelines are sparse and management is mostly based on physician experience. Consequently, treatment regimens differ throughout Europe. In 2012, a European initiative called SHARE (Single Hub and Access point for paediatric Rheumatology in Europe) was launched to optimize and disseminate guidelines for diagnosis and management for children and young adults with paediatric rheumatic diseases (PRD) such as vasculitides within Europe.

Objectives: To provide evidence-based recommendations for diagnosis and treatment of paediatric vasculitides, specifically PAN, GPA, MPA, EGPA and TA.

Methods: Evidence based recommendations were developed using the European League Against Rheumatism (EULAR) standard operating procedure. An expert committee was formed, consisting of paediatric rheumatologists from across Europe with expertise in vasculitis. The expert committee defined search terms for the systematic literature review, which was performed in summer 2013. Two independent experts scored each article for validity and level of evidence. Recommendations derived from the literature were evaluated using an online survey. Those with less than 80% agreement during the online survey were reformulated. Subsequently, all recommendations will be discussed at a consensus meeting using the nominal group technique [1]. Recommendations will be accepted if more than 80% agreement is reached.

Results: The systematic literature search yielded 7766 articles, including articles on two more common forms of paediatric vasculitides, Kawasaki Disease (KD) and Henoch Schönlein Purpura (HSP). After exclusion of these articles and articles that did not meet inclusion criteria, 93 articles on rare paediatric vasculitides were considered relevant. The expert committee then scored these for validity and level of evidence. Evidence supporting recommendations for diagnosis and treatment was extracted from the literature. Subsequently, statements on clinical symptoms, referral of patients, useful laboratory investigations, imaging techniques and treatment were formulated based on this evidence and expert opinion and were evaluated in an online survey. The outcome of this survey will be discussed at the next consensus meeting with the aim of yielding final recommendations on minimal standards of care for children with vasculitides throughout Europe.

Conclusion: The SHARE initiative provides recommendations for diagnosis and treatment of paediatric vasculitides and thereby facilitates improvement and uniformity of care for patients throughout Europe. Currently, similar processes are ongoing to add additional recommendations on diagnosis and treatment where consensus to date has not been reached, as well as recommendations regarding the holistic care of patients. As a final result, SHARE will provide standards of minimal care for different PRDs, including rare vasculitides (PAN, GPA, MPA, EGPA and TA) as well as more common vasculitides (KD and HSP).

Disclosure of interest: None declared.

P122
SHARE – workpackage 5: evidence-based recommendations for diagnosis and treatment of Kawasaki disease and Henoch Schönlein Purpura

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Pediatric Rheumatology 2014, 12(Suppl 1):P122

Introduction: Kawasaki Disease (KD) and Henoch Schönlein Purpura (HSP) are paediatric vasculitides that can lead to significant morbidity. Evidence-based guidelines are sparse and management is mostly based on physician experience. Consequently, treatment regimens differ throughout Europe. In 2012, a European initiative called SHARE (Single Hub and Access point for paediatric Rheumatology in Europe) was launched to optimize and disseminate guidelines for diagnosis and management for children and young adults with paediatric rheumatic diseases (PRD) such as KD and HSP within Europe.

Objectives: To provide evidence-based recommendations for diagnosis and treatment of paediatric vasculitides, specifically KD and HSP.

Methods: Evidence based recommendations were developed using evidence drawn from systematic reviews of the literature. An expert committee was formed consisting of paediatric rheumatologists from across Europe with expertise in vasculitis. Preliminary statements regarding recommendations on diagnosis and treatment of KD and HSP were developed. These recommendations were evaluated by the expert committee using an online survey. Those with less than 80% agreement in the online survey were reformulated. Subsequently, all recommendations were discussed at a consensus meeting in Genoa (Italy) in March 2014 using the nominal group technique [1]. Recommendations were accepted if more than 80% agreement was reached.

Results: Evidence supporting recommendations for diagnosis and treatment was extracted from the literature. Subsequently, 53 statements on diagnosis and treatment were formulated based on this evidence and expert opinion and were evaluated in an online survey. After discussion of the statements at the consensus meeting, 29 recommendations for KD and 15 recommendations for HSP were accepted with more than 80% agreement during the meeting. Topics covered were criteria for diagnosis, referral of patients, clinical symptoms, useful laboratory investigations, imaging techniques and treatment.

Conclusion: The SHARE initiative provides recommendations for diagnosis and treatment of paediatric vasculitides and thereby facilitates improvement and uniformity of care for patients throughout Europe. Currently, similar processes are ongoing to add additional recommendations on diagnosis and treatment where consensus to date has not been reached, as well as recommendations regarding the holistic care of patients. As a final result, SHARE will provide standards of minimal care for different PRDs including KD and HSP, as well as more rare vasculitides (PAN, GPA, MPA, EGPA and TA).
Reference

P123
Incidence and clinical features of Kawasaki disease in Catalonia (Spain)
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Pediatric Rheumatology 2014, 12(Suppl 1):P123

Introduction: Kawasaki disease (KD) is an acute self-limited systemic vasculitis relatively common in childhood. In Japan, last published study shows an incidence up to 239.6/105 children <5 years old (yo). In Madrid (Spain) a retrospective study with no well defined reference area showed an incidence of 15.1/105 children <5yo. Objectives: To ascertain the incidence and clinical features of KD in Catalonia, autonomous region in northeast Spain with 7.5 million inhabitants. Methods: Observational population-based study including all Catalan hospitals with Pediatric Units, both public and private management. Retrospective data retrieval was performed for the last 10 years (2004-2013). The presence of coronary aneurysms (CA) in echocardiography was based in the body surface area according to the American Heart Association. Results: Data from 399 patients from 33 different hospitals was analyzed. Of those, 233 (58.4%) patients had complete KD, 159 (39.8) incomplete KD and 7 (1.7%) were considered atypical KD. The mean annual incidence was 3.5/105 children <1<yo and 8/105 children<5yo (mean age 37±33 months(m), range 1.3-191.3m). KD was more frequent among boys (59.6%, p<0.01). Mean delay between onset of the disease and diagnostic was 7.2±5.3 days. Ethnic distribution was: Caucasian 279 patients(69.9%), North African 26 (6.5%), American 21 (5.2%), Asian 14 (3.5%) and Sub-Saharan 10 (2.5%). Ethnicity was not available in 55 (13.8%) patients. Distribution of classical manifestations for KD was: fever in 100% of patients, changes in extremities 40.3% (desmization in 31% of them), exanthema 84.2%, conjunctival injection 79.7%, changes in lips and oral cavity 55.6% and lymphadenopathy 28.8%. Other clinical findings reported were: sterile pyuria in 80(20%) patients, nausea and vomiting in 96(24%), abdominal pain in 85(21.3%), gallbladder distention in 14 (3.5%), transaminase elevation in 120 (36%), jaundice in 210 (5.1%), iritability in 118 (29.5%), aseptic meningitis in 16 (4%), sensorineural hearing loss in 2 patients, uveitis in 11 (2.7%) and arthritis or arthralgia in 55 (13.8%). Cardiologic findings were: perivascular brightness of the coronary wall in 42(10.5%) patients, pericarditis in 9(2.3%), myocarditis in 4(1%), mitral regurgitation in 28(7%) and CA in 53 patients(13.3%), 26(4%) of them disappearing before the 2nd month after the onset of KD. 4 patient had giant CA. Intravenous immunoglobulin (IVIG) was administered in 389 (97.5%) patients with response to the 1st dose in 332(83.2%). Day of IVIG administration was 7.5±3.1. Other treatment plans were: 2nd (69% response) and 3rd IVIG doses, oral or iv corticosteroids and abciximab (administered in 3 of the patients with giant CA). 97.3% of patients received anti-platelet dose aspirin in the convalescent phase. Conclusion: This is the first population-based study on the epidemiology of KD in Catalonia (Spain). It seems to be a higher incidence of CA in our cohort despite high rates of treatment response. Further analysis is required. Incidence rates, other clinical features and treatment plans are similar to dose described in studies in other European countries.

Disclosure of interest: None declared.

P124
Kawasaki disease in France, Kawanet: incomplete forms are frequent and associated with a high frequency of cardiac complications
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Pediatric Rheumatology 2014, 12(Suppl 1):P124

Introduction: KD is the main vasculitis affecting children before 5 years and the leading cause of acquired heart disease. The epidemiologic of KD is few reported in France within a population from different ethnic backgrounds. Even IVIG is still the standard treatment; the management of patients at risk for cardiac complications may change toward reinforced (and new) therapeutic approaches. Objectives: Kawanet is a clinical and biological data repository aimed to define the epidemiological characteristics of KD in France. Kawanet will compare clinical characteristics between distinct ethnic backgrounds and will define risk factors for resistance to standard treatment (IVIG) and for cardiac complications.

Methods: Targeted institutional physicians received information on a national registry for KD. All patients suspected with KD and seen since January 2011 were eligible to enter the study. eCRF was implemented in a web database. IRB approval for data storage were obtained. The included patients without the AHA international criteria were reviewed by an experts’ committee.

Results: 468 cases were entered by 84 physicians from 65 centers. The AHA classification gave: 280 complete (≥ 4 criteria), and 73 incomplete (≤ 3 criteria with coronary dilation). An expert consensus classified 48 other patients (≤ 3 criteria but agreement for IVIG treatment) leading 401 patients considered as KD (M229/F172). 45 patients were doubtful and 22 not classified for incomplete data. The median age at diagnosis for the Kawasaki was 3.1y (2m-14y). Their ethnic backgrounds were: European Caucasian 67%, Eastern Caucasian or North African 15% afro-Caribbean, 13%, Asian 4% and mixed ancestry 1%. The clinical symptoms were (%): conjunctivitis 84, cheilitis 82, diffuse exanthema 74, modification of the extremities 73, oral erythema 66, cervical adenopathy 52, raspberry tongue 49, seat erythema 26, perineal desquamation 18 and BCG erythema 5. The cardiac complications were: coronary dilation 30%, pericarditis 15%, coronary aneurysm 4%, and myocarditis 3% (1 death). 392/401 (98%) patients received IVIG, 21% (n=64) required 2 courses and 5 patients 3 courses. 11% required steroids, 93% received Aspirin and 1 Anti-TNF. The mean delay between fever onset and treatment was 6 days. The factors associated with the coronary abnormalities were: male gender (p=0.01), young age KD onset (p=0.03) and resistance to IVIG (p=0.03).

Conclusion: KD diagnosis remains challenging and overdiagnosis represents at least 10% of cases in this registry. Incomplete forms of KD account for 37% and are associated with coronary dilation/aneurysm (34%, p<0.01) and a high rate of IVIG resistance. Unlike previous studies, our population is very mixed with 28 % of children from the Middle East and Africa, in whom KD is still few reported.This study is supported by grants form APHP, PHRic2009, LFB and private (patient/family) donation

Disclosure of interest: None declared.

P125
Elicitation of expert prior opinion: application to the mypan trial in childhood polyarteritis nodosa
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Pediatric Rheumatology 2014, 12(Suppl 1):P125

Conclusion: The mypan trial in childhood polyarteritis nodosa proposal was strongly dependent on expert opinion. Further analysis is required. Incidence rates, other clinical features and treatment plans are similar to dose described in studies in other European countries.

Disclosure of interest: None declared.
Introduction: A major challenge in rare diseases is conducting clinical trials with sufficient power to inform best clinical practice when anticipated sample sizes are small. Historically, this has been a major barrier in rare paediatric autoimmun​e diseases. Bayesian methodology can be used to augment the sparse therapeutic data obtained from clinical trials in these circumstances. Objectives: We elicited expert prior opinion for a future Bayesian randomised controlled trial for a rare inflammatory paediatric disease, polyarteritis nodosa (MYPAN, Mycophenolate mofetil for polyarteritis nodosa). Methods: A Bayesian prior elicitation meeting was convened. Participating experts were drawn from across the EU and Turkey. Opinion was sought on the probability that a patient in the MYPAN trial treated with cyclophosphamide would achieve disease remission within 6-months, and on the relative efficacies of mycophenolate mofetil and cyclophosphamide. Expert opinion was combined with previously unseen data from a recently completed randomised controlled trial of mycophenolate mofetil versus cyclophosphamide in anti-neutrophil cytoplasmic antibody associated vasculitis. Results: A pan-European group of fifteen experts participated in the elicitation meeting. Consensus expert prior opinion was that the most likely rates of disease remission within 6-months on cyclophosphamide or mycophenolate mofetil were 74% and 71% respectively. This prior opinion will now be taken in to account and will be modified to formulate a Bayesian posterior opinion when data from 40 patients completing the trial randomised at a 1:1 ratio to either receive cyclophosphamide or mycophenolate mofetil are available. Conclusion: We suggest that this methodological template could be applied to trial design for other rare diseases, and is of particular relevance to rare autoimmune conditions that currently lack a good evidence base for treatment. Disclosure of interest: None declared.

P127 Prediction of methotrexate efficacy and adverse events in patients with juvenile idiopathic arthritis: a systematic literature review
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Introduction: Methotrexate (MTX) is the cornerstone disease-modifying anti-rheumatic drug in juvenile idiopathic arthritis (JIA). In JIA, it is important to start effective treatment early in the course of disease, the so-called window of opportunity, to avoid long term sequelae, such as joint damage. To accomplish this goal, it is essential to know beforehand who is going to respond well to MTX, so MTX monotherapy can be started in patients predicted to respond well, whereas other drugs, such as biologicals, could be prescribed to patients predicted to be non-responders. In addition, MTX adverse effects, such as MTX intolerance, occur frequently and can lead to non-compliance, thus hindering its efficacy. Therefore, to avoid inefficacy of an otherwise efficacious drug, the physician should timely be aware of these adverse events. Objectives: The aim of this study was to identify predictors for MTX efficacy and adverse events. Methods: A systematic literature search was performed in PubMed, Embase and The Cochrane Library, and 1,331 articles were identified. These were selected based on their relevance, and critically appraised according to predefined criteria. Predictors for MTX efficacy and adverse events were tabulated. Results: Twenty articles were selected. For MTX efficacy, some interesting outcomes were found, such as antinuclear antibody positivity, the childhood health assessment questionnaire score, the myeloid-related protein 8/14 level, long-chain MTX polyglutamates, bilateral wrist involvement and some single nucleotide polymorphisms (SNPs) in the adenosine triphosphate binding cassette and solute carrier transporter gene families. For MTX adverse events, potential predictors were alanine aminotransferase and thrombocyte level and two SNPs in the γ-glutamyl hydrolase and methylentetrafoldrofolate reductase genes. Validation of most predictors was still lacking. Conclusion: Interesting candidate predictors were found, especially for MTX efficacy. However, most of these have not yet been validated in independent cohorts. The results of some candidate predictors were quite variable in different cohorts, highlighting the difficulty to properly validate those, due to heterogeneity between studies. A clinically relevant way to validate these predictors is by means of a clinical prediction model. Disclosure of interest: None declared.

P128 Tumour necrosis factor-α levels are elevated in adolescent patients with juvenile idiopathic arthritis on etanercept therapy
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Introduction: Tumour necrosis factor (TNF) has been implicated in the pathogenesis of juvenile idiopathic arthritis (JIA). Etanercept is an TNF inhibitor which is currently the preferred biological therapy for severe and treatment-naïve JIA patients. However, its therapeutic benefit in these patients is not always clear. Methods: We performed a single cohort, cross-sectional, observational study. TNF was measured in 2014, 2014, 2014, 2014, adolescent patients with JIA who were treated with etanercept. Results: In 2014, 2014, 2014, 2014, patients, mean TNF level (±SEM) was 2014, 2014, 2014, 2014, ± 2014, 2014, 2014, 2014, and 2014, 2014, 2014, 2014, of control population was 2014, 2014, 2014, 2014, (p=0.001). Conclusion: Tumour necrosis factor-α levels are elevated in juvenile idiopathic arthritis patients on etanercept therapy.
**Introduction:** The use of etanercept, a tumor necrosis factor (TNF) inhibitor, has revolutionized the treatment of juvenile idiopathic arthritis (JIA). TNF is a key cytokine implicated in the pathogenesis of inflammatory arthritis and etanercept, which is a soluble TNF receptor fusion protein, binds and inactivates TNF-α and lymphotixin-A.

**Objectives:** The aim of this study was to profile serum levels of TNF-α in a large cohort of adolescent patients with JIA.

**Methods:** Serum TNF-α was measured in samples derived from 200 adolescent and young adult patients from JIA attending the adolescent and young adult rheumatology clinic at University College London Hospital using a commercial enzyme linked immunosorbent assay (ELISA) kit (eBioscience). Samples were tested in duplicate. Median age at sampling and median disease duration were 18 years and 8 years 9 months, respectively. Male:female ratio was 1:1.2. Equal numbers of patients with polyarticular (n=64) and enthesitis related arthritis (ERA, n=64) were tested in addition to 48 with oligoarticular, 16 systemic onset, and 8 psoriatic arthritis. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) measurements were also collected. Furthermore, an L929 cell viability bioassay was used to determine if the addition of etanercept abrogates the cytotoxic effects of TNF-α in L929 cells.

**Results:** Surprisingly, TNF-α serum levels were shown to be markedly elevated in patients on etanercept (median TNF-α on etanercept = 134.2pg/ml, IQR [49.4-207.1], median not on etanercept = 4.2pg/ml, IQR [1.8-9.1]) or disease modifying anti-rheumatic drugs alone (median = 4.2 pg/ml, IQR [1.1-12.9]), p<0.0001. In addition, ESR and CRP levels had a negative correlation with high TNF-α levels in patients on etanercept (p=0.0018 and p=0.0034 respectively). Etanercept was included at its therapeutic serum concentration (2.4ug/ml) to ensure there was no cross reactivity with the assay. Finally, we showed that the addition to TNF-α to human serum leads to cytotoxicity in a TNF-α sensitive cell line, while adding etanercept at its therapeutic concentration along with TNF-α significantly reduces cell death (p = 0.0277).

**Conclusion:** Patients treated with etanercept have higher levels of TNF-α. As the majority of patients with elevated TNF-α on etanercept were in remission, it is likely that this circulating TNF is biologically inactive. This is supported by our in vitro experiments in which the cytotoxic effect of TNF-α was abrogated upon addition of etanercept. Our hypothesis is that etanercept prolongs the half-life of circulating TNF-α. Further studies are needed to confirm these findings and dissect the mechanisms involved. As the association between high TNF-α and etanercept treatment is so strong, we hypothesise that it may be possible to measure TNF-α levels as a surrogate marker of adherence to this drug in this cohort of patients where adherence to medication can be a significant problem. This is a hypothesis that warrants further investigation.

**Disclosure of interest:** None declared.

P129
Mesenchymal stromal cells suppress synovial fluid-derived t cells from juvenile idiopathic arthritis patients in vitro

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**Introduction:** Mesenchymal stromal cells (MSC) are multipotent cells with an immunosuppressive capacity. In the last decade the feasibility and safety of MSC therapy has been established in various inflammatory diseases, including graft versus host disease. MSC are known to suppress T cell function and modulate T helper 17 (Th17) cells and regulatory T cells (Tregs), which play an important role in the pathogenesis of juvenile idiopathic arthritis (JIA). MSC may therefore serve as a new treatment option for JIA patients refractory to conventional therapies. However, it is unknown whether MSC are capable of suppressing the highly inflammatory synovial fluid mononuclear cells (SFMC), which have been shown to be resistant to suppression by Tregs. Furthermore, the effect of the inflammatory environment on MSC function is largely unknown, though it has been suggested that proinflammatory cytokines can enhance the suppressive potential of MSC.

**Objectives:** We aimed to study the in vitro immunomodulatory effects of MSC on SFMC from JIA patients, with a focus on T cell function. In addition, we assessed the influence of the inflammatory micro-environment, i.e. monocytes and proinflammatory cytokines, on the suppressive potential of MSC.

**Methods:** MSC were cocultured with either peripheral blood mononuclear cells (PBMC) or synovial fluid mononuclear cells (SFMC) from JIA patients (paired samples) or PBMC from healthy controls. We analyzed the effect of MSC on T cell proliferation and Th17 and Treg numbers by flow cytometry. Cytokine production was analyzed in the culture supernatant by Luminex assay. Furthermore, we depleted monocytes from culture and blocked the proinflammatory cytokines TNFα, IFNγ, IL-1β and IL-6 to assess the result on MSC-mediated suppression.

**Results:** MSC suppressed proliferation of PB T cells and SF T cells from JIA patients dose-dependently, but patient-derived T cells were less susceptible to suppression than healthy donor-derived T cells. MSC reduced Th17 numbers and increased Treg numbers in PBMC, but not in SFMC. Addition of MSC did not clearly affect IL-17 levels in the supernatant, but TNFα production was suppressed in both PBMC and SFMC. Contrary to previous reports, blockade of TNFα, IFNγ, IL-1β and IL-6 during in vitro culture did not reduce suppression, but rather enhanced suppression in PBMC from JIA patients. Similarly, depletion of monocytes increased MSC-dependent suppression of healthy control PB T cells.

**Conclusion:** MSC suppress proliferation of synovial fluid T cells from JIA patients in a dose-dependent manner. However, patient-derived T cells are less susceptible to immunomodulation than healthy donor T cells. We propose that reduction of proinflammatory stimuli in conjunction with MSC therapy may benefit the suppressive effects of MSC in JIA.

**Disclosure of interest:** None declared.

P130
Evaluation of the disease course of Italian children with juvenile idiopathic arthritis treated with etanercept: preliminary results in 172 patients

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**Pediatric Rheumatology** 2014, 12(Suppl 1):P130

**Introduction:** The advent of biologic medications has considerably increased the potential for treatment benefit in juvenile idiopathic arthritis (JIA), with clinical remission being now achievable in a substantial proportion of patients.

**Objectives:** To evaluate the outcome of etanercept (ETN) therapy in Italian children with JIA.

**Methods:** This is a multicenter, observational study that includes all children with JIA who were given ETN at Italian pediatric rheumatology centers after January 2000. Patients were classified in 2 groups: Group 1: patients who were no longer taking ETN at study start; Group 2: patients who were still receiving ETN at study start. Patients in Group 1 underwent only retrospective assessments, whereas patients in Group 2 underwent both retrospective and cross-sectional assessments. The primary outcome of the study were reasons for ETN discontinuation in patients in Group 1, and achievement of the states of inactive disease (ID), minimal disease activity (MDA) and parent- and child-acceptable symptom state (PASS, CASS) in patients in Group 2. The above states were assessed through both formal definitions and JADAS cutoffs. The secondary outcome was the evaluation of frequency and characteristics of ETN-related side effects.

**Disclosure of interest:** None declared.
Results: Twenty-five centers were asked to make a census of all patients followed at the center who met the inclusion criteria for Group 1 or Group 2. A total of 1230 patients were included in the census. Of these patients, 624 were still receiving ETN (Group 2), whereas 606 had discontinued ETN (Group 1). So far, the data of 772 patients (448 in Group 1 and 324 in Group 2) have been collected. Among the 448 patients in Group 1, reasons for ETN discontinuation included disease remission (57.1%), lack of efficacy (25.5%), and side effects (14.9%). The results of assessment of disease state through formal definitions in 305 children of the 324 children in Group 2 who had already undergone the cross-sectional evaluation were the following: ID 42.2%, MDA 63.6%, PASS 80.9%, CASS 76.2%. The percentages of patients who reached the same disease states assessed through JADAS cutoffs were: ID 45.7%, MDA 62.5%, PASS 71.1%, CASS 67.4%. Serious adverse events were seen in 10 of the 772 patients and included inflammatory bowel disease (4 pts), tuberculosis (1 pt), CMV hepatitis (1 pt), varicella complicated by bronchopneumonia (1 pt), bladder carcinoma (1pt), thyroid carcinoma (1 pt); 1 patient died of septic shock.

Conclusion: A substantial proportion of children currently receiving ETN were in the states of ID or MDA, or were satisfied with treatment outcome. More than half of the patients who had been discontinued from ETN before study start had the medication stopped because of disease remission. Serious adverse events were uncommon. Disclosure of interest: None declared.

P132
Indirect comparison of etanercept and abatacept efficacy and safety in patients with polyarticular juvenile idiopathic arthritis

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Introduction: The use of biological DMARDs have significantly improved the prognosis and prospects for patients with juvenile idiopathic arthritis (JIA). The main problem for pediatric rheumatologists when choosing JIA treatment is the absence of comparative controlled studies of efficacy and safety of different biological DMARD.

Objectives: To compare efficacy and safety of etanercept and abatacept in pediatric patients with polyarticular JIA.

Methods: The study enrolled 54 pediatric patients with polyarticular JIA, 32 of them received etanercept and 22 received abatacept. The demographic parameters were well matched across treatment groups. The mean age of children was 10.8 ± 3.7, the age at the disease onset was 5.4 ± 3.4, most of the patients were female. Prior to biological DMARD administration, all the subjects received multiple basic immunosuppressants. A total of 68.7% of subjects in the etanercept arm had disease activity grade II before biological DMARD administration, 31.3% had grade III; 54.6% of subjects in the abatacept arm had disease activity grade I, 31.8% grade II, and 13.6% grade III. American College of Rheumatology “pediatric” criteria (ACR pedi-30, -50, -70, -90), treatment compliance index and index LUNDEx were used to assess efficacy of the study treatment. Biological DMARD efficacy and safety were evaluated at Months 6, 12, 18 and 24 following therapy initiation. The drugs were given at standard doses.

Results: At least a 50% improvement according to ACR pedi was achieved in 84.3% of etanercept arm subjects and in 71.4% in patients receiving abatacept following 6 months of treatment. Drug-induced clinical and laboratory remission (ACR pedi 90,100) was achieved in 15.6% of subjects in the etanercept arm, and in 9.5% of patients receiving abatacept. After that, biological DMARD efficacy continued to increase. At Month 18, ACR pedi 50 was achieved in 100% and ACR pedi 90 in 31.0% of etanercept subjects; ACR pedi 50 was achieved in 83,3%, and ACR pedi 90 in 33.3% of abatacept subjects. The treatment compliance index at Month 18 was 0,97 in the etanercept arm and 0,8 in the abatacept arm. Index LUNDEx was 0.97 for ACR pedi 50, and 0.3 for ACR pedi 90 in the etanercept arm in the abatacept arm, it was 0.67 for ACR pedi 50, and 0.27 for ACR pedi 90. At Month 24 all the patients achieved a 50% response according to the ACR pedi criteria. Drug-induced clinical and laboratory remission was achieved in 43.0% of subjects in the etanercept arm, and in 67% of subjects in the abatacept arm. A greater treatment compliance index was obtained in the etanercept arm (0.94 versus 0.6 in the abatacept arm). Thus, when biological DMARD efficacy is compared using index LUNDEx to ACR pedi 50, the best result was obtained with etanercept when compared to abatacept, the values were 0.94 and 0.6, respectively. Index LUNDEx to ACR pedi 90, 100 was 0.4 in both arms. The difference between biological DMARD efficacy was not significant (p>0.05). Adverse drug reactions were more frequent in the abatacept arm (7%) than in the etanercept arm (2%). More patients were also more frequent with abatacept treatment (9%) than with etanercept (3%; p>0.05).

Conclusion: Etanercept and abatacept are highly effective drugs for pediatric treatment of polyarticular JIA. Etanercept has a better safety profile than abatacept.

Disclosure of interest: None declared.
P133 Implementation of a health education program for teenagers affected by systemic lupus erythematosus

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Introduction: Lupus is a chronic disease for which health education is an integral part of the treatment. Health education consists in teaching the patients how to manage everyday life with their illness.

Objectives: This study aimed to evaluate the benefits of health education programs among patients with lupus.

Methods: This experimental study was conducted by two doctors experienced in health education programs, one intern in paediatrics, and two trainee nurses. The health education program was offered to ten young women suffering from systemic lupus erythematosus, aged between 13 and 17 years old. It did not receive any financial support or benefit from additional human resources, and relied exclusively on the internal organization within the board and among the research team members.

Results: Seven of the ten women involved accepted to be part of the program. Every patient was first administered an educational assessment test, that was meant to evaluate the patients’ already acquired skills as well as their expectations from the teaching. The program was designed to develop such skills as a better knowledge of the disease, adequate self-care and other psychosocial skills (adaptability, capacity to speak about the disease, etc.)

To this day, two group sessions have already taken place and it has been our main concern to build them along with the patients. These sessions, of a duration of 2 hours and 45 minutes each, were scheduled some time away from the assessment session. Some educational tools were created during the sessions (card games, board games like ‘Time’s up’, ‘Photolanguage’, a game specifically designed to help expression of feelings around the disease, other educational games and activities). Additional tools are in the process of being built. They include a tryptic about the disease (its physiopathology, its consequences, the future with lupus), which is intended to the use of other young patients.

The patients’ satisfaction with the program was assessed individually and collectively.

This experimental program will be running until the end of 2014. It has been submitted to the Regional Health Agency for accreditation.

Conclusion: By revealing the patients’ demand for and satisfaction with the proposed health education sessions, this study has greatly encouraged us to continue this experimental health education program, which will soon be extended.

Disclosure of interest: None declared.

P134 Infectious adverse effects during treatment with IL-1 inhibitors in patients with systemic juvenile idiopathic arthritis and autoinflammatory diseases

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Introduction: IL-1 plays an important role in the pathogenesis of both illnesses. The anti-IL1 therapy (anakinra/ canakinumab) had been proved to be very effective in their treatment. The infections related to these treatments in children had been hardly described in literature.

Objectives: To describe the infectious complications in children with systemic juvenile idiopathic arthritis (SJJIA) or autoinflammatory diseases (AD) while receiving anti-IL1 drugs.

Methods: All the patients who had received IL1 inhibitors from January 2005 to January 2014 in our unit were included. We recorded the length of the exposition to anakinra or canakinumab, diagnosis, previous exposition to a different biologic treatment and moderate or severe infections.

The patients with SJJIA were defined by the ILAR criteria. In the AD group were included familiar mediterranean fever (FMF), Hiper IgD syndrome (HIDS), tumour necrosis factor receptor-associated periodic fever syndrome (TRAPS), Cryopyrin-Associated Periodic Syndrome (CAPS) and 1 pyogenic arthritis, pyoderma gangrenosum and acne syndrome (PAPA).

Results: Thirty nine patients were identified: 28 SJIA and 11 AD (7 HIDS, 2 TRAPS, 1 PAPA, 1 CAPS). Sixteen of them had received canakinumab, 35 anakinra and 12 had received both consecutively. Their mean age were 8.7 years (IQR 4.4-13.2).

At least one moderate-severe infection happened in 10/39 (25%) patients. The mean period from the first dose to the first infection was 1.78 years (range 0.3-3.75, IQR 1.05-2.65).

In the SJIA group 3/28 (10%) of the patients had at least one outstanding infection with a total of 7 episodes. In the AD group 5/11 (45%) developed at least one infection, with a total of 10 episodes, all of them in patients with HIDS. The 71% of patients with HIDS had at least one moderate-severe infection. Three patients accumulated the 52% of the episodes.

While receiving anakinra the infection rate was 11.6 episodes x 100 patients/year of treatment and 14, 4 while receiving canakinumab (RR 1.2).

Table 1(abstract P134)

<table>
<thead>
<tr>
<th></th>
<th>SJJIA 28 patients</th>
<th>AD 11 patients</th>
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</thead>
<tbody>
<tr>
<td>Canakinumab</td>
<td>1 pneumonia</td>
<td>1 Herpes Zoster</td>
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<tr>
<td></td>
<td>1 HPV infection</td>
<td>1 Soft tissue infection</td>
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<tr>
<td></td>
<td>1 severe VEB</td>
<td>1 Recurrent low urinary tract infection</td>
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<tr>
<td>Anakinra</td>
<td>4 pneumonia</td>
<td>1 pneumonia</td>
</tr>
<tr>
<td></td>
<td>1 sepsis</td>
<td>1 Recurrent low urinary tract infection</td>
</tr>
<tr>
<td></td>
<td>1 severe herpetic stomatitis</td>
<td>2 oropharyngeal candidiasis</td>
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</table>
**Objectives:** We aimed to analyse, in current practice, the switch to another ploy a system of post-graduate/workpackage 4 (WP4) aimed to identify current access to: Single Hub and Access point for 529 JIA patients, sex ratio: 0.5 (175M/354F), aged between 1 to 22 years in 16 centers 137 children with PF-JIA in CID on anti-TNF were treated with anti-TNF therapies (anti-TNF) for treatment at inclusion in the JIR cohort. The mean drug survival was not influenced by JIA subtype. We found a significant difference in patients having received more than two biotherapies, between SoJA and Poly (25%) compared to other JIA subtypes (5%).

**Conclusion:** Etanercept was the first biologic treatment used whatever the JIA subtype, in this retrospective study that includes patients treated since more than 10 years. Two third of cases were still treated with the first biologic after at the time of inclusion.

**Disclosure of interest:** None declared.

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**P136**

**Share – Package 4: addressing the need for health care for paediatric rheumatic diseases throughout europe**

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**Pediatric Rheumatology** 2014, 12(Suppl 1):P136

**Introduction:** A need for evidence-based guidelines for the management of paediatric rheumatic diseases (PRD) has been recognised. In 2012 the European Agency for Health and Consumers signed the contract for a new European initiative SHARE: Single Hub and Access point for paediatric Rheumatology in Europe (project number 2011 1202).

**Objectives:** Package 4 (WP4) aimed to identify current access to paediatric rheumatology services and practice in European countries in their complexity. Non-European countries from the PRINTO network were included in order to allow comparisons.

**Methods:** The survey questionnaires were developed through consensus meetings of the SHARE consortium partners and consultations with experts from across PR5 Working Groups. The Surveys have been stratified into 4 levels: Country-wide, Centre-specific, Disease-specific and Personal. Final survey texts were transformed into electronic web-based system hosted by PRINTO and presented to paediatric rheumatology community via PRINTO mailing list. Results of the country survey are presented here.

**Results:** The country survey was completed by representatives of 22 European countries (14 Western and 8 Eastern/Central) and 11 other countries. Results were grouped into 3 specific topics: 1. The healthcare system and organisation of paediatric rheumatology care, access to care. 2.Evidence based and qualified care. 3.Education and employment issues. In majority of European countries health professionals in PR care form an official working group or national society. Proportion of PR patients treated by general paediatricians or adult rheumatologists is low across Europe (mostly 12%). Proportion of patients treated in tertiary centres of university hospitals is higher in Eastern European countries. In Western Europe the similar proportion of patients are treated in paediatric departments of other than tertiary hospitals. National guidelines/recommendations are more frequently available in Western than Eastern European countries (64 vs 25%). When licenced biologics are available in all Western countries, this is not the case for Eastern Europe. Moreover, treatment limitations are more prominent in Eastern countries. Official recognition of paediatric rheumatology as a subspecialty varies. It is generally lower in Europe in comparison to non-European countries and reaches 37 (Eastern Europe) to 57% (Western Europe). Defined training scheme is available in over 60% of Western countries but only in 37% of Eastern ones. Availability of educational resources has been good for over 70% of all European Countries. The similar responses between Eastern and Western countries were also related to the availability of PR pre-graduate teaching. Only 35% of Western European countries employ a system of post-graduate/continuing education while such a system works in nearly 90% of Eastern European countries.

**Conclusion:** The WP4 of the SHARE project important information has been collected forming a thorough inventory of paediatric rheumatology practice in individual European countries. This will serve as a baseline for the formulation of internationally achievable best practices in PRD management. These practices will be presented to stakeholders such as individual paediatric rheumatology units, health authorities, health insurance companies and patient/parent organisations.

**Disclosure of interest:** None declared.

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**P137**

**Understanding the biology and use of TNF therapy in jia-clinical outcomes**

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**Pediatric Rheumatology** 2014, 12(Suppl 1):P137

**Introduction:** Treatment with anti-TNF therapies (anti-TNF) for polyarticular forms (extended oligo, Poly RF +/-) of JIA (PF-JIA) results in >50% demonstrating clinical inactive disease (CID).

**Objectives:** The aims of this study were to perform the first prospective, multicenter trial to determine the frequency, timing and predictors of flare upon withdrawal of anti-TNF in PF-JIA in CID.

**Methods:** In 16 centers 137 children with PF-JIA in CID on anti-TNF were enrolled and prospectively followed. If CID was maintained for the first 6 months of the study, then anti-TNF was stopped and the patients were followed prospectively by protocol. Background meds were stable.

**Results:** The study population included 18 (13%) extended oligoarticular, 17 (12%) RF+ Poly and 102 (75%) RF- Poly JIA patients. At enrollment, age (mean/median/range) was 11.3/11.6/5-14.0 years; disease duration was 4.0/4.6/0.5-16.8 yrs; 103 (75%) were Poly RF+ and 64 (47%) were Poly RF-.

Duration of CID at baseline was 1.2/0.5/0.5 day-.12.1 yrs. Anti-TNF was etanercept in 106 (77%), 25 (18%) adalimumab and 6 (5%) infliximab. 40% were on MTX at baseline (mean/median dose 0.4/0.4 mg/kg/wk). 17% were unable to maintain CID for the first 6 months despite stable background medications. For the extended oligo, Poly RF – and Poly RF- categories 94%, 82% and 60% respectively, maintained CID for the first 6 months (chi-square 0.7, p 0.03). ANA status, MTX use, and type of...
anti-TNF were not associated with the ability to maintain CID (chi-square p values 0.48, 0.14, and 0.75, respectively).

Upon stopping the anti-TNF therapy, the mean time to flare was 18.3 months with a median of 26 months (range 9-32 months). Longer disease duration at baseline was associated with an increasing risk of flare with stopping anti-TNF therapy (chi square 5.62, p = 0.017). Background MTX significantly decreased the risk of flare (p=0.05) and significantly increased the time to flare (p=0.05). JIA subtype was significantly associated with both risk of flaring (p=0.02) and time to flare (p=0.04) with RF+ Poly flaring less frequently than either RF- or Extended oligo which seem similar. RF+ patients were significantly less likely to flare than RF- (p=0.02). Age, gender, ANA status, duration of CID did not predict risk of or time to flare.

Conclusion: In these patients with Polyarticular forms of JIA in CID for 26 mos, upon stopping the anti-TNF therapy, 70% will experience a flare within 3.25 years but ≥ 50% will maintain CID for ≥17 months. Continuing background MTX both decreases the risk of flare and increases the time to flare. Disease duration and JIA subtype are the only predictive clinical parameters. Duration of CID was NOT predictive of risk of flare after stopping anti-TNF therapy.


Introduction: TNF receptor-associated periodic syndrome (TRAPS) is an autoinflammatory disease causing unprovoked fevers, myalgia, abdominal pain, rash, headaches, and, in severe cases, AA amyloidosis. It is an autosomal dominant condition resulting from variants in the TNF superfamily receptor 1A (TNFRSF1A) gene [1]. A hallmark of TRAPS is a huge overexpression of several genes associated with inflammatory response, including IL-1. Interestingly, IL-1 blockade normalized the overexpression of the disease-causing gene, TNFRSF1A, at the RNA level, suggesting a direct impact on the main pathogenic mechanism of TRAPS.


P139 Methotrexate in oligoarticular persistent juvenile idiopathic arthritis

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Pediatric Rheumatology 2014, 12(Suppl 1):P139

Introduction: Methotrexate (MTX) is recommended for children with juvenile idiopathic arthritis (JIA) with persistent oligoarticular course with high disease activity and features of poor prognosis or if they failed intraarticular glucocorticoid steroid injections following the 2011 ACR recommendations for the treatment of JIA. To date efficacy and safety of MTX for this JIA category have not been well studied.

Objectives: Evaluation of efficacy and safety of MTX in children with oligoarticular persistent JIA.

Methods: Baseline demographics, clinical characteristics and disease activity parameters have been prospectively documented in the German JIA BIKER Register. Efficacy was determined using the PedACR response criteria and the JADAS-10 until the last documentation or start of any biologic agent. Safety assessments were based on adverse events reports from the responsible physician.

Results: 343 patients with a total of 2039 visits were identified (894.7 total patient-years). 67% (n=231) were females. The median age at JIA onset was 4.7 (quartile (Q) 2.5/7.5) years. At treatment initiation the median age was 8.0 years (Q25/75 4.3/12.0) and the disease duration 1.1 years (Q25/75 0.5/3.1). ANA positivity has been found in 63.0%, HLB27 positivity in 11.1%. Prior MTX therapy 90.1% of children have been treated with nonsteroidal anti-inflammatory drugs (NSAIDs), 46.1% have received intraarticular glucocorticoid steroid injections. 88.3 of children were treated concomitantly with NSAIDs, 11.5% with corticosteroids and 2.6% with other disease-modifying antirheumatic drugs.

A high proportion of patients showed a significant response to treatment. Compared to baseline disease activity parameters at MTX initiation, at month 24 60.0%/63.9%/43.5% and at month 24 83.6%/80.0%/69.7% of patients met the PedACR response criteria of 30%/50%/70%. The median JADAS-10 at treatment start was 10.0 and decreased markedly to 2.1 at month 6, 1.4 at month 12 and 1.0 at month 24. At month 6 and month 12, 83 patients (33%) and 96 patients (42%) reached preliminary criteria for inactive disease. 113 patients experienced 216 adverse events (AE,24.7/100 patient-years). Four were reported as serious (0.4/100 patient-years (py)). The most
common reported AEs were nausea/vomiting (8.5/100 py), abnormal liver enzymes (4.7/100 py) and mild to moderate infections (3.6/100 py). 48 children (14%) suffered from uveitis prior treatment. None of these patients flared with uveitis. Four new uveitis index cases (1.1%) were reported while on treatment. 37 patients started a biologic agent, 16 of them switched from MTX to biologics while 21 patients were treated in combination with MTX. Treatment has been discontinued in 134 children for the following reasons: Inefficacy 3.2%, adverse events 9.8%, remission 24.3%, patients wish 16.5%, others 2.9%. 17 of 84 children (20.2%) who stopped MTX because of remission flared and re-started MTX.

Conclusion: Methotrexate appears to be highly effective in oligoarticular persistent JIA. The treatment is safe and well-tolerated. Few patients discontinued due to intolerance or inefficacy.

Disclosure of interest: None declared.

P140

Ten years of experience of biologics in juvenile idiopathic arthritis: focus for the reasons of withdrawals

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Pediatric Rheumatology 2014, 12(Suppl 1):P140

Introduction: Biologics are often used in therapy of DMARDs resistant JIA. The important problem is discontinuation of Biologics therapy due to different reasons.

Objectives: Evaluation of 10 years of the experience of Biologics in children, suffering from juvenile idiopathic arthritis (JIA) in single center focused for reasons of withdrawal.

Methods: The analysis includes data about 435 patients with JIA who have been getting Biologics in 2005 - 2014. The average age of patients is 10.5 years (from 1.5 to 18 years). Disease duration is 7 yrs avg (from 3 to 14 years). Clinical characteristics: sJuA - 70 (17%), JIA with polyarthicular course (poly) - 257 (61%), JIA oligo – 38 (9%), 51 (12%) patients suffered from active uveitis.

Results: During the observation Biologics were withdrawn in 123 cases (98 patients). For some patient we changed Biologics several times: in 21 cases - two times (21% of patients), in 2 cases (2%) - thrice. Distribution of reasons for the Biologics discontinuation is presented in Table 1 below:

Infliximab was withdrawn more often due to adverse events (infusion reactions), at the beginning of the treatment or several years later. The other reason is secondary inefficiency after 2-5 years of application. Abatacept was cancelled more often for the reason of inefficiency, adverse events were observed rarely. Etanercept was withdrawn in some cases because of uveitis de novo. Adalimumab was withdrawn basically due to organization problem. Favorable choice of Biologics is changed from 2005 till now. For new initiation we used different biologics in different time. Infliximab was administered in the past (from 2005 to 2012), maximum (14 patients) in 2011. Administration number decrees nowadays (3 in 2013, 1 in 2014). Adalimumab was not commonly administrated before 2011, from 2012 administration count increase from 10-11 per year to 39. Using of Etanercept was increased from 2010 (20-35) and achieved maximum in 2013 (49 patients). Usually we prescribe tocilizumab in systemic JIA and do not change in most cases.

Conclusion: Availability of Biologics therapy was increased during last ten years in Russia. That has improved survival of therapy and has given opportunity of using Biologics with good safety profile.

Disclosure of interest: None declared.

P141

Successful treatment of diffuse sclerosing osteomyelitis of the mandible/mandibular chronic non-bacterial osteitis with intravenous pamidronate: resolution of pain and radiographic bone inflammation with improved cosmetic appearance - a case study

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Pediatric Rheumatology 2014, 12(Suppl 1):P141

Introduction: Diffuse sclerosing osteomyelitis of the mandible (DSMO) is a form of chronic non-bacterial osteitis (CNO) and predominantly affects patients < 18 years. It can result in cosmetic disfigurement. No uniformly effective treatment exists. Intravenous pamidronate (IV-PAM) has been reported to be effective in multifocal CNO.

Objectives: To describe clinical and radiologic outcome of a DSMO patient following treatment with IV-PAM.

Methods: A 4-year old Caucasian female was diagnosed with DSMO and prospectively followed from 2007-2014. She presented with a 20-month history of facial asymmetry and painful bony expansion of the left hemimandible. CT-scan revealed bone expansion suggestive of fibrous dysplasia, but two consecutive bone biopsies revealed inflammatory cells only. Infectious osteomyelitis was also suspected, but cultures were negative and IV and oral antibiotics were of no benefit.

Focal MRI revealed bone marrow and soft tissue edema with perosteal reaction, consistent with DSMO. Subsequent whole-body MRI revealed no other bony lesions. Naproxen was of no benefit and she was started on monthly 1-day IV-PAM infusions (1st dose 0.5mg/kg; each subsequent dose: 1mg/kg). The response to treatment was assessed according to visual analogue score for pain (VAS, 0=no pain; 10=maximum pain), sequential MRIs and clinical photos.

Results: She received 8 monthly IV-PAM infusions. After 1st dose, VAS decreased from 10 to 0. MRI documented resolution of abnormal signal at 5 months with gradual mandibular remodelling. Clinical photos confirmed resolution of facial asymmetry over 5 years with sustained improvement at 7 years. She had a minor MRI confirmed flare at 67 months which responded to Naproxen monotherapy. She remains asymptomatic at 84 month follow-up.

Conclusion: DSMO is challenging to diagnose and treat due to its rareness and lack of uniformly effective treatment. IV-PAM was effective in this young refractory patient and resulted in resolution of pain, mandibular remodelling and cosmetic improvement.

Table 1(abstract P140)

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<th>Withdrawal reasons</th>
<th>All biologics</th>
<th>Infliximab</th>
<th>Abatacept</th>
<th>Tocilizumab</th>
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<th>Etanercept</th>
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<td>Two years</td>
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P142

Body composition, bone mineral density and serum adipokines in juvenile idiopathic arthritis with previous glucocorticoid therapy
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Pediatric Rheumatology 2014, 12(Suppl 1):P142

Introduction: Patients with juvenile idiopathic arthritis (JIA) are prone to alterations in bone health, body composition and adipokines.

Objectives: To evaluate areal bone mineral density (BMD), body composition measurements with dual X-ray absorptiometry (DXA), and serum leptin and adiponectin levels, but the results were unremarkable. Patients with JIA exposed to systemic GCs had normal BMD. Their lean mass for height and bone area for height were similar. Patients had lower Z-scores for whole body and bone-age-corrected lumbar spine BMD (p<0.001 and 0.009). Their whole body BMC and lean mass ratio was lower. Serum leptin and adiponectin were similar between groups even when adjusted for age and height, and no correlations with disease activity occurred. Patients (n=16) with low LS BMD (≤−1.0) were shorter, lighter and had lower BMI than those with normal BMD. Their lean mass for height and bone area for height were lower. In the low BMD group BMC to lean mass ratio was also decreased when adjusted for gender and height (p=0.002).

Conclusion: Patients with JIA exposed to systemic GCs had normal stature, body composition and serum leptin and adiponectin levels, but reduced whole body and lumbar spine BMD. Among the patients those with lowest BMD had delayed growth, but also evidence of sarcopenia and osteopenia.

Disclosure of interest: None declared.

P143

Bone mineral density in juvenile onset systemic lupus erythematosus from sultanate of oman
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Pediatric Rheumatology 2014, 12(Suppl 1):P143

Introduction: The survival of patients with systemic lupus erythematosus has increased over the last decade, which is associated with increased risk of morbidity. Osteoporosis remains one of leading morbidity associated with long term survivals. Multiple factors have been proposed to contribute to osteopenia, including limited physical activity, limited exposure to sunlight, duration of the disease activity, corticosteroid therapy, other immunosuppressant therapy, inadequate dietary intake of calcium and vitamins, and renal insufficiency. Children with Juvenile onset systemic lupus erythematosus (JSLE) are at even greater risk of developing osteopenia since the disease develops even before achieving their full potential peak bone mass.

Objectives: We evaluated bone mineral density (BMD) in Omani children with JSLE in order to detect potential predictors of reduction in bone mass.

Methods: BMD measurements were obtained in 27 JSLE patients and 97 healthy matched controls. The age, body mass index (BMI), BMD scores and Vitamin D levels were compared in both groups. Serial annual BMD was obtained in all JSLE patients and the first and last BMD scores were used for comparison. Factors that may play a role in BMD scores in the JSLE cohort including disease duration, disease activity, current steroid, cumulative steroid, immunosuppressive medication, vitamin D supplementation were recorded.

Results: In comparing JSLE with healthy matched controls, patients with JSLE had lower BMI (16±2 versus 19±5 kg/m2 p value 0.007) which was associated with lower overall BMD than normal healthy cohort (0.72±0.09 versus 0.84±0.10 gm/cm3 p value <0.001). There was no significant difference in cumulative steroid, immunosuppressive medication, vitamin D levels were compared in both groups. Disease duration seems to play a major role in decline in BMD score in the study. Other factors that may play a role in BMD measurements in JSLE patients, such as current and overall cumulative steroids and other immunosuppressive medication did not have a significant correlation with decline in BMD score in the study.

Conclusion: JSLE had lower BMI and BMD at disease onset than normal healthy cohort. Disease duration seems to play a major role in decline in Z score in the study. Other factors such as disease activity, vitamin D levels, current and cumulative steroids or immunosuppressive therapy did not seem to play a major role in decline in Z score. There was a significant increase in overall BMD in JSLE patients with JSLE which could be explained by effect of calcium and vitamin D supplementation. This study is not without limitation. A larger multi-centered study is needed to study the effect of JSLE on bone metabolism.

Disclosure of interest: None declared.

P144

Severe chronic non-bacterial osteomyelitis associated with MPO deficiency
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Pediatric Rheumatology 2014, 12(Suppl 1):P144

Introduction: We report a severe case of chronic non-bacterial osteomyelitis (CNO) associated with total myeloperoxidase (MPO) deficiency. Chronic non-bacterial osteomyelitis (CNO) is often considered an autoinflammatory disease. In pediatric literature CNO is often referred to as chronic recurrent multifocal osteomyelitis (CRMO). CNO is occasionally associated with extremely rare monogenic disease but in most cases the etiology is unknown.

MPO deficiency is characterized by low levels of leukocyte MPO, and in some cases even total lack of the enzyme. The condition is seldom associated with pathology; severe Candida infection occurs in about 5% and lumbar myelitis occurs in about 1% of cases. MPO and there is a slightly increased frequency of minor infections.

Objectives: The objectives of the case report are to describe a patient with CNO associated to MPO deficiency, including inflammatory markers, cytokines and phagocyte function as well as the response to treatment.

Methods: Measurements of clinical inflammatory markers, serum cytokines, as well as functional tests of innate immune cells.

Results: The patient, a girl of 18 years, was healthy until the age of 10 when she developed bilateral swollen and painful thighs. After a
A rare pediatric tumor: thymic carcinoma mimicking acute rheumatoid fever

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P145

Introduction: Malign diseases may mimic rheumatoid diseases. Joint involvement and leg pain are among frequently encountered symptoms particularly in the patients with leukemia. Sometimes, however, primary tumor may be asymptomatic and may mimic rheumatoid diseases because of metastasis. The present case, which admitted to our clinic with bone and joint pain continuing for 10 days and mimicking acute rheumatoid fever (ARF) and in which bone metastasis due to thymic carcinoma was detected when investigated, was presented for it is a rare condition.

Objectives: The present case, which admitted to our clinic with bone and joint pain continuing for 10 days and mimicking acute rheumatoid fever (ARF) and in which bone metastasis due to thymic carcinoma was detected when investigated, was presented for it is a rare condition.

Methods: A 13-year-old male patient presented to the pediatric polyclinic with joint swelling and leg pain that appeared 10 days ago. His history revealed that pain wakes him up at night and is remittent, spreads over his thigh and accompanied by knee pain, and that he has no history of recent infection or trauma.

The results of the laboratory analyses were as follows: erythrocyte sedimentation rate 120 mm/h, C-reactive protein 3.57 mg/dl and ASO 358 IU, and the patient was considered as ARF and admitted to the clinic for further analysis. Joint examination revealed swelling, but had no warmth or redness. Results of the analyses performed for joint pain including rheumatoid factor, anti-nuclear antibody, anti-dsDNA and other markers of collagen vascular diseases, as well as brucella and salmonella agglutination tests, were all negative. Bone marrow aspiration was normal.

MRI of hip, knee and sacroiliac joint were performed. Metastases were detected in all pelvic bones being more prominent in the left side including femur neck and proximal diaphysis, in bilateral sacrum and iliac bone with the largest was 28mm in the left iliac bone; multiple round-shaped metastases located in the femur, distal tibia and proximal diaphysis with the largest was 1 cm. Contrast enhanced thoracic CT demonstrated an approximately 10 x 7.5 x 5 cm heterogeneous hypodense solid-like mass lesion in the anterior mediastinum.

On PET/CT, increased FDG uptake was observed at malignancy level with a SUVmax measured to be 7 in a 76 x 46 x 49 mm mass, which completely fills the anterior mediastinum, suppresses the left lung, pushes the mediastinal strutures towards to the right and posterior, and invades the sternum. And there were increased FDG uptake in various areas of the lungs.

Increased FDG uptake at malignancy level with SUVmax measured to be 8.3 in bilateral humerus, bilateral scapula, sternum, extensively in C3, C7, thoracic and lumbar vertebrae, in the right 8th and left 5th and 6th costae, sacrum, bilateral iliac, acetabulum, head and neck of femur, pubis, and ischium.

Results: The result of the biopsy taken from the mass with the assistance of interventional radiology came up as thymic carcinoma.

Conclusion: The present case, which presented with the prediagnosis of ARF, is interesting because of having thymic carcinoma, is a rare case condition in childhood, and no complaint other than leg pain for 10 days was present despite extensive metastasis at the time of presentation.

Disclosure of interest: None declared.
P147
Neurophysiologic pain response in patients with juvenile idiopathic arthritis - a pilot study
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Pediatric Rheumatology 2014, 12(Suppl 1):P147

Introduction: Pain is a common symptom in children and adolescents with JIA. It has been hypothesized that frequent pain experiences sensitize pain processing pathways, resulting in hypersensitivity to later painful stimuli. A lower pain threshold (PT) and pain tolerance in JIA patients have been demonstrated in previous studies using pressure algometry and the cold pressor task.

Objectives: To investigate pain thresholds in adolescents with JIA compared to age and sex matched healthy controls, using several modalities for experimental pain testing.

Methods: Consecutive adolescents with JIA (16-18 years) were recruited from the pediatric rheumatology outpatient clinic at St. Olavs Hospital. Healthy controls were recruited from a local upper secondary school. Both completed a validated questionnaire on health and quality of life (SF-36), and reported pain from the last week (VAS scale). Quantitative sensory testing was conducted, and thermal detection pain thresholds (PTs) recorded. A thermal element was held against three specified locations of the participant’s skin, and the participant was instructed to press a button when he/she felt changes in temperature or pain. Pressure algometry was performed on two well-defined anatomical areas, giving the pressure pain threshold (PPT).

Results: Compared to 19 healthy controls, the 14 patients with JIA reported more pain during the last week, and had a less favorable score in the physical SF-36 domains, but no difference in the mental health domains. They displayed a lower PPT, but similar cold and warmth PT compared to the controls. When subdividing JIA patients with active and inactive disease, patients with inactive disease had a lower cold PT and PPT, and a tendency towards a lower heat PT compared to controls. Patients with active disease had a tendency towards higher PTs in all three modalities compared to both healthy adolescents and patients with inactive disease.

Conclusion: Our results indicate that JIA patients may be subject to a sensitization, giving lower pain thresholds in inactive disease, but once the disease is active, painful arthritis may act as a diversion leading to increased rather than lowered PT.

Disclosure of interest: None declared.

P148
Efficacy of TNF blockers from the perspective of growth velocity: slovak experience
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Pediatric Rheumatology 2014, 12(Suppl 1):P148

Introduction: In patients with polyarticular course of juvenile idiopathic arthritis (JIA) both, ongoing chronic inflammation with high levels of pro-inflammatory cytokines and corticosteroid treatment, may affect linear growth adversely, potentially leading to irreversible growth retardation. Biologic treatment of JIA may have the potential to enable normal growth in children with JIA.

Objectives: To retrospectively evaluate clinical efficacy, from perspective of growth velocity as a sensitive marker of well-being in children, of biologics in children with JIA in both centers in Slovakia.

Methods: 34 patients (17 girls, 17 boys) with DMARDs-resistant polyarticular JIA receiving TNFα blocker (28 etanercept, 6 adalimumab) + methotrexate were evaluated during their first year of biologic therapy. The mean age at anti-TNF treatment initiation was 10.52 (range 2.98-17.77). Median duration of disease was 4.42 years (range 0.89-10.63), 24 patients received corticosteroids. Control group, consisted of 21 patients (12 boys, 9 girls) with polyarticular course of JIA non-responsive to NSAIDs therapy and intraarticular corticosteroid injections, was evaluated during their first year of DMARDs treatment. Same inclusion and exclusion criteria, e.g. age and Tanner staging, were applied for both groups. Growth velocity was defined by change of height in standard deviation score (SDS). A positive value >0.1 indicated catch-up and negative value <0.1 indicated impaired growth. Values in the range -0.1 to 0.1 were labeled as “steady growth”.

Results: Efficacy of combination TNFα blocker + MTX treatment evaluated by ACR Pediatric 30 is increasing during the first year. In time of year control 34/31/25 patients reach criteria at least for ACR Pediatric 30/50/70 respectively. The number of joints with acute arthritis decreased by 9.19 % (from 309 to 25) compared to 91.33 % (from 173 to 15) in control group. TNFα blocker + MTX combination also shows a rapid corticosteroid-sparing effect. Only 4 patients received corticosteroids at the start of DMARDs treatment in control group. Clinical response in TNFα blocker + MTX group was accompanied by catch-up in 18 patients, “steady growth” and impaired growth were observed in 8 cases both. Clinical response in control group was accompanied by catch-up only in 3 cases, “steady growth” and impaired growth were observed in 6 and 8 patients respectively. The difference in growth velocity was statistically significant (0.106 ± SD 0.439 vs. -0.139 ± SD 0.385, t = 2.101 df = 53, p = 0.040).

Conclusion: Combination of TNFα blocker + methotrexate is highly effective in polyarticular course of DMARDs-resistant JIA. The clinical response is accompanied by an increase in growth velocity (catch-up) in most cases. The growth velocity compared with control group was on the border of statistical significance.

Disclosure of interest: None declared.

P149
Finding specific cut-off values of JADAS-10 and JADAS3-10 for disease activity levels in juvenile idiopathic arthritis: a finnish multicenter study
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Pediatric Rheumatology 2014, 12(Suppl 1):P149

Introduction: It’s crucial to observe the changes in disease activity in JIA in order to investigate reliably the effects of the new treatments and to optimize their use. Several tools for outcome measurements have been developed. Juvenile Arthritis Disease Activity Score (JADAS) is an independent measure of the therapy response and enables the comparison between cohorts. However, the use of ESR restricts the feasibility of JADAS. That’s why a JADAS index excluding ESR has been tested (JADAS3). In order to simplify the interpretation of the JADAS score, efforts have been made to define cut-off values of JADAS for low and high disease activity. Cut-off values of JADAS for disease activity levels, as defined by ACR, have not been developed. Neither have any cut-off values for JADAS3 been defined.

Methods: 70 patients (31 girls, 39 boys) were followed from January 2009 to December 2011 in two centers in Finland; 25 patients (12 girls, 13 boys) were followed from January 2009 to December 2011 in two centers in Slovakia. JADAS-10 and JADAS3-10 are defined in order to investigate reliably the effects of the new treatments and to enable the comparison between cohorts. However, the use of ESR restricts the feasibility of JADAS. That’s why a JADAS index excluding ESR has been tested (JADAS3). In order to simplify the interpretation of the JADAS score, efforts have been made to define cut-off values of JADAS for low and high disease activity. Cut-off values of JADAS for disease activity levels, as defined by ACR, have not been developed. Neither have any cut-off values for JADAS3 been defined.
Objectives: Our aim was to define the cut-off values for low, moderate, and high disease activity of JADAS-10 and JADAS3-10.

Methods: In a multicenter study consisting 20% of all patients with juvenile idiopathic arthritis in Finland (n=514), data on last registered visits and on visits fulfilling the criteria for high disease activity were obtained. JADAS-10 and JADAS3-10 were calculated, and the cut-off values of both of these scores were determined by 3 different ROC-based statistical methods.

Results: Of 514 patients included, 65.5% were females and 54.1% had polyarticular disease. The most suitable method for determining cut-off values was the 90% specificity index. The cut-off value for low disease activity was 0.2 for both JADAS-10 and JADAS3-10 in both oligoarticular and polyarticular disease. In oligoarticular disease, the cut-off value for moderate disease activity was 2.8 for JADAS-10 and 2.4 for JADAS3-10 and in polyarticular disease 4.1 for both JADAS-10 and JADAS3-10. In patients with polyarticular disease, the cut-off value for high disease activity of JADAS-10 and JADAS3-10 was 16.3 and 16.0.

Conclusion: Cut-off values for low, moderate and high disease activity were defined. In clinical setting, research and quality control, JADAS-10 can be used instead of JADAS-10. In the future, uniform, clinical disease activity levels need to be set. Valid and robust cut-off values of disease activity levels can guide both a clinician and a researcher, and equip in benchmarking.


Table 1 (abstract P150) Recommendations for screening for cardiopulmonary involvement in JSSc at baseline and follow-up (75% consensus defined as agreement)

<table>
<thead>
<tr>
<th>Cardiopulmonary</th>
<th>Baseline</th>
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<tr>
<td></td>
<td>All patients should undergo:</td>
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<td>- BP</td>
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<td></td>
<td>- 12 lead ECG</td>
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<td>- 24 hour ECG</td>
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<td>- ECHO with Doppler</td>
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<td>- Cardiac MRI with gadolinium</td>
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<td>- HRCT thorax</td>
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<td>- PFT with DLCO</td>
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<td>- 6MWT</td>
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Follow-up screening (for first 5 years from diagnosis)*

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<tr>
<td></td>
<td>6 monthly</td>
<td>12 lead ECG</td>
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<td>ECHO with doppler</td>
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<td>PFT with DLCO</td>
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<td>Annual</td>
<td>24hr ECG</td>
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<td>At 3 years</td>
<td>Repeat HRCT</td>
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*screening guidelines are based on asymptomatic patients. However, children may need more frequent monitoring depending on clinical status and abnormalities detected on previous investigation.

to treatment. The recommendations developed by this group aim to standardise care and improve outcomes in this rare disease.

Disclosure of interest: None declared.

Abbreviations: BP: blood pressure; ECG: electrocardiogram; ECHO: echocardiogram; MRI: magnetic resonance imaging; HRCT: high resolution computerised tomography; PFT DLCO: pulmonary function tests with diffusion capacity of lung for carbon monoxide: 6MWT: 6 minute walk test; NT BNP: N-terminal pro-brain natriuretic peptide; GORD: gastro-esophageal reflux disease.
Median disease duration is 8.5 years (IQR 7.3). Median JADAS 27 is 3.8 (IQR 6.9), active joint count is 0.0 (2.0), DAS 28 is 2.18 (1.37). MTX is ever or currently used in 78% of the patients, anti TNF in 15% and systemic corticosteroids in 24%. Early disease onset before the age of 8 years is present in 59% of the patients. Eleven patients are of non-Caucasian origin and 19 patients are older than 21 years, and are excluded from growth and puberty analysis. Median SDS length is -0.29 (IQR 1.38), SDS BMI -0.08 (1.71). PHG, Bre, PHB and Gen are delayed in all stages 2-5, more pronounced in stage 5. Median delay in PHG stage 5 is 3.4 years, Bre stage 5 3.4 years, Menarche 3.5 years, PHB stage 5 1.6 years and Gen stage 5 1.7 years. Progression of puberty is more delayed in stage 4 and 5 compared to healthy Dutch children. No significant differences are seen between users and non-users of systemic corticosteroids, MTX or anti TNF. Subtype of JIA, disease activity and age at onset of JIA did not significantly influence results.

**Conclusion:** Although disease activity is low due to intensive treatment, puberty is still remarkably delayed. Further investigation in clinical relevance and cause of delayed puberty is needed.

**Disclosure of interest:** None declared.

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**P152**

Clinical remission off medication in greek adults with juvenile idiopathic arthritis during a 17 year follow-up period

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**Introduction:** Clinical remission off medication (CR) in patients with Juvenile Idiopathic Arthritis (JIA) is the optimal aim of treat -to -target strategies. No relevant data have been published for Greek young adults so far.

**Objectives:** To assess the achievement of CR and identify CR’s predictors in adults with JIA over a-long-term disease course.

**Methods:** JIA patients ≥18 years, and ≥5 years disease duration were enrolled in this longitudinal retrospective cohort study. Radiographic damage was based on total modified Sharf/van der Heijde score (TmSvdHS), articular and extra-articular damage on JADI and physical ability on HAQ-DI.

**Results:** 98 patients (69 females) with a mean age at disease onset of 7.8 years, an interval from onset to last visit of 17.1 years and a current age of 24.9 years were studied. 37.8% achieved ≥ 1 episode of CR and 21.6% ≥2. The 7 JIA subtypes differed in respect to CR attainment (p=0.008), the worst being patients with polyarthritid RF positive (0%) and the best those with persistent oligoarthritis (87.5%). In 51.4% of them CR lasted for ≥5 years. Gender, age at disease onset, ANA and anti-CCP positivity were not correlated with CR. CR duration was significantly correlated with lower JADI-A (p=0.008), JADI-E (p=0.001), TmSvdHS (p=0.002) and HAQ-DI (p=0.018), while predictors of shorter CR state were polyarticular subtype (p=0.004) and longer duration of disease activity within the first 5 years (p=0.001).

**Conclusion:** Shrinking of disease activity periods in long-term JIA induced by improved treatments leads to extended CR periods and avoids structural damage and physical disability.

**Disclosure of interest:** None declared.

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**P153**

The evaluation of the disease advancement in patients with mucopolysaccharidosis

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Pediatric Rheumatology 2014, 12(Suppl 1)p153

**Introduction:** One of the most important manifestations of mucopolysaccharidosis (MPS) type I, II and VI is a progressive disease of the osteoarticular system. The evaluation of the disease advancement is difficult due to the complexity of symptoms. The characteristic features are progressive limitation of joint mobility and joint pain. These symptoms affect the quality of patient life. A uniform scale has not been developed for these patients.

**Objectives:** The aim of this study was to use the experience in the evaluation of disorders in rheumatic diseases (Juvenile Idiopathic Arthritis, JIA) in patients with MPS.

**Methods:** 6 patients with MPS VI were evaluated: 2 with advanced disease, 2 with moderate and 2 with slow progressing disease. The following parameters were selected for assessment: Physician global assessment of disease activity (PGA), Patient/parent global assessment of well-being (PGE), Functional ability (CHAQ), Number of joints with limited movement (LJC) and VAS pain – visual analogue scale for pain.

**Results:** The evaluation results are shown in Table 1.

**Conclusion:** The parameters used in JIA may be applied for assessment of the MPS severity. With their implementation, the progression of the disease and the effect of the treatment can be assessed and compared.

**Disclosure of interest:** None declared.

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**P154**

Medication therapy patients with juvenile idiopathic arthritis (JIA), who needed joint replacement in adult life

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Pediatric Rheumatology 2014, 12(Suppl 1)p154

**Introduction:** Well-timed administration of disease-modifying therapy is a keystone of contemporary treatment for patients with JIA.

**Objectives:** The objective is to analyze the effect of medication therapy carried out for patients in the first year of the disease and timeframe for disease-modifying therapy administration.

**Methods:** 23 adult patients of orthopedic surgery department who underwent joint replacement in 2010–2013. Based on patients survey and medical documents, we analyzed the age of the disease onset, arthritis type, mode of therapy taken in the first year of the disease, duration of the disease by the time of disease-modifying therapy administration and

<table>
<thead>
<tr>
<th>Patient</th>
<th>(years)</th>
<th>PGA 0-10cm</th>
<th>PGE 0-10cm</th>
<th>CHAQ 0-3</th>
<th>LJC 0-71</th>
<th>VAS pain 0-10cm</th>
<th>Score (104)</th>
<th>Severity of disease</th>
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<tr>
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<td>advanced</td>
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<td>37</td>
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social status during the study (education, job, marital status, age and disease duration by the time of the joint replacement).

Results: 87% of the patients examined were women. Mean age of the disease onset is 4.6 years (2–15 years). Polyrheumatism was found in 13 patients (56%), systemic and oligoarticular types were observed in 22% each. In the first year of the disease 4 patients were treated with glucocorticoids (GC) (intra-articular and systemic injection); non-steroid anti-inflammatory drugs (NSAID) were administered in 8 patients; 8 patients received combined therapy with these drugs and one woman received disease-modifying therapy in addition to the combination of these drugs. Average duration of the disease by the time of disease-modifying therapy administration was 6.5 years. In fact, 3 patients received methotrexate starting from the disease onset, two patients were treated only in hospital conditions. All patients finished school, 8 patients have been educated at home: a girl since the second form and others in senior school. 6 patients had vocational secondary education, 7 patients had a higher education, 7 patients were employed, 3 patients went on to further study, 5 patients had a family 3 of which were mothers. Mean age of the patients by the time of the first joint replacement was 23 years (17–35 years) and average disease duration was 15.9 years. One joint was replaced in 70% of patients, two joints in 20% and three joints in 10%. 60% of patients underwent hip replacement and 40% underwent knee replacement.

Conclusion: This treatment was inadequate in the majority of patients, though the condition of some patients was relatively satisfactory for a long period that allowed them to attend school. In 60% of patients with early onset of the disease, 47% had impairment in adolescent period. In one woman elbow replacement was associated with an error in rehabilitation: redressment after short duration of the disease led to fast ankylosing. Severe functional disorders and low social activity were caused by inadequate therapy administered at the early stage of the disease. Nowadays, almost all patients with chronic arthritis receive disease-modifying therapy in the first 3–6 months, which inspires hope for better functional and social results of their treatment in adult life.

Disclosure of interest: None declared.

**P155**

The spectrum of paediatric rheumatic diseases in two tertiary centres in Cape Town, South Africa

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Pediatric Rheumatology 2014, 12(Suppl 1):P155

Introduction: Access to paediatric rheumatology services in sub-Saharan Africa is currently very limited with major challenges such as lack of trained personnel, diagnostic and therapeutic resources. Knowledge of the spectrum and incidence of paediatric rheumatologic diseases is important to aid in the advocacy for making paediatric rheumatology more visible and to improve access to the services in areas such as sub-Saharan Africa where the greatest unmet needs exist. However, data on the occurrence and incidence of paediatric rheumatologic diseases in Africa is scant. Single centre registry studies may help bridge this gap and guide planning interventions to address the diagnostic, therapeutic and human resource needs.

Objectives: To determine the spectrum and frequency of diseases seen in the paediatric rheumatology service of two tertiary health care facilities in Cape Town, South Africa.

Methods: We reviewed patient folders and the electronic data base of the department of paediatric rheumatology at the Red Cross children’s and Groote Schuur hospitals in Cape Town. The demographic features and diagnosis for patients seen between 2010 and May 2014 was extracted, analyzed and descriptive statistics presented using StataIC 11 software.

Results: A total of 462 patients were in the data base; 264 (57.8%) female. The median age at first presentation at our centre was 10 (IQR 6-12.8) years. One hundred and fifty four (33.3%) were diagnosed with JIA. Other notable diagnoses included HIV associated arthritis 15 (3.3%), neutrophilic dermatoses 4 and periodic fever syndromes 6 cases. Less common conditions seen included fibrodyplasia ossificans progressiva 3, arcardi gutierrez syndrome 2 and poncet’s disease 4 cases. The findings are summarized in the table below.

Conclusion: A wide spectrum of paediatric rheumatologic diseases was seen in this study setting. JIA was the most frequent diagnosis at 33.3% of
cases. Connective tissue diseases e.g SLE, JDM and scleroderma for which scant reports exist from Africa comprised a significant part of the work load (10.4%). Vasculitis 22 (4.8%) of the cases may have been underestimated as most cases of henoch schonlein and kawasaki’s disease were followed up in the general paediatrics department. Cross sectional studies such as this could aid in understanding the scope of the problem of paediatric rheumatologic diseases, and in guiding the planning and identification of resource needs as well as preparation of practice guidelines.

Disclosure of interest: None declared.

**P156**

Influence of the cognitive aspects of caregivers in the adhesion of treatment in children and adolescents with chronic rheumatic diseases-preliminary data

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Pediatric Rheumatology 2014, 12(Suppl 1):P156

Introduction: The adhesion to treatment is a key factor for an effective treatment. Studies have showed considerable taxes in poor adhesion in children and adolescents with rheumatic diseases, which lead to long-term costs and consequences for the patient, the family, and society. Psychological conditions and familial support have demonstrated to be a strong influence in the adhesion to treatment.

Objectives: To study the psychocognitive and social aspects of the caregivers of patients with rheumatic diseases and evaluate its correlation with adhesion to treatment.

Methods: 42 caregivers of patients followed in our outpatient pediatric rheumatology clinic participated in this study, classified according to good or bad adhesion to treatment, according to the Morisky Green drug adhesion test. The sample was selected consecutively. We used a standard questionnaire to verify the socioeconomic level, the Family Apgar scale to verify family functioning. The Wechsler Adult Intelligence Scale (WAIS) to detect IQ, and clinical and demographic data.

Results: We observed good adherence in 6% of patients and bad adherence in 31%. In relation to socioeconomic class, 59% (n=17) of adherent patients belonged in the low middle class, against 77% (n=10) of non-adherent patients (p=0.31). The family functioning showed itself to be good in 79% (n=23) of adherent patients and 54% (n=7) of non-adherent patients (p=0.14). In the group of adherent patients, 59% (n=17) of caregivers received help from third parties in the care of patients, while 31% (n=4) of the non-adherent patient group received such help (p=0.18). The total IQ presented an average of 95.2 (SD=7.3) in the adherent patients group and 94.3 (SD=10.9) in the non-adherent patients group (p=0.77).

Conclusion: We noted a necessity in amplifying our sample size in order to reach statistical significance. Thus far, we observed a trend of higher social economic class in the group of adherent patients, as well as better family functioning and more support from other people in the care of the patients, in comparison with the non-adherent group. The overall

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**Table 1(abstract P155)** Frequency table of category of diseases seen

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Frequency</th>
<th>Percent</th>
<th>Cumulative</th>
</tr>
</thead>
<tbody>
<tr>
<td>JIA</td>
<td>154</td>
<td>33.3</td>
<td>33.3</td>
</tr>
<tr>
<td>Systemic CTDs</td>
<td>48</td>
<td>10.4</td>
<td>43.7</td>
</tr>
<tr>
<td>Uveitis</td>
<td>15</td>
<td>3.25</td>
<td>46.97</td>
</tr>
<tr>
<td>Vasculitis</td>
<td>22</td>
<td>4.8</td>
<td>51.77</td>
</tr>
<tr>
<td>Arthritis, HIV</td>
<td>15</td>
<td>3.25</td>
<td>55.02</td>
</tr>
<tr>
<td>Arthralgia other arthritis</td>
<td>81</td>
<td>17.5</td>
<td>72.52</td>
</tr>
<tr>
<td>Pain, CRPS and other</td>
<td>49</td>
<td>10.6</td>
<td>83.12</td>
</tr>
<tr>
<td>Other</td>
<td>78</td>
<td>16.9</td>
<td>100</td>
</tr>
</tbody>
</table>

Total 462 100

CTD=Connective tissue disease
average IQ seems similar in both groups. These preliminary results suggest the importance of healthcare teams in conducting reviews seeking global comprehension of the patient to aid in adhesion.

Disclosure of interest: None declared.

P157
Non-specific aorto-arteritis involving abdominal aorta branches in an adolescent girl (clinical case)
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Pediatric Rheumatology 2014, 12(Suppl 1):P157

Introduction: In children, the Takajans arteritis is one of the most frequent causes of renovascular hypertension.

Objectives: To present a clinical case on non-specific aorto-arteritis involving abdominal aorta branches in an adolescent girl.

Methods: Patient Dina Zh., female, 14 years old. The patient was admitted to the Department of cardiology and rheumatology of Chelyabinsk regional paediatric hospital on January 15, 2014. Fatigue, dyspnoe, headache, skin rash, BP increase up to 160/100 mm hg were reported. Severe disease was reported upon hospitalization; justification: Polyserositis; bilateral focal pleuroneumonia; class 2 respiratory failure, pancarditis (endomypopericarditis); class 2 heart failure, peritoneal exudation. Treatment resulted in stabilization; heart failure and respiratory failure symptoms were managed. Treatment – arterial hypertension (130/80 – 160/110 mm hg) persisted. Pink – to purple livedo-like rash appeared on the lower extremities and abdominal wall. Proteinuria (daily loss up to 310 mg) was reported; diuresis level -1350 ml/d. At hospitalization Day 3 hypertension attack was reported; it included BP increase up to 190/110 mm/hg, severe headache, spoor progressing to loss of consciousness, and seizures. CT of abdominal cavity with aortography: manifested narrowing of celiac trunk proximal regions, narrowing of superior mesenteric artery isthmus, narrowing of dextral renal artery. Blood circulation was not detected in proximal regions of the sinister renal artery. Inferior mesenteric artery: no significant changes reported. Diagnosis: non-specific aorto-arteritis (disease of Takajus), stenosis type 2 involving celiac trunk, superior mesenteric artery, and renal arteries; secondary arterial hypertension, symptomatic epileptic seizures.

Results: Treatment: pulse treatment with cyclophosphane (15 mg/kg dose), prednisolone (60 mg/dg, i/m injections), anti-hypertension treatment, anti-aggregation treatment. Due to presence of abdominal aorta branches, critical stenosis the patient was transferred to the Federal centre of cardiovascular surgery of Chelyabinsk. Operation: stenting of the affected arteries; sinister renal artery angioplastics. No complications were reported during the post-operation period. Improvements were reported, including recovery of consciousness, and BP normalization; the patient resumed oral feeding, and manifestations of heart failure were managed. The patient’s condition has improved; the girl was active. Normal blood pressure and no complaints were reported. The patient demonstrated normal appetite; weight gain was reported. US imaging: recovery of renal circulation was reported. Treatment was continued: methylprednisolone (16 mg/dg), methotroxate (12.5 mg/dg), folate acid (1 mg/day), brilinta (180 mg/day), nifedipine (20 mg/day). The patient was discharged on March 14, 2013; satisfactory health status was reported.

Conclusion: This case was associated with affection of abdominal aorta branches (renal arteries, celiac trunk, and superior mesenteric artery); thoracic and abdominal aortas were not involved. Latent disease progressed to manifestation phase after the development of arterial stenosis; development of the hypertension attack required emergency surgical intervention (stenting and angioplastics). Disease outcome was good.

Disclosure of interest: None declared.

P159
The late atlantoaxial subluxation in a patient with juvenile idiopathic arthritis
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Pediatric Rheumatology 2014, 12(Suppl 1):P159

Introduction: Atlantoaxial instability has been described as a manifestation of anklyosing spondylitis (juvenile and adult onset), reactive arthritis, juvenile idiopathic arthritis, and rheumatoid arthritis; however, it has rarely been reported as an early manifestation of these disorders (1). Instability of the atlantoaxial joint may lead to impingement on the cord and brainstem. There may also be cephalad encroachment of the odontoid into the foramen magnum. Locke and collaborators studied the atlanto-odontoid distance in 200 normal children aged 3 to 15 years, but the age and sex were not significant factors (2-4).

Objectives: To increase awareness of the condition in the hope that earlier recognition of this disease may prevent further serious injury.

Methods: We report the case of a 52-year-old woman who was diagnosed with JIA due to juvenile onset (at 16 years old), polyarthritus and a positive rheumatoind factor; the disease was persistent as active disease in adulthood.

Results: Our patient experienced persistent and worsening occipitocervical pain and signs of myelopathy after 36 years of disease and after one months of tumor necrosis factor a blockade. The atlantoaxial instability was appeared sudden in the night during sleep; she had woke up with dispnnea and she had fell on his bed. She was intubated and the diagnosis was established after tomography, in which we had noticed along cervical spine abnormalities like superior subluxation, odontoid fracture with cord compression, bone erosion and pannus formation. She was treated surgically with a C1-2 posterior instrumented fusion with a good evolution.

Conclusion: The atlantoaxial subluxation is a potential fatal complication and could be present even after many years of evolution.

Disclosure of interest: None declared.

P160
Musculoskeletal anomalies in a national cohort of children and adolescents with trisomy 21
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Pediatric Rheumatology 2014, 12(Suppl 1):P160

Introduction: Musculoskeletal complications of Down syndrome are common. Joint laxity, which may be associated with delayed ambulation, is almost universal. The combination of this ligamentous laxity and low muscle tone contribute to an increased risk of a number of musculoskeletal disorders in children with Down syndrome.
Objectives: 1. To describe the musculoskeletal anomalies observed in a National cohort of children with tisomy 21.
2. To calculate the average age children with Down syndrome walked unaided in our cohort.
3. To determine if in particular, musculoskeletal disorders in Down syndrome pose a greater problem for teenagers than children.

Methods: Over a 6-month period we performed a musculoskeletal examination on children and young adults with Down syndrome. We documented their Beighton hypermobility score, and any relevant orthopaedic history.

Results: 198 children and adolescents were examined, (56% male, 44% female). Median age was 7.2 years (0.6-18.6 years); 26% were adolescents (i.e. age ≥ 12 years). The average Beighton score for adolescents was 2 (0-6), which was significantly lower than that recorded for children, 4 (0-9) (p=0.001). There was no significant difference in the number of orthopedic conditions observed in children (10%) and adolescents (16%). They included scoliosis, patella instability, hip dislocation and C-spine anomalies. Pes planus was seen in 67% of children and 80% of adolescents with Down syndrome. However, only 42% of these children and 51% of the adolescents wore orthotics. The median age our cohort walked was 28 months (12-84 months). This is comparable to the literature that reports children with Down syndrome walk at 23 months (range 13-48), compared with 12 months (range 9-17) for the general paediatric population.

Conclusion: - Pes planus is common in children with Down syndrome, therefore early consideration of orthotics and life-long appropriate supportive footwear is advised.
- Significantly delayed ambulation is noted in children with Down syndrome. Early multi-disciplinary intervention is important to ensure these children obtain their full potential with regards to acquisition of walking unaided.
- Children with Down syndrome are at increased risk of a number of potentially debilitating orthopaedic conditions in addition to C-spine instability.
- Hypermobility becomes a less prominent musculoskeletal feature in the adolescent with Down syndrome.

Disclosure of interest: None declared.

P161 Phenotypes of juvenile idiopathic arthritis
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Pediatric Rheumatology 2014, 12(Suppl 1):P161

Introduction: The term “phenotype” comes from the Greek word “phaino” - to show. It is a mix of characteristics and properties of the body, formed in the process of individual development. In medicine phenotype has traditionally been viewed as the result of the interaction of the genotype (genetic characteristics of the organism to the conditions of external environment). Different authors in the allocation of individual phenotypes describe clinical and morphological characteristics of the disease, the most significant triggers, the presence of the leading link of the pathogenesis of the disease, as well as a unique response to treatment.

Objectives: The aim of our study was to learn structural (polymorphism C3435T MDR1 gene). Amplification was performed on the device “Cycler” (BioRad, USA) by standard scheme. Determination of cytokines (IL1, IL6, TNF-alpha) in the serum of patients with JIA was conducted by the method of solid-phase enzyme immunoassay. Determining the concentration of methotrexate in the blood serum were conducted on the analyzer TDxFLx firm Abbott method fluorescently-polarization immunoassay.

Results: For MDR1-dependent phenotype characterized by a higher activity of the disease, high levels TNFα and IL6. This phenotype is more common in patients with genotype CT and CC of polymorphism C3435T MDR1 gene, have higher relative amount of lymphocytes expressing P-glycoprotein as to stimulate IL2 and after; low MTX concentration in the serum. MDR1-independent phenotype characterized by lower activity of the disease, low content TNFα and IL6 in the serum, the most common genotype TT polymorphism C3435T MDR1 gene. Characterized by a relatively low number of lymphocytes expressing P-glycoprotein as to stimulate IL2 and after, and higher values MTX concentration in the serum.

Conclusion: After analyzing the obtained results we can assume that the study of the MDR1 gene polymorphism is necessary to assess the impact of different mechanisms on the concentration of methotrexate in patients with JIA, provides the ability to simulate dose methotrexate depending on the response to therapy. So, in patients with MDR-dependent phenotype can be considered earlier appointment of genetically engineered biological agents.

The selection of phenotypes diseases can afford to individualize the therapy to achieve better control of the disease.

Disclosure of interest: None declared.

P162 Management and prognosis of juvenile arthritis on the model of molecular genetic testing of gene p53
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Pediatric Rheumatology 2014, 12(Suppl 1):P162

Introduction: Juvenile idiopathic arthritis (JIA) is a multifactor chronic inflammatory joints disease that is characterized by long progressive course leading to development of contractures and loss of joint’s function. Currently, there are only several laboratory and radiological predictors of unfavorable prognosis of JIA. In recent years, scientists studied the molecular basis of the development and maintenance of chronic inflammation in the joint. Reduced sensitivity of cells to apoptosis is one the possible mechanisms contribution to progressive inflammation in synovial membrane. Polymorphisms Arg2Pro 4 exon, ins/del 16bp intron 3 and G13964C intron 6 gene P53 may change expression gene P53 and functional activity this protein, main factor of intrinsic apoptosis pathway (P.Dumont et al 2003; A.Sallivan et al, A.ghosh et al 2004).

Objectives: Identify predicting factors of course and outcome of JIA in children by based on comprehensive analysis of the clinical and instrumental, laboratory and molecular genetic tests.

Methods: Clinical, serological, x-ray manifestations, ultrasound and MRI data were analyzed in 126 children with JIA. Three polymorphisms gene P53 were detected by PCR-RFLP. 60 healthy children without family history of any autoimmunne disease were controls.

Results: We haven’t revealed significant differences distribution genotypes of Arg2Pro ex4, ins/del16bp intr3 and G13964C intr6 gene P53 between children with JIA and controls. But girls with oligo- and polyarthritis with genotypes containing three or more minor polymorphic variant 72Pro, ins16bp, 13964C gene P53 in any combination were with more severe variant articular lesion. By means of ROC-curve analysis and regression methods we assessed the contribution of molecular genetic, clinical, instrumental and laboratory factors on the disease with a view to determine the prognostic significance of these factors. The presence of erosions of the joints and carrier of genotypes containing allele 72Pro gene P53 were found in girls with JIA like highly information signs of prognosis “active” arthritis and the presence of erosions and debut JIA under the age of 3 years old - for boys. Also two signs were obtained for predicting remission in girls with JIA it’s early treatment by DMARS and carrier of homogenous genotype containing allele Arg22 gene P53.

Conclusion: In order to predict the nature of the disease and to identify children with risk group of the worst course of JIA is possible to use molecular genetic testing of gene P53 in combination with the study of clinical, instrumental and laboratory data.

Disclosure of interest: None declared.
P163
Muskoskeletal manifestations of mild form of mucopolysaccharidosis Iva - a clinical case
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Introduction: Mucopolysaccharidosis IVA (MPS IVA) is a rare inherited metabolic disorder caused by galactosamine-6-sulfate sulfatase (GALNS) enzyme deficiency that leads to progressive lysosomal accumulation of glycosaminoglycans (GAGs). MPS IVA has a variable age of onset and variable severity. Clinical presentation is heterogeneous, and some cases are only mildly affected. Key clinical features include short stature, skeletal dysplasia, dental anomalies, and corneal clouding. It is the milder forms of MPS that are often diagnosed late or misdiagnosed as an inflammatory joint disease.

Objectives: To describe a clinical case of muskoskeletal involvement in a patient with MPS IVA and to raise awareness for the timely diagnosis.

Methods: Case report.

Results: We present a case of a 12-year old boy with a 2-year history of hip and lower back pain, morning stiffness and disordered gait. A CT scan was performed prior to admission – it revealed changes in the femoral heads as a result of severe narrowing of the epiphyseal region, shallow acetabulum and femoral neck shortening. On admission the patient had hip pain and limited hip internal and external rotation, as well as lower back pain that worsens when bending, scoliosis, knee and ankle pain, inability to squat, abnormal gait. The boy had normal stature. Due to X-ray changes compatible with coxa plana, investigations to rule out MPS were made. The patient did not have corneal clouding. A thoracic and lumbar spine X-ray was performed – the observed changes were suggestive of MPS.

Urine and blood specimens were referred to the National Genetic Laboratory. The patient was found to have elevated GAG levels in his urine. Subsequent enzyme analysis revealed reduced GALNS enzyme activity, and the diagnosis of MPS IVA was made.

Conclusion: The boy was referred to the rheumatologist due to hip and lower back pain. The diagnosis of the classical forms of MPS is relatively easy due to the presence of typical clinical features. Diagnostic delays occur frequently in patients with mild forms of MPS which has an impact on the institution of appropriate therapy as early as possible.

Disclosure of interest: None declared.

P164
Total body MRI, a guide to diagnosis in patients with osteo-articular pain and inflammation
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Pediatric Rheumatology 2014, 12(Suppl 1):P164

Introduction: CRMO is an autoinflammatory bone disorder, characterized by aseptic multifocal osteitis. CRMO is classically used in measuring the extent and activity of the bone lesions and possible soft tissue involvement. Additionally, MRI may help to exclude other causes of osteoarticular inflammation.

Objectives: To demonstrate the usefulness of whole body MRI in the differential diagnosis of recurrent bone pain with inflammation in children.

Methods: Retrospective study of pediatric cases with bone pain and inflammation. Comprehensive imaging study including whole body MRI.

Results: Two patients were referred to our pediatric rheumatology outpatient clinic with the presumed diagnosis of CRMO. Since several months, they experienced episodes of articular pain and joint swelling (patient 1) and recurrent back pain and fatigue (patient 2). In the first patient initial blood evaluation showed mildly increased inflammatory parameters (CRP 75 mg/L) with a mild microcytic anemia (Hb 11 g/dL) and thrombocytosis (557x10^9/μL) with a normal leukocyte count. Conventional X-ray showed no abnormalities. MRI of both ankles confirmed arthritis/synovitis with presence of bone edema in ankle and tarsal bones. Initial treatment with NSAIDs was successful. In patient 2 additional investigations showed also increased inflammatory parameters (CRP 136 mg/L) with a mild anemia, slightly increased thrombocytosis and normal leukocyte count. Initial MRI of the spine showed mildly intense signaling of different vertebræ on STIR images. Bone scintigraphy demonstrated multifocal hypercapetration at the right skull, coracoid bone and multiple vertebræ. Additional bone marrow puncture was normal. NSAIDs were started systemically with success. In patient 1, pain returned. PET-CT showed increased metabolism at multiple skeleton foci. Additional bone marrow puncture in the posterior iliac crest returned normal with no arguments for a lymphoproliferative disorder. Persistent and worsening of clinical symptoms prompted us to perform whole body MRI which showed multiple, symmetric T1-hypointens signals in the peripheral bones (lower legs, underarms, feet, knees and elbows). Guided by these findings, a targeted bone marrow puncture was performed in the tibia which showed a malignant lymphoproliferative disorder, namely a pre-B ALL.

Conclusion: CRMO remains a diagnosis of exclusion in patients with osteoarticular pain and inflammation. In case of persistent and/or progressive pain, the physician should keep a high index of suspicion for malignancy. Whole body MRI can precisely define the characteristics and extent of the bone lesions (aspect and localization) as well as help in choosing the optimal localization for bone marrow puncture and/or bone biopsy.

Disclosure of interest: None declared.

P165
Value of ultrasound in detecting subclinical synovitis in polyarticular juvenile idiopathic arthritis (PJIA) in clinical remission (CR)
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Pediatric Rheumatology 2014, 12(Suppl 1):P165

Introduction: Ultrasonography (US) is a useful tool to determine synovial inflammatory involvement, anatomical damage, and "subclinical synovitis" in adult and juvenile pts with RA.

Objectives: To describe US findings in pJIA pts in CR.

Methods: Prospective study.

Inclusion criteria: pJIA patients (ILAR’01) with inactive disease (according to Wallace criteria). All patients underwent an ultrasound assessment within the week when clinical examination was done. The U.S. examiner was blinded to clinical findings and the US were carried out on previously affected joints. A Toshiba equipment, model Nemio, transducer 6-12 Hz was used. The following findings were considered pathological in U.S.: synovial hypertrophy, effusion and tenosynovitis (by gray scale) and positive Power Doppler (PD). Subclinical synovitis was defined as synovial hypertrophy and positive PD, in absence of clinical arthritis. Demographic, clinical- functional, laboratory and therapeutic variables were analyzed.

Results: A total of 19 patients were included, 15 females (79 %), median age 12.9 years (IQR 11.4-6.2), median disease duration 6.04 years (IQR 3.5-8.5) and median remission period 1.53 years (IQR 1.18-2.32). Sixteen out of 19 patients (84%) were in CR (17 MTX, 6 anti-TNF), and 3 in CR. The CHAQ score mean value was 0.02 (SD ± 0.06). Two hundred joints were systematically evaluated (clinical + US); structural alterations were found in 11/19 (58%) pts and in 14/200 (7%) joints (see table 1).

Conclusion: In our series, subclinical synovitis was not detected by U.S. The prevalence of abnormalities by grayscale was 58% pts (11/19), these findings suggest the possibility of persistent inflammation (in US exam) in spite of the absence of clinical finding related with “active disease”.

Disclosure of interest: None declared.
A 5-year-old boy presented with a 1 year history of right leg pain causing progressive pseudorheumatoid dysplasia. He received several courses of intravenous and oral antibiotics without improvement. NSAID regimen was ineffective too. Intravenous PPD is a non inflammatory skeletal disorder clinically simulating juvenile idiopathic arthritis. Treatment with corticosteroids (5 mg prednisolone/day), methotrexate (10mg/week), folic acid (5mg/week) and etanercept (25 mg/week sc). Upon examination the girl was unable to walk on her own. She had severe restriction of mobility of erarial spine, kyphoscoliosis, swelling and contractures of elbows, swelling of metacarpophalangeal and interphalangeal joints of both hands with limitation of extension of the fingers and severe restriction of mobility of coxofemoral joints, wrists and ankles. No active arthritis was detected. The girl had normal facial appearance and intelligence.

Results: Erythrocyte sedimentation rate, C reactive protein, rheumatoid factors and antinuclear antibodies were normal. X-rays of the hands showed widening of the metacarpal and phalangeal epiphyses and loss of joint space. X-rays of the hips showed degenerative changes with almost complete destruction of the joints. Radiographs of the spine revealed flattening of thoracic and lumbar vertebrae (platyspondylia). No soft tissue swelling or erosions could be seen. Peripheral computed tomography revealed extremely reduced trabecular volumetric density, cortical volumetric density and derived bone strength. The clinical and radiological findings suggested that our patient was suffering from PPD, a disease often misdiagnosed as Juvenile Arthritis. Genetic testing is currently under way.

Conclusion: PPD is a non inflammatory skeletal disorder clinically simulating early stages of JIA. Non-inflammatory joint involvement with characteristic radiological findings (ie enlarged epiphyses, and platyspondylia) should raise suspicion for this diagnosis. Early recognition of PPD could spare children of unnecessary treatment and lead to early initiation of appropriate rehabilitation therapy.

Disclosure of interest: None declared.
**P168**

**Chronic active EBV infection mimicking periodic fever syndromes: a new challenge for the paediatrician**

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**Pediatric Rheumatology** 2014, 12(Suppl 1):P168

**Introduction:** Chronic active EBV (CAEBV) infection is a rare condition associated with an abnormal activation of EBV and therefore to a chronic, potentially lifethreatening lymphoproliferation. Few cases of this condition have been described in the Asian population (with a prevalence of expansion of T and NK lymphocytes) and in North America (with a prevalence of expansion of B cells). This condition presents a poor prognosis: most of the patients not treated with bone marrow transplantation die for lymphatic malignancies.

**Objectives:** To describe the clinical course of two patients with CAEBV, initially misdiagnosed and treated as periodic fever syndromes.

**Methods:** We describe the clinical course of two patients presenting with a condition of periodic fever due to the chronic activation of EBV virus.

**Results:** A boy of consanguineous parents at the age of 15 months presented, in complete wellbeing, a febrile episode associated to tonsillitis with exudates, lateral cervical lymphadenopathy and hepatosplenomegaly; the blood test revealed an infectious mononucleosis. The clinical course of the disease was regular. In the following months the child presented recurrent episodes of high fever with exudative tonsillitis, adenitis, splenomegaly and sweating, lasting 3-5 days and treated with NSAIDS or antibiotics. The blood examinations revealed neurofilip leukocytosis and elevation of acute phase reactants. An autofluorescent condition with periodic fever was suspected and therefore on-demand steroidal treatment was suggested; this therapeutic approach was only partially effective. In the following months the boy continued to present periodic fever, occasionally associated to respiratory infections requiring antibiotics, and recurrent episodes of cholestasis. Several destructive dental caries were found as well as hyper sensibility to mosquitoes bite. In light of the persistence of the symptoms, monogenic periodic fevers were ruled out and immunologic test were performed: the level of plasmatic immunoglobulins was reduced and the lymphocytic count revealed an increase of CD20+ cells; the EBV PCR revealed 25000 copies for 100000 leucocytes with prevalence of infection in the B cells.

A second non-related patient of non-consanguineous parents, at the age of four years started to present recurrent episodes of high-grade fever with pharyngitis, oral atosis and abdominal pain with normal or slightly increased inflammatory markers. The genetic test for periodic fever revealed the presence of the R20Q variant in homoygenosis in the MEFV gene; the diagnosis of FMF was point out and treatment with colchicine was started, without a clear improvement of the clinical picture. Due to an increase of the transaminase and reduction of the platelets’ count, a bone marrow aspiration was performed, negative for malignancies. Several destructive dental caries were found requiring the avulsion of 11 teeth. Immunologic tests were then performed: immunoglobulins were normal, while the lymphocyte populations’ count revealed a relevant increase of the NK cells, with reduction of the other populations. Virologic investigations revealed a high replication of EBV virus (600000 copies for 100000 monocytes) with a prevalence of infection of NK cells.

**Conclusion:** Chronic active EBV infection is a rare condition, rarely individuated in the childhood. However this disease has to be ruled out in paediatric patients with periodic fever syndromes, especially in case of presence of unusual symptoms.

**Disclosure of interest:** None declared.

**P170**

**Clinical significance of hyper-iga in a pediatric laboratory series**

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**Pediatric Rheumatology** 2014, 12(Suppl 1):P170

**Introduction:** Very high levels of one or more classes of immunoglobulins can be found in children with various clinical conditions. Diagnostic protocols have been developed for defined forms of IgG, IgM or IgE hyperimmunoglobulinemia, which could be the expression of both chronic inflammatory disease and primary immunodeficiency syndromes. In contrast, except for well described conditions such as IgA nephropathy and Henoch Schonlein Purpura, much less is known about hyper-IgA.

**Objectives:** We analyzed and discussed the diagnostic significance of very-high IgA levels in the clinical practice of a tertiary care children hospital.

**Methods:** We collected all IgA determinations performed on children aged less than 16 years at the laboratories of Immunopathology of the Institute for Maternal and Child Health, IRCCS Burlo Garofolo, from 2009 to 2013. IgA values greater than three standard deviations above the mean, based on the local reference values for three age groups, were considered as ‘hyper-IgA’ (0 – 12 months, IgA > 113 mg/dl; 1 – 3 years, IgA > 225 mg/dl; 3-16 years, IgA > 368 mg/dl). For subjects with repeated hyper-IgA measures on different determinations, only the first value was recorded. To estimate the burden of diseases associated with hyper-IgA, a control age-matched group of 200 subjects with normal IgA values was randomly selected from the same laboratory series. Physicians who cared for each patient were asked to fill out a questionnaire regarding the clinical diagnosis and the interpretation of increased values of IgA. In addition, the levels of IgG and IgM greater than 2 standard deviations above the mean were recorded as well, where available. Subjects whose clinical records were not available were excluded from the analysis.

**Results:** A total of 12650 measurements of serum IgA were performed during the period of the study on 6364 subjects. Ninety-one subjects...
Juvenile Idiopathic Arthritis (JIA) is one of the most common chronic pediatric rheumatic diseases (PRD). As is the case for many PRD’s, evidence-based guidelines are sparse and management is based to a great extent on physician’s experience. Moreover, there are differences between nations regarding availability and financing of biological therapies. Consequently, treatment regimens differ throughout Europe. In 2012, a European initiative called SHARE (Single Hub and Access point for pediatric Rheumatology in Europe) was launched to optimize and disseminate diagnostic and management regimens in Europe for children and young adults with rheumatic diseases.

Objectives: To provide evidence based recommendations for diagnosis and treatment of JIA.

Methods: Evidence based recommendations were developed using the European League Against Rheumatism (EULAR) standard operating procedure [1]. An expert committee was instituted, consisting of pediatric rheumatologists from across Europe with expertise in JIA. The expert committee defined search terms for the systematic literature review. Two independent experts scored articles for validity and level of evidence. Recommendations derived from the literature were evaluated by an online survey. Those with less than 80% agreement during the online survey were reformulated. Subsequently, all recommendations were discussed by the experts at a consensus meeting using the nominal group technique [2]. Recommendations were accepted if more than 80% agreement was reached.

Results: The literature search yielded 4723 articles, of which 174 were considered relevant. The included articles were scored for validity and level of evidence. Recommendations were formulated based on the valid papers and were discussed and adjusted where needed during the consensus meeting. In total, 10 recommendations for diagnosis and 31 for treatment were accepted with more than 80% agreement. Topics covered for diagnosis and for treatment are shown in Table 1.

Conclusion: The SHARE initiative provides recommendations for diagnosis and treatment of JIA and thereby facilitates improvement and uniformity of care in this difficult to treat condition. Throughout Europe, the different phases of the project, best practices identified from literature will be completed with the ‘experts opinion’ in order to formulate diagnostic and management guidelines as best practices for care of JIA patients throughout Europe.

Disclosure of interest: S. Vastert Consultant for: Novartis, V. Boom: None Declared, A. Ravelli: None Declared, A. Martini: None Declared, H. Foster: None Declared, N. Wulffraat Grant / Research Support from: Abbvie, GSK, Roche, Consultant for: Novartis, Genzyme, Roche, Pfizer.

Table 1(abstract P171)

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<th>Juvenile idiopathic arthritis</th>
<th>Diagnosis</th>
<th>Treatment</th>
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<tr>
<td>The value of MRI in the diagnosis of arthritis</td>
<td>Steroids (locally and systemically administered)</td>
<td></td>
</tr>
<tr>
<td>The value of ultrasound in the diagnosis of arthritis</td>
<td>DMARDs</td>
<td></td>
</tr>
<tr>
<td>Biomarkers for diagnosis of JIA</td>
<td>Biologicals</td>
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<tr>
<td>Diagnosis of complications</td>
<td>Treatment of complications</td>
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</tbody>
</table>

References

**P172**

**Introduction:** Ultrasound (US) is a powerful tool for the assessment of joint disease in children with juvenile idiopathic arthritis (JIA) and has been shown to be more accurate than clinical examination in detecting synovitis. Parent’s proxy-report of joint involvement is potentially useful to obtain information on parent’s perception of the burden of child’s arthritis and may serve as surrogate for physician’s arcutaneous examination. However, it is unclear whether parents are reliable reporters of their children’s disease.

**Objectives:** To evaluate the level of agreement between parents’ proxy-report of joint involvement and US assessment of joint synovitis in children with JIA.

**Methods:** Before the study visit, parents of children with JIA were asked to complete the Juvenile Arthritis Multidimensional Assessment Report (JAMAR), which includes a standardized assessment of the presence of swelling or pain in 9 joints or joint groups, and several other parent-centered JIA outcome measures. At study visit, a pediatric rheumatologist, who was unaware of parent’s reports, performed a formal joint assessment and scored the presence or absence of swelling and tenderness/pain on motion in the same joints assessed by the parent. After the visit, a pediatric radiologist with more than 5 years of experience in US assessment in JIA evaluated independently the presence of synovial hypertrophy/effusion (gray scale US - GSUS) and Power Doppler (PD) inmetacarpophalangeal and interphalangeal joints, knees and ankles, and quantified each US feature on a 0-3 semi-quantitative scale. Agreement between parent, rheumatologist, and ultrasonographer joint assessment was computed by the Spearman’s kappa and was categorized as follows: 0.40-poor; 0.41-0.60-moderate; 0.61-0.80-substantial; >0.80 excellent.

**Results:** The JAMAR was completed by parents of 10 unselected patients, 8 with persistent oligoarthritis, 1 with extended oligoarthritis and 1 with rheumatoid factor-negative polyarthritis, aged 22 months to 8 years. The median (range) of JADAS71 in the 10 patients was 10 (0-19).

Table 1 shows the k values for agreement in joint assessment between parents, physician and ultrasonographer evaluation.

**Conclusion:** Our results show moderate-to-substantial agreement between parents’ proxy report of joint disease and US assessment. Concordance with US was similar for parents and physicians. This finding suggests that parents are reliable reporters of the extension and severity of their children’s arthritis. Overall, concordance was greater for PDUS than for GSUS and was lower for the ankle than for the other joints.

Disclosure of interest: None declared.

Disclosure of interest: None declared.

References

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Disclosure of interest: None declared.
A database at the study center including 785 patients who had Juvenile Idiopathic Arthritis (JIA) is the most chronic disease, requiring regular monitoring. The physician confirmed a morning stiffness lasting ≤ 15 minutes. However, it is still unknown whether the disease status of children with ID who have or do not have morning stiffness is comparable.

**Table 1 (abstract P172)**

<table>
<thead>
<tr>
<th>Joint</th>
<th>GSUS vs parent</th>
<th>PDUS vs parent</th>
<th>GSUS vs physician swelling</th>
<th>PDUS vs physician swelling</th>
<th>GSUS vs physician pain/LOM</th>
<th>PDUS vs physician pain/LOM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hand</td>
<td>0.62</td>
<td>-</td>
<td>0.62</td>
<td>-</td>
<td>0.62</td>
<td>-</td>
</tr>
<tr>
<td>Knee</td>
<td>0.70</td>
<td>0.67</td>
<td>0.62</td>
<td>0.77</td>
<td>0.62</td>
<td>0.77</td>
</tr>
<tr>
<td>Ankle</td>
<td>0.47</td>
<td>0.62</td>
<td>0.57</td>
<td>0.69</td>
<td>0.47</td>
<td>0.62</td>
</tr>
</tbody>
</table>

Not assessed because PDUS score = 0.

**P173**

Juvenile idiopathic arthritis: cross-sectional study of incidence and prevalence observed in a tertiary center of Spain

Marta Medrano SanIldefonso$^1$, Almudena Román Pascual$^{1,2}$

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**Introduction:** Juvenile Idiopathic Arthritis (JIA) is the most chronic musculoskeletal disease of pediatric population. Its incidence and prevalence vary considerably through the world. The Spanish Society of Rheumatology has estimated a incidence and prevalence of 8.22/100.000 and 0.7-4.0/100.000 respectively.

**Objectives:** Estimate the incidence and prevalence of juvenile idiopathic arthritis (JIA) in a paediatric tertiary care centre of Spain.

**Methods:** A 15-years (1997-2012), prospective, population-based study was then carried out to determine the incidence of JIA. Prospective and retrospective data retrieval was performed to calculate prevalence. The International League of Associations for Rheumatology (ILAR, Edmonton revision) classification criteria were applied. Data were compared by Chi-square, student t or wilcoxon test. Significance was set at 5%. Statistical analysis was performed with SPSS version 15.0 software.

**Results:** We identified 132 cases of JIA according to ILAR criteria: 81 girls (61.4%) and 51 boys (38.6%). Over the study period, 20 new cases of JIA were diagnosed in Zaragoza. The mean annual incidence was 14.8/100.000 children aged less than 16 years. In Aragón 23 new cases of JIA were diagnosed so the mean annual incidence was 14.8/100.000 and prevalence was 34.6/100.000 children aged less than 16 years. The mean age was 7.54 years (95% CI: 6.82-8.25). The most frequent form of onset was persistent oligoarticular arthritis, followed by enthesitis-related arthritis, psoriatic arthritis, rheumatoid factor negative polyarticular arthritis, undifferentiated arthritis, systemic disease and rheumatoid factor positive polyarticular arthritis.

In boys the most frequent category was arthritis - enthesitis (n = 28, 54.9 %) and in girls was oligoarticular JIA (n = 55, 67.9 %). The average age at which the arthritis was diagnosed was significantly earlier in the group of patients who of oligoarticular disease (6.4 years) than patients who polyarticular seropositive disease (10.74 years).

**Conclusion:** Incidence and prevalence rates are similar to those reported for several countries of Europe. To avoid underestimation of incidence and prevalence, epidemiological studies of JIA should be population-based rather than referral center-based. Further descriptive studies of JCA in different well-defined geographic areas are important to make valid comparisons. Such comparisons could give clues to etiological factors, both genetic and environmental.

**Disclosure of interest:** None declared.

**P174**

Is it worth allowing the presence of morning stiffness in the definition of inactive disease in juvenile idiopathic arthritis?

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1. Pediatric Rheumatology, Istituto Giannina Gaslini, Genova, Italy; 2. Paediatrics, Istituto Giannina Gaslini, Genova, Italy

**Introduction:** Morning stiffness is a major symptom of juvenile idiopathic arthritis (JIA) and it is usually associated with active disease. However, it is common view that children with disease quiescence may have some degrees of residual morning stiffness. The 2004 preliminary criteria for inactive disease (ID) in JIA did not include the assessment of morning stiffness, whereas the 2011 revision of the criteria has allowed the presence of morning stiffness lasting ≤ 15 minutes. However, it is still unknown whether the disease status of children with ID who have or do not have morning stiffness is comparable.

**Objectives:** To compare the disease status of children with JIA who meet the 2011 revised criteria for ID and have or do not have a morning stiffness lasting ≤ 15 minutes.

**Methods:** A database at the study center including 785 patients who had undergone a total of 2957 visits, which included a parent report of the presence and duration of morning stiffness, was analyzed to identify all visits in which patients met the criteria for ID. In each visit, the duration of morning stiffness was categorized as follows: ≤ 15 min, 15-30 min, 30-60 min, 1-2 hr, >2 hr. Clinical assessments included demographic features, and parent-reported outcomes. In case a patient met the ID criteria in more than 1 visit, only the first visit was retained.

**Results:** A total of 460 visits in which the patient met the criteria for ID were evaluated. Absence of morning stiffness was reported in 390 (84.8%) visits, whereas in 70 visits (15.2%) there was morning stiffness. Among the visits with morning stiffness, in 41 (8.9%) duration was ≤15 min, and in 29 (6.3%) duration was >15 min. Table 1 shows the comparison of disease duration and parent-reported outcomes between patients with absence or presence of morning stiffness.

**Conclusion:** Among patients who met the 2011 criteria for ID, those with morning stiffness ≤15 min had worse parent-reported outcomes than those without morning stiffness. This finding suggests that parents may not perceive their child’s disease state as true remission when lower degrees of morning stiffness are present. Notably, a sizeable proportion (6.3%) of children meeting the 2004 ID criteria had morning stiffness lasting >15 min. The change of the criterion “Duration of morning stiffness of ≤ 15 minutes” to “Absence of morning stiffness” in the definition for ID should be considered.

**Disclosure of interest:** None declared.

**P175**

Patient-reported joint count in juvenile idiopathic arthritis: the reliability of a mannequin format

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1. Paediatric Rheumatology, Erasmus MC Sophia Children’s Hospital, Rotterdam, Netherlands; 2. Rheumatology, Erasmus MC, Rotterdam, Netherlands

**Introduction:** Juvenile idiopathic arthritis (JIA) is a common chronic disease, requiring regular monitoring. Patient-reported outcomes can assist monitoring, may promote patient self-management and can be useful in epidemiological surveys.

**Objectives:** To evaluate reliability of a mannequin-format patient-reported joint-count in JIA, and to detect changes in a follow-up visit.

**Methods:** JIA patients aged 12-21 marked joints with active arthritis on a mannequin before their regular clinic visit. The physician performed a joint-count without having seen the patient’s assessment. For two subsequent clinic visits, agreement between the physician and patient-reported joint-counts was assessed using Intraclass Correlation Coefficient (ICC) and kappa statistics. The ability of the patient-reported joint-count to discriminate between active and inactive disease was evaluated using positive and negative predictive values. Sensitivity to change was estimated using Pearson’s rho and standardized response mean (SRM).

**Results:** 75 JIA patients were included. In general, patients had a low number of active joints (median 1 joint, indicated by the physician). ICC was moderate (0.61) and kappas ranged from 0.3-0.7. At the follow-up (n=33), kappas were similar; the ICC was 0.19. When a patient scored 0 joints, the physician confirmed this in 93-100%. When the patient marked ≥1 joints, the physician confirmed arthritis in 59-76%. Sensitivity to
change was moderate (Pearson’s rho: 0.44, p=0.001, SRM in worsening patients: 0.67).

Conclusion: Agreement between physician and patient on joint-counts was reasonable. Untrained patients tended to overestimate presence of arthritis when they marked active joints on a mannequin-format joint-count. When the patient indicated absence of arthritis, the physician usually confirmed this. The sensitivity to change was moderate for patients who worsened over time. The agreement did not improve at follow-up; future research should focus on the possibility of achieving this through training. For now, the patient-reported joint-count cannot fully replace the physicians’ joint-count in clinical practice; it may be used in epidemiological studies with caution.

Disclosure of interest: None declared.

P176

Nearly 20% of children are not correctly classified according to current ILAR classification in a PRINTO dataset of more than 12,000 juvenile idiopathic arthritis patients

Alessandro Consolaro, Francesca Bovis, Ekaterina Alexeeva, Violeta Panaviciene, Jordi Anton, Susan Nielsen, Gordana Susic, Maria Trachana, Troels Herlin, Nico Wulfraat, Pavla Dolezalova, Yosef Uziel, Nahid Shafaie, Ingrida Rumba-Rozenfelde, Valda Stanevicha, Nicolina Rupert, Daniel Lovell, Angelo Ravelli, Alberto Martin, PRINTO

Istituto Giannina Gaslini, Genoa, Italy

Pediatric Rheumatology 2014, 12(Suppl 1):P176

Introduction: Juvenile idiopathic arthritis (JIA) is an exclusion diagnosis that encompasses all forms of arthritis that begin before the age of 16 years, persist for more than 6 weeks, and are of unknown origin. In the ILAR classification, this heterogeneous group of chronic arthritides has been categorized on clinical and laboratory grounds to try to identify homogeneous, mutually exclusive categories suitable for etiopathogenic studies. However, the ILAR classification is complex and includes several inclusion and exclusion criteria. As a result, the correct placement of a patient in a specific category is not simple.

Objectives: To assess the rate of inappropriate classification in a large dataset of JIA patients collected by PRINTO members.

Methods: Patients enrolled in the multinational study of the European Pediatric Rheumatology, treatment and Outcome of Childhood Arthritis (EPOCA study) and in the Pharmacovigilance in patients treated with biologics±methotrexate study (Pharmachild) were merged in a single database, after exclusion of overlapping patients. The reasons that led to a “provisional” ILAR classification (i.e. lack of fitting into an ILAR category despite ILAR category attribution by the attending physician) in the two datasets and the queries regarding classification raised to the investigators by the PRINTO staff were analyzed and grouped into major categories according to the inclusion or exclusion criterion involved.

Results: A total of 12,141 patients were included in the study. The Table shows, for each JIA subtype, the most frequent drawbacks leading to a provisional classification. Most problems were related to the lack of 2 determinations of rheumatoid factor (RF) at least 3 months apart, the missing data in the indication of the presence or absence of psoriasis in the patient or in the presence or absence of a history of psoriasis in a first degree relative, the lack of assessment of RF or the inconsistency in indication of the presence of psoriasis in a first degree relative.

Disclosure of interest: None declared.

P177

Is there an evidence for the role of multidisciplinary team in the management of active juvenile idiopathic arthritis?

Sarka Fingerhutova*, Melanie Saifridova, Marketa Vanova, Pavla Dolezalova, Stanislava Sebikova, Marek Bohm, Dana Nemcova, Jitka Obralova

Paediatric Rheumatology Unit, General University Hospital in Prague, Prague, Czech Republic

Pediatric Rheumatology 2014, 12(Suppl 1):P177

Introduction: Complex management of JIA comprises of drug treatment, physiotherapy/occupational therapy, education and counselling. It should be provided by a trained multidisciplinary team of physicians and allied health professionals (AHP). In the traditional model, nursing and physiotherapy staff competencies are limited by the leading role of physicians and support of an equally important role of AHP is not automatically provided. A case for the importance of AHP needs to be presented to the healthcare providers and hospital managers. Objectives: The project has 2 parts: 1.To develop a comprehensive system of therapeutic interventions provided by AHP to paediatric patients with JIA (a subject to this report). 2.To prospectively test performance of these interventions in a cohort of JIA patients with active disease requiring new drug treatment.

Methods: Two trained rheumatology nurses and a physiotherapist contributed to the development of an AHP intervention plans as an add-on to the routine clinical care. Apart from the published literature the main resources included observations made by the team during their educational visits and the queries regarding classification raised to the investigators by the PRINTO staff were analyzed and grouped into major categories according to the inclusion or exclusion criterion involved.

Results: A total of 12,141 patients were included in the study. The Table shows, for each JIA subtype, the most frequent drawbacks leading to a provisional classification. Most problems were related to the lack of 2 determinations of rheumatoid factor (RF) at least 3 months apart, the
We conducted a retrospective analysis of a single-centre cohort. This included a review of the patient case notes, radiology and drug monitoring data of all children with JIA diagnosed between January 2013 and May 2014. From November 2013 to May 2014 total of 41 consecutive patients were eligible from which one family refused participation. Polyarticular JIA was present in 19 children, oligoarthritis in 14, psoriatic, enthesitis-related or systemic JIA in 7 patients. There were 24 patients with the new diagnosis of JIA, 16 had JIA relapse. Median age at study entry was 6.5 years (3.7-10.1), prior disease duration was 1.0 year (0.2-3.7). Median active joint count at study entry was 3 (1-6.5), JADAS 71 was 9 (6-18). From 21 patients in whom the first EU assessment was available, 10 received intraarticular triamcinolone-hexacetonide (in 2 cases with methotrexate, MTX), 6 received s.c. MTX and in 5 patients biologic therapy was added to MTX.

**Conclusion:** With this study we aim to accumulate better evidence on the importance of the trained nursing and physiotherapy staff in the multidisciplinary team caring for rheumatology patients in the country where such an approach is not fully supported by the existing system. Evaluation of the performance of interventions provided by AHP is a subject of ongoing study.

**Disclosure of interest:** S. Fingerhutova: None declared., M. Saifridova: None declared., M. Bohm: None declared., D. Nemcova: None declared., J. Obrsalova: None declared.

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### Table 1(abstract P176)

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<th>Reasons for provisional diagnosis</th>
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<tr>
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<td>Rheumatoid factor</td>
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<td>1365</td>
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<tr>
<td><strong>Oligoarthritis</strong></td>
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<tr>
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<tr>
<td><strong>Psoriatic arthritis</strong></td>
<td>433</td>
</tr>
<tr>
<td><strong>Enthesitis related arthritis</strong></td>
<td>1323</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>12141</td>
</tr>
</tbody>
</table>

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### P178

**Evaluation of an nhs juvenile idiopathic arthritis (JIA) treatment pathway compared to published international recommendations**  
Katherine L Green 1, Maninka Twilt1, Taunton Southwood2

1Paediatric Rheumatology, Birmingham Children’s Hospital, UK; 2Paediatric Rheumatology, NHS, Birmingham, UK  
Pediatric Rheumatology 2014, 12(Suppl 1):P178

**Introduction:** The ACR recommendations for the treatment of Juvenile Idiopathic Arthritis (ACR-JIA) were published in 2011 with the aim of providing an evidence-based therapeutic pathway for effective JIA treatment. Our aim was to determine the feasibility of applying ACR-JIA to a real-life paediatric JIA cohort and to evaluate the treatment pathway of those children.

**Methods:** We conducted a retrospective analysis of a single-centre paediatric JIA cohort. This included a review of the patient case notes, radiology and drug monitoring data of all children with JIA diagnosed with multi-joint (5 or more joint) disease in the 2 years since ACR-JIA were published. In total, 35 patients fulfilled ILAR criteria for the diagnosis of JIA since 2011: systemic arthritis (n=5), polyarthritis (n=25) and extended Oligoarthritis (n=5). Duration to Methotrexate and Etanercept treatments was calculated, and the frequency of drug monitoring noted.

**Results:** 25 females and 10 males (median age at onset 13, range 1.5-15 years) were included in the evaluation. Median age at disease onset for poly/extended oligoarthritis was 10 years (1.5-16), with a median of 12 joints (12-38) active at presentation, and for the systemic group median age at onset was 6 years (2-7), with a median number of 6 active joints (2-10). 3 polyarthritis patients were rheumatoid factor positive (0 extended oligoarthritis and 0 systemics). 22/30 patients with polyarthritis/extended oligoarthritis followed the ACR recommendations for treatment according to their disease severity, commencing methotrexate therapy within a median of 6 weeks (3-37) of diagnosis and etanercept (where relevant) within a median of 7 months (3-24) of diagnosis. 7 patients did not follow ACR-JIA guidelines due to experiencing excessive durations (for disease severity) between diagnosis and commencing methotrexate or etanercept treatment. One patient did not have sufficient regular drug monitoring tests. All patients with systemic arthritis followed the ACR-JIA recommendations for treatment and drug monitoring.

**Conclusion:** Overall, 27/35 patients followed the ACR-JIA recommendations. This evaluation highlights the difficulty of achieving rapid commencement of new JIA therapies and the challenging of regular drug monitoring.

**Disclosure of interest:** None declared.

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### P179

**Juvenile idiopathic arthritis: a single center Lebanese study**  
Rawane Dagher, Sami Assi  
Pediatric department, Notre Dame De Secours University Hospital, Byblos, Lebanon  
Pediatric Rheumatology 2014, 12(Suppl 1):P179

**Introduction:** Juvenile Idiopathic Arthritis (JIA) is the most frequent rheumatic disease in childhood. Many variations of JIA are described in different populations. Lebanon is a small middle-eastern country where Pediatric Rheumatology is still emerging as a subspecialty.

**Objectives:** To this day, the Lebanese experience concerning JIA is not published. Therefore, the aim of this study is to describe the disease characteristics through a single center series.

**Methods:** A retrospective chart review of children who consulted in Pediatric Rheumatology department of Notre Dame De Secours University Hospital between April 2010 and April 2014 was performed. Only patients who met the 2001 classification criteria of the ILAR (International League of Associations for Rheumatology) were included. Epidemiologic and clinical aspects of different types of JIA were studied.

**Results:** A total of 66 children were included. The overall sex ratio is 1:1. The average age at the onset of the disease is 5.2 years (range: 9 months - 14 years). The average age at diagnosis is 5.9 years. The average age at the first visit to the pediatric rheumatologist is 6.6 years. The distribution by types of JIA is as follows: systemic form 23%, persistent oligoarticular form 27%, extended oligoarticular form 4%, polyarticular form with negative Rheumatoid Factor (RF) 24%, enthesitis-related arthritis (ERA) 17%, undifferentiated arthritis 5%. Two sets of siblings are reported including one pair of monozygotic twins. ANA was positive in 15 patients (23%). Only 4 cases of urethritis were observed: 2 in ERA, 1 in persistent oligoarticular form and 1 in extended oligoarticular form. Osteoporosis with vertebral compaction was found in one patient of systemic JIA who had active disease for 4 years. A major growth delay is noted in another patient of systemic JIA who had active disease for more than 6 years.
In this series, diagnosis delay and late referral to the specialist are outlined. Late referral is linked to poor outcome. In comparison to published western data, we found a higher rate of male gender in JIA (50%). Gender distribution particularities are also found in some subtypes of the disease. Systemic and enthesitis related subtypes appear to be more prevalent than in JIA populations described in Europe and North America. Similarly to neighbouring countries, lower rates of ANA positivity and uveitis are noted.

Conclusion: To the best of our knowledge, this series is the first report on JIA in Lebanon. It shows a distinctive profile of JIA suggesting genetic and environmental roles in disease expression. A major challenge is encountered with late presentation to the pediatric rheumatologist. Larger prospective studies are needed to further elucidate the characteristics of JIA in Lebanon.

Disclosure of interest: None declared.

<table>
<thead>
<tr>
<th>JIA subtype</th>
<th>Disease severity</th>
<th>N=</th>
<th>Poor prognostic factors</th>
<th>RfH positive</th>
<th>Median duration to MTX</th>
<th>Median duration to etanercept</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic</td>
<td>Low</td>
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<td>0</td>
<td>0</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>N=5</td>
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<td>High</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polyarthritis &amp; extended oligoarthritis</td>
<td>Low</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>6 (3-37)</td>
<td>7 (3-24)</td>
</tr>
<tr>
<td>Polyarthritis &amp; extended oligoarthritis</td>
<td>N=30</td>
<td>Moderate</td>
<td>23</td>
<td>9</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>6</td>
<td>2</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Unknown</td>
<td>1</td>
<td>0</td>
<td>0</td>
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</table>

Results: 74 JIA patients (M/F 2.4:1), with a mean age of 12 years, were examined. The prevalence of TMJ involvement was 4-11%. The TMJ score required around three minutes to be used. The internal consistency of the tool was 0.78. Deleting the morphological items 'asymmetry' and mandibular retrognathism, with low agreement, the coefficient increased up to 0.85. For the history related items, the value ranged between 0.46 and 0.87; for the examination related items between 0.25 and 0.73. The kappa value for the total score, between the rheumatologist and the dentist, was 0.46. The tool seemed to correlate with JADAS, improving its value in indicating patients to refer to the specialist.

Conclusion: The TMJ score used in our study showed to be an easy tool, not time-consuming for the rheumatologist, to evaluate the TMJ in JIA patients. The internal consistency of the score was good. The low agreement between specialists highlights the need of adopting further measures, such as more specific training and attention on the examination of TMJ, in order to improve the skills of the rheumatologist in examining this joint. Our score does not aim in giving a validated tool, but it represents a practical instrument for the rheumatologist to support the diagnosis of TMJ arthropathy and the possible referral to a gnathologist.

Disclosure of interest: None declared.

**P180**

A three minute- screening tool for temporomandibular joint involvement in children with juvenile idiopathic arthritis

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Introduction: The temporomandibular joint (TMJ) is a possible localization of arthritis in patients with Juvenile Idiopathic Arthritis (JIA), with an estimated prevalence around 50%. Despite the decreasing involvement in the last years, maybe due to the current treatment strategies, TMJ remains one of the most clinically under recognized affected joints in JIA patients. The clinical examination of TMJ is often unreliable, even for experienced rheumatologists, leading to the need of more specific diagnostic tools.

Objectives: Aim of our study was to test a diagnostic score specific for TMJ, capable to shortly detect arthritis in the joint, as assessed by rheumatologist and dentist, the two specialists mainly involved in TMJ examination.

Methods: 78 consecutive patients (5-17 years of age), all affected by JIA, according to the ILAR classification, were selected in the outpatient clinic of our department. 76 gave informed consent and were examined between December 2013 and January 2014 (Table 1). Those with dental and facial disorders were excluded. Four rheumatologists were trained in TMJ examination by a dentist. On the day of consultation, the patient was first examined by the rheumatologist and then by the dentist, considered the gold standard examiner and blind to the findings of the rheumatologist. Both specialists were asked to use separately the score for the TMJ evaluation, composed by 11 items: five concerning patient history and six based on physical examination. Each item was scored as 1, when present, with a total score ranging from 0 (no TMJ involvement) to 11 (maximum severity of TMJ involvement). Juvenile Idiopathic Disease Activity Score (JADAS) was also calculated for each patient and correlated with the TMJ score. The internal consistency of the tool and agreement among specialists were determined through kappa statistics and pearson coefficient.

Results: 74 JIA patients (M/F 2.4:1), with a mean age of 12 years, were examined. The prevalence of TMJ involvement was 4-11%. The TMJ score required around three minutes to be used. The internal consistency of the tool was 0.78. Deleting the morphological items 'asymmetry' and mandibular retrognathism, with low agreement, the coefficient increased up to 0.85. For the history related items, the value ranged between 0.46 and 0.87; for the examination related items between 0.25 and 0.73. The kappa value for the total score, between the rheumatologist and the dentist, was 0.46. The tool seemed to correlate with JADAS, improving its value in indicating patients to refer to the specialist.

Disclosure of interest: None declared.

**P181**

Clinical depiction, treatment and long term follow up characterization of a group of enthesitis related arthritis - juvenile idiopathic arthritis patients from a spanish pediatric tertiary hospital

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Introduction: Enthesitis related arthritis (ERA) is a subtype of Juvenile Idiopathic Arthritis (JIA) that affects children >6 years of age. It presents with enthesitis, uveitis, peripheral and axial arthritis. It’s one of the less frequent subtypes of JIA. Data is scarce involving follow up and outcomes.

Objectives: Describe a case series of JIA-ERA patients of a Spanish cohort in a tertiary pediatric hospital. Report response to oral (OR) and subcutaneous (SC) methotrexate (MTX) in insufficient/non-responders to NSAID/intra-articular steroid infiltrations in these patients. Relate the persistence of symptoms on follow-up and course of treatment.

Methods: Retrospective and observational. Inclusion criteria: Edmonton classification criteria for ERA-JIA. Variables: age, sex, HLA-B27, date and delay of diagnosis, onset of symptoms, classification, start/finish of date of OR MTX, start/finish date of MTX SC, date of start of biologic treatment (as a variable of MTX inefficacy). Articular activity: number of swollen joints (NSJ) and number of painful joints (NPJ). Prospective data will be collected starting January 2014 of all ERA-JIA patients visited in our Unit. Local ethics committee approval was acquired.
Results: 11 patients all of which were male (100%), mean age of 15.3 (SD 4.6), age of first symptom 11.2, (SD 2.4), age of diagnosis 11.6 years (SD 2.3), delay in diagnosis 4.7 months (SD 6.3), follow up 55.6 months (SD 42.2). 90% were HLA-B27 positive. The rest of the clinical data are summed up on table 1. Number of painful joints (NPJ) varied from 0-4, number of swollen joints (NSJ) between 0 and 8. 90.9% (10 patients) required MTX. Six received OR MTX (54.5%), 4 of these patients switched to SC MTX (66.7%) due to inefficacy. A total of 8 of 11 patients received SC MTX. The average dose of MTX was 14.6 mg/week (SD 3.9). Two (20%) patients continued MTX on transition to the adult rheumatology clinic. The average time on MTX was 13.1 months (SD 7.6). One patient suspended treatment with MTX because of digestive intolerance and another because of inefficacy. One patient (9%) started Etanercept because of partial response to both OR and SCMTX.

Conclusion: Patients had a mean age of 11 years at time of diagnosis, are male, HLA-B27 positive and have low joint level activity. The majority of patients that started OR MTX switched to SC MTX due to inefficacy or insufficient response, with a mean weekly dose of 15mg/weekSC MTX. The rate of side effects was low (<10%). Several patients required active treatment (DMARD/biologic) after 4 years of follow-up. Our findings should be taken with a grain of salt as this analysis is preliminary and we will be completing data from all of our JIA-ERA patients in coming months.

Disclosure of interest: None declared.

P182
Myeloid related proteins 8 and 14 (mrp 8/14) - potential biomarkers of disease activity of arthritis in children and with trisomy 21
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Pediatric Rheumatology 2014, 12(Suppl 1):P182

Introduction: JIA is an umbrella term used to describe a heterogeneous group of diseases. To date no specific markers exist in clinical practice to predict disease activity & outcome. MRP 8/14 are calcium-binding proteins secreted by infiltrating phagocytes in synovial inflammation. Studies have shown that serum (Se) concentrations correlate sensitively & specifically with synovial inflammation in JIA. It is believed that they are predictive biomarkers that can identify subclinical disease activity, patients at risk of relapse during times of clinically inactive disease, and patients more likely to respond to Rx with MTX. To date there have been no studies looking specifically at their use in DA. Research Q(s) - 1. Are MRP8/14 accurate markers of inflammation in DA? 2. Do MRP 8/14 levels in Se correlate to Synovial Fluid (SF)?

Objectives: Evaluate the use of CRP, ESR & MRP 8/14 as biomarkers of disease activity in DA & JIA.

Methods: Between May 2013-May 2014, new cases of JIA & DA attending the NCPR had blood drawn to measure their CRP, ESR & MRP 8/14 levels at dx. Corresponding AJC was documented. Paired SF samples were taken for analysis from children requiring steroid JIs as Rx for their arthritis. Se & SF MRP 8/14 were determined by sandwich ELISA.

Results: 32 children (20 JIA, 12 DA) had Se samples taken for CRP, ESR & MRP 8/14 levels at diagnosis. 14 of these children had paired SF samples taken. Table 1 highlights accuracy of each measurement as a marker of disease activity. In DA, a significant correlation was detected between AJC & both ESR & MRP 8/14 (SF). Combining results for the DA & JIA cohort, a significant positive correlation was noted between paired samples of MRP 8/14 in Se & SF.

Conclusion: MRI with contrast remains the gold standard for dx of disease activity in DA & JIA.

Disclosure of interest: None declared.

Table 1(abstract P182)

<table>
<thead>
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<th>Variable</th>
<th>Variable 1</th>
<th>Correlation</th>
<th>p value</th>
</tr>
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<tbody>
<tr>
<td>CRP</td>
<td>ESR</td>
<td>Positive</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>MRP 8/14 SF</td>
<td>MRP 8/14</td>
<td>Positive</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Table 1(abstract P181)

<table>
<thead>
<tr>
<th>Joint activity</th>
<th>NPJ at onset</th>
<th>NPJ at end of follow up</th>
<th>NSJ at onset</th>
<th>NSJ at end of follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average</td>
<td>1.86</td>
<td>2.82</td>
<td>0.13</td>
<td></td>
</tr>
<tr>
<td>Standard deviation</td>
<td>1.34</td>
<td>3.28</td>
<td>0.35</td>
<td></td>
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</tbody>
</table>
Noteworthy detection of statistically significant higher level TNFα in patients receiving biological therapy, mainly TNF inhibitors. Apparently, the continuing high level of TNF, despite the use of inhibitors, characterizes this group of patients, as the most severe.

In the group of patients not treated with biological therapy level TNFα was significantly lower than in the group of children treated with this type of therapy. The main biological drugs, which were given to children with JIA were either direct blockers TNFα (infliximab, etanercept) or affecting the synthesis of Pro-inflammatory cytokines (tocilizumab, adalimumab).

Conclusion: It was natural to assume that in a group of children receiving anticytokine drugs the level of TNF-alpha will be lower. However, in our study we have received significantly higher level of TNF-alpha, which indicates a more severe disease, and on the other hand possible resistance to selected for treatment of biological drugs in these patients.

Disclosure of interest: None declared.

P184
Multicenter retrospective study of biological tolerance in juvenile idiopathic arthritis (JIR-cohort)
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Pediatric Rheumatology 2014, 12(Suppl 1)P184

Introduction: Ten years after the introduction of biologics in children, we assess the tolerance of these therapies among patients with juvenile idiopathic arthritis (JIA) in pediatric rheumatology centers.

Objectives: Study the epidemiology of JIA in 10 European centers of pediatric rheumatology and describe adverse events (AEs) to biologics at short and medium term.

Methods: Multicenter retrospective observational study in JIA patients who have been treated with biologics, in the 10 following pediatric rheumatology centers: Basel, Zurich, Aarau, Lucerne, Vaud (Switzerland), Lyon, Paris, Clermont-Ferrand, Strasbourg (France) and Leuven (Belgium) between June 1999 and March 2014.

Results: 531 patients were included in the study. Most of them suffered from polyarticular JIA (PA) RF negative (21.4 %, n = 115). Other JIA subtypes were distributed as follow: arthritis with enthesitis 19.3% (n= 102), oligoarticular JIA (OA) persistent 17.4% (n= 92), systemic JIA 16.6% (n= 88), OA JIA extent 10.6% (n= 56), psoriatic arthritis and JIA PA RF positive 5.1% (n= 27) and other arthrits 4.3%. Ocular involvement was found in all subtypes of JIA except for polyarticular RF+, consisting of 105 patients of which 19.8% (n=20) with positivity for antinuclear antibodies. Familial history of autoimmunity was identified in more than a quarter of cases (n=146, 27.6 %). A macrophage activation syndrome (MAS) was found in 20 patients, restricted to the systemic JIA subset. Enentercept was the most common drug and accounted for 47.5% of all biologics in the cohort. Most of AEs were mild, one third of AEs were due to reversible reactions at the injection (such as rash, fever and pain). Infections represented one third of the AEs and were more frequently secondary to viral agents. Tocilizumab was more often involved in AEs with a frequency of 0.27 AE patients/year, followed by infliximab and canakinumab with 0.17 AE patients/year. No AE was seen with rituximab but this drug represented an overall exposition of 7.7 patients/year. Severe AEs were found in 19 patients (3.4%) including two cases of Hodgkin’s disease. The mean exposure duration to biologics at the first occurrence of AEs was 14.4 months. No deaths were reported.

Conclusion: This multicenter study shows an overall good tolerance of JIA patients to biologics. The main AE are represented by infectious agents and preventive strategies including vaccination should apply. Notably, 2 cases of malignancy, both Hodgkin disease, were identified in the cohort. The prospective follow-up of children treated with biologics, and international efforts, such as Pharmachild project, will improve the quality of data collection and the identification of possible predisposing factors for AE.

Disclosure of interest: None declared.

P185
The role of steroid injection in joints and tendon sheaths in JIA in the biologic era
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Pediatric Rheumatology 2014, 12(Suppl 1)P185

Introduction: Intraarticular injections are commonly used in children with JIA to induce prompt relief of symptoms of active synovitis, and obtain disease remission as sole therapy or in combination with systemic treatment. In the recent years, the wider use of musculoskeletal ultrasound allowed to detect more precisely the exact site of inflammation and showed to be a safe guide for injection procedures also in tendons sheaths and periaricular tissue.

Objectives: The aim of the study was to investigate the role of intraarticular steroid injections and injection of tendon sheaths in the management of children with JIA in a pediatric rheumatology tertiary care center in the recent years.

Methods: The charts of all the patients with JIA that underwent to steroid injection of joints and/or tendon sheaths from January 2012 to April 2014 in our center were reviewed. Demographic and clinical data at the time of the steroid injections were registered, including ongoing therapy and decision to start a new systemic treatment. In the follow-up visits, remission of synovitis in the injected sites was clinically defined as the absence of swelling and/or pain on motion/tenderness associated to limited joint restriction.

Results: From January 2012 to April 2014 we performed 181 steroid injection sessions in 145 JIA patients. 25 patients (17%) underwent to more than one session: 51 sessions were conducted under local anesthesia, while 130 under general sedation. In 65 sessions only one joint or tendon sheath was injected; 2 injections were performed in 51 sessions; 3 or more injections in the same session were conducted in 75 sessions. The total number of sites injected was 456, 71 of which (16%) were represented by tendon sheaths or cysts. After a median period of 4.9 months 79% of the sites injected were in clinical remission. Of the 21% of sites with persistent synovitis at the first follow-up visit, 50% achieved remission without adding new treatments after a median of 7 months from the procedure, while 25% achieved remission only after the introduction of new systemic treatments; the remaining 25% were not in complete remission at the last follow-up visit yet.

Conclusion: Intraarticular and tendon sheaths injections in our center have been extensively performed in the recent years for the treatment of synovitis in one or multiple joint areas in children with JIA. Further longitudinal studies including imaging definition of remission should be performed to investigate the long term efficacy of these therapeutic procedures.

Disclosure of interest: None declared.

P186
Clinical classification of JIA in Albania
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Pediatric Rheumatology 2014, 12(Suppl 1)P186

Introduction: Juvenile idiopathic arthritis (JIA) is a group of heterogeneous disorders with different disease manifestations among various populations.
In our country is the first study made for the clinical patterns AUI. In this paper presented AUI clinical patterns encountered in University Hospital Center “Mother Teresa” in Tirana for the period July 2012-March 2014.

**Objectives:** To identify clinical patterns of JIA in our country. Design of therapeutic strategies based on relevant clinical model.

**Methods:** Hospital records of patients with a diagnosis of chronic arthritis with onset at the age of 16 years or less were analyzed. The anti-nuclear factor (ANF) test was used in the diagnosis of systemic JIA. Diagnostic criteria were based on the international JIA classification.

**Results:** In total, 39 patients were included in the study. The most frequent types of chronic arthritis were oligoarticular JIA and juvenile idiopathic arthritis (JIA) with polyarticular involvement, which accounted for 77% of the cases. The average age at disease onset was 3.7 years (range: 0.7-17.5 years). The study revealed strong correlation of the serum hepcidin level with clinical and laboratory characteristics of arthritis and the level of CRP. Serum hepcidin concentration correlated with the inflammatory activity indices. We revealed correlation (p<0.02) of serum hepcidin concentration with the number of swollen joints (r=+0.60), the number of painful joints (r=+0.71), with ESR (r=+0.63), with the level of CRP (r=+0.87), with leukocyte (r=+0.89), platelet (r=+0.89) and neutrophil blood cell counts (r=+0.79). Rather strong correlation of serum levels of hepcidin and ferritin (r=+0.90), sTfR (r=+0.51), iron (r=-0.49) and TIBC (r=-0.50) as well as with MCV (r=-0.63) and with MCH (r=-0.62) was also revealed. MCH was found to be the most sensitive to the level of serum hepcidin parameter, much more sensitive than total hemoglobin concentration.

**Conclusion:** The study revealed strong correlation of the serum hepcidin level with both clinical and laboratory indicators of the inflammatory activity of arthritis, as well as with indicators of the iron metabolism. Our results support the idea that anemia in JIA-children is almost exclusively controlled by hepcidin and is caused by disturbance of iron metabolism with the development of iron-restricted erythropoiesis.

**Disclosure of interest:** None declared.

**P188**

**Treat to target: temporomandibular joint (TMJ) arthritis in children with juvenile idiopathic arthritis (JIA) – experience of Centro Hospitalar Do Porto**

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**Introduction:** TMJ arthritis occurs in up to 80% of children with JIA and it has been described in all JIA subtypes. TMJ arthritis can develop anytime during the course of JIA, even when patients are asymptomatic or on biologic therapy. As it can also occur in the absence of clinically evident arthritis outside the TMJ, a precocious evaluation by maxillofacial surgery is suggested.

**Objectives:** Evaluation of TMJ in JIA and presentation of adopted guidelines in Centro Hospitalar Do Porto.

**Methods:** Selection of three polyarticular JIA cases with TMJ involvement followed in pediatric rheumatology unit. The protocol establishes oral-maxillofacial observation and high-resolution ultrasound at clinical presentation of polyarticular JIA. The need of contrast-enhanced magnetic resonance imaging, the periodicity of clinical observations and the decision to perform intraarticular corticosteroids injections is based on the clinical repercussion of TMJ arthritis.

**Results:** Case 1: 15 year old girl, with polyarticular JIA diagnosed in 2012 and on etanercept during the past 14 months. The TMJ response to biologic therapy was minimal and maximal incisal opening (MIO) was 37mm.Intraarticular corticosteroid injection (triamcinolone hexacetonide -1ml; 20mg/ml) was performed and three months after arthroscopy, pain relief was achieved and the TMJ function was good.

Case 2: 11 year old girl, with psoriatic JIA diagnosed in 2008, on etanercept during the past 22 months and intolerant to methotrexate. She has micrognathia, malocclusion of the teeth with overbite (class 2) and a painful TMJ. Condylar flattening was observed in the last magnetic resonance imaging.

Case 3: 14 year old girl, with polyarticular JIA diagnosed in 2012 and on etanercept during the past 12 months. Facial asymmetry and sporadic pain when opening the mouth were present. TM joint dysfunction with limited left condylar excursion was confirmed in the last high-resolution ultrasound.

**Conclusions:** The TMJ involvement in JIA, presented in the cases, was responsible for the recent creation of a multidisciplinary protocol joining pediatric rheumatology and oral-maxillofacial surgery of Centro Hospitalar do Porto. The main goal is to guarantee a precocious TMJ examination, with early treatment when necessary, to avoid some deleterious consequences that develop even in the absence of symptoms.

**Disclosure of interest:** None declared.

**P189**

**Respir: a network dedicated to children and adolescents suffering from chronic rheumatic diseases in the ile-de-france region**

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**Introduction:** The present network was created in 2012 and is dedicated to children and adolescents sufferen from chronic rheumatic diseases in the ile-de-france region.
Introduction: Introduction: chronic rheumatic diseases affect around 2000 children in the Ile-de-France region. Most patients suffer from juvenile idiopathic arthritis (JIA) that leads to chronic pain, fatigue and structural damage responsible for short- and long-term disability. Several physicians and health professionals may be involved in the treatment and care of these patients. This multidisciplinary approach is particularly important in managing paediatric rheumatic diseases, since many symptoms are chronic and change in severity over time. The RESRIP (Réseau pour les Rhumatismes Inflammatoires Pédiatriques) network has been created to improve and personalize patient care coordination.

Objectives: Objectives: improvement of patients care in a non-hospital setting, develop 2 of therapeutic education at home in order to ameliorate treatment adherence; supporting the transition period from paediatric to adult health care; reduction of costs thanks to lower need for hospitalization and medical transportation.

Methods: Methods: any patient aged equal or less than 18 years suffering from chronic inflammatory diseases having given informed consent could be enrolled in the network. Patients needed to meet at least two of the following criteria: disease complexity (impact on: physical or psychological status, school attendance, growth and/or development; complexity of treatment); association of two or more diseases; necessity of at least 3 different health professionals; social difficulties; demand of support expressed by the patient or the parents; transition to adult health care; patients referred in a peripheral hospital. Physician network coordinator evaluates patient needs, establishes care process and weaves relationships between the different health professionals. A patient notebook helps this process. Health professionals enter into the network after signing the specific informed consent too. Patients and health professionals inclusions started in September 2013.

Results: Results: at present 46 patients (29F; 17M, median age 10.8 years, median disease duration 3.1 years) have been included. Principal diseases were: JIA (32 patients: polyarticular 14, oligoarticular 10, psoriatic arthritis 3, enthesitis-related arthritis 3, systemic 2); connective tissue diseases (6), auto-inflammatory diseases 4, idiopathic uveitis 2, other 2. Seventy-five health professionals have adhered to the network.

Conclusion: Conclusion: RESRIP is the first French network dedicated to children and adolescents with chronic rheumatic diseases, which might improve patient care coordination and treatment adherence.

Disclosure of interest: None declared.

P190

Factors associated with choice of first biologic among children with juvenile idiopathic arthritis: a combined analysis from two UK paediatric biologic registers

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Pediatric Rheumatology 2014, 12(Suppl 1)P190

Introduction: The management of juvenile idiopathic arthritis (JIA) has been revolutionised through biologics such as etanercept (ETN), approved in the UK in 2002. Since that time, the use of other biologics in children and young people (CYP) has expanded. ETN is most often the first choice biologic in the treatment of JIA; however there may be occasions where ETN is not the preferred choice, for reasons of efficacy or safety.

Objectives: The aim of this analysis was to describe the choice of first-line biologics in UK CYP with JIA and explore possible reasons behind this choice.

Methods: Both the British Society for Paediatric and Adolescent Rheumatology Etanercept Cohort Study (BSPAR-ETN), and the Biologics for Children with Rheumatic Diseases (BCRD) study, are ongoing prospective observational cohorts, collecting detailed information on CYP starting biologics for JIA. At start of therapy, demographic and disease information is collected. Patients registered from 01/01/2010 starting a first biologic were compared between therapies using descriptive statistics. CYP starting ETN c2010 were also included to analyse changes in ETN prescribing since initial approval.

Results: To 07/04/2014, 870 patients were recruited starting a first-line biologic (123 BCRD; 747 BSPAR-ETN (582;2010, 165;2010) (Table 1). From 2010, CYP with systemic JIA (sJIA) were almost exclusively prescribed anakinra or tocilizumab. Choice of anti-TNF therapy was largely driven by prevalence of uveitis. Compared to ETN patients pre-2010, CYP starting ETN from 2010 had shorter disease duration, less uveitis, less sJIA, and less corticosteroid use.

Conclusion: Although ETN remains the most common biologic prescribed for JIA, there has been a shift towards the use of alternative biologics, some unlicensed, largely driven by disease subtype and the presence of uveitis. This channelling of certain children towards specific therapies is important in terms of future comparative effectiveness studies and also as a guide to ongoing research priorities within rheumatology.

Disclosure of interest: None declared.

P191

Long-term impact of juvenile idiopathic arthritis in the greek adults’ psychosocial life

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Pediatric Rheumatology 2014, 12(Suppl 1)P191

Introduction: Juvenile idiopathic arthritis (JIA) seems to have a negative impact on patients’ life style mostly due to the disease chronicity. No relevant data have been published for Greek young adults so far.

Objectives: To capture the impact of disease burden in the psychosocial profile of adults with JIA, 17.2 years after disease onset.

Methods: A total of 96 (66 females) patients were enrolled. Psychosocial distress was assessed by the Greek version of the self-completed paper-based General Health Questionnaire (GHQ-28). A second questionnaire regarding marital status, education level and employment status was completed by all patients. Disease activity status at the last follow-up visit was assessed according to the Wallace criteria, while the level of disease activity by the Disease Activity Score-28 (DAS-28). The patient’s assessment of global disease activity was measured on a Visual Analogue Scale (VAS) 0 to 10. Structural damage was scored by the Juvenile Arthritis Damage Index-Articular (JADI-A) and by the Total modified Sharp/van der Hejide Score (TmSvdHS). Physical ability was assessed by the Health Assessment Questionnaire-Disability Index (HAQ-DI).

Results: The GHQ-28 case score depicted impaired psychosocial status in 20% of adults with JIA, 17.2 years after disease onset.

Conclusion: Juvenile idiopathic arthritis is a chronic disease that significantly impacts patients’ life style and has a long-term impact on patients’ psychosocial life. The long-term impact on patients’ quality of life and the need for ongoing psychological support and rehabilitation services have to be taken into consideration when discussing treatment and disease management strategies.

Disclosure of interest: None declared.
**Table 1 (abstract P190)**

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>109 (67%)</td>
<td>30 (67%)</td>
<td>17 (59%)</td>
<td>14 (44%)</td>
<td>11 (73%)</td>
<td>384 (66%)</td>
</tr>
<tr>
<td>Age, years</td>
<td>11 (8, 14)</td>
<td>10 (6, 14)</td>
<td>8 (5, 10)</td>
<td>8 (4, 11)</td>
<td>3 (2, 13)</td>
<td>11 (8, 14)</td>
</tr>
<tr>
<td>Disease duration, years</td>
<td>2 (1, 5)</td>
<td>4 (2, 6)</td>
<td>3 (2, 6)</td>
<td>1 (1, 2)</td>
<td>0 (0, 1)</td>
<td>4 (2, 7)</td>
</tr>
<tr>
<td>ILAR Category</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systemic arthritis</td>
<td>5 (3%)</td>
<td>1 (2%)</td>
<td>1 (3%)</td>
<td>28 (88%)</td>
<td>15</td>
<td>70 (12%)</td>
</tr>
<tr>
<td>Oligoartthritis</td>
<td>39 (24%)</td>
<td>24 (53%)</td>
<td>16 (55%)</td>
<td>0 (100%)</td>
<td>117 (20%)</td>
<td></td>
</tr>
<tr>
<td>Polyarthritis</td>
<td>83 (50%)</td>
<td>9 (20%)</td>
<td>9 (31%)</td>
<td>3 (9%)</td>
<td>0</td>
<td>253 (43%)</td>
</tr>
<tr>
<td>Enthesitis Related Arthritis</td>
<td>10 (6%)</td>
<td>5 (11%)</td>
<td>2 (7%)</td>
<td>0 (0)</td>
<td>50 (99%)</td>
<td></td>
</tr>
<tr>
<td>Psoriatic arthritis</td>
<td>10 (6%)</td>
<td>5 (11%)</td>
<td>1 (3%)</td>
<td>0 (0)</td>
<td>44 (8%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>18 (11%)</td>
<td>1 (2%)</td>
<td>0 (0)</td>
<td>1 (3%)</td>
<td>0</td>
<td>48 (8%)</td>
</tr>
<tr>
<td>Concomitant MTX</td>
<td>77 (47%)</td>
<td>31 (69%)</td>
<td>26 (90%)</td>
<td>28 (88%)</td>
<td>12 (80%)</td>
<td>322 (55%)</td>
</tr>
<tr>
<td>Concomitant corticosteroids</td>
<td>15 (9%)</td>
<td>7 (16%)</td>
<td>5 (17%)</td>
<td>23 (72%)</td>
<td>7 (47%)</td>
<td>146 (25%)</td>
</tr>
<tr>
<td>Ever had uveitis</td>
<td>7 (5%)</td>
<td>31 (70%)</td>
<td>21 (72%)</td>
<td>0 (0)</td>
<td>54 (11%)</td>
<td></td>
</tr>
<tr>
<td>CHAQ [0-3]</td>
<td>1 (0, 2)</td>
<td>1 (0, 1)</td>
<td>0 (0, 1)</td>
<td>1 (0, 2)</td>
<td>2 (1, 2)</td>
<td>1 (0, 2)</td>
</tr>
<tr>
<td>JADAS-71</td>
<td>13 (8, 21)</td>
<td>10 (7, 17)</td>
<td>6 (3, 12)</td>
<td>19 (1, 22)</td>
<td>23 (7, 30)</td>
<td>16 (9, 23)</td>
</tr>
</tbody>
</table>

**P192**

Non-HLA gene polymorphisms in juvenile chronic arthritis: associations with outcome of disease

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**Introduction:** The etiology and pathogenesis of JIA are believed to be influenced by both genetic and environmental factors. Although several associations between the risk of developing JIA and gene variants both inside and outside the HLA region have been confirmed, no studies have examined associations between non-HLA gene polymorphisms and the disease outcome.

**Objectives:** Genes involved in immune regulation and signal transduction of cytokines were studied. The genes chosen were previously shown to be associated with JIA in independent validation studies. They were selected to test the hypothesis that Single Nucleotide Polymorphisms (SNPs) previously shown to be associated with JIA are also risk factors for a severe disease outcome.

**Methods:** A total of 500 children with JIA were included prospectively in a population based Nordic cohort study in 1997-2000. All patients had a recent diagnosis of JIA at inclusion. Not all centers were able to collect DNA from patients and at 8 years follow-up DNA was available from 217 patients. All eight categories of JIA were represented in the final cohort. Clinical data were collected longitudinally for the first eight years of disease. Remission was defined according to the preliminary criteria by Wallace et al. 2004. Associations between genotypes and clinical endpoints were found for WISP3, IL2RA, STAT4 and VTCN1, although with low level of significance, p= 0.02–0.03 (Fisher’s exact test). Carriage of the A:A genotype of STAT4 was associated with persistently active disease eight years after disease onset (p=0.03) with about 7 times increased risk, but was not associated with onset type or the use of second line treatment (MTX and/or biologics). The other 7 tested SNPs were not associated with disease outcome

**Conclusion:** In a JIA cohort with longitudinally collected data, we were unable to show robust associations between selected non-HLA genotypes and disease outcome. Data were suggestive of associations between STAT4 A:A and an aggressive course of JIA in which remission were not achieved at eight year follow-up. This is of interest because STAT4 mediates the transcription of cytokine inducible genes and the A:A genotype has previously been associated with an increased risk of developing JIA. These findings should be confirmed in larger patient cohorts.

**Disclosure of interest:** None declared.

**P193**

Juvenile idiopathic arthritis: the transition to adulthood

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**Introduction:** Juvenile Idiopathic Arthritis (JIA) is term used to classify a group of heterogeneous pediatric rheumatic diseases. Many of these conditions remain active until adulthood and when patients start to be followed by adult Rheumatologists there may arise some classification problems once AIA (Adult Idiopatic Arthritis) does not exist! Many published papers regarding the transition of JIA into adulthood miss this point.

**Objectives:** Our aim is to analyze the characteristics of 206 JIA patients, currently in their adulthood, that have been followed, in most of their disease, by the same Rheumatologist with a follow-up time superior to 30 years in some cases.

**Methods:** This study includes 206 patients currently in adult age from a sample of 369 JIA patients, continuously followed by the first author in the Children, Adolescent and Young Adult Rheumatology Outpatients Clinic at IPR and Private Practice. All these patients are registered in
Table 1(abstract P191)

<table>
<thead>
<tr>
<th>STAT4_rs3821236 genotype</th>
<th>Remission (%)</th>
<th>No remission (%)</th>
<th>Total n.</th>
</tr>
</thead>
<tbody>
<tr>
<td>AA</td>
<td>1 (13)</td>
<td>7 (87)</td>
<td>8</td>
</tr>
<tr>
<td>GA</td>
<td>37 (56)</td>
<td>30 (44)</td>
<td>67</td>
</tr>
<tr>
<td>GG</td>
<td>47 (41)</td>
<td>68 (59)</td>
<td>115</td>
</tr>
</tbody>
</table>

Fisher’s exact test p = 0.03

REUMA.PT, the National Registry for rheumatic diseases of the Sociedade Portuguesa de Reumatologia. The 2010 EULAR/ACR Criteria1 for the classification of RA and the ASAS Criteria for Classification of Axial2 and Peripheral Spondyloarthritides were used.

**Results:** The group included 126 female and 80 male patients, with a mean age of 30.0 +/-11.0 years, having mean disease duration of 21.5 +/-11.3 years. The presentations forms and definitive diagnosis are listed below. Sixty three of these three patients are in complete and prolonged off therapy remission. 112 patients were treated with methotrexate, 42 are or were previously treated with biological agents, and 33 had been subjected to intra-articular injections (triamcinolone hexacetonide). Other aspects concerning therapy, morbidity and mortality were also analyzed. All of these patients are registered in SPR database (REUMA.PT).

**Conclusion:** It’s clear that JIA is a group of several joint diseases that start in children and may continue to affect these patients throughout their adult life. A significative group of this patients can be classified as juvenile spondyloarthritis (75/206 = 36%) This analysis shows that JIAs are not a benign and self-limiting disease group, being essential to ensure the proper continuity of rheumatologic care for these patients in adulthood, preferably using a common language and approach to classify and treat these patients.

**Disclosure of interest:** None declared.

**P194**

**Identification of predictive parameters of juvenile idiopathic arthritis among a cohort of patients with musculoskeletal pain**

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**Pediatric Rheumatology 2014, 12(Suppl 1):P194**

**Introduction:** Musculoskeletal pain is a common complaint in the pediatric population and the children affected are often referred to the rheumatologist. Indeed, although the differential diagnosis in these children may be wide, a carefully guided anamnesis allows to orientate it in the majority of cases.

**Objectives:** To recruit children referred to our Centre for musculoskeletal pain and explore if some parameters, obtainable by a thorough medical history evaluation, would be good predictors of the final diagnosis. Secondary aim was to assess the distribution of the different etiologies of musculoskeletal pain in a cohort of patients referred to the pediatric rheumatologist.

**Methods:** Clinical records of children referred to our Unit for musculoskeletal complaints between June 2011 and December 2013 were collected during the first evaluation. A database was built, considering: characteristics of pain (frequency, pattern, precipitating factors), joint swelling, morning stiffness, constitutional symptoms, laboratory test results (ESR, CRP, ANA, RF), family history. After the final diagnosis was made, each patient was categorized according to three subgroups: JIA, post-infective arthritides, non-inflammatory disorders and the three categories were compared for each one of the parameters recorded. Leave-out cross validation and logistic regression model were used to identify the parameters associated with the final diagnosis of JIA.

**Results:** A total of 178 children were evaluated throughout this study. The final diagnosis were: JIA (36), infection-related arthritis (28), non-inflammatory disorders (114). The comparison between the three groups showed a pattern of signs and symptoms specific for each one of the categories, in particular JIA and non-inflammatory disorders: persistent joint swelling, the rest as precipitating factor, the presence of morning stiffness and a persistent pain were statistically associated with the diagnosis of JIA (all p values<0.0001), while absence of joint swelling, activity as a precipitating factor, recurrent pain on evenings/nights, resulted statistically associated with non-inflammatory disorders (all p values<0.0001). Focusing on JIA diagnosis, we then analyzed the impact of each one of the identified parameters on the final diagnosis, obtaining the formula y = k + b1x1 + b2x2 + b3x3 + b4x4 (Y= probability of having JIA; k=15.735; x1= joint swelling’s pattern; x2= precipitating factors; x3= morning stiffness; x4= pain frequency). This formula gives the probability that a child with musculoskeletal complaints will receive a final diagnosis of JIA (sensitivity 90.9%, specificity 95.3%).

**Conclusion:** Musculoskeletal pain is a common cause of rheumatological referral, but only a minority of patients will receive a diagnosis of JIA, indeed the majority of cases are secondary to non-inflammatory disorders. A detailed evaluation of the medical history turned out to be a valid tool to drive the differential diagnosis with high sensitivity. The obtained formula could be used to calculate the probability that a patient with musculoskeletal complaints could be affected by JIA. Obviously this formula cannot be interpreted as a substitute of a specialized evaluation but, if our results will be confirmed on larger cohort, it may be a valuable tool for primary care physician to address the differential diagnosis and the diagnostic work-up.

**Disclosure of interest:** None declared.

Table 1(abstract P193)

<table>
<thead>
<tr>
<th>Initial presentation</th>
<th>Number of patients</th>
<th>Current diagnosis</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oligo persistent</td>
<td>58</td>
<td>Still’s Disease</td>
<td>34</td>
</tr>
<tr>
<td>Oligo extended</td>
<td>31</td>
<td>Rheumatoid Arthritis</td>
<td>24</td>
</tr>
<tr>
<td>Poli FRGm +</td>
<td>17</td>
<td>Axial Spondylarthritides</td>
<td>14</td>
</tr>
<tr>
<td>Poli FRGm -</td>
<td>23</td>
<td>Peripheral Spondylarthritides</td>
<td>39</td>
</tr>
<tr>
<td>Systemic</td>
<td>34</td>
<td>Reactive arthritis</td>
<td>2</td>
</tr>
<tr>
<td>Arthritis/Enteritis</td>
<td>30</td>
<td>Psoriatic Arthritis</td>
<td>9</td>
</tr>
<tr>
<td>Psoriatic arthritis</td>
<td>7</td>
<td>Inflammatory Bowel Disease Arthropathy</td>
<td>11</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>6</td>
<td>Oligo/ANA+ with Chronic Uveitis</td>
<td>18</td>
</tr>
</tbody>
</table>

**Ocular manifestations**

**Uveitis** 25 [22 Chronic + 3 Acute]

**P195**

**Effect of physical therapy on static postural balance, lower extremity muscle strength and functional status in children with juvenile idiopathic arthritis**

Hristina Colovic1, Lidija Dimitrijevic1, Ivona Stankovic1, Vesna Zivkovic2, Marija Spalevic2

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**Pediatric Rheumatology 2014, 12(Suppl 1):P195**

**Introduction:** The aim of the study was to evaluate muscle strength and functional status in children with juvenile idiopathic arthritis (JIA) before and after a 6-months physical therapy program. The patients also had static postural sway and lower extremity muscle strength measured.

**Objectives:** To analyse static postural sway, lower extremity muscle strength and functional status in children with juvenile idiopathic arthritis before and after a 6-months physical therapy program.

**Methods:** The study included 66 children with JIA. They were divided into two groups. The first group received a 6-months physical therapy program. The second group received no treatment. The assessment of muscle strength, static postural sway, functional status and pain level were done before and after the program.

**Results:** The results showed improvements in muscle strength, static postural sway, functional status and pain level in the first group after the physical therapy program. The second group showed no improvements.

**Conclusion:** The results of the study showed that a 6-months physical therapy program can improve muscle strength, static postural sway, functional status and pain level in children with juvenile idiopathic arthritis.

**Disclosure of interest:** None declared.
Introduction: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatologic disease in children. It is defined as permanent arthritis of one or more joints that lasts 6 weeks in children younger than 16 years when all other causes of arthritis are excluded. It is characterized by pain, swelling, morning stiffness in affected joints and decreased quality of life. The goals of physical therapy are to increase joint range of motion, muscle strength, joint stability, physical function without pain and neuromuscular coordination adequate to the age.

Objectives: The aim of this study was to evaluate the effect of physical therapy on range of motion, muscle strength, balance and functional status in children with JIA.

Methods: The diagnosis of JIA was made according to the ILAR criteria. Patients with psoriatic arthritis and arthritis associated with enthesitis were excluded from the study. Twenty children (aged 6-18 years) manifesting lower extremity arthritis were assessed. Before and after physical therapy single-leg static balance was measured. Lower extremity strength, active range of motion and functional status (Childhood Health Assessment Questionnaire - CHAQ) were also assessed at the beginning and the end of the therapy.

Physical therapy included electrotherapy, laser therapy, kinesiotherapy, occupational therapy and hydrotherapy during 3 months. At the beginning all the children had 20 procedures, 5 days in a week. Kinesiotherapy, occupational therapy and hydrotherapy were continued 3 times weekly during 2 months.

Results: After physical therapy, range of motion, muscle strength, balance and functional status were significantly improved in all the patients (p < 0.05).

Conclusion: By increasing joint range of motion and muscle strength, physical therapy improves balance, proprioception and functional status in children with juvenile idiopathic arthritis.

Disclosure of interest: None declared.

P196
Polymarticular juvenile idiopathic arthritis (pJIA): clinical and serologic predictors of inactive disease (ID)
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Pediatric Rheumatology 2014, 12(Suppl 1):p196

Introduction: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatoid disease in childhood and the polyarticular subtype is associated with persistent activity and a low rate of remission. The goal of an early and aggressive treatment is to achieve remission preventing irreversible joint destruction and long-term disabilities.

Objectives: 1) To assess disease activity in patients with pJIA "under early therapy with MTX." 2) To determine predictors of ID in this cohort.

Methods: Clinical charts of 174 pJIA pts (ILAR ‘01), (1998 -2009) we reviewed. Inclusion criteria:pJIA pts under "early" MTX-follow up "a minimum of 12mo". Demographic, clinical, laboratory, and therapeutic variables were analyzed at disease onset, 12mo and last visit. Functional disability (CHAQ), damage (JADe Articular score) and Remission Criteria (Wallace) were properly assessed.

Results: Ninety eight patients were included , 85 girls, (86.7%) median age at onset 10 years ( IQR 6.6 -12), median disease duration 60 months (IQR :36 -74 ) and follow-up 48 months (IQR 24,5 -67); 34 pts (34.6%) were RF Positive. All patients received MTX; 32 /98 (32.6%) reached ID at median follow up time of 12 mo with a CHAQ mean value 0.37 and a JADI mean value 1.3. Nineteen out these 32 pts (60%) sustained remission for at least 37 mo. ID was associated with a less time of disease evolution (p<0.05), a better function CHAQ (p =0.5 ) and less damage (p =0.4)A higher prevalence but not significantly RF titers (40 vs 25%); seronegative ANA titers (60 vs 53 ) and RX damage (47 vs 32 ) were observed in the group of non responders pts to MTX. On multivariate analysis a less time of disease evolution was the only predictive risk factor associated to inactive disease (β 1.01 p =0.5).

Conclusion: In our series , only 32/98 (32.6%) pJIA pts reached ID, this clinical state was sustained in 60% of them longer than 2 years. A less interval between disease onset and Mttx start was the only variable predicting inactive disease.

Disclosure of interest: None declared.

P197
Lack of association between the HLA region RS7775055 polymorphism and JIA in patients from russia
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Pediatric Rheumatology 2014, 12(Suppl 1):p197

Introduction: Juvenile idiopathic arthritis (JIA) refers to a group of conditions involving joint inflammation that first appears before the age of 16. Juvenile idiopathic arthritis is thought to arise from a combination of genetic and environmental factors. Numerous associations between HLA polymorphisms and JIA subtypes have been reported in multiple populations. The HLA region SNP rs7775055 is a part of the HLA-DRB1*0801–HLA-DQA1*0401–HLA-DQB1*0402 haplotype, which has been shown to increase risk of JIA in UK and non-Hispanic Caucasians US patients. The recent study of Hinks and co-authors also showed the strong covariation of associations between rs7775055 and JIA (odds ratio (OR) = 6.01; p=3.14×10^-124) in patients from across the US, UK and Germany.

Objectives: The goal of the study was to test the hypothesis that the HLA region SNP rs7775055 could underlie susceptibility to JIA or its subtypes in patients from Russia.

Methods: The HLA region SNP rs7775055 was studied in 204 children with JIA and 207 healthy individuals, citizens of the Bashkortostan, Russia using real-time PCR. Statistical analysis was performed using Statistica v.6.0 and SNPStats programs.

Results: The genotypes distribution was in Hardy-Weinberg equilibrium in both groups. The HLA region SNP rs7775055 did not show an association either with JIA or any of the JIA subtypes in our cohorts. We revealed a trend tendency towards an increase of CC genotype under a recessive model in persistent oligoarthritis cohort, but it was not statistically significant (p=0.068, OR=6.88 95%CI 0.71-67.02).

Conclusion: In summary, we found no evidence of association between the HLA region SNP rs7775055 and JIA or its subtypes in patients from Russia.

Disclosure of interest: None declared.
significantly differences with control group (p<0.01). We concluded that the test for anti-CCP in poly JRA patients are significantly benefit in the clinical field.

Disclosure of interest: None declared.

P199
Reasons for stopping methotrexate treatment in patients with juvenile idiopathic arthritis
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Pediatric Rheumatology 2014, 12(Suppl 1):P199

Introduction: Patients with juvenile idiopathic arthritis (JIA) commonly have been using methotrexate (MTX) to improve the clinical course of the disease, however non adherence is frequently observed.

Objectives: To evaluate the reason for MTX interruption, if it was due therapeutic inefficacy or side effects.

Methods: Data were collected from medical charts of JIA patients followed at the pediatric rheumatology Unit from the State University of Campinas. Relevant clinical variables was observed as age, gender, age at diagnosis, subtype of JIA, age at start of MTX, the time from diagnosis to start the treatment with MTX (in months), response to MTX (yes / no) and whether there were adverse effects (yes / no) and the reason for discontinuation of MTX.

Results: We included 98 patients (median age 15.4 ± 7.5 years) who had a definitive diagnosis of JIA and used MTX. Seventy-six (78%) patients were females. The JIA subtype most frequently observed was polyarticular. Routes of administration of MTX observed were subcutaneous (55%) and oral (13%), but many patients throughout the treatment used both administration (32%) in order to improve adherence to treatment. After a mean follow-up time of 5 years, 51 (52%) of these patients discontinued treatment and 47 (48%) of them were still on treatment, but only 35 (74%) were adherent. Sixty-eight (69%) JIA patients reported the presence of sporadic episodes of adverse reactions during treatment. Episodes of adverse reactions related to MTX was mainly gastric intolerance (abdominal discomfort, nausea and vomiting). There were three cases of elevated transaminase levels and one case of neutropenia. The reasons for JIA patients discontinue treatment with MTX was presence of side effects (35%), interruption on their own decision (27%), treatment abandonment (12%) and other reasons such as pregnancy, chickenpox and lack of medication in the public hospitals (12%), improvement of the disease (8%), and inefficacy (6%). All patients who discontinued MTX on their own decision had additionally the presence of side effects.

Conclusion: Although MTX has a great therapeutic index, the side effects are still seen as a major form of abandonment of this pharmacological treatment. Therefore a careful history is essential to identify side effects and adequate treatment to increase adherence.


P200
Anaphylactic reaction to the first dose of subcutaneous methotrexate in JIA: a case report and literature review
Leonardo Campos1, Renata Sobral1, Vivian Almeida1, Rozana Almeida2, Marise Lessa2, Christianne Diniz2, Marta Rodrigues3, Sheila Oliveira3, Flavio Sztajnbok2
1Pediatric Rheumatology, Instituto de Pediatría e Puericultura Matogrosso Gesteira (IPPAG), Federal University of Rio de Janeiro, Brazil; 2Pediatric Rheumatology, Adolescent Health Care Center, State University of Rio de Janeiro (NEA/UERJ), Rio de Janeiro, Brazil; 3Pediatric Rheumatology 2014, 12(Suppl 1):P200

Introduction: Anaphylactic reaction is the first dose of subcutaneous methotrexate in JIA: a case report and literature review

Methods: To report a case of a 13-years old adolescent girl diagnosed with polyarticular JIA that had an anaphylactic reaction to the first dose of subcutaneous methotrexate.

Results: A 13-years old adolescent girl diagnosed with polyarticular JIA (RF-/ANA-/HLA-B27-) received the first dose of subcutaneous methotrexate in our Day Care centre due to refractoriness to NSAIDs. While she was leaving the building after 10 minutes of medication she developed urticaria, angioedema, shortness of breath and hypoxia (O2 saturation 85%). After administration of 0.5ml of 1:1000 adrenaline, 500ml of saline, 2.5mg of dexamethasone and 125mg of methylprednisolone she recovered and was discharged home after a short period of stay. The methotrexate she used was also for intrathecal administration and had only distilled water as suspension.

Conclusion: This is the first case report of anaphylaxis to methotrexate in a patient with JIA without previous exposure. Considering it is a very rare and fatal reaction, we suggest that the first subcutaneous dose should be administrated in a health center and the patient should wait 30 minutes before leave.

Disclosure of interest: None declared.

P201
Role of invasive and non-invasive additional imaging methods in pediatric rheumatology
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Pediatric Rheumatology 2014, 12(Suppl 1):P201

Introduction: Juvenile arthropathy it’s a term combining heterogeneous group of joint diseases in children, which are characterized by structural, morphological and functional changes of inflammatory nature and non inflammatory disorders. Chronic inflammatory process may be “driving” mechanism that is determine the nature of the articular lesions with specific clinical, instrumental and laboratory picture or maybe just one of the features of another pathology. Similarity of clinical and radiological picture, chronic nature of the flow, various of pathogenetic therapy and outcomes of the disease do this group one of the difficult to diagnose.

Objectives: To study the masks of JIA and no rheumatology pathology joint in children of Russian Federation.

Methods: Clinical, serological, x-ray manifestations, ultrasound, MRI, arthroscopy data were analyzed in more then 300 children which examined in hospital department with presumptive diagnosis JIA.

Results: All children were subjected to complete rheumatology examination, and remained under our observation for a long time in order to assess the dynamic of the articular lesion. Children with classic course of JIA were appointed basic anti-inflammatory drugs (methotrexate, anti-TNF, IL6 block). In cases when clinically atypical duration or laboratory “mute” of arthritis, long persistence monoarthritis and also variants with fever or destructive bones change we were applied deeper imaging methods such as MRI, arthroscopy, 3-phase osteo scintigraphy and other. Over five years were diagnosed six cases of tuberculous lesion of the joints (specific destruction of bone + biopsy), two cases of tuberculous periarthritis soft tissue (cyst formation with tyromatosi), fourteen cases of vascular anomaly (cavernous hemangioma, dysplasia of the superficial veins), five cases of atypical localization focus of osteoid-osteoma (the bottom of the acetabulum, the bottom of the fosa coronoidea humorous, processus posterior of the talus), six cases of pigmented villous and chronic hemorrhagic synovitis of the knee and ankle joint, several cases of the skeletal dysplasia, and in rare cases of histiocytosis, malignant B-cell lymphoma, osteomyelitis and other rare bones disorders. Not one cases of the CRMO. In many cases due to this methods, we were excluded such diagnosis like tumors of the joints, different forms osteochondropathy. Such typical changing of the bones in JIA are usually degenerative nature in chronic uncontrolled inflammation.
Conclusion: In some cases in undifferentiated arthritis, time of the diagnosis may determine the success of treatment. Any arthritis after failure of anti-inflammatory and antibacterial therapy should be questioned of rheumatic nature. Application invasive and non-invasive additional imaging methods can reduce the risk of incorrect diagnosis.

Disclosure of interest: None declared.

P202 Hand function assessment in patients with juvenile idiopathic arthritis: usefulness of duruöz hand index
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Pediatric Rheumatology 2014, 12(Suppl 1):P202

Introduction: Assessing hand function in juvenile idiopathic arthritis (JIA) is important.

Objectives: To assess if Duruoz’s Hand Index (DHI) was a useful instrument to evaluate functional disability in patients with JIA.

Methods: Patients diagnosed as JIA according to ILAR criteria in Pediatric Rheumatology Department of Dokuz Eylul University Hospital were consecutively enrolled in this cross-sectional study. Demographic, clinical and functional characteristics of patients were evaluated. Erythrocyte sedimentation rate, patients’ and physicians’ global VAS, number of involved joints were recorded as non-functional parameters related to active disease status. Functional assessment was performed by DHI, Childhood Health Assessment Questionnaire (CHAQ), Purdue Pegboard, grip strength and 3 kinds of pinch strengths. The correlation of DHI was assessed with the other functional parameters as well as non-functional parameters by Spearman’s test. We also compared the functional parameters of patients with hand involvement with the ones who did not have involvement. The study protocol was approved by the institutional ethics committee and informed consents were obtained.

Results: Forty JIA patients with a mean age of 12.3 ± 3.1 were recruited. Twenty seven of them (68%) were females. The average duration of disease was 3.4 ± 2.7 years (min: 0.5 max: 9 years). Twenty patients (50%) had hand involvement. DHI was significantly correlated with CHAQ scores (rho=0.576, p<0.005), grip strength (Dominant hand: rho=0.399, p<0.011 and non-dominant hand: rho=0.391, p=0.013), patients’ global VAS (rho=0.452, p=0.004), physicians’ global VAS (rho=0.493, p=0.001), ESR (rho=0.456, p=0.004), number of involved joints (rho=0.487, p=0.002) and hand involvement (rho=0.580, p<0.005). DHI was not significantly correlated with Purdue Pegboard scores and 3 types of pinch strengths (p>0.05). The patients with hand involvement had significantly higher DHI scores than the patients without (p=0.005). However, other functional scores did not significantly between 2 groups (p>0.05). Besides, the mean ESR, physicians’ global VAS and CHAQ score were significantly higher in patients with hand involvement than the patients without (p=0.014, 0.001 and 0.044, respectively).

Conclusion: The results of this study indicate that children with active disease have a greater risk of developing muscle weakness in the hands during the course of the disease. Hand strength in patients with JIA is mostly attributable to the activity of disease rather than hand involvement. DHI scores confirm these findings.

Disclosure of interest: None declared.

P203 A hospital based registry of juvenile idiopathic arthritis in Norway
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Pediatric Rheumatology 2014, 12(Suppl 1):P203

Introduction: In 1999 a registry of patients with juvenile idiopathic arthritis (JIA) and juvenile onset connective tissue diseases was established at Rikshospitalet, Oslo University Hospital. The purpose of the registry is to initiate clinical, epidemiological and laboratory research projects.

Objectives: To evaluate clinical characteristics in patients with JIA registered in the hospital based registry.

Methods: The registry is based on written informed consent. JIA patients were classified using ICD-10 codes and they were registered once. Gender, date of registration and year for disease onset was recorded, in addition to onset type, number of active joints and physician’s global assessment of disease activity (VAS 0-100 mm).

Results: A total of 1069 JIA patients were registered. Mean age at inclusion was 9 years, and 65% were female. The distributions in various ICD-10 subgroups are shown in table 1. The most frequent subgroups were pauciarticular and polyarthritis (seronegative).

Conclusion: The age at onset and gender distribution is as expected. Girls had higher physician’s global than boys and those with polyarthritis had higher physician’s global than both systemic and pauciarticular arthritis. Ideally the register should have been based on the ILAR criteria instead of the IC-10 codes. We consider the three subgroups pauci, poly and systemic to be the most consistent with the ILAR criteria. The registry will be an important database for studies concerning outcome in JIA.

Disclosure of interest: None declared.

P204Juvenile idiopathic arthritis in a child with nijmegen breakage syndrome
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Pediatric Rheumatology 2014, 12(Suppl 1):P204

Introduction: Nijmegen Breakage Syndrome (NBS) is a rare autosomal recessive DNA repair disorder, caused by mutation in the NBS1 gene on chromosome 8q21. The hallmark symptom is microcephaly, other characteristic features are facial phenotype, growth retardation, premature ovarian failure in girls. Psychomotor development is usually not disturbed. Immunological and hematological parameters are normal or slightly decreased. Patients with NBS have an extremely high risk for developing malignancy.

Objectives: We present 7 y.o. girl with NBS who developed arthritis.

Methods: The child was delivered in time, by cesarean section due to IUGR, with congenital defects syndrome (microcephaly, dysmorphic face, anal atresia, fistula to the skin of the perineum). She underwent surgery shortly after birth. Genetic consultation confirmed, c.657del5 mutation on both alleles of NBS1 gene, normal karyotype and aberration of chromosome 7 and 14. In first few years she suffered from upper respiratory tract infection, viral gastrointestinal infections. At the age of 5 years replacement IVIG was introduced. Since 3rd year of life the granuloma- like skin changes on ears, nose and hands had been observed (epitheloid granuloma in histopathological examination). The immunological assessment, done on IVIG showed slightly diminished level of IgG, normal IgA, and slightly increased IgM. Immunophenotyping of lymphocytes revealed severely diminished number and percentage of CD3+/CD4+ T cells (27.3%), CD3 +CD8+/CD4+ cells (5.3%), CD4+CD8+/CD4+ cells (15.8 %), with B cells and NK cells within the normal range. The in vitro response of lymphocytes to mitogenic stimuli such as phytohaemagglutinin, anty-CD3 and Pansorbin was deeply decreased. Slight reduction of lymphocytes with no leucopenia was observed.

Results: Since 3rd year of life inflammatory process in joints was observed: the swelling, effusion of right knee, swelling of right wrist and 3rd and 4th finger of the right hand. The X-ray of the right knee was correct. In ultrasound inflammation was confirmed in the knee, tendovaginitis of the extensor of 4th finger tendon and flexor of 3rd finger of the right hand.
ESR and CRP were in norm, trombocytosis 508G/L, Rheumatoid Factor-16 years old. While outcome of pregnancy in pregnant women with RA is well-known, at best of our knowledge there are limited data on the characteristics of six women affected by juvenile idiopathic arthritis (JIA).

Introduction: Pregnancy outcomes in women affected by JIA.

Objectives: To describe pregnancy outcomes in a case series of six women affected by JIA.

Methods: We report on six cases of women affected by JIA.

Results: A total of 1069 patients were included. The distribution of JIA patients according to ILAR category were: systemic arthritis 23 (7.5%), oligoarticular persistent 86 (28%), oligoarticular extended 8 (2.5%), RF positive polyarthritis 21 (6.8%), RF negative polyarthritis 71 (23%), ERA 94 (30%), psoriatic arthritis 4 (1.3%) and undifferentiated 1 (0.3%). 64% were female and mean follow up time was 55 months (9-192). Uveitis was present in 19 (6.2%) patients, 68% had oligoarticular extended disease. Of the study cohort, 54 (17.5%) patients were reported as ANA positive (≥1:160). Represented by oligoarticular persistent, RF negative polyarthritis, RF positive polyarthritis and ERA, 46%, 22%, 13% and 13%, respectively, ANA positive group, 81% were female sex and mean age of arthritis onset was 7y (2-14y). ANA dilution was in 65% ≤1:320. Uveitis was more frequent in ANA positive patients (17% vs. 0.4% p=0.002), in oligoarthritis and in early-onset JIA (<5y (p=0.003).

Conclusion: ANA positive patient group had a higher rate of female sex, younger age of onset and higher rate of uveitis. These findings are consistent with those reported by other authors. Furthermore, this cohort differs from that reported in the literature for the high frequency of ERA subtype and 13% of ANA positivity in these group of patients.

Disclosure of interest: None declared.

P305
ANA positivity in juvenile idiopathic arthritis: make a difference in a Colombian children population?
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Pediatric Rheumatology 2014, 12(Suppl 1):P205

Introduction: Juvenile idiopathic arthritis is the most common cause of chronic arthritis in children. JIA is a heterogeneous disease that has been classified by the International League of Associations for Rheumatology (ILAR) on seven different subtypes according to the most relevant clinical and serological features. Previous studies have demonstrated an association between the presence of antinuclear antibodies (ANA) and features like: early-onset oligoarticular disease, female predominance, asymmetric arthritis and higher frequency of uveitis. There are limited data on the characteristics clinical and analytical into different subtypes of JIA in Colombian children and their relationship with type of onset and clinical course.

Objectives: To describe a group of Colombian patients with JIA and analyze the clinical features according to ANA positivity (more or equal to 1:160) was considered as positive).

Methods: This is a descriptive case series study. Includes patients from three pediatric rheumatology clinics in Bogotá, Colombia. The associations between clinical and laboratory parameters were analyzed using chi square test. P values less than 0.05 were considered as significant.

Results: A total of 308 patients were included. The distribution of JIA patients according to ILAR category were: systemic arthritis 23 (7.5%), oligoarticular persistent 86 (28%), oligoarticular extended 8 (2.5%), RF positive polyarthritis 21 (6.8%), RF negative polyarthritis 71 (23%), ERA 94 (30%), psoriatic arthritis 4 (1.3%) and undifferentiated 1 (0.3%). 64% were female and mean follow up time was 55 months (9-192). Uveitis was present in 19 (6.2%) patients, 68% had oligoarticular extended disease. Of the study cohort, 54 (17.5%) patients were reported as ANA positive (≥1:160). Represented by oligoarticular persistent, RF negative polyarthritis, RF positive polyarthritis and ERA, 46%, 22%, 13% and 13%, respectively, ANA positive group, 81% were female sex and mean age of arthritis onset was 7y (2-14y). ANA dilution was in 65% ≤1:320. Uveitis was more frequent in ANA positive patients (17% vs. 0.4% p=0.002), in oligoarthritis and in early-onset JIA (<5y (p=0.003).

Conclusion: ANA positive patient group had a higher rate of female sex, younger age of onset and higher rate of uveitis. These findings are consistent with those reported by other authors. Furthermore, this cohort differs from that reported in the literature for the high frequency of ERA subtype and 13% of ANA positivity in these group of patients.

Disclosure of interest: None declared.

P206
Pregnancy outcomes in women affected by juvenile idiopathic arthritis (JIA)
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Pediatric Rheumatology 2014, 12(Suppl 1):P206

Introduction: JIA is the most frequent form of persistent arthritis in children that begins at or before 16 years old. While outcome of pregnant women with RA is well-known, at best of our knowledge there are a few scientific works about pregnancy in JA patients [1,2].

Objectives: Our aim is to describe pregnancy outcomes in a case series of six women affected by JIA.

Methods: We report on six cases of women affected by JIA with a median age of 32.8; median age at onset of 6.1; median age at first delivery of 25.7. (table 1).

Results: In all cases, pregnancy was associated with remission of disease activity, however a post partum flare appeared after 4 pregnancies (pt 1-4.5-6) and in the first year post-partum. The seven babies were in good condition, without apparent malformation or symptoms of neonatal illness. Only 1 woman was treated during her pregnancy: the number 5 patient received oral cyclosporine for the first 5 months of pregnancy and oral low-dose corticosteroids for all pregnancy; she had an active disease before pregnancy and she had an important flare a few months after delivery.
Introduction: Juvenile chronic arthritis (JCA) is the most common chronic rheumatic disease in children an important cause of disability. When only one joint is involved it may be difficult to make an early diagnosis. A detailed history and clinical examination is important to reach a correct diagnosis and appropriated treatment.

Objectives: To investigate the diagnosis of chronic monoarthritis.

Methods: Data were collected retrospectively for 69 consecutive chronic monoarthritis seen in our hospital during 2000 -2001. Minimal duration of arthritis ≥3 months 10 patients were excluded for not having complete information.

Results: There was two age more frequently 2 and 11 years (R: 0.10-14.4). Joint fluid: 90% inflammatory. Arthroscopic with pathology anatomic: 11 nonspecific chronic synovitis. Another diagnosis were: 5 body forein (pine needle, sliver, toothpick), 6 discoid meniscus, 3 synovial chordromatosis, 2 distention ligament, 2 osteochondritis, 2 synovial cyst, 1 Synovial haemangiomia, 1 Pigmented villo-nodular synovitis, 1 patient with agamaglobulinemia (Brutton Disease), 1 Tenosinovitis in Celiac disease. The laboratory tests include antinuclear antibody and ocular examination was not significative difference to diferenciate ACJ to another chronic monoarthritis (Fisher exact test, p> 0.27). On the other hand highly significative association between patients with ACJ and cronic synovitis (κ=0.3005) was found.

Conclusion: 40.6% of patients with chronic monoarthritis had ACJ, being the most frequent form: pauciarticular. MRI and the synovial biopsy arthroscopy play an important role in the diagnosis of a child that presents a chronic monoarthritis.

Disclosure of interest: None declared.

References

Table 1(abstract P206)

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (y,m)</th>
<th>Age at onset</th>
<th>Type</th>
<th>Therapy before pregnancy</th>
<th>Age at delivery [pS1] (y,m)</th>
<th>Sex of babies</th>
<th>Flare after delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 LS</td>
<td>29 7/12</td>
<td>12 y 2/12</td>
<td>poliarticular</td>
<td>None</td>
<td>18 11/12</td>
<td>♀♂</td>
<td>yes</td>
</tr>
<tr>
<td>2 GM</td>
<td>38 7/12</td>
<td>8 y</td>
<td>poliarticular</td>
<td>None</td>
<td>27 3/12</td>
<td>♀</td>
<td>no</td>
</tr>
<tr>
<td>3 GA</td>
<td>29 11/12</td>
<td>4 y</td>
<td>oligoarticular</td>
<td>none</td>
<td>25 9/12</td>
<td>♀♂</td>
<td>no</td>
</tr>
<tr>
<td>4 CE</td>
<td>37 11/12</td>
<td>1 y 4/12</td>
<td>poliarticular</td>
<td>none</td>
<td>26 9/12</td>
<td>♀</td>
<td>yes</td>
</tr>
<tr>
<td>5 RL</td>
<td>34 5/12</td>
<td>8 y 7/12</td>
<td>poliarticular</td>
<td>Cya, steroids</td>
<td>29 3/12</td>
<td>♀</td>
<td>yes</td>
</tr>
<tr>
<td>6 BA</td>
<td>26 10/12</td>
<td>2 y 8/12</td>
<td>poliarticular</td>
<td>none</td>
<td>26 2/12</td>
<td>♀</td>
<td>yes</td>
</tr>
</tbody>
</table>

[pS1]

As reported for pregnant patients affected by RA (Dolhain Rijmen 2010), in our cases pregnancy was associated with a remission of disease in 6/6 patients and flare in post-partum period in 4/6 patients, probably depending on increased levels of serum alfa 2 glycoprotein and elevated levels of sex hormones that influence a shift in cytokine production from a Th1 to a Th2 profile. In fact, oestrogens inhibit T-cell function, progestrone stimulates Th2 effects and cortisol has a general immunosuppressive effect.

The number 5 patient was treated with cyclosporine and steroids. No congenital anomalies or increase of death rate were observed in infants exposed to cyclosporine antenatally. Besides low-dose steroids therapy (5-15 mg prednisone daily) does not increase low-birth-weight or small for gestation age infants.

Conclusion: In conclusion, in JIA patients a stable disease or remission should be reached before pregnancy and should be used safe immunosuppressive drugs to avoid a flare during pregnancy and in post-partum period.

Disclosure of interest: None declared.

References

P207
Differential diagnosis of chronic monoarthritis in children
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Pediatric Rheumatology 2014, 12(Suppl 1):P207

Introduction: Juvenile chronic arthritis (JCA) is the most common chronic rheumatic disease in children an important cause of disability. When only one joint is involved it may be difficult to make an early diagnosis. A detailed history and clinical examination is important to reach a correct diagnosis and appropriated treatment.

Objectives: To investigate the diagnosis of chronic monoarthritis.

Methods: Data were collected retrospectively for 69 consecutive chronic monoarthritis seen in our hospital during 2000 -2001. Minimal duration of arthritis ≥3 months 10 patients were excluded for not having complete information.

Results: There was two age more frequently 2 and 11 years (R: 0.10-14.4). Joint fluid: 90% inflammatory. Arthroscopic with pathology anatomic: 11 nonspecific chronic synovitis. Another diagnosis were: 5 body forein (pine needle, sliver, toothpick), 6 discoid meniscus, 3 synovial chordromatosis, 2 distention ligament, 2 osteochondritis, 2 synovial cyst, 1 Synovial haemangiomia, 1 Pigmented villo-nodular synovitis, 1 patient with agamaglobulinemia (Brutton Disease), 1 Tenosinovitis in Celiac disease. The laboratory tests include antinuclear antibody and ocular examination was not significative difference to diferenciate ACJ to another chronic monoarthritis (Fisher exact test, p> 0.27). On the other hand highly significative association between patients with ACJ and cronic synovitis (κ=0.3005) was found.

Conclusion: 40.6% of patients with chronic monoarthritis had ACJ, being the most frequent form: pauciarticular. MRI and the synovial biopsy arthroscopy play an important role in the diagnosis of a child that presents a chronic monoarthritis.

Disclosure of interest: None declared.

References

P208
A family case of early onset juvenile idiopathic arthritis with uveitis: lessons of the past and the present
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Pediatric Rheumatology 2014, 12(Suppl 1):P208

Introduction: Early onset of juvenile idiopathic arthritis (eoJIA) associated with pauci/polyarticular joints involvement, antinuclear factor and uveitis is a special subtype of JIA. Generally accepted opinion of pediatric rheumatologists this JIA category isn`t belong to ankylosing spondylitis (AS)-related group of diseases.

Objectives: To present clinical observation of a family case (mother and daughter) of eoJIA with uveitis, homogenous clinical picture in the disease beginning and manifestation of severe AS in the mother in adulthood.

Methods: Cases report.

Results: Female patient was born in 1978. Disease onset was reported when she was 3 years old from arthritis of right knee and developed polyarthritis within 2 years. By the 3rd year of disease duration bilateral uveitis involved. She was treated by NSAIDs treatment, intra-articular glucocorticoid (GC) injections, and different (>5) DMARDs consequently;
multiple courses of GC pulse therapy, local ocular therapy and repeated surgical treatment of ocular complications, since 1996 - prednisolone (10 mg/day) continuously. Despite the treatment, polyarthritis and hight activity persisted, corneal spot developed. Significant aggravation was reported after the first labors (age 22 years); inflammatory back pain appeared. Ankylosis of neck and sacroiliac joints, osteonecrosis of left femoral head were observed. i.e. AS (HLA-B27-negative) was diagnosed after 20 years of disease duration. In 2004 hip replacement of left femoral joint performed. In 2009 after 2nd labor disease progression with high activity and osteonecrosis of right femoral joint developed, that required hip replacement. High activity persisted within next 4 years until adalimumab (ADA) therapy was started. Her daughter, which was born in 2009, developed oligoarthritis in the age of 2. Despite of therapy with NSAIDs, SSZ, i.a. GC injections arthritis was extended to polyarthritis with dactylyitis of 3rd fingers of hands and flexor contracture of knee joints. Bilateral uveitis was diagnosed and local eye treatment was initiated. MTX (s/c 12 mg/m2/week) was added to SSZ treatment. 4 months later cyclosporine A prescribed instead of SSZ, repeated i.a.GC injections were needed. ESR was 30 mm/h, C-reactive protein - 52.3 mg/l, HLA-B27 – negative, ANF positive (1/320). Hypertrophy of metaphyses on separate phalanxes by X-ray, bone marrow edema and synovitis of some hand’s fingers by MRA observed. In 2013 ADA was not approved for children younger than 4th in Russia. Considering the progression of clinical and functional disorders, local growth disturbances, periostitis, persistence of active uveitis, and bad outcome of the similar disease in her mother ADA 30 mg s/c once in 2 weeks was added to MTX. Initial effect was good for the arthritis and uveitis; but, later, within the next 2 months the efficacy level has somewhat decreased. ADA was increased up to 40 mg per injection with achievement of clinical remission by 1 year of therapy without any adverse event. ADA therapy started in her mother (1st pt) in the same time with good respond.

**Conclusion:** This clinical case demonstrates the same type disease in mother and daughter. It illustrates the possibility of AS development in female patients with eoJIA with ANA-associated severe uveitis, despite of HLA B27 negativity. Aggressive treatment strategy, including ADA in a very young patient, dose escalation ADA, seems to be justified in the case of high risk of unfavorable prognosis in order to prevent joint destruction and irreversible uveitis complications.

**Disclosure of interest:** None declared.

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**P210**

**Dissociation of T lymphocyte subpopulations in patients with juvenile idiopathic arthritis**

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**Pediatric Rheumatology** 2014, 12(Suppl 1)P210

**Introduction:** Introduction and objective: it is well known fact that the key point in the development of an autoimmune response in rheumatoid inflammation is the dissociation between subpopulations of T lymphocytes.

**Objectives:** The aim of our study was to analyze the quantitative changes in the spectrum of T-lymphocytes and the activity of the pathological process in children with juvenile idiopathic arthritis (JIA).

**Methods:** Materials and Methods: the main subpopulations of T-lymphocytes in peripheral blood were determined by laser flow cytometer - FacsCalibur using the program CellQuest. The study was conducted in patients with different stages of JIA. A following panel of antibodies: CD45/ CD14, IgG1/IgG2; CD3/CD19, CD4/CD8, CD2/HLA-DR, CD16/56, CD71 ; CD95/ CD54, CD38 was used to identify lymphocyte populations.

**Results:** Results of our study revealed the elevated levels of lymphocytes expressing CD3 + CD19 markers - 27.3 ± 3.4% (compared with the reference parameters - 9.5 ± 1.1%). Besides, decreasing of CD19+T-lymphocytes (51.6 ± 2.4% compared to healthy 76.2 ± 1.5%) was in direct correlation with the high activity of the process (P <0.05). Moreover, it was necessary to define two groups of results:

1. - a significant increase in T-helper cells ( CD4 + CD8-) to 44.9 ± 4.2% (control group -34.7 ± 2.1%) while the number of CD8 + T-lymphocytes was within normal parameters. These results indicate the predominant contribution of 2and 3 types hypersensitivity, which are cha-racterized with the production of autoantibodies during the pathology process.

2. - preservation of T helper population within the reference values while the content of T CD8 + effectors was increased that indicates the cell type of hypersensitivety. Growth of CD8 + T cells correlated with the activity of the process, while remaining normal in oligoarthritis with low laboratory activity (ESR, CRP). Deterioration of articular changes followed by increased levels of CD95+T-lymphocytes (12.8 ± 1.9% when a rate of healthy is 3.2 ± 0.6%). In our opinion, direct correlation between the CD95+T-lymphocytes and CD8+T-cytotoxic cells indicated the dependence between proliferation, cytotoxicity and apoptosis . The level of activated CD3 + HLA-DR+ T cells was significantly increased in JIA up to 9.7 ± 1.5% (com-pared with healthy children - 4 , 1 ± 0.5%). In one patient with systemic JIA (stage of severe rheumatoid inflammation) the level of activated CD3 + HLA-DR+ T-
lymphocytes increased dramatically up to 38.7%. It is necessary to point that our results did not reveal the growth of the serum immunoglobulins.

Conclusion: Conclusion: dissociation of T-lymphocyte subpopulations in children with JIA correlated with clinical activity of the disease. Screening of T lymphocytes populations is promising for a personified therapy selection in patients with JIA.

Disclosure of interest: None declared.

P211
Clinical and immunological characteristics of rheumatic diseases in children
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Pediatric Rheumatology 2014, 12(Suppl 1) P211

Introduction: The problem of rheumatic diseases (RD) in childhood is associated with increasing prevalence, severity and frequency of adverse events and complications. RD group of children are more common juvenile idiopathic arthritis (JIA), systemic lupus erythematosus (SLE) and juvenile scleroderma (JS).

Objectives: To investigate the clinical and immunological response and the role of infectious factors in the development of RD in children.

Methods: 60 patients with RD were examined in the 4th City Children’s Hospital in Minsk (31 children with JIA, 16 with JS, 13 with SLE). To identify organ pathology used general clinical research methods, including a complex of functional, instrumental and laboratory diagnostic tests, including the determination of levels of TNF-α and IFN-γ.

Results: 20 patients with JIA had an articular form, 11 children had a systemic form. 2 patients had diffuse form of systemic sclerosis (SS). 6 patients had a limited form of SS. 8 children had scleroderma. 8 children with JS, 13 children with JIA and all children with SLE had fever, weakness, weight loss at the onset of the disease. 3 children with JS, 12 children with JIA and 5 with SLE had lymphadenopathy. The most of children had in the blood IgG antibodies to herpes simplex virus (12 with JIA, 10 with JS, 6 with SLE), Epstein-Barr virus (8 with JIA, 3 with JS, 2 with SLE) and cytomegalovirus (6 with JIA, 3 with JS). IgG to Borrelia burgdorferi (17 with JIA, 9 with JS), to Chlamidia psittaci (10 with JIA). It can be assumed that these organisms can act as triggers for the development of this pathology. The same changes, characterized by a primary decrease CD8+-cells against a background of normal or elevated content of CD4+-cells been established in children with RD. Individual values of TNF-α in serum were elevated in 8 (88.9%) patients with JS, in 5 (62.5%) children with SLE and in 11 (84.6%) children with JIA. The positive relationship of TNF-α content with the content of CRP (P<0.04, P<0.01). The content of TNF-α was significantly higher in patients with high values of rheumatoid factor (RF) than in children with normal levels of RF (P<0.05). According to the results of the research content of IFN-γ in the serum of all patients with RD level of IFN-γ was significantly reduced compared with healthy children (P<0.05).

Conclusion: Revealed changes in the immune system of children with RD characterized by an imbalance of immunoregulatory subpopulations of T-lymphocytes, cytokine imbalance with pro-inflammatory and anti-inflammatory functions in conjunction with persistent viral and bacterial infection, are the basis for immunotherapy in treatment of children with RD.

Disclosure of interest: None declared.

P212
JIA-like in a boy with Ataxia-telangiectasia
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Pediatric Rheumatology 2014, 12(Suppl 1) P212

Introduction: Mechanisms of autoimmunity in primary immunodeficiencies (PID) are, in many situations, unclear. Despite being linked with many PIDs (namely humoral), juvenile idiopathic arthritis (JIA) has rarely been associated with DNA-repair disorders, such as Ataxia-telangiectasia (A-T).

Objectives: We report a case of JIA-like in a male patient with A-T.

Methods: A 3 year-old boy with A-T presented with pain and swelling of fourth metatarsophalangeal (MTP) joint of left foot. Six months later, this symptom persists and arthritis of the left knee was noted, so he was referred to rheumatology consultation.

Results: At first evaluation he had arthritis of both knees, left ankle and 4th MTF of the left foot and tenosynovitis of second finger of the right hand. His immune evaluation revealed an important CD4 naïf lymphopenia, abnormal proliferative responses to mitogens, skewed Vbeta repertoire and expanded gammadelta T cells, as well as conserved humoral response. Laboratory investigations showed erythrocyte sedimentation rate 25 mm/hr, C-reactive protein 14.5 mg/l, antinuclear antibodies positive (1/80), anti-cyclic citrullinated protein antibodies and rheumatoid factor were negative. A JIA-like disease was assumed, he started ibuprofen (30 mg/kg/day), and a chemical synovectomy with triamcinolone hexacetonide (TH) was performed (knees and ankle).

Ten months after diagnosis, knees and left ankle remain without active synovitis, but active 4th MTP of left foot and tenosynovitis of 2nd finger of right hand persists despite moderate improvement. Taking in account the underlying immune defect methotrexate was not an option and hydroxychloroquine (5 mg/kg/day) was started.

Conclusion: This case seems to be the first known pediatric patient with A-T who developed chronic, JIA-like disease. The management of these patients is particularly difficult because they are extremely susceptible to DNA damage and show an unusual susceptibility to viral infections (namely herpetic). These features are very important when considering the best therapeutic options for JIA-like disease.

Disclosure of interest: None declared.

P213
Identification of the best cut-off points and clinical signs specific for early recognition of macrophage activation syndrome in active systemic juvenile idiopathic arthritis
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Pediatric Rheumatology 2014, 12(Suppl 1) P213

Introduction: Macrophage activation syndrome (MAS) – is a severe life-threatening hematological condition, mostly complicated systemic juvenile idiopathic arthritis (SJIA). Early detection of MAS can lead to appropriate therapeutic interventions and change the outcomes. There are no strict criteria for early MAS detection in SJIA. Currently applied MAS criteria can determine only advanced stage of MAS, which lead to delay diagnosis, late start of specific treatment and associated with poor outcomes. There are several sets of preliminary criteria of MAS in SJIA.

Objectives: The purpose of our study was to detect early clinical and laboratory signs able to discriminate macrophage activation syndrome (MAS) from active systemic juvenile idiopathic arthritis (SJIA) without MAS.

Methods: Our retrospective study was based on reviewing the medical charts of the children, admitted to the rheumatology department with active SJIA and definite MAS (n=18) and without MAS (n=40). We evaluated the data related to SJIA and MAS at the moment of the patient’s admission. If the patient had signs of MAS since admission or developed definite MAS later during this flare he was referred to the main group. The children, who did not have MAS during the flare episode and did not have MAS in the past medical history, were in the control group. We calculated the cut-off points for MAS parameters, performed the analysis of sensitivity and specificity, identified the predictors and provided the preliminary diagnostic rule through “the number of criteria present” approach.

Results: The clinical signs relevant to MAS in SJIA: oligoarticular disease course (OR=5.6), splenomegaly (OR=67.6), hemorrhages (OR=33.0), respiratory failure (OR=11.3). The involvement of wrist (OR=0.2), MCP (OR=0.1) and PIP joints (OR=0.1) were protective against MAS development. The best cut-offs for laboratory parameters were PLTs≤211.10^11/l, WBCs<5.910^11/l, AST≥59.7 U/L, LDH>882 U/L, albumin<29 g/dl, fibrinogen<400 μg/l, α1-antitrypsin.<1.8 g/l, proteinuria. The laboratory
variables were more precise in the discrimination of early MAS than clinical: any 3 or more laboratorial criteria provided the highest specificity (1.0) and sensitivity (1.0) and OR = 2997.

Conclusion: We detected clinical and laboratorial markers and created preliminary diagnostic (laboratorial) guidelines for early discrimination of MAS in active SJIA.

Disclosure of interest: None declared.

P214

Macrophage activation syndrome during treatment with biological therapy in patients with systemic juvenile idiopathic arthritis

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Pediatric Rheumatology 2014, 12(Suppl 1):P214

Introduction: Macrophage activation syndrome (MAS) is a severe complication of autoimmune diseases. It is more often associated with Systemic Juvenile Idiopathic Arthritis (SJIA). It is difficult to distinguish the MAS from a flare of SJIA, infection or medicinal side effects. The MAS can occur during a flare, an infection, a change in the medication or as a side effect of the treatment administered for the treatment of SJIA. Paradoxically have been reported MAS cases in patients with SJIA treated with anti IL-1 or anti IL-6R.

Objectives: We report two cases of SJIA who developed MAS during the treatment with biological therapy.

Methods: Revision of two cases of MAS associated with SJIA treated with biological therapy in our clinic.

Results: Case1: Girl diagnosed at 9 years of SJIA, treated with Prednison and then MTX for persistent arthritis. A few years later, Anakinra treatment is started for persistent joint activity despite MTX, suspended after 5 weeks of treatment for suspected unconfirmed septic arthritis, treated with antibiotics and anti-inflammatory. A month after the resolution of the infectious process it was restart Anakinra, detecting eight days later deterioration of liver function and subsequent development of a analytical and clinically symptoms compatible with MAS. The clinical picture improved gradually after initiation of cyclosporine and high dose of prednison, achieving complete remission. Currently treated with Tocilizumab and with good clinical outcome, without new MAS episode.

Case2: Patient diagnosed of SJIA according to ILAR criteria at 2 years of age, debutting with typically clinical, laboratory and histological MAS, coinciding with very high disease activity. At 4 years of age it is initiated Etanercept that is suspended 1 year later for ineffectiveness. At age 8 he start Anakinra with good clinical response, that is maintained up to 14 years when it is suspended for clinical remission and local side effects (pain). Six months after the suspension he presents a new flare with new joint and systemic activity that is treated with Tocilizumab alone, without Prednisone. After the second infusion of Tocilizumab he presents upper respiratory infection, treated with Amoxicillin and anti-inflammatory treatment. Several days later he is hospitalized with clinical and laboratory tests compatible with MAS. The bone marrow biopsy confirms the presence of hemofagocytosis. The microbiological tests detected recent Epstein Barr Virus infection. It was initiated treatment with Cyclosporine iv Methylprednisolone with resolution of symptoms.

Conclusion: To our knowledge, there are reported a few cases of MAS associated with SJIA treated with biological therapy in our clinic.

Disclosure of interest: None declared.

P215

Effect of listeriolysin O (LLO) secreted by listeria monocytogenes on apoptosis of macrophages derived from patients with macrophage activation syndrome- in vitro

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Pediatric Rheumatology 2014, 12(Suppl 1):P215

Introduction: The term of macrophage activation syndrome (MAS) refers to a condition caused by excessive activation and expansion of T lymphocytes and macrophagic histiocytes that exhibit hemophagocytic activity. The expansion of these cells also leads to a massive systemic inflammatory response associated with pancytopenia, liver dysfunction, and coagulopathy consistent by disseminated intravascular coagulation (DIC). MAS has been reported in association with almost any rheumatic disease and most common in systemic onset JIA. However, the pathological mechanisms of MAS are not fully understood.

Objectives: In clinically similar primary HLH, the uncontrolled proliferation of T cells and macrophages has been linked to decreased natural killer (NK) cell and cytotoxic T cell function, often due to mutations in the gene encoding perforin. Deficient cytotoxic function lead to inefficient apoptosis and overactivated macrophages. Because high doses of LLO are known to cause cell death by necrosis or apoptosis, we decided to evaluate the effect of LLO on apoptosis of macrophages derived from patients with macrophage activation syndrome in vitro.

Methods: Blood from MAS patients and healthy donors was collected in Falcon tubes containing EDTA at 2 mM final concentration and incubated with enrichment antibody cocktail (50 μl per ml of whole blood) at room temperature for 20 minutes. Cells were then separated by density gradient using Ficoll-Paque™ PLUS (GE Healthcare). Platelets present in the enriched monocyte fraction were discarded by 3 washing steps in PBS, 2% FBS. Finally, monocytes were seeded in RPMI 10% FBS, 4 mM L-Glutamine with Pen/Strep at a concentration of 5×10^6 cells/ml in 12-well tissue culture treated plates for 6 days. The effects of various concentration of LLO (10%, 25%, 50%, 75% and more) were evaluated on apoptosis of macrophages in both groups.

Results: By using LLO less than 75%, there were no apoptosis in both normal and patients groups. However, 50% of macrophages of healthy donors and 82% of MAS patients showed apoptosis by LLO 75% and more.

Conclusion: High concentrated LLO may induce significant apoptosis in macrophages derived from patients with Macrophage Activation syndrome in vitro.

Disclosure of interest: None declared.

P216

Macrophage activation syndrome in a newborn infant born to a untreated mother with adult onset still disease

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Pediatric Rheumatology 2014, 12(Suppl 1):P216

Introduction: In neonatal lupus, macrophage activation syndrome (MAS) is very rare. Now, we reported a newborn infant with MAS born from a untreated mother with adult onset Still disease.

Objectives: In infant born from a mother with autoimmune disease, clinical manifestations of neonatal MAS were similar with neonatal sepsis. We have to consider neonatal MAS from a mother with autoimmune disease.

Methods: We reported a newborn infant with macrophage activation syndrome (MAS) born from a mother with positive anti-nuclear (ANA) and anti-SSA/Ro antibodies. The 2,500 g girl was born at 37 th weeks of gestation in good condition. Mother had been diagnosed with adult onset Still disease.
Macrophyage activation syndrome in children with systemic juvenile idiopathic arthritis: a retrospective analysis on 7 patients

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Pediatric Rheumatology 2014, 12(Suppl 1):P218

Introduction: macrophage activation syndrome (MAS) is life-threatening complication of rheumatic diseases and is most frequent seen in systemic juvenile idiopathic arthritis (sJIA). Prompt recognition and immediate therapy is life saving.

Objectives: to review clinical and laboratory data of MAS in 7 children with sJIA.

Methods: Clinical and laboratory data of 7 patients with MAS, treated in our hospital from January 2008 to December 2013, were analyzed retrospectively.

Results: Seven children (4 females, 3 males) were studied. Two children had incomplete MAS. The underlying disease was not identified in one child. MAS developed during the course of underlying disease (sJIA) in three children. Clinical manifestations at diagnosis included high persistent fever (7), skin rash (6), hepatosplenomegaly (7), lymphadenopathy (6), hemorrhages (5) and central nervous system dysfunction (6). Laboratory data included: high ferritin>10 000 (7), cytopenia (7), abnormal liver function tests (7), hypoalbuminaemia (7), hypertriglyceridaemia (5), coagulopathy (5), decreased erythrocyte sedimentation rate (5). Macrophage hemophagocytosis were found in 4 bone marrow aspiration. Rota virus was isolated in stool in 3 children. MAS was recurrent in two children (perforin gene done, negative). Six children responded on immunosuppressive therapy and are doing well, one child died.

Conclusion: MAS is rare but serious complication of systemic juvenile idiopathic arthritis in children. It is important to keep in mind suddenly clinical and laboratory disturbances in children with JIA, to recognize and immediate treat MAS in order to decrease mortality.

Disclosure of interest: None declared.

P219

Recurrent macrophage activation syndrome since toddler age in a patient with HLA B27 positive juvenile ankylosing spondylitis

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Pediatric Rheumatology 2014, 12(Suppl 1):P219

Introduction: Recurrent macrophage activation syndrome (MAS) is very rare. Recurrent MAS should be considered secondary cause including autoimmune disease. We experienced recurrent MAS since toddler age without definite etiologies. We reported a case of recurrent MAS in 16 year-old boy with HLA B27 positive juvenile ankylosing spondylitis.

Objectives: Recurrent MAS since toddler age is considered secondary autoimmune disease.

Methods: A 16-year-old boy was transferred from the department of surgery due to remittent fever with pancytopenia and splenomegaly despite improvement of septic shock after intravenous immunoglobulin (IVIG) and antithrombin III. He had received fístulectomy with colostomy because of intractable perianal abscess 2 months previously. He had been diagnosed with hemophagocytic lymphohistiocytosis (HLH) according to HLH 1994 guideline at 3 years of age and had been treated with IVIG. HLH recurred 3 years later, and he was treated according to HLH 2004 protocol for 8 weeks, and remained symptom free without maintenance therapy. He relapsed again at ages 7 and 8, but we were unable to identify any causes. He received maintenance steroid treatment for 2 years after the 4th attack. He remained symptom free until the development of back pain and...
right ankle joint pain with swelling at 15 years of age. He was diagnosed with juvenile ankylosing spondylitis compatible with bilateral active sacroiliitis and positive HLA B27. He received naproxen with methotrexate, but showed symptom aggravation. He showed improvement after Etanercept, but suddenly developed intracranial abscess.

Results: His laboratory data showed white blood cell count 1,240/µL, platelet 44,000/µL, ferritin 2,707ng/mL, triglyceride 343 mg/dL, aspartate aminotransferase 238 IU/L, alanine aminotransferase 145 IU/L, and fibrinogen 96 mg/dL. Bone marrow biopsy showed histiocytic hyperplasia with hemophagocytosis. There was no serologic evidence of any viral infection. He was treated with naproxen only, and improved without any other immunomodulatory medication. His laboratory data returned to near normal range within 4 weeks.

Conclusion: In our case, underlying autoimmune disease should be considered as the cause of recurrent HLH in a young patient after familial HLH has been excluded.

Disclosure of interest: None declared.

P220
Macrophage activation syndrome (MAS) in different pediatric rheumatic disease
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Pediatric Rheumatology 2014, 12(Suppl 1):P220

Introduction: Macrophage activation syndrome (MAS) is a life-threatening complication of chronic rheumatic disease in childhood.

Objectives: We aim to evaluate MAS findings and outcomes that differ according to disease in childhood.

Methods: We obtain 11 rheumatic patients followed in two different pediatric rheumatology units (Erciyes University and Ege University) who presented with MAS. We report their clinical and laboratory findings, therapies and outcomes.

Results: The primary diagnoses of the patients included in the study, respectively: systemic juvenile idiopathic arthritis (n=5), Systemic Lupus Erythematosus (n=2), juvenile dermatomyositis (n=2), a neonatal onset multisystem inflammatory disease (NOMID) and a microscopic polyarthritis nodosa. The mean age of the patients was 9.9 years old (1-14), and male to female ratio was 3:8. The mean duration of underlying disease was 6 months (1-24 months) at the diagnosis of MAS. We found MAS due to infection in four patients, while used medicine in a patient. MAS were developed spontaneously in 6 patients. The clinical manifestations of MAS included fever 7 (63.6%), mucosal bleeding 6 (54.5%), neurologic involvement 4 (36.4%) and hepatomegaly 6 (54.5%). We found thrombocytopenia in 9 (81.8%), leucopenia in 5 (45.5 %), increased AST in 7 (63.6%), hypofibrinogenemia in 6 (54.5%), increased ferritin in 11 (100%), decreased ESR in 4 (36.4%) and increased triglyceride in 10 (90.9%) patients. We investigated bone marrow in all patients, and hemophagocytosis were determined in 8 (72.7%). The medications were pulse methylprednisolone 6 (54.5%), intravenous immunoglobulin 8 (72.7%), plasma exchange 5 (45.5%), cyclosporine 6 (54.5%), dexamethasone 1 (9.1%), etoposide 1 (9.1%). The prognosis of patients were recovery 8 (72.7%), and exitus 3 (27.3%).

Conclusion: In conclusion, MAS can be developed in various pediatric rheumatologic disease and fatal. Prompt recognition and timely treatment can result good outcomes.

Disclosure of interest: None declared.

P222
Features of Japanese juvenile spondyloarthrits patients in our hospital
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Pediatric Rheumatology 2014, 12(Suppl 1):P222

Introduction: Spondyloarthritis (SpA) is thought to be very rare in Japan, because possession rate of HLA-B27 in healthy people is 0.4% and it is significantly lower than that of other countries (5%). This makes it difficult for Japanese physicians to diagnose SpA early. Since 10-20% of SpA patients experience symptoms in their childhood, it is very important to distinguish them from other chronic arthritis patients for pediatric rheumatologists.

Objectives: We investigated the actual situation among Japanese patients with chronic arthritis and the features of juvenile SpA patients in our hospital.

Methods: We checked age at disease onset, age at diagnosis, sex, hight SD, HLA and treatment.

Results: There are eleven SpA cases (14.4% of children with chronic arthritis in our hospital), containing 5 axial SpA and 6 peripheral SpA cases. One psoriatic arthritis patient and one SAPHO patient are included in peripheral SpA. Male to female is 6 to 5. Age at disease onset ranges from 1.5 to 13.6 years old (median: 8.0 years old). The duration from disease onset to diagnosed age ranges from 0.6 to 11 years (median: 1.8 years).

Disclosure of interest: None declared.

P221
Macrophage activation syndrome in a patient with juvenile systemic lupus erythematosus
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Pediatric Rheumatology 2014, 12(Suppl 1):P221

Introduction: Macrophage activation syndrome (MAS) is a rare but life threatening complication of infectious, neoplastic and rheumatic diseases. Clinically, patients usually have high fever, hepatosplenomegaly, lymphadenopathy and neurologic symptoms. In laboratory results pathognomonic are pancytopenia, decline in the value of sedimentation rate (ESR), increased levels of ferritin and coagulation abnormalities.

Objectives: The aim of the study is to present the case of Macrophage Activation Syndrome in a Patient With Juvenile Systemic Lupus Erythematosus.

Methods: The clinical course and results of the diagnostic tests were analyzed on the basis of the patient’s medical history.

Results: 16-year-old male patient 8 months prior to admission presented fatigue, weakness, weight loss and facial erythema with edema. On admission, the patient was confused, he had trembling extremeties, scanning speech and a fever of 38.8 °C. Physical exam revealed muscle atrophy, lymphadenopathy, oral ulcers, ecchymoses, palmar erythema and malar rash. An infectious process was ruled out with viral panel and bacterial cultures. The blood count showed pancytopenia, increased ESR, AST and ASP, hypocomplementemia, hypertiriglyceridemia and hyperferritirinemia. Subsequently the patient presented antinuclear antibody in titer 1:20480 with a speckled pattern, positive anti-Sm and positive anti-ribosomal P protein antibodies. Bone marrow biopsy showed no changes typical for MAS. With this data the diagnosis of SLE was reached and treatment with pulses of glucocorticoids and an IVIG was started. During the next three days of hospitalization laboratory results were constantly getting worse despite the treatment and new clinical symptoms occurred (neurologic symptoms and bleeding from mucous membranes). Based on clinical manifestation and results of laboratory tests the patient was diagnosed with Macrophage Activation Syndrome secondary to SLE and the treatment with cyclosporine was added. Despite the clinical and laboratory tests improvement in the next five days the patient had a seizure attack followed by a cardiac arrest and after successful reanimation he was transferred to an intensive care unit. After two weeks the patient was again admitted to the clinic, he was conscious and respiratory stable although there was no logical contact, no reflexes in upper limbs, weak reflexes in lower limbs, profound muscle atrophy and hydrocephalus. Blood cell counts, markers of inflammation and other abnormalities in biochemical returned to normal.

Conclusion: The diagnosis of MAS secondary to SLE is difficult due to common characteristics such as fever, pancytopenia, lymphadenopathy, neurological symptoms and skin manifestations. Careful assessment of laboratory results especially pancytopenia, hyperferritirinemia and hypofibrinogenemia is crucial and leads to a quick and accurate diagnosis which is very important as MAS is considered to be a severe complication which puts patient’s life at risk.

Disclosure of interest: None declared.
HLA-B27 possession rate is 30% and much higher than that of Japanese population. Possession rates of HLA-A2 and A24 are 50% respectively and also higher than those (25% respectively). Two peripheral SpA patients have family history. All three axial SpA patients with longer duration between onset and diagnosis than 1 year accompanied short stature (from -2.4 to -5.5 SD). All patients are treated with NSAIDs and nine patients are prescribed methotrexate (MTX). All five axial SpA patients need TNF inhibitors (etanercept for 2 cases and adalimumab for 3 cases) and three peripheral SpA patients need TNF inhibitor (adalimumab) to control disease activity. Sulfasalazine is adopted in two peripheral cases. Prevalence of SpA was originally reported to be 0.0095% and be significantly low in Japan. However Fujita recently reported that it amounted to 0.2% in their population survey held at Wakayama prefecture and insisted that real prevalence of Japanese SpA would be almost same as other countries. Low degree of recognition for SpA among Japanese physicians and difference of genetic background might account for this discrepancy. Similarly, juvenile SpA patients are thought to be very rare in Japan. Takei reported that enthesis-related and psoriatic types among JIA amount to be 1.6%, based on data from national medical profit project for chronic pediatric diseases. Our data shows that juvenile SpA patients amount to 14.4% of children with chronic arthritis in our hospital and does not differ big from other countries. One reason for this result could be that our hospital is a well-known center for pediatric rheumatism with trained medical specialists and diagnostic accuracy is higher. HLA-B27 negative patients or peripheral SpA patients are generally diagnosed inadequately. The other reason is that patients without apparent joint involvement tend to be referred to our facilities, so there can be some statistic bias. However, it is interesting that there are some numbers of SpA patients in Japan, the country at where prevalence of HLA-B27 does not high.

Conclusion: We hope that survey on juvenile SpA advances since now and pathlogy of HLA-B27 negative patients will be disclosed all over the world.

Disclosure of interest: None declared.

P224
Juvenile idiopathic arthritis is a diagnosis of exclusion
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Introduction: Juvenile Idiopathic Arthritis (JIA) is classified as an acquired autoimmune inflammatory disease. Problems in applying all classification criteria include the necessity to exclude other diseases with similar symptoms. There are no laboratory markers for SJIA.

Objectives: To analyze cases with cancer diagnosis who were in rheumatology department in SCCH of RAMS.

Methods: 13 patients were included in the analysis. All Patients were directed (referred) to our clinic like patients who were suffered from JIA from 2004 to 2014 years. We analyzed time concomitant therapy, symptoms of diseases, cancer diagnosis, diagnostic methods which helped to exclude JIA.

Results: 11 patients were directed with systemic JIA and 2 - with olygoarthritus. All patients with “JIA” had criteria for diagnosis according ILAR classification. All patients with “systemic JIA” had fever, hepatosplenomegaly, generalized lymphadenopathy, arthralgia or arthritis, high level of CRP, ESR, anemia. Patients with “oligoarthritus” had mononarthritis. The diagnosis was made at the place of residence. 6 patients received immunodepressants (methotreaxate, cyclosporine), 8 patients – glucocorticoids, 1 – tocilizumab. Disease duration was from 2 to 9 months, the duration of hospitalization until the diagnosis was verified was from 1 to 7 days. We performed ultrasound, radiography, CT scan, MRI, bone marrow function, biopsy of lymph node, biopsy of bone. There were 4 patients with neuroblastoma, 2 – with lymphogranulomatosis, 4 - with leukemia, 1- with malignant lymphoma from patients with “SJIA”. There was 1 patient with malignant histiocytoma and 1 patient with glyoma from patients with “oligoarthritus”. Concomitant treatment made difficult to verify right diagnosis.

Conclusion: JIA is still a diagnosis of exclusion. We should use modern diagnostic procedures to establish right diagnosis and mustn’t give antirheumatic drugs except NSAID to our patients until the diagnosis is verified.

Disclosure of interest: None declared.

P225
Pneumocystis pneumonia in a child with soja
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Pediatric Rheumatology 2014, 12(Suppl 1) P225

Introduction: Pneumocystis jirovecii pneumonia (PCP) is opportunistic infection caused by Pneumocystis jirovecii. PCP occurs in patients with thoracic and gastrointestinal manifestations. In the pediatric age group the incidence of PCP is reported to be 1-6 per 100,000.

Objectives: To describe the case of a child with known soja allergy who developed PCP.

Methods: The case of a 5 year old girl with known soja allergy, who presented with fever, cough, malaise and anemia is described.

Results: The patient was born 6 months premature at 24 weeks of gestation and was transferred to our hospital at 2 months of age with respiratory distress. She developed bronchopulmonary dysplasia and bronchiolitis obliterans. She had no previous history of PCP. She was hospitalised in the Pediatric Intensive Care Unit with respiratory distress syndrome and sepsis. She was anticoagulated for 6 months due to a coagulation defect. She developed a petechial rash on admission. At bronchoscopy a granulomatous disease with necrotizing angitis was found. She was treated with methylprednisolone and switched to oral methylprednisolone at a dose of 1.5 mg/kg/day. She received inpatient treatment for 4 weeks and was discharged home on oral methylprednisolone at the same dose.

Conclusion: PCP is a rare condition and has been reported in children with cystic fibrosis and immunodeficiency. PCP in children is most commonly reported in association with immunosuppressive therapy. In children with documented PCP in our hospital, P. jirovecii has been isolated from BAL. There is no evidence of, or history for, atopy in children with PCP. However, the association of PCP and atopy is well described. PCP was not considered in the differential diagnosis of this patient. She was treated with inhaled steroids and inhaled bronchodilators. She was not treated with the appropriate combination of antifungal therapy and corticosteroids as described by the American Thoracic Society. The diagnosis of PCP in children with atopy is challenging. PCP should be considered in the differential diagnosis of children with atopy and respiratory distress. The patient described in this case report developed PCP shortly after anaphylaxis to soja.

Disclosure of interest: None declared.
Introduction: Pneumocystis pneumonia (PCP) is an opportunistic infection affecting patients with congenital or acquired immunodeficiency. In rheumatology, PCP is occasionally seen as a life threatening event complicating the course and treatment of a variety of diseases, especially vasculitides and systemic connective tissue disorders. 

Objectives: To show possible complications of the immunosuppressive treatment of systemic onset juvenile idiopathic arthritis (soJIA) and also demonstrate possible adverse effects and alternatives of antimicrobial treatment of PCP.

Methods: A case report of a girl with soJIA and Pneumocystis infection.

Results: A 6-year-old girl with soJIA treated with high doses of corticosteroids and cyclosporine for 6 months was sent to the Paediatric Rheumatology Centre at the Paediatric Department of the University Hospital Brno, Czech Republic. For lasting systemic symptoms (fever, rash, high inflammatory markers) and active knee arthritis the therapy with tocilizumab was initiated after discontinuation of cyclosporine. There was a history of repeated antibiotic and antifungal therapy for upper respiratory infections before starting the biological treatment. At the time of the first tocilizumab infusion, chest radiograph was negative, white blood cell count including neutrophils and lymphocytes was normal, the total IgG level was only slightly reduced. After the second dose of tocilizumab the corticosteroids could be tapered, but the girl presented with nonproductive cough and dyspnea. On the basis of typical symptoms, HRCT findings and highly positive PCR for Pneumocystis jiroveci in bronchoalveolar lavage the diagnosis of PCP was established and tocilizumab was discontinued. The first line PCP treatment with IV. trimethoprim-sulfamethoxazole (TMP-SMX) for 17 days was successful, but it was complicated by agranulocytosis requiring application of colony stimulating factors and antibiotic treatment for febrile neutropenia. Granulocyte count was promptly normalized but simultaneously significant hypogammaglobulinemia occurred with the absence of CD20+ and significant decrease of CD19+ lymphocytes in peripheral blood, while the counts of T lymphocytes including CD4+ were normal. Monthly substitution by intravenous immunoglobulins (IVIGs) was required for six months until sustained normalization of plasma immunoglobulins was achieved. Intravenous pentamidine every 4 weeks has been used in the secondary PCP prophylaxis. The dose of corticosteroids could be significantly decreased because of inactivity of soJIA for a long period of expressed secondary immunodeficiency. However, eight months after setting the diagnosis of PCP the soJIA flared, possibly in connection with the restitution of the immune response. The therapy with anakinra was started with good response enabling corticosteroid withdrawal within 5 months. Now, the girl is without any difficulties, there are no clinical or laboratory signs of inflammation, her serum immunoglobulin levels are normal as well as the number of T-lymphocytes, even the B-lymphocyte count is almost normal. Secondary PCP prophylaxis still continues.

Conclusion: Pneumocystis pneumonia in rheumatology should be considered particularly in patients with secondary immunodeficiency complicating the immunosuppressive and combined immunosuppressive therapy. However, no specific guidelines have been established for primary PCP prophylaxis in patients without HIV infection. PCP treatment with high doses of TMP-SMX may be associated with significant side effects such as agranulocytosis, which requires the use of second line drugs, for example pentamidine. Criteria for discontinuing the secondary PCP prophylaxis have also not been clearly defined and an individual approach should be used.

Disclosure of interest: None declared.

P227 Complicated systemic JIA with macrophage activation syndrome and pulmonary hypertension responsive to a anti IL-1: case report

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Pediatric Rheumatology 2014, 12(Suppl 1):P227

Introduction: Systemic juvenile idiopathic arthritis (SJIA) is characterized by fevers, rash, and chronic arthritis, and interleukin-1 (IL-1) and IL-6 inhibitors seems to be effective treatments. Pulmonary arterial hypertension (PAH) and macrophage activation syndrome (MAS) is a rare and serious condition which can be fatal. It is known that IL-1β plays a key role in the pathogenesis of MAS, therefore IL-1 inhibitor is considered particularly in patients with secondary immune system disorders and also in patients with the systemic onset juvenile idiopathic arthritis (SoJIA) and also demonstrate possible adverse effects and alternatives of antimicrobial treatment of PCP.

Methods: A case report of a girl with soJIA and Pneumocystis infection.

Results: A 6-year-old girl with soJIA treated with high doses of corticosteroids and cyclosporine for 6 months was sent to the Paediatric Rheumatology Centre at the Paediatric Department of the University Hospital Brno, Czech Republic. For lasting systemic symptoms (fever, rash, high inflammatory markers) and active knee arthritis the therapy with tocilizumab was initiated after discontinuation of cyclosporine. There was a history of repeated antibiotic and antifungal therapy for upper respiratory infections before starting the biological treatment. At the time of the first tocilizumab infusion, chest radiograph was negative, white blood cell count including neutrophils and lymphocytes was normal, the total IgG level was only slightly reduced. After the second dose of tocilizumab the corticosteroids could be tapered, but the girl presented with nonproductive cough and dyspnea. On the basis of typical symptoms, HRCT findings and highly positive PCR for Pneumocystis jiroveci in bronchoalveolar lavage the diagnosis of PCP was established and tocilizumab was discontinued. The first line PCP treatment with IV. trimethoprim-sulfamethoxazole (TMP-SMX) for 17 days was successful, but it was complicated by agranulocytosis requiring application of colony stimulating factors and antibiotic treatment for febrile neutropenia. Granulocyte count was promptly normalized but simultaneously significant hypogammaglobulinemia occurred with the absence of CD20+ and significant decrease of CD19+ lymphocytes in peripheral blood, while the counts of T lymphocytes including CD4+ were normal. Monthly substitution by intravenous immunoglobulins (IVIGs) was required for six months until sustained normalization of plasma immunoglobulins was achieved. Intravenous pentamidine every 4 weeks has been used in the secondary PCP prophylaxis. The dose of corticosteroids could be significantly decreased because of inactivity of soJIA for a long period of expressed secondary immunodeficiency. However, eight months after setting the diagnosis of PCP the soJIA flared, possibly in connection with the restitution of the immune response. The therapy with anakinra was started with good response enabling corticosteroid withdrawal within 5 months. Now, the girl is without any difficulties, there are no clinical or laboratory signs of inflammation, her serum immunoglobulin levels are normal as well as the number of T-lymphocytes, even the B-lymphocyte count is almost normal. Secondary PCP prophylaxis still continues.

Conclusion: Pneumocystis pneumonia in rheumatology should be considered particularly in patients with secondary immunodeficiency complicating the immunosuppressive and combined immunosuppressive therapy. However, no specific guidelines have been established for primary PCP prophylaxis in patients without HIV infection. PCP treatment with high doses of TMP-SMX may be associated with significant side effects such as agranulocytosis, which requires the use of second line drugs, for example pentamidine. Criteria for discontinuing the secondary PCP prophylaxis have also not been clearly defined and an individual approach should be used.

Disclosure of interest: None declared.

P227 Complicated systemic JIA with macrophage activation syndrome and pulmonary hypertension responsive to a anti IL-1: case report

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Pediatric Rheumatology 2014, 12(Suppl 1):P227

Introduction: Systemic juvenile idiopathic arthritis (SJIA) is characterized by fevers, rash, and chronic arthritis, and interleukin-1 (IL-1) and IL-6 inhibitors seems to be effective treatments. Pulmonary arterial hypertension (PAH) and macrophage activation syndrome (MAS), which is a unremittting fever, coagulopathy, pancytopenia, and multiple organ dysfunction. These complications can be fatal and may be the result of severe uncontrolled systemic disease activity or influenced by medication exposure.

Objectives: Describe a 7 year old girl with systemic JIA complicated with macrophage activation syndrome and pulmonary arterial hypertension refractory to numerous treatments, with good response to canakinumab, IL-1 inhibitor.

Methods: Female patient was diagnosed with systemic JIA at seven year old. At eight years, she was hospitalized with disease reactivation in use of cyclosporin and oral prednisone. An echocardiogram showed mild pericardial effusion and moderate PAH (69mmHg), ferritin:8.65mg/dL, triglycerides 428mg/dL, fever, splenomegaly and macrophage activity in bone marrow fulfilled the macrophage activation syndrome (MAS) criteria. Methylprednisolone pulse was started and echocardiographic control showed mild improvement. Anti IL-6 therapy tocolizumab - 8mg/kg was started every two weeks, total of 2 doses. Initially, there was clinical improvement and decrease in pulmonary artery pressure (PAP) to 38 mmHg. However, one week later, a new echocardiogram showed mild PH (44mmHg), new pericardial effusion and acute relapse of disease symptoms (fever, rash, adenopathy) and new MAS (ferritin 30.000mg/dL, triglycerides 500mg/dL). The patient underwent a new pulse methylprednisolone and oral prednisolone resulting in clinical improvement and after the second dose of tocilizumab, high transaminases levels were observed indicating anti-IL-6 suspension. After one month, she had a new clinical decompensation with signs of heart failure requiring intensive care. Echocardiogram showed PAP of 55mmHg. A new methylprednisolone pulse therapy was prescribed. After clinical stabilization, received the first dose of IL-1 inhibitor. Second dose of Canakinumab was performed 4 weeks later, and, at this moment PAP was 48mmHg in absence of fever, rash, arthritis and reduced hepatosplenomegaly.

Results: In the present case, the patient developed MAS and pulmonary hypertension and had important clinical improvement with anti IL-1 therapy, MAS is thought to be an acquired form of hemophagocytic
lymphohistiocytosis, the real incidence in systemic JIA is not known, but studies show that there are histological changes in the bone marrow, even without clinical symptoms in many patients. HP is a rare condition where immunosuppressants and biological agents may be involved. Diagnosis is difficult, but we should have protocols to search it.

Conclusion: Systemic JIA can be complicated, among others, by MAS and pulmonary arterial hypertension (PAH). Further prospective studies are needed to determine the real factors associated with the development of pulmonary complications.


P228

Posterior reversible encephalopathy syndrome complicating macrophage activation syndrome in a patient with systemic juvenile idiopathic arthritis

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Pediatric Rheumatology 2014, 12(Suppl 1):P228

Introduction: Posterior reversible encephalopathy syndrome (PRES) is a distinct clinical entity presenting with a constellation of neurological symptoms and characteristic neuroradiographic findings of posterior cerebral white matter edema. In adults, PRES has been associated with a variety of conditions and predisposing factors, including acute hypertension, preeclampsia or eclampsia, renal disease, sepsis, and exposure to immunosuppressants. The syndrome has been reported less frequently in children, with only one publication reporting the association of PRES with macrophage activation syndrome (MAS) in a patient with systemic onset juvenile idiopathic arthritis (SoJIA).

Objectives: We report a case of newly diagnosed SoJIA complicated with MAS during the abatement of which developed PRES.

Methods: Case report.

Results: A newly diagnosed 8-year-old boy with SoJIA left the hospital on prednisolone (1 mg/kg p.o.), in order to re-examined after 10 days. At that time, he appeared with hemoglobin 104 g/L, leukocytes 17.44x10⁹/L, platelets 406x10⁹/L, ESR 120 mm and serum ferritin 1050 µg/L. One week later and despite his gradual clinical improvement, he re-admitted because he presented persistent high grade fever and rash. On re-admission, laboratory results have shown hemoglobin 96 g/L, leukocytes 5.60x10⁹/L, platelets 206x10⁹/L, ESR 60 mm, serum ferritin 7500 µg/L; fibrinogen 1.23 g/L; LDH 1526 U/L and triglycerides 582 mg/dL. With the tentative diagnosis of MAS, the patient was administered methylprednisolone pulses and cyclosporine (75 mg x 2 / day). His clinical picture and laboratory findings were rapidly improved but, on the fifth day from the initiation of treatment, elevation the blood pressure was appeared and tapering of prednisolone and cyclosporine was started. The day after, the patient presented tonic-clonic seizures that necessitated his admission in the intensive care unit for two days. Axial T2-w and FLAIR MRI images demonstrated characteristic findings of PRES, bilateral and symmetrical high signal intensity lesions involving cortical and subcortical areas of the posterior part of the hemispheres. Prednisolone and cyclosporine discontinued, and the neurological syndrome was completely controlled with antihypertensives and antiepileptics. Two weeks later the patient left the hospital on anakinra, prednisolone (1 mg/kg p.o.) and antiepileptics. After six months, prednisolone has been discontinued and the patient is free of inflammatory symptoms but any attempt to discontinue antiepileptics leads to the relapse of seizures. However, follow up MRI showed complete resolution of previously noted abnormal signal of PRES lesions.

Conclusion: The case reported highlights unusual evolution of congenital syphilis, despite conventional treatment of the disease in the neonatal period, the child presented clinical signs of infection later manifested as recurrent fever and severe anemia. Therefore, a past history of syphilis should always be valued.

Disclosure of interest: None declared.

P229

Recurrent fever, arthralgia and asymmetric genu varum of unexpected etiology

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Pediatric Rheumatology 2014, 12(Suppl 1):P229

Introduction: Congenital syphilis is still a public health issue worldwide. Beyond the neonatal period, clinical findings may be subtle and nonspecific. We report an unusual case of congenital syphilis with recurrent fever, knee pain and severe anemia in a 28-month-old boy, despite standard penicillin treatment early in life.

Congenital syphilis should be considered throughout early childhood, especially if past or familiar medical story of syphilis.

Objectives: Not applicable

Methods: Not applicable

Results: Case Report: A 28-month-old boy was referred to our pediatric rheumatology department for suspected Still’s disease. He had a 4-month history of recurrent fever, intermittent knee pain (especially at the onset of gait), normocytic normochromic anemia (hemoglobin 8.8 g/dL) and sedimentation rate 120 mm/hour. An asymmetric genu varum was the only finding on physical examination.

This child had a previous story of congenital syphilis diagnosed and treated in the neonatal period. At this time he was abandoned by his mother, and then was institutionalized until 4 months when he was adopted. At the age of 8 months a painful right parasternal mass was noted. Histology revealed “nonspecific inflammatory reaction” and resolution occurred in one month.

The Venereal Disease Research Laboratory (VDRL) test was 1:2 and T. pallidum hemagglutination (TPHA) test was reactive with a titer of 1:10.240. Posterior serological evaluations revealed a negative VDRL and declining of TPHA until 1:2560 in the second year of life. At 20 month-old he was referred to the orthopedics hospital department because of a bilateral genu varum. A “Blount’s disease” was diagnosed.

Given the past medical history of congenital syphilis, probably parasternal gummata at 8 month-old with TPHA titer of 10.240, penicillin treatment was started and maintained for 14 days. The treatment was successful and he became asymptomatic.

Conclusion: The case reported highlights unusual evolution of congenital syphilis, despite conventional treatment of the disease in the neonatal period, the child presented clinical signs of infection later manifested as recurrent fever and severe anemia. Therefore, a past history of syphilis should always be valued.

Disclosure of interest: None declared.

P230

A case of macrophage activation syndrome in a child with systemic juvenile idiopathic arthritis

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Pediatric Rheumatology 2014, 12(Suppl 1):P230

Introduction: Systemic type of juvenile idiopathic arthritis (JIA) is highly active autoimmune process. One of its severe complications is macrophage activation syndrome, seriously influenced the outcome of the disease. The aim of the report is to reveal the macrophage activation syndrome during the onset of JIA, before treatment.

Objectives: A patient 1.3 years old, in the onset of JIA.

Methods: All routine analyses, including the blood test, biochemical serum determination of antinuclear antibodies to autoimmune hepatitis, markers of viral hepatitis, antibodies to Epstein-Barr virus, CMV, herpes infection, toxoplasmosis, chlamydia, mycoplasmosis, HIV were performed. Instrumental methods included: chest radiography, tomography t, echocardiography, electrocardiography.
P231

Rare oncological diagnosis presenting as ‘rheumatic fever’

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Introduction: CML (Chronic myeloid leukemia) is a myeloproliferative disorder, with dysregulated proliferation and differentiation of granulocytes. CML is rare during childhood, incidence of 1 in 1,000,000 and accounts for less than 5% of childhood leukemia. There are 3 different stages: chronic phase, accelerated phase and blast phase.

Objectives: Discuss a case of CML, which presented as possible rheumatic fever.

Methods: Case report and review of literature.

Results: Case report: A 13-year-old Caucasian boy, while on a skiing holiday in Switzerland, developed fever, pharyngitis, erythematous skin lumps and arthralgia; investigations revealed significantly raised Anti-streptolysin-O titres. His blood count showed a transient neutrophilia and thrombocytosis. General practitioner diagnosed him with streptococcal infection and treated him with oral Penicillin; he made full recovery in five days and returned to the UK. However he continued to have episodes of fever, arthralgia associated with raised inflammatory markers for the next 5 weeks. These episodes seem to occur every 10 days, lasting 4 – 5 days. In between these episodes he would make full recovery. He was continuing oral Penicillin prophylaxis and Anti-streptolysin-O titres were improving. Acute rheumatic fever was one of the differentials, however towards the end of ‘febrile episode’, he became neutropenic- which is not a recognised feature of acute rheumatic fever. Detailed investigations including: screen for common and rare bacterial and viral pathogens, biochemical profile, whole body isotope bone scan and urinary catecholamines, were within normal limits. Abdominal ultrasound revealed mild splenomegaly. Due to the neutropenia a bone marrow examination was performed, microscopy showed normal cellularity and maturation of the haematopoietic cells. Routine cutrogenic analysis was performed which demonstrated the classical Philadelphia chromosome t(9;22) BCR-ABL, thus supporting diagnosis of Chronic Myeloid Leukemia (CML). At presentation he was in the chronic phase.

Discussion: In 2 recent case series of childhood CML, mean age at presentation was 11.5 years and 16 years. Chronic phase of CML is the most common type, seen in 92% childhood CML patients at presentation. Our patient presented with intermittent/periodic febrile episodes and neutropenia; these features were not described among a large case series of 430 CML patients (adult and childhood). In a childhood CML series, 2/13 children had fever as a presenting feature, the authors have not elaborated if this was periodic.

Conclusion: To the best of our knowledge, intermittent/ periodic febrile episodes have not been described before as presenting features of childhood CML.

Bone marrow examination is highlighted as an important examination to consider in children presenting with pyrexias of unknown origin especially if associated with haematological abnormalities.

Disclosure of interest: None declared.
left ankle; functional limitation of both elbows; Hb 10.8 mg/dl; ESR 95 mm/h; CRP 11 mg/dl. Then, in October 2012 the anti-TNF therapy was discontinued and replaced with canakinumab (150 mg/day subcutaneously), initially effective, but suspended in May 2014 due to the refractory disease. Currently, the patient has acute arthrosynovitis of both knees even though they have already been infiltrated with triamcinolone acetonide, a functional limitation of the left hip and an inflammatory anemia (Hb 10.3 g/dl; VES 75 mm/h; CRP 8 mg/dl; SAA 99 mg/l). Her current treatment is prednisone (0.4 mg/kg/day) associated with indomethacin and MTX.

Conclusion: Considering the efficacy of anti-IL-6 blockade described in s-JIA, we’re going to start the intravenous infusion of Tocilizumab (8 mg/kg over 60 minutes).

Disclosure of interest: None declared.

P233
Non-infectious pediatric uveitis in a single French tertiary center
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Pediatric Rheumatology 2014, 12(Suppl 1):P233

Introduction: Pediatric uveitis is a blinding disease in 15-20% of cases. Juvenile idiopathic arthritis (JIA) is the most common disease associated with uveitis (JIAU). Biologics have changed the treatment of uveitis in particular JIAU. Objectives: To describe epidemiological, clinical, ophthalmologic and therapeutic characteristics of non infectious pediatric uveitis followed in our center. Methods: We retrospectively collected data between 2004 and 2013 for children under 16 years of age followed for non-infectious uveitis in the Department of Ophthalmology and in Pediatric Rheumatology Unit of the Hospital of Tours. Results: Of 32 children included there were 62% of females and the mean age at diagnosis was 7.7 ± 3.4 years and 6.5 ± 3.8 years for JIAU. Ophthalmologic complications were present at the diagnosis in 72% of patients. Uveitis was unilateral in 56% of cases and anterior in 75% of cases. At the time of the last follow-up 41% were idiopathic uveits and 41% JIAU. The number of inflammatory cells in the uvea (Tyndall) was improved in 50% of cases and stabilized in 50% of cases. One third of patients had presented new ophthalmologic complications. Uveitis was recurrent in 84% of cases and 75% of uveits had relapsed at least once. Local corticosteroid was always used in combination with systemic treatment. Corticotherapy was used in 41% of cases, and associated to DMARDS (methotrexate) in 19% of patients. Anti-TNFx (adalimumab) was used in 42% of patients and 34% of JIAU. An improvement in the visual acuity of our cohort was found (4/10 initially versus 6.3/10). In the subgroup of JIAU (13 patients) visual acuity was modified from 4/10 to 5/10 and 23% patients used the systemic association; corticosteroid and methotrexate, 3 patients relapsed under adalimumab. Conclusion: The risk of visual impairment in child uveitis is important. JIAU was the underlying systemic disease in 23 patients. One patient was diagnosed with Cogan’s syndrome, in 22 patients no underlying systemic disease was found. ANA positivity was found in 24 out of 46 patients. In 40 patients, MTX use had been sufficiently long for analysis. In 28 of these patients, disease remission was achieved in (median) 26.7 (range 2.5-146) months. Patients treated with a lower maximum dose of MTX had a longer time to disease remission (median 26.1, range 2.8 – 147.1 months) than patients treated with a higher dose of MTX (median 19.7, range 2.5 – 29.8 months) (p-value 0.02). No statistical significant differences were found in steroid-sparing effect, cumulative dose MTX to disease remission and side effects.

Conclusion: In this retrospective study on pediatric auto-immune uveitis, high dose MTX seems to result in a quicker disease remission.

Disclosure of interest: None declared.

P234
Efficacy of high dose methotrexate in pediatric auto-immune uveitis
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Pediatric Rheumatology 2014, 12(Suppl 1):P234

Introduction: Efficacy of high dose methotrexate in pediatric auto-immune uveitis. Objectives: To compare the efficacy of high dose (±15mg/m²/week) Methotrexate (MTX) versus low dose (<15mg/m²/week) MTX in relation to time to disease remission. Methods: Retrospective analysis of 46 pediatric patients with uveitis with or without underlying systemic disease treated with MTX at the University Medical Center Groningen (The Netherlands) between 1993 and 2013. The SUN (Standardization of Uveitis Nomenclature) workinggroup criteria were used for endpoints. Other endpoints included visual outcome, steroid-sparing effect, cumulative dose MTX to disease remission and side effects. Results: Mean age at onset of uveitis was 6.6 years (1.7 – 18). Male:female ratio was 24/22. In 36 patients, bilateral disease was found. Most patients (n=27) had anterior uveitis, followed by intermediate (n=9), pan (n=8) and posterior uveitis (n=2). Ocular complications related to the uveitis were found in 36 patients. Cataract surgery was performed in 28 patients and glaucoma surgery in 20 patients. JIA was the underlying systemic disease in 23 patients. One patient was diagnosed with Cogan’s syndrome, in 22 patients no underlying systemic disease was found. ANA positivity was found in 24 out of 46 patients. In 40 patients, MTX use had been sufficiently long for analysis. In 28 of these patients, disease remission was achieved in (median) 26.7 (range 2.5-146) months. Patients treated with a lower maximum dose of MTX had a longer time to disease remission (median 26.1, range 2.8 – 147.1 months) than patients treated with a higher dose of MTX (median 19.7, range 2.5 – 29.8 months) (p-value 0.02). No statistical significant differences were found in steroid-sparing effect, cumulative dose MTX to disease remission and side effects.

Conclusion: The high dose MTX seems to result in a quicker disease remission.

Disclosure of interest: None declared.

P235
Ocular expressions of children behcet disease
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Pediatric Rheumatology 2014, 12(Suppl 1):P235

Introduction: Behcet disease is a systemic vasculitis, the diagnosis is difficult in child. The most frequent ocular signs in child is panuveitis with retinian vasculritis. Objectives: The aim of this study is to clarify the frequency and clinical characteristics of ocular attack in child behcet disease in our context. Methods: It’s a retrospective study concerning 13 cases of child behcet disease with ocular signs in service of pediatrie 4 and paediatric rheumatology consultation in Rabat children hospital during 5 years (April 2007- January 2013). We have studied the onset of symptoms, ocular anatomo clinical form, complications and therapeutic implications. Results: Our patients were 4 to 15 years old (average 10,78 years ). Ocular signs were found at 13 cases among 19 followed for behcet disease (68,4%). The attack was bilateral in 11 cases (84%). In 2 cases, ocular attack was inaugural. The uveitis was total in 3 patients, anterior in 3 others cases, intermediate in 2 cases, severe in one case. Papilar oedema was noted in 2 cases, retinian vasculitis in 3 cases. 4 patients had ocular complications: 2 optic atrophie, 1 cataract and 1 macular oedema. Conclusion: Ocular signs in Behcet disease was found in 10 to 52,5% in pediatric series. They are often bilateral. Panuveitis and anterior uveitis are the most frequent signs followed in our serie by intermediate uveitis. This finding concord with a tunisian serie. Visual prognosis is threaten by ocular complications which are precocious in child : cataract, macula oedema, optic atrophie indeed blindness. Disclosure of interest: None declared.

P236
Effects of anti-TNF therapy on ophthalmological complications in children with rheumatic diseases
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Pediatric Rheumatology 2014, 12(Suppl 1):P236

Introduction: Biologics started a new era in treatment of different aspects of rheumatic diseases. Authors present the effects of anti-TNF therapy on ophthalmological complications in their patients with juvenile idiopathic arthritis (JIA), juvenile dermatomyositis (JDM) and sarcoidosis. Objectives: To investigate therapeutic success of anti-TNF therapy on ophthalmological complications in children with rheumatic diseases.
Methods: Retrospective chart review of all rheumatic patients with ophthalmological complications treated with anti-TNF therapy at Division of Paediatric Rheumatology and Immunology, University Hospital Centre Zagreb, during 2009. – 2013. period. Results: Among 54 children treated with anti-TNF therapy at our Division during 2009. – 2013. period, 10 were detected with ophthalmological complications (8 girls, 2 boys), 8 with JIA, 1 with JDM and 1 with sarcoidosis. Nine patients had chronic uveitis (JIA, sarcoidosis) and 1 had …cotton wool” retinal lesions accompanied with bilateral papilar oedema (JDM). Avarage time between the beginning of disease and start of anti-TNF therapy was 2.9 years (28 days – 9 years). Initial anti-TNF therapy was adalimumab in 5 cases (4 JIA, 1 sarcoidosis), etanercept in 4 cases (JIA) and infliximab in 1 case (JDM). During therapy, etanercept was changed to adalimumab in 2 cases, due to ineffecivity on uveitis. Adalimumab was partially effective in 1 case (sarcoidosis). Infliximab, applied in patient with JDM and …cotton wool” retinal lesions accompanied with bilateral papilar oedema, led to fast and complete recovery of eye changes and other aspects of the disease. Conclusion: Anti-TNF therapy was successfull in 90 % of our cases. To our opinion, anti-TNF therapy should be early introduced in rheumatic patients with severe ophthalmological complications. Disclosure of interest: None declared.

P237

TNF inhibitors in the treatment of uveitis in the course of juvenile idiopathic arthritis
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Pediatric Rheumatology 2014, 12(Suppl 1):P237

Introduction: Uveitis is the most common extraarticular complication of juvenile idiopathic arthritis (JIA). TNF inhibitors are a promising new therapeutic option in the treatment of chronic uveitis in JIA.

Objectives: The aim of this study was to evaluate the efficacy of TNF inhibitors in children with chronic uveitis in the course of JIA. Methods: Data of 8 children with JIA and chronic uveitis treated with TNF inhibitors between 2010 and 2013 were analysed retrospectively. The clinical subtypes of JIA were: polyarticular – 2 patients (pts), oligoarticular - 6 pts (according to the ILAR criteria), 5 children were ANA positive. Clinical effectiveness assessment included JIA outcome parameters (PhGA, PaGA, CHAQ, ESR, CRP, number of joints with active arthritis; number of joints with limited range of motion) and ophthalmological examination.

Results: In all (8) pts the first used biological drug was ETA after unsuccessful treatment with two synthetic DMARDs (including methotrexate) and systemic glucocorticoid (6 pts) and topical glucocorticoid (8 pts). The treatment of ETA was started after a mean 4 ± 3,7 years of disease, and mean treatment of 3,8±3,9 after uveitis was diagnosed. In all patients, remission of uveitis was achieved during ETA treatment. ETA treatment was terminated after at least 18-month remission on the drug (according to the Polish therapeutic program). 3 pts (43%) developed a uveitis exacerbation after termination of ETA and the treatment was restarted. In 2 pts due to exacerbation of uveitis, ETA was switched to adalimumab with improvement. In all children systemic and topical glucocorticoids were terminated.

Conclusion: Anti-TNF therapy is effective in JIA patients with chronic uveitis. In case of active disease it is necessary to switch to another biological agent. Many patients developed a disease exacerbation after anti-TNF termination, reintroduction of therapy was needed. Disclosure of interest: None declared.

P238

The use of colchicine in PFAPA syndrome, the french experience and literature review
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Pediatric Rheumatology 2014, 12(Suppl 1):P238

Introduction: PFAPA syndrome is the most frequent periodic fever syndrome in non-Mediterranean patients. The cause remains obscure but overexpression of inflammasome-related genes and increase IL-1b during attacks suggest an autoinflammatory mechanism. We wondered whether colchicine could be used as effective prophylactic treatment in PFAPA syndrome.

Objectives: To compare 2 groups of PFAPA patients distinguished by their response to colchicine prophylaxis, and to identify the predictive factors of response to this treatment.

Methods: We performed a retrospective, multicentric, chart review of PFAPA patients under colchicine prophylaxis. We distinguished one responder group, defined as patients, who had no more, or twice fewer crises under colchicine and another one of non-responders. Subgroup analyses were performed using the nonparametric Mann-Whitney test for the quantitative data and calculating the odds ratio and confidence interval for qualitative data. The difference between the two groups was considered significant for p value <0.05 or a confidence interval different from 1.

Results: Twenty children, 65% of boys, were studied. Their mean age at disease onset was 2.3 ± 1.5 years. The mean duration of attacks was 3.2 ± 1.1 days (SD) (1 to 7 days) of strong fever (mean 39.9°C) with chills (30%), pharyngitis (85%), abdominal pain (75%), cervical adenitis (65%), asthenia (60%) and aphotic stomatitis (50%). Half of patients, 57% (8/14) were heterozygous in the MEFV gene. Nine patients were responders to colchicine. No significant differences were found between the two groups (responder and non-responder).

Conclusion: We observed a relatively high rate of response to colchicine; however our study could not sort out the predictive factors of this effect.

Disclosure of interest: None declared.

P239

A proposed treatment scheme for chronic recurrent multifocal osteomyelitis (CRMO): a case series of nine patients
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Pediatric Rheumatology 2014, 12(Suppl 1):P239

Introduction: CRMO is a rare, orphan auto-inflammatory disease characterized by recurrent episodes of pain associated with sterile bone inflammation. There is no consensus on the optimal treatment.

Objectives: The aim of this study was to review our CRMO patients and report our results with etanercept treatment in patients with a resistant course in CRMO.

Methods: Retrospective descriptive case series of nine children diagnosed as CRMO at the Department of Pediatric Rheumatology at Hacettepe University, Ankara, Turkey. Disease activity was assessed by acute phase reactants (ESR, CRP), physician and patient/parent visual analogue scales (VAS) (0-10 cm), and radiological findings (MRI and bone scintigraphy).

Results: The median age of symptom onset was 8.2 years, while the patients were diagnosed to have CRMO at a median of 10 years of age. Eight out of nine patients presented with extremity pain, while five of the patients had back pain on presentation. Eight out of nine patients presented with extremity pain, while five had back pain on presentation. The patients had a median of three lesions at the time of diagnosis. There was sacroilitis in seven patients. Four out of nine patients were treated with nonsteroidal anti-inflammatory drugs (NSAID) and methotrexate (MTX). Five patients did not respond to these treatments, thus etanercept therapy was started at an initial dose of 0.8 mg/kg/week after a median of 24 months from diagnosis. Acute phase reactants returned to normal, physician and patient/parent visual analogue scales significantly improved in all patients after etanercept treatment. We were able to show healing of lesions in imaging that correlated with the improvement of VAS and pain in the patients, suggesting that anti-TNF was effective on the bone inflammation. We have extended the time interval between two doses of etanercept from one week to two weeks after six months of remission with maintenance of the complete response in four of these patients.

Conclusion: Our treatment policy in CRMO is to start with NSAIDs and MTX. If the patient is refractory to these drugs, anti-TNF treatment is commenced. Anti-TNF treatment was effective in the treatment of our CRMO patients, We suggest that extending the dosing interval is an
effective option once they are in remission for 6 months. We also suggest that imaging may be included as an outcome measure in patients with CRMO. Further prospective studies are needed to determine the optimum outcome measures and treatment strategy.

Disclosure of interest: None declared.

P241 Evidence based recommendations for genetic diagnosis of Familial Mediterranean Fever
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Introduction: Familial Mediterranean Fever (FMF) is a disease that starts in childhood and can lead to significant morbidity. In 2012, a European initiative called SHARE (Single Hub and Access point for pediatric Rheumatology in Europe) has been launched to optimize and disseminate diagnostic and management regimens in Europe for children and young adults with rheumatic diseases. For FMF, attention was focused on genetics.

Objectives: The aim of the SHARE recommendations in FMF is to provide a diagnostic tool for inexperienced pediatric rheumatologists to cope with FMF in their clinical practice. This is possible through a correct interpretation of the diagnostic value of MEFV genotype mutations in predicting FMF phenotype.

Methods: Evidence-based recommendations were developed using the European League Against Rheumatism (EULAR) standard operating procedure. An expert committee was instituted, consisting of pediatric rheumatologists, and search terms for the systematic literature review were defined. Two independent experts scored articles for validity and level of evidence. Recommendations derived from the literature were evaluated by an online survey. Those with less than 80% agreement during the online survey were reformulated. Subsequently, all recommendations were discussed at a consensus meeting using the nominal group technique. Recommendations were accepted if more than 80% agreement was reached.

Results: The literature search yielded 3386 articles, of which 240 about genetics and, among them, 25 considered relevant and therefore scored for validity and level of evidence. 17 articles were scored valid and used in the formulation of the recommendations. 9 recommendations for diagnosis were suggested in the online survey and 8 were finally accepted with 100% agreement after the consensus meeting. Topics covered for diagnosis were: clinical versus genetic diagnosis of FMF; genotype – phenotype correlation; genotype – age at onset correlation; silent carriers and risk for amyloidosis; role of the specialist in FMF diagnosis.

Conclusion: The SHARE initiative provides recommendations for the diagnosis of FMF and thereby facilitates improvement and uniformity of care throughout Europe.

Disclosure of interest: G Giancane: None declared, N Ter Haar Grant/Research Support from: SHARE is funded by the European Commission (project N° 2011/2002), N. Wulffraat Grant / Research Support from: Abbvie, GSK, Roche, Consultant for: Genzyme, Novartis, Pfizer, Roche, B. Vastert Consultant for: Novartis, K Barron: None declared, V Hentgen: None declared, K Tilmann Grant / Research Support from: Novartis, Speaker Bureau of: Novartis, SOBI, H Oztoglan: None declared, J Anton Lopez Grant/Research Support from: Abbvie, Novartis, Pfizer, Consultant for: Novartis, Speaker Bureau of: Abbvie, Novartis, Pfizer, Roche, SOBI, P Brogan Grant/Research Support from: Novartis, Roche, Consultant for: Roche, L Cantarini: None declared, J Frenkel Consultant for: Novartis, Speaker Bureau of: SOBI, C Galeotti Grant / Research Support from: Novartis, MGattorno: None declared, G Grateau: None declared, M Hofer: None declared, J Kone-Paut: None declared, J Kuehmerle-Deschner Grant / Research Support from: Novartis, Speaker Bureau of: Abbvie, Novartis, Pfizer, Roche, SOBI, P Brogan Grant/Research Support from: Novartis, Roche, Consultant for: Roche, L Cantarini: None declared, J Frenkel Consultant for: Novartis, Speaker Bureau of: SOBI, C Galeotti Grant / Research Support from: Novartis, M Gattorno: None declared, G Grateau: None declared, M Hofer: None declared, J Kone-Paut: None declared, J Kuehmerle-Deschner Grant / Research Support from: Novartis, Speaker Bureau of: Abbvie, Novartis, Pfizer, Roche, SOBI, P Brogan Grant/Research Support from: Novartis, Roche, Consultant for: Roche, L Cantarini: None declared, J Frenkel Consultant for: Novartis, Speaker Bureau of: SOBI, C Galeotti Grant / Research Support from: Novartis, M Gattorno: None declared, G Grateau: None declared, M Hofer: None declared, J Kone-Paut: None declared, J Kuehmerle-Deschner Grant / Research Support from: Novartis, Speaker Bureau of: Abbvie, Novartis, Pfizer, Roche, SOBI, P Brogan Grant/Research Support from: Novartis, Roche, Consultant for: Roche, L Cantarini: None declared, J Frenkel Consultant for: Novartis, Speaker Bureau of: SOBI, C Galeotti Grant / Research Support from: Novartis, M Gattorno: None declared, G Grateau: None declared, M Hofer: None declared, J Kone-Paut: None declared, J Kuehmerle-Deschner Grant / Research Support from: Novartis, Speaker Bureau of: Abbvie, Novartis, Pfizer, Roche, SOBI, P Brogan Grant/Research Support from: Novartis, Roche, Consultant for: Roche, L Cantarini: None declared, J Frenkel Consultant for: Novartis, Speaker Bureau of: SOBI, C Galeotti Grant / Research Support from: Novartis, M Gattorno: None declared, G Grateau: None declared, M Hofer: None declared, J Kone-Paut: None declared, J Kuehmerle-Deschner Grant / Research Support from: Novartis, Speaker Bureau of: Abbvie, Novartis, Pfizer, Roche, SOBI, P Brogan Grant/Research Support from: Novartis, Roche, Consultant for: Roche, L Cantarini: None declared, J Frenkel Consultant for: Novartis, Speaker Bureau of: SOBI, C Galeotti Grant / Research Support from: Novartis, M Gattorno: None declared, G Grateau: None declared, M Hofer: None declared, J Kone-Paut: None declared, J Kuehmerle-Deschner Grant / Research Support from: Novartis, Speaker Bureau of: Abbvie, Novartis, Pfizer, Roche, SOBI, P Brogan Grant/Research Support from: Novartis, Roche, Consultant for: Roche, L Cantarini: None declared, J Frenkel Consultant for: Novartis, Speaker Bureau of: SOBI, C Galeotti Grant / Research Support from: Novartis, M Gattorno: None declared, G Grateau: None declared, M Hofer: None declared, J Kone-Paut: None declared, J Kuehmerle-Deschner Grant / Research Support from: Novartis, Speaker Bureau of: Abbvie, Novartis, Pfizer, Roche, SOBI, P Brogan Grant/Research Support from: Novartis, Roche, Consultant for: Roche, L Cantarini: None declared, J Frenkel Consultant for: Novartis, Speaker Bureau of: SOBI, C Galeotti Grant / Research Support from: Novartis, M Gattorno: None declared, G Grateau: None declared, M Hofer: None declared, J Kone-Paut: None declared, J Kuehmerle-Deschner Grant / Research Support from: Novartis, Speaker Bureau of: Abbvie, Novartis, Pfizer, Roche, SOBI, P Brogan Grant/Research Support from: Novartis, Roche, Consultant for: Roche, L Cantarini: None declared, J Frenkel Consultant for: Novartis, Speaker Bureau of: SOBI, C Galeotti Grant / Research Support from: Novartis, M Gattorno: None declared, G Grateau: None declared, M Hofer: None declared, J Kone-Paut: None declared, J Kuehmerle-Deschner Grant / Research Support from: Novartis, Speaker Bureau of: Abbvie, Novartis, Pfizer, Roche, SOBI, P Brogan Grant/Research Support from: Novartis, Roche, Consultant for: Roche, L Cantarini: None declared, J Frenkel Consultant for: Novartis, Speaker Bureau of: SOBI, C Galeotti Grant / Research Support from: Novartis, M Gattorno: None declared, G Grateau: None declared, M Hofer: None declared, J Kone-Paut: None declared, J Kuehmerle-Deschner Grant / Research Support from: Novartis, Speaker Bureau of: Abbvie, Novartis, Pfizer, Roche, SOBI, P Brogan

P242 Adrenomedullin levels in patients with Familial Mediterranean Fever: a long term follow-up
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Introduction: Familial Mediterranean Fever (FMF) is the most common periodic fever syndrome, characterized by recurrent fever and serositis attacks. It has been shown that there might be an ongoing subclinical inflammation between attacks. Adrenomedullin (ADM) is synthesized in endothelium, and has been shown to have high levels in patients with inflammation such as FMF. Colchicine is the treatment of choice and given once or twice daily depending on expert opinion.

Objectives: In this study, it was aimed to investigate ADM as a marker for inflammation in pediatric patients with FMF who are using colchicine in different dosage schema.

Methods: Pediatric patients diagnosed with clinically and genetically confirmed FMF diagnosis were included in the study. The Colchicine was started in one or two doses randomly. The clinical and laboratory parameters were assessed on six clinical visits made every two months. After the third visit the dosing schema was changed to twice or once depending on the schema at the beginning.

Results: A total of 37 patients were included in the study. Mean age of patients was 7.7±2.00 years, mean age at disease onset was 5.05 ± 3.04 years and mean age at diagnosis was 7.51 ± 2.66 years. Twenty patients received colchicine in once daily dosage while 17 patients had in twice daily dosage at the beginning of the study. There were 10 patients with heterozygote and 27 with homozgyote MEFV mutations. After the treatment was started all patients demonstrated improvement in clinical and laboratory findings such as erythrocyte sedimentation rate and C-reactive protein. However, ADM levels did not show any correlation with ESR and CRP levels. Mean ADM levels in six consecutive visits were as follows, first 322.19±161.92 ng/L; second 330.50±189.63 ng/L; third 339.5±168.03 ng/L; forth 378.11±177.63 ng/L; fifth 328.91±172.30 ng/L and sixth 326.25±165.87 ng/L. ADM levels were similar in all visits (p=0.954) and did not show any difference between the first and second three visits i.e. before and after changing the dosage schema (p=0.593).

Conclusion: The results indicated that patients using colchicine in once or twice daily doses did not demonstrate any difference considering clinical and laboratory findings and had similar effects in controlling
disease manifestations. ADM levels did not demonstrate any alterations in all visits which may suggest the continuation of subclinical inflammation in these patients.

Disclosure of interest: None declared.

P243
Validity and reliability of medication adherence scale in FMF (adult version)
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Pediatric Rheumatology 2014; 12(Suppl 1):P243

Introduction: MASIF (Medication Adherence Scale in FMF) is an instrument designed to measure adherence to treatment in children with Familial Mediterranean Fever (FMF). We have developed this scale for children with FMF and found valid and reliable.

Objectives: In this study, it was aimed to assess the validity and reliability of this adherence scale for medical treatment in adult FMF patients.

Methods: This study is multicentre and 14 centers participated to the study. Patients with FMF using medication at least for 6 months and accepted to participate constituted the sample of the study. Besides “Medication Adherence Scale in FMF Patients (MASIF)”, “Data collection forms about the sociodemographic and medical information (demographic, clinical and laboratory findings) of patients”, and “Morisky Medication Adherence Scale (MMAS)” were used as data collection instruments.

Results: There were 133 patients with FMF enrolled for the validation of the study. The median age of the patients (n=133) was 28.60 years (min.18.12-max.71.34) and 52.6% of them were female. The median number of the attack frequency was 13.50 (min. 0-max 99) in a year and 57.9% of the participants had irregular attacks. For internal consistency, Cronbach’s alpha was 0.764 for MASIF adult version. Also, there was a positive and significant correlation between test and retest score (t=0.971; p=0.000) and for the “structure” validity, factor analyzes and Kaiser-Meyer-Olkin tests were performed.

Conclusion: Approximately 10-15% of patients with FMF are non-responders but it was claimed that in fact they are non-compliers that causes these patients receive unnecessary biologic agent treatment procedures; which are hazardous as well as expensive. This scale will provide assessment and follow up of adherence to treatment patients and determine whether the patient is non-responders or non-compliers. It may help to determine the non-compliance and prevent unnecessary and expensive biologic agents.

Disclosure of interest: None declared.

P244
Canakinumab for the treatment of different refractory autoinflammatory disorders
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Pediatric Rheumatology 2014; 12(Suppl 1):P244

Introduction: Interleukin-1 (IL-1) is a powerful pro-inflammatory cytokine synthesized in the inflammosome complex of immune cells in response to injury and infection. The excess activity of this cytokine plays a fundamental role in the pathogenesis of the autoinflammatory disorders. An emphasis on pediatric rheumatology is given to systemic-onset juvenile idiopathic arthritis (SOJIA) and periodic fever syndromes. Until the last decade, there wasn’t an efficient alternative for the treatment of autoinflammatory syndromes refractory for conventional therapies. This scenario was modified with the introduction of biological agents, especially the IL-1 antagonist group (Anakinra, Rilonacept and Canakinumab). Canakinumab, a fully human anti-IL-1β monoclonal antibody, selectively binds to IL-1β, and intercepts the spread of inflammation. This medication was approved for treatment of cryopyrin-associated periodic syndrome (CAPS) in 2009, and SOJIA in 2013, and has shown to be an excellent tool for controlling these disorders.

Objectives: To report the clinical and laboratory response to the use of Canakinumab in pediatric patients with distinct autoinflammatory syndromes.

Methods: We performed a retrospective chart review of patients in use of Canakinumab in monitoring at the Rheumatology Department of a tertiary center in Curitiba (Brazil). Patients with arthritis (SOJIA and pediatric granulomatous arthritis) received a subcutaneous dose of 4mg/kg every 4 weeks, whereas patients with periodic fever syndromes received a subcutaneous dose of 2mg/kg every 8 weeks. The clinical and laboratory activity of these diseases were evaluated right after the first medication dose. The patients were monitored during the next years in order to evaluate the long-term response to Canakinumab.

Results: We reported 5 cases of autoinflammatory disorders: 2 cases of SOJIA, 1 neonatal-onset multisystem inflammatory disorder (NOMID), also known as chronic infantile neurological cutaneous and articular syndrome (CINCA), 1 familial Mediterranean fever (FMF) and 1 pediatric granulomatous arthritis (Blau Syndrome). All cases showed an excellent clinical and laboratory response after Canakinumab first dose. One SOJIA patient reported flare during the NSAID and corticoid tapering. With the reintroduction of NSAID, the patient satisfactory responded to the medication and the disease became inactive again. The Blau Syndrome patient had a flare after withdrawal therapy for 5 months, due to failure to receive the medication. As soon as Canakinumab was reintroduced, the disease was also remissioned. Neither patients showed adverse effects.

Conclusion: Although randomized, double-blind, controlled studies are still needed, the anti-IL-1β antibody Canakinumab has proven to be an excellent alternative for refractory autoinflammatory disorders, due to its high efficacy and safety.

Disclosure of interest: None declared.

P245
Can serum amyloid a level be used to support the Familial Mediterranean Fever diagnosis?
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Pediatric Rheumatology 2014; 12(Suppl 1):P245

Introduction: Familial Mediterranean Fever (FMF) is a periodic fever syndrome characterized by recurrent episodes of fever and serosal inflammation. The diagnosis is still based on clinical criteria. No laboratory test is diagnostic of FMF. During the attacks increased C reactive protein (CRP), serum amyloid A (SAA), fibrinogen, beta 2 microglobulin, erythrocyte sedimentation rate (ESR) and leukocytosis is observed. The increased levels of SAA in patients with FMF during the attack free period have been reported as a sign of subclinical inflammation. Also, studies have shown that during the attack the sensitivity of SAA and CRP was similar.

Objectives: The aim of this study was to evaluate the sensitivity of SAA and other acute phase reactants in the diagnosis of FMF.

Methods: We reviewed the medical files of 100 patients with FMF followed up in our center in which SAA was measured; mutation-analysis was performed and yet untreated. The diagnosis of FMF was established according to Livneh and Yalçınkaya criteria. Patients were divided according to the presence or absence of attack while the SAA measurement was performed. The level of white blood cells (WBC), ESR, CRP, fibrinogen and platelets that measured simultaneously with SAA were recorded. For each parameter the level above the normal range accepted as increased.

Results: Thirty one patients were evaluated during the FMF attack and 69 patients were evaluated during the attack free period. The median levels (minimum, maximum) during the attack: SAA 178 (5 - 1720) mg/L, CRP 4.5 (1 – 15.9) mg/dL, ESR 29 (4 – 88) mm/hour, fibrinogen 4.5 (2.2 – 8.1) g/L, WBC 9100 (3910 - 26700) /mm³ platelets 343000 (146000 - 694000) /mm³, during the attack free period: SAA 20 (1 – 351) mg/L, CRP 0.2 (0.1 – 7.6) mg/dL, ESR 7 (1 – 48) mm/hour, fibrinogen 3.3 (1.6 – 6.5) g/L, WBC 7480 (3730 -
In conclusion, we describe a typical CANDLE clinical syndrome in late CRMO phases. After Chronic recurrent multifocal osteomyelitis (CRMO) is the most common autoinflammatory osteomyelitis (CRMO) is characterized by non-bacterial osteomyelitis and primarily affects children and adolescents. The disorder has a relapsing and remitting course. While non-steroidal anti-inflammatory drugs (NSAIDs) are used as first-line treatment, glucocorticoids and disease-modifying antirheumatic drugs (DMARDs) are given the impression that SAA levels decreased specificity and PPV of SAA in predicting FMF attack confirmed CRMO all patients were treated with NSAID.

Table 1 Sensitivity, specificity, positive and negative predictive values of acute phase reactants for predicting FMF attack

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
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<tbody>
<tr>
<td>SAA</td>
<td>96%</td>
<td>28%</td>
<td>37%</td>
<td>95%</td>
</tr>
<tr>
<td>ESR</td>
<td>64%</td>
<td>88%</td>
<td>71%</td>
<td>84%</td>
</tr>
<tr>
<td>CRP</td>
<td>83%</td>
<td>85%</td>
<td>72%</td>
<td>92%</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>58%</td>
<td>82%</td>
<td>60%</td>
<td>81%</td>
</tr>
<tr>
<td>WBC</td>
<td>45%</td>
<td>81%</td>
<td>51%</td>
<td>76%</td>
</tr>
<tr>
<td>Platelets</td>
<td>25%</td>
<td>88%</td>
<td>50%</td>
<td>72%</td>
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20000 /mm³ platelets 325000 (173000 - 528000) /mm³. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for all parameters. (Table 1).

Table 1 Sensitivity, specificity, positive and negative predictive values of acute phase reactants for predicting FMF attack

Conclusion: Decreased specificity and PPV of SAA in predicting FMF attack gave the impression that SAA levels during the attack free period in FMF patient is increased. In this respect it is concluded that SAA can be used as an independent laboratory parameter to support FMF diagnosis.

Disclosure of interest: None declared.

P247

Pamidronate treatment in resistant cases of CRMO – our small case series

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Pediatric Rheumatology 2014, 12(Suppl 1):P247

Introduction: Chronic recurrent multifocal osteomyelitis (CRMO) is the most common autoinflammatory osteopathy. CRMO is characterized by non-bacterial osteomyelitis and primarily affects children and adolescents. The disorder has a relapsing and remitting course. While non-steroidal anti-inflammatory drugs (NSAIDs) are used as first-line treatment, glucocorticoids and disease-modifying antirheumatic drugs have been reported to be effective in some cases. In resistant cases, the effects of TNF-α inhibitors or bisphosphonates were observed.

Objectives: To describe a cohort of CRMO patients and to characterize treatment effects with focus on bisphosphonates in a retrospective study of a case series.

Methods: Between 1995 and 2014 we diagnosed CRMO in 17 patients (14 females and 2 males). The mean age at diagnosis was 9.2 years. The time between symptom onset and diagnosis of CRMO ranged from 3 to 72 months. We found multifocal lesions involving the tibia, clavicle, femur, vertebral bodies, pelvis and mandible. The average number of lesions per patient was 3.8. The diagnosis of CRMO was based on radiographic findings (X-ray, CT, MRI, scintigraphy) and biopsy. In the histopathology typical cell infiltrates – predominantly neutrophils in the early stages, monocytes, macrophages, lymphocytes and plasma cells in the later stages; and osteolyses with sclerosis and/or fibrosis in late CRMO phases. After confirming CRMO all patients were treated with NSAID.

Results: NSAID was ineffective in 8 out of 17 patients who then received a corticosteroid therapy. 4 of these patients (3 girls and 1 boy) did not fully respond and were treated with intravenous pamidronate. In 2 patients pamidronate was added to MTX and/or Sulphasalazine (n=2) while the other 2 patients were MTX/Sulphasalazine naive. In MTX/Sulphasalazine naive patients, 1 reached complete remission after a single dose and 1 after a double dose in a 6 month regimen. In these patients no corticosteroids were needed after pamidronate therapy. Two patients with previous MTX/Sulphasalazine treatment, the dosing regimen at 6-month intervals was inadequate, requiring a dose increase to 3-month intervals. One of these patients was treated with anti-TNF-α inhibitors prior to pamidronate, but without sufficient effect. These patients have improved only partially and required treatment with corticosteroids. In both groups no adverse effects were observed.

Conclusion: In accordance with published data, our experience confirms good effect of pamidronate therapy in patients with resistant CRMO, however more severe cases with multiple bone lesions and/or systemic symptoms (febrile, inflammatory skin disorders, weight loss or growth retardation) require higher dose regimen.

Disclosure of interest: None declared.

P249

Involvement of the IFN-γ-gamma pathway in a patient with candle syndrome carrying a novel variant of PSM88 gene

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Pediatric Rheumatology 2014, 12(Suppl 1):P249

Introduction: Chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature (CANDLE) syndrome is a newly described autoinflammatory disease.

Objectives: To describe clinical phenotype and cytokine profile of our patient.

Methods: A 10-year-old young girl presented at 10 months of age with recurrent fever, hepato-splenomegaly and nodular erythematous skin lesions of trunk and limbs; subsequently she progressively developed lipodystrophy, arthralgia, arthritis and edema of eyelids. Skin biopsy showed typical features of lobular panniculitis. Laboratory tests showed persistent elevated acute phase reactants with increased serum amyloid A, persistent chronic anemia, mild recurrent leucopenia, thrombocytopenia and decreased IgG, IgG and IgM levels. Immunological and cytogenetic studies performed on bone marrow were normal. Subsequently, the patient developed proteinuria with nephrotic syndrome. Renal biopsy revealed a minimal change glomerulopathy; she was started on a standard nephrotic syndrome high-dose glucocorticoid protocol with remission of proteinuria. Response to hydroxychloroquine, colchicine, cyclosphorine-A, and anakinra was unsatisfactory. Complete sequencing of TNFRSF1A and MVK genes showed no mutations. Analysis of the PSM88 (proteasome subunit 6 type 8) gene revealed the presence of c.220A>T (P74S) variant in heterozygotic status that has never been reported before. In order to assess the dysregulated inflammatory response in our patient, we evaluated the cytokine profile in patient’s sera using the Luminex multiplexing assay. Whole blood RNA analysis was also performed using a human immune array (TaqMan® Human Immune Array from Applied Biosystems), containing 92 genes typically involved in the immune response.

Results: Serum samples (n=4) were collected during the last two years. We found high levels of IFN γ (mean ± SD: 115.3 pg/ml ± 64.21), of IFN-gamma inducible protein 10 (IP-10), also called CXCL10 (164± 892.9 pg/ml) and of IFN-γ (mean ± SD: 892.5 pg/ml) and of IFN-gamma inducible protein 9 (IP-9, also called CXCL11) (582.9± 335.6 pg/ml) and especially of CXCL9, also known as monokine induced by gamma interferon (MIG) (18161± 6405 pg/ml), compared to healthy controls or pediatric patients with sJIA during active disease. Two whole blood RNA samples collected from our Candle patient were compared to 6 whole blood RNA samples collected from healthy controls comparable for age. We obtained results consistent with those obtained by serum cytokine measurement: IFNg, CXCL10 and CXCL11 mRNA expression were significantly increased compared to healthy controls (1.88, 32.7 and 4.1 fold higher respectively). We also found that the expression of the HLA-DRB1, a gene whose expression is known to be induced by IFN-gamma, was markedly upregulated (> 100.000 fold) compared to healthy controls. In both groups no adverse effects were observed.

Conclusion: In conclusion, we describe a typical CANDLE clinical phenotype in the absence of biallelic mutations of PSM88 gene. The presence of high levels of IFN-γ and of IFN-γ related chemokines points to a major pathogenic role of the IFN-γ pathway, which appears to be similar to what has been recently reported in CANDLE (Li et al). The pathogenic role of the variant T74S remains to be elucidated: a potential role is suggested by its presence in a patient with a classical phenotype and with
a dysregulation of the IFN pathway, taking also into account that this variant is close to the known pathogenic mutation T75M.

Disclosure of interest: None declared.
administration. Administration of canakinumab (150 mg/4 weeks) led to normalization of inflammatory markers for the first time since his birth. The patient remains asymptomatic after 4 doses of canakinumab.

The third case is a teenager who had been diagnosed with FMF at the age of 4 due to typical symptoms and homozygosity for the M694V mutation. The disease had been kept in remission with colchicine until the age of 14 when he presented every 3 weeks severe flares (mild fever but severe chest pain, arthralgias and fatigue followed by loss of weight), unresponsive to maximum doses colchicine. Canakinumab (150 mg/6 weeks) was initiated and led into remission. In a period of 2 years the patient presented 3 mild episodes.

No adverse effects were observed in anyone of the patients during the whole periods of canakinumab administration.

Conclusion: The reported cases indicate that canakinumab is effective and safe for the treatment of FMF patients resistant to colchicine as well as of those presenting adverse effects of the drug.

Disclosure of interest: None declared.

P254
Familial Mediterranean Fever in older children
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Pediatric Rheumatology 2014, 12(Suppl 1):P254

Introduction: Familial Mediterranean Fever (FMF) is an autosomal recessive disease, characterised by recurrent, self limited attacks of fever with serositis.

Objectives: The aim of this study was to compare the demographic, clinical and genetic features of FMF patients who had late onset disease to those with earlier onset during childhood period.

Methods: Files of patients who had been seen in our department (during routine follow-up visits) between January 2013 and January 2014 were retrospectively evaluated. Patients were divided into two groups according to age of disease onset (Group I: ≤8 years of age; Group II: >8 years of age).

Results: The study group comprised 317 FMF patients (170 females, 147 males) with a mean age of 12.2 ± 5.7 years. There were 267 patients (84.3%) in group I and 50 patients (15.7%) in Group II. Median attack frequency before colchicine therapy was 24/year in Group I and 12/year in Group II (p<0.05). Although the frequency of majority of the clinical features did not differ between the groups, fever was seen less frequently in Group II patients (p=0.003). M694V homozygosity was also less frequently detected in group II patients (p=0.022). Median disease severity scores and final colchicine dosages were lower in Group II (p<0.001; p=0.003). Median delay in diagnosis was 24 months in Group I and 12 months in Group II (p=0.002).

Conclusion: Only a small number of FMF patients had disease onset at older ages in childhood period. It seems that FMF patients with late onset disease have milder illness. However, more readily expression of their clinical findings in older ages yields earlier diagnosis in this group.

Disclosure of interest: None declared.

P255
The toll-like receptor 4 agonist MRP8/14 protein complex (calprotectin) in autoinflammation: potential biomarker in chronic nonbacterial osteomyelitis – a case report
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Pediatric Rheumatology 2014, 12(Suppl 1):P255

Introduction: The cytoplasmic S100 proteins derived from cells of myeloid origin. Calprotectin (MRP8/14 protein complex) might be a biomarker either for autoinflammation and autoimmuneopathy. Since autoinflammatory diseases might be a diagnostic challenge calprotectin may be helpful in the diagnosis of autoinflammatory diseases. Chronic nonbacterial osteomyelitis (CNO) is an autoinflammatory, noninfectious disease. CNO describes a wide spectrum from a monofocal bone lesion to the chronic recurring multifocal osteomyelitis (CRMO). Laboratory and histopathological findings are nonspecific. In some patients systemic inflammatory signs such as elevated acute phase proteins cannot be found.

Objectives: To test the ability of Calprotectin (MRP8/14 protein complex) serum concentrations to monitor disease activity in patients with CNO.

Methods: Serum concentrations of Calprotectin (MRP8/14 protein complex) in a patient with CNO were determined by a sandwich ELISA.

Results: Calprotectin (MRP8/14) level were raised heralding active disease when acute phase proteins (CRP, erythrocyte sedimentation rate). The calprotectin level was 7872.7 ng/ml (normal range 0-3000 ng/ml).

Conclusion: Calprotectin (MRP8/14) serum concentrations correlate closely with disease activity and may herald a flare before clinical manifestation. Therefore MRP8/14 serum concentrations are a biomarker indicating disease activity in CNO patients.

Disclosure of interest: None declared.

P256
Chronic recurrent multifocal osteomyelitis: experience from a single pediatric rheumatology center over the past ten years
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Pediatric Rheumatology 2014, 12(Suppl 1):P256

Introduction: Chronic recurrent multifocal osteomyelitis (CRMO) is a rare inflammatory disorder that primarily affects children. Its hallmark is recurring episodes of sterile osteomyelitis. The clinical presentation is insidious bone pain with or without fever. Pathogenesis is still unknown and there is no any effective treatment.

Objectives: The aim of our study is to describe our experience with CRMO over the past ten years.

Methods: We retrospectively evaluated patients with CRMO who had been diagnosed at or referred to Rheumatology Service of Institute for Maternal and Child Health - IRCCS Burlo Garofolo - between 2004 and 2014. History, diagnostic imaging, laboratory and histological data were obtained.

Results: We followed seven patients diagnosed as CRMO, 6 female and 1 male. Bone pain was the leading symptom; median age of first complaint was 11 years (range 8-14 ys). The majority of bone lesions were located in the metaphyses of the long bones (10 sites, 63%), clavicle (3 sites, 19%) and pelvis (2 sites, 12%). Five patients had more than one lesion at onset. Of the latter, one patient remained with only one bone focus. Bilateral involvement was presented in two cases. The male patient also had fever and severe acne, so received diagnosis of SAPHO (synovitis, acne, pustulosis, hyperostosis, and osteitis) syndrome. Blood examination revealed slight increased eritrosedimentation rate and normal C-reactive protein in all cases. In two cases, at any disease relapse, urine analysis showed calprotectin without other signs of renal involvement. One that showed a mesangial glomerulonephritis. In all patients X-rays were suggestive of osteomyelitis. In all patients diagnosis was formalized after biopsy, except for patient with SAPHO. The biopsy showed scattered inflammatory infiltrate and leukocytes with no evidence of bacteria or malignancies in any cases. No patients responded to non-steroidal anti-inflammatory drugs (NSAIDs) therapy. All patients received corticosteroids but only two of them reached clinical remission. Of the remaining, one received methotrexate and then infliximab with no benefit so switched to bispophonate with partial response and 3 received bispophonate with good clinical response. The patient with SAPHO received Infliximab with good response. After 4 years, patient with SAPHO is still on infliximab therapy as an attempt of withdrawal provoked a flare of the disease. Four patients are clinically asymptomatic with no therapy, one patient is on bispophonate therapy, and one patient showed recurrent course despite bispophosphonate and biological anti-TNFα therapy.

Conclusion: The clinical course of CRMO is variable. The metaphyses of the long bones remain the more affected sites followed by clavicle and pelvis. Laboratory tests are aspecific and the biopsy is necessary, especially in cases with singular localization. In two patients we also found intermittert proteinuria, that has never been reported so far. In our opinion two hypothesis could be considered: proteinuria is a sign of renal involvement in some cases of CRMO, or proteinuria is a side effect of treatment. In fact in one patient when infliximab was withdrawn, proteinuria permanently disappeared. Bispophonate therapy can be of benefit to patients with
relapsing symptoms. In refractory patients biologic therapy could be considered even if no controlled studies are disposable.

Disclosure of interest: None declared.

P257
The clinical and genetic features of patients with hyper-immunoglobulin D syndrome (HIDS)
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Pediatric Rheumatology 2014, 12(Suppl 1)p257
Introduction: Mevalonate kinase deficiency (MKD) is a rare autosomal recessive disorder causing 1 of 2 phenotypes, hyper-immunoglobulin D syndrome and mevalonic aciduria, presenting with recurrent fever episodes, often starting in infancy, and sometimes evoked by stress or vaccinations. This autoinflammatory disease is caused by mutations encoding the mevalonate kinase (MVK) gene and is classified in the group of periodic fever syndromes. HIDS is characterized by recurrent fever attacks of 3-7 days that begin in infancy and recur every 4-6 weeks. The febrile period is accompanied by lymphadenopathy, arthralgia, abdominal pain, diarrhea, aphthous ulcers, and varying degree of skin involvement. The course and severity of the disease may be quite different. There is no effective or proven therapy for HIDS.

Objectives: We aim to determine the clinical and genetic characteristics together with the underlying MVK genotypes in single center during a period of 2 years.

Methods: A retrospective review of medical records for patients referred for HIDS over 2 years. We obtain 40 patients (22 female, 18 male) and 25 healthy controls.

Results: The median age of first attack was 33 months (range 2-62 months). The median age of diagnosis was 60 months. The most common symptoms of high fever accompanied respectively: lymphadenopathy (n=27), abdominal pain (n=26), arthralgia (n=20), diarrhea (n=13), aphthous stomatitis (n=13), vomiting (n=12) and maculopapular rash (n=6) were determined. Amyloidosis was found in a patient (0.3%). The mean serum IgD level was 129±92 mg/dl, it was be normal in 43% of patients. We found mutations in 75% of patients (n=30) in exon 3 and 11 (c155G>A; c112G>C) in MVK gene. We applied colchicine therapy in 40% of patients while intermittent steroid therapy 20% of patients. Empiric colchicine (40%) and glucocorticosteroids (20%) controlled flares in majority of patients with HIDS. Three patients had also tonsillectomy. We used biologic therapy in 3 patients (canancinumab (n=2), anakinra (n=1)).

Conclusion: In conclusion, HIDS is characterized with early onset an autoinflammatory disease and may to result frequent and uncontrolled attacks.

Disclosure of interest: None declared.

P258
Increased frequency of psoriasis in the families of subjects with childhood Familial Mediterranean Fever
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Pediatric Rheumatology 2014, 12(Suppl 1)p258
Introduction: Familial Mediterranean fever (FMF) is an autosomal recessive disease characterized by periodic fever and polyserositis attacks. FMF can be associated with vasculitis, spondyloarthropathies, Behçet’s disease and inflammatory bowel disease. Psoriasis is another disease that can be associated with FMF. Psoriasis is a common disease affecting approximately 2% of the population. Although there are many clinical subtypes, the most frequent subtype is psoriasis vulgaris. Psoriasis vulgaris comprises 85-90% of all the psoriasis subtypes. The association of FMF with psoriasis has never been investigated so far.

Objectives: The aim of our study was to investigate the frequency of psoriasis among the family members (mother, father, sibling) and close relatives (uncle, aunt) of children with FMF.

Methods: The study group consisted of 202 FMF cases diagnosed according to the diagnostic criteria of Yalcinbay et al, 238 JIA cases diagnosed according to ILAR (International League of Associations for Rheumatology) who were followed up in Istanbul University, Cerrahpasa Medical Faculty, Department of Pediatric Rheumatology and 200 healthy controls. Patients with juvenile psoriatic arthrits in the JIA group were excluded from the study. The presence of psoriasis diagnosed by a dermatologist was questioned among family members and close relatives of all the enrolled cases.

Results: Psoriasis was detected in 41 (20.3%) of 202 FMF patients (M:25, F:16), 10 (4.2%) of 238 JIA patients (M:3, F:7), 12 (6%) of the family members and close relatives of 200 healthy children. Of the 41 FMF patients with psoriasis, dermatologist diagnosed psoriasis was detected in the mother; in the father; in the sibling; in the grandmother and grandfather; in the aunt and uncle; and in the cousin, in 5, 5,1,11,12,12 of them, respectively. The increased incidence of psoriasis among the parents and close relatives of cases with FMF than that of cases with JIA and healthy controls was statistically significant (p<0,0001).

Conclusion: The association of FMF with psoriasis has been reported in the medical literature only as case presentations. To our knowledge, this study is the first study investigating this association among FMF patients and their family members. We found an increased incidence of psoriasis in the family members of FMF patients. However, this association should be confirmed with further studies with larger sample sizes and the association of MEVF gene with psoriasis should also be investigated.

Disclosure of interest: None declared.

P260
Recurrent multifocal osteomyelitis (CRMO): effect of neridronate
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Pediatric Rheumatology 2014, 12(Suppl 1)p260
Introduction: Chronic recurrent multifocal osteomyelitis (CRMO) is an autoinflammatory bone disease of unknown etiology. Clinically, the disease is characterized by the insidious onset of local pain and swelling in affected bones. Its course is one of intermittent periods of exacerbation and remission with successive bones affected.CRMO most commonly affects the metaphysis of long bones, especially the tibia, femur, and clavicle. The spine, pelvis, ribs, sternum, and mandible may also be affected. Although lesions are mostly multiple, patients may present with a single symmetric focus. Treatment in CRMO is empiric, since placebo controlled randomized trials have not been performed.

Objectives: To describe the outcome of CRMO patients treated with neridronate.

Methods: We report 8 patients (3 M.S.F, mean age 8ys) Median age of first CRMO symptoms was 6.3 years (range 5-13). The more affected sites were the metaphys of the long bones, pelvis and coxofemoral joints.

Results: Seven patients failed to respond to NSAIDs therapy. Two patients received corticosteroids, without clinical disease remission. Four patients received neridronate (2mg/kg body weight every 3 months for 1 year), all with good clinical response and induction of clinical remission. After a median follow-up period of 3.2 years (range 1-5), three patients are clinically asymptomatic and one patient required another 6 months course to reach and sustain remission.

Conclusion: The treatment of CRMO is not standardized. Bisphosphonate therapy can be of benefit to patients with relapsing symptoms. Randomized controlled multicentric trials are needed to provide better evidence for definition of bisphosphonate therapy protocol.

Disclosure of interest: None declared.

P261
The role of genotype in Familial Mediterranean Fever
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Pediatric Rheumatology 2014, 12(Suppl 1)p261
Introduction: Familial Mediterranean Fever (FMF) is an autosomal recessive disease, characterised by recurrent, self limited attacks of fever with serositis. The gene responsible for FMF, designated as MEFV, encodes pyrin.

Objectives: The aim of this study was to compare the demographic and clinical features of FMF patients with heterozygous MEFV mutations to those with homzygous or compound heterozygous mutations.

Methods: Files of patients who had been seen in our department (during routine follow-up visits) between January 2013 and January 2014 were retrospectively evaluated. Six predominant mutations (p.M694V, p.M680I, p.M694I, p.V726A, p.K695R, p.E148Q) in the MEFV gene were studied in our center. Patients were divided into two groups: group I included patients with heterozygous mutations and group II included patients with homozygous or compound heterozygous mutations.

Results: The study group comprised 263 FMF patients (145 females, 118 males) with a mean age of 9.7 ±5.2 years. There were 83 patients in group I and 180 patients in Group II. Although age at disease onset and clinical findings did not differ between the two groups, age at onset of colchicine therapy was lower in group II (p<0.05). Family history of FMF was more frequently detected in group II (p=0.016). Acute phase reactant levels during the attacks before colchicine therapy and the attack-free period after colchicine therapy were higher in group II (p<0.05). Median PRAS severity score and final colchicine dosages were also higher in group II (p<0.05). Patients in group II had more severe clinical presentation compared to the patients in group I.

Conclusion: As an expected finding FMF patients with homozygous and compound heterozygous mutations have more severe disease during childhood period.

Disclosure of interest: None declared.

P262

NLRP12- associated autoinflammatory disorder: case report
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Pediatric Rheumatology 2014, 12(Suppl 1):P262

Introduction: During latest years, the identification of genes involved in the control of inflammation, apoptosis processes and a better comprehension of the mechanisms connected to an anomalous activation of the inflammasome, have made possible to delineate a new group of illness called * Monogenic autoinflammatory syndromes*.

Objectives: Report a case of recurring fever due to NLRP12 mutation.

Methods: E.M., 4 years old, comes to our observation because of the presence of recurrent episodes of fever lasting 4-5 days,since about one year, every 15 days, associated with diarrhea, urticaria-like rash decreasing spontaneously, mainly on the back and lower limbs.

From November 2012 to April, the patient presented daily fever (Tmax 40°C) associated with worsening rash, arthralgia and arthritis of knees and ankles , edema of eyelids and lips and palmar angioedema during 7 days. From April 2013, every 15 days, the child had again febrile episodes (Tmax 40°C) lasting about seven days with the associated symptoms already described. Each episode has been exclusively cured with Paracetamol. Blood tests revealed just a small increase of the inflammatory indexes. After excluding other common causes of persistent and recurrent fever in the pediatric age, we suspected an autoinflammatory disease. Then, we directed the patient to a third level structure, where analysis of the CIAS1 gene have been carried out. Suspecting strongly an auto-inflammatory disease, the NLRP12 gene has been examined too. Analysis of the CIAS1 gene didn’t reveal pathological mutations, while the analysis of NLRP12 gene resulted positive.

Results: Considering the clinical feature associated with increase of inflammatory indexes and the genetic analysis outcomes, the diagnosis of disease was NLRP12 associated autoinflammatory disorder (NLRP12AD).

Conclusion: The NLRP12AD is an autosomic dominant disease , due to mutation of NLRP12 gene which encode for the NLRP12 protein or "MONARCH-1", playing a crucial role in the immune mechanisms against pathogens agents. As for Cryopyrinopathies, symptoms can be induced by the exposure to the cold and are characterized by recurring fever episodes lasting 5-10 days, associated with rash, headache, lymphadenopathies, oral ulcers and abdominal pain. Therapy depends on the seriousness of the symptoms: in less serious cases , treatment is based on antihistamines, NSAIDs and corticosteroids; in more serious ones, the administration of Anakinra can be useful. In the refractory cases, further therapeutic strategies are based on Anti-TNF and ANTI-IL-6 agents.

Disclosure of interest: None declared.

P263

Does hyperbaric oxygen therapy truly help in the treatment of chronic recurrent multifocal osteomyelitis?
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Pediatric Rheumatology 2014, 12(Suppl 1):P263

Introduction: Chronic recurrent multifocal osteomyelitis (CRMO) is a non-infectious inflammatory bone disorder of yet to be determined etiopathology. However, it is considered that the imbalance between pro- and anti-inflammatory cytokines plays the main role in the disease expression. CRMO represents the most severe form of chronic nonbacterial osteomyelitis and predominantly affects children and adolescents, primary girls. The clinical presentation is variable onset of bone pain with or without fever, local soft tissue swelling or warmth with an unpredictable clinical course and spontaneous remissions. Metaphyses of long bones are the most specific affected sites. CRMO is a diagnosis of exclusion because of its clinical presentation and laboratory findings that are not disease-specific and vary between patients.

Objectives: Here we present two cases of CRMO, first in 9-year-old girl localized in left clavicle and the second one in a 5-year-old girl with oligo-focal form. In both cases onset of the disease was characterized with bone pain and local soft tissue swelling without fever. Laboratory findings included elevated inflammatory markers (C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), leucocytes count). Radiographs, bone scan and MRI in both girls showed specific signs indicating osteomyelitis (osteolytic lesions located in the metaphyses, nonaggressive periostal reaction, thickening of surrounding soft tissue). A needle biopsy was performed and the pathohistological findings indicated osteomyelitis. Microbiological findings were negative. Both patients were initially treated by antibiotic. During the first week of antibiotic therapy older girl was developed DRESS – drug rash with eosinophilia and systemic symptoms. The recurrence of the symptoms, multifocality, lack of evidence of causative factor and imaging characteristics of the bone lesions led us to CRMO diagnosis. In both girls we applied treatment with NSAID and corticosteroids (prednisone 1 mg/kg for two weeks with subsequent reducing of dosage for four weeks). In the same time both patients were subjected to hyperbaric oxygen therapy.

Methods: In the same time both patients were subjected to hyperbaric oxygen therapy. After six months clinical remission was achieved in the both children but with residual bone impairments on MRI scans.

Results: After six months clinical remission was achieved in the both children but with residual bone impairments on MRI scans.

Conclusion: Since CRMO is self limited and benign disease the question is whether oxygen barotherapy truly helps or is it natural course of the disease. According to the literature data residual bone impairments are expected, which suggest an up to 50% rate of residual impairments. Thus, the development of effective treatment algorithm and enlightened of pathophysiology of CRMO will be essential in the future.

Disclosure of interest: None declared.

P264

Familian Mediterranean Fever: genetic characterization in Georgian population
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Pediatric Rheumatology 2014, 12(Suppl 1):P264

Introduction: FMF is the most common mendelian autoinflammatory syndrome, resulting from autosomal recessive mutations in the MEFV locus. This disorder occurs most frequently among Sephardic Jewish, Arab, Armenian andTurkish populations. FMF occurs at lower frequencies in other Mediterranean populations and ethnicities.

Objectives: In Georgia this disorder was detected mainly in ethnic Jewish and Armenians. We present cases of FMF in ethnic Georgians, that we
have diagnosed in our department from the day of its foundation (2007) up today (2014).

Methods: We suspected FMF in 37 patients, the diagnosis was based on typical features. The FMF mutations were investigated in all patients. As a result FMF was proved in 37 cases is in investigation stage.

Results: Of the 37 patients 19(52.8%) are females, 18(47.2%) are males and the age ranged from 2 to 106. A positive family history of FMF was noted in 5(13.5%).Two patient has developed amyloidosis(mutationM694V/M694V). 27 of the patients had mutation M694V/M694V, 3 had mutation M680I/ M694V. Another had M680I/M694V, M680I/R761H, M680I/V726A, E148Q/ M694V/M694V/WT. We have not colchicines resistant patient.

Conclusion: Our study has approved that FMF occurs not only among Mediterranean population but among others including Georgians.In our population mostly frequent type of mutation is M694V/M694V.

Disclosure of interest: None declared.

P265
Trouble always comes in threes: three mutations for three autoinflammatory genes in a child and in his father

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P266
TNFRSF1A gen and R92Q and P46L variants. Association with other inflammatory diseases

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Disclosure of interest: None declared.

Introduction: Tumour Necrosis Factor (TNF) Receptor-Associated Periodic Syndrome (TRAPS) is an autoinflammatory disease with an autosomal dominant inheritance pattern. Structural mutations in the TNFRSF1A gen tend to have a penetrance higher than 90%, except for p.P46L and p.R92Q variants. The intensity of clinical manifestations in patients with these variants has been shown to decrease or even to disappear in the long term follow-up. It has been found a high prevalence of the R92Q mutation in patients with inflammatory diseases known to have a relevant TNF-alfa involvement.

Objectives: To describe the inflammatory pathologies associated with TNFRSF1A gen variants P46L and R92Q in 15 patients.

Methods: All the patients with a TNFRSF1A gen variants, discovered in the context of the study of a suspected autoinflammatory disease, between 2005 and 2014, were included.

Results: A mutation in TNFRSF1A gen was detected in 18 patients: 3 structural mutations, 13 R92Q variant and 2 P46L variant. Inflammatory disorders found in the group of 15 patients with a TNFRSF1A variant were: 4 vasculitis (Takayasu arteritis, Schölein-Henoch purpura, ANCA positive vasculitis, polyarteritis nodosa), 3 patients fulfilled criteria for systemic juvenile idiopathic arthritis (2 with macrophagic activation syndrome). In 2 patients a familial Mediterranean fever mutation was also found and 2 patients showed high fecal caproptin levels without inflammatory bowel disease symptoms at that moment.

Conclusion: Although R92Q mutation has been identified in healthy individuals, recent studies suggest that it may increase the susceptibility to other inflammatory conditions as multiple sclerosis, Behçet's disease, the occurrence of extraintestinal manifestations in Crohn disease and vasculitis.

Disclosure of interest: None declared.

P267
An experience of use of canakinumab IL-1 inhibitor in children with cryopyrin-associated periodic syndromes (CAPS)

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Disclosure of interest: None declared.

Introduction: Interleukin-1β (IL-1β) is a basic mediator of cryopyrin-associated periodic syndromes (CAPS). In this respect an experience of the use of IL-1 inhibitors has been gained in patients with CAPS. Canakinumab was approved by FDA and EMEA in 2009 and registered in the Russian Federation in 2011 for treatment of CAPS. Canakinumab is shown to have high efficiency and good tolerability in patients with CAPS.

Objectives: to present an experience of use of canakinumab IL-1 inhibitor in children with CAPS in Russia.

Methods: The study includes 4 patients with CAPS: two patients with Muckle-Wells syndrome and two patients with CINCA/NOMID syndrome including three girls (3.5, 5.5 and 8 years old) and a boy (17 years old). 1 female patient with MWS received glucocorticoids in a dose of 0.1 mg/kg and other patients received NSAID. All patients passed molecular genetic test to find NLRP3(CIAS1) gene mutation. Two patients with MWS had pThr436Ile and pThr438Ile mutations and two patients with CINCA/ NOMID were negative. Canakinumab was administered in a dose of 4 mg/kg for body weight under 15 kg or 2 mg/kg for body weight over 15 kg and injected subcutaneously every 8 weeks. By now, two patients have received 4 injections (32 weeks of observation) and two patients have received 3 injections (24 weeks of observation).

Results: All patients developed significant clinical improvement: recovery of well-being, relief of fever and rash, reduce in the level of acute phase markers. The effect is stable during the whole follow-up period. This allowed to discontinue glucocorticoid therapy in a female patient with MWS at all. No adverse effects were observed in any patients.
Conclusion: An experience of the use of canakinumab in patients with CAPS has shown high efficiency and good tolerability of the drug. Decrease in acute phase markers was appeared to be slower in patients with CNCA/NOMID syndrome as the most severe CAPS form.

Disclosure of interest: None declared.

P268
Familial case of TRAPS syndrome in Russia
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Pediatric Rheumatology 2014, 12(Suppl 1):P268

Introduction: TRAPS syndrome (tumor necrosis factor (TNF) receptor-1 associated periodic fever syndrome) is a typical representative of periodic auto-inflammatory fevers of monogenic character. We did not find any descriptions of TRAPS syndrome in the Russian population.

Objectives: To describe the case of TRAPS syndrome in three Russian family generations confirmed by molecular genetic tests.

Methods: In addition to standard rheumatologist examination, TNFRSF1A gene was partially tested in the patient, his grandmother and parents by direct sequencing with the study of exons 2, 3, 4.

Results: The patient is a boy of 9 years old of the Russian ethnic origin. The disease manifested at 6 months by fever episodes up to 39.5 °C, lasted for 7-10 days with 4-weeks intervals associated with intensive abdominal pain and increase in acute phase markers (ESR up to 43 mm/h, increase in CRP level, leukocytosis). During the periods between attacks the abovementioned indexes were considerably lower but did not return to normal values. In the follow-up period the patient developed pericarditis episode. At 7 years of age he underwent surgery for peritoneal concomitances. In February of 2012 he developed extensive hemorrhagic rash and hemorrhagic nephritis. Glucocorticoid therapy (GT) started in a dose of 0.8 mg/kg had partial effect. The symptoms relapsed with dose reduction. The diagnosis was established in April of 2013 at the age of 9 years. The patient has taken canakinumab since October of 2013 in a dose of 2 mg/kg once every 8 weeks with complete reversal of all symptoms and withdrawal of GT. The patient’s mother (36 years old) has been sick since the age of 4. The disease has been manifested by fever attacks up to 40.0 °C, intensive abdominal pain, periorbital redness and edema. At the age of 14 one of the episodes was evaluated as appendicitis but appendectomy was conducted without effect. Since 16 years she has developed episodes of extensive erythema of an upper limb associated with fever up to 38.0 °C for 3-4 days, transient elbow joint contracture on the side of lesion and intensive abdominal pains. The episodes lasted for 3 weeks and occurred twice a year. Acute phase markers were permanently increased (ESR 58 mm/h, CRP 62 mg/L, leukocytosis up to 12.0 x 10^9/L). The patient’s grandmother has clinical presentation similar to daughter’s disease appeared at the age of 14. Mutation of c.1129G>A (p.Val377Ile, also known as V377I) in heterozygous state was found in these three patients. This mutation recorded in Infevers database had been originally described in patients of German and Scottish origin.

Conclusion: A familial case of genetically confirmed TRAPS syndrome with known mutation originally detected in patients from the Western Europe was found in Russia for the first time. The treatment of the child has been well tolerated, and no side effects were observed. The steroids were dropped. The fever and rash were absent, but the acute phase reactants were still high. His blood samples were referred for genetic testing NOD2 mutations. Methotrexate was added to the treatment, but the flair was occurred two months later. NOD2 mutations were detected to be P268S heterozygote and V955I heterozygote. Since the patient’s response to anakinra was poor, TNF blocker was later added to the treatment.

Disclosure of interest: None declared.

P270
Interleukin 1 blockade with canacinumab for hyperimmunoglobulin B and periodic fever syndrome
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Pediatric Rheumatology 2014, 12(Suppl 1):P270

Introduction: Hyperimmunoglobulinemia D and periodic fever syndrome (HIDS; MIM# 260920) is a rare autosomal recessive autoinflammatory condition caused by mutations in the MVK gene, which encodes for mevalonate kinase. There is no standard treatment for HIDS.

Objectives: We report on a 2 year-old Austrian boy with recurrent episodes of fever, febrile seizures, arthralgias, and splenomegaly. Rash and abdominal pain were also seen occasionally. During attacks an acute-phase response was detected. Clinical and laboratory improvement was seen between attacks. These findings led to the tentative diagnosis of HIDS.

Methods: Sequencing of the MVK gene showed a homozygous c.1129G>A (p.Val377Ile, also known as V377I) mutation in the child, while the healthy non-consanguineous parents were heterozygous. The mutation is known to be associated with HIDS.

Results: Therapy with nonsteroidal anti-inflammatory drugs during attacks had poor benefit. A further febrile episode resulted in a status epilepticus. Treatment with canakinumab was initiated and a final dose of 4 mg/kg every 4 weeks resulted in the disappearance of febrile attacks and a considerable improvement of patient’s quality of life during a 6-month follow-up period. The drug has been well tolerated, and no side effects were observed.

Conclusion: Treatment with canakinumab is a therapeutic option for patients with HIDS.

Disclosure of interest: None declared.

P271
Interleukine-6 and TNFα blockers provide only partial and short-term temporal improvement in cryopyrin-associated periodic syndrome
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Introduction: Hyperimmunoglobulinemia D and periodic fever syndrome (HIDS; MIM# 260920) is a rare autosomal recessive autoinflammatory syndrome characterized by recurrent febrile attacks with polyclonal hyperimmunoglobulinemia, erythema nodosum, and joint pain.

Objectives: To evaluate the efficacy of interleukine-6 and TNFα blockers in the treatment of HIDS.

Methods: A 15-year-old boy with a history of recurrent febrile attacks with polyclonal hyperimmunoglobulinemia, erythema nodosum, and joint pain was treated with etanercept, adalimumab, and canakinumab.

Results: The patient had a remarkable improvement in clinical symptoms with the use of etanercept, adalimumab, and canakinumab.

Conclusion: Interleukine-6 and TNFα blockers provide only partial and short-term temporal improvement in cryopyrin-associated periodic syndrome.

Disclosure of interest: None declared.
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Diagnoses challenges and therapeutic response in Blau syndrome – case report

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Pediatric Rheumatology 2014, 12(Suppl 1):P272

Introduction: Blau’s syndrome is an autosomal-dominant, autoinflammatory disease characterized by a non caseous granulomatous inflammation, presenting with arthritis, dermatitis and uveitis, caused by mutations of the CARD15/NOD2 gene. Patients are treated with high doses of oral corticosteroids and if the therapeutic response is unsatisfactory, additional treatment with immunosuppressive agents is the best choice, such as: Methotrexate, Cyclosporine Anti-TNF and Canakinumab (Anti-IL-1). Objectives: To describe a case of Blau syndrome with early onset atypical manifestations and therapeutic response.

Methods: A 2 year old boy was referred to a Brazilian Pediatric Rheumatology center, in March/2009, with daily persistent high fever, diffuse and firm erythematous rash and polyarthritics since age of 3 months old. Laboratory tests showed: leukocytosis, anaemia and persistent elevation of platelets counts; Immunoglobulins, complements; Zinc, Calcium, Phosphorus, PTH, 25-hydroxivitamin D e Urine analysis: normal. Cytomegalovirus, Epstein Barr, toxoplasomiasis, Parvovirus B19, HIV, herpes, antinuclear antibodies (FAN, DNA, SSA, SSB, RNP, Sm, ANCA-p, ANCA-c, antecardiolipine e lupus anticoagulante): negative. VHS e PCR: elevated; PPĐ: nonreactive. Audiometry /impedanciometry: normal. Wrist X-Ray: nodular images in 2nd and 5th right metacarpals. Skin and synovial biopsies: granulomatous alterations. His mother presented similar history, diagnosed “systemic JIA” at age of 6, currently presenting articular deformities and visual loss. Indomethacin, cyclosporine, methotrexate, colchicine, etanercept and adalimumab were used but the patient remained with fever, rash and worsening of articular symptoms; ophthalmomathy in left eye and left ventricular dysfunction. However, there were no signs of neurological involvement. Canakinumab (Anti IL-1) was started with improvement of all the above symptoms. The genetic test detected genetic mutation in NOD2.

Results: Systemic JIA was initially considered. However, there were no significant improvement after treatment with prednisone, cyclosporine, NSAIDs and Methotrexate. Considering the very early onset, CINCA syndrome, caused by mutation of gene CIAS1, was also an important hypothesis. The manifestations of high fever and urticarial rash starting in first weeks of life; aspetic meningitis leading to sensorineural hearing and vision loss with persistent elevation of acute phase reactants, leukocytosis and chronic anaemia. In spite of the clinical resemblance, cutaneous granulomatosis and the lack of neurological symptoms rule out this diagnosis. Finally with the noncaseating granulomatous skin biopsy, we considered Blau’s syndrome. It usually manifests before the first decade of life, with small and big joint symmetric arthritis, variable erythematous rash (maculopapular or icthyiform) and uveitis. The early onset, the skin rash and the unsatisfactory response to the initial treatment brought us some doubts. But the gene mutation in NOD2/CARD15 was conclusive. Blau’s syndrome can be treated initially with NSAIDs and systemic corticosteroids, however, in cases with ineffective therapeutic response Anti-TNF and Anti-IL1 can be very beneficial, especially in patients presenting non responsive uveitis.

Conclusion: The atypical manifestation of this case shows the variable clinical spectrum of monogenic autoinflammatory syndromes and their resemblances, which makes the early diagnosis and treatment very challenging.

Disclosure of interest: None declared.

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Familial case of Muckle-Wells syndrome in the Russian population: a long way to the diagnosis

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Pediatric Rheumatology 2014, 12(Suppl 1):P273

Introduction: Muckle-Wells syndrome (MWS) is a rare auto-inflammatory disease related to the group of cryopyrin-associated periodic syndromes (CAPS) frequently complicated by amyloidosis. The disease is caused by mutation in NLRP3 (CIAS1) gene transmitted by autosomal dominant route.

Objectives: To describe genetically verified familial MWS case in mother and daughter of the Russian ethnic origin.

Methods: In addition to standard rheumatologist examination, NLRP3 gene was partially tested in the patient, her mother by direct partial sequencing.
Results: Case 1: female patient of 17 years old (daughter) has been examined in the Institute since the age of 8 (2004). Since the age of 10 months she has complained for periodic fever, transient macular and papular rash on different body areas without itching, arthralgia/arthritis without joint dysfunction, headache, abdominal pain, sore throat, nodal fever episodes, ulcerative stomatitis and genital ulcers. The patient has had a history of uveitis and frequent conjunctivitis since 8 years of age. Lucid asymptomatic intervals have been observed. Differential diagnosis: systemic juvenile arthritis, systemic vasculitis, periodic fever syndromes (FMF, TRAPS), Behcet's disease since 2006.

Case 2: Female patient of 40 years old (mother) has been examined in the Institute since 31 years of age (2004). She has complained for periodic arthralgia/arthritis without joint dysfunction since 7 years. Since 17 the patient has developed fever, transient macular and papular rash on different body areas without itching, sore throat, nodal fever and ulcerative stomatitis episodes, genital and rectal ulcers, abdominal pains and frequent conjunctivitis. Sensorineural hearing loss with progressive deafness has developed since 2000 (27 years). Differential diagnosis: acute rheumatic fever, Still's disease of adults, systemic lupus erythematosus, periodic fever syndromes (TRAPS), Behcet's disease since 2006. Acute phase markers (ESR, CRP, leukocytosis) are permanently increased in both patients. HLA-B51 is negative. Treatment with antibiotics, NSAID, disease-modifying anti-rheumatic drugs and colchicine had no effect and glucocorticoids led to temporary improvement. Molecular genetic test revealed NLRP3 (CIAS1)-pThr350Met gene mutation in mother and daughter in heterozygous state. CAPS – MWS syndrome was diagnosed in 2013.

Conclusion: MWS may occur in patients of the Russian ethnic origin and should be included in a range of differential conditions in patients with fever, rash and other inflammatory symptoms, particularly in the cases when similar signs are observed in the patient's family or if standard anti-rheumatic and anti-inflammatory therapy has no adequate effect.

Disclosure of interest: None declared.

P274

The complexity of diagnosis of FMF in children living outside typical of this disease in the region
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Pediatric Rheumatology 2014, 12(Suppl 1):P274

Introduction: Currently diseases from the group autoinflammatory syndromes pays much attention in the literature and real clinical practice. Among the diseases in this group is the most common Familial Mediterranean Fever (FMF). For this disease characterized by loss of patients of certain national groups, and also characterized by a specific geographical area of distribution. However, due to the growth of migration and assimilation processes, patients with this disease are increasingly can be detected outside the historically significant areas. In the absence of constant alertness doctors errors may occur in the diagnosis of this condition.

Objectives: To evaluate the clinical features of and difficulties in diagnosis of in children living outside typical for this disease territory.

Methods: The study was a retrospective study of all patients with FMF followed at the clinic of Hospital Pediatrics Saratov State Medical University named V.I. Rumovsky from September 2008 to January 2014. We reviewed the charts of 5 patients with FMF diagnosed according to the criteria of Tel-Hashomer that, however, adapted for populations with high some of the frequency of occurrence of this syndrome.

Results: Children with newly diagnosed FMF were aged 1 year 11 months to 17 years. National of 4 children - Armenians, 1 child - Greek. The onset of the disease is marked in the age of 4 years (8 months - 4 years). A child has been observed with different symptoms, reflecting the assumed acute inflammatory disease (pneumonia, and so on). Suspicion for the presence auto inflammatory syndrome is not expressed. All children showed mixed option FMF: in five cases were abdominal - fever syndrome, in 2 cases - articular syndrome in 2 cases - thoracic syndrome. In the General analysis of the blood - accelerated ESR up to 25-50 mm/h. All patients on the background of fever have been reported increase of CRP to high numbers to the rapid decline after knocking febrile syndrome. In none of the cases are not recorded signs of amyloidosis and adhesive disease. Draws attention to the fact that younger children noted the minimum number of criteria Tel-Hashomer. In 2 cases of large criteria was not revealed. However, the detection of even a small number of small or supporting criteria FMF amid careful exception important foci of infection in conjunction with national identity are a pretext to perform a genetic examination. In all 5 cases at the final stage of the survey were identified mutations characteristic of the FMF - mutations M694V and V726A in compound heterozygous condition; in 2 cases - mutation M694V in the homozygous state; in one case detected strengthening electrophoretic mobility exon 10 MEFV gene, which is located more than 90% of mutations that are logged when FMF, corresponding mutation M694V in the heterozygous state.

Conclusion: In pediatric practice even one symptom of recurrent fever combined with belonging to the respective ethnic group should be grounds for exclusion of FMF.

Disclosure of interest: None declared.

P275

A difficult case of juvenile dermatomyositis complicated by thrombotic microangiopathy and purtscher-like retinopathy
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Introduction: Juvenile dermatomyositis (JDM) is a multisystem disease of uncertain origin resulting in chronic muscle and skin inflammation. Disease’s complications are calcinosis and cutaneous ulcerations, lipodystrophy, joint contractures, interstitial lung disease, cardiac involvement, digestive and central nervous system vasculitis.

Objectives: We report here a case of severe JDM complicated by thrombotic microangiopathy (TMA).

Methods: Case report.

Results: A 16 year old girl was admitted for fever, diffuse pain, asthenia, sore throat and generalised papular rash. Initial work-up showed leukopenia, elevation in creatine phosphokinase (CK) (650 U/l) and transaminase. Epstein-Barr Virus (EBV) serology was compatible with acute infection and the initial treatment was symptomatic. Subsequent deterioration of general conditions, progressive polymyositis with regular increase in muscle enzymes (CK up to 39000 U/l), massive muscle swelling and maculo-papular rash were consistent with a diagnosis of JDM. MRI confirmed muscular inflammatory involvement.

Sudden onset of blurred vision, haemolytic anaemia (haemoglobin 53 g/l and schistocytes) and thrombocytopenia (21 G/l) lead to further investigation. Complete work-up showed Purtscher-like retinopathy, renal failure (creatinine 150 umol/l) and pancreatitis (lipase 570 U/l). Renal and Muscle biopsy showed microangiopathy with capillary endothelium necrosis and mild infammation consistent with JDM and TMA. Dosing of ADAMST-13 activity was normal.

Patient failed to respond to pulse therapy with methylprednisolone, intravenous immunoglobulin, plaquenil, rituximab and cyclophosphamide. Patient showed also partial response to plasma exchange therapy, with successive deterioration of clinical conditions and biological parameters. Treatment with Eculizumab, a monoclonal antibody against the C5 protein fraction of complement system, 900 mg once/week for 5 weeks and then 1200 mg once 2/week was effective in improving clinical condition and biological parameters.

Conclusion: This report emphasizes that early recognition of TMA and prompt treatment are important in children with severe JDM associated with anaemia and thrombocytopenia. Eculizumab is to consider when plasma exchange is not effective enough.

Disclosure of interest: None declared.
Juvenile dermatomyositis: clinical features, laboratory findings, treatment modalities and disease course (a single center experience) Ozgur Kasapcoglu1, Kenan Barut1, Pinar Ozceng Avar2, Salim Caliskan1, Lal Seve1, Nil Arsoy1
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Pediatric Rheumatology 2014, 12(Suppl 1):P276

Introduction: Juvenile dermatomyositis (JDM) is an uncommon vasculitis in childhood. JDM is the most prevalent idiopathic inflammatory myopathies of childhood. JDM is characterized by proximal muscle weakness and typical skin involvement.

Objectives: To describe demographics, clinical features, laboratory findings and treatment modalities of patients with juvenile dermatomyositis (JDM) at a referral pediatric rheumatology center in Turkey.

Methods: Retrospective review of forty three patients meeting Bohan and Peter criteria diagnosed as JDM at the Pediatric Rheumatology Department of Istanbul University Cerrahpasa Medical Faculty between the years 2003-2013.

Results: Forty three patients were identified; thirty of them (69.3%) were female, thirteen of them (30.2) male. Mean follow-up period was 48 months (3-168). Mean age for the beginning of the disease was 6.3±4.4, mean age for the diagnosis was 6.9±4.4. Forty two patients (97.9%) had heliotropic rash and Gottron papules, 39 patients (90.7%) had muscle weakness, 36 patients (87.3%) had erythroderma and 16 patients (37.2%) had calcinosis as the most common clinical features of the disease. Forty one of the patients (95%) had elevated acute phase responses at presentation. Twenty seven of the patients (62.8%) had anti-nuclear antibody (ANA) positivity. Anti-jo 1 and antibodies to extractable nuclear antigen were not found at all. Mean creatine kinase levels at presentation were 2245±3404 IU/L, median level was 564 IU/L. Mean time returning to normal levels was 6.6±17.8 months, median time was 3 months. Muscle biopsy was performed on 14 patients (32.6%) and all of them showed findings of inflammatory myopathy. Electromyography (EMG) was performed on 25 patients (58.1%) and all of them suggested inflammatory myopathy. All patients had been treated with corticosteroids at different dosages. Methotrexate was used in 41 patients (95.3%), at the mean dosage of 14.5±7.1 (7.5-40) milligrams per week and for the mean duration of 45.4±36 months. Cyclosporine was used in 16 patients (37.2%). In 13 of 16 patients with calcinosis (81.3%), alendronate was used. Muscle weakness was present in 39 patients (90.7%) in the beginning, mean duration for the recovery of muscle weakness was 7.9±10.1 months, median duration was 4 months. Only two patients on follow-up period could not achieve self-movement capability. Both were referred to our clinic after a long duration of the disease and had widespread calcinosis. There were no significant relationship between mean duration of the muscle enzymes to return normal values and mean duration of the disappearance of the muscle weakness (p>0.7).

Conclusion: Juvenile dermatomyositis is a rare systemic vasculopathy; however, it is an important disease because it may cause severe muscle weakness and paralysis. JDM should be keep in mind by its presentation as muscle weakness and different skin rashes in early childhood. It should be differed from some kind of genetic muscle diseases. Methotrexate and prednisolone should be first choices for the treatment of JDM. Disclosure of interest: None declared.

Juvenile dermatomyositis in Portuguese children: a case series report
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Pediatric Rheumatology 2014, 12(Suppl 1):P278

Introduction: Juvenile dermatomyositis (JDM) is a rare multisystem disorder that predominantly affects skeletal muscles and skin less frequently the gastrointestinal tract, myocardium, joints and lungs.

Objectives: To describe the main epidemiological, clinical and analytical features and outcome of children with JDM followed in our Pediatric Rheumatology Unit.

Methods: Retrospective review of the clinical records of patients with JDM attending our centre since January 2004.

Results: Seven patients were included, five of them were females. The median age at diagnosis was 10 years (range 4 – 17 years) and the median duration of signs and symptoms was 7 months (range 2 weeks – 2 years). All patients had skin alterations at presentation, which included Gottron papules (6/7), heliotropic rash (4/7), raynaud phenomenon (2/7), livedo reticularis (1/7) and vasculitis (1/7). Common initial manifestations were also muscle weakness (5/7), myalgia (5/7), constitutional symptoms (5/7), arthralgia (5/7) and arthritis (4/7). One patient presented with cutaneous calcinosis, another one had esophageal involvement and presented with dysphagia and dysphonia. All patients had elevated serum muscle enzymes, four had positivity for antinuclear antibodies and one for rheumatoid factor. Electromyography was done in all patients and was abnormal in five of them; muscle biopsy was done in two patients, cutaneous biopsy in one and magnetic resonance imaging in two, and the results showed changes compatible with dermatomyositis. All patients were initially treated with corticosteroids (n=7), to which it was added, alone or in combination: methotrexate (n= 5), hydroxycarbazine (n=2), azathioprine (n=1) and intravenous immunoglobulin (n=1). The median
follow-up time was 4 years (range 4 months – 10 years). One patient developed interstitial lung disease and another one had salivary calcinosis with parotiditis. One patient attained prolonged remission off medication after two years, five patients achieved remission on treatment in a median time of 2 years (range 4 months – 2 years), and one patient had partial response.

Conclusion: Although this is a small series it indicates that, if diagnosed early and treated adequately, JDM has a good outcome. The most frequent initial manifestations were cutaneous, musculoskeletal and constitutional. During follow-up one patient had gastrointestinal involvement, one developed pulmonary manifestations and other one had salivary calcinosis. Overall there were few complications and a satisfactory response to therapy.

Disclosure of interest: None declared.

P279
The role of etanercept in juvenile dermatomyositis (JDM) in children
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Introduction: Juvenile dermatomyositis is a rare autoimmune disease characterised by profound muscle weakness in addition to skin lesions, calcinosis, and underlying vasculopathy. Current treatment plans, including methotrexate and corticosteroids, are ineffective in some patients and may be associated with significant adverse events. The benefits and risks of etanercept in JDMSc are not well studied.

Objectives: The aim of this study is to review the benefit and safety of etanercept in JDM patients.

Methods: We performed a single centre retrospective analysis of all consecutive JDMSc patients treated with etanercept in a tertiary paediatric referral centre. Data collected included clinical and laboratory data, disease duration, the initial dose of etanercept, and other medication details. The outcome was measured by the Childhood Myositis Assessment Scale (CMAS) score before commencing Etanercept and at 12 months follow-up.

Results: Seven JDMSc patients (5 female) were treated with etanercept. Median age at diagnosis was 64 months (36-103 months). The most frequent symptoms at diagnosis included proximal muscle weakness in all patients, constitutional features in 6, muscle pain in 5, typical skin features in 4, and arthralgia in 3 patients.

Disease duration until etanercept was 35 months (10-60 months). All children were treated with prednisolone and methotrexate prior to commencing etanercept and continued prednisolone (in reducing doses) and methotrexate concurrently.

Median duration on etanercept was 20 months (range 6-85 months). Five children ceased etanercept; three due to a flare of disease activity, one child due to transfer of care, and one child due to disease remission. Two patients still receive etanercept at time of analysis. Two children who ceased etanercept commenced monthly infliximab therapy with marked disease improvement. The median CMAS score before etanercept was 44 (range 41-47), and at 12 months after commencing etanercept the median CMAS was 46 (range 41-53).

Conclusion: Etanercept did not demonstrate an appreciable or reliable improvement in the disease control of JDMSc. Whilst beneficial for some patients, caution should be taken when initiating etanercept for JDMSc. Further multicenter studies are necessary to confirm our findings.

Disclosure of interest: None declared.

P280
Juvenile polymyositis and leprosporiasis association: case report
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Introduction: The Polymyositis (PM) is an inflammatory myopathy with symmetrical proximal muscle weakness, especially in pelvic, shoulder girdle and cervical musculature. It may occur primary or secondary to other diseases. Diagnosis is made by exclusion of other etiologies, such as infections, endocrinopathies, metabolic diseases and Bohan and Peter criteria.

Leprosporiasis is a zoonosis of worldwide distribution, that can be asymptomatic, with clinical presentation ranging from an acute febrile illness, with headache, severe myalgia, fever, arthralgia, to a severe syndrome of multorgan dysfunction (Well syndrome) and the diagnosis may be missed unless the physician has a high index of suspicion for the disease.

Objectives: Describe an adolescent with juvenile polymyositis caused by a leprosporiasis infection.

Methods: Patient 14 years, female, reports that two weeks before admission, she developed fever, diffuse rash, arthritis of the left ankle with progressive ascendant loss of force in lower and upper limbs associated with progressive dysphagia initially to solids and later to liquids. The patient had absent patellar reflexes, decreased proximal muscle strength (grade II), CHAQ: 6.8. Initial laboratorials tests: creatine kinase (CPK): 8438; Aldolase: 110 U/L; AST: 236U/L; ALT: 141U/L; lactic dehydrogenase (LDH): 2468 U/L; cervical MR: normal, serologies: HIV, Epstein Barr, Hepatitis A, B and C, Coxackie B, Herpes, cytomegalovirus, parovirus and dengue were negative, but leprosporiasis serology was IgM positive and IgG negative. Patient received crystalline penicillin for 10 days, as recommended, but did not improved muscle strength and enzymes. Electromyography showed myopathic pattern and subsequent muscle biopsy: inflammatory myositis; ANA, anti-yo-2 and anti-Jo-1 negatives. Patient improved after methylprednisolone pulses, and subsequent treatment with oral prednisone, associated with methotrexate.

Results: There are reports of infectious diseases preceding inflammatory muscle diseases which may suggest an association between late infections and inflammatory diseases. The association of PM with leprosporiasis has been described in few cases in the literature. Leprosporiasis can occur in children mimicking a polymyositis and increasing CPK levels. There is an immunologic relationship of leprosporiasis infection with atypical onset of inflammatory response, such as rheumatic manifestations. In our case, after the initial diagnosis, proper treatment and repeat serology (Ig M became negative), the patient did not improved and was subsequently diagnosed as juvenile inflammatory polymyositis.

Conclusion: Leprosporiasis is a condition that leads to clinical and laboratory muscular disorders and should be considered in endemic areas, it can simulate or trigger a polymyositis.

Conclusion: As the result of this article we conclude that midfoot arthritis is an alarming sign in children because of the association with malignancies. So it is important to exclude malignancies in children whom presenting with only midfoot arthritis.

Disclosure of interest: None declared.

P282
Diagnosis of tuberculosis infection in pediatric patients treated with inhibitors of the tumour necrosis factor alpha. A multicenter national study comparing tuberculin skin test and igra tests
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Introduction: In the last years, inhibitors of tumor necrosis factor alpha (antiTNFα) have been a major advance in the treatment of many rheumatic diseases and inflammatory bowel disease, also in the pediatric patient. However, antiTNFα use is associated with an increased risk of serious infections, including tuberculosis (TB). In adults, the new interferon γ release assays (IGRA) tests for the diagnosis of TB infection appear to show better sensitivity and specificity than the tuberculin skin test (TST) in these patients. Data in children are still very scarce. We have previously reported a latent tuberculosis infection (LTI) prevalence rate of 1.4% (95%CI: 0.2-2.9) in children on antiTNFα treatment, which is similar to that reported in healthy pediatric population studies in Spain. LTI was diagnosed in 3 adolescent girls (out of 221 patients) in whom QTF tested positive, while TST was positive in only one of them.

Objectives: To establish the sensitivity and specificity of IGRA tests in the diagnosis of LTI compared to the TST in pediatric patients by the implementation of antiTNFα treatment.

Methods: We present an ongoing national multicenter retrospective/prospective cross-sectional study (hosted by the Spanish National Societies of Pediatric Rheumatology, Infectious Diseases and Gastroenterology) including pediatric patients in whom LTI is to be ruled out simultaneously by TST and IGRA test, prior to initiating treatment with antiTNFα drugs. Medical history related to the underlying disease, the risk of LTI and the results of the TST and IGRA tests will be collected.

Conclusion: This study will observe the prevalence of LTI in this cohort, identify risk factors associated with LTI and analyze the sensitivity, specificity and negative predictive value of IGRA tests as compared to TST in children before antiTNFα initiation.

Disclosure of interest: None declared.

P283
Capillaroscopic findings in children and adolescents with raynaud’s phenomenon: results from study in 92 patients
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Pediatric Rheumatology 2014, 12(Suppl 1)P283

Introduction: Raynaud’s phenomenon (RP) appears to be underestimated in the pediatric population and its prevalence is unknown. However, RP is the earliest and the most common clinical manifestation of diffuse connective tissue diseases. Nailfold capillaroscopy is an easily performed, non-traumatic and low cost technique, with a confirmed role in discrimination between primary and secondary RP, playing an important role in the assessment of autoimmune rheumatic diseases.

Objectives: Identify all patients registered as RP in a Pediatric Rheumatology Unit. Describe the demographic and clinical features of these patients. Assess nailfold capillaroscopy in these children and adolescents with RP and the relation of the clinical features to the capillaroscopic pattern.

Methods: Medical records (2003-2013) from patients with RP followed in our Pediatric Rheumatology Unit were reviewed for demographic data, familial history, trigger factors, Raynaud pattern, clinical manifestations, associated conditions and auto-antibodies positivity. Capillaroscopic patterns were defined as normal (NP), nonspecific pathological (NPP) and specific pathological (SPP). Capillaroscopy was performed, distinguishing primary RP (PRP), secondary RP (SRP) and undifferentiated RP (URP). Associated autoimmune rheumatic diseases: systemic sclerosis (SSc), juvenile dermatomyositis (JDM), systemic lupus erythematosus (SLE), mixed connective tissue disease (MCTD).

Results: 101 patients with RP, F:M 84:16. Age at onset 10,42 +/- 3,70 years old. RP classification: 28% PRP, 35% SRP, 37% URP. Familial history: 20% rheumatic disease, 7% RP. Trigger factor: 73% cold, 8% stress, 8% exercise. Raynaud pattern: 31% single-phase, 53% two-phase, 16% three-phase. Clinical manifestations: livedo reticularis 66%, arthritis 34% and digital ulcers 16% in SRP; arthralgia 40%, pemirosis 28%. Associated conditions: 7 MCTD, 8 JDM, 10 SLE, 3 SSc, 2 localized scleroderma, 1 CREST syndrome, 2 antiphospholipid syndrome (APS), 3 juvenile idiopathic arthritis, 1 Behçet’s disease. Auto-antibodies: ANA + 48%, ENA+ 10%, DNA+ 7%. Capillaroscopy was performed in 92 patients, with mean follow-up time of 5.45 years. Out of 92 patients, 56 (61%) had NP, 14 (15%) NPP, 22 (24%) SPP. NP: 38 PRP, 9 SRP, 10 URP. NPP: 5 SRP, 9 URP. SPP: 20 SRP, 2 URP. Autoimmune rheumatic diseases with capillaroscopic pattern: SSc (1NP, 2 SPP), JDM (2 NP, 6 SPP), SLE (4 NP, 2 NPP, 4 SPP), MCTD (1 NP, 6 SPP), CREST (1 SPP), APS (1 NP, 1 SPP). During the follow-up, 7 patients with NP changed to SPP (3 MCTD, 2 SLE, 1 CREST and 1 SSc). 54% were treated with transdermal nitroglycerine, 30% with nifedipine and 5% with bosentan.

Conclusion: In our series we found a marked female predominance of RP, with a mean age of onset 10 years old. Compared with RP in the adulthood, we found a more frequent single- or two-phase pattern, and a higher association with systemic connective tissue diseases. These results are similar to those reported in other series.

Disclosure of interest: None declared.

P284
Five cases of rheumatic fever diagnosed after onset of Sydenham chorea
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Pediatric Rheumatology 2014, 12(Suppl 1)P284

Introduction: Acute Rheumatic fever is still a challenge for physicians, it is often not diagnosed at onset and adequately treated.

Objectives: To describe five cases of Rheumatic Acute fever. Patients came to our department with symptoms of Sydenham’s chorea from 2011 to 2014.

Methods: A. 12 y.o., came to our observation for involuntary, arrhythmic movements of the upper limbs. She had a history of pharyngitis with negative throat swab three months before and a 2/6 murmur on cardiac examination. Blood tests showed ESR and TAS increased. On ECG activity unstable and poorly regulated. On Doppler-echocardiography: mild mitral and moderate aortic regurgitation. Rheumatic Chorea was diagnosed and confirmed by a neuropsychological evaluation. She started penicillin, ASA, and haloperidol therapy. After responding poorly we added Pregabalin, with regression of neurological symptoms. She was on penicillin when Chorea came back nine months after. She is currently on pimozide.

E. 6.5 y.o., admitted to our Department for involuntary movements of the proximal portion of the upper limbs. She had medical history of two pharyngitis treated with antibiotics, in the last year. Performed tests showed high levels of TAS. Rheumatic Chorea was diagnosed. She started penicillin prophylaxis and haloperidol with remission. Three months later there was a relapse. Was added valproate because of an EEG doubt for temporal lobe epilepsy, then responded.

E. 7.7 y.o., had aimless movements of left arm. She was hospitalized for FUO five months before. We did haematological and neuro-radiological examinations. On Doppler-echocardiography: mild aortic and moderate
mitral insufficiency. We diagnosed Rheumatic Chorea and Carditis. She started penicillin prophylaxis, valproic acid (8 months) and prednisone (3 months) with disappearance of the symptoms. A year later movements relapsed with extension to left emisoma. She became haloperidol with remission 6 months after.

R. 12 y.o. came to our observation for involuntary movements of limbs and trunk. She had no pathological findings on brain NMR, EEG and echocardiography. Blood tests showed high ESR and TAS value, throat swab positive for GAS. She started penicillin and valproic acid. Two months after she had a severe hypotonia of the right arm so she began prednisone with remission of the symptomatology. Two years later, because of a relapse she started Clonazepam.

C.10 y.o. presented dyskinetic movements of face and limbs. Blood tests and MRI were negative. On Doppler-echocardiography: mitral regurgitation. He started penicillin and haloperidol. Then, because of the onset of psychosis the dosage was increased. Currently He is in remission.

Results: CS diagnosis relies on clinical criteria. Therapy is not clearly codified.

Conclusion: CS is a late neurological consequence of Rheumatic Disease. CS incidence is 10-20%, symptoms may last up 2 years, some of them recurring. The therapy is based on pharmacological correction of neurochemical imbalance of the basal ganglia with antipsychotic, antidepressive drugs and reduction of inflammation of basal ganglia (corticosteroids). In refractory forms IgG vein can be effective. From 2011 to 2014 we diagnosed 5 cases of SC. Has rheumatic disease changed or can we not diagnose it early enough?

Disclosure of interest: None declared.

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**P285**

Polyarticular arthritis as presenting feature of farber disease: a lysosomal storage disease involving inflammation

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Pediatric Rheumatology 2014, 12(Suppl 1):P285

Introduction: Farber lipogranulomatosis (Farber Disease; FD) is an ultra-rare lysosomal storage disorder resulting from the inherited deficiency of the enzyme acid ceramidase, and the accumulation of the lipid substrate, ceramide. Ceramide is a pro-inflammatory and pro-apoptotic lipid that has been implicated in the pathogenesis of cartilage disorders. Farber Disease has a heterogeneous presentation ranging from a severe phenotype with respiratory and CNS involvement with an average life expectancy of 1.3 years, to a moderate phenotype, which generally includes joint swelling, contractures and pain. The clinical similarity between the moderate Farber phenotype and the more severe forms of Juvenile Idiopathic Arthritis (JIA) suggests that moderate Farber Disease cases may be diagnosed as JIA in some cases.

Objectives: To demonstrated the presentation, phenotype and pathophysiology of Farber Disease, and to show that moderate Farber Disease should be considered in certain cases of early-onset polyarticular arthritides in children. In addition, we address how the diagnosis of Farber Disease is established and the potential effectiveness of enzyme replacement therapy.

Methods: We present a case study to demonstrate the moderate Farber phenotype and the results of a literature search of Farber Disease case studies since 1990. The background for enzyme replacement therapy (enzyme uptake and decrease of ceramide levels in vitro) also is outlined.

Results: The patient described was originally diagnosed with JIA. The clinical suspicion of Farber Disease was raised by a pediatric rheumatologist with experience in lysosomal storage diseases. His leukocyte acid ceramidase activity is ~4% of his parents, and his ceramide levels are ~2 times that of his parents. Genetic testing revealed a homozygous mutation in the ASAH1 gene. He is currently 9 years old and receiving anti-inflammatory therapy including a TNF-alpha blocker. He has no CNS involvement, but his joint disease continues to progress. Of the published Farber Disease case studies since 1990, 40% (n=14) described patients with moderate disease. 36% (n=5) of these patients were initially diagnosed as having JIA. To establish proof-of-concept for enzyme replacement therapy of Farber Disease, recombinant human acid ceramidase was produced in Chinese hamster ovary cells and added to the culture media of human Farber cells, resulting in a significant reduction in ceramide levels.

Conclusion: A high percentage of moderate Farber Disease patients are likely initially suspected of having JIA. Given this finding, it is important to increase awareness of Farber Disease in the pediatric rheumatology community. Differential diagnosis can be made by accounting for the comparatively early onset, progressive symmetric arthritis, presence of subcutaneous nodules in the joints, scalp and/or spine, and an unusual, hoarse cry or voice (due to nodule formation on the larynx) in Farber Disease patients. Based on experience with Farber Disease cells and with bone marrow transplantation in Farber Disease patients, enzyme replacement therapy could reduce ceramide levels and resolve or significantly attenuate the arthritis phenotype in patients. Such therapy is currently under development. We propose that Farber Disease can account for specific cases diagnosed as JIA, and that clinically guided screening of the JIA population will reveal patients who will benefit from disease-specific care and treatment.

Disclosure of interest: A. Sölyom Consultant for: Plexcera Therapeutics LLC, N. Karabul: None declared., B. Hügel: None declared., C. Simonaro: None declared., E. Schuchman Shareholder of: Plexcera Therapeutics LLC.

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**P286**

Effect of infliximab in sweet’s syndrome-pyoderma gangraenosum overlap syndrome

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Pediatric Rheumatology 2014, 12(Suppl 1):P286

Introduction: Both Sweet’s syndrome and pyoderma gangraenosum are neutrophilic dermatoses with abrupt onset of painful skin lesions. In Sweet’s syndrome systemic symptoms such as fever, headache and leucocytosis together with painful skin papules are often seen. Corticosteroid therapy is often sufficient treatment. Pyoderma gangraenosum is characterized by the development of painful ulcerative skin lesions and can be managed with anti-TNFα (infliximab).

Objectives: We report a symptom overlap between these two conditions with an excellent response to infliximab.

Methods: Case presentation.

Results: A 7-month-old girl, first child of non-consanguineous Danish parents, was admitted with multiple painful inflammatory skin lesions. Pregnancy and delivery were without complications. The child was born at term with a birth weight of 3970 g and received her first vaccination (diphtheria, pertussis, tetanus, haemophilus influenzae and polio) 3 months old without any complication. Two weeks after she received the second vaccination 6 months old she developed a 3 x 4 cm large skin lesion consistent with pyoderma gangraenosum, at the injection site on her right thigh. The following month she developed numerous ½-1 cm large, round, necrotic, painful ulcerations on the extremities and the neck. CRP was elevated to 106 mg/L; haematology and immunoglobulins were normal. Biopsy showed lesions with diffuse, neutrophilic infiltrates but without granuloma or vasculitic abnormalities; the findings were therefore compatible with Sweet’s syndrome. On high-dose corticosteroid treatment with pulse methylprednisolone (10 mg/kg/day for 3 days) followed by oral prednisolone (2mg/kg/day) the initial response was marked. However, on repeated attempts of tapering off prednisolone she flared on even high doses of prednisolone (2 mg/kg/d) and azathioprine. She then received treatment with infliximab (7-8 mg/kg) resulting in a rapid and dramatic response within few days and went into remission and corticosteroids were finally tapered off. After 6 doses of infliximab the treatment was stopped. Remission has currently lasted one year after termination of medical treatment.

Conclusion: This case shows that the clinicians have to be aware of the overlap between Sweet’s syndrome and pyoderma gangraenosum in order to identify patients that might benefit from anti-TNFα therapy.

Disclosure of interest: None declared.

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http://www.ped-rheum.com/supplements/12/S51
P287
Case autoimmune pancreatitis in children
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Pediatric Rheumatology 2014, 12(Suppl 1):P287

Introduction: Autoimmune pancreatitis represents 2% of chronic pancreatitis, most often in adult male presentation associated with IgG4. We present a case of a patient 6 years old, with a dependent pancreatic and bile duct obstruction abdominal mass, which is interesting because this presentation in children is more common with autoimmune pancreatitis that malignancies. Objectives: Show an exceptional case in pediatrics rheumatology. Methods: Presentation of case. Results: Female 6 years old, previously healthy, 3-year evolution gastric recurrent vomiting, abdominal pain intermittently mesogastria, adding hipoxia, jaundice and increased waist circumference, with palpable mass in the right upper quadrant. Cholestatic syndrome, 857 Lipase, amylase 137 Immunglobulin IgG subclass 4: 23mg/dl (5-6 years: 1-121). CT: dilatation of intra and extra hepatic bile duct. Level space-occupying hepatic hilum extending to pancreatic head and esophagogastric junction mass. Gonadotropin and alpha-fetoprotein: negatives. Cholecystectomy, incisional biopsy of tumor, liver biopsy was performed. He reported: lymphoplasmacytic sclerosing pancreatitis. (chronic autoimmune pancreatitis).

Conclusion: This is a rare autoimmune disorder that resembles a pancreatic neoplasm with biliary obstruction, occurring primarily in adults, making it an exceptional case in pediatrics. As part of an IgG4-associated systemic disease, serum level may be normal in up to 40 %, being positive in pancreatic tissue. Disclosure of interest: None declared.

P288
Femoral osteochondrosis mimicking chronic arthritis
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Pediatric Rheumatology 2014, 12(Suppl 1):P288

Introduction: Osteochondrosis or osteochondritis are alterations characterized by failure in sub-chondral ossification and affects the immature skeleton of children and teenagers. It may affects any epiphyseal growth plate and may affect the femoral condyle, as presented, and may affect considerably the quality of life. General physicians, pediatricians and specially rheumatologists and orthopedic surgeons should be alert to this condition. Attention should be given to any child or teenager who complains of chronic articular pain or has growing disturbance because this condition may lead to severe deformities, as presented, and may affect considerably the quality of life. Disclosure of interest: None declared.

P289
A case of neurosarcoidosis with aggressive characteristics
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Pediatric Rheumatology 2014, 12(Suppl 1):P289

Introduction: Here we are presenting a case of sarcoidosis with extensive systemic and neurologic involvement. Although different immunosuppressant modalities were used, the neurologic symptoms recurred. Management of neurosarcoidosis can be challenging and needs multidisciplinary approach. Objectives: Presenting a case of sarcoidosis with extensive systemic and neurologic involvement. Methods: A male patient, who was 14 years old at that time, applied to the emergency department 4 years ago with right sided hemiplegia, right sided hemianopsia and disarticulated speech. Cranial MRI showed T2 and flair hyperintensities on optic tractus and chiasma opticum. This finding was consistent with either neoplastic diseases or aggressive inflammatory processes. Lomber punction revealed no specific finding. As the patient had pansitopenia, bone marrow aspiration / biopsy was performed. Paratrabecular granuloma was found in the bone marrow biopsy. To analyse pansitopenia and Hepatosplenomegaly, the patient underwent portal Doppler USG imaging. Splenic vein calibration seemed to be increased. A gastroscopy was performed and grade 1 esophagus varices were visualized. Abdominal CT scan showed many lymph nodes of 2 cm or larger. Hepatic biopsy showed non-necrotizing granulomatous lesions and EZN stains were negative. Abdominal lymph node biopsy was performed by a laparotomy and Schaumann bodies were seen at the microscopic analysis. The patient was given 60 mg methylprednisolone daily and 20 mg MTX weekly. MRI after 3 weeks showed minimal regression and clinical signs of the patient ameliorated. Steroid was continued by tapering the dose and MTX was given for 6 months. As the neurological signs of the patients couldn’t be cured, patient was re-admitted after 6 months. MRI showed prominent progression in the lesions. Spinal MRI showed sequel lesions due to involvement of the spinal cord. Infliximab treatment was planned but couldn’t be continued as allergic reaction developed. Cyclophosphamid treatment was started but had to be stopped after 5 doses because of side effects (nausea, vomiting). In order to manage the procedure to reduce articular deformity and epiphysisodesis of bilateral distal femur. After 5 years, when the patient was 15 years old, his cousin, who lived in a different city, showed similar symptoms of the same disease. In this case, the disease started at 6 years old, triggered by a trauma after falling in the ground. After one week, he started presenting progressive swelling and pain on the right knee. After one month, the left knee also presented significant local edema with flogistic signs and he was sent to a rheumatologic clinic. He was treated as JIA for one year with naproxen, MTX and prednisolone and developed severe bilateral valgism deformity. After knowing of the similarity of his cousin’s disease he came to our clinic and was diagnosed as bilateral femoral condyle osteochondrosis. Results: Osteochondrosis is a heterogeneous clinical condition regarding its clinical presentation and severity, and has been described in medical literature for a long time. The course of the history showed that the repetitive trauma and excessive stress may have a role in the pathogenesis of osteochondrosis (DOUGLAS, 1981). Another important etiologic factor to be considered is the insufficient blood supply. Several animal models studies have demonstrated an important association of inadequate perfusion of cartilaginous channels and the subsequent development of local osteochondrosis (YTREHUS, 2004).

Conclusion: Although femoral bilateral osteochondrosis is very rare, its clinical presentation and severity, and has been described in medical literature for a long time. The course of the history showed that the repetitive trauma and excessive stress may have a role in the pathogenesis of osteochondrosis (DOUGLAS, 1981). Another important etiologic factor to be considered is the insufficient blood supply. Several animal models studies have demonstrated an important association of inadequate perfusion of cartilaginous channels and the subsequent development of local osteochondrosis (YTREHUS, 2004).

Disclosure of interest: None declared.
progressive neurologic findings Rituximab (4 doses in total) was applied. However patient presented with recurrent neurological findings and Adalimumab treatment was given. Hepatic sarcoids were regressed in abdominal USG but gastrosopic images showed grade 2 esophagus varices. Patient had received a total of 3 doses till now and seems to have a slow regression for neurological findings.

Results: Adalimumab treatment can be effective for neusarcoidosis.

Conclusion: Management of neuusarcoidosis could be challenging despite usage of many immunosuppressant modalities.

Disclosure of interest: None declared.

P290
Sjögren’s syndrome in a child presenting with cutaneous findings

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Pediatric Rheumatology 2014, 12(Suppl 1):P290

Introduction: Sjögren’s syndrome (SS) is a systemic autoimmune disease that presents with inflammation of lacrimal and salivary glands and accompanied by extraglandular complications. The spectrum of disease extends from sicca symptoms to systemic involvement. In childhood, SS is an extremely rare autoimmune disorder (1). Here we present a girl with SS who was first presented with cutaneous lesions.

Objectives: A 12-year-old girl was admitted to our hospital due to large erythematous lesions on pretibial region that has been seen for three years. These lesions were started with hyperemic, tender and nodular forms then changed to a dark brown macular coloration and persists afterward. She did not suffer from dry mouth or eye. However, when the medical history was examined carefully, she pointed out that she had no teardrops. Erythrocyte sedimentation rate (ESR) was 43 mm/hour, C-reactive protein (CRP) was 0.43 mg/dl, antinuclear antibody test was 1/320 (+), anti-Ro and RF was positive and anti-La was negative. She had bilateral positive Schirmer test (2mm/2mm). Biopsy of the salivary gland revealed lymphocytic infiltration. With positive Schirmer test, positive anti-Ro antibody and ANA and supportive biopsy findings, the diagnosis of SS was established. She was started 200 mg/day hydroxychloroquine and symptomatic therapy with eye drops.

Methods: Case report.

Results: Case report.

Conclusion: Skin lesions may be the first symptoms of an underlying autoimmune disease. Although cutaneous involvement is highly seen in patients with SS, it is an uncommon disorder in pediatric population (2). Therefore, pediatricians should be aware of the possibility of a coexisting disease especially when the lesions are unusual.

Disclosure of interest: None declared.

P291
Rapidly progressive glomerulonephritis, thrombotic microangiopathy and amebic colitis: a challenging case report

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Pediatric Rheumatology 2014, 12(Suppl 1):P291

Introduction: Thrombotic microangiopathy (TMA) describes a pathological process of microvascular thrombosis, consumptive thrombocytopenia and microangiopathic haemolytic anaemia, leading to end-organ ischaemia and infarction. TMA is a feature of a number of clinical disorders, most commonly hemolytic uremic syndrome (HUS) and thrombotic thrombocytopenic purpura. Several molecular mechanisms mediating TMA have been elucidated; however, challenges remain in distinguishing specific causes of TMA in the presence of overlapping clinical features.

Objectives: We aim to report a case of thrombotic microangiopathy, rapidly progressive glomerulonephritis and amebic colitis.

Methods: A 12-year old previously healthy boy was admitted with acute renal injury, requiring dialysis. Initial lab exams revealed urea of 213 mg/dL, creatinine 6.0 mg/dL, hematocrit 18%, hemoglobin 7 g/dL, thrombocytopenia, LDH 5900 mg/dL, urine protein-to-creatinine ratio of 4.3, and low C3. Due to evolution with myocardial dysfunction and pericardial tamponade, IV methylprednisolone (MP) pulses were started and he developed massive gastrointestinal bleeding due to amebic colitis, evidenced at colonic biopsy. Plasmaphersis, gammaglobulin, metronidazole and teclozan, were initiated, and after infection control: MP pulses, Rituximab, cyclophosphamid and therapeutic low-molecular weight heparin. Renal biopsy revealed crescentic glomerulonephritis, IgG and C3 on glomeruli, and C1q tubular deposits, but also arteriolar TMA. Despite this, he developed end stage renal disease. Serial autoantibodies tests were negative. ADAMTS13 activity assay was 80%. Immunological investigation performed after immunosuppression showed persistent and marked reduction of serum IgA/IgM/IgG and lymphocyte, even after discontinuation of cyclophosphamide and rituximab. This patient currently has mild thrombocytopenia, leukopenia, lymphopenia, labatorial signs of hemolysis, and livedo reticularis. Genetic studies for complement-mediated diseases are pending.

Results: This is a case with severe evolution, characterized by rapidly progressive glomerulonephritis and TMA. The main question is whether this patient has atypical HUS, perhaps associated with amebic dysentery, or an antiphospholipid syndrome. The persistently negative autoantibodies, and the partial response to the adopted treatment, made pSLE less probable.

Conclusion: The persistent active disease and the extreme difficulty of vascular access for renal replacement therapy make it urgent to perform kidney transplantation. Considering the high risk of disease relapse and subsequent loss of renal graft, it is essential to confirm the diagnosis to decide to use eculizumab (anti-C5 monoclonal antibody) or not, and especially to ensure better post-transplant prognosis.

Disclosure of interest: None declared.

P292
Clinical manifestations of four patients diagnosed with early-onset sarcoidosis or sarcoid-like syndrome

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Pediatric Rheumatology 2014, 12(Suppl 1):P292

Introduction: Sarcoidosis is a rare multisystemic granulomatous disease. Pulmonary involvement is common in adults, but any organ can be affected.

Objectives: To describe the main features of 4 pediatric patients diagnosed with early-onset sarcoidosis (EOS) or sarcoid-like syndrome.

Methods: Medical charts were reviewed.

Results: Four patients were enrolled, 2 female (cases 1 and 2) and 2 male (cases 3 and 4). Their main characteristics are shown in table 1. The age at disease onset was 1.5, 10, 0.6 and 11 years respectively. The time until diagnosis ranged from 4 days to 8 years. The two cases with EOS (1 and 3) had been previously diagnosed as Juvenile Idiopathic Arthritis. Both started at a short age with the classical triad and carried a heterozygous gain-of-function NOD2 mutation. Patient 2 seemed to be a late-onset sarcoidosis but persistent hypogammaglobulinemia and poor antibody production suggested a CVID, despite she did not suffer from recurrent infections. Other granulomatous lung diseases were dismissed in this case. Finally, diagnosis in patient 4 was made according to his clinical manifestations and the slight increase in ACE level.

Conclusion: Diagnosis of sarcoidosis in pediatric patients is often delayed because the disease is not suspected. Pulmonary involvement occurs less frequently in pediatric than in adults patients. This condition requires multidisciplinary management.

Disclosure of interest: None declared.
Table 1 (abstract P293) Main features of the four enrolled children

<table>
<thead>
<tr>
<th></th>
<th>Clinical data</th>
<th>Analytical data</th>
<th>ACE</th>
<th>Non-caseating granulomata</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Arthritis, rash, uveitis</td>
<td>Heterozygous p.R334Q mutation at NOD2 gene</td>
<td>27.5</td>
<td>Skin</td>
<td>EOS</td>
</tr>
<tr>
<td>2</td>
<td>Splenomegaly, lymphadenopathy, interstitial/nodular lung disease</td>
<td>Lymphopenia, Thrombocytopenia, Hypogammaglobulinemia</td>
<td>92</td>
<td>Lung</td>
<td>CVID, sarcoid like syndrome</td>
</tr>
<tr>
<td>3</td>
<td>Arthritis, rash, uveitis</td>
<td>Heterozygous p.C495Y mutation at NOD2 gene</td>
<td>19</td>
<td>Skin</td>
<td>Blau’s syndrome</td>
</tr>
<tr>
<td>4</td>
<td>Right facial paralysis, parotid enlargement, uveitis, high fever</td>
<td></td>
<td>74.8</td>
<td></td>
<td>Heerfordt’s syndrome</td>
</tr>
</tbody>
</table>

ACE = angiotensin converting enzyme serum level (normal 10-50 IU/l)
CVID = common variable immunodeficiency

P294
Update of the japanese national registry of pediatric rheumatic disease
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Pediatric Rheumatology 2014, 12(Suppl 1):P294

Introduction: We, Pediatric Rheumatology Association of Japan (PRAJ), have set up new online national registry of pediatric rheumatic diseases. 

Objectives: We report the first several months of enrollment to PRICURE (Pediatric Rheumatology International Collaboration Unit Registry).

Methods: Professor Shuji TAKEI, the former chairman of PRAJ had ordered his working group to set up a new registry system in 2012. Ethical issues about the registry in which we use clinical information were discussed by ethics committee of PRAJ and it had been approved in 2013. We started to collected basic information (e.g. name of rheumatic disease, age of onset, sex, clinical course) and further information (e.g. clinical symptoms, laboratory examination abnormalities, radiological examination abnormalities, treatment, complications) by web-based way in spring 2014.

Results: In the end of May 2014, 394 cases had been registered in the PRICURE. The number of cases of each diseases are as follow, Juvenile Idiopathic Arthritis 174, Systemic Lupus Erythematosus 65, Juvenile Dermatomyositis 43, Sjogren syndrome 26, Systemic Sclerosis 12, Behcet Disease 8, Vasculitis 16, Autoinflammatory Disease 38.

Conclusion: We hope that this registry contribute to the development of clinical research in the field of pediatric rheumatology.

Disclosure of interest: None declared.

P295
Pain threshold in adolescents with juvenile idiopathic arthritis and fibromyalgia
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Pediatric Rheumatology 2014, 12(Suppl 1):P295

Introduction: Pain is a frequent complaint in pediatric practice and is present in several chronic organic diseases, such as juvenile idiopathic arthritis (JIA). While JIA patients show symptoms such as inflammation of the joints and other structures, such as the heart and eyes, patients with idiopathic musculoskeletal pain (IMP) experience a painful condition that is not associated with presence of tissue injuries. Juvenile fibromyalgia (JFM), disorder characterized by recurrence of disabling pain, is a classic example IMP. This study shows preliminary data of a protocol for evaluation of brain activation using functional magnetic resonance imaging (fMRI) after a painful stimulus produced by pressure.

Objectives: To evaluate and compare the pain threshold in adolescents with JIA and JFM that will be examined by fMRI scan.

Methods: Twenty nine adolescents were divided into 3 groups: 10 adolescents with JFM, 9 adolescents with JIA and 10 healthy adolescents without complaints of pain.

Using a mechanical system, designed for experiments with fMRI, a series of discrete pressure stimulus were performed, with duration of 5 seconds, applied on the left thumb by a stiff rubber tube connected to a hydraulic piston, enabling a controlled and reproducible stimulation. Participants were asked to grade the intensity of pain sensation evoked by an ascending series of pressure stimulus, until the subjective rating of pain reported was graded as 4 (four).

Results: The amount of pressure used in the pressure stimulus was significantly different between groups (p = 0.0003). The pain threshold was lower in JFM group (mean pressure used = 3.70 kg/cm²), followed by the group of healthy adolescents (4.45 kg/cm²) and the JIA group (4.88 kg/cm²). All participants reported the same subjective pain rating 4 (four).

Conclusion: Adolescents with JFM presents a decrease in the threshold for pain, which was significantly lower when compared with adolescents with JIA with long history of organic pain.

Disclosure of interest: None declared.

P296
Prevalence of joint hypermobility in children with inguinal hernia
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Pediatric Rheumatology 2014, 12(Suppl 1):P296

Introduction: The Joint Hypermobility Syndrome (JHS) is a multi-system inherited connective tissue disorder caused by defective fibrous tissue matrix proteins such as collagen. Joint hypermobility has been occurred more frequently in children, with diminishing occurrence as age increases in population studies. The prevalence of hypermobility in children has been reported to be between 2.3 and 30%. Hypermobility is associated with weakness of abdominal wall and pelvic floor and predisposes to increased risk of hernia, hiatus hernia, and rectal prolaps.
Objectives: The aim of this study is to determine the relation between joint hypermobility syndrome (JHS) and unilateral and/or bilateral inguinal hernia in children.

Methods: A case-control study has been conducted in which 67 patients with inguinal hernia (unilateral and/or bilateral) were accompanied by 86 healthy control group (age between 4 to 16 years old). The joint hypermobility was assessed by searching in all of the possible joints according to Beighton scoring system. Student’s t-test and Chi-squared test were used for the test of significance where applicable and P < 0.05 was considered significant.

Results: The prevalence of joint hypermobility in children with inguinal hernia (unilateral and/or bilateral) was 80.6% (54 of 67). The 60 out of 67 patients (89%) had unilateral and 1 (1.4%) cases had bilateral hernia. The prevalence of joint hypermobility in the group with unilateral hernia was 80%(48 of 60) and in bilateral hernia was 14.3% (1 of 7). Comparison of the prevalence of disease between case and control groups indicated statistically significant difference (P<0.001).

Conclusion: In our study, there was a significant correlation between joint hypermobility and both unilateral and/or bilateral inguinal hernia.

Disclosure of interest: None declared.

P297 A new mutation in blau syndrome: case report
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Pediatric Rheumatology 2014, 12(Suppl 1):P297

Introduction: Blau syndrome is a rare autoinflammatory granulomatous disease and inherited as autosomal dominant. The classical triad of Blau syndrome is granulomatous dermatitis, symmetric arthritis and recurrent uveitis. However, all of these findings may not be together in the patients. In the majority of patients, the disease is characterized by early onset that usually before 3-4 years of age. The ocular findings of Blau syndrome occur usually after the articular and skin findings.

Objectives: Our aim is to describe a new mutation of Blau syndrome here. The defective gen of Blau syndrome is located 16q12.2-13 locus and NOD2 gen is found in this locus. So far, ten NOD2 mutations have been described that causes Blau syndrome. In addition, seven NOD2 mutations have been described that may be associated with Blau syndrome. These mutations are heterozygous state mostly.

Methods: Five years old male patient had developed papular rash that lasted one year at 5 month old, bilateral knee and ankle arthritis at 4 year old and right anterior uveitis at 5 year old. His papular rash and anterior uveitis was compatible with granulomatous vasculitis and granulomatous uveitis, respectively.

Results: Blau syndrome gen studies revealed heterozygous missense NOD2 mutation (P507S [c.1519C>T]).

Conclusion: Up to date, 10 Blau-associated genetic mutations have been identified within thisgene, almost in heterozygous state. Two of these mutations are heterozygous state mostly.

Disclosure of interest: None declared.

Reference

P298 Eosinophilic granuloma: case report
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Pediatric Rheumatology 2014, 12(Suppl 1):P298

Introduction: Lameness is a symptom very common in childhood, it depends on inflammatory, neoplastic, infective, orthopedic diseases.

Objectives: To describe a clinical report of a Eosinophilic Granuloma beginning with lameness.

Methods: V. 29 months old comes to our hospital because of persistent lameness. The symptoms began three months before, after a trauma. For persisting pain and lameness the child was checked by an orthopaedist who diagnosed “hip transitory synovitis”. Infact radiography and ultrasonography of the hip and femoral head were negative. The child was prescribed therapy with NSAIDs. At first the child’s conditions improved, but after sometime his leg was in pain again. When he came to our observation in the articular examinations revealed pain, functional limitation of the right leg and lameness, inflammatory indexes (EBS and CRP) were normal. Suspected of having a Perthes disease the child underwent to another right leg radiography that revealed the presence of a remodelling area with an osteolytic lesion near the big trochanter. The CT scan confirmed the osteolytic lesion with sclerotic regular margins eroding the cortical bone. Scintigraphy performed with tc99 showed solitary bone lesion with a slightly increased blood flow and metabolism. So we decided to perform a needle biopsy to define the diagnosis.

Results: Histologic examination of the lesion revealed connective proliferation, edema, with different subtypes of immune cells (lymphocytes, granulocytes, eosinophils) and histiocytes. So was made diagnosis of Eosinophilic Granuloma and was performed a surgical curettage of the lesion.

Conclusion: Eosinophilic granuloma (EG) is a rare histiocytic disease due to clonal proliferation of Langerhans cells. It is characterized by single or multiple bone lesions involving cranium, mandible, pelvis, ribs, spine and long bones, in particular femur. Eosinophilic granuloma onsets with pain, getting worse during the night, and edema, in this phase laboratory tests are normal. Imaging (radiography, CT scan, scintigraphy,magnetic resonance) shows single or multiple osteolytic lesions, with cortical erosion. This disease has to be differentiated by a destructive lesion includes malignancy such as Ewing sarcoma, lymphoma, leukemia, and metastasis as well as osteomyelitis. Biopsy of one of the lesions is often needed for diagnosis.

Disclosure of interest: None declared.

Reference

P299 Study of the bone tissue structural-functional state in children in the East of Ukraine
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Pediatric Rheumatology 2014, 12(Suppl 1):P299

Introduction: The problem of osteopenia and osteoporosis in children turned from a rare pediatric problem to a frequent pathology which is difficult to diagnose. This problem is especially urgent for the present-day in Ukraine because the level and quality of therapeutic and diagnostic care as well as nutrition quality are influenced by the transformation of the society. The critical years for building bone mass are during childhood and adolescence. This is when a new bone is formed more quickly than the old bone is removed, causing bones to become larger and denser.

Objectives: The 1126 children aged 9-17 residing in the East of Ukraine.

Methods: The ultrasound densitometry.

Results: According to the findings of population study we worked out special nomograms for evaluation of structural-functional state of the bone tissue in children population in Ukraine for the use by medical practitioners. Active accumulation of the bone mass is observed between the age of 11-12, its increase equals 7-8% per year. The periods of intensive growth and active bone mass accumulation occur at the same time. The incidence of osteopenic disorders in the bone tissue structural-functional state in children aged 9-16 in a large industrial area is (20.5± 1.1%) and changes with the age, gender, residence from (14.6±2.3%) to (30.3±4.0%). In the children, the incidence of stage 1 osteopenia is (9.3± 1.1%), stage 2 – (7.1±0.8%), stage 3 – (4.1±0.5%). Thus, the most frequent variant of osteopenia is stage 1 disturbance (43.3% of the cases), 20.0% of cases are marked osteopenic disorders (stage 3). Age- and gender-related differences in the values of osteopenia prevalence in children are characterized by prevail of its frequency in the young group (9-12 years) over the older group, which is more pronounced in girls (24.8±1.8%) and (18.2±2.0%), respectively, p<0.05, first of all due to the larger frequency of stage 3 osteopenia (16.4±1.2%) and (3.5±0.8%), respectively, p<0.05. In girls from rural regions, osteopenia incidence was (16.7±1.9%), in the younger age group, stage 1 and stage 3 osteopenia were more prevalent (9±3.3%) and
The necessity of implementation of nomograms for S. pyogenes infection to PANDAS, another pediatric neuropsychiatric disorder. 40% of patients (66.9%) showed a complete or partial remission of the initial OCD/tics, whereas 53.1% of patients (7/103 patients (6.5%). Out of these whom, 3 presented a recent Ebstein Barr virus infection, 3 had signs of a recent M. pneumonia infection and in 1 patient a recent B. burgdorferi infection was demonstrated. As specified in “patients and method”, 77 patients were evaluated by MRI, EEG, and echocardiography, which were normal in all subjects. All patients were treated with amoxicillin and benzathine benzylpenicillin. Sixty nine patients (66.9%) showed a complete or partial remission of the initial symptoms.

Conclusion: Our data confirm that patients with PANDAS present an acute abrupt clinical onset at mean age of 6±2 years. This neuropsychiatric disorder is mainly observed in males, commonly having other relatives suffering from neuropsychiatric disorders (about the 50% of them). Seven patients did not present evidence of S. pyogenes infection, and these patients may be collocated in the PANS group. Antibiotic therapy seemed to be efficacious also in the latter patients, with a complete or partial remission of symptoms. Our data highlight the close clinical similarity between PANDAS and PANS. In clinical practice, these two disorders may be distinguishable only using laboratory test with the aim of identifying their etiologic agents.

Disclosure of interest: None declared.

P301
Internet access and utilisation of adolescents attending a national centre for paediatric rheumatology
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Pediatric Rheumatology 2014, 12(Suppl 1):P301

Introduction: With emerging interactive and communication technologies now available, the internet has become one of the top health information resources for adolescents (Stinson et al., 2010). Adolescents are typically the early adapters of new technologies, with in particular, the internet providing innovative opportunities for engaging youths. Traditional sources of health information are now becoming defunct and young people are increasingly going online for health related information.

Objectives: To assess internet access and utilisation of adolescents.

Methods: A convenience sample of 25 patients completed an online questionnaire. The questionnaire assessed the following: 1. Adolescents access and utilisation of the internet. 2. Adolescents utilisation of the internet to access health related information.

Results: From the 25 respondents 52% were female, 48% male. The mean age was 14.5 years (S/D: 11-18 years).

1. Access & utilisation of the internet: 100% stated they have access to the internet on a daily basis with 85% using the internet 7 days per week. The reported time spent online ranged from 1 to 9 hours per day, mean: 2.9 hours. Table 1.

2. Adolescents utilisation of the internet to access health related information: 65% stated they use the internet to look up health information. Of these, 85% researched their own medical condition/diagnosis followed by medications (35%), pain/coping with pain (21%), other medical conditions (21%), alcohol and medication (14%) and sexual health (7%).

When asked to list recent search items used to look up health information the following were listed: pain, explaining arthritis to others, drinking alcohol on methotrexate, hypermobility syndrome, lupus, methotrexate, medications and pregnancy, and TNF medications. 52% of respondents use the internet to communicate with peers who have a similar diagnosis. Of these, 100% use a facebook page linked with a community support group for adolescents and young people with rheumatic diseases.

Conclusion: The internet has become an important tool for many people with health concerns; adolescents being no exception. Health professionals

Table 1(abstract P301) Respondents had numerous ways to access the internet

| Mobile phone | 76% |
| Personal laptop | 68% |
| Tablet | 60% |
| Game Console | 40% |
| Home PC | 76% |
| School Computer | 36% |
must know how to guide and advise adolescents in need of health related information to material that is both reputable and of a high standard while being age appropriate and appealing (Skinner et al., 2003).

**Disclosure of interest:** None declared.

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**P302**

**Use of internet in adolescents and young adults with JIA**

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**Pediatric Rheumatology 2014, 12(Suppl 1):P302**

**Introduction:** Internet-use is increasing since it is an efficient way to find information. Information obtained via Health Related Internet (HRI) sites, or online peer support groups might increase knowledge and self-management in adolescents and young adults with Juvenile Idiopathic Arthritis (JIA).

**Objectives:** To evaluate the frequency of use and perceived relevance of HRI and its association with demographic, disease-related and psycho-social variables

**Methods:** In a cross-sectional study, JIA patients (age 10 - 27 years) were asked to complete a self-reported questionnaire. Frequency of using HRI-sites (regarding information about JIA, medication-use and aspects of JIA related to social life) as well as having online contact with fellow patients were evaluated. Perceived relevance of HRI and contact with fellow patients were also questioned. Demographic variables, disease activity, medication and emotional behavior and coping were assessed as possible predictors.

**Results:** 142 patients were included. 71% had used internet to search general information on JIA, but specific topics like medication, were less searched for. 25% had ever visited a forum or had online peer contact. Perceived relevance of HRI-sites and opportunities for online peer contact was rated low (median 2.0; scale 0-10). Demographic and disease related factors, apart from female gender, were not associated with HR use. Among psychological variables, in male, only coping styles “confrontation” and “reassuring thoughts” were associated with HR use. Emotional behavior was not associated.

**Conclusion:** Health Related Internet cannot be used as the only source of information for JIA patients since they use it infrequent and consider its relevance low.

**Disclosure of interest:** None declared.

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**P303**

**Tocilizumab for the treatment of refractory pediatric mixed connective tissue disease (MCTD), in two patients**

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**Pediatric Rheumatology 2014, 12(Suppl 1):P303**

**Introduction:** Mixed Connective Tissue Disease (MCTD) is a rare autoimmune disease of unknown origin. The diagnosis is suggested when there are overlapping symptoms of lupus, scleroderma and dermatomyositis. Kasukawa criteria are the most commonly used in pediatrics. Treatment should be tailored to the clinical symptoms but no specific recommendation regarding the therapeutic management has been established to date. Tocilizumab (TCZ), an inhibitor of interleukin 6 is used in juvenile idiopathic arthritis (systemic and polyarticular JIA) and Castleman’s disease. Only one case has been reported with TCZ in the context of a MCTD with pulmonary hypertension in a 45 year-old man with a favorable outcome.

**Objectives:** We report on two children diagnosed for a MCTD who presented with active arthritis despite various therapies including methotrexate (MTX) and TNFa blockers.

**Methods:** Description of two clinical cases.

**Results:** Case 1: A 7 year-old girl was initially diagnosed for a polyarticular JIA and was in remission under MTX and etanercept (ETA) combination. 8 years later (at the age of 15), she presented with a relapse with Raynaud’s phenomenon, sclerodactyly and polyarticular arthritis. Laboratory tests revealed the presence of ANA (1/1600), positive anti-DNAdb (30 UI/l) and positive anti-ENA (anti Sm-RNP at >8 UA/ml and anti U1RNP at >8 UA/ml). Because of low tolerance to MTX and joint manifestations in the foreground, treatment with TCZ was initiated. The joint outcome under treatment was shortly favorable. Regarding other autoimmune manifestations, the evolution was marked by the appearance of positive Coombs test with asymptomatic anemia, neutropenia, mixed, and an increase of anti-DNA titer. Other treatments consisted in a low dose steroids and hydroxychloroquine (HCQ).

Case 2: A 12 year-old girl presented with juvenile dermatomyositis and was successfully treated by steroids and MTX. 2 years later, she presented a relapse with Raynaud’s phenomenon, sclerodactyly, and a Gougerot-Sjögren’s syndrome. Autoantibody screening revealed positive ANA (1/1600) with anti-DNA 7,4 (Far assay) and positive anti-ENA (anti -SSA, anti -Sm, anti- Sm-RNP and anti -U1RNP). Various therapies including MTX, mycophenolate mofetil, HCQ, ETA did not manage to control arthritic symptoms. TCZ in combination with MTX was started at the age of 17 and was shortly associated to remission. Other manifestations, including Raynaud’s syndrome and liver disease, tended to persist. Other therapies consisted in a low dose steroids and HCQ with irregular compliance.

**Conclusion:** This is the first description of the use of TCZ for articular manifestations of pediatric-onset MCTD. These two observations suggest that TCZ is effective and safe on articular manifestations of MCTD. However, systemic autoimmune manifestations including leucopenia and hepatitis were not improved by the treatment. TCZ is as a therapeutic option in the MCTD with polyarticular manifestations refractory or intolerant to basic treatment.

**Disclosure of interest:** None declared.

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**P304**

**Histopathological and molecular analysis in dermis and epidermis of patients with systemic and localized scleroderma**

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**Pediatric Rheumatology 2014, 12(Suppl 1):P304**

**Introduction:** Scleroderma is a highly complex disorder in its clinical manifestations and pathogenesis. It has a wide range of clinical manifestations due to varying degrees of vasculopathy, autoimmunity, altered endothelium function, and abnormal fibrinosis which were accused in the pathogenesis of the disease.

**Objectives:** The aim of this study be made of the cases diagnosed in childhood with immune histochemical analysis is to shed light on the pathogenesis of the disease.

**Methods:** Single-blind clinical trial. The tissue samples obtained from patients PAS, hematoxylin and eosin, E-Cadherin, CTGF, Tunnel, and staining for TGF-β1 is applied and evaluated by light microscopy. Additionally, we have analyzed both TGFβ1 level and mRNA expression analysis in plasma and tissue samples from patients. A total of 15 patients were enrolled in the study. These patients, who were chosen from, systemic (n = 8) or localized (n = 7) scleroderma patients clinically received, and for the disease of any systemic untreated and scleroderma other than skin disease.

**Results:** In the study a total of 22 tissue samples (15 diseased tissue, healthy tissue and 7) were used. The mean age of onset was 9.2 ± 1.2 years and the mean age of diagnosis was 15.3 ± 3.2 years. All patients with systemic sclerosis have antinuclear antibody (ANA) titer 1/160-1/640. ANA positivity in patients with localized scleroderma were no. Clinically with different
characteristics in the two subgroups of the histopathology examination was shown to be distinct from the tissue level.

Conclusion: Playing a fundamental role in the pathogenesis of the TGF-B levels in both plasma and skin have been shown to be locally high. Particularly in patients with systemic scleroderma this elevation was found to be more pronounced. Treatment for this disease is still questionable. results obtained will throw light on new treatment possibilities.

Disclosure of interest: None declared.

P305
Localized scleroderma in a cohort of juvenile idiopathic arthritis children
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Pediatric Rheumatology 2014, 12(Suppl 1)P305

Introduction: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in childhood. Localized scleroderma also known as morphea is an inflammatory, fibrosing skin disorder that leads to sclerosis of the dermis and eventually of the underlying tissues. The prevalence is estimated to be 1-5/100,000 with the onset before 30 years of age in 2% of patients. The association between different autoimmune diseases is well described, but few studies have been performed to investigate the relationship between JIA and other autoimmune diseases, in particular very little is written about the possible association between arthritis and morphea. In these cases articular involvement in terms of arthralgia, impaired joint mobility, or joint contracture, may be related to a mechanical etiology secondary to the contracture of the overlying skin.

Objectives: To describe the association of morphea and JIA in our cohort.

Methods: We analyzed a total of 440 patients carrying the diagnosis of JIA followed in our Centre from January 1, 2010 to January 1, 2014.

Results: We found four children that were diagnosed to have also morphea: a 12-year-old boy with polyarticular JIA that presented on the inner surface of the right thigh a well demarcated plaque of about 5 cm in diameter, a 8-year-old girl with polyarticular JIA who had a linear lesion extending from the posterolateral surface of the right elbow to the back of the wrist as well as a small patch of 2 cm in diameter on the volar surface of the same elbow, a 7-year-old female with oligoarticular JIA with a patch on the anterior surface of the right leg and two similar, smaller lesions over the dorsum of the left foot and one over the dorsum of the right foot, and an 11-year-old Chinese boy with HLA-B27 positive enthesis-related arthritis that presented a linear skin lesion on the medial surface of the left knee. Except for the boy with the polyarticular form in which morphea preceded by one year the joint involvement, in the other cases morphea followed the arthritis, appearing in periods in which the disease was in remission and off any therapy. The boy with polyarticular arthritis was not treated because the lesion appeared already in the atrophic stage at the time of the first visit, while the other 3 children were placed on therapy with methotrexate at a dose of 15 mg/sq week per week subcutaneously for approximately one year in combination with 3 months of oral prednisone, 1 mg/kg/day. All of them achieved a clinical remission for a mean duration of 12 months.

Conclusion: In our series of children with JIA we documented the appearance of morphea in 0.9% of cases, which is more than would be expected by chance alone, and we observed an association with different types of articular onset. In these patients arthritis was localized in different and distant sites from those affected by morphea, removing the possibility of a mechanical phenomenon or of a misdiagnosis. Although localized scleroderma is considered an autoimmune disease limited to the skin the association with JIA could suggest a systemic imbalance of the immune system.

Disclosure of interest: None declared.

P306
Infectious agents in juvenile scleroderma
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Pediatric Rheumatology 2014, 12(Suppl 1)P306

Introduction: The problem of juvenile scleroderma (JS) is determined by a variety of clinical manifestations, tendency to early generalized process with the development of peripheral and visceral lesions. In the last decade various forms JS associated with Borrelia infection, as evidenced by the discovery of a skin biopsy patients spirochete Borrelia Burgdorferi afzelii, garrini and the presence of specific antibodies in the blood of patients. Besides bacterial relevant theory and molecular “mimicry” the herpes viruses, providing a provocative role in the development of JS.

Methods: 65 children with juvenile scleroderma were examined. Patients were divided into 2 groups: 41 patients with scleroderma (S) (mean age 13,1±0,4 years) and 24 with systemic sclerosis (SS) (mean age 12,7±0,5 years). All patients underwent bacteriological examination with nasopharyngeal flora definition of sensitivity to antibiotics. Antibodies in the blood was determined by Borrelia burgdorferi, Chlamydia psittaci, Herpes Simplex Virus Types 1, 2 and Cytomegalovirus. The concentration of interferon-gamma (IFN-γ) in the serum was determined by ELISA using kits from Immunotech (France).

Results: The most of children with the S (56.1%) and SS (87.5%) had chronic foci of infection (chronic tonsillitis, chronic pharyngitis, adenoids, chronic periodontitis). Staphylococcus aureus was allocated from the nasopharynx in 19.5% of patients with S and 25% of children with SS, β-hemolytic streptococcus was allocated from 17.1% of children with S and in 30.8% of the SS. Antibodies to Borrelia burgdorferi in blood serum identified in 39.1% of children with S and 37.5% of children with SS. Antibodies to Chlamydia psittaci in blood serum identified in 12.2% of patients with S and 16.7% of the SS.

The presence of chronic CMV infection revealed in 17% of children with the S and 20.8% of the SS. The presence of the herpes simplex virus infection revealed in 14.6% of patients with S and 25% with SS. Level of IFN-γ in serum was significantly lower in all children with S and SS than in healthy children (0.76±0.2 pg/ml). Reduction of IFN-γ plays a role in reducing the antiviral immunity and confirmed the role of RNA viruses in the development and progression of juvenile scleroderma.

Conclusion: The foci of chronic infection alter the reactivity of the organism causing an imbalance in the immune system of children, and is likely to play a pathogenic role in the occurrence of juvenile scleroderma. The presence of persistent viral infection and a significant decrease of IFN-γ in children with SS and S suggests a role of viral infection in the development and progression of juvenile scleroderma.

Disclosure of interest: None declared.

P307
The frequency of pulmonary hypertension in juvenile scleroderma
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Pediatric Rheumatology 2014, 12(Suppl 1)P307

Introduction: Juvenile scleroderma (JS), represents a rarely seen group of connective tissue disease with multiple organ involvement. Although quite rare in childhood, cardio-vascular and pulmonary involvements are the most important mortality and morbidity factors. Pulmonary arterial hypertension (PAH), the most important sequelae of pulmonary involvement, could be determined by echocardiographic examinations. Early cardio-vascular and pulmonary involvement determination is extremely important in reducing mortality of patients.

Objectives: The aim of the study was to use non-invasive methods (echocardiography, pulmonary function tests) to examine cardio-pulmonary involvement of the disease in patients. Treatment of patients with positive findings in the early stage of the disease possibly reduces the morbidity and mortality.

Methods: Totally of 35 patients with scleroderma, followed up at Cerrahpasa Medical Faculty, Pediatric Rheumatology Department with diagnosis of juvenile scleroderma were included in the study. Doppler echocardiography was performed at Cerrahpasa Medical Faculty, Pediatric...
Cardiology Department and pulmonary function tests were performed at Laboratory for pulmonary function tests at Cerrahpasa Medical Faculty. FVC and DLCO were measured in order to investigate pulmonary fibrosis. The assessment of PAP and risk factors for PAH was made by measurement of maximum tricuspid insufficiency (TI), end diastolic pulmonary insufficiency (PI), AT/ET, RAP and contraction of vena cava inferior during inspiration.

Results: The values of TI, PI, AT/ET and PAP were found to be normal and statistically significant different from the pathological values. The results of FVC and DLCO were found to be statistically significant above normal values. In other words, no patient was found to have cardio-pulmonary involvement.

Conclusion: Although quite rare in juvenile scleroderma, cardiovascular and pulmonary involvement is the most important factor in the prognosis of the disease. Early diagnosis, regular follow up and appropriate treatment are important in reducing the cardio-vascular and pulmonary complications of the disease.

Disclosure of interest: None declared.

P308
Raynaud and digital ulcers in patients with juvenile systemic sclerosis: ambulatory iloprost protocol. A single center experience
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Pediatric Rheumatology 2014, 12(Suppl 1):P308

Introduction: Raynaud Phenomenon (RP) and digital ulcers (DU) are the main clinical manifestation of vasculopathy secondary to Juvenile Systemic Sclerosis (JSSc). Accepted treatment for RP is calcium channel blockers. Iloprost is indicated if active ulcers are present or if RP is refractory to treatment.

Objectives: The aim of this study was to assess the safety and efficacy of ambulatory treatment with intravenous prostanooids in children with RP and DU secondary to JSSc.

Methods: Three patients with JSSc and active digital ulcers were treated with intravenous iloprost. Our protocol establishes two treatments in the cold months: one in the beginning and the second 3 months later, of a continuous five day intravenous infusion of iloprost in a dose of 0.4-0.6 mg/kg/min perfusion through an elastomeric pump.

Results: Since 2007 we treated three patients with JSSc and active digital ulcers: two girls, 12 and 13 years, and a boy of 18 months old at time of first treatment. A total of 19 treatments of iv. iloprost were done, 15 of these in ambulatory basis with the elastomeric pump. Outcomes were good with a reduced number and severity of RP attacks in all patients, and reduced pain associated with RP and DU. No disabling or severe side effects were observed. Two patients, the girls, had no more active digital ulcers after the second treatment with a follow-up of 2 and 3 years respectively. One patient, male, has recurrent digital ulcers, but number has decreased from 4 to 1 not interfering with daily activities.

Conclusion: Iloprost iv. perfusion with the elastomeric pump at ambulatory is a safe and effective treatment for patients with refractory RP to calcium channel blockers and in patients with digital ulcers. The authors suggest two treatments in the winter season with reduction of number and severity of R and ulcer healing.

Disclosure of interest: None declared.

P309
Gain-of-function mutation in IFIH1 can cause both acardi-goutières syndrome and systemic lupus erythematosus with LGa-deficiency
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Pediatric Rheumatology 2014, 12(Suppl 1):P309

Introduction: Gain-of-function mutations in IFIH1 were identified in Aicardi-Goutières syndrome (AGS), a rare neuroinflammation disorder associated with elevated levels of type I interferon and characterized by leukoencephalopathy, brain atrophy and intracranial calcifications leading to profound intellectual disability, spasticity and dystonia. IFIH1 functions as an intracellular innate immune receptor that senses viral nucleic acids and leads to the induction of type I interferon and proinflammatory cytokines.

Objectives: We aimed to identify the underlying genetic defect in a 16-year-old girl with severe early-onset and refractory systemic lupus erythematosus (SLE), LGa-deficiency and mild lower limb spasticity without neuroradiological manifestations.

Methods: Whole-exome sequencing was performed on the index patient and her parents. Extensive immunological analysis was performed on serum and on peripheral blood mononuclear cells (PBMC) of the patient.

Results: We independently identified the same de novo p.Arg779His IFIH1 mutation in a young patient with severe refractory SLE with antiphospholipid syndrome as was described in two patients with an AGS phenotype without major immunological manifestations. The index patient in our study, a girl of European Belgian ancestry, was initially seen before the age of 1 year with frequent respiratory infections. Immunological testing revealed LGa-deficiency. By the age of 2.5 years she developed spasticity of the lower limbs, with normal cognitive and clinical development. Magnetic resonance imaging (MRI) of the brain and spine showed no abnormalities. At the age of 8 years the patient was diagnosed with SLE with secondary antiphospholipid syndrome. Clinically, she manifested arthritis, livedo rash, necrotizing cutaneous vasculitis and she developed a deep venous thrombosis. Blood analysis showed a marked inflammatory response, complement activation and highly increased levels of anti-dsDNA, anticardiolipin and anti-thyroid antibodies. Further analysis also showed elevated serum levels of interferon α and upregulation of IFIH1 on the RNA-level in patient PBMC. Single-photon emission computed tomography (SPECT) of the brain showed no signs of intracerebral vasculitis and brain CT and MRI did not show any microcalcifications or other abnormalities. Despite systemic immunosuppressive treatment, signs of autoimmune activation remained with persistently increased levels of circulating autoantibodies and complement activation, as well as persistently elevated interferon α in serum and IFIH1 upregulation in patient PBMC. Attempts at decreasing immunosuppressive medication were associated with disease flares. The lower limb spasticity has stabilized, cognitive functioning has remained excellent and all neuroradiological examinations have remained normal.

Conclusion: This finding adds a new gene association to Mendelian lupus erythematosus: what's the weight of the headache?

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Disclosure of interest: None declared.

P310
Neuropsychiatric manifestations in juvenile systemic lupus erythematosus: what’s the weight of the headache?
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Introduction: Juvenile Systemic Lupus Erythematosus (JSLE) as an autoimmune disease characterized by multiple organ involvement. The nervous system is often affected, with a higher frequency in children than in adults.

Objectives: To examine prevalence and features of neuropsychiatric manifestations in JSLE, focusing on headache.

Methods: The records of all patients satisfying the ACR criteria for JSLE admitted to our Hospital from 1980 to May 2014 were retrospectively reviewed. Disease activity at onset was measured by SLE disease activity index (SLEDAI); organ damage was assessed at last follow-up using the SLICC/ACR Damage Index (SDI). Using the 1999 ACR nomenclature for neuropsychiatric (NP) lupus syndromes, patients were divided in patients with (NPSEL) and without (nNPSEL) NP involvement. Headache was defined
as in the ACR nomenclature (ACR headache), as in SLEDAI (SLEDAI headache) and as “severe persistent headache: may be migrainous” (LHA).

Results: Of 97 patients included in the study 84.5% were female. The female to male ratio was the same both in NPSLE and nNPSLE. Our population was predominantly white (90.7%). The mean ± SD age at onset was 11.8 ± 6.9 years and at diagnosis 12.9 ± 6.9 years. Mean ± SD length of follow-up was 6.6 ± 5.7 years. The mean ± SD age at onset of NP manifestations was 14.4 ± 9.3 years. The overall prevalence of NPSLE manifestations was 52.6%; NP syndromes were already present at the onset in 20.6% JSLE patients. In Table 1 we display the most common central nervous system syndromes reported in our NPSLE patients. The mean SLEDAI score at onset was 15.5 ± 7.7 in NPSLE and 12.6 ± 6.3 in nNPSLE. Mean SDI was 0.84 ± 0.9 in NPSLE and 0.5 ± 1.3 in nNPSLE. NP involvement was significantly associated with a SDI ≥ 1 (p < 0.05). Lupus anticoagulant (LAC) was present in 50.9% NPSLE and 19.6% nNPSLE patients. Antiphospholipid antibodies (APL) were detected in 50.9% NPSLE and 10% nNPSLE patients. In the subset of NPSLE patients, positivity of LAC and APL wasn’t significantly associated with headache. Magnetic Resonance Imaging (MRI) was performed in 37 NPSLE patients and normal in 12. LHA definition was fulfilled in all patients with headache and pathological MRI.

Conclusion: Consistently with the literature, more than a half of our JSLE patients presented NP involvement. Headache is a frequent manifestation: it was reported in 38.8% JSLE and 72.5% NPSLE patients. Headache in JSLE deserves an accurate investigation. In the subset of NPSLE patients, positivity of LAC and APL did not significantly correlate with headache, which may also be due to small number of cases. Further prospective studies are needed to better understand and define headache in JSLE.

Disclosure of interest: None declared.

P311

Long-term outcomes in childhood-onset systemic lupus erythematosus: preliminary results of the CHILL-NL study

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Pediatric Rheumatology 2014, 12(Suppl 1):P311

Introduction: Childhood-onset systemic lupus erythematosus (cSLE) is a more severe disease when compared to adult-onset SLE, with higher disease activity at onset and during disease course, higher percentage of major organ involvement and more rapid accrual of damage. Long-term outcome studies on cSLE are rare.

Objectives: This study aims to describe the long-term outcomes of patients with cSLE that have reached adulthood.

Methods: All Dutch rheumatologists, immunologists, nephrologists, haematologists, neurologists were asked to refer cSLE patients to the CHILL-NL (CHILdhood Lupus in the NetherLands) study team. The study was promoted in magazines and on websites of the Dutch SLE patient organizations. Interested adult cSLE patients were asked to approach the study team. All patients were seen for a single study visit. Patients’ current health status was assessed with an extensive medical interview and physical examination. All previous medical correspondence was retrieved, including information regarding cumulative multisystem involvement, auto-antibody profiles, drug use and comorbidities. SLE disease activity index-2K (SLEDAI-2K) and SLICC damage index (SDI) was calculated. Quality of life and related factors such as educational and work status, fecundity, fatigue and depressive symptoms were assessed.

Results: 31 patients (87% female) are currently included with a median age at diagnosis of 13 years (range 9–18) and median disease duration at time of visit was 15 years (range 4–36). At time of visit, median SLEDAI-score was 4 (0–9). 20/31 (65%) patients had an SDI-score of at least 1 (median 1, range 0–7). Current medication use included hydroxychloroquine in 63% of all patients, prednisone in 52%. 48% of the patients were treated with at least one DMARD (MMF (27%), Azathioprine (25%) and others). Half of the patients ever had CNS involvement. Two thirds of patients ever had renal involvement. Of these patients, 33% had current proteinuria (>50 mg/mmol). Four (13%) patients had a renal transplantation. During their disease course, 32% of the patients had been hospitalised at least once due to a severe infection. Analyses on factors related to quality of life are pending. Table 1.

Conclusion: cSLE is associated with significant long-term consequences, including frequent renal and CNS involvement, accrual of damage in the

Table 1(abstract P310) Most common central nervous system neuropsychiatric syndromes

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Frequency (median + range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis</td>
<td>13 years (9 – 18)</td>
</tr>
<tr>
<td>Disease duration</td>
<td>15 years (4 – 36)</td>
</tr>
<tr>
<td>SLEDAI-score</td>
<td>4 (0 – 9)</td>
</tr>
<tr>
<td>SDI</td>
<td>1 (0 – 7)</td>
</tr>
<tr>
<td>Cumulative organ involvement</td>
<td></td>
</tr>
<tr>
<td>Skin</td>
<td>90%</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>83%</td>
</tr>
<tr>
<td>Haematological</td>
<td>83%</td>
</tr>
<tr>
<td>Renal</td>
<td>65%</td>
</tr>
<tr>
<td>Central nervous system</td>
<td>48%</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>46%</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>36%</td>
</tr>
<tr>
<td>Abdominal</td>
<td>19%</td>
</tr>
<tr>
<td>Peripheral nervous system</td>
<td>10%</td>
</tr>
<tr>
<td>(Vertebral) fractures</td>
<td>23%</td>
</tr>
<tr>
<td>Severe infections (hospitalization necessary)</td>
<td>32%</td>
</tr>
</tbody>
</table>

Table 1(abstract P311) Medication use

<table>
<thead>
<tr>
<th>Medication use</th>
<th>Current</th>
<th>Ever</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prednisone</td>
<td>52%</td>
<td>100%</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>25%</td>
<td>64%</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>0%</td>
<td>36%</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>63%</td>
<td>85%</td>
</tr>
<tr>
<td>Rituximab</td>
<td>0%</td>
<td>11%</td>
</tr>
<tr>
<td>MMF</td>
<td>27%</td>
<td>46%</td>
</tr>
</tbody>
</table>

Family history

<table>
<thead>
<tr>
<th>Degree</th>
<th>1st degree</th>
<th>2nd degree</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLE</td>
<td>14%</td>
<td>0%</td>
</tr>
<tr>
<td>other auto-immune diseases</td>
<td>55%</td>
<td>57%</td>
</tr>
</tbody>
</table>
P312

Sense of smell, anti-ribosomal p antibodies and neuropsychiatric manifestations in childhood systemic lupus erythematosus

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Pediatric Rheumatology 2014, 12(Suppl 1):P312

Introduction: Neuropsychiatric involvement in cSLE has a prevalence ranging from 20 to 95% and results in significant morbidity and mortality. Multiple autoantibodies have been reported in association with NPSLE. Anti-P seem to be highly specific for SLE and might also be a marker for SLE disease activity. In SLE population the prevalence of anti-P varies from 6% to 46% depending on ethnicity, age and clinical variables analyzed. Anti-P are able to binding neuronal cells of the limbic areas that are associated whit olfact dysfunction. Decreased olfaction was observed in patients with several central nervous system CNS diseases in which immune-mediated mechanisms might be implicated. Evidence that olfactory dysfunction is an early sign of neurologic diseases makes a patient’s sense of smell of direct relevance to the rheumatologist

Objectives: To assess the olfactory functions in cSLE patients compared with age- and sex-matched healthy controls, to examine the association between the sense of smell, anti-P, disease activity, damage and CNS involvement.

Methods: Olfactory functions were evaluated using the Sniffin Sticks test. All individuals were submitted to a standardized neuropsychiatric evaluation. Mood disorders were determined through Beck Depression and Beck Anxiety Inventory (BDI and BAI). Active neuropsychiatric lupus was diagnosed according to ACR guidelines. In SLE, disease activity was evaluated through SLE Disease Activity Index (SLEDAI), damage through Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SLICC-SDI). Anti-P was measured by ELISA kits, p<0.05 was considered significant.

Results: We included 61 patients (91.8% women) mean age of SLE patients was 17.51± 3.42 years and 61 controls matched for age and sex (p=0.701). Mean age of SLE patients was 17.51±3.42 years and 61 controls matched for age and sex (p=0.701). Smell deficit correlated with duration of disease (r=-0.295; p<0.05) and anxiety (r=0.279; p<0.05). A decrease in the sense of smell was observed in cSLE patients (31.14%) and control (27.87%) (p=0.697). Not observed olfactory alterations olfactory (p=0.518). Anti-ribosomal P antibodies were identified in 23% of cSLE patients (n=14) and 21% of controls (n=13) (p=0.721). Anti-ribosomal P antibodies were not associated with CNS involvement (p=0.561), but when we analyzed each manifestation separately, we only observed an association between the presence of anti-ribosomal P antibodies and convulsion (p=0.05).

Conclusion: Comparing cSLE patients and matched controls, we observed a significant decrease in the olfactory abilities in cSLE patients, which was correlated with duration of disease and CNS manifestations. Anti-P are predominantly found in the serum of children suffering from lupus with neuropsychiatric involvement, especially psychosis in adults, therefore, monitoring longitudinal these patients is needed for see whether will present during the disease neuropsychiatric manifestations and if decline olfactory might be a useful and easy tool for the physician in early diagnosis of CNS involvement in autoimmune diseases.

Disclosure of interest: None declared.

P313

Analysis of rituximab’s usage for the treatment of pediatric systemic lupus erythematosus

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Pediatric Rheumatology 2014, 12(Suppl 1):P313

Introduction: Systemic lupus erythematosus (SLE) is a heterogeneous autoimmune disease characterized by chronic inflammation that potentially leads to organ damage. Severe manifestations make the management of SLE difficult and challenging. Nonsteroidal antiinflammatory drugs (NSAIDs), antimarial drugs, glucocorticoids, immunosuppressive and cytotoxic agents are the mainstays of treatment. Unfortunately, these agents are related to a vast toxicity. For an amount of patients, these approaches arent enough to achieve disease activity control, especially in those with cytopenia, nephritis and neuropsychiatric lupus. For these cases, Rituximab (RTX) – a chimeric mouse/human monoclonal antibody specific for human CD20 B-cell – has been widely prescribed. It is known that B-cells have a central role in SLE pathogenesis, being precursors of plasma cells production autoantibodies, precipitating inflammation by producing cytokines, activation T-cells by presentation of self-antigens, and regulating T-cells activity via co-stimulatory molecules. Although the clinical trials of RTX in SLE had controversial results, RTX seems to be a valuable option as an off-label drug for refractory patients.

Objectives: To report the experience of a tertiary pediatric rheumatology center with RTX for patients with refractory SLE.

Methods: We performed a retrospective chart review of patients with SLE that received RTX in some moment of their disease from September 2009 to February 2013 due to refractory to traditional therapies. A satisfactory response was defined as reaching SLEDAI reduction in at least 50%, urina protein/creatinine ratio (UPCR) <50 mg/mmol (equivalent to proteinuria <0.5g/24h), and corticoid tapering to at least 50% of initial dose.

Results: Seven patients were in use of the medication in the revised period. All of them were female. Six patients had the diagnosis of lupus nephritis, and 1 had refractory plaquetopenia to standart drugs. Two patients had an inadequate response to RTX. One of them persisted with refractory plaquetopenia and the other died due to complications related to SLE. Out of the 6 patients with lupus nephritis, 4 (66%) achieved SLEDAI reduction of at least 50% after 4-6 months of RTX, as well showed an important reduction of proteinuria (≤0.5g/24h) and corticoid tapering.

One patient had improvement of her disease, however without achieving the parameters of satisfactory response to the RTX. For this reason, this patient was considered to have a partial response to the RTX. The results are according to those found in similar studies.

Conclusion: It is suggested that RTX continues to be used as a therapeutic option for patients with refractory SLE or with contraindication to traditional drugs. Prospected studies are still needed to evaluate efficacy and safety of RTX in pediatric patients.

Disclosure of interest: None declared.
A rare presentation of systemic lupus erythematosus: diffuse alveolar hemorrhage in an infant

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Introduction: Systemic lupus erythematosus (SLE) is a multisytem autoimmune disease characterized by a variable clinical picture and serological abnormalities. Children and adolescents generally have a more severe disease presentation; develop disease damage more quickly than adults with SLE. Diffuse alveolar hemorrhage (DAH) is a rare life-threatening complication in SLE. In this report a case of infantile onset SLE with DAH and negative ANA is presented.

Objectives: In this report a case of infantile onset SLE with DAH and negative ANA is presented.

Methods: Case report: A 1-year-old boy presented with petechia on his legs. Physical examination was notable for ecchymoses and petechiae in the lower extremities. He had a 2/6 systolic murmur and hepatomegaly. Arterial blood pressure was 121/81 mm/Hg (> 95th percentile). On admission, the patient’s hemoglobin was 7.2 g/dL, white blood cells (WBC) 15900/mm3, platelets 50200/mm3, BUN 25 mg/dL, creatinine 0.53 mg/dL, alanine aminotransferase 120 U/L, aspartate aminotransferase 99 U/L. Urinalysis revealed Ph 5.0, density 1020, blood 3+ and protein 2+. Spot urine protein creatinin ratio was 5.7 mg/mg. Complements C3 was 23 mg/dL (90-180 mg/dL) and C4 was 2.9 mg/dL (10-40 mg/dL). Direct Coombs was +4 positive. Bone marrow aspiration revealed hypercellular bone marrow with an increased myeloid series. Echocardiography revealed pericardial effusion. With the preliminary diagnosis of SLE, a renal biopsy was performed. Diffuse global proliferative nephritis (Class IV-G(A)) was confirmed. Glomerular deposits of IgG, IgM and complement C3 was seen with immunofluorescence microscopy. However, antinuclear antibody (ANA) and anti-dsDNA were negative.

Results: The patient was diagnosed as SLE with Systemic Lupus International Collaborating Clinics (SLICC) criteria which were reported to be more sensitive than ACR (American College of Rheumatology) criteria. The initial SLE Disease Activity Index (SLEDAI) was 15. Intravenous methylprednisolone was administered at a dose of 30 mg/kg/day. In the second day of treatment he suddenly developed dyspnea. Chest radiograph demonstrated diffuse alveolar shadows in both lungs without cardiomegaly. He was transferred to the intensive care unit with the diagnosis of acute respiratory distress syndrome (ARDS) and supported with mechanical ventilation. During this support severe lung bleeding was inspected from the endotracheal tube. Intravenous cyclophosphamide 500 mg/m2 was added to therapy and response to treatment was observed in a few days. He was successfully weaned off ventilator support after 7 days. In his 4th follow-up month, he is in remission with monthly cyclophosphamide and prednisolone.

Conclusion: Children and adolescents generally have a more severe disease presentation; develop disease damage more quickly than adults with SLE. Diffuse alveolar hemorrhage (DAH) is a rare life-threatening complication of SLE. It is an uncommon complication with estimates ranging from < 2 to 5.4 % in cohorts of lupus patients. DAH usually occurs in patients with established diagnosis of SLE; however, cases have been reported where DAH was initial presentation of SLE. DAH can often mimic severe pneumonia or ARDS. Optimal management of DAH has not been established. Use of cyclophosphamide has been linked to better survival as in our case. This case is having a combination of the rarely known presenting features of SLE as infantile onset, DAH and negative ANA.

Disclosure of interest: None declared.

P316
Psychiatric symptoms as the first manifestation of juvenile SLE complicated with Klinefelter’s syndrome

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Introduction: Systemic Lupus Erythematosus (SLE) is an autoimmune, multisystem disorder with diverse manifestations. There are limited reports on the neuropsychiatric findings as the first manifestation of systemic lupus erythematosus in children.

Objectives: A 14-year-old Iranian boy with two years history of cognitive dysfunction, behavioural problems and recent history of epistaxis was referred to Moffid’s Children Hospital, Tehran, Iran. His work-up ended to a diagnosis of Klinefelter’s syndrome associated with juvenile systemic lupus erythematosus.

Methods: It is a case report. It just reports a patient with unusual manifestation of systemic lupus erythematosus. The patient also had a chromosomal abnormality discovered by chromosomal study and the diagnosis of Klinefelter’s syndrome was confirmed.

Results: Patients with Klinefelter’s syndrome may exhibit behavioural problems and psychological distress. These psychiatric disorders will be more prominent if be complicated with Lupus in children. In fact, psychiatric symptoms can occur as the first manifestation of juvenile SLE.

Conclusion: In pediatric patients with psychiatric disorders, especially in those who do not respond well to the classical psychiactric treatments, a diagnosis of systemic lupus erythematosus must be strongly considered, especially if the patient has a positive family history of SLE.

Disclosure of interest: None declared.

P317
From symptom onset to diagnosis: a critical exploration into the experiences of young people with juvenile systemic lupus erythematosus (JSLE)

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The UK JSLE Study Group, Bernie Carter1,3
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Introduction: There is a paucity of literature relating to the experiences of young people before and during diagnosis of JSLE. An understanding of young people’s experiences and the issues relevant to them could help improve outcomes and facilitate the development of standards of care in JSLE.
Objectives: To describe the journey from onset of symptoms to diagnosis in JSLE from a young person’s perspective by exploring the stories they tell.

- Ascertain key points if any in the journey to diagnosis to generate deeper insight into access to care for young people with SLE.

Methods: An exploratory qualitative approach was used in one UK centre for paediatric rheumatology with young people who were participating in the UK JSLE Cohort Study and who had received their diagnosis after January 2010. The study utilised in-depth interviews with eight young people who told their story of their own ‘journey to diagnosis’. Data were subjected to thematic analysis (Braun & Clarke 2006). All ethical issues were addressed.

Results: Four themes were generated and are linked by a meta-theme ‘passing of time’. This was not a static concept; it moved slowly in the first two themes but was experienced as a single point in time in theme 3.

1. ‘Emerging Illness’ encompasses the first descriptions of a change in health, the emergence of physical symptoms and the impact of these symptoms on the young people’s lives. The main physical symptoms were tiredness, pain, rash, sickness and other non-specific symptoms. These symptoms gradually affect their lives preventing them from doing ordinary things. Often symptoms were dismissed or ignored.

2. ‘Seeking Help’ lasted from weeks to up to 2 years and covered the first and ongoing contacts with health services. All first contacts were with a General Practitioner; most young people experienced dissatisfaction with how their symptoms were dealt with.

3. ‘Diagnosis of Lupus’ was a significant time point as the young people experienced a change in health status. For some, diagnosis was a relief; others were worried by the implications of the condition. They all talked about how their diagnosis impacted on them and how it affected their family.

4. ‘Resilience, Reflection & Recovery’ encompasses the experiences that had occurred after diagnosis. It is characterised by things that went well and things that did not.

Conclusion: This study reveals how young people may not recognise symptom-related changes. It also shows the struggle they/their parents often have in being taken seriously when they seek help. All young people should have the opportunity to tell their ‘journey to diagnosis’ story to a care team member. This would allow experiences to be contextualised and support offered. Raising awareness about emerging symptoms of lupus and increasing support after diagnosis is also recommended. Understanding young people’s experiences of ‘symptom onset to diagnosis’ has the potential to reduce the impact and burden of this disease.

Disclosure of interest: None declared.

P319 Neuronal biomarkers and hippocampal volume in childhood-onset systemic lupus erythematosus
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Pediatric Rheumatology 2014, 12(Suppl 1)P319

Introduction: Hippocampal atrophy is associated with corticosteroid use and may be related to cognitive impairment in systemic lupus erythematosus (SLE). Some biomarkers associated with neuronal injury have been associated with neuropsychiatric SLE, but their roles in the pathogenesis and its validity and clinical applicability has not been studied in childhood-onset systemic lupus erythematosus (cSLE).

Objectives: To determine the possible relationship between hippocampal volume loss and S100β e subunit of high molecular weight neurofilament (NF-H).

Methods: We included consecutive cSLE patients followed in a cohort at the pediatric rheumatology unit at the State University of Campinas and age and sex matched healthy controls. All patients had disease-onset before the age of 18. Magnetic resonance imaging (MRI) scans were obtained through a standardized protocol (3Tessla Philips). Volumetric 1mm T1 weighted images were used for manual volumetric measurements. Volumes smaller 2 standard deviation from the means of controls were considered abnormal. Non-parametric-tests and correlation were used for statistical analysis. S100β and NF-H protein levels were measured by enzyme-linked immunosorbent assay using commercial kits from BioVendor, inc (Czech Republic) and compared by non-parametric tests.

Results: We included 71 cSLE patients (64 female; mean age 18.8 ±4.06 years) and 50 healthy controls with similar age and sex distribution. cSLE had a mean disease duration of 6.38 ±4.54 years. Neuropsychiatric manifestations were observed in 49 (69.0%) patients. The volumes of right (mean volume 3.38±0.57 cm3) and left (mean volume 3.40±0.60 cm3) hippocampi were significantly smaller when compared to controls (right: mean volume 4.45±0.5 cm3, p < 0.001; left: mean volume 4.43±0.45 cm3, p < 0.001). Hippocampal atrophy was identified in 46 (64.8%) patients. NF-H protein levels were increased in cSLE (101.80±89.40 pg/mL) when compared to controls (57.12±13.28 pg/mL, p=0.038). Serum S100β levels were significantly increased in cSLE (148.98 ±102.73 pg/mL) compared to controls (48.10 ± 38.52 pg/mL, p<0.001). No association of S100β and NF-H levels in cSLE patients with and without neuropsychiatric manifestations was observed. No association between S100β and NF-H with hippocampal volumes or hippocampal atrophy was observed.
Conclusion: Neuropsychiatric manifestations and hippocampal atrophy is frequently observed in cSLE patients, however no association with neuronal biomarkers was observed. Further studies need to be done to determine biomarkers for hippocampal involvement in cSLE.


P320
Cardiovascular risk assessment in adolescents with systemic lupus erythematosus: biomarkers related to lipid metabolism
Thais Ortiz, Simone Silva, Daniele Machado, Eugênia Khazaal, Milena Correia, Sonia Hix, Fabiola Souza, Roseli Sami, Maria Teresa Tenre, Claudio A. Len
Pediatric Rheumatology 2014, 12(Suppl 1):P320

Introduction: Juvenile systemic lupus erythematosus (JSLE) is a chronic, autoimmune and multisystem disease. Adult patients with SLE have an elevated risk of premature atherosclerosis and myocardial infarction. Dyslipidemia is a risk factor for the development of future chronic diseases and is associated with disease activity, corticosteroids use (CTC), renal impairment, among other factors. Other biochemical markers have been proposed for identification of cardiovascular risk, among them the protein components of lipoproteins (apolipoproteins - Apo) and enzyme related to cardiovascular risk (paraoxonase - PON).

Objectives: To evaluate the biochemical markers related to cardiovascular risk in adolescents with JSLE.

Methods: Cross-sectional and controlled study including 33 female adolescents with JSLE and 33 healthy controls. We evaluated: lipid profile, Apo A1, Apo B, PON activity and body mass index (BMI). For classification of lipid profile we considered cutoff points proposed by the American Academy of Pediatrics. Statistical analysis: Mann Whitney test.

Results: The median age and SLEDAI of the patients were 16 years and 2 (0, 12), respectively. We observed SLEDAI > 4 in 33 %, nephrotic syndrome in 12%, CTC use in 75.8% [median dose 0.18 (0.05, 0.6) mg/kg/day] and hydroxychloroquine use in 93.9% of the patients. Overweight/obesity was observed in 36.4%; dyslipidemia in 39.4 and 21.2% of patients and controls, respectively. Hypertriglyceridemia and low HDL-C were the frequent alterations. Apo A1 concentrations were significantly higher in controls (p = 0.01). There was no statistical difference in the lipid profile, in the concentrations of Apo B (p = 0.85) and in PON activity (p = 0.062). There were statistical differences in the relations Apo B/Apo A1 (p = 0.000) and LDL/Apo B (p = 0.000).

Conclusion: Low concentrations of Apo A1 in patients suggest a dysfunctional HDL cholesterol, possibly due to inflammation. The results indicate increased cardiovascular risk in adolescents with JSLE compared with healthy controls.

Disclosure of interest: None declared.

P321
B lymphocyte stimulator, interferon-c and HMGB1 interrelation in childhood onset systemic lupus erythematosus: associations with disease activity and severity
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Pediatric Rheumatology 2014, 12(Suppl 1):P321

Introduction: The role of B lymphocyte stimulator (Blys) in Childhood onset Systemic Lupus Erythematosus (cSLE) has not been elucidated.

Objectives: To investigate the role of Blys and its association with biomarkers related with the cSLE disease activity and severity.

Methods: 34 cSLE patients (study group), 51 with other rheumatic or autoimmune diseases and 26 healthy children (control groups) were studied. For evaluating the disease activity, SLEDAI and ECLAM scores were used. For estimating the disease severity the criteria were: involvement of 3 vital organs (kidneys or CNS or blood or combination of ≥2 organs), increased anti-dsDNA titres, low C3 /C4 concentrations and high concentrations of serum IFN-α and HMGB1 (high mobility group box 1) protein.

Results: Mean Blys levels were significantly higher in cSLE patients in respect to patients of all control groups, in patients with active as compared with patients with inactive disease and in patients with vital organ involvement as compared with patients without such involvement. Moreover, mean Blys levels were positively correlated with anti-DNA titer, IFN-α and HMGB1 levels but negatively correlated with C3 /C4 concentrations.

Conclusion: Taking together, results of our study indicate that: high levels of Blys are mainly found in serum of JSLE patients and they may be involved in the increased anti-DNA plus other autoantibody production. Moreover, they are associated with the disease activity and severity, meaning that Blys is a specific biomarker for the selection of patients who will need more aggressive and possibly more targeted than conventional therapy.

Disclosure of interest: None declared.

P322
The diagnosis of juvenile systemic lupus erythematosus with SLICC
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Pediatric Rheumatology 2014, 12(Suppl 1):P322

Introduction: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease that can involve any organ system, and may lead to significant morbidity and even mortality. Childhood-onset SLE (cSLE) is a rare disease with an incidence of 0.3-0.9 per 100.000 children-years and a prevalence of 3.3-8.8 per 100.000 children.

Objectives: SLE is called the great mimicker, as the disease shares characteristics with many other (autoimmune) diseases. Especially when the classic malar rash is absent, diagnosing SLE can be a challenge. Most patients who are diagnosed with juvenile SLE fulfill 4 or more of the American College of Rheumatology (ACR) classification criteria for SLE. The Systemic Lupus International Collaborating Clinics (SLICC) have recently suggested a new set of criteria for the classification of SLE. In recently study, SLICC criteria performed better, was more sensitive (p < 0.001), and less specific (p = 0.016) than ACR criteria in childhood.

Methods: JSLE patients (n = 83) from 2 different centers whose diagnosis fulfilled four or more of the ACR criteria were divided into two groups: those with at least one ACR mucocutaneous criterion (ACR skin feature positive) and those without (ACR skin feature negative) at diagnosis. The relative frequency of skin involvement was described by the paediatric adaptation of SLICC.

Results: We studied 83 patients (83% female; 17% male) with SLE from two regions of Turkey. The mean age at diagnosis was 13±2.95 years. The common criteria besides ANA in ACR all patients were, respectively, haemato logical (n = 55 (66%), musculoskeletal (n = 45 (54%), and renal (n = 40 (48%)). Forty-five patients (54%) had ACR-defined skin involvement with no significant demographic differences compared with those without. ACR skin feature positive patients showed greater major organ involvement (haemato logical (68% vs 66%), renal (51% vs 45%). At the time of diagnosis, median SLICC score was 8 in ACR skin feature positive group while 6 in others. Fifty-eight per cent of ACR skin feature negative patients had skin involvement using SLICC (n=13), which included maculopapular rash (76%), toxic epidermal necrosis (0.8%), bullous rash (19%), photosensitive rash (92%). The thirteen patients showed greater musculoskeletal, haematological and renal involvement at diagnosis (P=0.005).

Conclusion: There are a number of other important mucocutaneous manifestations commonly found in JSLE patients apart from the four listed in the ACR criteria. These additional lesions are also associated with major organ involvement.

Disclosure of interest: None declared.
P323
Cognitive functions and metabolic syndrome in childhood-onset systemic lupus erythematosus
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Pediatric Rheumatology 2014, 12(Suppl 1):P323

Introduction: Childhood-onset systemic lupus erythematosus (cSLE) have a high prevalence cognitive involvement and inflammatory mechanisms and autoantibodies were hypothesized to be involved in its pathogenesis. The underlying factor for an association between the metabolic syndrome (MetS) and cognitive decline might be a subclinical inflammation.

Objectives: To determine if cognitive functions are impaired in cSLE patients with MetS.

Methods: We performed a cross sectional study of 63 consecutive cSLE patients and 63 healthy age and sex matched controls. All individuals were assessed for anthropometric and MetS features according to international Diabetes Federation (IDF) criteria. Neurological manifestations were analyzed according to the ACR classification criteria. Cognitive evaluation was performed in all participants using Wechsler Intelligence Scale for children (WISC-III) and Wechsler Intelligence Scale for adults (WAIS), according to age and validated in Portuguese. Mood disorders were determined through Becks Depression and Anxiety Inventory in all participants. SLE patients were further assessed for clinical and laboratory SLE manifestations, disease activity (SLE Disease Activity Index (SLEDAI)), damage (Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI)) and current drug exposures. Total dose of corticosteroids and other immunosuppressant medications used since the onset of disease were calculated by data obtained by careful review of the medical charts.

Results: We observed higher hip circumference (p=0.030), waist-to-hip ratio (p=0.005) and hypertriglyceridemia (p=0.005) in cSLE patients. Controls had a higher height (p=0.003) and higher levels of HDL-c (p=0.004). MetS was present in 11 (17.4%) cSLE and in no control. Cognitive dysfunction was observed in 12 (50.8%) cSLE patients. We observed an inverse correlation with height and corticosteroid total dose adjusted by weight in cSLE patients (-0.285; p=0.022). Rey complex picture on memory subtest was correlated with body mass index (r=-0.249; p=0.05) and hypertriglyceridemia (r=0.282;p=0.028). Total cholesterol levels was correlated with Boston naming test (r=-0.258;p=0.047).

Conclusion: MetS was observed in 18% of our cohort and not associated with worse cognitive performance. However, features of MetS, such as total cholesterol, hypertriglyceridemia and obesity can influence some cognitive functions in cSLE.


P325
Clinical and serological features of juvenile systemic lupus erythematosus in an ITALIAN tertiary centre of pediatric rheumatology
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Pediatric Rheumatology 2014, 12(Suppl 1):P325

Introduction: Juvenile systemic lupus erythematosus (JSLE) is a multisystem autoimmune disorder that is characterized by widely variable clinical presentations and uncertain course.

Objectives: to evaluate the clinical and serological features of JSLE in a long lasting observation of a single Italian centre.

Methods: 104 patients affected by JSLE (<18 years) were enrolled in thirty one years from 1982 to 2013). 11 patients were male. The mean age of onset was 13 (SD 3.18); 41 were 12 years old or less. The mean disease duration was 163 months (SD 118).

Results: Fever and fatigue were frequent symptoms at onset, occurring respectively in 47 (45.1%) and 39 (37.5%) patients. The most common organ involvement was skeletal, affecting 89 (85.3%) of patients, 87 (97.7%) of whom were affected by non erosive arthritis. Jaccoud’s arthropathy was observed in 7 (6.7%) patients. Malar rash, leukopenia and non scarring alopecia were common findings. They occurred respectively in 60 (57.6%), 59 (56.7%) and 52 (50%) patients. Clinical evidence of renal involvement occurred in 42 (40.3%) patients. 31 patients had 1 or more renal biopsies: 22 (70.9%) resulted a glomerulonephritis, 3 (9.6%) by membranous nephropathy. Cutaneous vasculitic lesions, observed in 38 (36.5%) patients, were an important cause of morbidity. Oral ulcers and serosis were found in 27 (25.9%) and 25 (24%) patients respectively. Neurologic involvment occurred in 20 (19.2%) patients. Seizures were observed in 8 (7.6%) patients. Infections remain a major problem in morbidity: serious infective manifestations occurred in 21 (20.1%) patients. Avascular necrosis of bone occurred in 7 (6.7%) patients association whit disease activity, laboratory and treatment features and Mood and anxiety disorders.

Methods: We included 63 consecutive cSLE patients [median age 18 years (range 11-25) and 59 healthy controls [median age 20 years (8-33)]. Controls were age and sex-matched to cSLE patients. SLE patients were further assessed for clinical and laboratory SLE manifestations, disease activity [SLE Disease Activity Index (SLEDAI)], damage [Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI)] and current drug exposures. Total dose of corticosteroids and other immunosuppressant medications used since the onset of disease were calculated by data obtained by careful review of the medical charts. Mood and anxiety disorders were determined through Becks Depression (BDI) and anxiety inventory (BAI). Th1 (IL-12), Th2 (IL-6 and IL-10) and Th17 (IL-17) cytokines levels were measured by ELISA and compared by non-parametric tests.

Results: Serum IL-6 (p=0.001), IL-10 (p=0.006), IL-12 (p=0.027) and IL-17 (p=0.0001) levels were increased in cSLE patients when compared to healthy controls. IL-6 levels were significantly increased in patients with active disease (p=0.008). IL-6 (p=0.032) and IL-12 (p=0.028) levels were significantly increased in patients with active nephritis. We observed that IL-17 was associated with migraine (p=0.045), IL-6 with thrombocytopenia (p=0.022) and IL-12 with the presence of anxiety (p=0.048). No association between cytokine levels and SDI scores or medication was observed.

Conclusion: Cytokines play a central role in cSLE. IL-6 is associated with SLEDAI and may be a biomarker of disease activity. Th1 and Th2 responses may play a role in lupus nephritis and Th1 and Th17 may play a role in neuropsychiatric symptoms in cSLE. Longitudinal studies are necessary to confirm their ability to predict SLE related manifestations.


P324
The relation of cytokines TH1, TH2 and TH17 in childhood-onset systemic lupus erythematosus
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Introduction: Childhood-onset Systemic lupus erythematosus (cSLE) is an autoimmune disease with a wide spectrum of clinical manifestations, characterized by periods of activity and remission. Hematological and immunological abnormalities are commonly found. Laboratory evaluation, including the cytokine profile, assists in the diagnosis, determination of disease activity and may predict future damage caused by the disease.

Objectives: To determine the serum levels of TH1 (IL-12), TH2 (IL-6 and IL-10) and TH17 (IL-17) cytokines in cSLE and healthy controls. To evaluate their
patients, 3 of whom suffered more than 1 episode. Six (5.7%) patients developed steroid induced cataract. Tender rupures were observed in 4 (3.8%) patients. Growth failure and established osteoporosis, resulting from prolonged corticosteroid treatment in chronically active disease, were unfrequent but severe complications in our jSLE series occurring respectively in 8 (7.6%) and 5 (4.8%) patients. Cushingoid features and stria rubrae were frequent problems observed in 17 (16.3%) patients, due to disease itself and/or its treatment, that caused increased psychological distress, particularly in adolescents. Finally there were 4 deaths. Two due to infection complications and two due to myocardial infarction.

Conclusion: these data show that JSE is not necessarily associated with poor prognosis. Survival has improved, but morbidity due to disease itself and complications of therapy remain a significant problem.

Disclosure of interest: None declared.

P326
Simultaneous presentation but contrasting clinical features in 2 female siblings with juvenile systemic lupus erythematosus (JSE)
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Introduction: SLE is an autoimmune disease characterized by the presence of antinuclear antibodies and multitudes involvement. The presenting clinical features can be variable and the course of disease unpredictable. Studies have shown increased incidence of SLE in siblings of individuals with the disease.

Objectives: We report 2 female siblings who presented with juvenile SLE simultaneously in May 2013 but had contrasting clinical features.

Methods: Fifteen year old sibling 1 presented with history of low grade fevers since 2 months, oral ulcers, malar rash, alopecia, paller, arthralgia, history of loss of weight and appetite. Investigations revealed anaemia, leucopenia, high ESR, and low C3, C4 levels. She also had ANA +ve 1:1280, ds DNA +ve, lupus anticoagulant +ve, anti cardiolipin antibody +ve, normal urine protein creatinine ratio and normal BP. She was treated with oral steroids, hydroxychloroquine, azathioprine and calcium supplements. 10 year old sibling 2 presented at the same time with history of high grade fever since one week with no obvious focus. She was initially worked up for infective cause and treated symptomatically. During second week of illness she developed rashes in her lower limbs with arthritis in her ankle joints. Within next few days she developed acute abdominal pain, pedal oedema, elevated blood pressure and seizures. Her investigations revealed anaemia, leukopenia, elevated ESR, low C3, C4 ANA +ve +ve 1:1000, dsDNA positive, elevated urine protein and high BP of 160/110 mmHg. US abdomen showed mild ascites, CT angiogram of abdomen was normal and renal biopsy showed evidence of necrotising vasculitis. She was treated with intravascular steroids followed by oral steroids, IV cyclophosphamide, hydroxychloroquine, antihypertensives and antoconvulsants.

Results: Two female siblings presented with contrasting clinical features of SLE at the same time. The elder sibling had a chronic history and aggressive clinical course. The younger sibling presented with a very short history and aggressive clinical course. Genetic studies were not done as this is not available in our country.

Conclusion: The occurrence of SLE in the 2 female siblings at the same time probably points to an environmental factor as a trigger in these two patients. The presenting clinical features however were in complete contrast and representative of the two ends of spectrum of the disease.

Disclosure of interest: None declared.

P327
Liver and spleen biometrics in childhood-onset systemic lupus erythematosus patients
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Introduction: Involvement of the reticuloendothelial system occurs in 20-50% childhood-onset systemic lupus erythematosus (c-SLE) patients at disease onset, usually associated with disease activity. Hepatomegaly and/or splenomegaly may also be associated with abnormal liver function tests. Abdominal ultrasound can be used to assess liver and spleen measurements in children and adolescents without risk of radiation. However, a systematic evaluation of these visceral organ dimensions has not been performed in c-SLE population, particularly during the disease course.

Objectives: To evaluate liver and spleen dimensions in c-SLE patients and healthy controls and to assess possible associations between abnormalities in liver and spleen sizes with demographic data, clinical features, disease activity, cumulative damage and treatment.

Methods: 30 c-SLE patients and 30 healthy control volunteers underwent abdominal ultrasound. The following two liver measurements were performed in left hepatic lobe: cranio-caudal and anteroposterior and three in right hepatic lobe (RHL): posterior craniocaudal (PCC-RHL), anterior craniocaual and anteroposterior. Three spleen dimension measurements were also evaluated: longitudinal, transverse and anteroposterior. Demographic, clinical and laboratorial data, and treatment were assessed. Disease activity was evaluated according to SLE Disease Activity Index 2000 (SLEDAI-2K), European Consensus Lupus Activity Measurement (ECLAM) and Systemic Lupus Activity Measure (SLAM) scores.

Results: Mean current age was similar in c-SLE and controls (17.03±27.81 vs. 16.4±39.25 months; p=0.486), likewise the frequency of female gender (77% vs. 63%, p=0.398). The mean of PCC-RHL dimension was significantly higher in c-SLE compared to controls (13.30±1.85 vs. 12.52±0.93, p=0.044). There were no differences between the other hepatic biometrics and splenic parameters (p>0.05). Further analysis in c-SLE patients according to PCC-RHL dimension > 13.3 cm (mean of this biometric measurement in 30 c-SLE patients) versus < 13.3 cm showed that the median of SLEDAI-2K [8 (0-18)] vs. 2 (0-8), p=0.004, ECLAM [4 (0-9)] vs. 2 (0-5), p=0.019 and SLAM [5 (1-13)] vs. 2 (0-14), p=0.016 were significantly higher in patients with higher PCC-RHL dimension, likewise the mean of erythrocyte sedimentation rate (33.7±16 vs. 22.0±13 mm/1st hour, p=0.038). The frequencies of nephritis were significantly higher in patients with PCC-RHL dimension > 13.3 cm versus < 13.3 cm (77% vs. 29%, p=0.010). The median of serum liver enzymes were similar in both groups (p>0.05). Positive correlation was observed between SLEDAI-2K and PCC-RHL (p=0.001, r=0.595). Negative correlation was evidenced between disease duration and longitudinal dimension of spleen (p=0.031, r=−0.394).

Conclusion: Our data raises the novel possibility that disease activity could lead to a subclinical and localized hepatomegaly during the disease course. Long disease duration resulted to spleen atrophy in c-SLE patients.

Disclosure of interest: A. Guariento: None declared., M. F. Silva: None declared., P. S. Tassoteno: None declared., S. M. Rocha: None declared., L. M. Campos: None declared., M. Valente: None declared., C. Silva Grant/ Research Support from: This study was supported by Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP - grants: 2006/58939-4 to CAS), by Conselho Nacional do Desenvolvimento Científico e Tecnológico (CNPq – grant 302724/2011-7 to CAS), by Federico Foundation to CAS and by Núcleo de Apoio à Pesquisa “Saúde da Criança e do Adolescente” da USP (NAP- CriAd).

P328
The systemic lupus erythematosus in paediatrics: Moroccan experience of a unit of pediatric rheumatology
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Introduction: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease characterized by multi-organ involvement. Its pathogenesis remains controversial. Diagnosis in children is also based on the ARA criteria (American Rheumatism Association).

Objectives: We propose to report the epidemiological, clinical, immunological, therapeutic and evolutive profile of childhood’s SLE through this retrospective study in the Pediatric Rheumatology Service of the Children’s Hospital of Casablanca, conducted between December 2001 and January 2014.

Methods: We report a series of 30 children, including 25 girls, mean age of onset is 12 years, with a range of 7-16 years, the average time from...
diagnosis is 6 months. The mode of presentation of the disease is classical (general signs, skin and joints involvement) in 56% of cases, by lupus nephritis in 26.6 % of patients, or a Macrophage Activation Syndrome “MAS” in 13.3 % of cases and lupus nephritis associated with MAS in one patient.

Results: The clinical picture showed fever in 76.66% of patients, the frequency of joint locations (90%), skin (86.66%), kidney (66.6%) , hematologic (50%) lung (36.66%), gastrointestinal (30%), neuropsychiatric (26.66%) and cardiac (23.3%) involvement. The hematological involvement was detected in 76.66% of our patients, an inflammatory syndrome in 83.3%, immunological disturbances with positive titers of anti-DNA AC (90%), ANA (93.6%), and a reduction of the complement (83.3%) . False syphilis serology completed by anti- j2Glycoprotein1 antibodies (26%) and anti- cardioline were positive in respectively 40, 26 and 20% of cases. Renal involvement is manifested by renal insufficiency in 43% of cases, a significant proteinuria in 50% of cases and prevalence of class IV on biopsy. A case of kikushi fujimoto has been reported as 5 hemophagocytic syndromes. All patients were treated with systemic corticosteroids and hydroxychloroquine. The use of methylprednisolone bolus was indicated in cases of SAM or severe renal impairment associated with cyclophosphamide/MMF and anti-proteinetic medication.

Conclusion: The prognosis of pediatric SLE remains unpredictable; however it is assigned to the renal, neurological and the occurrence of MAS. We mourn two deaths one by neurological attack and other by renal failure.

Disclosure of interest: None declared.

P329
Use of SIICC / ACR damage index in adolescents with SLE
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Pediatric Rheumatology 2014, 12(Suppl 1):P329

Introduction: System Lupus Erythematosus (SLE) is one of the most severe and unfavorable to its course of rheumatic diseases. Poor prognosis of SLE development has irreversible changes of internal organs. The number and type of there have accounted for by SIICC/ACR Damage Index in adults. However, such changes have found in children also.

Objectives: In order to timely diagnosis of irreversible changes of internal organs in systemic lupus erythematosus (SLE) 44 adolescents with SLE medical history have analyzed.

Methods: The age of patients at the time of the study were 12.67 ± 3.17 years. SLE debut age equaled 12.65 ± 2.87 years. Duration of illness was 39.36 ± 4.17 months.

The diagnosis of SLE exhibited respectively ACR classification criteria (1997). SIICC/ACR Damage Index was assessed in all patients. Comparison of estimates of the index had conducted at duration of illness before and more than three years.

Results: SLE manifested the following clinical syndromes: articular (84.3%), skin (82.3%), renal (55.4%), cardiac (59.8%), pulmonary (35.7%), cerebral (31.2%), Blood disorders (64.3%), antiphospholipid syndrome (11.9%). Most patients had subacute start option (61.4%) and moderate activity of SLE (45.4%).

All adolescents were treated with glucocorticoids; the mean total dose was 11326 ± 2435 mg per patient. Combination therapy with glucocorticoids and cytotoxic drugs was at 70.3% of patients. Ultrahigh doses of methylprednisolone (“pulse”- therapy) have conducted in 37.5% of patients.

The authors have found that 90.9% of adolescents with SLE have the damage that includes the scale SIICC/ACR Damage Index for adult patients. Average score SIICC / ACR Damage Index in adolescents with SLE was 2.72 ± 0.84 points. Frequency of cumulative damage and the total score SIICC/ACR Damage Index increased with disease duration of more than three years.

Conclusion: Research proves that children with SLE should be have evaluated to assess the scale of damage. Adaptation of these scales have needed for children and adolescents.

Disclosure of interest: None declared.

P330
Juvenile systemic lupus erythematous in Iranian children
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Pediatric Rheumatology 2014, 12(Suppl 1):P330

Objectives: Juvenile systemic lupus erythematous (JSLE) is a multi-system autoimmune disorder of unknown origin. Involvement of the mucocutaneous, musculoskeletal system and kidney disease are the most common manifestation of JSLE. This investigation was performed to define the demography and clinical manifestation of JSLE in Iran.

Methods: Fifty nine patients with JSLE were enrolled in this retrospective study. All patients fulfilled the American College of Rheumatology revised criteria 1982 for the diagnosis of SLE and had shown classical manifestations of the disease before the age of 16.

Results: A total of 59 patients, 49 (89%) were female and10 (16.9%) male. The female to male ratio was 4.9:1. The mean age of onset was 10.5 years (range 2-16). The mean duration of disease from diagnosis was 2 years (range 7 months-5 years). The most common of constitutional sign was fatigue (76.3%) and the other signs were fever (32.2%), Nocturnal pain (20.3%), Mood disorder (20.3%) and Weight loss (22%). The most common manifestation of JSLE were as follows: 48 patients (81.35%) had mucocutaneous involvement, 46 patients (77.9%) had musculoskeletal involvement, 25 children (42.37%) suffered from renal disease, hematological abnormalities were detected in 19 patients (32.2%), 10 patients (16.94%) had cardiovascular disease, 33 patients (55.93%) presented nervous system involvement, 12 patients (20.33%) had pulmonary disease, and 13 patients (22.03) experienced infection complications. During the follow up period(3years) two patients died, one from renal failure, one from infections.

Conclusion: A high index of suspicion must be preserved for the diagnosis of SLE in adolescent children, particularly girls. Juvenile systemic lupus erythematous (JSLE) is a critical multi-system organ disease. JSLE still has a significant mortality rate high, although it has a high remission rate with early diagnosis and treatment.

Disclosure of interest: None declared.

P331
Persistent sLe activity related to untreated reactivation of pulmonary tuberculosis
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Pediatric Rheumatology 2014, 12(Suppl 1):P331

Introduction: SLE patients are at risk of tuberculosis (TB) infection due to both secondary immunosuppression and intrinsic defects in innate immunity. On the other hand infection can also perpetuate the development of an autoimmunity [1,2].

Objectives: Here we report a case of pulmonary tuberculosis reactivation in a SLE patient. The lupus activity was not responsive to heavy immunosuppressants. It was only controlled after commencement of anti TB treatment.

Methods: WLS was diagnosed SLE at the age of 16 with fever, rash, oral ulcers, cytopenia, lupus nephritis (type II and III), retinal vasculitis and positive anti dsDNA. She was started on systemic steroid and Azathioprine. Symptoms became better and steroid was gradually tapered. However 3 months later she developed relapse of lupus activity with worsening lupus nephritis (active urinary sediments, heavy proteinuria up to 7.6g/day), cytopenia and high anti dsDNA titre. ESR was high but CRP was normal, a pattern commonly seen in active lupus. Azathioprine was switched to Mycophenolate Mofetil without much success. CXR was performed which showed prominent horizontal fissure of right lung. HRTC thorax scan, to our surprise, showed features of early TB reactivation. She had absolutely no respiratory symptom. Girl's TST and CXR before commencement of steroid were negative. Gamma Interferon Releasing Assay (IGRA) was positive.
Bronchoscopy finding was normal. Only the BAL of the RUL bronchus grew Mycobacterium Tuberculosis.

Upon further questioning the parents recalled that the girl’s uncle died from pulmonary TB 4 years ago. She stayed with his family during a summer holiday 8 years ago.

After commencing anti TB treatment, her SLE activity remitted with resolution of proteinuria and cytopenia, allowing steroid tapering.

**Results:** Table 1. 

**Disclosure of interest:** None declared.

**References**


**P332**

**Sensorineural hearing loss: a new manifestation of neonatal lupus erythematosus?**

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Pediatric Rheumatology 2014, 12(Suppl 1)P332

**Introduction:** Neonatal lupus erythematosus (NLE) is a rare acquired autoimmune disease, characterized by the transplacental passage of maternal antibodies (anti-SSA/Ro and/or anti-SSB/La) into the fetal circulation system, inducing clinical manifestation in the neonate. The most serious clinical manifestation of NLE is a nonreversible complete congenital heart block (CHB), and other common manifestation included skin rash, hepatobiliary and hematologic abnormalities, which are usually reversible.

**Objectives:** Central nervous system involvement is not uncommon, but up to now there have been no reports of inner ear involvement in NLE.

**Methods:** We describe the clinical case of a 13-year-old Caucasian boy, born from mother with Sjögren syndrome and anti-SSA/Ro antibodies, who developed a complete congenital heart block (CHB), treated with pacemaker implantation at birth. No other clinical manifestations were present in the perinatal period, and anti-SSA/Ro antibodies positivity disappeared in the first 6 months of life.

**Results:** When 12-year-old he developed nausia, nystagmus, dizziness, tinnitus, vertigo, and hearing loss, so he was admitted in a community hospital, where laboratory test revealed leukocytosis, with normal CRP and ESR. Cultures for bacteria and viruses from blood, throat, and urine were all negative. Cardiological examination showed a normal heart rate induced by pacemaker; neurological examination, Brainstem Auditory Evoked Potentials (BAEPs) and brain CTscan were negative. ENT examination revealed a moderate right sensorineural hearing loss (SNHL). Initially a diagnosis of labyrinthitis was made, and a treatment with oral prednisolone (1 mg/kg daily) was started. Nausea, nystagmus, dizziness, tinnitus and vertigo disappeared in a few days, while a persistent moderate right SNHL was confirmed in the following ENT evaluations. Ten months later, the boy referred headache, and dizziness, and was admitted in our hospital, where audiometry showed a severe right SNHL, worsened when compared to the previous examination. Neurological and cardiological examinations were normal. Routine laboratory test and inflammatory markers were normal. The genotype study of GJB2 (connexin-26) and GJB6 (connexin-30) mutations were negative, so hereditary hearing loss was excluded. The study of NLRP3 gene mutations was normal, so Muckle-Wells syndrome was also ruled out.

Autoantibodies against inner ear showed a positivity for anti-reovirus peptide antibodies, and a strong positivity for anti-peptide 12 (Cogan peptide), anti-Peptide CD148 and anti-connexin 26 antibodies. The patient was diagnosed as having autoimmune hearing loss and was started on oral prednisone (1 mg/kg/day). Headache and dizziness rapidly disappeared, and prednisone were tapered after 3 months and hearing loss was resolved.

**Conclusion:** The transplacental passage of maternal antibodies, SSA/Ro and SSB/La, into the fetal circulation system induced CHB. To our knowledge, the coexistence of congenital heart block and SNHK has not been previously reported. Interestingly, the autoantibodies which are able to induce tissue damage on binding of cell-surface molecules present on the sensory epithelia of the inner ear and on endothelial cells can cross-react with anti-SSA/Ro. We are currently investigating the pathogenetic role of anti-Ro in inner ear damage.

**Disclosure of interest:** None declared.

**P333**

**Social phobia in childhood-onset systemic lupus erythematosus**

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Pediatric Rheumatology 2014, 12(Suppl 1)P333

**Introduction:** Anxiety is frequently observed in systemic lupus erythematosus, however the prevalence of phobia has rarely been reported.

**Objectives:** To evaluate the frequency of social phobia in patients with childhood-onset Systemic Lupus Erythematosus (cSLE) and to verify possible associations with clinical, laboratory manifestations, and the use of corticosteroids.

**Methods:** In this cross-sectional study 48 patients with cSLE followed at the Pediatric Rheumatology Unit of the State University of Campinas during the May and August of 2013 were included. The control group was composed by 53 age and sex matched controls. The presence of symptoms of social phobia was assessed by the Liebowitz Social Anxiety Scale (LSAS), validated in portuguese. Neuropsychiatric manifestations were classified according to the criteria established by the American College of Rheumatology. SLE patients were further assessed for clinical and laboratory SLE manifestations, disease activity (SLE Disease Activity Index (SLEDAI)), damage (Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI)) and current drug exposures. Total dose of corticosteroids and other immunosuppressant medications used since the onset of disease were calculated by data obtained by careful review of the medical charts.

**Results:** Social phobia was observed in 9 (18.75%) patients and was associated with the current age (p = 0.003), age at diagnosis (p = 0.008), disease duration (p = 0.007), SLEDAI (p = 0.009), cumulative corticosteroid dose adjusted by weight (p = 0.002), current dose (p = 0.004) and the cumulative dose over time (p = 0.001). When analyzed by severity, moderate social phobia was observed in 5 (10.42%) patients and associated with disease duration (p = 0.005), SLEDAI adjusted over time (p = 0.02), headaches (p = 0.048) and cumulative dose of corticosteroids (p = 0.009). Severe social phobia was observed in 3 (6.25%) patients and...
was associated with current age (p = 0.035). Very severe social phobia was observed in one (2.08%) patient and associated with SLEDAI (p = 0.036). There was no significant association between social phobia and cumulative damage and other neuropsychiatric manifestations.

Conclusion: Social phobia was frequently observed in cSLE and associated with disease activity and corticosteroid dosage. Social phobia should be screened routinely it can influence the quality of life of cSLE patients.

Disclosure of interest: None declared.

P335
Childhood-onset bullous systemic lupus erythematosus
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Pediatric Rheumatology 2014, 12(Suppl 1):P335

Introduction: Bullous systemic lupus erythematosus (BSLE) has rarely been described in pediatric lupus population and to our knowledge the prevalence of childhood BSLE has not been reported.

Objectives: To evaluate the prevalence and describe cases of BSLE in childhood-onset SLE (c-SLE) patients.

Methods: From 1983 to 2013, 303 c-SLE patients were followed at the Pediatric Rheumatology Unit of the Children’s Institute of Hospital das Clínicas da Faculdade de Medicina da Universidade de Sao Paulo. Three of them (1%) presented BSLE and are described herein.

Results: Case 1: A 10-year-old boy presented fever, arthritis and generalized tense vesicles and bullae on the face, oral mucosa and trunk. Biopsy of a vesicle showed a subepidermal blister with neutrophilic microabcesses in dermal papillae and perivascular lymphocytes and neutrophils infiltration. Direct immunofluorescence (DIF) revealed IgG/IgA/IgM deposits at BMZ. After 1 month, he presented oral ulcers and pleural effusion. Laboratory findings showed hemoglobin 9.3g/dL, WBC 7,300/mm³ (73%neutrophils, 21%lymphocytes), platelets 398,000/mm³, C3 45mg/dL and C4 6mg/dL. Urinalysis showed leukocytes 1,000/ml and erythrocytes 21,000/mL. Immunological tests showed positive ANA 1:640, anti-dsDNA, anti-Sm, anti-Ro/SSA and anti-La/SSB autoantibodies. He fulfilled Camisa and Sharma diagnostic criteria. At that moment the SLEDAI-2K score was 18. He was treated with methylprednisolone pulse therapy (30mg/kg/day for 3 days), followed by prednisone (1.0mg/kg/day), hydroxychloroquine and dapsona. After one month, the vesicles and bullous lesions improved immensely.

Case 2: A 10-year-old girl presented recurrent bullae and vesicular lesions on the trunk for two months. Two months later, she presented oral ulcers, arthritis, pericarditis, and arterial hypertension. A skin biopsy showed neutrophilic bullous dermatitis with subepidermal cleavage. DIF revealed deposits of IgG/ IgM/IgA/C3 at the BMZ. Hemoglobin was 10.9g/dL, WBC 7,590/mm³ (87% neutrophils, 9%lymphocytes) and platelets 354,000/mm³. C3 38mg/dL and C4 3mg/dL. Proteinuria was 0.6g/day. Immunological tests showed positive ANA 1:1280 and positive anti-ds DNA, anti-Sm, anti-Ro/SSA autoantibodies. The renal biopsy showed focal proliferative lupus nephritis. The SLEDAI-2K score was 24. She was treated with methylprednisolone pulse therapy, followed by prednisone, monthly intravenous cyclophosphamide (500-1000mg/m²) and hydroxychloroquine. After 4 months, she progressively improved, with complete resolution of bullous lesions with residual pigmentation changes.

Case 3: A 6 years girl, presented with fever and vesicles and bullous lesions on the neck, lower limbs, and oral mucosa for 2 months. Skin biopsy showed subepidermal blister with neutrophil inflammation in the upper dermis and DIF showed deposition of IgA, IgM and IgG. Two months later, the patient developed eyelid edema and oral ulcers. Hemoglobin was 7.9g/dL, ANA 1:200 and positive anti-Sm and proteinuria was 0.6g/day. Renal biopsy revealed mesangial proliferative lupus nephritis. She received methylprednisolone pulses, prednisone, hydroxychloroquine and dapsona. After 4 months, she presented progressive improvement of the bullous lesions.

Conclusion: In the last 30 years, the prevalence of BSLE in childhood was 1% in our tertiary University Hospital. Vesiculobullous skin involvement was the first disease manifestation in all three cases. A diagnosis of SLE should always be considered in children with recurrent tense vesiculobullous lesions especially with systemic manifestations and specific autoantibodies.

Disclosure of interest: None declared.

P336
Autoimmune hepatitis and juvenile systemic lupus erythematosus: 2 for 1?
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Pediatric Rheumatology 2014, 12(Suppl 1):P336

Introduction: Autoimmune hepatitis (AIH) and juvenile systemic lupus erythematosus (JSLE) are often referred as two different diseases with different etiopathogenesis and different clinical outcomes. In this study, we report a case of a patient who had both AIH and JSLE.

Case Report: A 12-year-old girl was referred to the Pediatric Rheumatology Unit of the Hospital de São João, Porto, Portugal with a 2-month history of fatigue, weight loss and jaundice. The patient was born full-term and had no congenital abnormalities. The family history was unremarkable. She had been diagnosed with JSLE 9 months before the presentation to our unit and was treated with corticosteroids (dexamethasone 0.3mg/kg/day) and hydroxychloroquine. At presentation, the patient had a body weight of 35 kg, height of 145 cm and body mass index of 13.8 kg/m². Physical examination revealed jaundice and a palpable liver. Laboratory tests showed hemoglobin 9.8g/dL, WBC 8,700/mm³ (81% neutrophils, 16% lymphocytes), platelets 269,000/mm³, alanine transaminase 533 U/L, aspartate transaminase 515 U/L, total bilirubin 9.4 mg/dL and direct bilirubin 6.5 mg/dL. Anti-nuclear antibodies (ANAs) were positive (1:640), anti-smooth muscle antibodies (AMSAs) were positive (1:1280), anti-mitochondrial antibodies (AMAs) were negative, and rheumatoid factor (RF) was negative. Antinuclear antibodies (ANAs) were positive (1:640). Seven days later, the patient developed jaundice and ascites and was referred to the Pediatric Gastroenterology Unit. Total bilirubin was 14.2 mg/dL, direct bilirubin 11.4 mg/dL, albumin 3.3g/dL, alanine transaminase 1106 U/L, aspartate transaminase 1225 U/L, and γ-glutamyl transpeptidase 1980 U/L. Anti-smooth muscle antibodies (AMSAs) were positive (1:1280), anti-mitochondrial antibodies (AMAs) were negative, and rheumatoid factor (RF) was negative. Anti-neutrophil cytoplasmic antibodies (ANCA) were negative. The patient was treated with methylprednisolone pulse therapy (30 mg/kg) and prednisone (1mg/kg/day) and her condition improved gradually.

Conclusion: The coexistence of AIH and JSLE is rare. Our patient had severe liver involvement with jaundice, ascites and anemia. The clinical outcome in this patient was favorable with improvement after the treatment with corticosteroids and hydroxychloroquine. Further studies are needed to evaluate the long-term outcome of patients with AIH and JSLE.
Introduction: Autoimmune hepatitis (AIH) is characterized by increased liver enzymes, hypergammaglobulinemia, specific autoantibodies and typical histologic findings. Extrahepatic autoimmune phenomena may coexist with type 1 AIH. Systemic lupus erythematosus (SLE) is a chronic multisystem autoimmune disease associated with the production of autoantibodies. Although it has the potential to affect any organ, clinically significant hepatic involvement is considered to be uncommon and liver dysfunction is not a diagnostic criteria. Objectives: The authors present a clinical case and discuss the challenges posed by the differential diagnosis between AIH type 1 and SLE. Methods: A previously healthy 12-year-old girl was referred to our Gastroenterology Unit due to the incidental finding of high transaminases (30 fold upper limit of normal [ULN]). Besides fatigue there were no other symptoms, and physical examination was unremarkable. Laboratory investigations showed hypergammaglobulinemia, no colestasis and negative viral serologies. Anti-1 anti-trypsin deficiency, hemochromatosis and Wilson’s disease were excluded. Transcutaneous biopsy revealed liver cirrhosis with chronic interface hepatitis and lymphoplasmocytic infiltrates. AIH antibody panel was negative, including smooth muscle, liver/kidney microsome type 1, liver-specific cytosol type 1 and soluble liver antigen/liver pancreas antibodies. A very high titer of antinuclear antibodies (ANA) (>1/17,110) raised suspicion and led to additional studies which showed very high dsDNA antibodies and positive anti-nucleosome antibodies. The remainder antibody panel was negative, including antiphospholipid and antinuclear P protein antibodies, with normal complement. There was a positive direct Coombs test (4 out of 5, IgG specific), without anemia or active hemolysis, normal platelets and discrete intermittent lymphopenia. Results: 3 months after the initial presentation, malar rash and frequent oral ulcers appeared, with no renal abnormalities, photosensitivity or joint complaints. A juvenile SLE diagnosis was thus established: lymphopenia + malar rash + oral ulcers + immunologic criteria. After 4 months of treatment with prednisolone, azathioprin (2 mg/kg/day), hidroxchloroquin and urodeoxyacetic acid, there is a partial response with liver enzymes decreasing to 2.3 fold ULN. Conclusion: The distinct between SLE and type 1 AIH can be difficult, and we cannot exclude an overlap phenotype. In the present case, the absence of liver specific antibodies and a very high titer of ANA raised the diagnostic suspicion. Cooperation with the Rheumatology Unit led to a diagnosis of SLE with implications in the monitoring, management and prognosis of the patient. Recent case series report a much higher prevalence of liver involvement in juvenile SLE patients compared with adults, which may often precede the other symptoms. On the other hand, juvenile patients with AIH have a significant risk of developing SLE, which calls for an increased awareness in the follow-up of these patients.

Disclosure of interest: None declared.

P338
Prescribed but not approved: biologic agents used without approval in juvenile idiopathic arthritis in Switzerland, France and Belgium
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Introduction: Biologic agents (BA) have profoundly changed the outcome of juvenile idiopathic arthritis (JIA), making inactive disease and clinical remission an achievable goal for treatment. An increasing number of BA has become available in the last 15 years. However, some BA that have been associated to efficacy in some clinical conditions are not approved by legal authority for the use in pediatric population. Objectives: To evaluate the frequency of pediatric patients with JIA treated with BA not approved by medical supervisory authorities in Switzerland, France and Belgium at initiation of therapy. Methods: Multicenter, retrospective study using the juvenile inflammatory rheumatism (JIR) cohort, including ten Swiss, French and Belgian centers for pediatric rheumatology. Results: A total of 7,965 BA treatments in 3,531 patients were collected. Mean age at start of first biologic therapy was 10.9 (SD ± 4.61) years. Etanercept, the first approved BA for pediatric use, was initiated in 378 patients (47.5%), of whom 377 (99.7%) after the approval date of the European medical agency (EMA) or Swismedic (SM). Adalimumab, infliximab and golimumab were used in 147 (18.5%), 106 (13.3%) and 14 (1.8%) patients, respectively; 75 (51.0%) patients were started on adalimumab before EMA/SM approval, whereas all patients on infliximab and golimumab were treated without EMA/SM approval. Atabecap was given in 26 patients (3.3%), of whom 10 patients (38.5%) before EMA/SM approval. Tocilizumab was used in a total of 48 patients (6.0%); for systemic-onset JIA and non-systemic JIA, it was prescribed in 8 of 27 patients (17.9%) and 16 of 20 (80%) before EMA/SM approval, respectively. Canakinumab used for the treatment of systemic-onset JIA was given in 14 patients (77.8%) without approval for this indication. Anakinra was identified in 49 patients (6.3%) for the treatment of systemic-onset JIA, although EMA/SM approval is pending for this disease. When more than one BA was used in a patient, 167 out of 265 treatments (63%) were given without approval. In total, 303 treatments (37.7%) were started without authorization by EMA/SM.

Conclusion: In pediatric rheumatology clinical practice, a significant number of BA lacks authority approval for the treatment of JIA. Pediatric clinical trials and registers are crucial to assess effectiveness and safety of BA in this rare disease, substantiating an unequivocal decision making of both doctors and their patients.

Disclosure of interest: None declared.

P337
Tuberculosis the great simulator, really is lupus? A clinical case report
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Pediatric Rheumatology 2014, 12(Suppl 1):P337

Introduction: The post disease is an infection caused by mycobacterium tuberculosis in bone, was first described in 1779, this being a polivertebral condition, in children the most affected region is the dorsal column at 51%, followed by Lumbar 20 % and 17% back pain. Extra pulmonary Tuberculosis (EPT) has a global percentage of 25%, and 20% in children, Mexico represents 5.3% of the reported cases of tuberculosis, with a mean age of 12.3 ± 5.5 years. In particular pott disease represents 10-15% of all EPT. 1 Infection with M. tuberculosis (TB) and autoimmune diseases share many symptoms: fever, myalgia, arthralgia/artitis, rash, multiorgan involvec well as a variety of antibodies that are usually in positive titers during latent infection, as antibodies antinuclear (ANA), anti double-stranded DNA (dsDNA anti), anti Smith (anti SM), anti ribonucleoprotein (RNP anti), antinuclear antibodies (ANCA’s), anti- cyclic citrullinated peptide antibodies(anti CCF), also elevation antibodies to Antiphospholipid syndrome, Anti β2 glycoprotein 1, Anticardiolipins 3. It has been found that after 6 months of treatment for TB , both as antibodies and symptomatology will to be negative.4 Present the case of a female patient of 12 years old with a history of 5 -month with chronic cough,fatigue, weakness , weight loss , predominantly nocturnal fever with deformity lumbar spine, in magnetic resonance imaging is observed vertebral destruction with spondylodiscitis L3 and L4 , and probably secondary to osteomyelitis evidenced Tuberculosis and immunologically impaired positive antibodies for Systemic Lupus erythematosus (SLE) and triple positive marker for antiphospholipid syndrome. The patient underwent surgical procedure for vertebral destruction approach to immune disease begins by the previously mentioned positive antibodies and the high risk of thrombosis.

Disclosure of interest: None declared.
P339

Efficacy and safety of TNF-alpha antagonists in children with juvenile idiopathic arthritis who started treatment under 4 years of age

Introduction: The experience in the use of tumour necrosis factor (TNF) antagonists in children below 4 years is limited, although there are some trials in the literature which support safety and efficacy under this age.

Objectives: To assess efficacy and safety of TNF-alpha antagonists (anti-TNF) in a cohort of patients with Juvenile Idiopathic Arthritis (JIA) who began treatment under 4 years old. Assess relapse rate after methotrexate and/or anti-TNF withdrawal.

Methods: We made a retrospective charts review of our non-systemic JIA patients treated with anti-TNF under 4 years of age between January 2006 and April 2013. Demographics, epidemiologic, clinical, laboratory data and rate of relapse after treatment withdrawal due to clinical remission were collected. Efficacy and safety endpoints included side-effects and time to achieve clinical remission.

Results: We included 27 patients, 23 received etanercept and 4 adalimumab with a median age of 3.01 (range 0.88-3.97) years at anti-TNF beginning and 1.94 (range 0.18-5.44) and 2.39 (range 0.18-7.24) years of treatment and follow up respectively. All patients had previously received Disease Modifying Antirheumatic Drugs at optimal dose. Nineteen patients reached clinical remission on treatment in a median time of 9.1 (range 6.23-21.17) months. Four of those relapsed during treatment. Six developed mild side-effects (22.2%): 3 primary non complicated varicella zoster virus infections, 1 pneumonia, gastrointestinal and respiratory mild infections in a patient with primary immunodeficiency and 1 case of constipation. None serious side-effects were described. Eleven patients who reached clinical remission relapsed after treatment withdrawal. None achieved clinical remission off treatment.

Conclusion: Most patients reached clinical remission on anti-TNF. In our cohort of patients, etanercept and adalimumab were safe, with mostly mild infections and no serious side-effects. We observed a high relapse rate during treatment withdrawal.

Disclosure of interest: None declared.

P340

Administration of adalimumab in paediatric patients with juvenile idiopathic arthritis in South Ural region

Introduction: Juvenile idiopathic arthritis (JIA) is a severe disabling disease affecting paediatric population. 507 children with JIA are monitored in Chelyabinsk region. Oligo-articular and poly-articular types of JIA are often associated with affection of eyes (uveitis). In patients resistant to traditional basic treatment (methotrexate and cyclosporine) F-alpha inhibitors are recommended. Adalimumab, approved for treatment of children older than 4 years in the Russian Federation, is a treatment of choice in patients with JIA associated with uveitis.

Objectives: Evaluate adalimumab effectiveness and safety in JIA patients from Ural regions, Russia

Methods: 11 JIA patients (age 8-17 years, mean age 12.2 years, 7 M, 4 F) were monitored. Disease duration: from 1 year to 11 years (mean 7.4 years). JIA diagnosis was based on the ILAR criteria. Oligo-arthritis was reported in 5 children, seronegative polyarthritis was reported in 4 children. Systemic (without active systemic manifestations) and enthesitis – associated JIA types were reported in 1 patient each. 7 children had uveitis (bilateral uveitis was reported in 6 of them). High disease activity was reported in 7 patients. X-ray activity (stages 1-2) was reported in 8 children. All patients had functional class 2 disease. Methotrexate (15 mg/m²) was ineffective in all children. All patients were receiving adalimumab (40 mg s/c EOW).

Treatment course duration: from 3 months to 3.5 years (mean 1.3 years). ACR pedi criteria were used to evaluate the disease activity and treatment efficacy.

Results: High disease activity (both joint syndrome and uveitis) was reported in all children prior to adalimumab initiation. Mean number of joints affected by severe arthritis: 5 [3, 8] (25; 75%). Number of joints with dysfunction: 4 [3, 8]. Mean ESR (as measured by Panchenko’s method): 20 [15, 32] mm/hour; C-RP level: 25 [13, 40] g/l. Bilateral uveitis was reported in 6 patients; unilateral uveitis was reported in 1 patient. Number of affected eyes: 13. Uveitis was mild and associated with uveitis, resulting in lens replacement in 11 affected eyes. Adalimumab treatment resulted in disease activity decrease in all patients. Mean number of joints affected by active arthritis was 0 [0, 3] (25; 75%) (P = 0.003). Number of joints with function disorder – 0 [0, 3] (P = 0.003). Mean ESR level: 4 [2, 15] mm/hour (P = 0.005), C-RP level: 6.5 [3; 15] g/l (P = 0.008). CHAQ function index: 0.19 [0; 0.5] (P = 0.003). Investigator’s assessment of disease activity (VAS): 20 [15, 30] (P=0.003). Patients/parents assessment of disease activity (VAS): 20 [20, 30] (P = 0.003). Clinical remission (ACR pedi criteria >90%) was reported in 8 patients within 3.6-12 months of treatment. 2 patients were lost for contact within 3 and 6 months of treatment; last reported efficacy was 50%. Insufficient efficacy was reported only in 1 patient with systemic JIA (50% within 2.5 treatment years, resulting in treatment change). Remission of uveitis within 3 months of treatment was reported in 2 children; remission within 6 months of treatment was reported in 3 children. Significant decrease of uveitis activity was reported in 2 children.

Adverse event (transient myositis) was reported in 1 patient; treatment withdrawal was not required.

Conclusion: In patients with JIA, including uveitis-associated cases, adalimumab treatment was highly effective and safe. Clinical remission was achieved in 70% of children. Disease activity decrease was reported in 100% of patients. No severe adverse events were reported.

Disclosure of interest: None declared.

P341

Evaluation of the JIA treatment with adalimumab in UKRAINE

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Objective: To summarize the short-term experience of adalimumab treatment in patients with different types of JIA.

Methods: During the 2013 in the National Children’s Hospital “Ohmatdyt” 79 patients with JIA were treated, aged 5 to 16 years (median -12.5 years), 31 boys and 48 girls. Among girls dominated persistent oligoarthritis and systemic arthritis (50% and 29%, respectively). Boys mostly had polyarthritis, RF-negative and persistent oligoarthritis (48.2% and 22.8%, respectively). 7 children (8.8%) were HLA B27 positive: 6 boys and 1 girl. 7 of all patients were treated with adalimumab and DMARDs. All children on adalimumab were boys with age from 9 to 16 years (adalimumab in Ukraine is approved from 4 y.o.). 6 children had polyarthritic course of JIA, 1 – systemic arthritis. Among them 1 was RF-positive, 1 HLA-B27 positive and 1 had uveitis. RF, HLA-B27 positive patients and patient with systemic arthritis had recurrent courses of disease.

Children with body weight less than 30 kg were given 20mg of adalimumab, and if body weight was 30 kg and more – 40mg eow. All patients previously failed to answer to NSAIDs, methotrexate, sulfasalazine or cyclosporine A. The duration from onset of the disease varied from 2 to
P342
Renal disorder and biological treatment in juvenile idiopathic arthritis
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Pediatric Rheumatology 2014, 12(Suppl 1):P342

Introduction: The paper will present and discuss the renal complications occurred after two years of biological treatment in the case of an 8-year-old female patient, who was previously diagnosed with a polarticular form of Juvenile Idiopathic Arthritis.

Objectives: The authors take into discussion the occurred kidney disorder as a side effect of the biological treatment.

Methods: Long term follow up of the patient contained periodical clinical examination and laboratory investigation. Imagistic methods and renal biopsy were also needed in the evaluation process.

Results: The patient was diagnosed with Juvenile Idiopathic Arthritis when she was 3 years and 2 months old, for which she was previously treated with a polarticular form of Juvenile Idiopathic Arthritis.

Conclusion: The occurrence of renal impairment is discussed as a side effect of the biological treatment. Similar, still rare references can be found in medical literature.

Disclosure of interest: None declared.

P343
Off-label use of rituximab in refractory pediatric rheumatic diseases: a single-center experience
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Pediatric Rheumatology 2014, 12(Suppl 1):P343

Introduction: Rituximab (RTX) is a chimeric monoclonal antibody directed against the CD20 antigen on the surface of B lymphocytes. It binds to CD20 and causes B cells death by different mechanisms. In what concerns rheumatic diseases, it is only approved for the treatment of rheumatoid arthritis. However, there is growing evidence of its utility in other diseases, including in pediatric patients.

Objectives: To describe the efficacy, tolerability and safety of RTX in patients with juvenile rheumatic diseases attending our Pediatric Rheumatology Unit.

Methods: Retrospective review of medical records of patients that were treated with RTX between January 2009 and May 2014. The information collected included: age at diagnosis and at the time of initial treatment with RTX, gender, race, baseline rheumatic disease, previous treatments, indication for RTX, regimens used, follow-up time and data for evaluation of efficacy and adverse events.

Results: We included five patients, four female, four caucasian and one black child. Four of them had juvenile systemic lupus erythematosus (jSLE) and one had extended oligoarticular juvenile idiopathic arthritis (JIA). The median age at diagnosis was 10 years (range 1-17) and median evolution time until receiving RTX was 6 years (range 5 months – 15 years). Previous treatments included high-dose prednisolone (N=5), methylprednisolone pulses (N=5), cyclophosphamide pulses (N=3), methotrexate (N=2), hydroxychloroquine (N=3), mycophenolate mofetil (N=3), azathioprine (N=2), leflunomide (N=1) and etanercept (N=1). The indication for receiving RTX was refractory class IV lupus nephritis in 3 patients, jSLE with refractory multisystem involvement in one patient and severe polyarthritis in a patient with JIA who had had anti-TNFα-induced lupus-like nephritis. The regimens used were variable. The median follow-up time after receiving RTX was 1 year (range 4 months – 5 years). In general, the response to treatment was satisfactory: all the patients showed clinical and analytical improvement after 3 – 12 months. In three patients there was deterioration of the disease between 7 and 14 months after initiation of RTX, and two of them received a second cycle with favorable results. It should be noted that during and/or after RTX patients with jSLE continued therapy with mycophenolate mofetil and prednisolone and the patient with JIA continued corticosteroids, but it was possible to gradually reduce the dose of these drugs. In what concerns adverse events, it was recorded only one case of respiratory tract infection, which was resolved with antibiotics without any complications.

Conclusion: RTX is an anti-CD20 antibody with off-label use in various rheumatic diseases, including in pediatric population. In this case series we found an overall favorable response to RTX, although some patients needed to repeat RTX pulses more than 6 months after the first treatment, which may be related to its mechanism of action. The drug was well tolerated with only one respiratory tract infection reported. Limitations of this study include its retrospective nature, small sample size and short follow-up period. In conclusion, RTX may be a plausible therapeutic choice in rheumatic diseases with more severe and refractory course.

Disclosure of interest: None declared.

P344
Effectiveness of tnf inhibitors therapy in children with juvenile idiopathic arthritis aged 2 to 5 years
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Pediatric Rheumatology 2014, 12(Suppl 1):P344

Introduction: Juvenile idiopathic arthritis (JIA) therapy in the youngest patients (pts) is particularly difficult. Etanercept (ETA) and adalimumab (ADA) are approved for use in moderate and severe JIA in pts older than 2 years, but available data about treatment in the youngest children are limited.

Objectives: The aim of study was the evaluation of the effectiveness of TNF inhibitors in pts with JIA who had started therapy before the age of five.

Methods: 13 children aged 2 to 5 years with polyarticular JIA -2 or extended oligoarticular JIA -11 pts (according to the ILAR criteria) treated with anty-TNF were included in the study (2007-2003). All pts at the start of anti-TNF treatment received two synthetic modified drugs (including methotrexate) and glucocorticoids (GC), in 10 pts intraarticular GC injections were used. The assessment of clinical effectiveness included

Disclosure of interest: None declared.
**P345** Myositis as a rare complication after tocilizumab treatment

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Pediatric Rheumatology 2014, 12(Suppl 1):P345

Introduction: Tocilizumab (TCZ) is an anti-interleukin-6 receptor antibody. It has been accepted as a biological treatment in some subtypes of Juvenile Idiopathic Arthritis. Off-label it has been used (compassionate use) in refractory pediatric autoimmune disorders. Despite being an effective treatment in most cases, this drug isn’t exempt of adverse events.

Objectives: To describe a patient affected by an overlap autoimmune syndrome who presents an inflammatory myopathy as a rare complication during TCZ treatment.

Methods: A 6-year-old boy affected by an overlap autoimmune syndrome characterized by facial skin lesions chilblain lupus like (histopathologically compatible with leukocytoclastic vasculitis), recurrent skin urticarial episodes and a severe lung disease (in the anatomopathologic study is a lymphoid interstitial neumonitis). He presents antinuclear antibodies positivity (maximum title reported 1/640), an undetermined antiDNA antibodies title (values around 31 UI/ml), no complement consumption of C3 neither C4, positives antiβ₂-glycoprotein and anticardiolipin IgG antibodies with persisting elevation of acute phase reactants highlighting an ESR permanently around 100 mm/h and thrombocytosis around 500x10⁹/µl platelets. An extended auto-antibodies study was repeatedly performed without finding other auto-antibodies positivity. Several therapeutic strategies with different agents were previously tested (corticoids, azathioprine, hydroxychloroquine, anakinra, mycophenolate, gammaglobulin, tacrolimus). All of these therapies were discontinued because of inefficacy or lack of efficacy, and resolution of symptoms wasn’t achieved.

Results: After a multidisciplinary evaluation TCZ treatment was initiated. After the first dose he presented improvement of general condition, of skin lesions and of the exortential dyspnea and a dramatical decrease in the acute phase reactants values. Two months later he referred subacute inflammatory pain in both lower limbs, predominantly proximal and symmetrical. The blood test revealed elevation of liver and muscular enzymes: alanine aminotransferase 91 UI/L, aspartate aminotransferase 59 UI/L, creatine kinase 1008 UI/L, aldolase 34.3 UI/L, lactate dehydrogenase 695 UI/L. A bilateral lower limb MRI was performed confirming enhanced STIR signal and edema affecting multiple muscles: right transverse abdominal muscle, bilateral gluteal muscles (maximus, medius and minimus), almost all muscle groups in both thighs respecting the intermedius and medialis vastus, the short and long adductors, and partially the Magnus adductor. Inflammatory lesions of practically all muscle groups in both legs were also observed. To sum up, a bilateral inflammatory myopathy was detected from abdomen to ankles. Intravenous gammaglobulin 1mg/kg/14 days treatment was introduced and TCZ discontinued achieving a fast improving in pain, function and normalizing blood parameters related with muscle inflammation. Two months later the myositis episode was on clinical and biological remission but the autoimmune disease continues.

Conclusion: We report a case of inflammatory myopathy attributed as a rare complication after Tocilizumab treatment. To our knowledge, this adverse event of Tocilizumab treatment wasn’t previously described.

Disclosure of interest: None declared.

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**P346** Clinical response to the canakinumab in crotan’s disease related arthritis

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Pediatric Rheumatology 2014, 12(Suppl 1):P346

Introduction: Crohn’s disease (CD) is an inflammatory disorder of the gastrointestinal (GI) tract that is both chronic and relapsing. In addition to affecting the GI tract, CD has several extra-intestinal manifestations. Arthritis is a common, occurring in approximately 30% of CD patients. Here we report a patient with CD who had treatment resistant arthritis.

Results: A 4 years old girl was admitted because of right hip pain. When she was 1 year old was diagnosed with Crohn’s disease and taken sulfasalazine and corticosteroid. She had septic arthritis in her right hip one year ago. On admission, we have found pain and limitation in right hip. Also she was growth retardation. In her laboratory findings, acute phase reactants were elevated (white blood cells ≥20 500 /mm³, Thrombocyte : 596 000/ mm³, ESH:120 mm/h, CRP 50,2 mg/L). She had also anaemia (Hemoglobin : 8 gr/dl). We found ANA and HLA B27 were negative. We detected arthritis in right hip joint and bilateral sacroiliac joints in her MRI. Glucocorticoids and metotrexate (MTX) was started effectively; however, the patient did not reach complete remission. Therefore etanercept was added her therapy. We found homozygote MEFV mutation (M694V/M694V) and cholecine was added in her therapy.

After one year, a severe arthritis flare occurred, with an aggressive polyarticular course. In consideration of the lack of control obtained through the etanercept administration. We then decided to switch from etanercept to infliximab), which was administered at 7 dose. Despite this therapy, symptoms and laboratory findings did not regress. We started canakinumab (2mg/kg/month) therapy. Her arthritis was recovery on canacinumab in 3 months.

Conclusion: Interleukin-1 (IL-1) is a highly active pro-inflammatory cytokine that lowers pain thresholds and damages tissues. Monotherapy blocking IL-1 activity in autoimmune inflammatory syndromes results in a rapid and sustained reduction in disease severity, including reversal of inflammation-mediated loss of sight, hearing and organ function. The pathogenesis of CD may be mediated by IL-1, and canakinumab may be useful when this disorder is unresponsive to more conventional treatments.

Disclosure of interest: None declared.

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**P347** Complete regression of hip structural damage with anakinra: a case report

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Pediatric Rheumatology 2014, 12(Suppl 1):P347

Introduction: Systemic juvenile idiopathic arthritis (SJIA) is an autoimmune inflammatory disease characterized by the presence of intermittent spiking fever, evanescent erythematous rash, arthritis, lymphadenopathy, hepatosplenomegaly, serositis and elevated inflammatory markers. It accounts for only 10-20% of all patients with JIA but is associated with higher morbidity and mortality. Despite the variety of treatments available, in some cases the disease is difficult to control and has a refractory course. The recent knowledge of the key role of certain cytokines (interleukin
(IL-1, IL-6 and IL-18) in its pathogenesis makes them potential therapeutic targets. Anakinra is a recombinant form of human IL-1 receptor antagonist (IL-1Ra) that has been used in SJIA refractory cases and as first line therapeutic agent in selected patients.

Objectives: To describe a case of clinical and imaging complete remission with Anakinra treatment in a patient with SJIA and severe coxitis.

Methods: The authors report the case of a fourteen-year-old Caucasian girl diagnosed with SJIA by the age of four, when she presented with prolonged febrile syndrome, polyarthritis, evanescent salmon pink rash and pericardial effusion. She was initially treated with oral corticosteroids (prednisolone 1 mg/kg/day). In spite of clinical improvement, systemic and articular activity of the disease persisted with 1-2 exacerbations a year and in the beginning of the year 2007 she started subcutaneous methotrexate (10 mg/week). Despite methotrexate treatment escalation, the patient developed severe left coxitis with major limitation of hip joint mobility, which did not respond to triamcinolone hexacetonide injection.

Results: Due to the persistence of arthritis and elevated inflammatory markers she started Anakinra (1 mg/kg/day) in July 2009. Since then there has been sustained improvement with resolution of clinical symptoms, normalization of laboratory parameters and complete clinical and radiological resolution of coxitis, which allowed discontinuation of methotrexate and corticosteroids. Anakinra was well tolerated and there were no adverse events. The patient achieved prolonged remission.

Conclusion: A significant number of patients with SJIA has persistent disease despite the treatments used. In this case we report the therapeutic success with Anakinra in a patient with refractory systemic and articular manifestations emphasizing complete regression of structural damage of the hip joint.

Disclosure of interest: None declared.

P349
Prospective analysis of Kawasaki disease cases in Catalonia (Spain) from March 2013 to March 2014

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Introduction: Kawasaki disease (KD) is an acute self-limited systemic vasculitis relatively common in childhood. In Japan, last published survey shows an incidence up to 239.6/10^5 children <5 years old (yo). In Madrid (Spain) a retrospective study with no well defined reference area showed an incidence of 15.1/10^5 children <5yo.

Objectives: To ascertain the incidence and clinical features of KD in Catalonia Catalonia, autonomous region in northeast Spain with 7.5 million inhabitants, over a prospective period of one year.

Methods: Observational population-based study including all Catalan hospitals with Pediatric Units, both public and private management. Prospective communication of new cases of KD was performed from March 2013 to March 2014. The presence of coronary aneurysms (CA) in echocardiology was based in the body surface area according to the American Heart Association. Giant CA was considered if the CA was higher than 8 mm.

Results: The study included 33 different hospitals from Catalonia. Over the one-year study period 49 new cases of KD were collected. The annual incidence was 4.1/10^5 children <14yo and 12.3/10^5 children <5yo (mean age 34±23 months (m), range 3.3-105.1 m). There were not differences between boys and girls. Mean delay between onset of the disease and diagnostic was 8.6±9.8 days. Ethnic distribution was: Caucasian 42 patients (85.7%), North African 4 (8.1%), Amerindian 2 (4%) and Asian 1 (2%). Distribution of classical manifestations for KD was: fever in 100% of patients, changes in extremities: edema and erythema 51% and desquamation 44.9%, exanthema 85.7%, conjunctival injection 91.8%, changes in lips and oral cavity 77.5% and lymphadenopathy 24.8%. Other clinical findings reported were: sterile pyuria in 20 (20%) patients, nausea and vomiting in 13 (26.5%), abdominal pain in 12 (24.4%), gallbladder distention in 1 (2%), transaminase elevation in 13 (26.5%), jaundice in 3 (6.1%), irritability in 20 (40.8%), and arthritis or arthralgia in 13 (26.5%).

Cardiologic findings were: perivascular brightness of the coronary wall in 8 (16.3%) patients, myocarditis in 2 (2%), mitral regurgitation in 3 (6%) and CA in 8 (16.3%) patients, disappearing before the 2nd moth of disease in 2 patients. No giant CA were reported. Intravenous immunoglobulin (IVIG) was administered in 47 (95.9%) patients with response to the 1st dose in 40 (91.6%). Day of IVIG administration was 7.8±3.3. Abciximab was administered in 2 patients. 97.9% of patients received anti-platelet dose aspirin in the convalescent phase.

Conclusion: During the prospective period incidence of KD in Catalonia (Spain) was higher than the one ascertained in the retrospective analysis. Further analysis may be performed in order to know if this is due to a better diagnosis, a better registry o a real incidence increase. It seems to be a higher incidence of CA in our cohort despite high rates of treatment response. Further analysis is required. Incidence rate, other clinical features and treatment plans are similar to dose described in studies in other European countries.

Disclosure of interest: None declared.

P348
Can neutrophil-to-lymphocyte ratio predict cardiac involvement in Kawasaki disease?

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Pediatric Rheumatology 2014, 12(Suppl 1):P348

Introduction: Kawasaki disease (KD) is an acute self-limited vasculitis, in which 1/3 of patients develop coronary artery lesions (CAL) if untreated. Although studies have explored potential biomarkers to predict patients with KD who are at risk of CAL, no useful single marker exists. The blood neutrophil to lymphocyte ratio (NLR) is identified as a potentially useful marker of clinical outcome in inflammatory diseases.

Objectives: To evaluate NLR in patients with KD and to investigate the relationship with coronary artery involvement.

Methods: The hospital charts of patients who were diagnosed as KD in a single center between 2004 – 2014 were analyzed retrospectively. Demographic, clinical, and laboratory data were assessed.

Results: Sixty KD patients were evaluated. Male:female ratio was 1:8:1. The mean age at onset of disease was 45±29 months (min: 3 max: 120 months). The mean duration of disease at the time of diagnosis was 8.2±4.6 days. The frequencies of the criteria for KD in all patients were as follows: fewer than 5 days 97%, oral mucosa changes 83%, conjunctivitis 78%, rash 73%, lymphadenopathy 51%, and extremity changes 60%. Twenty three patients (38%) had CAL. The frequencies of the criteria for KD were similar in patients with and without CAL. The duration of fever and platelet counts on admission in patients with CAL were significantly higher (p=0.004 and p=0.007, respectively) and age at onset was significantly younger (p=0.05) than the patients without CAL. The blood neutrophil to lymphocyte ratio was similar between patients with and without CAL (p=0.82). Besides; the mean platelet volume, leukocyte count, hemoglobin level, serum sodium, serum albumin and C-reactive protein level were insignificant between groups (p=0.79, p=0.16, p=0.18, p=0.51, p=0.86 and p=0.26, respectively).

Conclusion: The significantly increased platelet count and longer fever duration along with younger age in KD patients with CAL are in agreement with those in previous literature. The results of this study suggest that blood neutrophil to lymphocyte ratio cannot predict CAL.

Disclosure of interest: None declared.
Kawasaki shock syndrome: a case report

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Pediatric Rheumatology 2014, 12(Suppl 1):P350

Introduction: Kawasaki disease is the second most common systemic vasculitis of childhood and may result in life-threatening coronary artery abnormalities in up to 25% of untreated patients. Adolescents often present with an atypical/incomplete presentation of KD with a delayed diagnosis. Kawasaki Shock syndrome (KDSS) is a rare KD presentation and has been recently defined as the presence of any of the following conditions: systolic hypotension (< 2 SD blood pressure defined for age and sex), a decrease in systolic blood pressure from baseline of >20% or clinical signs of poor perfusion with accompanying features of KD [1].

Objectives: To describe a case of KDSS and to increase awareness for this rare condition among paediatric rheumatologist and intensivists.

Methods: We report the case of 15-year-old boy presenting with atypical KD complicated by severe shock syndrome and successfully treated with high-dose intravenous immunoglobulins (IVIG).

Results: A 15-year-old boy presented to another hospital after four days of high-grade fever, diffuse abdominal pain, diaphoresis and a maculo-papular cutaneous rash. He received antibiotic therapy and underwent laparoscopic abdominal exploration in the suspicion of appendicitis, which was ruled out. The postoperative period was complicated by fever persistence and a by general clinical worsening with clinical signs of shock and of left ventricular dysfunction: a presumptive diagnosis of viral myocarditis was made and the boy was transferred to our ICU where he required mechanical ventilation, fluid resuscitation and inotropic support. Microbiological test failed to identify any infectious agent. Because of the persistence of high grade fever, the sequential appearance of other four KD criteria (chilblains, rash, non-secretive conjunctivitis, oedema of hands and feet) and the sonomorphological demonstration of left coronary artery hyperechogenicity, a diagnosis of KDSS was made and he was administered two courses of IVIG with rapid improvement. Eventually he was discharged with low-dose aspirin; two weeks later he showed periangual peeling of fingers and toes. No further complications appeared, and at last follow up visit, 24 months after diagnosis, he was completely asymptomatic with normal laboratory tests and echo-cardiogram.

Conclusion: KDSS is a rare aetiology for shock in childhood; the diagnosis could be missed because of its atypical presentation. Because of the need for proper diagnosis and rapid treatment, paediatricians and paediatric intensivists should maintain a high index of suspicion.

Disclosure of interest: None declared.

Reference

Fulminant skin necrosis and massive deep venous thrombosis as a part of a clinical presentation of polyarteritis nodosa -case report

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Pediatric Rheumatology 2014, 12(Suppl 1):P351

Introduction: Polyarteritis Nodosa (PAN) is a systemic, necrotizing vasculitis that affects medium-sized and small muscular arteries resulting in microaneurysm formation. In the presteroid era, mortality was high and the diagnosis was exclusively made postmortem.

Objectives: Our goal is to present very challenging, biopsy proven, case of PAN which resulted in massive necrotic skin lesions and deep venous thrombosis.

Methods: We report the case of 8 year old boy who was referred to our hospital with 11 days history of high fever (39.5°C), fatigue, anorexia and weight loss. Two days prior to admission he began to complain of pain in the calves muscles, developed petechial skin rash and hematomas, gross haematuria and gastrointestinal (GI) bleeding. At admission was febrile, in very poor condition, hyperventilating, with calf muscle tenderness (mostly gastrocnemius and soleus muscles), scrotal pain, unable to walk. Skin findings: livedo reticularis, multiple hematomas, petechie, subcutaneous nodules. On the second day he developed cutaneous necrosis, five days after admission bilateral legs edema was observed. Doppler ultrasonography showed massive deep end superficial venous thrombosis. He was tested negative for hepatitis C antibodies, perinuclear antineutrophil cytoplasmic antibody (pANCA) and cytoplasmic antineutrophil cytoplasmic antibody (cANCA). A deep skin biopsy was performed and showed fibrinoid necrosis of small muscular arteries with leukocytic infiltrate; finding compatible with polyarteritis nodosa. Kidney biopsy was contraindicated because the boy had agensis of the right kidney.

Results: Patient responded well to the aggressive immunosuppressive therapy in terms of halting progression of skin necrosis and gradually resolving haematuria, GI bleeding, muscle and scrotal pain. Thrombosis were treated with intravenous and subcutaneous heparin with good response. Cutaneous necrosis required skin transplantation. At present time, 18 months after disease onset, PAN is in remission and there are total resolution of deep and superficial lower extremities veins.

Conclusion: PAN is life-threatening disease that often presents with multorgan invollment, but is rarely associated with deep venous thrombosis. Pain and swelling of the lower extremities is not always a symptom of the disease itself, but may indicate another very serious condition such as deep venous thrombosis. Disease requires prompt diagnosis and aggressive immunosuppressive treatment to reduce morbidity and mortality.

Disclosure of interest: None declared.

Successful treatment of refractory hughes stovin syndrome with infliximab

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Pediatric Rheumatology 2014, 12(Suppl 1):P352

Introduction: Hughes-Stovin Syndrome (HSS) is a very rare clinical disorder characterized by pulmonary artery aneurysm and forming deep venous thrombosis. Typical symptoms are recurrent fever, chills, haemoptysis and it usually affects young men. The natural course of the illness is usually fatal because of fulminant haemoptysis. The aetiology of Hughes-Stovin syndrome is still unknown; however it is supposed to be a clinical variant manifestation of Behçet disease.

Objectives: While several case reports have shown infliximab to be efficacious in patients with Behçet’s syndrome and pulmonary arterial aneurysm, no experience exists about its use in Hughes Stovin Syndrome.

Methods: In the present report we describe the first successful use of infliximab in refractory Hughes Stovin Syndrome.

Results: A 12-year-old albanian boy was first admitted to local a Children Hospital with fever, diplopia, headache and repeated vomiting lasting for weeks. There was no prior medico-surgical illness history. Cerebral MRI (magnetic resonance imaging) revealed thrombosis of right sigmoid and transverse sinuses. Acetyl salicylic acid treatment was started and the boy was discharged. Shortly thereafter he started complaining high fever and left leg pain. Computed tomography (CT) angiography revealed a right femoral artery pseudoaneurysm. Echocardiography showed a large tricuspid valve vegetation. In the suspicion of bacterial endocarditis antibiotic therapy was instituted, without improvement of symptoms. Because of refractory fever the boy was so referred to our Children Hospital. Inflammatory markers were markedly elevated. Echocardiography confirmed the presence of a tricuspid valve vegetation and detected a large atrial thrombus. The boy was put in heparin and referred to a Cardiocosurgery Department where cardiac thrombus and large atrial thrombus were surgically removed. Nevertheless, fever persisted. Thoracic angio-CT-scan was performed, that showed three partially thrombosed aneurysms of right segmental pulmonary arteries. On the basis of pulmonary artery aneurysms, sinus thromboses and femoral pseudoaneurysm a diagnosis of Hughes-Stovin syndrome was made. HLA B-51 allele was detected. There where no other findings consistent with...
Behçet disease. Pulse intravenous cyclophosphamide plus oral prednisone was started with prompt amelioration of symptoms and disappearance of fever. Antiaggregation and coagulation were discontinued to avoid the risk of hemoptysis. Two months thereafter pulmonary aneurysms resulted only partially reduced and inflammatory markers were still slightly elevated. Episodes of relapsing remitting fever occurred. His treatment was so changed to intravenous infliximab with methotrexate to which he showed an excellent response with complete regression of aneurysms at contrast enhanced pulmonary MRA and normalization of inflammatory markers. This permitted successful and quick steroid tapering.

Conclusion: Anti-TNF inhibitors should be considered in patients affected by Huges Stovin Syndrome who do not respond to treatment with corticosteroids and cyclophosphamide.

Disclosure of interest: None declared.

P353

Behçet disease – although rare can be present in children

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Pediatric Rheumatology 2014, 12(Suppl 1):P353

Introduction: The child’s history reveals frequent faringitis accompanied by oral lesions (4-5 episodes/year), bilateral ankle joint swelling and weight loss. Behçet disease (BD) is characterized by a triple-symptom complex of recurrent oral aphthous ulcers, genital ulcers, and uveitis. Hippocrates may have described Behçet disease in the fifth century BC; however, the first description of the syndrome was attributed to the Turkish dermatologist Hulusi Behçet in 1924. In 1930, the Greek physician Adamantiades reported a patient with inflammatory arthritis, oral and genital ulcers, phlebitis, and iritis. Since then, the syndrome has been referred to as Behçet disease.

Objectives: Behçet disease is most common among persons aged 20-40 years. Cases that develop before age 25 years are more likely to involve eye disease and active clinical disease. The mean age at onset is 25-30 years.

Methods: The author present the case of a 16 years old child that comes to our office for oral aphthous ulcers (for the last 3 months), genital ulcers and nodular lesions on the legs (for the last month).

Results: The International Study Group for Behçet’s Disease has emphasized the presence of recurrent oral ulcers as a primary consideration in the diagnosis of Behçet disease. In response, the pathogens above have been targeted for study in hopes of establishing a direct link between their presence and disease activity. Unfortunately, researchers have been unable to generalize results across geographic populations so far.

Conclusion: Behçet disease, although rare, is present in children. This is why pediatricians with rheumatology concerns and beyond, need to know about it and to take it into consideration when needed. Clinical examination of a child with symptoms similar to that present, makes the diagnosis difficult.

Disclosure of interest: None declared.

P354

Aortitis and uveitis. A challenging case of Takayasu or Behcet disease?

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Pediatric Rheumatology 2014, 12(Suppl 1):P354

Introduction: Childhood vasculitis is a group of conditions that are defined as the presence of blood vessel inflammation, and they are grouped in base of the size of vessels involved. In 2008 were presented the PRES revised classification criteria for childhood vasculitis.

Objectives: We describe the case of a vasculitis interesting the aortic arch in a boy with panuveitis, HLA-B51 positive and proteinuria.

Methods: We presented a challenging case of vasculitis classified considering the EULAR/PRINTO/PRES c-Takayasu Arteritis criteria of 2008 and the International Criteria for Behcet disease of 2013 (ICBD)

Results: B. is a ten years old boy born in Columbia. At the age of nine, he presented fever that lasted for about 1 month. In the suspect of Kawasaki disease, he was administered Immunoglobulin, without resolution, that persisted until administration of intravenous steroid. His clinical conditions were characterized by asthenia, arthralgia and photophobia. He also presented a heart murmur of 2/6 at centrum cordis. He presented high inflammatory markers, HLA-B51 positivity and proteinuria. Chest radiography, abdomen ultrasound, brain MRI, lumbar puncture and cardiac ultrasound were negative. Instead total body PET and MRI showed inflammation of aortic arch and signs of previous pericarditis. The eye examination showed panuveitis with retinitis. The therapy administered was based on systemic and ocular steroids and on mycophenolate mofetil with benefit Table 1.

Conclusion: Making the diagnosis of vasculitis is often challenging, because presenting symptoms may be subacute, non-specific and non-diagnostic. Our patient had clinical manifestations, signs and symptoms of TA and BD. The TA criteria were satisfied by the presence of the aorta thickening and high inflammatory markers, however clinical features such as pericarditis, uveitis and HLA-B51 positivity are suggestive for BD, even if the BD criteria are not fulfilled. Vasculitis classifications are useful for patient categorization however other clinical characteristics must be considered in distinguishing ambiguous situations.

Disclosure of interest: None declared.

Table 1(abstract p354) Clinical features of our patient and differential diagnosis based on PRES c-TA and BD criteria

<table>
<thead>
<tr>
<th>Angiographic abnormality</th>
<th>Our patient</th>
<th>ICBD-point score system</th>
<th>Sign/symptom</th>
<th>Score</th>
<th>Our patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Pulse deficit or claudication</td>
<td>Not</td>
<td>Ocular lesion</td>
<td>Genital aphthosis</td>
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<td>2. Blood pressure discrepancy</td>
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<td>Oral aphthosis</td>
<td></td>
<td>2</td>
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</tr>
<tr>
<td>3. Bruits</td>
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<td>Skin lesions</td>
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<td>4. Hypertension</td>
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<td>Neurological manifestations</td>
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<td>5. Acute phase reactant</td>
<td>Yes</td>
<td>Vascular manifestation</td>
<td></td>
<td>1</td>
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<tr>
<td></td>
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<td>Positive pathergy test</td>
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<td>not performed</td>
</tr>
</tbody>
</table>

P355

Takayasu arteritis treatment in children

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Pediatric Rheumatology 2014, 12(Suppl 1):P355

Introduction: Takayasu arteritis (TA) is a rare chronic inflammatory disease of unknown origin mainly involving the large vessels, such as the aorta and its primary branches. There is no uniform strategy of therapy TA in children owing to a rarity of this pathology and no specificity of clinic.

Objectives: Efficacy of 3 treatment regiments (TR) was retrospectively analysed in 38 children with TA aged from 3 till 16 years. Follow up period was 36 mo. In 27 of 38 patients diagnosis was established after a year from emergence of the first symptoms and characterized by widespread inflammation in the aorta and its main branches.

Methods: Group 1 (36 patients) received the combined therapy by glucocorticoids (P) and methothrexate (MTX). Cyclophosphamide (CYC) used at 2 patients as first therapy with widespread inflammation and in 6 – at inefficiency of primary treatment of MTX (group 2). In 5 children with refractory TA – infliximab (INF) (group 3). TR efficacy was estimated by TA activity index (AI), based on Birmingham scale of vasculitis activity (erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), clinical symptoms and results of Doppler ultrasound, etc.).
Results: 1 TR was effective in 67% patients, 2 TR show reliable decrease in an index of activity in 6 months, remission is noted in 12 months therapy. The success of 3 months INF treatment was evaluated according to the normal significances of ESR, CRP and lack of active disease symptoms, after 6 months – reduced of vessel wall thickness. Our data suggests that remission achieved in 32 patients (84%) within 2 years therapy. Full remission is reached at all patients, the diagnosis by which about 6 months from an onset of the illness and at 65% with diagnosis term were established more than 12 months.

Conclusion: At early diagnostics and the localized type of aorta damage as starting basic therapy use of the combined therapy Pr and MTX is expedient. At MTX inefficiency, late diagnostics and widespread type of defeat of the vascular course, vazorenal arterial hypertension - should use CYC and INF.

Disclosure of interest: None declared.

P357

Plasma exchange therapy for severe gastrointestinal involvement of Henoch Schonlein purpura in children

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Pediatric Rheumatology 2014, 12(Suppl 1)P357

Introduction: Henoch-schönlein purpura (HSP), which is predominantly a disease of childhood, is a small vessel vasculitis. It is characterized by non-thrombocytopenic purpura, arthritis and arthralgia, abdominal pain, gastrointestinal hemorrhage and glomerulonephritis. Prognosis and treatment opportunities depends on the clinical severity and organ involvement. Some reports have been published suggesting the beneficial effects of plasma exchange in HSP nephritis, but there have been only some small case series discussing the efficacy of plasma exchange in gastrointestinal system (GIS) involvement.

Objectives: The aim of this report is to evaluate the plasma exchange as a choice for the treatment of life threatening GIS involvement in HSP when refractory to conventional therapies.

Methods: We respectively reviewed the medical records of HSP patients whom had plasma exchange therapy due to massive GIS involvement. We reported age, gender, initial HSP presentation, etiological or triggering factors and disease course. Treatment modalities, side effects and their outcomes were noted.

Results: Seven patients who had plasma exchange therapy due to GIS involvement were identified. All patients had pulse methylprednisolone (MPZ) treatment and then continued with oral prednisolone (2mg/kg/day) therapy. All patients’ complaints continued, G1 bleeding and the severity of disease did not improve. Therefore, pulse cyclophosphamide was added to the treatment. Two patients received intravenous immunoglobulin (IVIG) therapy. Gastrointestinal manifestations did not improved and plasma exchange was performed. All patients improved after plasma exchange management.

Conclusion: Treatment of GI involvement in HSP with plasma exchange have been mainly based on case reports. According to our data, we propose that, plasma exchange may be a safe and efficient management choice in pediatric HSP patients with massive GIS involvement.

Disclosure of interest: None declared.

P358

A case of Henoch-Schönlein purpura associated with posterior reversible encephalopathy and review of literature

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Pediatric Rheumatology 2014, 12(Suppl 1)P358

Introduction: Henoch-Schönlein purpura (HSP) is a vasculitis that involves small vessels and seen in children predominantly. Main symptoms are purpuric rashes on body, especially on lower extremities, arthralgia, abdominal pain, and nephritis. Uncommonly, nervous system can be involved.

Objectives: PRES can occur in HSP infrequently. Here we will review our case, a first reported Korean case, and compare with published cases to find out which symptoms and signs should be aware.

Methods: First, our case is reviewed retrospectively by electrical medical record. And then, we searched Pubmed database, terms including HSP, PRES, RPLS, and encephalopathy. We compared collected cases and our case.

Results: A 6-year-old girl visited our hospital complaining abdominal pain and purpuric rash on lower extremities and buttock. On hospital day 7, there were two brief events of generalized tonic-clonic seizure. She complained dizziness and blurred vision. Brain MRI demonstrated increased signal intensity in the cortex and subcortical white matter, in the parietooccipital area, and impression was PRES. She was discharged on day 19 without any complication. Table 1.

Conclusion: In HSP patients, hemodynamic change due to severe hypertension and renal insufficiency, and CNS vasculitis can cause PRES. JI Shin suggests IL-6 and VEGF can play a role in this situation. Neurological involvement is not common in HSP. But when patients complain headache or blurred vision, it can be manifestation of CNS lesion, including PRES. Adequate assessment and manage should be performed to avoid neurologic sequela.

Disclosure of interest: None declared.

P359

Risk factors for refractory Kawasaki disease: clinical records of the paediatric clinic of palermo

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Pediatric Rheumatology 2014, 12(Suppl 1)P359

Introduction: Kawasaki disease (KD) is an acute, self-limited febrile illness that mainly affecting small- to medium-sized vessels and occurs in early childhood. The etiology is currently unknown, however it likely results from an immunologic response triggered by microbial agents, with documented genetic susceptibility. Intravenous administration of immunoglobulin (IVIG) is the gold standard therapy for coronary arteritis in the acute phase of KD; some patients do not respond to IVIG and coronary aneurysms continue to develop in 5%. The most serious complications are coronary vasculitis and aneurysms. 15% of these patients do not respond to IVIG (Refractory KD:RMK) and have a higher risk of aneurysms.

Objectives: To predict RKD, Kobayashi et al. suggested a score system including: age, gender, days of the disease at IVIG start, neutrophils and platelets count, AST, CRP. Na. Recent reports suggest the utility of a combined treatment with IVIG and steroids or Infliximab to reduce the risk of coronary involvement in RKD. We analyzed Kobayashi criteria and we also considered D-dimer and gamma-GT, to elevate the sensitivity of the score.

Methods: We analyzed the clinical records of the Paediatric Clinic of Palermo, since January 2008 till april 2014: 65 patients with KD (68% Typical KD; TKD; 4% Atypical KD: AKD; 28% incomplete KD: IKD).

Results: 33 (51%) are males; 32 (49%) females, with a M/F ratio of 1.03, lower of that reported (1.5-1.7). Age at the diagnosis was 2±1.8 years. The fever at the admittance was since 5.39±2.40 days; the most frequently relieved symptoms were: conjunctivitis (88%), stomatitis (85%), rash (71%). IVIG were administered 6.7±2.5 days later the fever start. Defervesence occurred 36.8±24 hours after IGEV. 53 patients (82%) received 1 dose of IVIG; 18% had a RKD, with persistent fever after IVIG. 11% responded to the second dose; 5% to three doses; one patient to Infliximab. 15 patients (23%) had aneurysms (20% in responders; 36% in RKD); 64% (7/11) of RKD vs 44% (24/54) of responders showed cardiac involvement. Preocurious, encephalopathy was associated with and more precocious than coronary involvement.

Age was lower in RWD (1.4±1.1). The days of fever pre-IVIG were inversely correlated with IVIG doses. 5/11(45%) of RKD received the first dose <5days. None had platelet count <30.000 mm3 or % neutrophils >80%. 2 had AST>100. 82% (9/11) of RKD had Na<133 vs 26% of responders. Leucocytes were significantly directly correlated with fibrinogen pre-IVIG (p<0.001). IVIG doses were directly correlated with CRP post-IVIG (p<0.044),

Disclosure of interest: None declared.
gamma-GT pre-IGEV (p:0.008), D-dimer pre-IGEV (p:0.014). In RKD D-dimer was 1188±724 ng/ml, significantly higher than in responders (798±662). Days of fever at the recovery were inversely correlated with pre-IVIG AST (p:0.034), and ALT (p:0.013). Conclusion: Our data well correlate with Kobayashi score. However we stress the role of D-dimer and gamma-GT as prognostic criteria for RKD. The role of neutrophils, platelets reduction is decreased.

Disclosure of interest: None declared.

P360
Seidlmyer’s purpura: five cases and review of the literature
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Pediatric Rheumatology 2014, 12(Suppl 1) P360

Introduction: About 100 cases of AHEI have been published in medical literature worldwide. Although initially considered a variant of Henoch-Schönlein purpura (HSP), it is now considered a separate entity: in fact it shows infrequently visceral involvement and IgA skin depositions. Furthermore these patients show a better prognosis than HSP patients. Onset age for AHEI usually ranges between 4 and 24 months but it spreads from birth to 60 months. AHEI, also defined Seidlmyer’s purpura (SP), is characterized by the triad: fever, oedema and purpura. The latter is usually rosette-, annular- or targeted-shaped primarily over the face, ears and extremities in a nontoxic infant. The development and the rapidity of the skin lesions’ onset are typical and more frequent in winter. Skin lesions are dramatic both in appearance and rapidity of onset. In some cases viral or bacterial infections, drugs, vaccinations are documented.

Objective: However AHEI is a self-limited short-duration disease, usually lasting less than 3 weeks. Long-term sequelae are unlikely and relapses are uncommon.

Methods: We report five cases of SP, age: 8-11 months, admitted since January 2013 till April 2014. The purpuric lesions were localized on the face, on the distal ends of limbs on gluteal region. Leucocytes, CRP, transaminases, urine, BUN, creatinin were in the normal ranges. The good clinical conditions of the children allowed excluding a septic framework. The abdomen scan excluded the presence of intestinal loops thickening, suggestive of an involvement of small vessel district. A dermatological evaluation confirmed the suspicion of SP. Serological test of IgM and IgG for Epstein-Barr, Parvovirus, Adenovirus, Coxsackie, Mycoplasma Pneumoniae, Chlamydia did not confirm a recent infection. Anti-nuclear antibodies (ANA) and antineutrophil cytoplasmatic antibodies (ANCA) were undetectable. A nasopharyngeal swab was negative for pathogen bacteria and virus as influenza, Parainfluenza, Respiratory Syncytial virus, Beta-hemolytic group A Streptococcus in 3, positive for Parainfluenza virus in 1, Haemophilus Influenzae in 1. In 2 patients skin lesions were detected 1-2 days after amoxicillin plus clavulanic acid were started.

Results: In 3 patients the fecal occult blood was positive; in 2 fecal occult blood and the urine examination were negative during the acute phase of the illness and the follow up. The patients with the fecal occult blood positive, skin lesions had an ulcerative evolution in the fingers, toes and/or the ears. The worsening of skin lesions suggested the treatment with methyyprednisolone (1mg/kg/die) with benefit, tapering on the fifty-sixth day and completely suspended after 7-8 days).

Conclusion: In most cases no specific treatment is required for SP. The role of corticosteroids is limited to forms with intestinal involvement. In 30% of our patients corticosteroids were necessary due to the severity of dermatological lesions, with a successful improvement in the clinical outcome. Recognition of this rare purpura will avoid misdiagnosis, anxiety for parents and inappropriate therapeutic approaches. Disclosure of interest: None declared.

Table 1 (abstract P358)

<table>
<thead>
<tr>
<th>Our case</th>
<th>Days of fever</th>
<th>Main symptom</th>
<th>Neurologic symptom</th>
<th>Blood pressure</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>F</td>
<td>8yr</td>
<td>Abdominal pain, bloody tinged stool, Purpura</td>
<td>GTC, Blurred vision</td>
<td>144/86</td>
<td>MX pulse Tx, anti-hypertensive drug, anti-convulsive drug</td>
</tr>
<tr>
<td>Dassanathi, et al.</td>
<td>1yr</td>
<td>Abdominal pain, vomiting, purpura</td>
<td>GTC, complete loss of vision</td>
<td>112/67</td>
<td>Supportive Tx</td>
</tr>
<tr>
<td>SivIoglu, et al.</td>
<td>5yr</td>
<td>Purpura, arthralgia, abdominal pain</td>
<td>Headache seizure</td>
<td>180/110</td>
<td>Anti-hypertensive drug, anti-convulsive drug, dialysis</td>
</tr>
<tr>
<td>Sasayama, et al.</td>
<td>13yr</td>
<td>Abdominal pain, purpura</td>
<td>Generalized seizure, cortical blindness</td>
<td>180/120</td>
<td>MXP pulse Tx, anti-hypertensive drug</td>
</tr>
<tr>
<td>Fuchigami, et al.</td>
<td>7yr</td>
<td>Abdominal pain, arthralgia, purpura</td>
<td>Sudden loss of vision GTC</td>
<td>190/100</td>
<td>PL, anti-hypertensive drug, anti-convulsive drug</td>
</tr>
<tr>
<td>Woolfenden et al.</td>
<td>10yr</td>
<td>Fever, RLQ pain, bloody diarrhea</td>
<td>Bi-temporal headache, nausea, vomiting, bilateral visual loss seizure</td>
<td>Not known</td>
<td>MXP pulse Tx, anti-convulsion drug</td>
</tr>
<tr>
<td>Ozcákar et al.</td>
<td>10yr</td>
<td>Fever, palpable purpura, arthralgia</td>
<td>Seizure</td>
<td>130/90</td>
<td>Steroid, anti-convulsive Tx, anti-hypertension drug</td>
</tr>
<tr>
<td>Endo et al.</td>
<td>7yr</td>
<td>Abdominal pain, purpura</td>
<td>Seizure unconsciousness loss of vision</td>
<td>190/100</td>
<td>PL, anti-hypertensive drug, anti-convulsive drug</td>
</tr>
</tbody>
</table>

A child with cPAN as only manifestation of FMF
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Pediatric Rheumatology 2014, 12(Suppl 1) P361

Introduction: Cutaneous Polyarteritis Nodosa (cPAN) is a rare type of vasculitis affecting small-to-medium-size arteries. It is distinct from systemic PAN in that it lacks significant internal organ involvement. Familial Mediterranean Fever (FMF) is the most common inherited autoimmune disease, characterized by recurrent, self-limited attacks of fever and aseptic polyarthritis. PAN is considered one of the four types of vasculitis associated with FMF. FMF is widespread in Armenia and there is a higher than expected frequency of FMF-associated vasculitis which may in some cases be the first indication for MEVF mutation analysis.

Objective: We want to introduce the importance of MEVF gene analysis in the patients with vasculitis in population with high prevalence of FMF.

Methods: A case report of a patient diagnosed and followed in a multidisciplinary unit.

Results: A 7 years old girl was admitted to the hospital with the following complaints: high grade fever for 3 days, stomatitis, ulcers on the feet, swelling and tenderness of the left ankle joint. Past history was unremarkable. The physical examination revealed livedo reticularis on the
lower extremities, painful subcutaneous nodules and ulcers on the left leg and foot, arthritis of the left ankle joint. Blood pressure was normal. No signs of internal organ involvement were found. Initial laboratory findings indicated: mild anemia, (Hbg-100g/l), thrombocytopenia -700,000/mcl elevated acute phase reactants - leukocytes -26,000/mcl with 81% of neutrophils, ESR 70 mm/h, and CRP 96 mg/l. An extensive diagnostic work up including blood culture and serology (ANA, anti dsDNA, ANCA, ACA, HBs Ag …), biochemical examination, bone marrow aspirates and imaging studies did not reveal any pathology. Despite of absence of FMF symptoms, genetic analysis of MEFV mutations was done and 2 mutations in compound homodimer-sized arteries with fibrinoid necrosis were found. Along with prednisone, aspirin was started. After 1 year, his blood pressure was normal, he gained weight and the rash, arthralgia, and epigastric pain disappeared. Today he is 12 years old on clinical remission. Conclusion: We described three PAN cases all with very aggressive presentations, central nervous system involvement and ANCA negative, with relatively good response to immunosuppression. Only one remained with sequelae, but all have currently good organic and cognitive prognosis and no disease relapses.

Disclosure of interest: None declared.

P363
Atypical hemolytic-uremic syndrome associated with antiphospholipid antibodies and antiphospholipid syndrome; a novel presentation
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Introduction: Atypical hemolytic-uremic syndrome (HUS) is defined by the presence of microangiopathic hemolytic anemia, acute renal failure, and thrombocytopenia without a diarrheal prodrome. It is responsible for only ten percent of cases in children. The role of genetic deficiencies of complement regulation, Von Willebrand factor cleaving protease (ADAMTS13), and intracellular defects of vitamin B12 metabolism has been known in pathogenesis of disease. Antiphospholipid antibodies (aPLs) are autoantibodies against negatively charged phospholipids or phospholipid binding plasma proteins. It is clear that their presence is associated with thrombosis, pregnancy morbidity, hematologic, skin, neurological conditions, and microangiopathy.

Objectives: To our knowledge, there are only two pediatric case series that showed a high frequency of anticardiolipin antibodies in children with typical HUS. Microangiopathic antiphospholipid-associated syndrome (MAPS) was also described in a child with atypical HUS. Herein we reported a 5.5-year-old boy who was presented with atypical HUS associated with antiphospholipid antibodies and antiphospholipid syndrome in his father.

Methods: A 5.5-year-old boy from Azerbaijan was referred to Mofid Children’s Hospital, because of edema, hypertension, anemia and acute renal failure. He was healthy until 4 weeks before admission while he had fever and sore throat. Then generalized edema, ecchymosis, gross hematuria and severe paleness occurred. The history of diarrhea was negative. On presentation, he was ill, pale but afebrile.

Results: His laboratory data on admission were as following: white blood cell (WBC): 18800/μL, hemoglobin (Hb): 11g/dl, lactate dehydrogenase (LDH): 6236 IU/ml, creatin phosphokinase (CK): 1039 IU/L, Erythrocyte sedimentation rate (ESR): 40 hr, C-reactive protein (CRP): 11 mg/l, blood urea nitrogen (BUN): 98 mg/dl, creatinin: 3.7 mg/dl, uric acid: 16.8 mg/dl, Aspartate transaminase (AST): 298 IU/L, Alanine transaminase (ALT): 371IU/L. His urinalysis showed hematuria (many RBC) and proteinuria (2+). He had low level of C3: 30 mg/dl (normal range: 90-180) and his C4 level was 11(10-40) mg/dl. His C4 level was 11(10-40) mg/dl. Conclusion: On the basis of microangiopathic hemolytic anemia, thrombocytopenia and acute renal failure, he was diagnosed as having atypical HUS. To our knowledge, in the literature, there is no report of this association between aHUS , aPS and aPLs as predisposing factor.

Disclosure of interest: None declared.
Introduction: We reported a patient with mercury poisoning who presented as systemic vasculitis.

Results: A 12-year-old girl was admitted to our hospital with complaints of weakness, weight loss (10 kg in the last month), excessive sweating, and abdominal and joint pains. Her complaints started 6 weeks prior to admittance when she began to suffer from intermittent fever, arthralgia, back and abdominal pain. Also she was found to have red painful hands, a blood pressure 170/120 mm Hg, and tachycardia. In laboratory examinations, acute phase reactants were very high while viral markers, ANA and ANCA were negative. Renal doppler ultrasound and MR angiography were normal. We found sensorial neuropathy in her legs. Her blood pressure was controlled with 2 different antihypertensive medicines. The patient’s symptoms were not controlled with steroid treatment, we continued our research. A blood mercury concentration of 12.4 Mcg/L (ref value 0.3 mcg/L) and spot urine mercury concentration of 18.8 Mcg/L (ref value 0.15 Mcg/L) were discovered. The girl was treated with metalcaptase 25mg/kg three times daily for 5 days, then every 12 hours for another 2 weeks (total duration, 19 days).

Conclusion: Symptoms of mercury poisoning can vary greatly and mimic many acute diseases. Cardiovascular symptoms have been reported with acute poisoning. We conclude that inclusion of mercury intoxication in the differential diagnosis in vasculitis early on can help avoid unnecessary and invasive diagnostic tests and therapeutic interventions.

Disclosure of interest: None declared.

P365
Intracardiac thrombus in a child with behçet’s disease
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Pediatric Rheumatology 2014, 12(Suppl 1)P365

Introduction: Behçet’s disease (BD) is recognized as a systemic vasculitis involving both arteries and veins of any size and characterized by recurrent oral aphthous ulcers, genital ulcers, and uveitis and skin lesions. The mean age of onset is in the fourth decade.

Objectives: Childhood BD accounts for 1–3% of all cases. Intracardiac thrombus in BD is rarely seen. We present an adolescent with a severe manifestation BD who had an intracardiac thrombus.

Methods: A sixteen-year old male patient was admitted with painful localized swelling of the legs, high fever and cough. Medical history revealed that he had suffered from recurrent oral ulcers for 5 years, recurrent painful nodules on his legs and uveitis in the last one year. He was diagnosed with BD at another center; colchicine and eye drops were started. However, he didn’t use the pills and eye drops, regularly. Family history revealed a maternal uncle who died due to BD.

Results: His height and weight were below 3%. Oral ulcers, vision loss in the left eye and erythema nodosum on the lower extremities were observed. Eye examination showed a serious sequel of uveitis, but there was no evidence of active uveitis. Although azathioprine, prednisolone and colchicine were prescribed, he did not use the medications, regularly. After 3 months, he applied with chest pain, cough and abdominal pain. Physical examination showed pale appearance, slightly hyperemic tonsils, postnasal drip. Laboratory investigations showed: Hgb: 12.7 g/dL, Ptt:487000 K/Ul, WBC11700 K/Ul, AST:71 IUL, ALT:141 IUL, C-RL:17 mg/dL, and erythrocyte sedimentation rate: 40 mm/hr. Abdominal ultrasound showed many lymph nodes (largest one 10 x 15 mm), and chest X-ray demonstrated irregularity and notches in the right diaphragm. Thorascopich echocardiography showed a 15 x 8 mm mass linked to trabecular muscle in the right ventricle. Thorax CT angiography showed a hypodense filled defect of 22 x 9 mm in the right ventricle, with focal consolidation, micro emboli and intracardiac thrombus, low molecular weight heparin, pulse methylprednisolone (3 consecutive days), oral prednisolone 2 mg/kg/ day and pulse cyclophosphamide (for 6 doses-monthly) were started. Clinical improvement was observed and control echocardiography showed reduction in the size of the mass in the right ventricle. Steroid (with reducing doses), colchicine and anticoagulant treatment were continued. During this period oral ulcers and erythema nodosum did not recur and there were no active uveitis attacks. Thrombosis panel showed heterozygote mutations of an allele of factor V Leiden (G1691A) and prothrombin (G20210A). A control thorax CT angiography in the 5th month of treatment showed that intracardiac mass had disappeared, regression of the fibrose-focal consolidation areas in the parenchyma of both lungs and the frost-glass opacity nodule had disappeared.

Conclusion: In Behçet’s disease intracardiac thrombi are rarely seen. However it is related with high mortality and morbidity. Thus, early diagnosis and treatment is very important from the point of view of prognosis. Instead of surgical treatment intense immunosuppressive treatment with anticoagulant therapy may be more beneficial in these type of patients.

Disclosure of interest: None declared.

P366
Eosinophilic granulomatosis with polyangiitis (churg-strauss syndrome) without respiratory symptoms in a boy
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Pediatric Rheumatology 2014, 12(Suppl 1)P366

Introduction: Eosinophilic granulomatosis with polyangiitis or Churg-Strass Syndrome (CSS) is rare in children. It is characterized by eosinophilia, extravascular necrotizing granuloma, and eosinophilic infiltration of multiple organs particularly lungs, but may also involve the gastrointestinal tract, heart, and the kidneys.

Objectives: The condition is usually associated with a preceding history of asthma or allergic sinuitis. It has rarely been reported in children, where most of the cases had pre-existing asthma, allergic rhinitis, or atopic disease. We present a boy with CSS, without history of asthma or allergic rhinitis and respiratory symptoms or signs.

Methods: A fourteen-year old male patient was admitted to our pediatric rheumatology department with a 7 days history of severe extremity pains and generalized body rash. Past medical history revealed that he had no asthma and other allergic diseases, recurring sinuitis, familial Mediterranean fever or vasculitis.

Results: During physical examination, he was very irritable and agitated due to severe leg pain. Blood pressure, weight, height, respiratory rate and body temperature were normal. He suffered from severe pain in all extremities. Neurological examination revealed 1–2/5 strength in all muscle groups of his lower and upper extremities. He had sensation loss similar to gloves or socks type, and mucosal rash on the back of hands and soles of feet. Respiratory system and other systems were normal. Laboratory investigations revealed peripheral blood eosinophilia (30%), slight thrombocytopenia (112,000/mm3), high muscle enzymes (CK: 2700U/L, AST: 47U/L, LDH: 249mg/dL), slightly high CRP (1.1mg/dL), IgE (103mg/dL) and ASO (266 IU/mL) levels. All viral, bacterial and parasitological investigations, full urine exam, other biochemical parameters, rheumatologic serological investigations, heavy metal levels (lead and mercury), eye exam, chest X-ray, echocardiography and bone marrow evaluation, abdominal MR and selective renal angiography were normal. Electroneuromyography (ENMG) showed sensorimotor polyneuropathy in all extremities especially in the upper. Skin biopsies revealed necrotizing eosinophilic vasculitis. Thorax MRI showed peripheral infiltration of the anterior segment of the left upper lobe and the patient was diagnosed as CCS. After three days of pulse methylprednisolone, 60 mg/day oral steroid therapy (1 month) was started, then while monthly reduction of steroid continued, IV pulse cyclophosphamide (once a month for 6 months, twice for lower dosage) and then azathioprine (2 mg/kg/day), gabapentin, oral vitamin D and calcium treatment were given. Meanwhile physical therapy was commenced. All clinical, laboratory and MRI findings were resolved in the first 2 months of treatment. Polyneuropathy was checked by ENMG every 6 months and noted clear improvement in all extremities. On the last visit of the patient in the 20th month, he noted minimal weakness of left hand muscle associated with minimal hypoesthesia.
Conclusion: In cases suspected of CSS, even without respiratory symptoms, detailed imaging and pathology will establish the exact diagnosis. As in our case, though all findings regress with intense immunosuppressive treatment in the early period, it takes a long time for neuropathy to resolve completely.

Disclosure of interest: None declared.

P367
Forever interesting disease: Kawasaki vasculitis – case series
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Introduction: Kawasaki disease (KD) typically presents in children younger than 5y as a febrile illness with mucocutaneous changes. If untreated, KD can result in coronary aneurysms in 25% patients.

Objectives: Analysis of 6 patients diagnosed as KD, at Children’s Hospital Sarajevo from 2008 to 2014.

Methods: Retrospective analysis of clinical features, coronary artery abnormalities and treatment outcome.

Results: Youngest patient was 3 months, oldest 13 years, far more boys 83% (5/6). Seasonal peak was during winter (Jan-Feb) in 50%. Clinical presentation (figure 2) was consistent with literature. All patient had high inflammatory markers, anemia (patients 1, 2, 5), thrombocytosis. Patient 1. had incomplete KD, with coronary artery aneurysms seen before therapy. Completely responded well to one dose of IVIG. Patient 2.was diagnosed od day 7 of fever; received IVIG, but had unusually prolonged systemic inflammation requesting second IVIG dose and pulses of IVMP plus MTX. Patient 3. is a child with suspected primary immunodeficiency (neutrophil dysfunction in observation). Patient 5. presented with pleuropneumonia requesting active pleural drainage and had prolonged inflammation. Responded well to second IVIG + IVMP. Patient 6.had splitter haemorrhages on his nails.

Conclusion: KD is diagnosed on clinical basis with supportive laboratory evidence and imaging. Once identified, timely initiation of treatment is imperative in order to quell the inflammatory response and decrease the incidence of long-term sequelae, specifically coronary artery aneurysms. Longitudinall follow-up should be implemented based on risk stratification and individualised to each patient.

Disclosure of interest: None declared.

ORAL PRESENTATIONS

Y1
Y1M-013. Development of novel protein biomarkers for the prediction of response to treatment in juvenile idiopathic arthritis
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Introduction: Standard management of Juvenile Idiopathic Arthritis (JIA) is heavily dependent on the use of methotrexate (MTX), which induces clinical benefit in about 65% of patients. We have previously demonstrated that children with high serum levels of MRP8/14 protein prior to starting MTX have a high chance of good response to MTX. However, among children whose MRP8/14 serum levels are moderate or low, prior to MTX, some respond well whilst others respond poorly to MTX. We have taken a proteomics approach to identify novel biomarkers present in serum prior to treatment that correlate with response or non response to MTX.

Objectives: The aim of this study was to identify novel protein biomarkers in serum from JIA patients to help and inform the clinicians at time of diagnosis whether the patient is likely to respond well to MTX.

Methods: Blood serum samples and clinical data were obtained from 83 JIA patients from the Childhood Arthritis Response to Medication Study (CHARMS) before starting MTX treatment. The study has full ethical approval and consent. To assess clinical response to medication, core set variables and Definition of Improvement (DOI) for JIA was used, comparing data at 0 and 6 (range 4-8) months. MRP8/14 was measured in these patients and used to classify cases into three groups: non-responders, responders with low MRP 8/14 levels pre MTX, and responders with high MRP 8/14 levels pre MTX. To screen for proteins which distinguish future MTX non-responders from responders, 5 serum samples from age-matched patients from each group were pooled; pooled samples were enriched for low abundant proteins, and fractionated on a 1D PAGE. Proteins were identified and quantified by Msx- label free quantitation and analysed using Nonlinear Dynamics Progenesis LC-MS software for differential expression.

Results: A total of 648 unique proteins were identified in serum pools (just prior to commencing MTX treatment). Patients were defined as responders, R (those reaching ACR50 or above) or non-responders, NR (reaching only ACR30 or below). Forty proteins were found to be differentially represented in the serum pools, using a level of >2 fold difference between MTX responders and non-responders. This group included 26 proteins with high abundance in the responder group and 14 proteins with high abundance levels in the non-respondor group. Using a more stringent cut off of fold difference > 4 identified 12 proteins that showed a significant difference between R and NR groups. In contrast to our previous data with MRP8/14, these 12 novel biomarker proteins were highly differentially expressed in serum of both the groups of responders (i.e. MRP high and MRP low responder groups), compared to NR cases, prior to MTX use. This indicates that these protein biomarkers may function to distinguish R from NR patients more efficiently than the MRP8/14 biomarker.

Conclusion: This study has identified a number of potential novel protein biomarkers which may be able to discriminate between patients who will respond or those who will fail to respond to MTX, when measured prior to starting the treatment. Forty protein biomarkers were able to significantly differentiate between response and non response. Using a higher cut off of >4 fold difference produces 12 proteins that we envisage to be more reliable than MRP 8/14 for predicting response. Further testing and analysis of these proteins is required to validate those which can most reliably recognise patients who will respond to MTX therapy, or those who will fail to respond.

Disclosure of interest: None declared.

Y2
Y2M-020. Standardization and performance of cone beam CT scan for the evaluation of linear scleroderma of the face
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Introduction: Up to now, standardized and validated methods for monitoring linear scleroderma of the face are still lacking. Therefore, it is difficult to assess, in these patients, the disease progression both for therapeutic purposes and maxillofacial surgery procedures. The Cone Beam Computed Tomography (CBCT) is an imaging technique that has good sensitivity for both soft and the bony tissues, is fast to be performed, does not require sedation and the irradiation is 50 times lower than traditional CT scan.

Objectives: We evaluated the performance of Cone Beam CT scan for evaluation of linear scleroderma of the face.

Methods: The study was conducted in two phases. Five CBCT transverse sections were identified, in 8 patients, from the entire face volume: mental symphysis (MS), mandibular foramen (MF), maxillary sinus (MS), mandibular condyle (MC) and supraorbital ridge (SR). From the intersection axes an origin point was generated and from this one, 30° and 60° lines, crossing bony and soft structures, were drawn. For each given degree, the total thickness, the soft tissue thickness, and the inner skeletal thickness, were measured. Sixty measures were therefore evaluated for each patient by...
using the software Onis 2.4 free edition. The intra- and inter-operator correlation were tested, ICC values were interpreted as follows: > 0.7 excellent, 0.40–0.75 fair to good and <0.40 as poor.

Results: The lack of reproducible bony landmarks allowed us to discard two transverse sections: the superorbital ridge and the mandibular symphysis, which represent the more external sections of the face. Three judges evaluated 5 patients’ CBCTs twice, with a time interval between the first and second analysis of one month. The same evaluators analyzed 10 patients’ CBCTs singularly and blindly to the others and to the disease site. The intra-operator concordance resulted optimal in almost all cases, varying from a minimum of 0.70 to a maximum of 1. The inter-operator concordance between judges was statistically significant in the 75% of cases, with an ICC ranging between 0.40 and 0.92. About 25% of the parameters had an optimal ICC (> 0.75). The best performances were obtained at the level of the MF and MC planes.

Conclusion: CBCT has shown to be a reliable method to assess skin and bone lesions in patients with linear scleroderma of the face. It is fast to be done, safe and reproducible. While it is not applicable for frontal lesions, it provides a reliable assessment in the remaining parts of the face. A prospective validation to confirm its relevance in evaluating the disease progression is on going.

Disclosure of interest: None declared.

POSTER PRESENTATIONS

Y3
YIM-P22. Extracellular vesicle induced macrophage differentiation; developing a disease in a dish model
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Pediatric Rheumatology 2014, 12(Suppl 1):1/Y3

Introduction: Extracellular vesicles (EVs) are small membrane vesicles of endocytic origin. EVs can be found in a plethora of body fluids and are known to carry both vesicle as well as parental cell specific proteins. The content of the particles is dependant on the stimulation and/or micro-environment surrounding the donor cell. Content analyses reveal the presence of proteins involved in targeting, adhesion, membrane trafficking, signal transduction, chaperones, enzymes and functional miRNA and mRNA, with particle release being a highly regulated process induced by biological, chemical or mechanical stimuli. EVs play a functional role in immune responses providing both activating and suppressive signals to target cells. This is exemplified by the fact vesicles from FMA-differentiated THP-1 cells have been shown to induce naive THP-1 cell differentiation. Systemic juvenile idiopathic arthritis (sJIA) is a subtype of childhood arthritis that is characterized by its systemic manifestations, severe symptoms and, on a cellular level, polarization of monocytes to a pro- or anti-inflammatory phenotype depending on the active/remissive state of the patient.

Objectives: EVs are biological vectors, carrying important messages from one cell to another. We aimed to develop a system in which the influence of sJIA patient plasma vesicles could be analyzed in order to determine their influence on monocyte differentiation and phenotype.

Methods: THP-1 cells where cultured and differentiated into macrophages. Upon differentiation into macrophages, cells where further skewed toward a pro- or anti- inflammatory phenotype. Vesicles where subsequently harvested from the culture supernatant of differentiated cells and placed on undifferentiated THP-1 or M0 macrophages. Cytokine production and cell surface markers were used as read out for cell differentiation.

Results: Upon polarization, elevated CD80 signified M1 differentiation while CCL22 was upregulated in M2-polarized macrophages. Vesicles harvested from M1-polarized macrophages skewed naive macrophages towards an M1 phenotype while M2 vesicles may skew macrophages towards a more regulatory phenotype.

Conclusion: Data provides evidence towards the functional role of EVs in macrophage differentiation. By optimizing our system, this model could be used to analyze the function and activity of EVs in sJIA, allowing us to determine the influence of these particles on disease pathology and possibly inferring the future active or remissive state of a patient.

Disclosure of interest: None declared.

Y4
YIM-P44. Reduced expression of cd73 on jia synovial lymphocytes is related to cell proliferation
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Pediatric Rheumatology 2014, 12(Suppl 1):1/Y4

Introduction: The nucleoside adenosine exerts regulatory functions prompting T cell anergy and preventing release of inflammatory cytokines. The main source of extracellular adenosine is AMP dephosphorylated by CD73. The resulting product can be taken up by the cell or further metabolized by ADA (Adenosine deaminase) expressed extracellularly when bound to the membrane via coupling to CD26 protein, a surrogate marker for ADA expression. We have shown that CD73 expression and its AMPase activity are reduced on JIA (juvenile idiopathic arthritis) SFMC (synovial fluid mononuclear cells), particularly on CD8+ T cells and CD19+ B cells; we hypothesise that this may lead to a defect in generation of anti inflammatory adenosine in JIA.

Objectives: To investigate the mechanisms which lead to reduced cell surface expression of adenosine-generating and degrading ectoenzymes on JIA synovial inflammatory cells.

Methods: PBMC and FACS sorted CD8+CD73+ from healthy donors were stimulated with anti-CD3mAb and anti-CD28 mAb or CpG, CHO CD40L or anti-IgG/IgM F(ab’2)2 and then analysed by flow cytometry for surface markers and the nuclear protein Ki67. In some experiments, cells were labelled with CFSE before culture to allow assessment of proliferation. Culture supernatants were analysed for soluble CD73 by ELISA. Data are expressed as medians, analysed by GraphPad Prism.

Results: Stimulation of T cells through the TCR in vitro resulted in reduced CD73 expression on CD8 cells. Higher levels of CD73 protein were found in culture supernatants of TCR stimulated cells (53.8 ng/ml) than that of cells cultured in medium alone (29.9 ng/ml; p=0.03) suggesting that TCR stimulation leads to shedding of CD73 protein. Co-stimulation was not required for this reduction in CD73 expression, as it was still evident after culture with α-CD3 antibody alone. TCR stimulation of sorted CD8+CD73+ cells demonstrated that CD73 downregulation is related to cell proliferation, as only those cells which had entered cell cycle had lost their CD73 expression. B cell stimulation via use of TLR9 ligand CpG and CHO cells transfected with CD40ligand led to a significant reduction in CD73 expression on B cells, while culture with anti-IgG/IgM F(ab’2)2 induced only a minor, non-significant reduction in CD73 on CD19+ cells. Culture in cytokines IL-1, IL-6, TNFα, known to be elevated in the JIA synovium and SF (synovial fluid) did not affect CD73 expression of either T or B cells. Expression of ADA-binding protein CD26 was also found to be reduced on JIA synovial CD8+ T cells (24.7%) compared to both JIA PBMC (63.3%, p < 0.0001) and healthy PBMC (62.9%, p < 0.0001). This result was unexpected as CD26 is known to be a marker of activation and JIA SFMC have an activated phenotype.

Conclusion: These data show that low expression of CD73 on T and B cells in the inflammatory site is related to cell proliferation and shedding of the protein and suggest that diminished CD73 expression on T and B cells found in the joints of children with JIA may have followed stimulation by proliferative signals at the inflamed site.

Disclosure of interest: None declared.

Y5
YIM-P58. Macrophage activation syndrome: the role of infectious triggers
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Pediatric Rheumatology 2014, 12(Suppl 1):1/Y5

Introduction: Macrophage activation syndrome (MAS) is a potentially fatal complication of childhood rheumatic diseases (RD), due to excessive activation and proliferation of macrophages. It belongs to secondary forms of Hemophagocytic lymphohistiocytosis (HLH), including HLH-infection associated forms (HLH-IA).

Using the software Onis 2.4 free edition. The intra- and inter-operator correlation were tested, ICC values were interpreted as follows: > 0.7 excellent, 0.40–0.75 fair to good and <0.40 as poor.

Results: The lack of reproducible bony landmarks allowed us to discard two transverse sections: the superorbital ridge and the mandibular symphysis, which represent the more external sections of the face. Three judges evaluated 5 patients’ CBCTs twice, with a time interval between the first and second analysis of one month. The same evaluators analyzed 10 patients’ CBCTs singularly and blindly to the others and to the disease site. The intra-operator concordance resulted optimal in almost all cases, varying from a minimum of 0.70 to a maximum of 1. The inter-operator concordance between judges was statistically significant in the 75% of cases, with an ICC ranging between 0.40 and 0.92. About 25% of the parameters had an optimal ICC (> 0.75). The best performances were obtained at the level of the MF and MC planes.

Conclusion: CBCT has shown to be a reliable method to assess skin and bone lesions in patients with linear scleroderma of the face. It is fast to be done, safe and reproducible. While it is not applicable for frontal lesions, it provides a reliable assessment in the remaining parts of the face. A prospective validation to confirm its relevance in evaluating the disease progression is on going.

Disclosure of interest: None declared.
Objectives: The aim of our study is to assess the prevalence of clinical and laboratory features, possible triggers and outcomes of MAS.

Methods: We retrospectively evaluated a cohort of 12 patients with MAS and HLH-IA, observed at the U.O.S. Pediatric Rheumatology, from 2005 to 2014. Here we report: sex, ethnicity, RD; age at the onset of the rheumatic disease, age at the onset of MAS, duration of the disease pre-MAS; clinical and laboratory features; results of the bone marrow biopsy if performed; trigger factors, treatments and outcomes.

Results: We identified 12 patients: 9 MAS and 3 HLH-IA; 9 females and 3 males; 10 Caucasians, 1 Egyptian and 1 Latin American. The mean age at diagnosis of MAS was 9.25 years. 9 children had RD: 6 systemic juvenile idiopathic arthritis, 1 dermatomyositis, 1 autoinflammatory disease and 1 systemic lupus erythematosus. In 3 cases MAS occurred during the first presentation of the RD. In all cases, RD status was active during MAS. The mean age at onset of RD was 7.8 years. HL-A and IA MAS could occur at the onset of the RD with an interval of 22 days or later in the course of RD with an interval of 1105 days on average. Organ involvement was: hepatomegaly 12, splenomegaly 7, lymphadenopathy 5, bleeding 2, central nervous system 6, heart 8, lung 4, kidney 5 and gallbladder 2.

Table 1 summarizes patients’ characteristics, the clinical and laboratory features and number of cases.

In 11 cases the possible trigger was an infectious episode. We identified 5 bacterial infections (Chlamydia pneumoniae, Mycoplasma pneumoniae, Clostridium difficile, group A beta-hemolytic Streptococcus, Staphylococcus aureus), 2 viral infections Chickenpox virus, Epstein-Barr virus and one multiple protozoal infection (Entamoeba histolytica, Endolimax nana). In 4 cases there were signs suggestive of infection, including lower respiratory tract infection, skin infection, urinary tract infection, gastroenteritis, but it was not possible to identify a pathogen.

All patients were treated with methylprednisolone and cyclosporine. 9 received transfusions of fresh frozen plasma, 7 blood transfusions and 4 intravenous immunoglobulins. Regarding the outcomes, 1 patient died. 3 had sequelae: seizures in 1, 1 spastic quadriplegia and 1 flaccid paralysis of half body, with a motor type polyneuropathy.

Conclusion: In our cases, RD was in active phase at the time of diagnosis of MAS, regardless of the time elapsed since the first diagnosis. The infection appears to have a triggering role in the MAS, including Entamoeba histolytica and Endolimax nana, as far we are aware, are not reported in the literature.

Disclosure of interest: None declared.

Y6

YIM-P59. Relationships between the Th17 and innate lymphoid cell signature in enthesitis related arthritis

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Pediatric Rheumatology 2014, 12(Suppl 1):y6

Introduction: Enthesitis related arthritis (ERA), a subtype of juvenile idiopathic arthritis (JIA) has a close association with HLA-B27. Previous studies suggest a role for Th17 cells in disease pathogenesis; at present the link between Th17 immunity and HLA-B27 is unknown. Innate lymphoid cells (ILCs) form a bridge between the innate and adaptive immune systems, producing signature cytokines in response to cytokine stimulation. ILCs lack common surface markers associated with known leukocyte lineages, but constitutively express the IL-7 receptor-α(CD127). ILCs can be divided into 3 types (1, 2 and 3) which mimic the T cell subsets (Th1, Th2 and Th17) based on their transcription factor and cytokine profiles.

Objectives: To investigate Th17 and ILC populations in the joint and blood of ERA JIA patients.

Methods: Th17 cells and ILCs from the peripheral blood mononuclear cells (PBMC) of healthy controls and ERA patients and synovial fluid mononuclear cells (SFMC) of ERA patients were analysed by flow cytometry (n=7). Th17 cells were identified as CD3 positive CD4 positive T cells which secreted interleukin (IL)-17 after stimulation with PMA and ionomycin . ILCs were identified as lineage negative (CD3, CD14, CD16, CD1a, CD34, CD94, CD103, CD127, CD11c, CD11b, CD16) negative, CD45 positive, CD127 positive cells.

Results: Th17 cells (CD3+CD4+IL-17+) were enriched in the joint compared to the blood of ERA patients and healthy blood (p=0.0446). Within the Th17 populations, an increase of IL-17/IFNγ double-producing cells was found in the joint compared to the blood of ERA patients. Compared to available data in other types of JIA, the number of Th17 cells was higher in ERA (median = 4.1%) than other JIA subtypes, including extended oligoarthritis (median = 1.99%). An enrichment of ILCs was observed in the joint of ERA patients (0.15-0.5%) compared to healthy blood (<0.1%) (p=0.0114). Interestingly, a positive correlation between Th17 and ILC numbers in the joint of ERA patients was demonstrated (r=0.6).

Conclusion: These data show that Th17 cells and ILCs are enriched in the joints of ERA JIA patients. Further work is warranted to explore the interplay between these two immune cell populations in the context of ERA.

Disclosure of interest: None declared.