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Abstracts

Oral Abstracts

O 01

Distinctive gene expression in patients with juvenile spondyloarthropathy is related to autoinflammatory diseases

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INTRODUCTION: Juvenile Spondyloarthropathies (jSpA) are characterized by dysregulation of the inflammatory processes and bone metabolism which may be clarified by gene expression profiles.
OBJECTIVES: To identify genes with disease-specific expression patterns of patients diagnosed with jSpA and healthy controls using microarray-based methods.
METHODOLOGY: Peripheral blood samples of 6 HLA-B27/B7, double positive" patients (OR=14.9) with new onset, untreated disease were analyzed for expression patterns that correlated with disease characteristics using Human Genome U133 PLUS 2.0 GeneChip, Affymetrix, (6x106 SNP's). For comparison, gene expression profiles were obtained from 4 healthy controls. Real-time PCR was used for confirmation of gene expression differences.
RESULTS: Statistical analysis of gene expression patterns identified 369 differentially expressed genes at statistical cutoffs fold change 1.5 ($p<0.05$, max>100). There were also 163 mRNAs with significantly increased expression, and 197 mRNAs with significantly decreased expression. The genes represented by these probe sets were enriched for functions related to inflammatory modulation, MAP kinase pathway, TGF-beta family, as well as other enzymes and receptors (myosin light chain kinase, NRLP3 (inflammasome), thrombomodulin, protein-tyrosin phosphahase, receptor type 2 (PTPRN2), TRAF1, and ZAP-70. Using network, DAVID, and GSEA analysis we discovered gene hubs among the differentially expressed genes based on correlation of expression (T-cell regulation, energy metabolism, RNA processing).
CONCLUSIONS: This study demonstrates that jSpA patients exhibit complex patterns of gene expression for functions related to inflammatory and defense response, MAP kinase and cell cycle, chromatin modulation and transcription, cell death, apoptosis, and interestingly, gene closely linked to autoinflmmatory diseases (NRLP3).
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O 02

Autoinflammatory gene polymorphisms and susceptibility to UK juvenile idiopathic arthritis: association with an exonic single nucleotide polymorphism in mevalonate kinase

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BACKGROUND: Autoinflammatory syndromes, also called hereditary periodic fever syndromes, are a heterogeneous group of diseases, unified by a common feature of cyclical episodes of unexplained inflammation and fever. Autoinflammatory syndromes have several overlapping features with JIA, especially with systemic-onset JIA. We have previously studied SNPs in 4 genes that cause autoinflammatory diseases (NLRP3, NOD2, MEFV, and PSTPIP1) and shown association with psoriatic onset JIA (Day TG et al. 2008, Arth & Rheum, 58(7), 2142-6). Here we have studied SNPs across MVK, located on chromosome 12q24, responsible for hyper-IgD syndrome (HIDS), and TNFRSF1A, located on chromosome 12p13.2, responsible for TNF receptor-associated periodic syndrome (TRAPS). In addition, we studied SNPs across NALP1, a homologue of the autoinflammatory gene NALP3. SNPs in NALP1 have recently been associated with vitiligo-associated autoimmune disease, autoimmune Addison's disease, and type 1 diabetes.
METHODS: DNA was available for 1054 UK Caucasian JIA patients. Pair-wise tagging SNPs were selected within 10kb up and down stream of each gene using an r2 cutoff ≥ 0.8 and MAF ≥ 0.05. SNP genotyping was performed using the Sequenom iPlex® MassARRAY platform according to manufacturers instructions. A 90% sample quality control rate and 90% SNP genotyping success rate was imposed on the analysis. Control samples genotype data was available from the Wellcome Trust case control consortium 2 (WTCCC2) (n=5380). Genotype and allele frequencies were compared between cases with JIA and controls using the Cochrane-Armitage trend test implemented in PLINK and allelic odds ratios (ORs) and their 95% confidence intervals (CIs) calculated.
RESULTS: This study had >80% to detect an odds ratio >1.25 for SNPs with allele frequencies >0.1. Two SNPs in the MVK gene, rs1183616 (ptrend=0.006 OR 1.17 95% CI 1.04-1.30) and rs7957619 (ptrend=0.005 OR 1.23 95% CI 1.07-1.43) are significantly associated with JIA. These two SNPs are in modest linkage disequilibrium (r2=0.36, D'=1). Logistic regression of the two SNPs, after conditioning on the most significant SNP, found that the rs1183616 SNP was no longer significant (p=0.3), suggesting that the association is a single effect driven by the rs7957619 SNP. This SNP lies within exon 3 of the MVK gene and is a Serine to Asparagine substitution at position 52. There was no significant evidence of a difference in allele frequencies between the seven ILAR subtypes for the rs7957619 SNP (p=0.32).
One SNP at the 3' end of the TNFRSF1A gene, which actually lies within the adjacent gene SLCNN1A, rs2228576, was associated with protection from JIA (ptrend=0.009 OR 0.87 95% CI 0.78-0.97). There was no significant evidence of a difference in allele frequencies between the seven ILAR subtypes (p=0.94). None of the 16 SNPs studied across the NALP1 gene were found to be associated with JIA susceptibility.
DISCUSSION: We have utilised the largest cohort of JIA cases available in Europe and identified associations between JIA and polymorphisms 3' of TNFRSF1 and within MVK. Replication of these findings in other JIA populations is required. These observations support the value of extrapolating from monogenic to complex disease phenotypes.

O 03

Clinical and microarray follow-up of SOJIA patients treated with anakinra: lessons learned over the past 7 years

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OBJECTIVE: To evaluate the response to IL-1 blockade over the past 7 years in SOJIA patients treated with anakinra at the clinical level including the durability of response, long term complications, and steroid sparing effect as well as to utilize blood gene expression profiling for insight into potential mechanisms of pathogenesis.
METHODS: Clinical/laboratory data of all children with SOJIA treated with anakinra at our institution with at least 6 months of follow-up were reviewed. Whole blood gene expression profiling (Ilumina bead chip array) were obtained in a subset of 12 patients before and after initiation of IL-1 blockade.
RESULTS: 31 SOJIA patients (18F/13M) with median disease duration of 2.6 years (range 0 days post dx-11.6yrs) and median of 3 active joints (range 0-34) at initiation of anakinra were treated with a mean dose of 2.34 mg/kg (range 1.33-5.95) with an average follow-up of 4.16 years (range 0.49-6.79)on anakinra. All children had a SOJIA signature as previously described (1)by microarray analysis. After IL-1 blockade, significant improvements were seen in rash (p=0.0008), fever ($p<0.0001$), number of active joints ($p<0.0001$), WBC ($p<0.0001$), hemoglobin (p,0.0001), platelets (p=0.0004), and ESR($p<0.0001$).
Two patients with clinical MAS at initiation of anakinra had complete resolution. Pre-anakinra 14 patients (46%)received IVMP (the primary method of steroid treatment at our institution)with only 2(7%)still receiving it 6 months post anakinra (p=0.0005).
25/31 (81%) patients met Wallace criteria for clinical remission off medications. Four children (13%) had a partial response with important clinical improvements and were able to stop or greatly wean steroids. Two children (6%) had no sustained response, one of whom took anakinra for less than 6 weeks due to painful injections.
At last clinic visit 12 patients were on anakinra monotherapy, 1 on anakinra was tolerating a prednisone wean (3mg/d), 3 were on anakinra/MTX,5 patients were on no medications. Two patients who stopped anakinra later flared with arthritis only and were controlled with etanercept. One patient developed hepatitis and had to stop anakinra. Six new onset patients and 4 polycyclic patients with new disease flares have been successfully treated with anakinra monotherapy.
Most side effects were minor although 1 patient who had just received IVMP died of complications related to sepsis. One patient continued anakinra throughout pregnancy and delivered a normal term baby.
Gene expression profiling showed a remarkably homogeneous pattern of IL-1 related gene dysregulation (1) which normalized in the most patients after anakinra. In some patients there was a time lapse between clinical response and correction of gene expression suggesting that immune alterations are not completely resolved at time of first clinical response. Most upregulated transcripts encoded innate immunity related proteins.Down regulated transcripts encoded proteins involve in cytoxic/NK cellfunction and protein synthesis. In this cohort, interferon inducible genes were upregulated especially in patient who had never received steroids and 5/7 of these showed normalization post anakinra.
CONCLUSIONS: Anakinra is safe and effective in controlling clinical disease and correcting gene expression alterations in most children with SOJIA both in combination with methotrexate and or steroids and as monotherapy. Anakinra allows significant steroid sparing, a major cause of morbidity in these patients.
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O 04

Methotrexate is protective against the new onset of uveitis under etanercept treatment. Data from the German Etanercept Registry

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INTRODUCTION: Uveitis occurs in 10 % of patients with juvenile idiopathic Arthritis (JIA). Several publications from retrospective data reviews suggest that etanercept do not decrease the occurrence of uveitis in patients with JIA. To explore this issue, we reviewed our prospectively collected data from our database regarding the occurrence of uveitis comparing two treatment arms.
METHODS: We evaluated the prevalence of Uveitis in patients of the German Etanercept and Methotrexate Registry according two different treatment arms, etanercept monotherapy, etanerecpt plus methotrexat as a combination therapy.
RESULTS: We reviewed the data of 868 patients, and selected 74 patients, who were treated only with etanercept and 246 patients, who were treated with the combination of methotrexate plus etanercept. We excluded the other patients from this analysis. The mean of disease onset was 8.46 in the monotherapy and 8.72 years in the combination therapy group. The mean disease duration was 4.66 in the monotherapy and 4.01 years in the combination group. The mean duration of the etanercept therapy was 1.4 years in the monotherapy and 1.76 years in the combination group. 7 of the 74 patients in the monotherapy group (9.5%) and 20 of the 246 patients in the combination group(8.3%) had already a uveitis flare before the initiation of etanercept. Under the etanercept therapy 4 patients evolved new onset uveitis in the etanercept group (5.4%) and 4 under the combination therapy (1.62%). The number (of new onset??) of uveitis per 100 patients year were 3.5 in the monotherapy and 0.9 in the combination group.
DISCUSSION: The combination therapy of etanercept with methotrexate seems to be protective against new onset of uveitis under etanercept therapy and decrease the number of uveitis flares at all compared to monotherapy of etanercept.

O 05

Methotrexate in children with Juvenile Localized Scleroderma: a randomized, double-blind, placebo-controlled trial

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BACKGROUND: Juvenile localized scleroderma (JLS) is a chronic progressive fibrotic process of the skin causing permanent disability and aesthetic damage. Although no universally accepted effective treatment is available, recent studies seem to support the use of methotrexate (MTX).
OBJECTIVES: We aimed to assess the safety and efficacy of methotrexate in patients with JLS.
METHODS: We performed a double-blind, randomised controlled trial. Patients with active JLS, with linear, generalized or deep subtypes, were randomly assigned to receive oral MTX, at a dose of 15 mg/m2 once a week (max 20 mg), for 12 months or until flare of the disease (MTX arm), or placebo at the same dose and timing (placebo arm). Oral prednisone (1 mg/Kg/day, max 50 mg), in a single morning dose for 3 months then tapered down until stopping in one month, was added to both groups. The randomization rate MTX/PLAC was 2:1. The extension of the skin lesions was evaluated by a computerized scoring system1 and changes were quantified by the skin score rate (SSR) (skin score at timen/ skin score at time0). Clinical examination and serial thermographies monitored the changes of active lesions2. The primary endpoint was the rate of response to treatment. Responders were defined those patients who satisfied the following 3 criteria: SSR<1; decrease of the temperature at thermography of at least 10% compared to baseline; absence of new lesions. Disease relapse was defined when was present at least one of the following: SSR>1; unchanged or increased lesion temperature; appearance of new lesions. All analyses were intention-to-treat.
RESULTS: 85 patients entered the screening phase and 70, aged 6-17 years, from 13 centres in Italy, were enrolled. 46 patients were randomized in the MTX arm and 24 in the placebo arm. Groups were homogeneous as far as clinical and immunological features, mean disease duration was 2,1 years in both groups. After an initial response in all patients, disease relapse occurred in 15 MTX patients (32,6%) and 17 placebo patients (70,8%) (p<0.005), mean SSR value decreased from 1 to 0.79 with MTX vs 1,1 with placebo. The mean target lesion temperature decreased 44% vs 12.1%. New lesions appeared in 3 MTX patients (6.5%) vs 4 on placebo (16.7%). 26 patients (56,5%) of MTX group and 11 patients of the placebo group (45,8%) presented mild side effects related to treatment. None was severe enough to stop treatment.
CONCLUSIONS: MTX is an effective and well tolerated treatment for patients with juvenile localized scleroderma.
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O 06

Authorisation of new medicines for children with rheumatic diseases in Europe

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BACKGROUND: After years of neglect children are placed at the forefront in the process of development of new medicines. In 2006 the EU adopted a Regulation (1) which requires a Paediatric Investigation Plan (PIP) that needs to be agreed at the early stage of development. Not only do new products trigger the Paediatric Regulation, but also new indications, new pharmaceutical forms or new routes of administration of already authorised medicines. The submission of an agreed PIP (or a waiver) is necessary for the validation of marketing authorisation applications for adults.
OBJECTIVE AND METHODS: To analyse the outcomes of the Paediatric Committee of the European Medicines Agency (PDCO), with focus on paediatric rheumatic (PR) indications. Discuss the scientific and regulatory challenges of development of new treatments in this field.
RESULTS: From its creation until May 2010, the PDCO reviewed 838 applications covering 1205 indications. Among them, 23 were proposing treatment for arthritis (incl. JIA), 4 for Kawasaki disease (KD), 2 for SLE, 2 for autoinflammatory diseases (AD) and 1 for dermatomyositis (DM). The PDCO adopted opinions on 17 PIPs for arthritis, 3 for KD, 1 for SLE, 2 for AD and 1 for DM. 5 applications were withdrawn during the evaluation process and the 3 were ongoing.
Several clusters of difficulties and challenges were identified in PR PIPs.
1. Terminology and classification of rheumatic diseases in children and their relationship to adult diseases. Need for better understanding of underlying biology of individual disease "subtypes" and individual patient responsiveness to treatment.
2. Feasibility of trials in different subtypes of JIA and other rare conditions in children. Agreement on suitable trial designs (e.g. active control vs. placebo, randomised withdrawal) and endpoints. Availability of children for trials.
3. Extrapolation opportunities from adult data and limitations. Clustering of study populations ("polyarticular course JIA"). Age of patients to be studied.
4. Safety issues (e.g. anti-TNFs and malignancies, B-cell depleting agents). Need for patient registries to measure the long-term risks and efficacy.
In December 2009 the European Medicines Agency convened an advisory meeting with experts from 12 European countries and the USA, to share experience with development of medicines for PR diseases and address related scientific and regulatory challenges. The presentations and the outcome of the meeting have been published on the Agency's website (2).
CONCLUSION: The Paediatric Regulation requires that the PIPs are submitted not later than upon completion of the human pharmaco-kinetic studies in adults. The development in children can be often deferred after completion of adult development. As the consequence the full impact of the new legislation on the market availability of new authorised treatments in paediatric indications is not yet measurable. However despite all the difficulties real and perceived, the development of better medicines for children, including children with rheumatic diseases, has become a reality through trials. The need for "off label" treatment, that was so typically the only option for paediatric rheumatologists and their patients, is becoming the thankfully forgotten past.
REFERENCES: 1. Regulation (EC) No 1901/2006 of The European Parliament and of the Council on medicinal products for paediatric use.
http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-1/reg_2006_1901/reg_2006_1901_en.pdf
2. http://www.ema.europa.eu/htms/human/paediatrics/workshops.htm

O 07

Functional and psychosocial outcomes 10 and more years after onset in adults with juvenile arthritis

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Some studies have shown that Juvenile arthritis (JA) is often self-limiting; about 60% of pts reach adulthood with no active sinovitis or functional limitation. However, many pts experience detrimental effects, including joint deformity and destruction, growth abnormalities and retardation and other problems, impaired psychological health or difficulty with daily living.
OBJECTIVE: To determine functional and psychosocial status in adults with JA 10 and more years after disease's onset.
PATIENTS AND METHODS: 213 adult pts with JA were included in the study (woman-72,8%) in the age from 18 to 60 years (mean 23,9+6,5 years). The mean duration of the disease at assessment was 17,4+6,8 years (range 10 to 53 years). All pts were assessed individually by interview, 97 of them were clinical examined. The functional disability and daily activities at the individual level were assessed by the Health Assessment Questionnaire (HAQ). Educational achievements, marital and employment status were recorded.
RESULTS: 43,3% of pts subjectively estimated their health status as good or very good, 39,8% - satisfactory, just 16,9% -bad. There was relationship between the health status and HAQ (R=0,6,p<0,001), the age of pts (R=0,3,p<0,001), disease duration (R=0,3,p<0,001). The mean HAQ score was 0,8. The half of pts did not have physical disability (HAQ score =0), HAQ=0,1-1,0 was in 33,5% of pts. The percentage of all pts with severe disability (HAQ score >2) was 6,6. HAQ was associated with the age of pts and disease duration (p<0,001).
The majority of pts (78,9%) were studing or working at the moment of our study. 48,8% of pts had high level of education. 6,8 % of pts didn\'t have a possibility to work due to the health-related reasons. 31,7% were married, 46 pts had children. Marital status, sexual activity and pregnancy did not depend on the health status and functional disability (HAQ).
CONCLUSIONS: Our study has shown, that the majority of adult patients suffering from JA 10 and more years had favorable functional and psychosocial outcomes. They had a high level of educational achievement, they were able to work and to conform in a daily life. But there were pts who had more serious prognosis and needed good transition from pediatric to high-quality adult rheumatology care.

O 08

Fatigue in adolescents with JIA and the impact on their quality of life

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BACKGROUND: Fatigue is present in many patients with rheumatic disorders (1), and is, therefore, a prevalent problem. It considerably affects daily functioning of afflicted patients (2). However, fatigue in pediatric and adolescent patients with juvenile idiopathic arthritis (JIA) is an understudied area (3).
OBJECTIVE: The aims of this study were (i) to examine the prevalence of fatigue in adolescents with JIA; (ii) to compare scores on different dimensions of fatigue with those of healthy controls; and (iii) to investigate the association between fatigue and quality of life (QoL).
METHODS: This cross-sectional, descriptive study is part of a larger project on transitional care in adolescents with JIA. We included 31 adolescents (8m/23f) with a median age of 16 (Q1=15.2;Q3=17.2) years. Patients could be included if they were treated for JIA in our center; aged 14–18 years; and Dutch speaking. Fatigue was measured using the Multidimensional Fatigue Inventory (MFI-20), a 20-item questionnaire, comprising 5 subscales, each with a scoring range of 4-20. MFI-20 has good psychometric properties (4). Norm data of healthy subjects were obtained from a previous study, conducted in the United States (5). Overall QoL was assessed using a Linear Analog Scale (LAS). This is a valid and reliable instrument consisting of a 10-cm, vertical, graded scale, ranging from 0 (worst imaginable QoL) to 100 (best imaginable QoL). Differences in fatigue between JIA patients and controls were expressed as mean standardized differences, and tested with a one-sample t-test. The association between fatigue and quality of life was tested with partial Spearman\'s rho correlation.
RESULTS: Fatigue, defined as a score of ≥ 15.0 on the general fatigue subscale, occurred in 19.4% of the patients. In comparison with healthy controls, the scores of JIA patients on all subscales were higher. Only for 'physical fatigue' and 'reduced activity', statistical significance was reached. Using Cohen's cut-offs (6), the differences were however small. The LAS scores for QoL ranged from 10 to 97, with a median of 74 (Q1=68.0;Q3=90.0). 'General fatigue' (rho= -0.52, p<0.01), and 'physical fatigue' (rho= -0.58, p<0.01) were strongly associated with overall QoL. 'Reduced activity' (rho= -0.47, p<0.01) was moderately associated with overall QoL.
CONCLUSIONS: One-fifth of JIA patients reported substantial fatigue. Patients reported significantly more physical fatigue and reduced activity than healthy controls, although, the difference is small. Fatigue should receive sufficient attention by healthcare professionals, because it impacts patients' QoL.
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O 09

Canakinumab provides rapid response and sustained remission in children across different disease severity phenotypes of cryopyrin associated periodic syndrome (CAPS)

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BACKGROUND: Canakinumab provides sustained interleukin 1-beta (IL-1β) blockade and is effective in the treatment of CAPS (comprising of familial cold auto-inflammatory syndrome [FCAS], Muckle-Wells syndrome [MWS], chronic infantile neurologic, cutaneous and articular syndrome [CINCA]/neonatal-onset multisystem inflammatory disease [NOMID]).
OBJECTIVES: To evaluate long-term safety, tolerability, and efficacy of canakinumab in pediatric CAPS patients.
METHODS: In this ongoing, open-label, single-treatment arm study, pediatric patients (n=19; 5–17 years) were canakinumab-naïve (n=11) or rolled-over (n=8) from earlier conducted Phase II/III studies. Patients received canakinumab 150 mg s.c. or 2 mg/kg s.c. (≤40 kg) every 8 weeks. Complete response was assessed for canakinumab naïve patients, while roll-over patients entered the study allowing continuous treatment every 8 weeks. In case of incomplete response patients received an additional dose of canakinumab 300 mg s.c. or 4 mg/kg s.c. (≤40 kg). Results of an interim analysis are reported here.
RESULTS: Of 19 patients (11 children; 8 adolescents [≥12 years]), 2 were diagnosed with FCAS, 13 with MWS, 3 with MWS/NOMID overlap and 1 discontinued as protocol violator (final diagnosis cold urticaria not related to CAPS). Complete response was achieved in most (n=9, 81.8%) of canakinumab-naïve patients within 7 days. The median duration of exposure to study drug was 86 (29–176) days at the data cut off for this interim analysis. Majority of canakinumab treated pediatric patients were relapse free (11 out of 18), 3 MWS patients experienced one relapse, 3 had missing relapse assessments and 1 MWS/NOMID patient did not achieve complete response and dose was up-titrated. 7 patients (36.8%) received at least one protocol defined dose adjustment (first dose doubled) or at least one frequency adjustment. For canakinumab-naïve patients median CRP and SAA reached normal levels within 7 days (1.3 and 3.3 mg/L) and were maintained at normal levels (<10 mg/L) during the study (both in naïve and in roll-over patients). The most frequent adverse events (AEs) were headache, joint sprain and pyrexia. 2 serious AEs were reported (intra-abdominal abscess and appendicitis) in one child (both resolved during the study). Most patients (94.7%) had no injection site reactions. No anti-canakinumab antibodies were detected.
CONCLUSION: Canakinumab every 8 weeks induced rapid and sustained clinical and biochemical remission in pediatric patients across all severity of CAPS phenotypes, and was well tolerated.

O 10

Long term effect of adalimumab in the treatment of Juvenile Idiopathic Arthritis and associated Uveitis

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AIMS: To investigate the long term effect of adalimumab, a tumour necrosis factor alpha antagonist, in the treatment of juvenile idiopathic arthritis (JIA) and associated uveitis.
PATIENTS AND METHODS: Adalimumab was initiated in 94 JIA-patients because of active arthritis and/or active associating uveitis. In 18 patients the therapy

was finished shortly because of inefficacy or side effects. In 49 JIA patients with uveitis the duration of treatment was mean 24, 4 months and in those 27 without uveitis mean 14, 6 months. The activity of uveitis was evaluated at the beginning of the Adalimumab treatment and at the end of the study using the SUN criteria and clinical evaluation. The activity of arthritis was examined by evaluating the number of swollen or active joints at the onset of the Adalimumab and at end of the study.
RESULTS: At the end of the study uveitis was in good clinical control in two thirds of the patients: 33% did not need any local treatment for uveitis and 35% used only 1-2 corticosteroid drops a day. One third of the 49 patients had active uveitis and used ≥ 3 corticosteroid drops a day. According to SUN criteria the response to Adalimumab treatment was good in 29% and worse only in 14% of uveitis patients. In this group of JIA patients the activity of arthritis diminished from 69% to 27% of patients and arthritis was in remission with medication in 73% of patients.
Remission of arthritis with medication was reached in 41% of JIA patients without uveitis and the number of active joints diminished from 93% to 59% of patients.
Systemic corticosteroid treatment could be tapered in 22% of uveitis patients and in 11% of those without uveitis (P=0.222). Most of the patients had received Methotrexate or other immunosuppressive therapy and/or other biological drugs before initiating Adalimumab.
CONCLUSION: Adalimumab is a valuable option in the treatment of refractory JIA and associated uveitis. The arthritis in JIA patients without uveitis seems to be more often chronic polyarthritis and more refractory to treatment than in those with uveitis.

O 11

10 years experience in the German JIA Etanercept Registry: lessons from changing patient populations

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BACKGROUND: For 10 years treatment of JIA with Etanercept has become a valuable option changing outcome perspectives for patients with previously refractory arthritis.
OBJECTIVES AND METHODS: To report on a changing population of JIA patients documented in the German Registry with analysis of pre-treatment, concomitant treatment and disease activity parameters. Efficacy was assessed using the PedACR30/50 and 70 criteria and the proposed criteria for inactive disease and remission on medication. Safety assessments were based on adverse events reports.
RESULTS: Since 2000 a cohort of 1260 JIA patients have been enrolled in the German JIA Etanercept registry. The recruiting rate increased from 88 patients in the first year to a maximum of 174 patients in 2007. At start of the registry 26% of patients belong to the soJIA category, this quote decreased to 2 % while the quote of ERA-JIA patients increased from 2% to 17%. While initially patients have been pretreated with numerous antirheumatic agents including cytotoxic agents pretreatment markedly decreased from a mean of 3.4 (up to 9 DMARDs in a single patient) to 1.3 DMARDs/patient. There was a marked reduction of concomitant treatment as well. Concomitant treatment initially consisted of corticosteroids in 83%, methotrexate in 95% and other DMARDs in 45% of patients (up to 3 in a single patient) while in patients starting treatment in 2007 to 2009 these numbers decreased to 31%, 61% and 14%, respectively. Moreover, the disease duration before treatment decreased from 6.1 (mean) to 3.4 years (median 4.5 to 2.3 years). While initially only 17% of patients received etaneercept during the first 2 years of theoir disease, this quoat oincreased to over 40% in the recent years.
The number of patients reaching a PedACR70 response after the first 12 months of treatment increased from 57% to 74% of patients. Inactive disease within one year was documented initially in 24% of patients while this rate increased to 54%. Furthermore, the number of adverse events in the first year of treatment (initially 0.37/pat.) decreased to about 0.2/patient and the rate of serious adverse events decreased from 0.13/pat to 0.02/pat.
CONCLUSION: These data indicate that patients starting etanercept in the recent years were treated earlier, received less pre-treatment, received less concomitant treatment with corticosteroids and DMARDs but in contrast had a better outcome with regard to the number of patients reaching a PedACR70 and "inactive disease" after 1 year of treatment. They also experienced less adverse events and less serious adverse events. During a 10 year period there were marked changes in characteristics of patients in whom etanercept treatment has been started and treatment led into an improved outcome due to a an earlier treatment and better selection of patients.

O 12

Outcome of Systemic Juvenile Idiopathic Arthritis: a comparison between the nineties and the noughties

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BACKGROUND: The treatment of JIA has changed in the last decades particularly with the addition of more effective therapies (including biologics) around the year 2000. However, a significant improvement in the outcome of patients with Systemic JIA (SJIA) is still to be demonstrated.
OBJECTIVES: To compare treatment modalities and the outcome of patients with SJIA followed in 2 different decades.
METHODS: The prospectively built patient database of our service was used to retrieve relevant data. Inclusion criteria: patients with SJIA first seen at our clinic during disease onset (first 6 months of the disease course) and followed regularly thereafter. Patients with follow-up duration < 2 years or with incomplete records were excluded. Patients were divided into "old" (disease onset before year 1998) and "new" (disease onset on or after year 2000). Selected observation points were disease onset, and subsequent visits with annual intervals up to year 5 after disease onset. Analysis of observations from old patients was limited to visits occurring prior to year 2000. Variables assessed in each observation were number of active joints, number of joints with limitation of motion, ESR, presence of systemic activity (rash, fever, and/or organomegaly), inactive disease, remission (as per Wallace et al. criteria, adapted for visits occurring before 2004), radiographic damage (bone erosions/fusion), use of corticosteroids, MTX, biologics, and disease course pattern (monocyclic, polycyclic, persistent). Both groups were compared using Mann-Whitney test or Chi square as appropriate.
RESULTS: 80 patients were included (34 old, 46 new; 49 girls; age at onset 4.5 years). Patients were followed during the period December 1992-December 2009. Median follow-up: 55 months. Baseline variables were not different. Biologics were used in 50 % of new patients (anti-TNF agents in 23, abatacept in 2, anakinra in 2 patients each) and in none of the old patients. MTX was used more frequently in new patients both at 1 year (91 % vs 62 %) and 2 years (87 % vs 65 %) after disease onset; corticosteroids were used more frequently in old patients. New patients showed a significantly lower frequency of radiographic damage (4% vs 24 % at 1 year, 9% vs 26 % at 2 years, 14% vs 42% at 3 years, 22% vs 44% at 4 years, 29% vs 58% at 5 years after disease onset). Disease activity outcome measures (including inactive disease and remission rates) and disease course pattern were similar in both groups (monocyclic 40% vs 50%, polycyclic 27% vs 26%, and persistent 40% vs 50% in new and old patients respectively).
Conclusions: patients with disease onset in the 2000s were exposed to a more intensive and early therapy (with MTX and biologics) than patients from the 90s. A probable consequence, radiographic articular damage is less prevalent in the former group. Disease course pattern does not seem to be altered by these new treatments. Functional capacity and quality of life assessments should be assessed in future studies. It is expected that IL-1 and IL-6 inhibiting strategies may have a deeper impact in the outcome of patients with SJIA.
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O 13

Tocilizumab Is efficacious in patients with Systemic Juvenile Idiopathic Arthritis (sJIA) across baseline disease characteristics and prior/baseline treatments: 12-week data from the Phase 3 TENDER Trial

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BACKGROUND: Systemic juvenile idiopathic arthritis (sJIA) is a debilitating disease characterised by arthritis and systemic and/or laboratory features such as intermittent fever, rash, anaemia, thrombocytosis and elevated levels of acute phase proteins such as C-reactive protein (CRP). Current treatment options for sJIA commonly include non-steroidal anti-inflammatory drugs (NSAIDs), oral corticosteroids (CS) and methotrexate (MTX). Interleukin-6 (IL-6) has been implicated in sJIA pathogenesis, and tocilizumab (TCZ), an IL-6 receptor inhibitor, has been shown to be effective in a Japanese, phase 3, placebo-controlled trial in patients with sJIA refractory to conventional treatment.
OBJECTIVES: To evaluate response to TCZ in patients with sJIA by baseline disease characteristics and prior or baseline treatments in the 12-week, double-blind, placebo-controlled part of the global phase 3 TENDER trial.
METHODS: Patients with active sJIA (aged 2-17 years, disease duration of ≥6

months, and inadequate response to prior NSAIDs and CS) were randomly assigned (2:1) to receive TCZ every 2 weeks (8 mg/kg for patients ≥30 kg body weight; 12 mg/kg for patients <30 kg) or placebo (control). Stable doses of NSAIDs and MTX were continued, and CS tapering was permitted at weeks 6 and 8 for patients who met criteria: JIA ACR70 response and erythrocyte sedimentation rate <20 mm/h plus absence of fever. Patients who qualified for rescue therapy received standard of care and were offered open-label TCZ and considered non-responders. The post hoc analysis presented herein is of the primary end point (proportion of patients with JIA ACR30 response plus absence of fever) and the secondary end point (JIA ACR70 by baseline disease characteristics and prior/baseline treatments [ITT analysis]).
RESULTS: The ITT population consisted of 112 patients (37 controls, 75 TCZ). Baseline characteristics were similar between the groups. At week 12, significantly more TCZ patients experienced JIA ACR30 plus absence of fever and JIA ACR70 response compared with controls (85% vs 24% and 71% vs 8%, respectively; p<.0001, all comparisons). Patients were grouped by baseline disease characteristics including age, disease duration, number of active joints, fever status, CRP level, and platelet count; by oral CS dose and MTX use at baseline; and by previous biological treatment (anakinra, TNF-α inhibitors). In each of the evaluated subgroups, at wk 12, considerable proportions of TCZ patients achieved JIA ACR30 plus absence of fever or JIA ACR70 response (**Table**). The proportions of patients achieving JIA ACR30 response plus absence of fever or JIA ACR70 response were generally independent of baseline characteristics and previous or concomitant treatments (Table).
CONCLUSIONS: Our findings demonstrate that TCZ is well tolerated and effective in patients with sJIA across multiple baseline disease characteristics and prior/concomitant treatments including patients with longer disease duration or very active disease (e.g. fever, higher number of active joints, higher CRP levels) and patients who have been previously treated with biologic therapy.

O 14

Efficacy and safety of tocilizumab in patients with Systemic Juvenile Idiopathic Arthritis (sJIA): 12-week data from the Phase 3 TENDER trial

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BACKGROUND: Treatment options for sJIA, a disease associated with substantial morbidity and mortality, are limited. Excessive IL-6 production has been implicated in several manifestations of sJIA. Tocilizumab (TCZ), an IL-6 receptor inhibitor, improved arthritis and systemic symptoms of sJIA in a Japanese, placebo-controlled, withdrawal-design phase 3 trial in patients with sJIA refractory to conventional treatment.
OBJECTIVE: To determine the efficacy and safety of TCZ in the 12-wk, double-blind, placebo-controlled, parallel-group part of the global 3-part, 5-yr, phase 3, multicentre study in patients with active sJIA.
METHODS: Patients aged 2–17 yrs with active sJIA for ≥6 months and inadequate response to systemic corticosteroids (CS) and NSAIDs were randomised 2:1 to TCZ (8 mg/kg if body weight ≥30 kg; 12 mg/kg if <30 kg) or placebo (control) administered every 2 wks for 12 wks. CS tapering was permitted at wks 6 and 8 in patients with JIA ACR70 response, erythrocyte sedimentation rate <20 mm/h and no fever. Stable doses of NSAIDs and methotrexate were continued and could be altered or discontinued only for safety reasons. Patients who qualified for escape received standard-of-care rescue therapy; they were offered open-label TCZ every 2 wks and considered non-responders. The primary efficacy end point was proportion of patients attaining JIA ACR30 response at wk 12 and no fever (no temperature ≥37.5°C in preceding 7 days).
RESULTS: The intent-to-treat population comprised 112 patients. Baseline characteristics were similar between arms **(Table)**. By wk 12, 1 control (3%) and 2 TCZ patients (3%) withdrew, and more control than TCZ patients required rescue therapy (54% vs 3%). Significantly more TCZ than control patients (85.3% [64/75] vs 24.3% [9/37]; p<0.0001) attained the primary efficacy end point. JIA ACR70 and ACR90 responses were significantly (p<0.0001) greater in TCZ than control patients (Table). Among patients with fever, rash or anaemia at baseline, significantly more TCZ than control patients were afebrile, had no rash or had normal haemoglobin levels, respectively, at wk 12 (p≤0.0008) (Table). Mean percentage decrease from baseline to wk 12 in the number of joints with active arthritis was significantly greater in TCZ than control patients (70.6% vs 37.2%; p=0.0012). Moreover, a significantly greater mean decrease from baseline to wk 12 in CHAQ-DI score occurred in TCZ than control patients (0.9 vs 0.2; p=0.0029). Furthermore, of patients who were receiving oral CS at baseline, a significantly greater proportion of TCZ than control patients (24.3% [17/70] vs 3.2% [1/31]; p=0.028) achieved JIA ACR70 response at wk 6 or 8, allowing them to reduce their CS dose by ≥20% without subsequent JIA ACR30 flare or occurrence of systemic symptoms. Four serious adverse events were reported in 3 patients, all in the TCZ group (angio-oedema and urticaria in 1 patient, bacterial arthritis and varicella infection); all resolved without sequelae.
CONCLUSIONS: Results from this first global phase 3 study demonstrate that TCZ is highly effective and generally well tolerated in the short-term (12-wk) treatment of patients with sJIA.

O 15

A novel fully automated system for the quantification of synovial volume using MRI

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BACKGROUND: The goal of new treatment is to obtain total suppression of joint inflammation to prevent erosive damage; therefore future outcome measures in both clinical trials and clinical practice, should comprise sensitive and robust measures of inflammation. Synovial volume (SV) measured by MRI, has proven useful in assessing disease activity, response to therapy and in predicting progressive joint destruction in RA. However the currently available tools for the assessment of SV are time-consuming (manual outlining of the inflamed membrane), or showed poor reproducibility and accuracy (semi-automatic methods).
OBJECTIVES: To develop a fully automated tool for the MRI SV measurement, and to assess its validity and reproducibility in patients with JIA.
METHODS: An algorithmic approach, based on supervised voxel classification, for fully automatic estimation of SV in a 3D MRI was developed. 58 wrist MRI of JIA patients were included in the analysis. A subset of 15 studies has been manually annotated; these annotations were used to train the SV estimation system, as well as for providing the reference measure to assess its precision and accuracy. 18 patients performed a follow-up MRI after 1 year.
RESULTS: The agreement between the automated estimation of the SV and the manual measurements was excellent (ICC 0.93 (95% CI: 0.79-0.98)). Significantly higher SV values were found in patients with higher wrist swelling (2.45=4.28, p<0.0005) and pain (2.26=3.92, p<0.0002) scores. SV correlated with: OMERACT MRI synovitis score (r=0.39, p<0.005), physician's global assessment of overall disease activity r=0.42, p<0.002), number of swollen joints (r=0.36, p<0.01), the Juvenile Arthritis Disease Activity Score for 71 joints (JADAS-71)(r=0.35, p<0.01), ESR (r=0.30, p<0.05). A significant difference in SV values has been found between baseline and follow-up (3.61 to 1.61; p<0.002; standardized response mean (SRM)=1.1)in the TNF inhibitor therapy group. Radiographic damage progression was strongly correlated with the baseline SV (r=-0.82, p<0.02).
CONCLUSIONS: The proposed fully automated tool allows fast and objective measurement of SV, which represents a promising imaging biomarker of disease activity in JIA; SV, in fact, has been shown to correlate well with other measures of acute inflammation, respond to treatment and to predict erosive progression.
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O 16

Functional splint treatment can reduce mandibular asymmetry caused by unilateral temporomandibular arthritis in JIA patients

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BACKGROUND: In JIA patients with unilateral temporomandibular joint (TMJ) arthritis asymmetric mandibular growth is often observed which can lead to unstable occlusion, reduced TMJ and masticatory function with an asymmetric loading, TMJ pain and a compromised aesthetic appearance.
OBJECTIVES: To evaluate the effects of a full-time worn orthopedic appliance with the aim to reduce asymmetric mandibular growth.
METHODS: In a cohort of JIA patients with unilateral TMJ arthritis 22 out of 42 patients met the criteria for inclusion. The 22 patients included (mean age 7.5 years, range: 3.8-13.8 years) were diagnosed with unilateral TMJ arthritis and a distinct asymmetric mandible. All of these patients received treatment with a distraction splint (mean treatment time 5.1 years, range: 1.2-11.1 years). This is an acrylic splint covering the occlusal surfaces of the teeth in the lower dental arch where the posterior height of the splint is gradually increased every 8th-10th week in the arthritic side in order to increase the posterior face height in the affected side by a pivot effect on the TMJ and to normalize the dentoalveolar vertical development. Orthopantomograms were taken prior and post treatment. At both of these time-points the ratio between the healthy and the affected side of the mandible was evaluated related to differences in condylar height and the vertical ramus length.
RESULTS: The mean ratio between the affected and the healthy side decreased from 1.20 to 1.10 in terms of condylar height (std.dev: 0.22) and from 1.12 to 1.06 in terms of ramus length (std.dev: 0.09). Functional treatment significantly

improved mandibular appearance because significantly reduced ratios were seen in both variables evaluated after treatment with the distraction splint ($p<0.05$).
CONCLUSIONS: Distraction splint treatment can reduce mandibular asymmetry in JIA patients with unilateral TMJ arthritis and support mandibular growth and vertical development in the affected side with TMJ arthritis.

O 17
Ongoing disease-activity in a majority of children in a Nordic Juvenile Idiopathic Arthritis (JIA) cohort

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BACKGROUND: Juvenile idiopathic arthritis (JIA) is an umbrella term for chronic childhood arthritides, and the disease often extends into adulthood. Recent studies on long-term outcome have shown a higher proportion of children with active disease when followed over time, than previous cross-sectional studies.
OBJECTIVES: The aim of the study was to describe disease characteristics and remission status during the first eight years after disease onset in a cohort of Nordic children with JIA in a population-based setting.
MATERIALS AND METHODS: Consecutive cases of JIA from defined geographical areas of Denmark, Finland, Sweden and Norway with disease onset in 1997 to 2000 were included. The incidence of JIA in the study area in 1997-98 was 15 per 100 000. The study aimed to be as close to population-based as possible, as centres participated only if they were able to include all children diagnosed with JIA in their catchment area. JIA subtypes were determined according to the ILAR criteria. Clinical data and disease activity were registered at regular follow-up visits.
RESULTS: Of 500 included children, 440 (88%) had a follow-up visit seven years or more after disease onset (median 96 months, range 84-147). The number of visits varied between 2- 10 (median 5). Among the 500 included children, 66% were female, median age at onset was 6 years and 52% were oligoarticular. Uveitis developed in 88 (20%). Synthetic and/or biologic DMARDs were reportedly used in 254 (58%) children during the disease course. At the last follow-up, 42% of the children were in remission off medication, 9% were in remission on medication and 49% were not in remission.
CONCLUSIONS: During the disease course the majority were treated with DMARDs including biologic agents. Importantly, a majority of the children were not in remission or still using regular medication for JIA at their last follow-up, indicating significant ongoing disease activity seven or more years after onset in this prospective Nordic cohort study.

O 18
Maternal microchimerism in muscle biopsies from children with Juvenile Dermatomyositis

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BACKGROUND: Recent advances in molecular techniques have revealed bi-directional transfer of cells between mother and child during pregnancy, and the presence of a mother's cells in her child has been termed maternal microchimerism (MMc). Haematopoietic and tissue-specific maternal cells have been identified, raising the possibility that MMc could be effector cells of the immune system, a target of autoimmunity or alternatively, could contribute to tissue repair. Previous studies on JDM have suggested that the frequency of MMc is increased in JDM tissue.
OBJECTIVE: The aim of this study was to determine whether maternal (female) nuclei could be detected in frozen muscle sections from 7 boys (age range 3-13 years) with JDM participating in the UK and Ireland Juvenile Dermatomyositis National Registry & Repository and 2 control muscle sections (age range 12-17).
METHODS: Fluorescent-labelled probes were used to detect X (Cy3) and Y (FITC) chromosomes by fluorescent in situ hybridization (FISH) on 7μM muscle sections. At least 500 nuclei from each section underwent confocal imaging through the nuclei to avoid counting nuclei that are products of non-disjunction,
Results: The frequency of MMc was higher in JDM muscle (0.42-0.99%) than in controls (0.01-0.12%).
CONCLUSIONS: These preliminary data confirm an increased frequency of MMc in male JDM tissue. FISH with concomitant immunohistochemistry studies are ongoing to determine whether these nuclei are heamatopoietic or tissue specific in origin. Understanding the role of MMc in JDM may provide insights for future therapy.

O 19
A survey of current practice in the management of Juvenile Dermatomyositis in the UK and Ireland

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BACKGROUND: Juvenile Dermatomyositis (JDM) is the most common childhood idiopathic inflammatory myopathy. There is limited published evidence regarding the current assessment and management of JDM.
OBJECTIVES: To identify current practice in the management of JDM in centres throughout the UK and Ireland. It is anticipated that the results of this survey will be used to develop consensus treatment guidelines and inform the development of future therapeutic studies.
METHODS: 16 Paediatric Rheumatology centres were contacted by email to arrange a time to complete a simple telephone questionnaire. All results were anonymised.
RESULTS: 15/16 centres responded. All centres routinely used MRI to investigate JDM. All used similar blood tests with slight variation in muscle enzymes measured (depending on laboratory availability). Only 2/15 routinely use muscle biopsy and 1/15 EMG. All used the Childhood Myositis Assessment Scale (CMAS) to assess muscle strength.
To assess response to treatment 13/15 measured muscle enzymes, 13/15 Childhood Health Assessment Questionnaire (CHAQ), 11/15 Physicians Global Assessment (PGA) and 7/15 MRI. No centre routinely used an objective tool to measure assess skin severity.
As first line treatment for a new patient with JDM and mild or absent weakness 13/15 centres use a combination of methotrexate and steroids, 1 centre would use steroids alone and 1 would use only methotrexate. As first line treatment for a patient with JDM & moderate weakness all centres use methotrexate and steroids. 11/15 use IV methylprednisolone; 12/15 use subcutaneous methotrexate. With severe weakness, ulceration or systemic disease all centres use IV methylprednisolone as first line treatment, 13/15 also use methotrexate. 9/15 would routinely use or consider cyclophosphamide including both centres that would not use methotrexate.
There was widespread variation in the choice of second and third line agents across all categories. Drugs used included IVIG, hydroxychloroquine, anti-TNF agents, rituximab, ciclosporin, azathiaprine, cyclophosphamide and MMF.
All units had access to appropriate nursing and allied health professional support other than 1 centre which lacked easy access to occupational therapy.
CONCLUSIONS: Our study shows emerging consensus throughout the UK & Ireland regarding the first line management of JDM. Steroids and methotrexate form the basis of treatment in all centres. There is variation in practice when choosing therapeutic agents for patients with an inadequate response to first line therapy, reflecting the lack of an evidence base for their use. Future research should be directed at this area.

O 20
The enlarging clinical spectrum of mevalonate kinase deficiency

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OBJECTIVE: To describe the spectrum of clinical and genetic manifestations of mevalonate kinase (MVK) deficiency (MKD)
METHODS: A retrospective French and Belgian study of patients identified by MVK gene mutations.
RESULTS: Fifty patients belonging to 38 different families were identified, including 1 asymptomatic patient. The first symptoms occurred within the first 6 months of life in 28 patients (62%) and before the age of 5 years in 48/50 (96%). Symptoms consisted of febrile diarrhea and /or rash in 23/35 (66%) patients. Febrile attacks were mainly associated with lymphadenopathy (71%), diarrhea (69%), arthralgia (67%), skin lesions (67%), abdominal pain (63%), and splenomegaly (63%). Beside these typical febrile attacks, inflammatory bowel disease, erosive polyarthritis, Sjogren syndrome and other persistent neurological, renal, pulmonary, endocrine, cutaneous, hematological and ocular symptoms occurred in 27 children or adults. Recurrent and/or severe infections, and hypogammaglobulinemia were observed in 13 and 3 patients respectively. Nineteen genomic mutations were identified, most frequently the V377I mutation (26/38 families). Three patients died from MKD related causes. Among 32 symptomatic alive patients followed up for more than 5 years, 17 patients continued to disclose a high disease activity, while the remaining 15 patients became asymptomatic or had mild disease activity. Anti-interleukin-1 (IL1) antagonists were the most effective biological agents tested, allowing complete or partial remission in 10/11 patients.
CONCLUSION: The present study suggests that MKD is at the interface between autoinflammatory syndrome, multisystemic inflammatory disorder and possibly immunodeficiency. A long-lasting multiorgan involvement was evidenced in a subset of patients.

O 21

The Spectrum of Pediatric Sarcoidosis: an immunohistochemical study of granulomas

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BACKGROUND: Pediatric sarcoidosis (PS) is a granulomatous inflammatory disorder comprising different entities including pediatric granulomatous arthritis (PGA or Blau syndrome/EOS), panniculitis with systemic granulomatosis (PSG) and adult type pediatric sarcoidosis. PGA is an auto-inflammatory disease characterized by a triad of granulomatous uveitis, arthritis and dermatitis. It is caused by mutations in the nucleotide-binding oligomerisation domain (NOD/NACHT) of the NOD2 protein expressed in pathogen sensing cells such as macrophages, neutrophils, dendritic cells and Paneth cells. (1-5)
OBJECTIVES: The relation between NOD2 mutations and granuloma formation is unknown. To help elucidate pathogenic pathways, we compared the cellular composition and cytokine expression in the first immunohistochemical study of mutation proven affected tissues.
METHODS: Biopsies were available from 11 cases of PS: 5 PGA patients, including 1 with the Blau syndrome, 4 PSG and 2 ATPS patients. Granulomas were studied with hematoxylin & eosin (H&E) and immunohistochemically (IHC) stained paraffin and cryostat sections. MoAbs targeting leukocyte markers (CD4, CD8, CD20, CD68, HLA-DR, IL23R), inflammatory cytokines and chemokines (IL6, IL10, IL12, IL17, IL23, IFNγ, TGFβ, TNF-α) and apoptosis related proteins (Bcl2, Fas, FasL, actCasp3) were used.
RESULTS: Large granuloma complexes with a prominent lymphocytic corona consisting mainly of CD4+T-cells were typically seen in PGA. Microgranulomas and separated granulomas with a looser lymphocyte border consisting mainly of CD8+ T-cells were seen in PSG. HLA-DR expression in lymphocytes was intense in granulomas from all diagnoses. We found substantial expression of IL6, IL17 and IL23 in the granulomas together with IL23R+ T-lymphocytes scattered in the surrounding tissue suggesting involvement of the Th17 axis in PS, particularly in PGA. Emperipolesis of CD4+ T-cells in multinucleated giant cells (MGCs) was seen in NOD2+ PGA; subsequent MGC death was associated with Fas/FasL expression but not with activated caspase 3 staining.
CONCLUSIONS: Our findings suggest that the Th17 axis may be relevant in the pathogenesis of granuloma formation and persistence in PGA. Emperipolesis of CD4+ T-lymphocytes in MGCs seems to be a morphological feature characteristic for PGA granulomas.
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FIGURE LEGEND: Emperipolesis of lymphocytes in MGCs in a PGA patient. A) H&E staining: emperipoletic vacuoles containing T-lymphocytes in the MGC border and microvesicular degeneration in the MGC centre can be distinguished morphologically. Ingested T-lymphocytes seem to be transported to the MGC centre where they are destroyed. This process might produce the substrate for refractive Schaumann body formation. B) IHC staining for CD4: CD4+ T-lymphocytes that infiltrate the granulomas are ingested by MGCs that show weak CD4 positivity as well.

O 22

Padua-J3S: a preliminary disease severity score for Juvenile Systemic Sclerosis

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BACKGROUND: Disease severity scores for adult patients with systemic sclerosis (SSc) are not applicable in pediatric patients because of clinical and auxological differences and different approaches for the evaluation of organ function.
OBJECTIVES: To develop a preliminary disease severity score for Juvenile Systemic Sclerosis (Padua-J3S score) and compare it with the Medsger score1, which is the most used in adult population
METHODS: The study was conducted following an evidence-based and consensus-based procedure, which included four phases: 1. Prospective data collection of demographic, clinical, laboratory and treatment characteristics of patients with JSS, followed for at least 4 years or until death. 2. Blinded evaluation of the disease profiles of the enrolled patients by three JSS experts using Delphi technique. Patients were classified as having mild, moderate or aggressive course. If consensus for a particular patient was not achieved, the patient was discussed by the whole group and a second vote was taken. If consensus was still not attained, the patient profile was declared indefinable. Patient profiles for which physician consensus was achieved were used as "gold standard" for the following phase 4. 3. Definition of a pediatric severity score according to adult existing scores and clinical evidence-based experience with pediatric patients. The Padua-J3S score included 9 organ systems (general, peripheral vascular, skin, joint/tendon, muscle, gastrointestinal, respiratory, cardiac and renal) and 0 to 4 severity levels. Conversely from the Medsger score1, a "coefficient of severity", to weight specific organs involvement was introduced. 4.The ability of the two candidate severity scores, Medsger and Padia-J3S, to classify individual patients as having improvement or worsening of the disease, was compared with gold standard profiles in order to define the severity score with the best performance in terms of construct validity and responsiveness to clinical change through the Standardized Response Mean (SRM).
RESULTS: Forty-two patients entered the study. Validation analysis was conducted on 35 patients, which were classified as having an aggressive (8), moderate (10) and mild (17) course. Seven patients' courses were indefinable. The Spearman\'s rank correlation coefficient (Rho) were high in both scores (0.80 and 0.86, $p<0.001$). The comparison histogram showed a lower dispersion of Medsger score with a better distribution of patients evaluated with the Padua-J3S score. The SRM of the Padua-J3S score was significantly higher than the Medsger score, showing a better performance particularly in patients with moderate (0.89 vs 0.52) and aggressive course (0.82 vs 0.75).
CONCLUSION: The Padua-J3S score is a valid instrument for assessment of disease severity in JSS. Once validated in different cohorts of patients, it may help standardize the conduct of clinical research, outcome studies and therapeutic trials.
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O 23

Longitudinal study on growth failure and height deflection in Juvenile Systemic Lupus Erythematosus (JSLE): the result of a prospective multicentre PRINTO study

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OBJECTIVE: The goal of the study was to obtain longitudinal data on growth in a large-scale, multi-national cohort of patients with JSLE followed for 26 months.
MATERIALS AND METHODS: This prospective, multi-centric study on JSLE was carried out in 39 countries from Northern and Southern Europe, Latin America, US and Asia between 2001 and 2004. Patients seen at the participating centers with diagnosis of JSLE, at active phase, and age younger than 18 years at enrollment were included.
RESULTS: Data was collected from 557 patients with JSLE. There was a significant reduction in parent-adjusted height z score with time in females and males ($p<0.0001$) with a significant gender difference ($p<0.0001$), male height being most affected. Median BMI z score peaked at 6 months and was still significantly above baseline after 26 months ($p<0.01$) with no gender difference. Standardized height reduction was inversely related to age at disease onset in females, especially pronounced at onset age <8 years. Females with onset age <12 years had a median parent-adjusted height z score of -0.87 with no catch-up growth. At the end of the study, growth failure was seen in 14.7% of the females and 24.5% of the males. Height deflection (less than-0.25/year) was found in 20.7% of the females and 45.5% of the males.
CONCLUSIONS: The longitudinal effect on height is modest in JSLE females with age at onset ≥12 years. In spite of all our knowledge and careful treatment, females <12 years at onset and males are still at risk of experiencing a considerable height loss during the course of the disease.

O 24

Impaired vasculogenic function of endothelial progenitor cells in children with primary systemic vasculitis

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BACKGROUND: Primary systemic vasculitis (PSV) is characterized by inflammation of blood vessels, paralleled by the detachment of necrotic endothelial cells. The repair of such endothelial injury is crucial for the maintenance of cardiovascular health. Bone marrow-derived endothelial progenitor cells (EPCs) are thought to play a pivotal role in the regeneration of damaged endothelium(1), and are known to influence the prognosis of cardiovascular disease in adults. We previously reported that EPC numbers are increased in the peripheral blood of children with active PSV, perhaps indicative of an attempted vasculogenic repair response (2). The functionality of these increased EPCs in PSV remains unknown, however.
OBJECTIVE: To investigate the vasculogenic function of EPCs in children with PSV.
METHODS: 16 children (9 males) of, median age 11.6 years (5 – 16.5) with PSV at various stages of disease activity were studied. Disease activity was measured using a modified Birmingham Vasculitis Activity Score (BVAS). PSV was classified as: polyarteritis nodosa (n=5); Wegener's granulomatosis (n=6); Churg Strauss Syndrome (n=1); Kawasaki disease (n=1); Behcet's disease (n=1) and unclassified (but biopsy proven) vasculitis (n=2). 5 healthy paediatric controls were also studied, median age 4 years (3.6 – 10). Peripheral blood-derived mononuclear cells (PBMCs) were cultured in angiogenic medium. The endothelial-like phenotype was confirmed, and the colony forming unit (CFU) capacity in tissue culture monolayers was determined. Vasculogenic function of EPCs was further quantified by their potential to form clusters in matrigel, and by their ability to incorporate into human umbilical endothelial cell (HUVEC) vascular structures in matrigel. All data were expressed as median and range unless otherwise stated, and data were compared between groups using the Mann-Whitney U test.
RESULTS: Compared to healthy child controls EPC-colony forming units (CFU) were significantly reduced in children with active PSV (BVAS 4/63; range 2-23/63), p= 0.03; but not in patients with inactive disease (BVAS 0/63), p=0.31. The number of EPC incorporated into the tubular network formed by HUVEC was reduced in children with active vasculitis (p=0.02), versus healthy child controls. No such differences were observed in patients with inactive disease (p=0.06). There was a similar but non significant trend for the potential to form matrigel clusters in both vasculitis groups compared with healthy controls.
CONCLUSIONS: Vasculogenic function of EPCs is impaired in children with active systemic vasculitis, despite increased EPC numbers in peripheral blood. Thus the pathogenesis of vasculitis involves severe endothelial injury and impaired repair response from EPCs. This unfavourable balance is likely to result in the severe vascular injury associated with systemic vasculitides.
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O 25

PED-BD: An international cohort study on pediatric Behçet's disease: one-year data of 110 patients

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BACKGROUND: Behçet Disease (BD) is exceptionally observed before the age of 16 years and raises diagnosis problems because there is no specific biologic marker. Sets of clinical criteria have been proposed for adult patients only. They lack of specificity in children where the disease is often uncompleted or atypical.
OBJECTIVES: Aim of the study is to set-up an international cohort of patients suspected with BD and selected on homogenous criteria for definition of the disease in children, reflecting the natural history.
METHODS: Centers specializing in pediatric BD have been called to collaborate documenting their patients into a database, available online. An international expert committee has defined inclusion criteria as follows: first sign related to BD before 16 years, new patient or patient followed since less than 3 years, patient being able to be followed during 4 years, consent obtained, and recurrent oral aphthosis [OA] (more than 3 attacks/year) associated to at least one of following symptoms: genital ulceration [GU], erythema nodosum, folliculitis, pustulous/acneiform lesions, positive pathergy test, uveitis, venous/arterial thrombosis, family history. Data are updated every year and patient's files are examined by the BD expert committee for classification into 3 groups: definite BD, probable BD and not BD. Statistical analysis are performed to compare the 3 groups.
RESULTS: In January 2010, 110 patients (56M/54F) from 16 centres of 11 countries have been included. Mean age: at inclusion was 13.5y, at first symptom 8.1y and at BD suspicion 11.8y. 38 % of them had only 1 symptom associated with OA, 31% had 2 and 31% had at least 3.106 first visits have been done. 93% were receiving treatment. 57 patients underwent first year visit.36 had no new symptom, 12 had one, and 9 had 2. The expert committee has examined 46 files and classified 28 as definite and 18 as probable. 15 patients had 2 or less symptoms; 11 of them were classified as probable and 4 as definite. 33 patients had 3 or more symptoms, 26 being classified as definite and 7 as probable. Therefore, having 2 or more symptoms was significantly associated with classification as definite BD (p=0.0005). Among our patients classified as definite, 26/30 (87%) fulfilled the ISG criteria, while 17/18 classified as probable did not meet the international criteria.
CONCLUSION: The expert committee has classified the majority of patients in the BD group although they did not fulfil the international BD classification criteria (for adults).

O 26

No Oral. See P 093

O 27

New genetic variations in the PSTPIP1 gene leading to autoinflammation distinct from classical PAPA syndrome

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INTRODUCTION: Hyperzincaemia and hypercalprotectinaemia is an extremely rare auto-inflammatory disorder associated with recurrent infections, hepatosplenomegaly, arthritis, anemia, cutaneous inflammation, and failure to thrive. So far no genetic cause has been identified in these patients. While the clinical appearance is heterogeneous all affected individuals present with extremely elevated S100A8/S100A9 (calprotectin) serum concentrations (1.5-9.0 g/l (normal range <0.001 g/l)).
AIM: Based on the observation that elevated S100A8/S100A9 serum concentrations are a feature of some autoinflammatory diseases, screening of candidate genes in five hyperzincaemia and hypercalprotectinaemia patients was used for identification of common mutations in this disease.
METHODS: Candidate exons were amplified by PCR. Amplification products were purified and sequenced on an ABI 3130 genetic analyzer. Furthermore serum concentrations of S100A8/S100A9 were analyzed in 6 patients with hyperzincaemia and hypercalprotectinaemia by a sandwich enzyme linked immunosorbent assay (ELISA) and compared with A230T positive PAPA-patients with and without treatment.
RESULTS: Four of the six patients were heterozygous carrier of a glutamic acid250 (GAG) ®lysine (AAG)/p.Glu250Lys/E250K substitution encoded by exon 11 of the PSTPIP1 gene. S100A8/S100A9 concentrations were extremely elevated in these patients (0.9-8.8. g/l) compared to PAPA patients (0.020-0.040 g/l) whose levels where still very high in comparison to normal controls.
CONCLUSION: The PSTPIP1 E250K mutation causes an autoinflammatory disorder known as hyperzincaemia and hypercalprotectinaemia. This disease shows a heterogeneous spectrum of symptoms which only partially overlaps with the appearance of the classical PAPA syndrome.

O 28

Rheumatoid Arthritis susceptibility loci; PTPRC, PTPN2, IKZF3, c5orf30, BLK and CD247 are also associated with Juvenile Idiopathic Arthritis

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BACKGROUND: Rheumatoid arthritis (RA) shares similar clinical and pathological features with juvenile idiopathic arthritis (JIA); indeed the strategy of investigating whether RA susceptibility loci also confer susceptibility to JIA has already proved highly successful in identifying novel JIA loci, such as PTPN22, IL2RA and TRAF1/C5. There has been a plethora of newly validated RA loci reported in the last year. Therefore the aim of this study was to test SNPs robustly associated with

RA in a large cohort of JIA cases and controls to investigate the overlap between these diseases and identify novel JIA loci.
METHODS: 29 SNPs that showed validated association with RA and had not been investigated previously in JIA were genotyped in JIA cases (n=1337) and healthy controls (n=2781) using Sequenom MassArray technology. Genotype and allele frequencies were compared between cases with JIA and controls using the Cochrane-Armitage trend test implemented in PLINK and allelic odds ratios (ORs) and their 95% confidence intervals (CIs) calculated.
RESULTS: Strong evidence for association with JIA was seen for eight SNPs. These include a SNP, rs10919563, in PTPRC (ptrend =2.5 x 10-6 OR 0.68 95% CI 0.58-0.8) rs7234029, in PTPN2 (ptrend =0.0003 OR 1.26 95% CI 1.11-1.43), rs2872507 in IKZF3 (ptrend =0.0004 OR 1.21 95% CI 1.09-1.34), rs26232 in c5orf30 (ptrend =0.002 OR 0.84 95% CI 0.75-0.94), rs2736340, in BLK (ptrend =0.003 OR 1.19 95% CI 1.06-1.34) and rs1773560 in CD247 (ptrend =0.005 OR 0.87 95% CI 0.79-0.96). There was additional evidence for association of two novel SNPs in genes previously associated with JIA, rs13119723, in the IL2/IL21 region (ptrend =7.5 x 10-6 OR 0.71 95% CI 0.61-0.83) and rs706778 in the IL2RA gene (ptrend =0.0002 OR 1.22 95% CI 1.1-1.35).
CONCLUSIONS: The association of PTPN2 with JIA in the current study validates the findings of a previous US study, confirming it as a JIA locus. The other loci identified are novel and will require validation in independent JIA datasets. To date we have investigated 44 RA loci in JIA and of those 27 are associated with both diseases. The overlap is remarkable for two diseases which, although sharing some phenotypic features, are clinically distinct entities.
ACKNOWLEDGEMENTS: Childhood arthritis prospective study (CAPS), UKRAG consortium and BSPAR study group.

O 29
Anti-TNFalpha therapy in juvenile idiopathic arthritis primarily affects effector T cells instead of regulatory T cells

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BACKGROUND: Anti-TNFalpha treatment has become a leading therapy in rheumatoid and juvenile idiopathic arthritis (JIA) patients who are refractory to conventional drugs. Infliximab, when used in adult rheumatoid arthritis, seems to exert its effects at least in part by modulation of defective regulatory T cells. In children, treatment with etanercept is clinically very effective, although arthritis tends to relapse immediately after etanercept is stopped.
OBJECTIVE: To examine the effect of etanercept on regulatory (Treg) and effector T cell populations in JIA.
METHODS: 20 patients with poly-articular or extended-oligo articular JIA were analyzed before and after 3 months of etanercept-treatment. Cytokine-profiles in plasma were assessed by Luminex directly *ex vivo*. Frequency, characteristics and functionality of regulatory T cells were analyzed by flowcytometry and by suppression assays in which sorted effector T cells (CD4+CD25-) and CD4+CD127low Treg were cocultured and studied for proliferation and cytokine production. Quantitative and qualitative responses to heat shock proteins (HSP60) were studied in T cell proliferation assays. We performed short stimulation assays using PMA/Ionomycin to study changes in cytokine production of CD4+ and CD8+ T cells before and after etanercept therapy.
RESULTS: Etanercept treatment downregulates disease activity, reflected by improvement in clinical disease parameters. This is accompanied by lower levels of IL-1alpha and IL-6 in plasma of JIA patients after treatment. The frequency and phenotype of Foxp3+CD4+ regulatory T cells was unaffected by etanercept treatment. Suppression assays with Treg and effector cells (including crossover experiments in which Treg pre-etanercept were cocultured with effector T cells post-etanercept and vice versa) showed that etanercept treatment did not result in an increased suppressive capacity of Treg on the proliferation of CD4+CD25- effector T cells nor on the cytokine production of anti-CD3 stimulated T cells. Finally, proliferative responses to human HSP60 significantly decreased after etanercept treatment.
CONCLUSION: Unlike an effect on regulatory cells as seen with infliximab treatment in adult rheumatoid arthritis, these data show that the clinical response by etanercept treatment in JIA is not mediated by changes in the frequency or function of Tregs. Our data indicate that etanercept primarily affects effector T cells and is associated with decreased T cell responses to human HSP60.

O 30
Overexpression of CREMalpha accelerates the onset of autoimmune mediated disease in a murine model of lupus

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The transcription factor cAMP response element modulator (CREM) is a widely expressed transcriptional repressor which is important for the termination of the T cell immune response and contributes to the abnormal T cell function in patients with systemic lupus erythematosus (SLE). Overexpression of CREMα in human SLE T cells results in an anergic phenotype with decreased IL-2 production. To explore the relevance of CREMα in vivo we used the well-established murine lupus model MRL/lpr, which is characterized by the introduction of a mutation in the CD95 (Fas) locus. We generated a transgenic mouse with a selective overexpression of CREMα in T cells and introduced a Fas -/- phenotype into the CREMα transgenic mice. CREMα transgenic Fas -/- mice developed a severe lymphadenopathy as early as 11 weeks of age, while the wildytpe Fas -/- mice did not at this early age. Additionally the CREMα transgenic Fas -/- mice showed a markedly enhanced splenomegaly compared to the wildtype Fas -/- mice. Lymphadenopathy and splenomegaly is paralleled by a massive expansion of pathogenic CD3+CD4-CD8- double negative T cells. Consistently with human SLE T cells, in which CREMα binds to CD3ζ chain promoter leading to a decreased CD3ζ chain expression, we found a decreased expression of the CD3ζ chain in T cells of the CREMα transgenic animals compared to wild type animals. Furthermore T cells of CREMα transgenic Fas -/- mice showed an enhanced production of IL-21 compared to wildtype Fas -/- mice. IL-21 has been linked towards SLE before and the blockade of IL-21 *in vivo* reduces disease pathology in lupus prone mice.
Therefore our data suggest a critical amplifying role of CREMα in autoimmune prone conditions like SLE.

O 31
Anakinra Treatment prior to Steroids In Newly Diagnosed Systemic Onset JIA; Changing the Biology?

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BACKGROUND: Systemic Onset Juvenile Idiopathic Arthritis (SoJIA) is the most severe subtype of JIA and is characterized by systemic inflammation and chronic arthritis. Many studies have implicated a role for cytokines (IL-1, IL-6, IL-18) and NK cell dysfunction in the pathogenesis of the disease. Current treatment involves NSAIDS, corticosteroids and methotrexate as first line drugs. Anakinra (IL1Rα antagonist) has been reported to be efficacious in refractory SoJIA patients. We describe the use of Anakinra in steroid naïve patients. This study was approved by our local ethical committee.
OBJECTIVES: To evaluate both clinical and immunological effects of anakinra treatment prior to steroids in newly diagnosed SoJIA patients.
METHODS: Thirteen consecutive patients with newly diagnosed systemic onset JIA were included. Clinical response was evaluated using the validated core set parameters for JIA. Disease activity was given as percentages improvement compared to baseline values (ACR-Ped scores). Biochemical parameters of disease activity (ESR, CRP, Ferritin, NK cell function, sIL-2R, cytokine profiles, Myeloid Related Proteins (MRP\'s) were collected at standardized timepoints.
RESULTS: We observed a fast clinical response in all patients, resulting in normalisation inflammatory parameters (sIL2R, ferritin, CRP and ESR), body temperature, disappearance of exanthema, and improvement in arthritis scores within 3 days. After 3 weeks of treatment 75% of patients achieved an pACR90 score. Clinical improvement was accompanied by normalisation of IL-1, IL-6 and MRP levels. After 1 year follow up our cohort can been divided into 3 groups: A) good responders (n=6) in which anakinra could be tapered and stopped after 3 months. B) good responders (n=4) in which patients remain anakinra dependent and cannot be tapered after 3 months. C) patients who flared during anakinra therapy requiring addition of steroids (n=3).
During the 1 year follow-up, NK cells numbers increased initially and remained stable throughout treatment. Specific lysis was restored to normal within just 3 days, but returned to baseline (low) values after 1 months of therapy. Intruigingly, specific NK cell lysis was normalised at D3 compared to normal controls but subsequently decreased again to baseline levels (i.e. significantly decreased compared to healthy controls). Absolute NK cell numbers increased during anakinra treatment and stayed persistently elevated compared to baseline. Moreover, the NK cell responsiveness to IL-18 was restored shortly after initiation of anakinra treatment. This was sustained throughout the treatment and follow-up.
CONCLUSION: In this cohort we show the response to anakinra in newly diagnosed sJIA patients prior to standard steroid treatment. Of these patients 75%

achieve an ACRp90 score and remain in remission during 1 year follow-up. Furthermore, in 50% of these patients anakinra can be tapered after 3 months and stopped without relapsing during follow-up. Interestingly, it seems that the pattern of IL6, IL-18 and MRP's precede the clinical response to anakinra. Moreover, the early use of anakinra in patients with a short disease duration induces restoration of the IL18 NK cell axis. These data suggest a change in the biology of the disease when interfering with the IL-1 route early in the disease process.

O 32

Evidence for persistent endothelial injury and subclinical inflammation in juvenile dermatomyositis

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BACKGROUND: Vasculitis and/or occlusive vasculopathy are considered central to the pathogenesis of juvenile dermatomyositis (JDM), although the pathogenesis of this vasculopathy remains uncertain.
OBJECTIVES: To assess whether biomarkers of endothelial injury (circulating endothelial cells; CECs) and markers of subclinical chronic inflammation provide insight into the pathogenesis of JDM.
METHODS: 20 JDM patients (13 girls), median age 9.58 years (2.84 - 17.09) and median disease duration 37.94 months (8.9 – 109.9) were studied. Disease activity was assessed using the Disease Activity Score (DAS) and Childhood Muscle Assessment Score (CMAS). Disease activity was defined according to the presence/absence of rash, CMAS, systemic and laboratory indices of inflammation. CECs were quantified by immunomagnetic isolation using staining for CD146 and UEA-1. Cytokines (TNF-α, IL1β, IL6 and IL10) and chemokines (VEGF, MCP1 and IL8) were measured by electrochemiluminiscence. 19 healthy children were controls.
RESULTS: CECs were higher in JDM patients compared to 19 controls (p=0.0001), which was true for those defined as having active disease (p=0.0025), and those with clinically inactive disease (p=0.0033). Patients with calcinosis had higher CECs than those without. VEGF, MCP1 and IL8 were higher in JDM than controls (pVEGF=0.0013, pMCP1=0.0084 and pIL8=0.0446). There was no correlation of CMAS, DAS scores or hs-CRP, serum amyloid A, CK or LDH with CECs, cytokines, or chemokines.
CONCLUSIONS: Children with JDM have persistent endothelial injury irrespective of clinical disease activity or therapy. Increased IL-8 and MCP-1 could be driving this subclinical vasculitis, whilst increased VEGF could indicate an endothelial repair signal as suggested in other vasculitides.

O 33

A novel defect: CD39+ T cells are enriched in the inflamed joint but do not suppress

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BACKGROUND: Regulatory T cells have been recently shown to suppress via ectoenzyme CD39-mediated hydrolyis of ATP and subsequent generation of anti-inflammatory adenosine. These cells are thought to play a role in resolution of the mild form of arthritis in children, persistent oligoarticular juvenile idiopathic arthritis, JIA.
OBJECTIVES: To characterise phenotype and function of CD39+ T cells in JIA.
METHODS: Mononuclear cells from healthy control blood (PBMC) and JIA patient blood and synovial fluid (SFMC) were assessed for CD39, Treg markers and cytokine expression by flow cytometry. ATP hydrolysis and adenosine production was measured by HPLC. Suppression of cell proliferation was measured using thymidine incorporation after *in vitro* stimulation with anti-CD3/CD28 (ratio of regulatory cells: responder cells, 1:1). All samples from patients with JIA and controls were used with full ethical consent.
RESULTS: We found a population of CD39+ Foxp3- CD4 T cells which is significantly enriched in the synovial fluid of patients with JIA ($p<0.001$) compared to blood of JIA or controls. Unlike CD39+Foxp3+ Treg, this novel population produces the proinflammatory cytokines IFNγ and IL-17 and also IL-2. There is also altered expression of Treg markers CD127 and CCR4 on these cells. CD39+Foxp3- cells have similar ATP hydrolysis activity to classical Treg, but fail to suppress cell proliferation *in vitro*. We tested if adenosine production was intact and show for the first time that although mononuclear cells from JIA synovial fluid have enhanced ATPase activity mediated by CD39+ cells compared to peripheral blood, these cells are significantly reduced in their ability to generate anti-inflammatory adenosine. These data are the first demonstration of this defect in the human inflammatory site.
CONCLUSIONS: We show that Foxp3 and CD39 expression on CD4 T cells can be dissociated in the human inflamed site and that expression of CD39 on CD4 T cells is not sufficient for regulatory function.
This study was supported by SPARKS UK and the Big Lottery Fund. KN is supported by an ARC Fellowship (Ref. 17998).

O 34

Preliminary definition of the remission and minimal disease activity cut-points for the Juvenile Arthritis Disease Activity Score (JADAS)

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BACKGROUND: Recent advances in therapeutic options, namely the introduction of biologic agents, have markedly increased the potential for achieving a remission or minimal disease activity (MDA) state. Therefore, accurate criteria for defining remission and MDA are needed.
Disease activity status can be defined using a categorical model, which requires simultaneous fulfilment of multiple criteria, each of them with a threshold value, or using a dimensional model, which is based on pooling individual measures of disease activity into a composite disease activity score and enables definition of remission through the calculation of a numeric cut-point. The first approach has been followed in the development of the current JIA remission criteria (Wallace criteria) (1), and in the preliminary definition of MDA(2).
OBJECTIVE: The identification of the remission and MDA cut-points of the recently developed composite disease activity score for JIA, the JADAS (3).
METHODS: For the purposes of this study, the JADAS-10 version was used. The JADAS-10 is computed as the simple sum of 4 variables, each with a 0-10 range: the physician's global assessment, the parent's global assessment, the normalized ESR and the reduced active joint count.
A total of 602 consecutive patients were included in the study. At each visit, all main physician- and parent-centered outcome measures were recorded. JADAS-10 could be calculated for 432 patients in 914 visits. At each visit, both physicians and parents were asked to rate independently the disease status as remission or active disease. Furthermore, we assessed the presence of remission by Wallace criteria and, after grouping patients in oligoarthritis or polyarthritis, of MDA by the preliminary definition.
In the first step, we calculated the JADAS-10 values corresponding to the 75th percentile of score distribution among patients' who were classified as having disease remission by physician's and parent's subjective rating and Wallace criteria, or having MDA. In the second step, we calculated, by means of the receiver operating characteristic (ROC) curve analysis, the JADAS-10 values that showed the best trade-off between sensitivity and specificity (i.e. the best accuracy) in discriminating between patients who had remission or active disease according to the physician, the parent, or the Wallace criteria, or who had MDA according to the preliminary definition.
RESULTS: The results in the 2-step analysis are shown in table. The numbers obtained for each definition using the 75th percentile or ROC curve method were then averaged. The values obtained for remission were further averaged achieving the value of 2.0, The values obtained for MDA are 2.3 for oligoarthritis and 2.9 for polyarthrtritis
CONCLUSION: The value of 2.0 is the remission cut-point for the JADAS-10 proposed for use in future clinical trials on JIA. The proposed cut-points for MDA in oligoarthrtitis and polyarthritis are 2.3 ad 2.9, respectvely.
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O 35

Therapeutic approaches for the treatment of active Juvenile Dermatomyositis an international multicenter study

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BACKGROUND: Recently published articles have documented a marked improvement in long-term outcome and survival of juvenile dermatomyositis (JDM) patients but little information is available on standardized evaluations of response to therapy based on current treatment options.

OBJECTIVE: Our aim was to evaluate in large prospective cohort of JDM patients the response to therapy over a 24 months period, according to the PRINTO JDM response criteria.
PATIENTS & METHODS: Clinical, laboratory and therapeutic modalities were collected prospectively between 2001 and 2004 in JDM patients by PRINTO/PRCSG members from 36 countries. Patients with probable or definite JDM, age < 18 years, in an active phase of their disease, at 4 time points (baseline, 6, 12 and 24 months), were included. The validated core set variables were the global assessment by the physician and parent, muscle strength, functional ability, quality of life and disease activity tool. Patients were defined as improved if able to demonstrate at least 20% (50, 70, or 90) improvement from baseline in 3 of any 6 core set variables with no more than 1 of the remaining worsening by more than 30%, which cannot be muscle strength. Remission was defined as patients with normal muscle strength (CMAS ≥48; nv 0-52) and physician global assessment of disease activity ≤ 0.5 cm (nv 0-10) and normal CPK (≤150 U/L)
RESULTS: The analysis data set included 275/294 (94%) patients. Patients median ages at onset and disease duration visit were 7.2 and 6 months respectively with 168 (61%) being female. The greatest improvement in clinical and laboratory measures was observed in the first 6 months of therapy and maintained thereafter. At baseline treatment options included steroids in 269 (97.8%), metotrexate (MTX) in 134 (48.7%) with 91 newly started, cyclosporine A in 44 (16%), hydroxychloroquine in 37 (13.5%), and IVIG in 38 (13.8%). Oral steroids dose at baseline and 6 months were 1 and 0.3 mg/kg/day respectively, at 24 months 91 patients (52.3%) were still on steroids at 0.21 mg/kg/day; steroids pulses were used in 100 (36.4%) at baseline. **Figure** reports the 20, 50, 70, 90 response and remission over time. A substantial improvement was observed in the initial 6 months (PRINTO 20 criteria 84%) and maintained thereafter.
CONCLUSIONS: Six months of therapy lead to a significant improvement in JDM core set measures and response criteria, that was maintained up to 2 years follow-ups. These data provided standardized response to therapy data in patients with JDM treated according to the current available options.

O 36
Validation of Birmingham Vasculitis Activity Score in childhood vasculitis

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BACKGROUND: Unlike for adults patients with systemic vasculitis, there are no validated tools to measure disease activity status in childhood (c-) systemic vasculitis.
OBJECTIVES: Our aim was to validate the last version of Birmingham Vasculitis Activity Score (BVAS v.3) and the Disease Extend Index (DEI) for comprehensive assessment of paediatric primary c-systemic vasculitis.
METHODS: We extracted from the PRINTO database all patients who fulfilled the Henoch-Schoenlein (HSP), childhood (c) polyarteritis nodosa (c-PAN), c-Wegener (c-WG) and c-Takayasu (c-TA) EULAR/PRINTO/PRES c-vasculitis classification criteria and whose disease duration at the time of diagnosis was ≤ 3 months. Data were also available for follow-up evaluation ≥ 3 months after diagnosis. The validation of the BVAS and DEI were examined by assessing discriminant ability among the 4 vasculitis, convergent validity by Spearman correlation coefficient with physician's global assessment of disease activity (MD global), indexes of inflammation (ESR/CRP), responsiveness to change over time through the standardizes response mean (SRM); A SRM value <0.5 is considered small, ≥0.5 and <0-8 moderate, and values ≥ 0.8 represent large effec.
RESULTS: The analysis data set included 796/1124 (71%) patients (M:F 0.96:1): there were 669 HSP, 80 c-PAN, 25 c-WG and 22 c-TA. The median age of the diagnosis was 6.99-year (6.6-11.96) and median delay for the diagnosis from the onset of signs or symptoms was 0.01 (0.003 - 0.027) years. In the table are reported the 9 subscore of the BVAS, the total BVAS score, the DEI, the MD global and indexes of inflammation.
The BVAS was able to discriminate between the 4 c-vasculitides with total BVAS scores equal to 9 (6.0-14.0), 17.5 (11.5-24.5), 23 (19-29), 15 (11-20) in HSP, c-PAN, c-WEG and c-TA respectively (see table). The cutaneous and cardiovascular sub-score are able to distinguish TA patients from the others; the ENT sub-score shows a significant ability to discriminate the c-WG patients from the others.
A strong correlation was found between the BVAS and DEI (rs=0.80) while correlation with MD global were moderate (rs=0.49) and poor with CRP and ESR (rs=0.34, rs=0.31). Responsiveness was large for BVAS total score (SRM=1.38), DEI (SRM=1.9), MD global (SRM=1.3) and ESR (SRM=0.85).
CONCLUSION: BVAS and DEI showed adequate discriminant ability and sensitivity to change but, but poor to moderate convergent validity. Further work is needed in order to improve activity measurement in c-vasculitides.

Poster Abstracts

P 001
Update of the juvenile systemic sclerosis inception cohort. www.juvenile-scleroderma.com

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BACKGROUND: Juvenile systemic sclerosis (jSSc) is a rare autoimmune disease. Currently just retrospective data exist regarding organ involvement, and evolvement of the disease, without a standardized assessment of the organ involvement. Our project is the first projects, where prospectively and with standardized assessment data of early jSSc patients, beginning in the first 24 months of disease duration, are collected.
METHOD: Using the proposed standardized patient assessment protocol patients with early jSSc , less than 18 months disease course, are prospectively assessed. All participating centres approved the protocol over the own IRB.
RESULTS: Up till now 42 centres from 20 countries applied worldwide to participate on the project. The assent and consent forms were translated into German, Spanish, Portuguese and Ivrit. Up till now 14 patients were enrolle d, the mean follow up in the cohort is 1.6 years. 1 is followed for 12 , four for 6 months, all others were just recently recruited. Twelve of the 14 patients were female. The mean age at the onset of the non-Raynaud symptomatic were 12.4 years. Seven of the 14 have diffuse subtype , one of them have overlap feutures and 7 of the 14 have a limited subtype and 3 of these have overlap features. The mean modified Rodnan Skin Score was 16.5 (range, 2 to 46). 12 were ANA positive, and 5 of them were anti-Scl 70 positive. None of them was anti-centromere positive. Twelve of the 14 have Raynaud's, 9 of them have capillary changes and 4 of them already ulcerations. 6 of them have cardiopulmonary invovelvement, 4 of them interstitial lung disease, 1 sign of pulmonary hypertension. One has renal involvement associated with hypertension. Seven of them have gastrointestinal involvement, and 5 of them oesophageal involvement. Twelve of ten have musculoskeletal involvement, 9 of them with joint contractures.
CONCLUSION: We present the data on the first 14 prospectively assessed patients with jSSc. The current recruitment data confirms the previous observations from retrospective data collection, but we are only at the beginning of this project and hope to recruit up to 50 patients and follow them prospectively over the next 2 to 4 years at least.

P 002
Fatal haemophagocityc lymphohystyocytosis in severe systemic lupus erythematosis boy after rituximab administration

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BACKGROUND: Haemophagocityc lymphohystyocytosis (HLH) is a severe life-threatening haemtologic condition, complicated different rheumatic diseases. The triggering factors could be also viruses, bacteria and medication. There a few of articles about potential triggering role of biologics in HLH developing
METHODS: we describe a patient with fatal HLH in severe systemic lupus erythematosis (SLE) boy after rituximab administration.
RESULTS: 14 y.o. boy with SLE – severe progressive nephritis: nephrotic syndrome with massive proteinuria (max 30 gr/24 h), hypoalbuminemia, mild hematuria, casts and hypertension. Immunologic tests: ANA, antidsDNA, LE cells were positive. In 2 months was 1st episode of generalized seizures, next episode was 1 month later and CT scan was revealed white matter lesions. Treatment with steroids - po and IV metylprednisolon (MP) pulses with cyclophosphamide (CTX) during 4 months was ineffective and boy at first was admitted to our rheumatology department there lupus-nephritis IV class was diagnosed. We continued steroids, CTX and added MMF (2000 mg\\day), but our treatment was ineffective too and rituximab (RTX) therapy with CTX pulse was started. The initial effect was very impressive, in 1 month boy was in remission, but after 1st infusion we observed unusual hematological changes: transient leucopenia, decreased number of platelets and mild anemia with very intensive left shift of neutrophils (bands near 30%, myelo-

cytes and metamyelocytes both near 20-30% and single blasts. Myelogramme was revealed: foci of macrophage storage without evidence of haemophagocytosis. After 2nd RTX administration proteinuria was mild and lupus serology was negative, but relapsed febrile fever with leucopenia occurred. Antibiotics, IV acyclovir, fluconazole were ineffective and only infusion of IVIG ceased the fever. There were no signs of lymphadenopathy and splenomegaly, only mild hepatomegaly. Third fever episode was very impressive: fever, bicytopenia, high ferritin, triglicerides, at first high ALT, AST, very high LDH, low protein and albumine level, low sodium, high CD25, low NK-cells and high γ-interferon. Relapsed course of reactive HLH was diagnosed. We started again IVIG and cyclosporine A. Next fever relapse in 3 weeks, at that moment pulse with solumedrol had short effect, IVIG have been at first ineffective, severe fever with agranulocytosis, severe anemia, low platelets and hyperferritinemia. Myelogramme was repeated: a low number of bone marrow cells with evidence of severe hemaphagocytosis. HLH-94 protocol was started (dexamethazone and etoposide). CMV was detected and gancyclovir was added. In 2 weeks after start of etoposide boy developed sepsis. After recovery boy again developed signs of severe HLH, resistant to steroids, IVIG, cyclosporine A and etoposide. Boy had very high signs of inflammatory activity (CRP>200 mg/dl) and high TNF-α and to stop the HLH course we used infliximab with positive initial effect: fever and inflammatory activity was ceased, ferritin and LDH were decreased but before 2nd infliximab administration boy had HLH flare, 2nd infliximab infusion with short-term improvement, boy developed severe respiratory distress syndrome and died. Postmortal examination revealed severe HLH with diffuse pneumonia, respiratory distress syndrome. There were no signs of active SLE, kidney examination show improvement of nephritis compared with 1st nephrobiopsy.
CONCLUSIONS: Our data show that using rituximab, effective medication for severe SLE with lupus-nephritis can be trigger of HLH.

P 003

Epidemiology and biologic use among adults with Juvenile Idiopathic Arthritis: data from the British Society for Rheumatology Biologics Register (BSRBR)

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OBJECTIVES: To document the use and outcome of biologics in adults with JIA.
METHODS: Patients with disease onset <16 years were identified from the BSRBR. Further information was requested from the physician to facilitate stratification into ILAR JIA subtypes. Patterns of biologic use, remission rates (defined using DAS28<2.6) and drug survival are reported.
RESULTS: 225 patients were identified. 168/225 (75%) were "labelled" with diseases other than JIA (RA:129, AS:23, PsA:16). The ILAR subtype was determined for 154/225 (68%). 73% were female with median age at commencement of first biologic 29 years (IQR 22-38). Median baseline HAQ was high (1.7 (IQR 0.6, 2.0). First biologic used was etanercept (56%), infliximab (25%) adalimumab (18%) and anakinra (1%). 32% received more than one biologic during follow-up (2 biologics: n=26, 3 biologics: n=18, 4 biologics: n=5). Remission rates at 6 and 12 months were 19% and 31% respectively. Drug survival at 1, 2 and 3 years was 82%, 65% and 57% respectively. At all 3 time points patients were more likely to stop from inefficacy than from adverse events.
CONCLUSIONS: Very little is known about the optimum management of disease activity in adults with JIA. This study is the first to describe patterns of biologic use in a national cohort of adults with JIA. The phenomenon of switching between biologics has not previously been reported in adults with JIA. Remission rates and drug survival were higher than those reported for RA, albeit the DAS28 has not been validated in JIA.

P 004

Efficacy of rituximab retreatment in refractory juvenile idiopathic arthritis

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RELEVANCE: Chimeric monoclonal anti-CD20 B-cell antibody (rituximab) is promising drug for the treatment of JIA refractory to immunosuppressive drugs and TNF-α-blockers.
PURPOSE OF THE STUDY: To evaluate clinical efficacy of rituximab retreatment in patients with severe juvenile idiopathic arthritis (JIA).
PATIENTS AND METHODS: 55 patients were enrolled in the study, 25 boys and 30 girls with JIA. Range of age was from 2 ,3 to 17 years; mean disease duration was 4,5±1,4 years. Rituximab was administered at a mean dose of 375 mg/m2/administration according to the following regimen: 1 dose once a week for 4 consecutive weeks every 24 weeks. The next course of Rituximab was administrated if patients had systemic manifestations, active joints, increasing level of CRP and ESR in 24 weeks after Rituximab treatment. 55 patients have received one treatment course (24 weeks), 54 children have received 2 courses (48 weeks), 42 children have received 3 courses (72 weeks), 25 – 4 courses.
RESULTS: The ACR Pedi 30, 50, 70 were achieved by 98%,50%, 40% and 0% of patients at Week 24, and by 95%, 71%, 70% of patients at Week 48 (N=7), respectively. At week 72 ACR pedi 50 and 70 were achieved by 93 % of patients. The remission was achieved by 25 % of patients at Week 24, by 52% of patients at Week 48, by 93% of patients at Week 96.
CONCLUSION: Rituximab is effective drug of treatment in patients with severe juvenile idiopathic arthritis/ The remission was achieved by 93% of patients at Week 96.

P 006

Result of a multinational survey regarding diagnosis and treatment of the temporomandibular joint involvement in juvenile idiopathic arthritis

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INTRODUCTION: Temporomandibular joint (TMJ) involvement occurs up to 80% of patients with juvenile idiopathic arthritis (JIA). Currently they are no standardized procedures regarding diagnosis and treatment of this common presentation of JIA.
AIM OF THE STUDY: To assess the current clinical practices regarding diagnosis and treatment of TMJ involvement in JIA.
METHODS: Paediatric rheumatology colleagues were asked to fill out a survey with 8 items regarding diagnosis and treatment of TMJ involvement. The survey was distributed over the worldwide Paediatric Rheumatology electronic list-serve.
RESULTS: 77 centres responded to the survey by March 2010. Forty of the centres followed more than 300 patients with JIA. All responding centres were actively screening for TMJ involvement, 75 by history, 77 by physical exam and 2 by imaging. Sixty-seven (87%) were screening at first visit and 66 (86%) at each follow-up visit. If imaging was requested, 76% asked for MRI, 11% for ultrasound, 8% for CT and 33% for Xray. The centres reported the following prevalence of TMJ involvement: over 50% - 4% of the centres, between 25 and 50% -11% of the centres; between 10% and 25% - 49% of the centres, less than 10% - 36% of the centres. The first line treatment of the TMJ involvement was a DMARD in 35%, an NSAID (34%), an intraarticular corticosteroid injection (27%) and an anti-TNF agent (4%). Overall, 51 of the centres (66%) were using intraarticular corticosteroid injections as treatment; of these centres 30 (58%) were using MRI, CT or ultrasound imaging for guidance during injections.
CONCLUSION: TMJ arthritis is common among children with JIA, but a wide array of diagnostic and therapeutic approaches are being employed. An expert opinion/consensus statement regarding TMJ arthritis in JIA will likely benefit patients worldwide.

P 007

The Eurofever registry: results of the first 6 months of enrolment

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INTRODUCTION: 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 (agreement n 2007332, EAHC) is to build a network on Autoinflammatory diseases. In the first part of the project a common web-based registry for all Autoinflammatory diseases was built in collaboration with the Eurotraps Project (FP7, HEALTH-F2-2008-200923).
AIMS: To evaluate the number of patients enrolled in the Registry in the first six month after starting the enrolment.
PATIENTS AND METHODS: A web-based registry collecting baseline and 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 Rheumatology centers of the PRINTO network and adult centers with a specific interest in Autoinflammatory diseases The following monogenic autoinflammatory

diseases were considered: FMF, CAPS, TRAPS, MKD, Blau's syndrome, PAPA, DIRA, NLRP12-mediated periodic fever. Information on CRMO, Behcet's disease, PFAPA and undefined periodic fevers were also collected.
RESULTS: During the first six months from the beginning of the enrolment 650 patients from 21 different countries have been entered in the registry. So far clinical and genetic information on the following patients has been collected: 175 FMF pts; 48 CAPS pts, 40 TRAPS pts, 42 MKD pts; 12 Blau's disease pts; 7 PAPA pts, 2 DIRA pts, 3 pts with NLRP-12 mediated periodic fever. Data on 146 PFAPA patients, 91 CRMO, 28 pediatric Bechet disease and 54 patients with undefined periodic fever are also available.
CONCLUSIONS: A common registry for collection of patients with Autoinflammatory disease is available and the enrolment is ongoing. Data will be available for analysis of the clinical presentation, outcome and response to treatment of Autoinflammatory diseases and for comparative studies among different Autoinflammatory conditions.

P 008

Acute Chorea in children: the value of Single Photon Emission Computed Tomographic Scan (SPECT) and Magnetic Resonance Imaging (MRI) findings

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BACKGROUND: Chorea is a neurological disorder characterized by involuntary and purposeless movements, caused by many genetic and acquired disorders that affect basal ganglia. In childhood, chorea is most often acquired acutely or subacutely and etiology includes autoimmune, vascular/hypoxic-ischemic, mitochondrial, toxic and even psychogenic causes. Sydenham chorea, a major manifestation of rheumatic fever, is the most common cause of acquired chorea in the young.
OBJECTIVES: The aim of this study was to find out possible correlations between MRI and SPECT findings and clinical course in our series of pediatric patients with acute chorea.
PATIENTS AND METHODS: Eleven children (3 boys, age range 5-10 years) were admitted to the Pediatric Rheumatology Unit of Federico II University in Naples between 1999 and 2010 with a diagnosis of acute chorea. Nine children had Sydenham's chorea (SC) (3 males, mean age 8 years and 3 months) with associated rheumatic carditis in three cases. One girl received a diagnosis of Systemic Lupus Erythematosus (SLE) and the last one showed clinical symptoms of chorea without any inflammatory signs. At presentation, chorea was generalized in 7 patients (63.6%) and localized (hemichorea) in 4 (36.4%), with subsequent generalization in 2 of them. Two patients had a recurrence of chorea after 1 and 3 years respectively. In patients with SC, laboratory tests were within normal limits, while the child with SLE showed leucopenia, increased inflammatory parameters, decreased complement, positive ANA, antiDNA and antiphospholipid antibodies. Brain MRI was performed in 10 patients and revealed normal findings in 8 and small foci of white matter gliosis in 2. Brain ECD SPECT scans, also performed in 10 cases (8 with SC) during the acute phase, showed asymmetric perfusion of the basal ganglia in 6/10 patients (60%), revealing unilateral increased perfusion as compared with the cerebral cortex. In only 2 patients with SC SPECT was performed again after the acute phase and found within normal limits.
CONCLUSIONS: In conclusion, our study confirms the increased incidence of acute chorea in girls SC being the most frequent cause. Based on our experience, SPECT scanning can be a good diagnostic and accurate tool to monitor the course of the disease.
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P 009

A rare cause of vasculitis – Idiopathic Hypereosinophilic Syndrome

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INTRODUCTION: Idiopathic hypereosinophilic syndrome (HES) is defined as sustained eosinophilia with an absolute eosinophil count ≥1.5x10^9/L for >6 months with target organ damage but without identifiable course. It is a rare disorder which carries significant mortality. Skin rash & fever were the most commonly presented symptoms among the paediatric population. However, the presence of vasculitis had not been reported. We report a case of secondary vasculitis due to idiopathic HES presented with vasculitis.
CASE REPORT: A 16 year old healthy Chinese female was admitted to the A&E Department with 3 weeks history of abdominal pain, vomiting, diarrhoea and newly onset skin rash on both sole in 2007. Physical examination on admission found splinter haemorrhage & tender vasculitic rash on both sole. Initial workup was unremarkable & the patient was given symptomatic treatment with little improvement. Gastrointestinal (GI) symptoms & vasculitic rash persisted.
At the same time, the patient developed cough with increasing severity. On Day 8 of admission, she was admitted to the PICU for further management of bilateral pleural effusion with desaturation & ascites. Oxygen supplement & thoracentesis were required.
Further workup showed elevated WCC up to 28.5x10^9/L with eosinophilia (20x10^9/L). Other cell lines showed no abnormality. ESR & autoimmune markers were normal. Sepsis workup was negative. Bronchoscopic examination was unremarkable. Pleural fluid showed high WCC with 80% being eosinophil. Cultures were negative for bacterial, viral, Mycobacterium & fungal growth. Cytology examination showed no malignant cell. CT Abdomen showed gross ascites & diffuse bowel wall thickening. OGD showed mucosal edema over the antral area, while gastric & duodenal biopsy showed evidence of chronic inflammatory infiltrate with sprinkle eosinophils in lamina propria. Skin biopsy showed features compatible with small vessels vasculitis. Perivascular infiltration by neutrophils, eosinophils & lymphocytes was noted. Echocardiogram showed increased endocardium & myocardium echogenicity which were suggestive of inflammatory cause. With the presence of elevated troponin I level, myocardial injury was confirmed. Liver & renal function tests were normal. Bone marrow aspiration & trephine biopsy showed features compatible with bone marrow eosinophilia. Cytogenetic study showed normal karyotype & there was no evidence of FIP1L1-PDGFRA arrangement. Extensive investigations had been done to rule out reactive eosinophilia or clonal eosinophilia as underlying cause. Idiopathic HES was confirmed.
IV Methylprednisolone 500mg Q24H for 3 days was given with good response. GIl symptoms & pleural effusion fully subsided. Vasculitic rash gradually faded out. No more eosinophil detected after on D3 of Methylprednisolone administration. Oral Prednisolone was given as maintenance, starting at 15mg tds and weaned down gradually. Regular out-patient follow up with cell count monitoring showed that the patient was dependent on a low dose of oral Prednisolone 5mg on alternate day without side effect.
CONCLUSION: The case illustrated that idiopathic HES could be one of the underlying cause of secondary vasculitis. Early recognition & initiation of treatment is important. Steroid is the mainstay of treatment but no standard regime is available yet. Many reports had suggested the use of oral steroid to bring about remission but we believe that pulse Methylprednisolone should be used to bring about disease control rapidly, which could be life-saving as in our patient.

P 010

Mutations in GALNT3 GENE: Two adolescents with tumoral calcinosis-hyperphosphatemia

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BACKGROUND: Tumoral Calcinosis (TC) is a rare congenital disease characterised by ectopic calcifications around large joints and hyperphosphatemia due to enhanced renal tubular phosphate reabsorption. Mineral depositions manifest as soft tissue masses especially around hips and shoulders. The occurrence of the disease is often associated with dental abnormalities and inappropriately normal or elevated levels of 1-25 (OH)2D3 and hyperphosphatemia. An inactivating mutation in GALNT3 gene encoding an enzyme responsible for initiating O-linked glycosylation of proteins triggers calcinosis.
PATIENTS AND METHODS: We report on 2 adolescents, a 16 year-old Caucasian girl and a 15 year- old Moroccan boy affected by TC. In the families, no other members were affected by the disease. Both pts developed the first features of the disease at the age of 13 and 12 years respectively, and in both the true diagnosis was missed up to adolescence. They presented to our attention with a rock-hard enlargement of glutea that hampered flexion, internal and external rotation of both hips. In addition, the boy had a rock-hard mass at the right shoulder and left elbow that prevented all joint movements. A pelvic MRI showed a mass with some cystic formations and several calcifications. Both pts had abnormal laboratory tests with serum Pi of 7.9 mg/dL and 5.4 mg/dL respectively (n.v.:2.5-5), a tubular Pi reabsorption rate (TmP/GFR) of 9.4 mmol/L and 6.3 (n.v.: 0.7-1.45), inappropriate levels of 1-25(OH)2 D3 52,1 and 110 pg/mL (v.n.:16-65) respectively. The girl had low levels of FSH, LH and 17 βE2 while boy had normal values. Additionally, low levels of serum intact FGF23 and high level of C-terminal fragment were found in both patients. Skull CT showed the presence of cerebral calcifications in both patients. Histopathologic findings of the ectopic calcified lesions were characterised by a diffuse deposits of calcium; by polarized light an amorphous to finely granular organisation, with dark blue-purple aggregates without a crystalline structure

were detected. These deposits were surrounded by a chronic inflammatory infiltrate composed of lymphocytes, histiocytes and several foreign body-type multinucleated giant cells.
METHODS: Genomic DNA was extracted from peripheral blood using a microvolume extraction method, QIAamp DNA Mini Kit (Qiagen GmbH, Hilden, Germany) according to the manufacturer's instructions.
RESULTS: We found a novel homozygous splice site mutation in intron I (IVS1-2a>g) likely leading to skipping of exon 2 and a described G>A transition at cDNA position 1524+1 which abolishes the consensus splice donor site. A coetaneous biopsy was obtained in order to perform functional studies.
CONCLUSIONS: Mutations of GALNT3 gene should be investigated in patients with wide hard calcifications around the joints not explained by concomitant connective tissue diseases as Juvenile Dermatomyositis and Scleroderma, thus avoiding invasive tests and expensive therapies. Functional studies should be critical in understanding the role of GALNT3 in the glycosylation and activity of FGF23 in order to manage targeted therapies.
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P 011

Novel mutations of Camptodactyly Arthropathy Coxa vara Pericarditis (CACP) syndrome

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BACKGROUND: The Camptodactyly Arthropathy Coxa vara Pericarditis (CACP) syndrome is an autosomal recessive disease characterised by congenital camptodactyly, no inflammatory arthropathy, joint failure, synovial hyperplasia, coxa vara, and thickening of the pericardium. The causative gene for CACP is PRG4 that is located on chromosome band 1q25-31 and consists of 12 exons. It encodes for a mucin-like glycoprotein named "proteoglycan-4" (PRG-4) which acts as the major surface lubricant for joint and tendons.
OBJECTIVES: To investigate possible genomic alteration in pts with CACP clinical manifestations, and to perform a comprehensive analysis of the PRG-4 gene.
PATIENTS & METHODS: 6 unrelated patients and 2 pairs of siblings (2 sisters, 1 sister,1 brother) with a phenotype resembling CACP syndrome were referred to us for mutational analysis of PRG-4 gene. The age of onset was mainly at birth (median age at diagnosis 5.5 years). Genomic DNA was extracted by peripheral blood and polymerase chain reaction was performed to amplify PRG-4 exon sequences including intro-exon boundaries using specific primers. The coding regions were sequenced, with the exception of 800bp, within exon 6 due to highly repetitive motifs.
RESULTS: 6 novel homozygous mutations within CACP gene were identified in 7 pts. The 2 sisters harboured the same nonsense alteration (Y1216X) that cause a frame-shift that creates a premature stop signal leading to the production of a truncated protein. Four mutations were small deletions of 1bp, 2bp and 5bp, three of which located within exon 6. These deletions cause frame-shift mutations and create a premature stop codon. In the remaining pts, we detected one substitution affecting the donor splice site (IVS8+3A>G); the bioinformatics analysis of this alteration predicts a decrease of the strength of the new splice site sequence that could be responsible for an aberrant splicing of the premature transcript. The analysis of CACP protein would be necessary to test the predicted effect of the mutations.
CONCLUSIONS: CACP syndrome is a rare disorder often misdiagnosed with other paediatric connective tissue diseases. This is the first study analysing the largest PRG-4 coding region and it allowed identifying a new set of molecular aberrations associated with the occurrence of CACP syndrome.
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P 012

Cross-talk between signals induced by IL-6 and TLR ligands causes increased inflammatory response in mouse and human macrophages. Implication for macrophage activation syndrome

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BACKGROUND: Macrophage activation syndrome (MAS) is often triggered by infections and occurs in patients with systemic JIA, which is characterized by high levels of IL-6.
OBJECTIVES: To evaluate if chronic exposure to IL-6 *in vivo* in IL-6 transgenic (IL6TG) mice and *in vitro* in human macrophages induced hyperresponsiveness to TLR ligands.
METHODS: IL6TG mice with high circulating levels of IL-6 were injected i.p. with TLR ligands at different doses: survival was recorded and blood and bone marrow were collected at different times. Moreover, splenocytes and peritoneal macrophages were isolated for in vitro studies. Cells were stimulated with TLR ligands and inflammatory cytokines levels were dosed in the supernatants. The activation status of STAT3, ERK and NF-kappaB was evaluated from cell lysates by western blot or confocal microscopy. Human macrophages were pretreated with IL-6 in combination with soluble IL-6 Receptor for 4 days, stimulated with LPS and analyzed as above.
RESULTS: Treatment of IL6TG mice with TLR ligands induced increased lethality and increased production of inflammatory cytokines, such as IL-6, IL-1β and TNF-α. Stimulation of murine splenocytes with TLR ligands led to a similar increase in inflammatory cytokine production. Analysis of signalling pathways showed an increased phosphorylation of STAT3, of ERK MAPK and IkappaB and increased NF-kappaB nuclear translocation upon TLR ligands stimulation in peritoneal macrophages from IL6TG mice. We reproduced these results in a human system by treating human macrophages with IL-6. Similarly to the murine peritoneal macrophages, we found increased STAT3 phosphorylation, ERK and NF-kappaB activation in these cells. In addition to increased lethality, IL-6TG mice treated with TLR ligands showed decreased platelet and neutrophil counts, increased serum levels of sCD25 and ferritin.
CONCLUSION: Our data show that high levels of IL-6 predispose to increased macrophage responses to TLR stimulation and implicate an ERK/STAT3/NF-kappaB activation pathway in this exaggerated inflammatory response both in mice and in human macrophages. TLR ligands treated IL-6 TG mice showed hematologic and biochemical features similar to those of patients with MAS. We hypothesize that MAS may be the consequence of abnormal response to TLR stimulation caused by high levels of IL-6.

P 013

Sclerosing peritonitis as a complication of lupus peritonitis in childhood systemic lupus erythematosus

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Sclerosing peritonitis (SP) is a rare chronic inflammatory disease characterised by fibrosis and adhesion of the peritoneum. SP is an unusual complication observed in continuous ambulatory peritoneal dialysis , or secondary to the use of beta-blockers and peritoneo-venous shunts. We describe an 11 year old Black-African female with systemic lupus erythematosus (SLE) who developed SP with chylous ascites secondary to chronic lupus peritonitis. In 2007, at the age of 9, she was diagnosed with SLE when she presented with severe skin lesions (lupus perniones), pancytopenia, hypocomplementemia and positive serology. One year after diagnosis, lupus peritonitis appeared with abdominal fullness, painless massive ascites and pleural effusion, responding to treatment with IV pulse methylprednisolone (1g for three days) and diuretics. 22 months later she redeveloped asymptomatic progressive abdominal distension. Abdominal CT demonstrated multiple adhesions of the small bowel, with thickening of the bowel wall and massive ascites. Abdominal tap revealed a milky fluid with triglycerides 1180 mg/dL, 2470 leukocytes/μL (90 % lymphocytes), albumin 2.29 g/dL, and glucose 1.10 g/L; without malignant cells or cultured bacteria. The Gram and Ziehl-Nielsen stains were negative. Laparoscopy showed a sclerosing peritonitis with multiple adhesions of the small bowel and colon transversum. Histology indicated diffuse fibrosis and sclerosis with a chronic inflammatory infiltrate and small vessel vasculitis. Lymphoscintigraphy showed partial obstruction of the abdominal ductus thoracicus and lympaticus dexter. A diagnosis of SP was established based on these features. To the authors\' knowledge this is the first case report of SP in childhood SLE.

P 014

Pleuropulmonary manifestations of childhood-onset Systemic Lupus Erythematosus: a descriptive study of 18 patients

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OBJECTIVE: Childhood-onset systemic lupus erythematosus (SLE) is a multisystemic autoimmune disease that can involve multiple organs such as: skin, kidney, musculoskeletal system, brain, and others as well as lungs. Pulmonary manifestations may be an initial or life-threatening complication of SLE in children. Pulmonary involvement is relatively frequent in adult patients; it has rarelly reported in children with SLE.
The aim of this report is to describe pleuropulmonary manifestations of childhood –onset SLE via description of our patients.
METHODS: We retrospectively studied medical records of children with childhood-onset or JSLE, admitted to Children's Medical Center from 1995 to 2005. were retrospectively evaluated for evidence of pleuropulmonary involvement. All patients fulfilled at least four of the classification criteria of the American Rheumatism Association.
We obtained data regarding the age, sex and clinical and laboratory features, Informed consent was obtained from all patients.
RESULTS: Overall, sixty four patients were eligible to participate in our study. Fifty five patients (86%) were female and 9 patients (14%) were male. Eighteen out of 64 cases (28%) had pulmonary involvement. pulmonary complications included: pleuritis in 33.3%, acute lupus pneumonitis in 11%, chronic interstitial pneumonitis (CIP) in 5%, infectious pneumonia in 33.3%, pulmonary vasculitis in 5%, and pulmonary embolism in 5%.
CONCLUSION: This is the largest collection of childhood-onset SLE from the Iran. It shows that childhood-onset SLE is more common in Iranian children than was previously believed, and has a higher rate of organ involvement..The pleuropulmonary manifestations of childhood-onset SLE range from the minor pleuritic pain caused by serositis to life-threatening consequences of pulmonary hemorrhage.
KEYWORDS: Childhood-onset Systemic Lupus Erythematosus, pulmonary involvement

P 015

Childhood Systemic lupus erythematosus (SLE): analysis of clinical and immunological findings in 74 patients

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OBJECTIVE: The aim of this report is to describe the first instance of the clinical features of childhood lupus erythematosus. To define the pattern of disease expression in patients with childhood onset (SLE).
MATERIAL AND METHODS: We studied prospectively 74 patients with childhood-SLE who were seen consecutively either as inpatients or outpatients between 2000 and 2008. All the patients fulfilled the 1982 (ACR) revised criteria for SLE and had the disease at or before the age of 16 years. In 74 patients, defined as the initial manifestation clearly attributable to SLE, occurred before the age of 16, and they represent the childhood onset group described in this report.
RESULTS: A fifteen -year retrospective analysis of the clinical features and survival of 74 Iranian children with (SLE) was made. Sixty five (88%) patients from the childhood onset group were female and nine male (12%) (ratio female/male, 7/1). Range of age at onset was 3-16 years (Mean age10 + - 2). During the evolution of the disease, the childhood onset patients had the mode of presentation was as follows: 74% had skin involvement, 77% had musculoskeletal involvement, 43% had renal disease, 33% had hematological abnormalities, 24% had pulmonary involvement, 17% had central nervous system involvement, and 16% had cardiovascular disease.
Anemia in 59% of patients. Autoimmune thrombocytopenia purpura in 45% cases, Leukopenia with lymphopenia was the presenting feature in 16 % cases. ESR >85 in 78% cases, and positive (C-reactive protein) in 59% patients.
Hematuria was the most frequent finding in these patients (47%). Proteinuria was the second finding in our patients (43%). Raised BUN and creatinine was seen in (21%). The Coombs\' test was positive in 21% children, false positive VDRL in 16% patients with childhood-SLE.
ANA positivity was detected in 97% of cases at presentation; the mean titer was >1:160 in all patients except 2 cases. All 2 children who were ANA-negative had at least a malar rash, oral ulcer, and associated with several mild manifestation.
Anti-d DNA was positive in 83 % patients. Antiphopholipid antibody was in 13% patients. 10% of patients with SLE will be anti-Sm positive, low C3 (85%), low C4 (41%), and low CH50 complement (85%).
CONCLUSIONS: Childhood-SLE is not a common illness in the pediatric population. Although Childhood-SLE has been reported in children in first the 10 to20 years of life, it is rare in children under 5 years of age, childhood onset patients as presenting clinical manifestations, while malar rash, photosensitivity, musculoskeletal involvement, hematological abnormalities, and renal disease were more common during the evolution of the disease.
KEYWORDS: Systemic lupus erythematosus, malar rash, ANA, Antiphopholipid antibody.

P 016

Cold-induced autoinflammatory disease associated with NLRP12 mutations. New insights into clinical presentation and pathogenesis in a Caucasian family

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INTRODUCTION: Mutations of the NLRP12 gene have recently been described in patients affected with a new Autoinflammatory disease. NLRP12 belongs to the NLRPs family and its role in the activation of the inflammasome and regulation of NF-kB activation is currently being under investigation.
AIMS: We report about a Caucasian family, some of whose members display clinical features consistent with FCAS-like phenotype and associated with a novel p.D294E missense mutation of the NLRP12 gene affecting the Walker B sequence of the protein crucial for ATP binding.
PATIENTS AND METHODS: Four individuals, carrying the p.D29E NLRP12 mutation were analyzed. NF-kB activity was evaluated in NLRP12-mutated monocytes after 24 hour of TNF stimulation using TransAM NFkB p65 Kit. IL-1ß secretion, production of ROS and activation of antioxidant systems in resting conditions and after PAMPs stimulation were also assessed. In vitro analysis of the NLRP12 mutation effect on NF-kB activity was performed after co-transfection of a luciferase-NF-kB promoter reporter construct with the mutant and wild type NLRP12 expression plasmids in HEK293 cells.
RESULTS: In the family, the p.D294E mutation segregates in association with a particular sensitivity to cold exposure (especially arthralgia and myalgia), but not always with an inflammatory phenotype (urticarial rash or fever). The p.D294E mutated protein did maintain the same inhibitory activity shown by wt NLRP12. Unexpectedly, this was also observed when the already reported p.Arg284X nonsense mutation (Jéru et al., 2008) was analyzed in the same system. Consistently, NLRP12-mutated monocytes showed neither increased levels of p65 NF-kB activity nor higher amounts of IL-1ß secreted . However, the kinetics of PAMP-induced IL-1ß secretion was significantly accelerated, and a high production of ROS and an upregulation of antioxidant systems were demonstrated, in patients carrying NLRP12 mutations compared to healthy controls.
CONCLUSIONS: Even with a variable range of associated manifestations, the extreme sensitivity to cold exposure represents the main clinical hallmark of individual carrying the p.D294E mutation of the NALP12 gene. The regulation of NF-kB activity does not seem to be affected in NLRP12-mutated patients. Redox alterations and accelerated secretion of IL1ß may be responsible for the mild autoinflammatory phenotype observed

P 017

Role of IL-1beta in the development of human TH17 cells: lesson from patients carrying NLPR3 gene mutations

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BACKGROUND: Interleukin 17 (IL-17)-producing CD4+ helper T cells (TH-17) represents a lineage of effectors CD4 T cells abundant at mucosal interfaces, where they contain infection with pathogenic bacteria and fungi. Beyond this function TH-17 cells have been linked to the pathogenesis of several inflammatory and autoimmune diseases. At present, understanding of Th-17 differentiation is limited to the mouse system and in humans as abremains still a puzzled issue. Recently it has been proposed IL-1 pivotal cytokine in driving Th-17 differentiation. Cryopyrin-associated periodic syndromes (CAPS) are a group of inflammatory diseases associated to mutations of NLRP3 gene encoding the inflammasome component cryopyrin. These mutations determine an exaggerated IL-1b secretion by monocytes upon Toll like receptors (TLRs) stimulation.
OBJECTIVE: We have investigated whether the altered IL-1b secretion, secondary to NLPR3 mutations, could affect the IL-23/IL-17 axis in CAPS patients.
METHODS: IL-17 serum level has been evaluated by ELISA assay. Expression of CCR6 and CD161, two TH-17 specific markers, has been analyzed on CD4+ memory T cells by flow cytometry Frequency of TH-17+ cells has been quantified upon stimulation with staphylococcus entherotoxin B (SEB). Production of IL-1β and IL-23 by monocyte derived dendritic cells (MoDCs), in response to TLRs lig-

ands, has been quantified by ELISA. CAPS patients have been analysed before and after anti-IL1β treatment.
RESULTS: Untreated CAPS patients display significant increased level of serum IL-17 as well as of Th-17+ T cells respect to age matched controls. Both IL-7 serum levels as well as Th-17 frequency decrease after IL-1β treatment. Also production of IL-1β and IL-23 by MoDCs is increased in CAPS patients, and after anti IL-1β treatment production of both cytokines is significantly reduced.
CONCLUSION: These findings further support a central role of IL-1β in the differentiation of TH 17 in human inflammatory conditions.

P 018
Characterization of tonsil infiltration and gene expression profile of Toll-like receptors in PFAPA patients

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INTRODUCTION: Periodic fever, aphthous stomatitis, pharyngitis (PFAPA) syndrome is a chronic disease classified in the group of autoinflammatory syndromes characterized by periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis in young children. The etiology of this disorder is still unknown. Palatine tonsils are sites where innate immunity leads to onset of the adaptive immunity, mediated by B and T lymphocytes. Toll-like receptors (TLRs), that are espressed in tonsil tissue are able to recognize conserved molecular structures on pathogens (PAMPs) and activate innate immune response.
AIM: This study aimed to investigate differences in leucocytes subpopulations and TLR gene expression of palatine tonsils cells and peripheral blood from patients with PFAPA.
METHODS: We have collected tonsil tissue and peripheral blood from two groups of pediatric patients undergoing tonsillectomy: PFAPA patients whose genetic testing excluded hereditary periodic fevers (HPFs) during flares and asymptomatic intervals (n=10), and patients undergoing to tonsillectomy due to recurrent bacterial tonsillitis (control group, CG) (n=10) .We performed staining of subpopulations on tonsils cells and tissues using flow cytometry and immunoistochemistry. We analysed TLR gene expression by quantitative real-time RT-PCR.
RESULTS: The histology of tonsils in PFAPA patients showed non specific chronic inflammation, characterized by lymphoid and follicular immunoblastic hyperplasia, focal histiocytic cluster, and hyalinizing fibrosis similar to that observed in CG. At cytofluorimetric analysis a wide range of subpopulations such as T and B cell subset, NK cells, DC cells, plasmacitoid DC cells, monocytes and neutrophils were variably expressed. Preliminary results showed an higher number of activated CD4+ and CD8+ T cells in PFAPA patients compared to CG. Moreover, we observed an increase of suppressive regulatory T cells (IL-7R-CD25hi Foxp3+) and NK cells in PFAPA patients with respect to CG. Tonsil cells expressed a broad repertoire of TLRs in both PFAPA and control group. The comparative analysis is ongoing.
CONCLUSIONS: Preliminary results indicate a possible activation and recruitment of T cells to secondary lymphoid organs in PFAPA patients, confirming the probable involvement of the adaptive immunity in the pathogenesis.

P 019
S100 calgranulin gene polymorphisms and JIA susceptibility

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BACKGROUND: Calgranulins comprise of three proteins, S100A8 (Calgranulin A, myeloid-related protein (MRP) 8), S100A9 (Calgranulin B, MRP14) and S100A12 (Calgranulin C, Enrage). They are calcium-binding proteins expressed by neutrophils, monocytes and activated macrophages. Serum levels of S100A8, A9 and A12 proteins are raised in JIA and a strong correlation with disease activity has been described. S100A12 remains elevated in JIA cases that go onto relapse and S100A8 protein has been described as a marker of subclinical inflammation in JIA cases that relapsed following cessation of methotrexate. S100A12 expression differentiates systemic onset JIA from other causes of fever of unknown origin. The genes for S100A8, 9 and 12 lie in a cluster on Chr1q21. No previous study has investigated SNPs in S100 calgranulin genes and JIA susceptibility.
METHODS: DNA was available for 1242 UK Caucasian JIA patients. The numbers genotyped per ILAR subgroup were: Systemic onset (n=179), persistent oligoarthritis (n=380), extended oligoarthritis (n=159), Rheumatoid factor (RF) negative polyarticular JIA (n=259), RF positive polyarticular JIA (n=76), enthesitis related JIA (n=74), psoriatic JIA (n=93) and unclassified (n=22). Pair-wise tagging SNPs were selected across the gene cluster (Chr1: 151596802-151637709, genome build 36.3) using an r2 cut-off ≥ 0.8 and MAF ≥ 0.1. SNP genotyping was performed using the Sequenom iPlex® MassARRAY platform according to manufacturers instructions. A 90% sample quality control rate and 90% SNP genotyping success rate was imposed on the analysis. Control samples genotype data was available from the Wellcome Trust case control consortium 2 (WTCCC2) (n=5380). Genotype and allele frequencies were compared between cases with JIA and controls using the Cochrane-Armitage trend test implemented in PLINK and allelic odds ratios (ORs) and their 95% confidence intervals (CIs) calculated.
RESULTS: This study had > 90% power to detect an odds ratio ≥1.3 for SNPs with MAF ≥ 0.1. The six SNPs genotyped resulted in 96% coverage across the 3 genes. No significant associations were seen with JIA as a whole; rs12119788 ptrend 0.46, rs724781 ptrend 0.18, rs3014875 ptrend 0.98, rs3014878 ptrend 0.92, rs3006485 ptrend 0.13 and rs6680386 ptrend 0.51. On subgroup analysis rs3006485 was found to be protective for systemic onset JIA (OR 0.6 95% CI 0.39-0.93, ptrend 0.02).
DISCUSSION: The S100 calgranulin genes are pro-inflammatory molecules that play important roles within the innate immune response. We find a weak association with protection from systemic onset JIA with a SNP 9Kb from the 5' end of the S100A12 gene. This finding requires independent replication. In addition, correlation of rs3006485 genotypes with S100A12 protein expression needs to be undertaken.

P 020
An exploration of biomechanical foot function in Juvenile Idiopathic Arthritis (JIA)

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INTRODUCTION: Foot and ankle disease has previously been associated with impairments and disability in Juvenile Idiopathic Arthritis [1], and altered gait patterns have been described [2] . However, the extent to which disease-related foot impairments impact on localised biomechanical foot function remains unknown.
OBJECTIVES: The aim of this study was to compare disease activity, foot function and gait characteristics between patients with JIA and healthy participants using standard clinical metrics, musculo-skeletal ultrasound (US) and instrumented gait analysis techniques including a novel 7-segment foot model.
METHODS: 14 JIA patients with a history of foot disease and 10 healthy controls were recruited. The Juvenile Arthritis Foot Disability Index (JAFI) and CHAQ were completed by each participant. US scores for effusions and synovial hypertrophy, tender/swollen foot joint counts, and Structural Index (SI) fore- and rear-foot deformity scores were recorded to assess localised disease activity, impairments and disability status. Each participant underwent 3D gait analysis, plantar foot pressure and spatio-temporal gait evaluation at one single time point. Mean differences between the groups and 95% confidence intervals (CI) were calculated for core variables using the t distribution. For core inter-segment kinematic variables, statistical outliers greater than 2 standard deviations from the normal group mean were identified and displayed graphically using a colour-coded reference scale [3].
RESULTS: In the JIA group there were low but variable levels of localised disease activity indicated by low median (range) scores for tender [0 (0-4) and 0 (0-5)], and swollen foot joints [0 (0-3) and 0 (0-3)], and US effusions [2 (0-6) and 3 (0-7)] and synovitis [0 (0-3) and 0 (0-2)] for left and right feet respectively. Mild to moderate foot related impairments [JAFI median (range); 1 (0-3)] and foot deformity scores [SI forefoot; 2 (0-7) left, 0.5 (0-5) right, rearfoot; 2.5 (1-5) left, 3.5 (2-5) right] were observed. No significant differences were observed between group means for all core variables except right peak mid-foot dorsi-flexion [mean (95% CI) difference -3.04° (-5.79, -0.30)]. There were trends towards reduced walking velocity [mean difference 7.81cm/s (-8.26, 23.88)], greater variability in mid-foot contact area [mean (SD) 19.77 (11.63) left, 19.04 (12.27) right JIA group versus 19.31 (5.29) left, 19.01 (4.46) controls], and lower peak forefoot pressures in the JIA group [mean difference 59.33 (-58.38, 177.03) kPa left, 13.36 (-121.02, 147.73) kPa right].
CONCLUSIONS: At the group level, foot function was normal in these JIA patients despite moderate levels of self reported impairment and disability. However, at the individual level detailed changes in foot function were detected, particularly related to flat-footedness or highly arched foot types (see fig1). Preliminary findings suggest that these foot types may be associated with various combinations of abnormal foot segment rotations. Further study is required to identify abnormal foot biomechanics in clinically meaningful homogeneous subgroups of JIA patients. 3D gait analysis appears to be a feasible technique with good patient acceptability and face validity for measuring foot function in JIA.
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Figure 1. Control group mean ±1SD versus individual outliers with JIA.

P 021

Immune response to influenza vaccination in children treated with methotrexate and/or tumor necrosis factor-alpha inhibitors

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INTRODUCTION: In children treated with methotrexate (MTX) and/or tumor necrosis factor-alpha (TNF-alpha) inhibitors, immunization is recommended due to greater risk of infections. It is still unclear if adequate antibody response to vaccinations can be achieved.
METHODS: In a prospective open label study, we assessed seroconversion and seroprotection after influenza vaccination during 2 seasons (6 different strains) in 36 children treated either with MTX (n=18), TNF-alpha inhibitors (n=10) oder both (n=8) and a control group of 16 immunocompetent children. In season 2007/2008, we included 31 children in the therapy group and 10 in the control group, in season 2008/2009 15 resp. 6 children in therapy resp. control group. Ten children of the therapy group were vaccinated as well in 2007/2008 as in 2008/2009. Influenza antibody titres were determined by haemagglutinin inhibition assay, before and 4-8 weeks after vaccination.
RESULTS: Pre-vaccination seroprotection titre ≥1:40 of ≥2 of 3 influenza strains) was present in 42% of the treatment group and 30% of the control group in season 2007/2008 and 33% resp. 50% in season 2008/2009. After vaccination, a protective titre was achieved in 87% of the treatment group and 90% of the control group in season 2007/2008 and 73% resp. 83% in season 2008/2009. Seroconversion was defined as the change from a negative titre(<1:40) to a protective titre (>1:40) with at least a 4-fold titer increase. This was documented in 57% resp. 50% (B strain), 46% resp 75% (A/H3N2 strain) and 58% resp. 80% (A/H1N1) in the treatment group resp. control group in season 2007/2008 and 50% resp. 67% (B strain), 44% resp. 60% (A/H3N2 strain) and 67% resp. 100% (A/H1N1 strain) in season 2008/2009. Safety evaluation of vaccination showed no serious adverse events.
CONCLUSION: -inhibitors can be safely and effectively immunized against influenza. Children under MTX and/or TNF-

P 022

The experience of young people with Juvenile Idiopathic Arthritis who have been transferred from Paediatric to Adult services

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BACKGROUND: Of patients with Juvenile Idiopathic Arthritis (JIA) at least one third will have active inflammation as adults requiring transfer to an adult rheumatology service.
There is an acknowledged need for adolescent transition but it has been suggested that even with the presence of an established transition programme there is no guarantee of successful transfer.
At Starship Children's Hospital, in Auckland New Zealand, there is no formal transitional care program and prior to this study little was known about the challenges young people with JIA face as they move from a paediatric to an adult setting. We therefore undertook a qualitative study to elicit adolescent's views in relation to the experience of transfer.
OBJECTIVES: To identify the factors that facilitates or challenges the transfer of young people with JIA from paediatric to adult services.
METHOD: A descriptive qualitative study was undertaken. Data was collected via a semi-structured focus group interview with 8 young people with JIA , who had recently transferred from paediatric to adult rheumatology service. Interviews were tape-recorded and transcribed verbatim. Data was analysed using thematic analysis.
RESULTS: The study identified three themes which describe young people's perception of the transfer process. It's time to move on signalled the young person's readiness for transfer. Preparing for transfer described the process of getting ready to move and Blending in indicated their arrival and adjustment to adult services.
CONCLUSIONS: This study indicates that when a young person signals readiness for transfer, a transparent and individualised process needs to be put in place. The need for details surrounding the adult setting was essential and emphasized that adult rheumatology services need to allow time for the young person to adjust and integrate into the new environment.
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P 023

Clinical and ultrasound (US) assessment of foot disease in juvenile idiopathic arthritis (JIA): interobserver agreement between a paediatric rheumatologist, podiatrist and a sonographer

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BACKGROUND: The use of US for the assessment of inflammatory joint disease is increasing in popularity. Recent studies have demonstrated that subclinical synovitis is common is children with JIA [1], and frequent discordance has been reported between clinical and US findings, particularly in the tendons and small joints of the feet [2,3].
OBJECTIVES: To compare clinical evaluation by a paediatric rheumatologist and podiatrist, and US evaluation of articular and peri-articular foot disease in JIA.
METHODS: Thirty patients with JIA and a history of foot disease underwent clinical examination of 24 foot joints (2 ankle, 2 subtalar, 10 metatarso-phalangeal; MTP and interphalangeal; IP joints) by the paediatric rheumatologist and podiatrist. Joints were assessed for the presence of absence of active synovitis by the rheumatologist, and tenderness and swelling by the podiatrist. In addition 10 tendons (2 tibialis posterior, flexor digitorum longus, flexor hallucis longus, peroneus brevis and longus tendons), and 6 other soft tissue sites (2 Achilles tendon calcaneal insertions; TA, retro-calcaneal bursae; RCB, plantar fascia calcaneal origins; PF) of the feet were assessed independently for tenderness and swelling by the podiatrist. The same assessment sites were evaluated independently by a trained sonographer for the presence or absence of effusion, synovial hypertrophy, power Doppler signal (PS), tenosynovitis, or abnormal tendon thickening as appropriate. The level of agreement between each clinical and US feature was estimated using Cohen's unweighted kappa (κ) (>0.4 = moderate agreement) with corresponding 95% confidence intervals.
RESULTS: 720 joints, 300 tendons and 180 soft tissue sites were assessed. Clinically detected synovitis, tenderness and swelling were recorded in 42 (5.8%), 78 (10.8%) and 73 (10.1%) joints respectively. US-detected effusions, synovial hypertrophy and PS were recorded in 88 (12.2%), 47 (6.5%) and 12 (1.7%) joints respectively. Ankles and subtalar joints were most frequently affected clinically and on US. Clinically detected tenderness and swelling were recorded in 29 (9.7%) and 16 (5.3%) of tendons and 28 (15.6%) and 9 (5%) of soft tissues respectively. US-detected tenosynovitis and PS were detected in 7 (2.3%) and 6 (2%) tendons. Abnormal thickening of the PF origin and TA insertion were detected at a frequency of 4/60 (6.7%) and 1/60 (1.7%), and 3/60 (5%) effusions were recorded at the RCB. Subclinical foot disease was found in 52 (7.2%) joints, 5 (1.6%) tendons and 4 (2.2%) soft tissue sites. Agreement was consistently less than moderate (κ<0.4) for each clinical and US interaction **(see figure 1).** There was moderate agreement between the rheumatologist and podiatrist for active synovitis versus joint swelling. Disagreement was greater for interactions with the podiatrist assessment of joint, tendon and soft tissue tenderness.
CONCLUSIONS: There is frequent discordance between clinical and US assessments of foot disease in JIA. Subclinical foot disease appears to be common; however clinical examination also detected features of active disease in structures that were recorded as normal on US examination. Further research comparing clinical examination, US and magnetic resonance imaging are required in order to optimise the evaluation of foot disease in JIA.
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P 024

At risk: health related quality of life in children and adolescents with JIA

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BACKGROUND: In the Netherlands the estimated prevalence of children with Juvenile Idiopathic Arthritis (JIA) is about 4000 children with yearly around 300 new patients. These children experience functional impairment due to joint manifestations of the disease, morning stiffness and fatigue. Based on previous studies, children with JIA seem to have lower Health Related Quality Of Life (HRQOL) scores compared to their healthy peers. However, comparison between studies is hampered because of heterogeneity of age cohorts, recruitment protocols and differences in national health care systems.

OBJECTIVES: To investigate HRQOL in JIA patients by the use of Patient Reported Outcomes (PROs) in outpatient daily clinical practice
METHODS: This study is part of the 'KLIK study', which assesses the effect of identifying and discussing HRQOL problems using PROs. Patients or parents (of children 6-7 years) are invited to complete questionnaires online, at home, before visiting the rheumatologist. HRQOL is measured using the Pediatric Quality of Life Inventory 4.0 (Pedsql 4.0), which assesses four domains of HRQOL; physical health, emotional, social and school functioning. Also a total and psychosocial sum score are included. The study sample includes all JIA patients (6-18 years) visiting four pediatric rheumatology outpatient clinics in Amsterdam in the period February 2009 until March 2010. For analysis, the study sample is compared with healthy controls and a chronic health condition using one sample t-tests. Effect sizes are calculated by dividing the difference in mean score of children with JIA and the healthy sample with their pooled SD.
RESULTS: Approximately 70% of the eligible patients participated (n=157). Data of 14 children aged 6-7 years (mean 7.1 yrs), 63 children aged 8-12 years (mean 10.9 yrs) and 78 adolescents aged 13-18 years (mean 15.9 yrs) were available for analysis. Both children (8-12) as well as adolescents (13-18) with JIA differed on almost all domains significantly with healthy controls and children with a chronic health condition. Effect sizes were moderate to large, with the exception of emotional functioning **(table 1)**.
CONCLUSIONS: HRQOL is severely affected in children and adolescents with JIA. Children with JIA report significant impairments in physical health, emotional, social and school functioning. These findings underline the need to systematically pay attention to HRQOL in clinical daily practice and to investigate the effectiveness of HRQOL feedback to the pediatric rheumatologist.

P 025
Nutritional status of children with juvenile idiopathic arthritis

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BACKGROUND: A review of studies published 1986-2008, concerning nutritional status of children with juvenile idiopathic arthritis (JIA), indicated that reduced muscle mass, growth retardation and lack of specific nutritional components occur and there were differences between the subgroups of JIA.
OBJECTIVE: The aim of this study was to investigate the nutritional status of children with JIA based on anthropometric and bioelectrical impedance measurements.
METHODS: A total of 46 patients with JIA aged 5-15 attending the Department of Rheumatology, Rikshospitalet, Oslo University Hospital, were included in this study. Eleven patients had oligoarticular arthritis, 20 had polyarticular or extended oligoarticular arthritis and 15 had systemic arthritis. Z-scores for height and BMI relative to the age and sex specific reference population from the World Health Organisation (WHO) were estimated, and the mid arm circumference was assessed. Total body water, fat mass, fat free mass and muscle mass was estimated, based on bioelectrical impedance measurements.
RESULTS: Children with systemic JIA had significant higher standardized BMI than both children with polyarticular and oligoarticular JIA ($p<0.001$). In a multivariate linear regression model disease category and current use of corticosteroids explained 21% of the variation in standardised BMI. When controlled for the use of corticosteroids, the systemic group was significantly different from the polyarticular group. Children with systemic JIA tended to have lower z-score for height than children with oligoarticular JIA, but the difference was not significant ($p=0.06$).
CONCLUSIONS: The study showed a high BMI in the group with systemic arthritis and a tendency of low BMI for children with polyarticular arthritis. Clinicians should be aware of the nutritional challenges among children with JIA. Larger studies of both undernutrition and overweight in JIA are needed.

P 026
Combination therapy with rituximab and cyclophosphamide in two girls with refractory lupus nephritis

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INTRODUCTION: Despite an increasing armamentarium of immunosuppressive agents, there is still a significant morbidity and mortality associated with childhood-onset systemic lupus nephritis. The ideal therapeutic strategy for children and adolescents with SLE should provide the right amount of tretment to allow normal growth, development and fertility while reducing the disease activity and damage that can be accured over the years. Modern therapeutic strategies include reduced doses and use of corticosteroids and intravenous cyclophosphamide respectively, with increased use of azathioprine, MMF and, more recently, rituximab.
MATERIALS AND METHODS: Two female patients, 12 and 13 years old at the beginning of treatment, with active lupus nephritis that were resistant to standard immunosuppressive agents (corticosteroids and mycophenolate mofetill), were treated with Rituximab (R) 700mg/m2 (max 1g) and ciclophosphamide (C) 750mg/m2, during the 12 months period, according to experimental protocol for class IV glomerulonephritis in patients with SLE. Patients had three cycles of R+C administered two times in two week period. First cycle was at the beginning of treatment. After that followed the four months induction therapy with C administred every one month, after which followed second cycle of R+C. Third cycle of R+C followed after six months. Clorpheniramin, paracetamol and methylprednisolone were given prior to rituximab administration, and before and after cyclophosphamide administration we used ondansteron and mesna. Both patients underwent complete clinical investigation including kidney biopsy before, during and after treatment. Global disease activity measure scores were obtained at the time of each visit, as measured by the European Consensus Lupus Activity Measure (ECLAM), the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), or the Systemic Lupus Activity Measure (SLAM).
RESULTS: Prior to treatment one patient had Class IV active LN, and other class IIIa. After the treatment one patient had class IIIc, and another class V, subsequently. We also recorded decrease in values of disease activity measures, for both patients. Prior to treatment one patient had ECLAM 10.5, SLEDAI 39 and SLAM 13. After the treatment all the scores were 0. Another patient prior to treatment had ECLAM 11, SLEDAI 41 and SLAM 14. After the treatmen ECLAM was 0,5, SLEDAI was 4 and SLAM was 1. No serious side effects or effects on growth and development were recorded.
DISCUSION: Before the treatment our two patients had very active kidney disease with lower values of GF, proteinuria, immune complex deposition, crescents, endocapilar proliferation, etc. After the combined treatment active disease was converted to chronicity, with almost no activity, either in kidney or serology.
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P 027
Croatian expiriences in treatment of juvenile idiopathic arthritis with biological agents

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AIM: Our aim was to assess long-term efficacy and tolerability of etanercept and infliximab in patients with JIA who had experienced an inadequate response to standard therapy of JIA in the routine care setting.
MATERIALS AND METHODS: This was an observational, retrospective study of 38 patients treated with anti-TNF therapy in two tertiary pediatric rheumatology centers in Croatia between 2005 and 2009. Seventeen patients were treated with etanercept, fourteen with infliximab and seven patients were switched from one medication to the other due to the lack of efficacy. Infliximab was administered as an intravenous infusion (3-5 mg/kg, loading dose + q 6 wks) and etanercept as subcutaneous injection (0.4 mg/kg twice a week, or 0.8 mg/kg once a week). Data on age, gender, diagnosis, duration of disease, and duration of the therapy were recorded. At the beginning of the therapy, after 6 months, after 12 months, as well as after 2 years Core Set Criteria for improvement in Juvenile Idiopathic Arthritis was gathered, and DAS28 and JADAS-71 were calculated. Some patients with hand involvement underwent radiographic imaging of wrist before the beginning of the therapy, as well as after 24 weeks. Images were scored according to the modified SHARP criteria by experienced radiologist in the field
RESULTS: Twenty-four weeks after the beginning of therapy 35 patients (92.1%) achieved ACR 20, 33 patients (86.8%) ACR 30, 31 patients (81.6%) ACR 50, 28 patients (73.7%) ACR 70 and 20 patients (52.6%) ACR 90. In the same period of time 19 patients (50%) had good DAS28 response, 12 patients (31.6%) had moderate response, and 5 patients (13.2%) did not respond to therapy. Statistically significant difference was shown in the average value of JADAS-71 before the beginning and 24 weeks after introduction of anti-TNF therapy; JADAS-71 dropped from 19 to 4.71 ($P<0,0001$). Flare had 11 patients (28.9%). After twelve months 15 patients fulfilled criteria for clinical remission on medications. Eleven patients have fulfilled criteria for clinical remission off of medications. In patients with polyarticular JIA (n=9) we found no statistically significant difference between modified SHARP score before and after 24 weeks of anti-TNF therapy ($P=0,5715$). We recorded serious adverse events in only two patients. One girl developed osteomyelitis six months after beginning of therapy with etanercept. Another patient developed reactivation of EBV infection, splenomegaly and hypersplenism after 9 months on etanercept.
DISCUSSION: Our study describes the experience of the two major pediatric rheumatology tertiary centers in Croatia with anti-TNF therapy in JIA patients. Although significantly improved in recent years, the outcome for children with JIA

is still far from ideal. Early, aggressive control of inflammation is essential in order to prevent long-term disability. For those children that are resistant to standard therapy, the introduction of biologic therapy offers new hope.
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P 028
Sedation for intra-articular corticosteroid injections in juvenile idiopathic arthritis: the views of patients and their parents

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BACKGROUND: Intra-articular corticosteroid injections (IACI) are one of the mainstays of treatment for children with juvenile idiopathic arthritis (JIA). The most important disadvantage of IACI is the pain associated with the procedure. Little is known about the children or parents' perception of this pain.
OBJECTIVE: To determine whether patients and their parents prefer sedation to receive IACI or not and why.
METHODS: A questionnaire was presented to patients and/or their parents from January to March 2010. It consisted of 4 questions on the choice of anesthesiologist-controlled deep sedation vs no sedation-no local anesthesia and the reasons for it. All participants had experienced the 2 options. In addition, there were 2 visual analogue scales (VAS) to evaluate pain associated with blood draws and IACI respectively. Clinical data were collected from patients' medical records.
RESULTS: 45 patients and their parents responded to the questionnaire. There were 34 females (75.6%), the mean age was 10.2 ± 4.2 years and the mean duration of the disease was 7 ±3.9 years. Mean VAS score was 2.4 ±2.8 for pain associated with blood draws and 6 ±3.1 for IACI. The graph shows the preferences of parents and patients and their reasons.
Children who preferred sedation for IACI were younger (p=0.02) and had a shorter course of disease (p=0.01).
CONCLUSIONS: While most children prefer to receive IACI under sedation, a majority of parents prefer to avoid its risks. Children who prefer IACI without sedation are significantly older and have a longer course of disease.
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P 029
Norwegian children with juvenile idiopathic arthritis (JIA) have the same level of physical activity as healthy children

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BACKGROUND: Children with JIA are reported to be less physical active than their healthy peers. Recent evidence concludes that physical activity and exercise are safe for children with JIA, and do not increase the inflammation process. Based on results from previous published studies there are no restrictions regarding physical activity for children with JIA and the children are encourage to participate in physical activity at the same level as their peers.
OBJECTIVE: The main purpose of this study was to compare the level of physical activity in Norwegian children with JIA with healthy children without any known diseases.
METHODS: The level of physical activity was measured by a self-administered questionnaire in children with JIA and healthy children. The questionnaire consists of 18 questions measuring the amount and intensity of physical activity within the last week. The total amount of minutes per day with moderate to vigorous physical activity (MVPA) is then calculated. MVPA is defined as activities with intensity above 3 METs (Metabolic Energy Turnover). The disease subtype and number of active joints (measured by active joint count) were registered in the children with JIA
RESULTS: A total of 35 children with JIA were included in the study (mean ± SD age 12.5 ± 1.6 years).They were compared to a normative sample consisting of 217 healthy children (mean ± SD age 11.4 ± 1.1 years). In the JIA group, 18 children were diagnosed with polyarticular JIA, 14 with oligoarticular JIA and 3 with systemic JIA. In 26 children there was no sign of disease activity (measured by active joint count), while in 9 children disease activity was measured in 1 or 2 joints. The children with JIA had the same level of daily MVPA as the healthy children, 78 minutes ± 63 minutes and 77 minutes ± 35 minutes, respectively. The public health recommendations of ≥1 hour daily moderate to vigorous physical activity were met by 51 % of the children with JIA compared to 70 % in the reference group. There was a wide range in the level of MVPA within both groups, especially in children with JIA.
CONCLUSIONS: Children with JIA have the same level of daily physical activity as healthy children. This is not in agreement with a previous study, which reported that Dutch children with JIA are less physical active than healthy children. A higher proportion of the healthy children compared to the children with JIA met the public health recommendations for daily level of physical activity. However, the mean level of MVPA was the same in the two groups, indicating that the level of physical activity varies to a greater extent in children with JIA. It is important to increase the percentage of children with JIA meeting the public health recommendations of daily physical activity.

P 030
Development and preliminary validation of a wrist ultrasound scoring system for the assessment of disease activity and damage in JIA: a comparison with MRI and clinical examination

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BACKGROUND: Musculoskeletal ultrasound (US) has emerged as a tool with the potential to enhance disease assessment and management in patients with inflammatory arthritis. Standardized scanning methodology and validated scoring system are warranted in order to use US for quantifying pathological features and monitoring therapy in JIA.
OBJECTIVES: To devise a wrist US scoring system for the assessment of disease activity and damage in JIA, and to test its construct validity.
METHODS: The US score was devised by a consensus between pediatric rheumatologists and radiologists, and tested in JIA patients with wrist involvement seen at the study Unit between 2007 and 2009. All the patients performed on the same day US, conventional radiography and MRI of the most affected wrist, coupled with standard clinical assessment and biochemical analysis.
RESULTS: 114 US examinations were included in the study. Gray-scale US (GSUS) revealed synovitis in 86.8% of patients, while power Doppler US (PDUS) in 41.4%. Extensor tenosynovitis was observed in 40.5% ,while flexor tenosynovitis in 25.6% of the patients.
As reported in the table GSUS synovitis score showed weaker correlation with measures of disease activity compared with PDUS synovitis score; there were no significant correlation between US erosion score and conventional measures of damage. A statistically significant relationship between extensor and flexor tenosynovitis scores and clinical markers of disease activity was found.
Agreement between US and MRI was moderate for synovitis (ICC 0.55) and tenosynovitis (extensor tendons: II Cohen's k =0.5, IV k= 0.55, VI k =0.37 and flexors k= 0.39). Very poor agreement was found between US and MRI in depicting bone erosion (Cohen's k ranged from 0 to 0.21). With MRI as the reference method, the sensitivity/specificity of GSUS in detecting synovitis was 0.86/0.39 for radiocarpal, 0.51/0.86 for radioulnar and 0.76/0.67 for midcarpal joints. The specificity of PDUS was excellent (all values >0.95) in all joint recess; an substantial specificity (all values >0.80) of US was found for all the extensor tendons (II, IV and VI) and flexors; less satisfactory values were observed for sensitivity. Conclusions: Our results indicate that the proposed US scoring system is a valid method for assessing disease activity in patients with JIA. We demonstrated the value of the proposed US score in detecting and grading synovitis and tenosynovitis against comparator such as MRI. PDUS had the potential to improve the specificity of US in inflammation assessment. The US score was not suitable for the assessment of structural damage.
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P 031
Anti-infliximab antibodies in pediatric patients with rheumatic diseases treated with infliximab

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OBJECTIVES: To investigate the anti-infliximab-antibody response in pediatric patients receiving infliximab for juvenile idiopathic arthritis and other pediatric rheumatic diseases and use epitope mapping to analyze the binding sites of these antibodies.

METHODS: A total of 111 serum samples were tested from 21 pediatric patients (mean age 11 years, range 4-18 years) who were receiving infliximab for the treatment of rheumatic diseases. We used ELISA-based assays to measure the serum through levels of infliximab, the serum levels of anti-infliximab antibodies and the ability of the anti-infliximab antibodies to inhibit the binding of infliximab to tumour necrosis factor. Additionally, we used overlapping synthetic peptides covering both infliximab variable domains in an effort to analyze the epitopes of the anti-infliximab antibodies.
RESULTS: Anti-infliximab antibodies developed in 43% of patients receiving infliximab therapy. All of the serum samples that tested positive for anti-infliximab antibodies also tested negative for infliximab, indicating an inverse relationship between the trough serum levels of infliximab and the levels of anti-infliximab antibodies.. Neutralization studies showed that in all of these patients, the antibodies were directed towards the variable domains of infliximab, as they inhibited binding of infliximab to tumor necrosis factor. A more precise determination of the antibody epitopes using synthetic peptides was not achieved, indicating that all of the antibody binding sites were composed of discontinuous segments of infliximab.
CONCLUSIONS: The formation of anti-infliximab antibodies was invariably associated with the formation of neutralizing antibodies that are most likely the cause of the decrease in infliximab efficacy in these patients.

P 032
Sulfasalazine in patients with juvenile idiopathic arthritis – a single centre experience

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Some forms of juvenile idiopathic arthritis (JIA) are known not to be associated with any autoimmune phenomena. There are also data establishing a pronounced arthritogenic effects in JIA of some enteropathogenic bacteria. These facts suggest that probably some patients require an anti-inflammatory rather than an immunosuppressive treatment. The mode of action of sulfasalazine (SSZ) was shown as combining: anti-inflammatory, bacteriostatic and uncertain immunosuppressive effects.
OBJECTIVE: The aim of this study is to determine the clinical efficacy of SSZ in JIA patients with negative ANA and IgM- RF after one year treatment, based on the ACR clinical remission criteria or ACR Pedi 100.
PATIENTS AND METHODS: 132 JIA patients (56 with persistent oligoarthritis,3 with extended oligoarthritis, 14 with IgMRF- negative polyarthritis, 55 with enthesitis- related arthritis and 4 with psoriatic arthritis) aged 2-17 years with mean duration of the disease 12.8 months have been enrolled in the 1-year follow-up study. All eligible patients had negative routine tests for ANA, dsDNA and IgMRF. Thirty two patients (24%) had positive HLA-B27 antigen. The majority of patients 114 (86.4%) had not been treated prior the study except with NSAIDs. All patients had active disease with at least 1 active joint and mean values of ESR- 32.46 mm and CRP -26.47 mg/l. All patients have been examined every 4 weeks over the study period. Disease activity measures were recorded at the 3rd, 6th month and at each follow-up visit after that until the 12 month.
RESULTS: At the 6th month 129 patients (97.7%) achieved at least ACR Pedi 30 response. At the end of the study 97 patients (73.3%) achieved ACR Pedi 100 or clinical remission. The treatment was discontinued in 5 (3.8%) patients due to the lack of efficacy or adverse reactions. The most beneficial outcome was associated with the persistent oligoarthritis (p=0.001), followed by the IgMRF-negative polyarthritis (p=0.042).
CONCLUSIONS: Our results showed that SSZ is an effective drug for treatment with a high remission rate and improvement at the and of the first year in JIA patients not expressing laboratory autoimmune phenomena. This is probably due to the anti-inflammatory effect of the drug and suppression of suggested autoinflammatory mechanisms in some patients.

P 033
Safety and efficacy Tocilizumab therapy in children with juvenile idiopathic arthritis

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OBJECTIVES: To evaluate safety and efficacy of tocilizumab treatment in children with juvenile idiopathic arthritis (JIA).
METHODS: A retrospective observational study on JIA patients taking tocilizumab (n=16, patients with polyarthritis – 1, systemic arthritis – 15). Tocilizumab was administered intravenously at a dose of 8 mg/kg every 2 weeks (n=12) and 4 weeks (n=4). All patients received DMARDs. Efficacy end points included the American College of Rheumatology (ACR) Pediatric 30 (Pedi 30), Pedi 50, Pedi 70, and Pedi 90 criteria for improvement.
RESULTS: A total of 16 patients (8 boys and 8 girls) were included in this Median age was 7 years (range; 3 to 14 years) and median disease duration was 4,2 years (range; 0.5 to 9 years). A total of 4 of the 16 patients (25%) entered the fifth month of continuous tocilizumab treatment. The frequently observed non-severe adverse events were nasopharyngitis, upper respiratory tract infection and gastroenteritis. No cases of opportunistic infections, malignancies, autoimmune diseases, or death were reported. 6 patients had incidences of reversible grade 3 neutropenia.The ACR Pedi 30, 50, 70 and 90 were achieved by 82%,47%, 29% and 12% of patients at Week 4, and by 100%, 75%, 56%, and 13% of patients at Week 8 (N=16), respectively. At week 16 ACR pedi 30, 50, 70, 90 were achieved by 100%, 100%, 83%, 33% of patients (N=6). During the treatment, 2 patients reduced doses (< 50%) of corticosteroids at Week 8.
CONCLUSION: Clinical improvements in the signs and symptoms of systemic JIA were also achieved in favorable levels in tocilizumab in the treatment of children with JIA.

P 034
Performance of Tuberculin Skin Test and Interferon Gamma Assay for the diagnosis of Latent Tuberculosis Infection in Juvenile Idiopathic Arthritis

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OBJECTIVES: The objective of this prospective cross-sectional study was to compare a M.tuberculosis –specific IFN-γ ELISA (QFT-TB Gold In Tube) test with a classic TST for detection of LTBI in patients with juvenile idiopathic arthritis (JIA).
To our knowledge, this is the first study evaluating the performance of QFT-G in comparison with TST in JIA.
METHODS: A cross-sectional study of 39 children with JIA and 40 healthy controls (2 to 17 years of age) was conducted in İzmir, Turkey. Blood was for drawn for the QFT-TB Gold In Tube assay prior to administration of the TST using 5 TU of RT 23 purified protein derivative. A positive TST was defined as ≥10mm for JIA and ≥ 15 mm for controls.
RESULTS: There were no significant differences between JIA patients and controls for age, sex, bacillus Calmette-Guerin vaccination. 70% of patients had active JIA disease. TST detected significantly less LTBI among JIA (%49) patients than controls (72.5). The median TST enduration was 5,8 mm (±5,7mm) in JIA and 10,7 mm (±4,5mm) in the control group The percentages of patients who showed no reaction to TST was 38%, and 93% were in active disease. Negative correlation was found between TST and erythrocyte sedimentation rate (ESR) in the study group (r=-0.325, p=0,044). One of the two patients who have positive IFN-γ results but negative TST was systemic type, other one had polyarticular type JIA. Overall agreement between TST and QFT-G was low both in JIA concordance 18/39 (% 46) (k value=0.019) or control group concordance 12/40 (%30)(k value=0.10).
CONCLUSION: In a TB-endemic population, the Quantiferon-TB Gold In Tube assay seemed to be a more accurate test for detection of LTBI in JIA patients compared with the TST. The IFN-γ assay may be useful to identify false-negative TST response of latent Mycobacterium tuberculosis infection in juvenile idiopathic arthritis.
KEY WORDS: Juvenile idiopathic arthritis, latent tuberculosis, tuberculin skin test, Quantiferon TB Gold

P 035
Anti-TNF agents for the treatment of JIA-related Refractory Uveitis: 2010 UPDATE from the Italian Registry

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BACKGROUND: Uveitis is an uncommon but serious manifestation of juvenile idiopathic arthritis (JIA) with the potential for significant sigh-threatening ocular complications. Since 2007 an inception cohort registry, reporting all patients with JIA-related uveitis treated with anti-TNFα agents, have been established in Italy.
OBJECTIVES: To report the results on safety and efficacy of anti-TNFα treatment in refractory uveitis, associated to JIA.

METHODS: A multicenter Italian cohort of children treated with anti-TNFα agents for refractory JIA-related uveitis between January 2007 and December 2009 were followed by a standardized protocol. Uveitis course including structural complications, type and dosage of anti-TNF agents used, tapering of steroids and side effects have been analysed at the beginning of treatment, after one, two and three years follow-up (F/U). Descriptive statistics, absolute and relative frequencies have been reported.
RESULTS: Up to December 2009, 98 patients (79 female, 19 male) have been included in the registry, mean age 10.4 years, mean follow-up 16.1 months. All patients failed previous traditional immunosuppressive treatments (MTX, CyA, MMF). Fifty patients were initially treated with adalimumab (ADM), 48 with infliximab (IFX). Fourteen patients (14.3%) experienced drug shift during treatment: 12 from IFX to ADM due to infusion reactions or inefficacy; two patients shifted from ADM to IFX and Abatacept, respectively. The mean IFX dosage was 4.7 mg/kg (range 2.7-6.0), the mean ADM dosage was 1.0 mg/kg (range 0.1 -1.3 mg/kg). Sixty subjects (61.2%) had at least one year F/U, 30 (30.6%) at least two years F/U. Side effects have been reported in 12 patients (12.2%) including, during IFX treatment, headache (3), infusion reactions (3), irritability (1), recurrent upper respiratory tract infections (4), and, during ADM treatment, site injection reactions (2), urticarial rash (1), hypertransaminasemia (2), HZV infection (1). Structural complications were present, at the treatment start, in 23 (38.3%) out of 60 subjects with at least one year F/U: cataract (25.0%), vitreitis (21.7%), cystoid macular edema (10.0%) and ocular hypertension (8.3%). After one year of anti-TNF treatment, structural complications disappeared in 8 patients (34.8%) and only 3 patients (5%) developed new complications.
CONCLUSIONS: Anti-TNF agents, namely IFX and ADM, appear to be effective and safe, at a short-medium term, for the treatment of refractory JIA-related uveitis. National registries represent important innovative instruments to improve the quality of the clinical research and to address safety issues for the health regulatory agencies.

P 036
Experience in the treatment with etanercept in patients with juvenile idiopathic arthritis under 4 years

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BACKGROUND: Therapy with etanercept (ETN) is approved by the AEMPS, EMEA and FDA in Juvenile Idiopathic Arthritis (JIA) Polyarticular older than 4 years, non-responders to Methotrexate (MTX). The efficacy and safety of ETN in children under 4 years is not clearly established.
OBJECTIVES: To evaluate the efficacy and safety of ETN in JIA patients under 4 years.
PATIENTS AND METHODS: A total of 16 children with polyarticular JIA non responders to MTX under 4 years were given ETN. All parents signed informed consent. Epidemiological data were considered, age at diagnosis of the disease and initiation of treatment, duration and concomitant therapy. ETN was administered at a dose of 0.8 mg / kg / week. Efficacy was assessed using the ACR improvement criteria pedi-30, 50, 70 and 90.
RESULTS: A total of 16 children (10 girls and 6 boys) with a mean age of 20.1 months (15-42). Forms of JIA: 11 (68%) patients had polyarticular RF negative, ANA +; 2 (12.5%) extended oligoarthritis, ANA +; 2 (12.5%) systemic onset polyarticular and 1 psoriatic polyarticular ANA +, RF negative. All patients received methotrexate (MTX) and corticosteroids. The average age of onset of ETN was 29 months (21-45) and the average duration of the treatment of 13.12 months (1-42). As shown in Figure 1, all patients achieved ACR-Pedi-50 in the 6th month of treatment. Two of the patients had been treated with ETN three months, so why not included in the efficacy analysis at 6 months. The average number of active joints at the beginning of was ETN 11.7 (8-20) and limited joint 0.74 (0-2). The start ESR rate was 60.8 mm/hour (48-78), CRP 47.4 mg/dL (30-80), Hb 10.9 g/dL (10.2 to 12.9) and serum iron 45.57 mcg/dl (13-93). One patient discontinued treatment after 45 months in remission. 2 patients relapsed (14%) between 8-12 months. Were detected during follow-up of infectious processes in 4 patients (25%): 2 IRS with a fever that did not require interrupting ETN, a pneumonia that not required hospitalization, an infection by Varicella and 1 uncomplicated anterior uveitis. Showed no serious adverse events.
CONCLUSIONS: It should be noted as characteristic of this group of pediatric patients with polyarticular JIA children under 4 years, the high number of active joints compared to the low number of joints limited, the moderate increase in acute phase reactants and the presence of iron deficiency anemia. ETN acted as an effective treatment without serious adverse effects found, so it should be considered as a therapeutic alternative in the non-responder to standard treatment.
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P 037
Psychological Treatment of adolescent with fibromyalgy

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OBJECTIVE: Identify the main components of the psychological therapy with teenagers with a diagnostic of fibromialgy.
MATERIAL AND METHOD: From the Rheumatology Pediatric Unit of La Fe Children Hospital of Valencia have explored the application and the adaptation of the treatment and procedures employed in the psychological therapy of patient adults to the patient teenagers.
RESULTED: The protocol of psychological intervention with teenagers with fibromialgy would have to include the following components (based in Comeche, Diaz and Vallejo, 2005): 1) knowledge of the characteristics of the illness and the psychological factors associated, 2) cognitive restructuring. Identification of the out negative thoughts about pain, illness and other problems of their life, 3) identify the situations that generate muscular tension and use the relaxation; 4) identify the main emotions (anger, depression and anxiety) like this like the situations in which manifest; 5)focus on activities abandoned by fault of the pain and recover them gradually, inr this way patients restored their usual style of life; 6) research of a responsible attitude of acceptance that foment a balance between obligations, rest and entertainment; 7) learn to control the emotions in distinct situations; 8) copy with the insomnia and the anxiety in front of the examinations.
CONCLUSIONS: The conclusions based in the treatment along these last four years aim to the suitability othe cognitive-behavioral therapy in the treatment of teenagers with fibromialgy. Special mention deserves the improvement of the patient quality of life of, the adaptation of the techniques to the adolescence characteristics and the importance of the parental education.

P 038
The disease presentation and outcome in juvenile Behçet's syndrome

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OBJECTIVE: To assess clinical characteristics and outcome among patients with juvenile onset Behçet's syndrome all attending a single dedicated center.
METHODS: We reviewed the charts of around 7000 patients registered between July 1977 and December 2009 at our multidisciplinary Behçet's syndrome outpatient clinic. We surveyed patients who fulfilled the International Study Group (ISG) criteria for BS and who were 16 or younger at their initial visit. We attempted to contact all these patients and called back to the outpatient clinic for a formal evaluation. Those patients who could not come to the hospital were re-evaluated, by a detailed telephone interview.
RESULTS: There were 166 patients (86 boys, 80 girls). The mean age at first visit was 14.2±1.9 years, the mean age at appearance of first symptom 10.9 ± 3.1 years, and the mean age at ISG fulfillment 13.1 ± 2.6 years. At the time of first visit, patients had oral ulcers (100 %; 166/ 166), genital ulcers (68 %; 113/ 166), pathergy positivity (63 %; 104/166), papulopustular lesions (57 %; 94/166), erythema nodosum (42 %; 69/166), arthritis (20 %; 33/ 166), eye disease (48 %; 80 /166), vascular disease (13 %; 22/166) and neurological disease (8 %; 13/ 166). The clinical manifestations at first visit such as genital ulcer, papulopustular lesions, erythema nodosum and arthritis were less frequent compared to the adult population (1). The dural sinus thrombi type of neurological involvement was the most common type of involvement (85 %; 11/ 13). Familial history of BS was present in 41(25 %) patients. Information on the onset of puberty was available only in 94 patients. The onset was prepubertal in 39 and postpubertal in the remaining 55. While erythema nodosum was more common among those with prepubertal onset (24/ 39 vs 16/ 55), genital ulcer was more common among those with postpubertal onset (18/ 39 vs 44/55). A total of 13 (8 %) were lost to follow-up after a single visit. Six (4%) (all males) had died. The median follow-up time in the remaining was median 10 years [4- 17]. Causes of death in 6 males were pulmonary artery aneurysms (n=2), hepatic failure due to Budd-Chiari syndrome (n =1), suicide (n =2) and pneumonia (n= 1). At the end of follow-up 18 (14 M/4 F)patients (22.5 %) had lost useful vision (bilateral: 8, unilateral: 10). The visual acuity in either eye was between 0.6-1.0 in 44(20 M/ 24 F)(56 %) and between 0.5- 0.1 in the remaining 18(13 M/ 5 F)(22.5 %). Two patients (all males) with neurological involvement had severe neurological deficit (hemiplegia and optic atrophy). Among 77 patients (50 M/ 27 F) in whom a final evaluation was available after a median of 9 [4-18] years, we observed that oral ulcer (90 %) and papulopustular lesions (55 %) were the most frequent lesions, whereas genital ulcers (18 %), erythema nodosum (29 %) and arthritis (14 %) were the least frequent lesions.

CONCLUSION: Pediatric cases made up around 0.2% of all Behçet patients. As in the adults, BS runs a severe course among the boys considering overall mortality in addition to the vascular and neurological involvement. The frequency of skin-mucosa lesions and arthritis decreased in frequency with time, again similar to adults.
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P 039
Atypical Pachydermodactyly

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INTRODUCTION: Swelling of the interphalangeal joints may be caused by periarticular thickening or by synovial effusion. This is different from swelling due to granuloma anulare, leukocytoclastic vasculitis. xanthoma or chilblain lupus lesions. Nodules found on the interphalangeal joints may be the consequence of an epidermic thickening (callus, knuckle pads, warts). As for pachydermoperiostosis several tissue plains including the periosteum are affected. This disease entity is often associated with clubbing. Finally pachydermodactyly is characterised by fibrosis of the dermis with acanthosis. The etiology is unknown. Pachydermodactyly is painless and mostly affects young adults.
CASE REPORT: A 14-year-old boy was referred to our rheumatology clinic with suspected polyarthritis. He presented with fusiform swelling of his proximal interphalangeal joints of nearly one years duration. He indicated that pain and inability to form a fist had started 6 months prior. There was no morning stiffness, pain was worst on writing and in the evenings. There was no other notable medical history. The mother recalled that her son has the habit of overextending and shaking his fingers when concentrating or stressed.
Physical examination revealed symmetrical swelling and tenderness of PIPs of Dig. II-V, there was limitation in the flexion of the affected PIP joints. Mild keratosis was found on the dorsal face of Dig. II and V.
Laboratory parameters did not show any inflammation, ANA and RF were negative, HLAB27 positive, serology was non contributive. X-ray of the hands showed no erosions, but soft tissue swelling. No synovial enhancement was seen on MRI.
There was limited response to non steroidal antirheumatic drugs and no subjective improvement on low-dose steroids. Swelling seemed to improve somehow with azulfidine according to the family. Following regular ergotherapy using cooling of the joints prior to excercise the boy was able to close his fists completely and painlessly.
Histology showed hypertrophy of the epidermis with hypergranulosis and major thickening of the sutratum corneum with mucinous deposits between collagen fibres. Our hypothesis is one of fibromatosis rather than rheumatic disease.
CONCLUSION: The patient who had been referred with suspected polyarthritis had no inflammatory signs nor bone pathology. Histology showed changes compatible with pachydermodactyly. This benign fibromatosis has however not been described with associated pain upon flexion.

P 040
Is foot posture in children related to their level of joint hypermobility?

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BACKGROUND: Many studies on hypermobile populations have noted a high prevalence of flat feet. In these studies, the assessment of foot type has been subjectively assigned, wtihout the use of an objective measure of the foot position. With the development of the Foot Posture Index (FPI-6), it is now possible to objectively define the standing foot position. The FPI has been validated in adults and has been shown to be reliable when used in paediatric practice. This measure has not previously been used to assess the foot in hypermobile children.
Joint hypermobility can be measured in a clinical situation using many different criteria but only two of the assessment systems available have been tested for validity and reliability (Hospital del Mar criteria & Lower Limb Assessment Score).
OBJECTIVE: The aim of this study is to investigate the relationship between joint hypermobility and foot posture in children through the application of valid and reliable measurement systems. This is a novel approach.
METHOD: Children attending the rheumatology unit at Great Ormond Street Hospital with a diagnosis of joint hypermobility were included in the study. Children were included if aged between 4-15 years old, had a diagnosis of hypermobility made by a rheumatology consultant or specialist physiotherapist. Children were excluded if they had a co-existing systemic, orthopaedic or neurological condition that prevents normal weightbearing through either feet, or which results in a fixed foot position. Each child was assessed using the Hospital del Mar criteria (HelM) and the Lower limb Assessment Score (LLAS) to ascertain their level of hypermobility. After marching on the spot for a count of 10 seconds, the participant stood still and the FPI-6 was recorded.
RESULTS: A total of 35 children were included. There was no significant difference between left and right feet for any of the variables ($p>0.32$) therefore further analysis considered right-side data only. The relationship between foot posture and hypermobility scores was tested using Spearman's correlation due to the categorical nature of the data generated from the assessment scores. The null hypothesis that there was no relationship between foot posture and joint hypermobility score was tested. A moderate correlation was seen between FPI-6 and LLAS ($r=0.62$, $P<0.001$). A weaker correlation was seen between the score of generalised hypermobility and FPI-6 ($r=0.39$, $p=0.02$).
Using the descriptive categories of the FPI-6, only 14% of children were considered to have a normal foot position, whilst 54% has an abnormally pronated foot type and 32% had a highly pronated foot type.
Of note, 43% of included children were diagnosed as being hypermobile but did not reach the threshold for diagnosis of generalised hypermobility (HDelM threshold >7) and 26% of children did not reach the threshold for diagnosis of lower limb hypermobility (LLAS threshold >7).
CONCLUSION: Foot posture is related to the level of joint hypermobility, being positively correlated with lower limb hypermobility scores, but it is not well correlated with the measure of generalised hypermobility. When the categorical descriptors of the Foot Posture Index are applied, it can be seen that the abnormally pronated and highly pronated foot types are most frequently seen in children diagnosed with joint hypermobility.
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P 041
Paediatric Systemic Lupus Erithematosus (p-SLE). Lupus Nephritis

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BACKGROUND: SLE is a multisystem inflammatory autoimmune disease that is infrequent in childhood. 10-20% of cases occurring in this population. Several studies suggest that both clinical and biological features of SLE are influenced by age at disease onset, and that SLE may be more severe in childhood than in adult onset. SLE is associated with renal involvement in a great part of affected children and it is an important cause of renal dysfunction in pediatric population. It is a treatable condition, and the survival rates for affected children have improved significantly over the last 30 years.
OBJECTIVE: To assess the epidemiologic, clinical and evolution characteristics of patients diagnosed with Juvenile SLE.
PATIENTS AND METHODS: Descriptive, longitudinal and retrospective study of patients of the Rheumatology Pediatric Unit of the Hospital Ramón y Cajal followed in the last 35 years.
RESULTS: 34 patients with p-SLE were included in this study. The mean time of follow-up was 15,14 ± 9,87 years (median 12 years). 22 of the total (64.7%) had renal involvement, 20 girls and 2 boys. Ethnic Groups: 20 Caucasian and 2 Latin Americans. 9 of these 22 had renal affection at the start of the disease and the rest developed it during the evolution. The current mean age is 32.3 years (rank 14-53). The mean age at onset of symptoms was 12.8 years (rank 6 -16 years) and the mean age at diagnosis was 14.13 years (8-26 years).
LABORATORY TEST: ANA (100%), anti-DNA antibodies (95.4%), Sm (27.2%), RNP (36.36%), anti-Ro /SSA(27.27%),anti- La/SSB (3.7%), FR (3.7%), lower levels of complement: C3b (86.36%), C4b (81.81%). Anti-phospholipid antibodies are seen in 2 patients with lupus nephritis with thrombotic episodes associated.
17 of 22 (77%) patients had renal biopsy. The patterns of glomerular damage found were: 1 WHO class II histology (5.8%), 1 class III (5.8%), 12 class IV (71%) and 3 class V (17%).
The treatment after biopsy was: 7 patients received methylprednisolone pulses, 7 intravenous cyclophosphamide pulses and 3 Azatioprine. Maintenance treatment: 6 Mycofenolate mofetil, 6 Azatioprine and different doses of prednisone all of them (100%)
Two patients required dialysis and one of them needed renal transplant with a renal survival of 14 months.
DISCUSSION: Children with p-SLE were found to have more active disease at presentation and over time, especially active renal disease than do adults with SLE. In our serried around 65% have renal involvement, more than others publicated series.
This condition continues to cause significant mortality and morbidity. Pediatric rheumatologists are obliged to recognize that therapeutic decisions made early may carry important implications. Lupus nephritis requires long-term, careful follow up of affected patients over decades and intensive attention is required to optimize patient outcome.

P 042
A retrospective study on Kawasaki disease

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AIMS: Kawasaki disease (KD), a systemic vasculitis, is the most common cause of acquired heart disease among children in Western countries. The aim of this study was to assess clinical presentation, course, treatment options and prognosis of KD patients referred to Pediatric Rheumatoly Unit, Institute of Child Health, IRCCS Burlo Garofolo.
METHODS: This is a retrospective chart review study. All patients affected by KD, referred to our hospital from 1988 to 2009, were enrolled. Medical records from onset to the end of follow-up were reviewed.
RESULTS: Our population consisted in 45 patients (29 males, 16 females). Median age at diagnosis was 32 months (range 18-53) and 79% of patients presented within first 5 years. Atypical and incomplete forms represented 14% and 18% respectively. Atypical presentation was associated with older median age (75,8 months, SD=45,2; p=0,014) and diagnostic delay than other forms. The most common atypical presentations were aseptic meningitis (38%), liver enzyme elevation (27%), arthritis (22%), sterile pyuria (15,5%) and gall bladder hydrops (15,5%). Patients treated with higher dose of ASA (80-100 mg/Kg) compared with those treated with lower dose, were less likely to undego a second IVIG infusion (25% vs 39%; p= NS) and to present cardiac abonomalities (16 vs 44%; p=NS).
24% of patients developed cardiac complications, most of them mild, with high frequency of valvular involvement (18%). Coronary aneurism developed in only 1 patient (2%). Older age, higher CRP levels, lack of response to the first IVIG infusion and IVIG dosage <2 gr/kg seemed to predict higher risk of cardiac involvement (p=NS), while no difference was found between classical and non classical forms.
CONCLUSIONS: Atypical and incomplete forms represent one third of all KD forms; they are characterized for an older age at onset and a diagnostic delay. Although the low incidence of coronary aneurisms, we report an uncommon high incidence of valvular involvement.
Pediatricians should be aware of atypical manifestations or incomplete forms of Kawasaki in order to promptly diagnose and treat them.

P 043
Health-related Quality of Life in Adults with Juvenile Dermatomyositis

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BACKGROUND: Few studies have focused on quality of life outcomes within Juvenile Dermatomyositis (JDM).
OBJECTIVE: The primary objective of this study was to acquire knowledge regarding health-related quality of life from the perspective of adult patients with JDM.
METHODS: Patients with probable or definite JDM according to the Bohan -Peter criteria, diagnosis after 1970, disease onset < 18 years of age, age ≥ 18 years were identified from Norwegian hospital registries. The study had a cross-sectional design, where 39 patients were compared with 39 age and sex matched healthy controls. Demographic information, including education and occupation, was obtained by questionnaire, and health-related quality of life (HRQoL) data were acquired by Medical Outcome Study 36-item Short Form (SF-36). Disease activity was measured by Disease Activity Score (DAS) and physical disabilities by Health Assessment Questionnaire (HAQ). Mann-Whitney-Wilcoxon and Fisher's exact tests were used for group data comparison, and Spearman rank 0.05 was considered<coefficient to identify correlation. P-value statistically significant.
RESULTS: The patients median age was 32.7 (range 18.3 - 55.4) years with a median disease duration of 22.2 (range 1.8 – 36.1) years. Patients and controls had similar levels of education and no significant differences regarding occupation. Compared to the controls, patients had reduced health-related quality of life in the SF-36 physical component summary score (PCS) (median 52.6 vs 56.4, p = 0.039) including subscales of physical functioning (p = 0.011) and general health (p = 0.009). There were no differences between patients and controls in the SF-36 mental component summary score (MCS) (p = 0.893), nor within any subscale of the MCS. Disease activity (DAS) correlated with PCS, rs = -0.422 (p= 0.007), physical functioning, rs = -0.484 (p = 0.002), role physical, rs= -0.418 (p = 0.008) and general health, rs= -0.367 (p = 0.022). An association was also found between physical disabilities (HAQ) and PCS, rs = -0.516 (p= 0.001), physical functioning, rs = -0.735 (p < 0.001), role physical, rs = -0.378 (p = 0.018), general health, rs = - 0.362 (p = 0.024) and social functioning, rs = -0.333 (p = 0.038).
CONCLUSIONS: JDM has a significant impact on patient HRQoL in adulthood leading to impaired HRQoL in physical domains, but not in mental domains.

P 044
Severe arthritis associated with systemic scleroderma refractory to cyclophosphamide and successfully treated with etanercept

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BACKGROUND: Systemic sclerosis (SSc) is a fibrosing connective tissue disease characterized by deposition of collagen and other components of extracellular matrix in the skin and target internal organs. Clinically articular involvement, arthritis is seen less frequently than arthralgia. We report a SSc patient complicated by severe arthritis successfully treated with etanercept, soluble TNF receptor fusion protein.
CASE REPORT: The patient was a man of 24 years of age, in whom SSc had been diagnosed in 2003, at 17 years of age, had been experiencing scleroderma, general fatigue, and weight loss for a few months. Skin thickness had been well controlled with oral prednisolone. However, polyarthritis, especially remarkable in hand and foot, had been recognized 24 months after the diagnosis was made. Blood examination revealed elevated levels of CRP (2.02mg/dL), serum amyloid-A (650μg/mL), ESR (37mm/1h), anti-CCP (>100U/ml), Rheumatoid Factor (155 IU/ml). Methotrexate (10mg/week), oral cyclophosphamide (100g/day), and additional intravenous cyclophosphamde pulse for developed lung fibrosis and gastroesophageal reflux were administered, but these treatments failed on arthritis, resulting in contracture of proximal interphalangeal, subdislocation of metacarpophalangeal joints, bone erosion and overgrowth of synovium recognized by MR image. Pathological evaluation of metacarpophalangeal joints of right middle finger revealed proliferating both fibrous connective tissue and synovium tissue. Subcutaneous injection of 25 mg of etanercept twice a week was started in 2007 at the age of 20. Joint pain was suppressed with improved inflammatory markers. Hot spots recognized in multiple joints by 18F-FDG PET (Fluorodeoxyglucose-Positron Emission Tomography) has disappeared though 12 months of etacercept.
CONCLUSION: Intravenous pulsed cyclophosphamide has benefitted patients with systemic sclerosis. In this case, severe arthritis poorly respond to cyclophosphamide. It suggests pathogenesis of arthritis seen in SSc might be different from skin and other organ involvements.

P 045
Three years experience of spanish registry of Juvenile Scleroderma: "REPESIN"

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BACKGROUND: Juvenile scleroderma (JSc) and mixed connective tissue disease (MCTD) are rare diseases in childhood above all systemic forms. JSc includes juvenile localized scleroderma (JLS) and juvenile systemic sclerosis (JSS).
OBJECTIVES: To study the spectrum of JSc seen in referral centers of paediatric Rheumatology in Spain with the long-term goal of developing a national registry.
METHODS: A multicenter prospective chart review was conducted of all patients diagnosed of JSc and MCTD during the period from November 2005 to November 2008. Demographic, clinical, immunological and therapeutic data were collected by previously designed questionnaire approved during the Spanish Paediatric Rheumatology celebrated in November 2005. The questionnaire was available for any paediatric specialists at the web site of the Spanish Paediatric Rheumatology Society. All the questionnaires received during this period were analyzed.
RESULTS: Thirteen paediatric rheumatologyst of eight centers, collected information about their patients. Seventy five patients with JSC from eight centers were enrolled into the study. The mean age at the first symptoms was 9 years (1-17). Period between first symptoms and diagnosis was 18.1 months (0-75). 20 patients(26%) had to be admitted to hospital. 12 patients had a positive family for rheumatic or autoimmune diseases and 7 of them another were diagnosed for other autoimmune disease. JLS was most frequent 68.9%, JSS 17.5%, 12,1% MCTD and prescleroderma 6.5%. 59 were females and 16 were males. Linear Scleroderma (LS) and plaque morphea (PM) were the most frequent subtypes with 28,5% each one followed by MCTD (12,1%), limited cutaneous SSc (lcSSc) (11,4%), generalized morphea (GM) (8.6%), diffuse cutaneous Ssc (dcSSc), deep morphea (DM), prescleroderma 6.7% and 1.3 unclassified. As many 15 patients had a mixed subtype. AAN were positive in 40 patients. 15 of them were JLS, 7 had anticentromere antibody and 5 antitopoisomerase 1 antibodies. 23 patients (33%) had Raynaud´s phenomenon (RyP), 22 tendon retractions, 16 myositis and arthritis, 8 gastroesophageal reflux, 5 calcinosis and digital ulcers, 4 dyspnea and a restrictive respiratory patern and 3 interstitial lung disase. Oral corticosteroids was the treatment more frequent used (46.6%) followed by methotrexate 41.3%, topical corticosteroids 13.3%, nifedipine 12%, bosentan 10.6%, d-penicilamine 8%, hidroxicloquine and mophetil micophe-

nolate 5.3%, colchicine, azathioprine and cyclophosphamide 2.6% and losartan, prostaglandines, cyclosporine, sulphasalazine and sildenafil 1.3%.
CONCLUSIONS: This is the first report of the experience of the Spanish REGISTRY OF JUVENILE SCLERODERMA (REPESIN). We need largest collection of patiets for obteining conclusions but is the largest collection of patients with JLS reported in Spain.

P 046
Juvenile Localized Scleroderma of the face: a neuro-cutaneous disease?

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BACKGROUND: Neurological involvement has been reported in few case reports of patients with Juvenile Localized Scleroderma of the face (JLS-F). Aim of the study was to systematically investigate frequency, clinical and radiological features of CNS involvement in JLS-F.
METHODS: A cohort of consecutive patients with JLS-F (including en coup de sabre (ECDS) and Parry Romberg syndrome (PRS)) underwent a comprehensive clinical evaluation, EEG and brain MRI. All radiographic films were analyzed by 2 neuroradiologists who were blinded to the patients' identity and clinical records. Parenchymal lesions were assessed by a standardized protocol (1) and classified by number, laterality, gray or white matter involvement and concordance with the skin lesion.
RESULTS: 34 patients with JLS-F entered the study, F:M ratio was 1.4:1, mean age at disease onset 8,6 years. Twenty nine patients (85.3%) had linear scleroderma of the face, 5 (14.7%) presented a mixed subtype, 23 patients (67.6%) had ECDS, 11 (32.4%) PRS. CNS involvement was found 21 (61.8%) patients, 11 (32,4%) had neurological symptoms such as chronic headache (5), seizures (3), hemiparesis (1), behavioural abnormalities (1) and cranial nerve palsy (1). Ten patients (29,4) presented MRI abnormalities without symptoms. EEG was abnormal in 5 patients (14,7%), all symptomatic and/or with MRI changes. Cerebral MRI resulted abnormal in 17/34 patients (50%). Twelve patients underwent more than one brain MRI which worsened in 5 patients (41,7%), unchanged in 5 (41,7%) and persisted normal in 2 (16.6%). Eight patients had a single brain lesion, 9 a multiple pattern. In 88,2% the site of skin and neurologic lesions were concordant. White matter involvement was present in 10/17 (58,8%), lesions extended to the grey matter in 7 (41,2%).
Four group of patients have been identified: group 1 patients with neurological symptoms and organic brain lesions (mainly multiple with white and grey matter involvement) concomitant or following the onset of the scleroderma skin lesion (no.7), group 2 (no.10) patients with just organic brain lesions following the skin lesions by 1-18 years, mainly single white matter lesions concordant with the site of skin lesion, group 3 (no. 4) patients with neurological symptoms but no organic brain lesions and group 4 (no.13) patients with no neurological involvement.
CONCLUSION: The high prevalence of neurological involvement in JLS-F reinforces the hypothesis of a possible pathogenetic link CNS-skin in localized scleroderma and confirms the need for a careful clinical and radiological monitoring of every patient since the disease onset.
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P 047
Pediatric patient with end-stage renal disease due to AA amyloidosis secondary to Hyperimmunoglobulin D Syndrome

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BACKGROUND: Hyperimmunoglobulin D syndrome (HIDS) is a rare condition associated with an autosomic recessive mutation in the MVK (mevalonate kinase) gene which provokes periodic recurrent fever with early debut in the childhood. Amyloidosis is a rare complication, with only two previous cases reported in adult patients.
Herein we present a case with HIDS and pediatric-onset amyloidosis.
CASE REPORT: A 6-month-old female infant began with autolimited recurrent fever episodes, frequently accompanied by diarrhea, lymph nodes, pharyngitis and elevation of acute phase reactants. At 6 years old, nephrotic range proteinuria was discovered. She was diagnosed of Familial Mediterranean Fever (FMF). Two years later, she developed a nephrotic syndrome with amyloidosis in a renal biopsy. She required a renal allograft at 12 years, which functioned well until 17, when it was lost due to an acute renal failure. Recurrent fever episodes continued despite colchicine from the diagnosis of FMF.
At 18 years old, she began with episodes of presyncope. Due to altered ecogenicity in echocardiogram, endomyocardial biopsy was performed, showing amyloid deposition. It was also confirmed in an intestinal biopsy, and it was suspected by abnormal ecogenicity in the thyroid gland. Genetic survey was conducted for Hereditary Recurrent Fever Syndromes and a heterozygous mutation in both loci of the MVK gene was found (p.Ile-268-Thr and p.Val-377-Ile, previously associated with HIDS). She began with anti-IL1 therapy (anakinra) in September 2010 with clear improvement of fever episodes from the first months.
CONCLUSIONS: HIDS must be taken into account for differential diagnosis in a pediatric patient with amyloidosis and a suspected Hereditary Recurrent Fever Syndrome.
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P 048
TRAPS: an unusual case

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INTRODUCTION: Tumor necrosis factor receptor-1-associated periodic syndrome (TRAPS) is the most common autosomal dominant autoinflammatory disorder and is caused by mutations in the TNFRSF1A gene encoding the 55-kDa receptor for tumor necrosis factor (TNF)-alpha The clinical features are recurrent attacks of fever, typically lasting from 1 to 3 weeks, myalgia, arthralgia or arthritis, periorbital edema and migratory erythematous plaque simulating erysipela. However not often this clinical features are typical and the diagnosis is delayed months or years.
The authors report the clinical case of a 5 year old child with no relevant familiar or personal diseases. In April 2008 was admitted to hospital with fever with 16 days of evolution, abdominal pain and myalgia. Laboratory tests showed: high ESR (95 mm1 h) and slight increase in transaminases. The pulmonary xray and abdominal ultrasound showed no change. The Mantoux test and serology were negative.
Three months later was again hospitalized for febrile syndrome, with 8 days of evolution, and abdominal pain without any other associated symptoms. Physical examination: pallor of the mucous membranes, abdominal pain in the palpation of the right quadrant and hypogastric with palpable liver. No palpable glands. In the laboratory study: Hgb: 9.3 g / dL, ESR: 111 mm, CRP: 111.4 mg / L, SGOT: 45 IU / L, ALT: 39 IU / L, LDH: 736 IU / L. The genetic showed the R92Q mutation. Corticosteroid was efficacious and since then he has been asymptomatic
Penetrance of TRAPS is close to 100%. The typical and more severe phenotype is associated with mutations involving cysteine. The mutation R92Q is considered low-penetrance, is associated with a phenotype less severe but also more unusual, suggesting that some forms of TRAPS may be underdiagnosed

P 049
Macrophage activation syndrome revealing familial Mediterranean fever

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We report the first case of macrophage activation syndrome (MAS) in association to familial Mediterranean fever (FMF).
A.Y., 4 years, was referred for prolonged fever, fatigue and hepatosplenomegaly; laboratory tests showed hepatic cytolysis, pancytopenia and clotting abnormalities. Liver biopsy showed hepatic fibrosis and a predominantly lymphocytic inflammatory infiltrate. Once infectious and toxic causes were ruled out, a diagnosis of autoimmune hepatitis was made (despite specific autoantibodies negativity), and treatment by methylprednisolone and azathioprine was started. After transient improvement, fever, associated with skin rash, reappeared. He had severe pancytopenia (Hb 5.6 g/dL, WBC 2530/ mm3, PLT 69000/ mm3), persistent clotting abnormalities, hyponatremia and hypofibrinogenemia. Bone marrow aspirate evidenced decreased cellularity and hemophagocytosis. MAS was recognised and

cyclosporine treatment was started. A few weeks later, he developed acute episodes of fever associated with peritonitis, pleuritis, and systemic inflammation. Careful medical history revealed Sephardic Jews ancestry and recurrent episodes of high fever lasting 2-3 days, accompanied by abdominal and articular pain, since the age of 18 months. FMF was confirmed by genetic testing showing M694V homozygosity in MEFV gene.
FMF is the most common hereditary autoinflammatory syndrome, observed predominantly in Sephardic Jewish and Mediterranean populations.
MAS is caused by excessive activation and proliferation of macrophages and T lymphocytes leading to uncontrolled production of inflammatory cytokines. There are 2 types of MAS: primary (positive familial history and/or genetic mutations), and secondary, associated with infections, malignant disorders, rheumatic diseases and drugs. Among patients with autoinflammatory diseases, MAS has been reported in 1 patient affected by chronic infantile neurologic, cutaneous, articular syndrome (CINCA), in 1 affected by mevalonic aciduria and in 1 with cytophagic histiocytic panniculitis. At our knowledge this is the first report of MAS in a child with FMF.

P 050

Idiopathic Juvenile Osteoporosis in a series of 24 children, evolution and review of the literature

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BACKGROUND: Idiopathic juvenile osteoporosis is a rare disease of unknown cause. Less than 100 cases have been reported, mostly as case-reports.
OBJECTIVE: To describe the demographic features, clinical and bone mineral density (BMD) at presentation and during the course of children with idiopathic juvenile osteoporosis (IJO).
PATIENTS AND METHODS: A retrospective multicenter study of children with IJO followed between 1986 and 2009 in 5 reference centers of paediatric endocrinology, paediatric rheumatology and genetics.
RESULTS: 24 patients were included, with a mean age of 12 years (range, 3 to 16 years) at the time of diagnosis. History of fractures and/or proven osteoporosis were present in the family (at least one member) of 6 patients; IJO was associated with a diabetes and a family history of other auto-immune diseases (1 patient) or with a family history of rheumatoid arthritis (1 patient) or Crohn's disease (1 patient). The diagnosis of IJO was considered because of the fortuitous discovery on X-rays of bone demineralisation (14 children), repeated long bone fractures (6 children), pain due to fractures of vertebrae (3 patients) and limping (1 patient). Eleven of the 24 patients presented with vertebral fractures, either alone (5 patients) either in association with long bone fractures (6 cases). The number of long bone fractures ranged from 3 to 17 fractures in the same patient with a mean score of 6 fractures per patient. Dual energy x-ray absorptiometry (DEXA) revealed an initial mean z-score of -3 DS below the mean for age and height (range -5.3 to -2 DS) and a final mean z-score of -2 DS (range -1 to -4,3 DS) (15 patients). At diagnosis, the calcium, phosphore and vitamin D levels were normal in 24/24 patients, alkaline phosphatases in 23/24, telopeptide C terminal of collagen I in 10/10 and osteocalcin in 11/11.Ten out of 13 investigated patients had a normal or even elevated urinary calcium/creatinin ratio suggestive of high bone turn-over, whereas the remaining 3 children had undetectable urinary calcium excretion suggestive of severe calcium deficiency and/or low bone-turn-over. All the known causes of osteoporosis were exluded. Complete remission of IJO was defined by a clinical remission (no pain and no recidive of fractures) and a normalization of BMD; partial remission was defined by a clinical remission and an increase without complete normalization of BMD, and the absence of remission by the persistence of clinical symptoms and/or the decrease of BMD. Among the 19 patients followed more than 3 years (mean follow-up 6 years; range 3 - 13 years), a complete (n=3) or partial (n=13) clinical remission was observed in 16 patients (84%) and absence of remission in 3 patients (16%). Among these 19 children the percentage of complete or partial remission did not differ significantly between the 8 children treated with bisphosphonates (75 %) and the 11 children not treated (35%) (p=0.16). Six children (25%) developed moderate orthopaedic sequellas.
CONCLUSION: Our series is one of the largest reported. We identified a familial predisposition to bone fragility in a subset of patients, suggesting a possible genetic origin of the disease, and an association to autoimmune disorders in others. Other studies are required to determinate the indication of bisphosphonates in the treatment of IJO.

P 051

Chronic recurrent multifocal osteomyelitis (CRMO): clinical features and outcome in 21 Czech and Slovak children

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BACKGROUND: Chronic recurrent multifocal osteomyelitis (CRMO) in children has been considered a part of the autoinflammatory bone disease spectrum. It is characterised by recurrent episodes of systemic inflammation with individual combinations of constitutional symptoms, arthralgia/arthritis, bone pain and non-musculoskeletal symptoms, mainly pyogenic skin manifestations. Bone lesions vary in their inflammatory activity resulting in episodic nature of the condition. Psoriasis, palmo-plantar pustulosis, inflammatory bowel disease and arthritis may run in families of affected children.
OBJECTIVES: To describe clinical features and disease outcome in a cohort of children with CRMO.
METHODS: Retrospective chart review of 21 children followed in 4 paediatric rheumatology units in Bohemia, Moravia and Slovakia over the years 2002-2010.
RESULTS: All 21 patients (12 girls) were Caucasian with mean age at onset of 10.5 years, mean follow-up was 1,9 years (2-84 months). The interval from disease onset to diagnosis varied significantly and ranged from 2 to 60 months. In total there were 69 bone lesions identified in different locations of the skeleton with the following distribution: upper extremities incl. clavicle 26%, lower extremities incl. pelvis 52%, vertebral bodies, sternum and ribs 19%, mandible 3%. Multifocal involvement was present in 19/21 children, two had only one lesion each. Bone biopsy was performed in 15/21 children showing non-specific inflammation in all cases. Cutaneous manifestations were present in 4 and arthritis in 2 children, one had significant scoliosis and one diffuse osteoporosis prior to the treatment initiation. Practically all children were treated with antibiotics before the diagnosis was made. Monotherapy with NSAIDs induced remission in 4/21 children , 4 children had NSAIDs with vitamin D and calcium, one with calcitonin, two with the short courses of oral corticosteroids (CS). Remaining 11 children required administration of second-line agents: sulphasalazine or methotrexate (MTX), each alone or in combination with CS. Three patients responded finally to pamidronate administration, which was given after the failure of aforementioned medications. One patient has had treatment-free remission 23 months after the third cycle of pamidronate. Majority of patients continue to have varying degree of relapsing disease course with relatively acceptable long-term quality of life with minimal functional limitations.
CONCLUSIONS: CRMO has not been infrequently recognised in patients presenting with musculoskeletal pain with non-specific inflammatory activity. Paucity of published information makes diagnostic as well as therapeutic decision-making processes difficult. Our heterogeneous case series illustrates the importance of collaborative efforts in this area (e.g. EUROFEVER initiative).

P 052

Venous malformation of knee masquerading as juvenile idiopathic arthritis

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We present a five-year-old girl with intermittent episodes of swelling of the right knee and limping during the last three years. There weren´t other affected joints and the pain easily eased with rest and treatment with ibuprofen over a period of few days. There were neither other symptoms nor personal history of interest. On physical examination right knee swelling with associated warmth was present. Movements of the affected joint were limited and painful only at extremes. The overlying skin was normal.
Laboratory investigations revealed a normal complete blood count with a erythrocyte sedimentation rate (ESR) of 40 mm/hour and a C reactive protein (CRP) of 2.4 mg/dL. Antinuclear antibodies and rheumatoid factor were negative. An X-ray of the knee was normal. She had been diagnosed elsewhere of juvenile idiopathic arthritis. In the follow up, the patient was asymptomatic between episodes of knee swelling, with normalization of ESR and CRP. An ophthalmological examination was normal.
An ultrasound examination of the knee revealed joint effusion and soft tissue swelling of quadriceps (vastus lateralis) with an altered echotexture (increased vascularization). A magnetic resonance imaging of the knee revealed a cystic mass in the suprapatellar bursa that extended to the vastus lateralis muscle, compatible with the diagnosis of low flow vascular malformation (venolymphatic type). An incisional biopsy of the mass was performed and the histological examination revealed the morphological features consistent with a venous malformation of the knee. At present, surgical excision or sclerosis of the mass are being evaluated by surgical plastic department of our hospital.

P 053
Tocilizumab in a case of multiple drugs refractory systemic onset-juvenile idiopathic arthritis

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BACKGROUND: Systemic arthritis belongs to a heterogenous group of pediatric rheumatic diseases known as juvenile idiopatic artrhitis (JIA). Patients with systemic arthritis (SJIA) have a range of other prominent features, including elevation of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), leukocytosis with high neutrophil counts and thrombocytosis. Ferritin concentrations are high and correlate with systemic disease activity. Systemic arthritis is often extraordinarily resistant to treatment.
OBJECTIVES: To encourage the use of new medications based on the increasing knowledge of JIA pathogenesis, drugs that are not yet licensed for children.
CASE REPORT: Our patient (17 y.o., caucasian female), was diagnosed with Systhemic Onset -JIA at 9 y.o.; she relapsed five years after the remission induced with steroids. Anamnestic, physical and lab findings confirmed the diagnosis of systemic arthritis – second evolutive cycle. In order to control the severe and persistent articular and, especially, extraarticular symptoms, accompanied by a intense biologic inflammatory syndrome, almost every conventional or unconventional therapeutic protocols were used: NSAIDs, Prednisone (PO), Methylprednisolone (pulsetherapy, over 20 series of 3 days), Methotrexate (6 mo), Cyclosporin A (6 mo), Etanercept and Methotrexate (6 mo), Infliximab and Azathioprine (10 mo), Rituximab (6 mo), Methotrexate associated with Leflunomide and Prednisone (6 mo).
In the 4 years following the relapse, the evolution was catastrophic: high fever, rash, hepatosplenomegaly, cachexia, secondary amenorrhea, severe anemia, hypoalbuminemia, osteoporosis, symmetric polyartrithis affecting 38 big and small joints. Biologic inflammatory syndrome persisted during all this time with extremely high values (ERS 126 mm/h, CRP 386,6 mg/L, ferritine 20,081ng/ml, leukocytes 37,220/mmc with 75% neutrophyls).
The patient was included in a tocilizumab treatment protocol : 8mg/kg IV infusion, every 2 weeks, during 9 mo. Tocilizumab was well tolerated, without side effects, and efficient, with gradually remission of fever and rash (after 2 mo), hepatosplenomegaly (after 4 wk), anemia (6 wk), amenorrhea (6 mo), biologic inflammatory syndrome (2 mo), and finally partial slow improvement of arthritis (3-4 mo). The coxofemoral ankylosis imposed hip replacement, six months after remission. The active disease relapsed after the surgical treatment. Unfortunately, in this case Tocilizumab came too late.
CONCLUSIONS: Despite its late introduction, the treatment with Tocilizumab was efficient and safe. It remains to be licensed after clinical trials for systemic arthritis.
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P 054
Early juvenile arthritis – prospective two-year follow-up

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OBJECTIVE: To study clinical and laboratory manifestations of different forms of juvenile arthritis (JA) at the disease's onset and during prospective two- year follow up.
MATERIAL AND METHODS: The study was performed as a part of Institute of Rheumatology early arthritis examination program "RADIKAL". It included 130 pts with early JA (60,7%-girls) with disease's duration from 2 weeks to 6 months (mean 2,9+1,6 months) aged 1,5-16 years (mean 7,9+5,0 years). 13(10%) pts had systemic-onset JA, 45(34,6%)-polyarticular-onset and 72(55,4%)-oligoarticular-onset subsets of JA. General state, joint status, systemic and organ manifestations as well as immunological parameters (ANA, RF), disease activity, functional status (Steinbrocker classes and Child Health Assessment Questionnaire- CHAQ) were assessed at baseline, and after 6, 12, 24 months of follow up.
RESULTS: Oligoarticular subset of JA prevailed at onset and after 2 years (57,6%-55,6%). During the observation systemic features were noted in reduced form as single manifestations. Morning stiffnes was absent in half of children or lasted more than 1 hour in 16,4% of pts. Rheumatoid nodules appeared in 1 pt after 1 year. Uveitis developed in 7 children (5,3%) and to the end of follow up it appeared in 2 more pts. Most of pts had minimal or moderate functional disability (Steinbrocker classes I and II, CHAQ score 0,1-1,5) during follow up. Disease activity at onset did not exceed 1 or 2 grade (80,2%) and after 2 years the disease was not active in half of pts. To the end of follow up remission was achived in 59% of pts, more often in pts with oligoarthritis and in those who received disease modifying antirheumatic drugs. In 23,2% of pts mostly in those with polyarticular JA continued to recure independently on treatment.
CONCLUSIONS: Timely administered complex therapy hampered disease progression, induced remission and improved quality of life in most children with JA. Pts with oligoarthritis had most favorable course of the disease. Pts with polyarthritis required early administration of aggressive therapy.

P 055
Vitamin D status and Juvenile Idiopathic Arthritis (JIA): is there an association with disease activity?

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BACKGROUND: Vitamin D has an immunosuppressive role in many aspects of the immune system. 1,25(OH)2D inhibits B cell proliferation, decreases production of antibodies, inhibits T cell proliferation and activation. In the murine model of collagen-induced arthritis, Vitamin D receptor agonists prevent disease expression and also suppress established disease. In adults with rheumatoid arthritis, several studies have demonstrated an inverse association between disease activity and vitamin D levels. However, this association has never been reported in children with JIA.
OBJECTIVES: In children with JIA, (1) determine the rates of and risk factors for vitamin D deficiency and insufficiency; (2) examine the association between serum levels of 25(OH)D and disease activity.
METHODS: This is an ongoing cross-sectional study. Disease activity is measured using JADAS-27. Serum 25(OH)D levels are measured by liquid chromatography at the same clinic visit. A minimum of 150 patients will be enrolled to detect a correlation of 0.23 between 25(OH)D levels and JADAS-27, with a power of 80%. A structured interview collects demographic and health information and a comprehensive food frequency questionnaire retrieves dietary information. When enrollment is completed (Sept 10), rates of vitamin D deficiency and insufficiency will be determined; a logistic regression model will analyze potential risk factors for vitamin D deficiency/ insufficiency. The association between abnormal levels of 25(OH)D and potential risk factors including age, ethnicity, time since disease onset, subtype of JIA, body mass index, season, use of supplements containing vitamin D, history of recent travel or tanning, and dietary vitamin D will be examined. In addition, a linear regression model will be developed to analyze the association between 25(OH)D levels and JADAS-27. This model will be adjusted for age, gender, JIA subtype, ethnicity, use of NSAIDs, methotrexate or biologics, season, and time since disease onset. Interactions between vitamin D and ethnicity, season, use of NSAIDs, methotrexate, and biologics will be determined.
RESULTS: To date, 105 children with JIA (mean age 11.3 yrs [range 3-19 yrs], 59% female, 88% Caucasians) have been enrolled. Mean body mass index is 20 (95% CI 19.1-20.9); 20% are overweight. Of the 105 patients, 41% have oligoarthritis, 22% enthesitis-related arthritis, 20% RF-negative polyarthritis, 10% psoriatic arthritis, 4% systemic-onset arthritis, and 3% RF-positive polyarthritis. Mean time since disease onset is 48.8 months (95% CI 39.7-58). Current medications include NSAIDs (52%, mean duration 13 months), methotrexate (25%, mean duration 8 months), and biologic agents (21%, mean duration 4 months). 24% of patients are not taking any medications, while 40% are taking >1 medication. 44% of patients are taking supplements containing vitamin D3 (dose 400 IU - 2,000 IU/day). In patients studied to date, mean 25(OH)D is 27.8 ng/ml (± 8.8 ng/ml); 17% are vitamin D deficient (<20ng/ml), 42% are vitamin D insufficient (20-29 ng/ml), and 41% have adequate levels of 25(OH)D. JADAS-27 mean is 7.1 ± 6.2 (range 0-30.7).
CONCLUSIONS: High rates of vitamin D deficiency and insufficiency are found in children with JIA. This population has a wide range of JADAS-27 scores. We will analyze the association between JADAS-27 scores of disease activity and 25(OH)D levels. These results will provide one of the first available analyses of this association.

P 056
Significance of M694V mutation in the course and outcome of JIA in Armenian patients

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BACKGROUND: MEFV gene mutation frequency is very high (20%) in Armenian population and is increased in patients with Juvenile Idiopathic Arthritis (JIA).
OBJECTIVES: To study the frequency of M694V mutation and its influence on the disease course in the patients with JIA.
METHODS: Retrospective chart review of all patients with JIA for MEFV mutations and JIA disease course. Refractory arthritis was defined as persistently active arthritis despite treatment with classical disease modifying drugs and/or intraarticular steroid injections.
RESULTS: 112 patients (85 males) mean age 9.93 years (range 1-18) with JIA were screened for MEFV gene mutations. All received standard treatment for JIA. 33/112 had confirmed diagnosis of FMF and received colchicine in addition to JIA treatment. 64/112 (57%) carried one or two MEFV gene mutations: 36/64 heterozygous, 20/64 compound heterozygous, 8/64 homozygous. M694V mutation was found in 46/64 (72%) cases: homozygous in 7/64 (15%), compound heterozygous in 17/64 (37%), heterozygous in 22/64 (48%). Refractory arthritis was found in 51/112 patients (45%), 35/64 (55%) patients with MEFV mutations and 16/48 (33%) patients without MEFV mutation (p<0.04, Chi square). 28/35 (80%) patients with refractory arthritis carried a M694V mutation (6 homozygous, 15 compound heterozygous, 7 heterozygous).
CONCLUSIONS: In our cohort of JIA patients MEFV gene mutations were associated with a higher rate of refractory arthritis. Especially homozygous or compound heterozygous M694V mutation carriers seemed to have a worse prognosis for their JIA.
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P 057
Spinal MRI in juvenile idiopathic arthritis: high prevalence of abnormalities

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OBJECTIVE: To assess the prevalence and the characteristics of spinal MRI findings in children with polyarthritic or systemic juvenile idiopathic arthritis (JIA).
MATERIALS AND METHODS: This cross-sectional study included patients with severe JIA treated in a tertiary rheumatologic center. Spinal MRI (0.23T) was performed and vertebral deformities, endplate irregularities, intervertebral disc involvement, back muscle status, the spinal canal and neural foramina were analyzed.
RESULTS: Altogether 50 patients (41 females; median age 14.8 y, median disease duration 10.2 y) with systemic arthritis (12%), seronegative polyarthritis (54%), seropositive polyarthritis (2%), extended oligo-arthritis (28%) and psoriatic arthritis (4%) were included. Only 38% had normal MRI, 62% had various abnormalities. Vertebral compressions (altogether 66 compressed vertebrae; from 1 to 16 affected vertebrae per patient) were seen in 28% of the patients and the majority were located in Th7-Th12. Endplate changes were noted in 28% and anterior corner lesions in 14%. Altogether 46% of the patients had intervertebral disc changes (14% had protrusions, 4% had prolapses); in 54% these were in the lower thoracic spine. Two patients had spinal canal narrowing without medullar involvement, none had neural root compression. Six (12%) had mild atrophy of the back muscles.
CONCLUSIONS: Patients with severe JIA have a high prevalence of vertebral, endplate and intervertebral disc abnormalities in the subcervical spine on MRI; the majority are located in the lower thoracic spine. Further studies are needed to assess the clinical relevance of these findings.

P 058
Vascular and cardiac diastolic function in children with Juvenile Idiopathic Arthritis

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BACKGROUND: Juvenile idiopathic arthritis (JIA), is a chronic inflammatory condition with its origin in childhood. Its adult form, rheumatoid arthritis, has been associated with impaired vascular and cardiac function, predisposing to atherosclerosis and cardiovascular disease even after adjustment for traditional risk factors. However, data concerning the association of JIA with early vascular and cardiac alterations is limited.
OBJECTIVE: To assess whether vascular and cardiac diastolic function is impaired in children with JIA.
METHODS: Thirty children with JIA were compared to 33 age-matched controls (aged 12.3 +/- 2.8 vs 11.7 +/- 2.2 years respectively). In all children, the following were measured: 1) brachial artery flow-mediated dilatation (FMD) to assess endothelial function, 2) carotid intima-media thickness (cIMT), 3) arterial stiffness indices: carotid-femoral wave velocity (PWV) and Augmentation Index (AIx) using applanation tonometry, 4) vascular compliance indices: large and small artery elasticity index (LAEI and SAEI) using diastolic pulse contour analysis, 5) cardiac systolic and diastolic function using classic, tissue Doppler, classic and color M-mode echocardiography and 6) biochemical inflammatory markers.
RESULTS: FMD was significantly decreased in JIA compared to control children by 28%, (p<0.05), while cIMT, PWV, AIx, LAEI, SAEI and cardiac diastolic function indices did not differ between groups (p=NS). FMD was not influenced by disease activity or duration or type of medications used. Serum ICAM levels were higher in children with JIA compared to controls (p<0.05).
CONCLUSIONS: Impaired endothelial function is detected early in children with JIA, despite preservation of other vascular and cardiac function indices in our population. Further research is needed to demonstrate whether reduced endothelial function in these children may indicate induction of atherosclerotic vascular disease earlier in adulthood.
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P 059
Economic impact of juvenile idiopathic arthritis and familial Mediterranean fever in Turkey

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OBJECTIVES: To determine the economical impact of juvenile idiopathic arthritis (JIA) and familial Mediterranean fever (FMF) in Turkey.
PATIENTS AND METHODS: A total of 100 patients (69 F/31 M) with JIA and 100 with FMF (68 F/32 F) who were consecutively seen in the outpatient clinic of the pediatric rheumatology department at Cerrahpasa Medical School between August 2008 and January 2009 were studied. Cost data were collected through a questionnaire filled out by the parents.
RESULTS: The mean age (JIA: 11±5; FMF:12±4) and mean disease duration (JIA: 5 ±3; FMF:4±3) of the patients were similar. JIA patients were assigned to 5 subtypes (polyarticular: n=45, oligoarticular: n=30, systemic onset: n=13, psoriatic: n=6 and enthesitis related arthritis: n=6). 49 % of the patients with JIA were treated with anti-TNF drugs and 37% with DMARDS with or without corticosteroids. All patients with FMF were using colchicine. The total annual cost of JIA (3864±3969 Euro) was considerably higher than that of FMF (157±75 Euro) (p< 0.001). Medication fees were the major determinant of total costs in both diseases constituting 85% in JIA and 39% in FMF. Among the subtypes of JIA total annual costs were highest among patients with polyarticular type (5850± 3946 Euro) and lowest in the systemic (1737±2196 Euro) and oligoarticular type (1796±2744 Euro).
DISCUSSION: Medications especially, anti-TNF drugs were the major contributor among all determinants of costs in JIA. The low costs of health care system especially that of health care providers and prominent changes in the health care policies for the last 5 years in Turkey might have played role in our findings.

P 060
A case of MTX-resistant poly Juvenile Idiopathic Arthritis treated by anti-TNF agent safely, after initial infection of Epstein-Barr virus

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BACKGROUND: Safety of anti-TNF agent(anti-TNF) to adult Rheumatoid Arthritis(RA) who were infected with Epstein-Barr Virus(EBV) previously were reported, and risk of reactivation of EBV were low. Children (and adolescents) are at high risk of initial infection of EBV than adults, but there are few information about safety of using anti-TNF in that situation.
OBJECTIVE: Considering about basis for initiation of anti-TNF to Juvenile Idiopathic Arthritis(JIA) patients with initial infection of EBV.

METHODS: We made criteria for initiation of anti-TNF to patients after initial infection of EBV.
1. Improvement of liver function test (less than 2-times the upper limit of normal)
2. Positive anti Epstein-Barr virus nuclear antigen antibody test
3. Negative of EBV DNA in quantitative polymerase chain reaction
4. No mosquito allergy
Patients have regular physical examination and blood examination (liver function test, EBV DNA) , after initiation of anti-TNF.
RESULT: A 7 year old girl who was refractory poly JIA treated with MTX was infected EBV and developed infectious mononucleosis during preparation of anti-TNF. She responded to symptomatic treatment after withdrawal of MTX. She satisfied this criteria on 129th day, and anti-TNF(Adalimumab) was administered. After that she was in remission without reactivation of EBV.
CONCLUSIONS: We initiated anti-TNF to our patient using this criteria and administered it safely until now. We need to accumulate experience of administering anti-TNF to patients infected with EBV to prove the validity of this criteria.
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P 061
A peculiar case of lameness due to spinal muscular atrophy

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BACKGROUND: Lameness is a symptom frequently found in children.Many causes can determine it.Accurate anamnesis and careful physical examination are necessary for a correct diagnosis.
OBJECTIVES AND METHODS: We describe the case of a little girl came to our attention at age of 2 years and 6 months for the presence of lameness following to infection of the upper airways about a month ago.Family history shows that the maternal aunt suffers from psoriatic arthritis,a paternal cousin has celiac disease,and 2 cousins suffer from a myopathy with increased CK undergoing diagnostic definition.She is the daughter of nonconsanguineous parents and her psychomotor development is normal.Clinical objectivity shows a height-weight growth in the standard and osteo-articular examination reveals only minimal limitation of the movement of abduction of hips right.Blood tests,inflammatory indices and serology practiced on this occasion are all normal;the detection of antinuclear antibody is negative. Abdominal ultrasound excludes the presence of expansive masses.Joint ultrasound shows the presence of intra-articular effusion in both hips,more to the right side. In suspicion of a transitory coxitis,it was started an anti-inflammatory therapy with slight improvement of clinical symptoms.After about a month,she come back to clinical check-up for the persistence of abnormal deambulation associated with frequent falls.At clinical examination our patient appears lively and collaborative,she drags the right leg walking on tiptoe,she presents difficulties in climbing and descending stairs holding on to the handrail,Gowers's sign is positive.Neurological examination highlights hypotonia of the pelvic girdle and of the quadriceps muscles and absence of patellar reflex bilaterally.Dosage of muscle enzymes CK and LDH with the corresponding isoforms appears to be normal in our patient and in both her parents.Magnetic resonance imaging of the brain and spine is negative,while electroneurography shows signs of neurogenic muscular suffering.In view of the clinical picture and because of suspicion of Spinal Muscular atrophy(SMA),it was decided to perform molecular genetic investigation.
RESULTS: Analysis of patient DNA revealed the presence of the deletion of exons 7 and 8 of Survival Motor Neuron-1 gene(SMN1)in homozygosity.Also,it was highlighted the presence of three copies of SMN2.This report is therefore compatible with the diagnosis of SMA.
CONCLUSIONS: SMA is a relatively common neuromuscular disease that is transmitted as an autosomal recessive,characterized by muscle weakness and atrophy due to degeneration of spinal motor neurons and nuclei of cranial nerves. Clinical picture varies widely.Currently,there is no effective treatment for this disease that,in severe forms,it seriously compromises the quality of life of patients affected.Severity of SMA phenotype is inversely correlated with the number of copies of SMN2.SMA type I patients usually have 1-2 copies of the gene,those with the intermediate form have 2 or 3 copies,while patients with benign forms they usually possess 3-4 copies or more.However,the influence of the number of SMN2 copies is not categorical because 3 SMN2 copies are sometimes also seen in SMA patients more severe.
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P 062
Pandemic Influenza A H1N1 vaccination in children with chronic rheumatic diseases and long-term therapy

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Every fall and winter, the families of patients with chronic rheumatic diseases (CRD) ask pediatricians whether their children should be vaccinated for influenza. This season, with escalating concerns regarding the novel H1N1 influenza virus and its recently approved vaccine, this question has become more frequent and increasingly urgent. There are no randomised controlled trials addressing the issue of vaccination against influenza in patients with CRD. Two small prospective open-cohort studies in Juvenile Idiopathic Arthritis (JIA) suggest that vaccination is safe, and that children with JIA are able to develop a protective response to vaccination equivalent to that of healthy children (1,2). Vaccination does not seem to have a noticeable effect on disease activity.
On November 2009, 22 children (F:M 14:8) with CRD (JIA = 18, Systemic Lupus Erythematosus = 1, Polyarteritis Nodosa = 3) aged 15 months-17 years (mean age 11.6 years) received H1N1 vaccine (Focetria), authorised under 'Exceptional Circumstances' for the influenza A (H1N1) pandemic that was officially declared by the World Health Organization on 11 June 2009. Therapeutic regimens were: 1 pt prednisone (PDN), 1 pt PDN plus ciclosporin, 3 pts PDN plus mycophenolate mofetil, 1 pt methotrexate (MTX) plus abatacept, 1 pt adalimumab, 2 pts MTX plus anakinra, 13 pts MTX plus etanercept. Clinical and laboratory evaluation were performed before and at 1, 3 and 6 months after vaccination. Blood samples were collected before and one month after vaccination and the antibody titers will be measured. 2/22 patients reported local reactions (pain at the site of the injection). No patient was found to fulfill criteria for deterioration or flare of the underlying disease. No patient reported "flu-like" symptoms during the 6-month period of follow-up.
We conclude that there is evidence that children with CRD receiving long-term therapy at conventional doses are able to respond to influenza vaccination, without serious adverse reactions or disease flares, regardless of their age or therapeutic regimen. The current evidence does not indicate whether influenza vaccination is actually protective against developing symptoms of influenza illness, or whether children with CRD are more at risk of developing severe influenza infection with secondary complications. Until this is addressed, the risk:benefit ratio of influenza vaccination in patients with CRD is uncertain. However, our small experience suggests that because this intervention is safe, inexpensive, and widely available, vaccination for seasonal influenza and the novel H1N1 strain is indicated.
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P 063
Vitamin D Levels in children with rheumatologic disorders

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BACKGROUND: Vitamin D deficiency has been linked to development of autoimmune diseases such as inflammatory bowel disease, type 1 diabetes, multiple sclerosis, rheumatoid arthritis, and systemic lupus erythematosus (SLE). However, literature about this subject in children is sparse.
OBJECTIVES: To evaluate the prevalence of vitamin D deficiency and to determine if there was a difference in vitamin D levels among children with autoimmune disorders versus non-autoimmune conditions attending a pediatric rheumatology specialty clinic.
METHODS: Observational study of all consecutive visits at a pediatric rheumatology clinic between November 2008 and September 2009 (N=254; F:M 171:83).
RESULTS: Of these patients, 169 had autoimmune rheumatologic disorders (SLE, juvenile idiopathic arthritis, dermatomyositis, scleroderma, vasculitis) and 85 had non-autoimmune conditions (Lyme, patello-femoral syndrome, hypermobility, etc). Mean age was 12.3 years (range 18 years). Vitamin D deficiency (25(OH)D levels < 20 ng/ml) was detected in 39 (23%) children with autoimmune rheumatologic disorders and in 12 (14%) children with non-autoimmune conditions. Vitamin D insufficiency (25(OH)D levels 20-29 ng/ml) was found in 56 (33%) children with autoimmune rheumatologic disorders and in 32 (38%) children with non-autoimmune conditions. Combined rates of vitamin D deficiency and insufficiency were 56% and 52%, for children with and without autoimmune diseases, respectively. There was not an association between the specific autoimmune diagnosis or disease activity and vitamin D levels. Prednisone intake in children with autoimmune diseases was associated with lower levels of vitamin D (p=0.005), although this

variable was not significant after the multivariate analysis. Ethnicity (p<0.0001), body mass index (p=0.019), age (p=0.011) and season (p<0.0001) were risk factors for vitamin D deficiency. African-Americans (17.9±10.4), Asian Indians (20.2±8), Asians (21.1±8.6), and Hispanics (21.3±8.4) had lower levels of vitamin D than Caucasians (30.7±10.4). Overweight children had lower levels of vitamin D than those with normal body mass index (24.1±12.3 versus 29.5±10.6). Age correlated inversely with vitamin D levels (r=-0.15, p=0.011). Vitamin D levels were higher during summer (36±10.2), than during fall (27.7±10.9), spring (26.3±10.8), or winter (25.7±9.5). Supplement intake was associated with higher levels of vitamin D (p=0.0002). However, only children taking supplements with doses>400IU of vitamin D3 had higher levels of vitamin D than those who were not receiving supplements (p=0.0001). Vitamin D levels in children receiving supplements with ≤400IU of vitamin D3 did not differ from children not receiving supplements.
CONCLUSIONS: Over 1/2 of children attending a pediatric rheumatology specialty clinic were vitamin D deficient or insufficient. Factors contributing to low vitamin D levels included age, body mass index, ethnicity, and season. Autoimmune disorder did not appear to be a specific risk factor for vitamin D deficiency.

P 064
Uveitis in children: single center experience

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BACKGROUND: Pediatric non-infectious uveitis remains a rare but potentially sight-threatening group of diseases. However, early screening and treatment can improve outcomes. We evaluate retrospectively, etiologic and clinical features and ocular manifestations of our patients with uveitis.
MATERIAL AND METHODS: Hospital records of 23 children (ages: 6-17 years, 13±3.6 years, F/M: 10/12) who presented with uveitis were evaluated. The mean duration of follow-up was 32.9±29.6 months. Patients with and without any rheumatic disease were grouped as Group 1 and 2 respectively, Characteristics such as onset, severity, anatomical subtype, systemic association or etiology, recurrence rate, response to treatment, and complications were identified. Detailed clinical parameters were reviewed, including highly sensitive C-reactive protein (hs-CRP), rheumatoid factor (RF), anitnuclear antibody (ANA), anti-cardiolipin antibodies, and HLA type.
RESULTS: Rheumatologic diseases were found to be the reason of uveitis in 10 (43%) children (Group 1). Four of them were diagnosed as Behcet's disease and 6 of them as juvenile idiopathic arthritis (JIA) during their follow-up. 13 patients were enrolled in Group 2 and uveitis was found to be idiopathic in 50% of them. Herpes Symplex and Toxoplasma infections were detected in 3 (13%) and Lyme disease in one patient. Bilateral uveitis was observed in 7 patients both in Group 1 and 2. Panuveitis was found in 4 patients in Group 1 and all of them were diagnosed as Behcet's disease after detailed rheumatologic investigation. Intermediate uveitis was also found in 4 patients in Group 1 while; anterior uveitis was the dominant diagnosis in group 2. Serum CRP level was significantly higher in Group 1 as expected. Positivity of ANA was found in 3/10 patients in Group 1 while only in 1/13 patients in Group 2. HLA positivity was found in 6/10 patients in Group 1 and 3/13 patients in Group 2 (p>0.05). Two patients in Group 1 were found to have a treatment resistant uveitis while there wasn't any in Group 2. Ten patients out of 12 had experienced a long term remission in Group 2 while only 7 had remission in Group 1.
CONCLUSION: Patients with uveitis should have an extensive etiologic investigation. Behcet's Disease is frequent and the presence of HLAB5 and panuveitis was associated with Behcet's disease. Association of a rheumatologic disease to uveitis should alert the physician about the prognosis and those patients need closer follow-up. A close relation should be fostered between rheumatologist and ophthalmologist to effectively monitor these children

P 065
Prospective study of infliximab use in pediatric uveitis

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BACKGROUND: Uveitis is a persistent disease for which there is little prospective data on treatment. Previous retrospective studies suggest TNF blockade may be efficacious for treatment of uveitis, but do not address time to response or optimal dose.
METHODS: Ongoing 9 month multi-center prospective study of infliximab for treatment of persistent pediatric inflammatory uveitis (onset < 16 yrs), randomizing subjects to one of 2 initial doses: 5 mg/kg or 10mg/kg monthly. Scheduled ophthalmologic exams utilized the Standardization of Nomenclature (SUN) criteria1 and were performed prior to infusions. Entry criteria: > 1+ anterior chamber inflammation, failure of at least one DMARD, on stable dose of mtx. Primary outcome variable was percent of subjects who had improvement per SUN criteria.
RESULTS: 14 subjects (9 female, mean age 11.8 [range 6-19]) with persistent inflammatory uveitis (1 sarcoid, 13 idiopathic) from 6 CARRA sites were randomized to receive 5 mg/kg (N=8) or 10 mg/kg (N=6) initial infliximab dose. At the baseline visit, 5 had unilateral and 7 bilateral inflammation.
Inflammation grade Baseline After 1st After 4th After 8th
(cells per hpf) dose dose dose
N=12 N=11 N=11 N=11 N=7
OD OS OD OS OD OS OD OS
3+ (26-50) 0 0 0 0 0 0 0 0
2+ (16-25) 1 2 0 1 0 0 0 0
1+ (6-15) 6 7 2 2 0 0 1 1
0.5+ (1-5) 1 2 4 3 5 4 2 1
0 (0) 3 1 5 6 6 7 4 4
* Inflammation is reported utilizing SUN criteria. Anterior chamber inflammation is graded as cells per high power field (hpf).
CONCLUSION: Infliximab works rapidly to decrease inflammation with a third of the subjects having 0 inflammation in both eyes after one infusion. Low grade inflammation may persist despite treatment. Improvement persisted 9 months after initiation of infliximab.
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P 066
Magnetic Resonance Imaging succesful outcome after antiTNF alpha switching to Adalimumab in a 12yo ERA-JIA male patient

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BACKGROUND: Juvenile idiopathic arthritis (JIA) is the most common childhood rheumatic disease (1). The pain and functional disability associated with JIA cause a significant burden for patients and their families and caregivers, affecting on health-related quality of life and well-being (2). TNF alpha blockers (infliximab, adalimumab, etanercept) and abatacept, are now a therapeutic option that offers both good efficacy and safety outcomes (3) when classic DMARDs fail. If a TNF alpha blocker has to be discontinued, the possibility to switch to another biologic agent to reach clinical remission should be considered (4).
OBJECTIVE: We present the first case report to document hip MRI improvement after TNF alpha blocker switching in a ERA patient.
METHODS: We describe a 12yo ERA-JIA male patient\\\'s clinical course receiving a TNF alpha blocker switching. We also present corresponding MRI imaging.
RESULTS: A 12-years-old male patient complaining of left hip pain at playing sports for 6-month was attended in June 2006. Physical exam showed both internal and external rotation limitation, Schöber test of 7 cm, finger-floor distance of 18 cm. We performed several tests which showed the following results: blood test (positive B27-HLA, normal acute phase reactants, hip joint ultrasound (left hip joint sinovitis), 99T-scintigraphy (left hip arthritis), and hip MRI (left hip effusion, head femoral bone oedema, subchondral and cartilaginous erosions (IMAGE 1).
A ERA-JIA subtype was diagnosed. He started on prednisolone 6 mg daily and methotrexate 15 mg/m2 subcutaneous weekly, and received a local steroid injection (triamcinolone). After three months-therapy he did much better, he had not hip pain, physical exam improved, and hip ultrasound showed minimal hip joint effusion. He complained of vomiting after methotrexate administration, he started oral sulfasalazine and discontinued methotrexate. Two months later, he referred his previous hip pain back, as well as hip MRI worsening. He started on etanercept 0.4 mg/k subcutaneously twice weekly. After one-year treatment he remained asymptomatic, although hip MRI still showed synovitis, cartilaginous abnormalities, bone oedema and synovial effusion (IMAGE 2). We decided to switch etanercept by adalimumab 40mg every 2 weeks, looking for a better radiological outcome.
Twelve months later, the patient not only had clinical remission, but also presented minimal MRI changes (minimal synovial effusion, lack of new cartilage lesions, and lack of bone oedema (IMAGE 3), which means radiologicalI improvement.
CONCLUSION: Although clinical remission may be reached in these patients, many of them do not get such response and need other treatment attempts. Switching between biological agents has shown effective, although there are only a few published articles about it. There is no evidence of radiological improvement evidence in ERA-JIA TNF alpha switching in the literature. We present the first case to demonstrate it, as we show in several MRI images.
Further studies are needed to confirm these findings.
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P 067
Spondyloepiphyseal dysplasia tarda with progressive arthropathy mimicking juvenile chronic arthritis; report of 8 cases

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BACKGROUND: SED is on of a group of skeletal dysplasia (dwarfing condition) caused by changes in type II collagen. Two major types of SED are recognized , SED congenita and SED tarda. SED tarda is milder and late in onset, and appearance may be normal at birth. They present with short stature and symmetric joint pain caused by epiphyseal changes. A progressive \"pseudo rheumatoid\" arthritis has been described in some children with SED tarda.
CASES REPORT: This is a case series study including 8 cases from four families (5 girls and 3 boys). They were 9-17 years old and onset of clinical manifestations were 2-6 years old. Parents were first- degree relatives in three families. All of cases were normal at birth. The most common signs were swelling, stiffness, range of motion limitation movements and contracture joints particularly knees, elbows and PIP and DIP of both hands and feet. All of patients were short stature,
CONCLUSION: SED tarda is a x-linked recessive disease (milder form is AD),characterized by abnormal gate, short stature, stiffness and contracture of joints. The clinical presentation mimic JCA and all of the patients primarily treated as JCA. It should be considered as differential diagnosis of familial disorders with contractures of stiff joints and familial disorders of short stature.
KEY WORDS: Spondlyloephiphyseal dysplasia tarda, Short stature.

P 068
Macrophage activation syndrome in two girls with SLE

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BACKGROUND: Macrophage activation syndrome (MAS) is a life-threatening complication in juvenile systemic lupus erythematosus (SLE). Diagnosis of MAS may be particularly challenging in patients with this disease because it may mimic the clinical and laboratory features of the underlying disease.
OBJECTIVE: To describe the clinical and laboratory features of MAS as an early complication of juvenile systemic lupus erythematosus.
METHODS: We report two cases of 15 and 10 yo girls with MAS in Juvenile SLE occurring acutely in the first 6 months after the onset at the time of first presentation in our hospital.
RESULTS: The clinical features and laboratory data were analyzed. The main laboratory findings of macrophage activation syndrome were present: pancytopenia, abnormal serum hepatic enzyme levels, coagulopathy, neurologic symptoms, hyperferritinemia, hypertriglyceridemia, decreased erythrocyte sedimentation rate, hyponatremia, hypoalbuminemia and macrophage hemophagocytosis in the bone marrow aspirate sample. The treatment comprised intravenous methylprednisolon, immunoglobulins, cyclophosphamide pulse (one case), transfusions (PT, FFP, PRC) and supportive therapy.
CONCLUSION: Diagnosis of MAS can be difficult because some of its clinical features overlap those of lupus itself. The occurrence of unexplained fever and pancytopenia associated with increased hepatic enzyme levels, coagulopathy, hyperferritinemia, should promptly raise the suspicion of macrophage activation syndrome.
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P 069
Clinical presentation and outcome in a spanish cohort of patients with paediatric onset Systemic Lupus Erythematosus

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BACKGROUND: Systemic Lupus Erythematosus (SLE) is a systemic autoimmune disease that usually affects young women in fertile age with uncommon onset before sixteen years old (10-17%). Several studies suggest that childhood onset worsens the prognosis and mid-term outcome.
OBJECTIVE: Describe the characteristics of a spanish cohort of patients with paediatric onset SLE (pSLE) followed in specialized rheumatologic consults of a tertiary center in last 35 years.
METHODS: A retrospective analysis of 34 patients with pSLE followed by Paediatric Rheumatology Unit of our service for at last six months since diagnosis was made collecting demographic, clinical manifestations and serological characteristics available in the patient's charts. Collected data were age of diagnosis, gender, ethnicity, family history of autoimmune disease, clinical and serological features, accumulated damage rates measured by SLICC / ACR, type of treatment received and mortality during follow-up.
RESULTS: 34 patients with pSLE were included in this study: 30 girls (88,2%) and 4 boys (11,8%). The mean age of onset was 12,88 ± 2,55 years. 3 patients (8,8%) developed the disease before puberty onset, 9 (26,5%) during peripubertal period and 22 (64,7%) in postpubertal period. Most patients were caucasian (32, 94,1%). 7 patients (20,6%) had positive family history for LES in first and second degree relatives. The mean time of follow-up was 15,14 ± 9,87 years. Clinical features of pSLE involved haematological organ in 28 patients (82,4%), non erosive arthritis in 26 (76,5%), lupic nephritis in 23 67,6%), serositis in 11 (32,4%), antiphospholipid syndrome (APS) in 5 (14,7%), and neuropsychiatric involvement with psycosis in 4 (11,8%) and epilepsy in 7 (20,6%), mucocutaneous manifestations like photosensitivity in 19 (54,8%), oral aphthae in 14 (41,2%) and malar erythema in 28 (82,4%). 8 patients (23,5%) developed Raynaud\\\'s syndrome during the follow-up. Immunological tests showed a very high frequency of ANA (100%) and anti-dsDNA antibodies (91,2%). 10 patients were positive RNP (29,4%) and 13 had anti-Ro/SSA antibodies (38,2%), but only 1 (2,9%) was positive anti-La/SSB. Different types of antiphospholipid antibodies were evaluated finding 8 patients (23,5%) with positive lupic anticoagulant and 7 (20,6%) with transient positivity for anticardiolipin IgG type. We found too lower levels of C3 and C4 in 25 (73,5%) and 26 (76,5%) patients, respectively. To assess severity of pLES outcome we used SLICC/ACR Damage Index for SLE at end of follow-up time and found 24 patients (70,6%) with SLICC score ≥ 1, showing a significant cumulative damage. All patients received corticosteroids at some moment of the disease. Most of patients required multiple immunosuppressive treatments. 8 patients (23,5%) received intravenous methylprednisolone pulses, 7 (20,6%) intravenous Cyclophosphamide, 17 (50%) Azathioprine, 6 (17,6%) Mycophenolate mofetil, and 22 (64,7%) antimalarials. Only one patient died (2,9%) and cause of this mortality was an infectious complication (abdominal sepsis).
CONCLUSIONS: The main objective of our study was to describe demographic, clinical and biological characteristics of a spanish pSLE cohort and evaluate the cumulative and irreversible damage that result from the disease activity and adverse effects of medications. Our findings are similar to other studies studies that suggest that pSLE tends to be more severe than adulthood onset SLE. We found too higher SLICC values indicating an earlier risk of damage in paediatric population.

P 070
Towards Defining Clinical Remission in Juvenile Systemic Lupus Erythematosus (jSLE)

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BACKGROUND: There is no established definition for global clinical remission in jSLE.
OBJECTIVES: To develop a definition of global clinical remission in jSLE and to identify candidate criteria for measuring jSLE clinical remission.
METHODS: Pediatric rheumatologists from all over the world (n=137) were surveyed about issues pertaining to defining and measuring clinical remission in jSLE. Consensus for the Delphi survey was set at 70%. Survey-responses were compared to prospective clinical data from a cohort of jSLE (n=33) considered to be in clinical remission by the treating physician.
RESULTS: Survey response rate was 65%. There was consensus that 'clinical remission' needs to be discriminated from 'minimal disease activity' in jSLE. There was consensus that a jSLE patient in clinical remission (a) may have some subjective symptoms (i.e. fatigue, joint pains, headaches) but should not have any objective physical signs of disease activity; (b) may have a persistently positive ANA but should not have abnormal ESR, C3 level, complete blood count and urine sediment; and thus (c) may have disease activity scores > 0. No consensus was reached as to whether remission constitutes a time point or a time period and if medication use is

important in its definition. Clinical data of jSLE patients considered to be in remission supported the survey-responses **(see Table1).**
CONCLUSIONS: Consensus has been reached on preliminary variables useful to define and measure clinical remission in jSLE. Further studies are in progress.

P 071
Hepatitis B vaccination in juvenile systemic lupus erythematosus

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BACKGROUND AND OBJECTIVES: Systemic lupus erythematosus (SLE) is a chronic multisystem autoimmune disease. Infections are one of the most common causes of death due to immunosuppressive treatment and disease related immune dysfunction. Vaccination is a primary tool for protection against infections. There has been limited number of studies about the efficacy of vaccination in this group of patients since it is believed that infectious agents and vaccines might induce autoimmunity. In this study, we examined the antibody responses after recombinant hepatitis B vaccine in juvenile SLE patients and whether antibody levels were affected by immunosuppressive therapy.
PATIENTS AND METHODS: This study consisted of 64 juvenile SLE patients and 24 healthy controls. We evaluated HBsAg, Anti-HBs and Anti-HbcIgG titers in SLE patients. 24 patients (37%) were nonimmunized, 39 patients were immunized (61%) and 1 patient (1,5%) was chronic hepatitis B carrier. Of the 24 nonimmunized patients, 3 had active disease (SLEDAI>10) and 1 was being treated for tuberculosis infection so they were not included in the vaccination program.
Twenty nonimmunized SLE patients were given 3 recombinant hepatitis B vaccine doses at 0,1,6 months. Clinical and laboratory evaluations were done for each patient one month after the vaccination. AntiHBs antibody titer >10 IU/mL one month after the last dose of vaccine was accepted as seroconversion.
RESULTS: Since two patients had SLEDAI score >10 after the first 2 doses of vaccine and one patient had SLEDAI score >10 after the first dose, these patients were given only two doses of hepatitis B vaccine. These patients had already seroconverted. One patient had exacerbation of the disease one month after the third dose of the vaccine.
After 3 doses of vaccination, 16 (80%) of SLE patients and all of the healthy controls had seroconversion. Protective antibody responses were statistically insignificant between the two groups (p=0.49). Geometric mean antibody titers of SLE patients were lower than those of the healthy controls. Adequate antibody response was not affected by immunosuppressive treatment as prednisone, azathioprine, and hydroxychloroquine.
DISCUSSION: Juvenile SLE patients could reach an adequate antibody response after recombinant hepatitis B vaccination and this response is not affected by immunosuppressive treatment. More studies with larger sample sizes are needed to evaluate the efficacy and reliability of this vaccine in this group of patients.

P 072
Papilledema, a possible underestimated physical sign in Kawasaki disease

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ABSTRACT: Aim. In the context of Kawasaki disease (KD), apart from bilateral nonpurulent conjuntivitis, other ocular signs have been described (anterior uveitis, punctuate keratitis, vitreous opacities, retinal ischemia, vascular occlusions and periorbital vasculitis). We describe the case of a 13- year-old latin-american boy, affected by Kawasaki disease with complete clinical presentation who was treated in our hospital and presented papilledema, a previously rarely reported finding..
CASE REPORT: Upon admission the patient was irritable, without other signs of neurological involvement; he showed complete classical criteria for KD and was properly treated with IVIG. An ophtalmologic evaluation showed normal visual acuity, conjunctival bilateral hyperemia, and marked bilateral papilledema with vascular congestion in posterior chamber. A head CT scan was then performed, with normal findings. Papilledema persisted even after IVIG treatment, and despite quick resolution of all other signs took several weeks to resolve.
CONCLUSION: Papilledema is an uncommon finding in the context of KD. Previous reports correlate papilledema with angiographic findings, supporting the hypotesis that this sign can be a consequence of the vasculitis.
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P 073
Churg-Strauss syndrome in childhood: a rare form of systemic vasculitis posing a great diagnostic challenge

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Churg-Strauss Syndrome (CSS) is characterized by eosinophil-rich granulomatous inflammation involving the respiratory tract, necrotizing vasculitis affecting small to medium-sized vessels and is associated with asthma and eosinophilia. To date there have been very few case reports of CSS in the literature in the paediatric population. We describe a case of a 16 year old female patient with CSS and highlight the diagnostic challenges associated with this condition.
A 16 year old girl, offspring of a Caucasian non consanguineous couple, presented with periorbital oedema, low grade fever and malaise. She subsequently developed respiratory distress, subcutaneous oedema, a vasculitic rash on the lower limbs and arthritis. In the previous 3 years, she had five hospital admissions due to severe asthma.
Positive findings from the investigations performed were: raised WCC (22000/mm3) with marked eosinophilia (9000/mm3), thrombocytosis (600/mm3), and raised ESR (118mm/h), CRP (160 mg/dl) and total IgE (3200 KU/L); p-ANCA was weakly positive. High resolution CT of her chest revealed microvascular changes, pulmonary infiltrates and interstitial changes. MRI of her sinuses showed sinusitis of the frontal sinuses. In the context of primary eosinophilic disorders considered T cell clonality studies were normal and she tested negative for FIP1L1-PDGFRA mutation.
Based on the findings of persistent asthma, paranasal sinusitis, peripheral blood eosinophilia and pulmonary infiltrates she was diagnosed with CSS. She was treated with corticosteroids and six intravenous pulses of cyclophosphamide at monthly intervals. Nine months following initial presentation she remains asymptomatic. Remission is sustained with low dose prednisolone and azathioprine.
Prompt diagnosis and initiation of intensive treatment has contributed to satisfactory control of the disease activity, although long term sequelae are yet to be determined. CSS is an extremely rare entity in the paediatric population; however, it should be considered in a systematically unwell patient with late onset asthma resistant to standardized treatment. Differentiation from primary eosinophilic syndromes remains challenging.

P 074
Two cases of livedoid vasculitis in children

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BACKGROUND: Livedoid vasculitis (LV), a type of small vessels vasculitis of the skin, is a cutaneous occlusive vasculopathy characterized by recurrent painfull ulcers occuring especially in the vicinity of the ankle in association with persistent livedo reticularis. LV is a very rare condition in children.
OBJECTIVES: To distinguish those cases of local cutaneous vasculitis difficult to diagnose and classify in the absence of definite criteria in children.
METHODS: This is a case presentation of 2 girls presenting with unusual chronic ulcerative cutaneous lesions around the ankles.
RESULTS: Based on clinical features (livedo reticularis), histopathologic changes (fibrin in the walls and thrombi within the lumen of venules in the reticular dermis) and the evolution (heal with atrophie blanche) a diagnosis was made, after the exclusion of other vasculitis types. Complex laboratory investigations were done in order to do this. Finally, the diagnosis in both cases was livedoid vasculitis.
CONCLUSIONS: Proper diagnosis of ankle ulceration is very important because ulcers may result from a variety of small vessel vasculitis which do not require the same treatment. Patients with livedoid vasculitis may have multiple defects in thrombolysis, so a complete coagulation workup is required.
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P 075
Henoch-Schönlein purpura in Turkish children

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BACKGROUND: Henoch-Schönlein purpura (HSP) is an acute leukocytoclastic vasculitis that primarily affects children. Most patients present from autumn to spring, and HSP often follows a upper respiratory infection.
OBJECTIVE: To examine epidemiological, clinical, and outcome in Turkish children affected with HSP.
METHODS: Retrospective study of children discharged with a diagnosis of HSP from the Erciyes University Medical Faculty, Department of Pediatric Nephrology and Rheumatology, between 1992 and 2008. Epidemiological, clinical, laboratory data, treatment, and outcome were collected by reviewing medical charts.
RESULTS: Two hundred thirty nine children entered the study: The male:female ratio was 1.4:1.The mean age at the time of diagnosis was 8.1+/-3.1 years. Purpura was present in all cases, arthritis/arthralgias in 76.2%, abdominal involvement in 62.3%, scrotal edema in 5.9%, renal involvement in 30.1%, pulmonary involvement in 0.8% and central nervous system involvement in 0.4 %. Joint involvement and scrotal edema were more frequently in patients whose disease began in autumn. Abdominal involvement was more frequently in children whose disease began in spring.
CONCLUSION: It may be relationship between season of onset HSP and frequency of some system involvement. The prognosis was excellent; although severe system involvements (pulmonary and brain) which were life-threatening was found in a small percentage of the children.

P 076
Identification of a new polymorphism of the FGF23 GENE: a possible predictor of coronary damage in Kawasaki Disease (KD)

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BACKGROUND: Vascular endothelial cell damage is pivotal in KD, acute systemic vasculitis with arterial dysfunction. Intimal thickening and fibrosis are reported in KD coronary arteries. Several pts timely treated with IVIG also develop CAA with risk of ischemic heart disease. Phosphatonins are new hormones involved in the regulation of phosphate homeostasis and bone mineralization. FGF23, the master phosphatonin, acts through FGFr1 present in vasculature and heart. Fgf23 knockout mice are characterized by ectopic calcification, vascular and heart damage with serum FGF23 that may contribute to the development of vascular damage.
AIMS: 1.To measure serum level of intact FGF23. 2. To evaluate the association between FGF23 levels and CAA 3.To screen KD pts for mutation in FGF23 gene to assess a possible role of FGF23 allelic variants in cardiac damage pathogenesis.
PATIENTS AND METHODS: 95 KD pts (58M, 37F, median age 30.5 mths) entered the study. 30 age and sexes matched healthy children acted as controls. All pts had received IVIG and aspirin. In all pts, at baseline and at study entry lipid profile (total cholesterol, HDL, LDL, triglycerides) was evaluated. The serum intact FGF23 concentration was measured after informed consent, using an ELISA assay (Immunotopics Inc. San Clemente, CA, USA). Genomic DNA was extracted from peripheral blood and the three FGF23 exons, including the intron-exon boundary regions, were PCR-amplified and analyzed on ABI Prism 3100 Genetic Analyzer (Applied Biosystems, Foster City, CA).
RESULTS: KD pts have higher levels of intact serum FGF23 than controls (72 +/-40SD vs 12,3+/-3.2SD pg/ml; Student's T Test: p=0.01). DNA analysis shows a new C insertion in the intronic region between -36 and -37 nucleotide close to the exon 2 (rs3832879: NM_020638.2:c.212-37_212-36insC). To verify the frequency of the rs3832879 variant, and to evaluate the presence of polymorphic change, DNA analysis of 100 Caucasian voluntaries confirmed this change, and the insertion as a polymorphic site. The polymorphism was associated with coronary damage; all pts (18M,10F) carrying out the polymorphic allelic variant have CAA. These pts, display higher levels of serum FGF23 than pts without polymorphic site (120+/-40 vs 38.2+/-5).
CONCLUSIONS: FGF23 is an important hormone that contributes to the development of cardiovascular damage in several diseases as chronic kidney disease though its exact role has to be defined. The high amount of serum FGF23 may be in part responsible of the pathogenesis of vascular and heart damage in KD. So far, no individual genotype data are available for FGF23 gene polymorphism. From these preliminary results the segregation of the FGF23 genotype with the CAA opens the possibility of a functional role of the new polymorphism in KD. These data point to FGF23 gene polymorphism and serum FGF23 levels two potential useful predictors of high risk of CAA in KD.
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P 077
Decreased exercise capacity in juvenile dermatomyositis – a long-term follow-up study

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BACKGROUND: This study describes long-term outcome on fitness in juvenile dermatomyositis (JDM) patients. It has previously been shown that patients with active JDM have decreased fitness (1,2), however, it is not known whether these patients regain their physical fitness after recovering.
OBJECTIVES: Our aim was to measure fitness in JDM patients in a follow up study 2-36 years after disease onset.
We hypothesized that fitness:
- Is decreased in patients with active JDM
- Improves after remission
- Is affected by prolonged JDM

METHODS: JDM patients were identified from the National Register of Patients. Controls were historic controls from recent Danish surveys. Maximal oxygen uptake (VO2max) was defined by incremental cycle ergometry test. Muscle function was tested with Manual Muscle Strength Test (MMT) and Child Myositis Assessment Scale (CMAS). Disease Activity Score (DAS) and the Myositis Damage Index (MDI) scored disease activity and damage, respectively.
RESULTS: 56 patients were identified; 51 patients (91 %) agreed to participate. Three patients were excluded due to pregnancy/lactation, one patient was too small for the cycle and one could not fulfill the exercise test; thus 46 patients, (31 females), were included.
The patients were characterized as shown in **table 1.**
OUTCOME: 15 patients (33%) had normal VO2max and 31 (67%) had decreased VO2max. VO2max was higher in healthy controls vs. patients with JDM (p=0.003, CI 8.3-19.3). However, when divided by sex no difference in VO2max was found in the males (p=0.15) only in the females (p=0.004).
Patients with active disease had significantly lower VO2max compared to those in remission (p<0.001), but even patients in remission > 5 years had decreased VO2max compared to normal controls (p<0.001).
Decreased VO2max was negatively correlated with CMAS, and MMT-score (p<0.001), and positively correlated with DAS-score (p<0.001). No correlations were found between VO2max and disease duration, follow up time delay and time from remission.
CONCLUSIONS: Patients with active JDM have decreased fitness and persists several years after remission.
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P 078
Pulmonary status in a long term follow up of juvenile dermatomyositis patients

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BACKGROUND: In children with juvenile dermatomyositis (JDM) only a few studies describes the pulmonary aspects of the disease, indicating that 5-30% of JDM patients develop restrictive pulmonary lung function or interstitial lung disease (ILD).
OBJECTIVES: The objectives of the study were to describe:
- Long term pulmonary involvement in a JDM-cohort
- The correlation between pulmonary involvement in JDM and the severity of the disease

METHODS: 52 patients with JDM were identified and screened with a conventional spirometry. The scores of Myositis Damage Index (MDI) and Myositis Damage VAS (MYODAMvas) were used to estimate JDM-outcome.
RESULTS: 51 patients (37 females) could perform spirometry with acceptable measurements. None of the patients reported of any pulmonary symptoms.

Thirty-eight patients (74%) had normal lung function, eight patients (16%) demonstrated obstructive pattern
FEV1/FVC ratio<0.8) with a positive reversibility for beta-2 agonist in 4 patients. Five patients (10%) had restrictive lung function, in which 3 of those were previously diagnosed with ILD by CT-thorax **(table 1)**. The other patients had no known history of pulmonary disease and had never been pulmonary evaluated.
Restrictive lung disease was correlated with increased long-term damage estimated by MDI and MYODAM VAS ($p < 0.01$)
CONCLUSIONS: In a long term follow up study of JDM patients 10% of the patients had decreased pulmonary function with at restrictive pattern after a mean follow up time of 12 years, indicating a need for repetitive pulmonary follow up in JDM patients. Conventional pulmonary disease like asthma should also be considered. Restrictive pulmonary involvement was correlated to increased long-term damage.

P 079
Evaluation of the Durometer to access skin thickness in healthy children

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The evaluation of the skin thickness manually for the Modified Rodnan Skin Score has a low correlation coefficient. In several studies with adult patients the Durometer was applied to access the skin thickness. The measured arbitory score from 0 to 100 does changes during treatment trials. The are currently no norm values for children.
AIM OF THE STUDY: To establish norm values for different body in children.
METHODS: Consecutive patients of the paediatric rheumatology clinic with juvenile idiopathic arthiritis , excluding the psoriatic form and the systemic form with rash, were prospectively for the assessment of the skin thickness with the manual Rex Digital Durometer evaluated. Patients with comorbities involving the skin were excluded. The points of the assessment of the anatomic areas were standardized. Certain anatomic areas with an underlying bone structure were excluded.
RESULTS: In 244 consecutive patients the skin thickness with the Durometer was evaluated. The mean age of the patients was 11.9 (range 6.4-17.2)years. The mean Tanner score was 2.1 (range 0-4). The mean values were for the upper arm 24.4, for the lower arm 29.8, for the hand 15.9, for the upper leg 30.5, for the lower leg 28.8, for the back of the feet 24.5, for the abdomen 19.8, for the subclavicular region 14.5. The mean values for the region over the finges were 50, because of the bony underlayer.
CONCLUSION: We established the norm values of skin thickness for certain anatomic areas with the durometer for healthy controls. The durometer can not be applied in regions , where there is bony structure directly under the skin surface. The values for the upper arm are in the similar range as established in healthy adults. The norm values are significantly lower, that in areas with sclerodermatous skin involvement. The application of the durometer will help to have a more objective way to access the MRSS, as one of the primary outcome measures in therapeutic trials for systemic sclerosis.

P 080
Preliminary results for 6 minute walk values in healthy German children

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INTRODUCTION: 6 minute walk is a primary outcome measure in therapeutic studies for patients with pulmonary hypertension. Currently we have a two of sets of data (Lammers1 et al and Li 2et al)regarding test results in the 6 minute walk test (6MWT) in healthy children with a large span in the norm values in the different age groups.
AIM OF THE STUDY: To establish norm values for healthy German children for the 6 Minute Walk Test.
METHOD: The team of an occupational therapist and a study nurse is visiting schools, were previously the parents agreed on the participation of the students on the test. Always just students from one class are invited to participate in the test. The students are performing the test according the international guidelines. The demographic data of the students are collected and the parents fill out a short survey regarding the physical activity and the health condition. Children with chronic diseases, which decrease the stamina are excluded.
RESULTS: Up till now 208 students participated from the age 7 to 10 years. 90 of the 208 were female. 30 in the age group of 7; 50 in the age group of 8 years; 67 in the age group of 9 years and 61 in the age group of 10 years. The mean 6 minute walk distance was 463.73 m in the age group of 7; 479.09 m in the age group of 8 ; 492,72 m in the age group of 9 and 488.32 m in the age group of 10.
CONCLUSION: Our results are in the range of the patients from the UK published by Lammers et al 1 and are in significantly lower range than in the Chinese population collected data by Li et al.2. This reflects the importance of this study to gain norm values for our patient population.
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P 081
Anti-interleukin-1 treatment in SoJIA patients carrying or not MEFV mutations

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INTRODUCTION: A high frequency of MEFV mutations has been detected among patients with systemic juvenile idiopathic arthritis (SoJIA) from the Turkish population. The prevalence and significance of the MEFV mutations in SoJIA remain unknown.
CASE REPORTS: Six patients with persistent arthritis, cutaneous rash and daily high fever were diagnosed as SoJIA according to the ILAR criteria. They were screened for MEFV mutations by specific PCR-amplification and bidirectional sequencing. Three children were heterozygous for previously described mutations.
All patients received corticosteroid therapy, but when the dose was tapering symptoms reappeared, in spite of association with methotrexate in 4 cases, and etanercept in 2. Due to the persistence of active disease, IL-1 receptor antagonist (IL-1Ra) was started.
Table shows patient characteristics and response to IL-1Ra therapy.
CONCLUSIONS: Despite the small sample size, there were three out of six SoJIA patients carrying MEFV mutations. Complete response to Il-1 blockade was observed in 5 children independently they had MEFV mutations associated.
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P 082
Expanding clinical and genetic diversity of TRAPS syndrome by means of identification of the novel p.K132R TNFRSF1A mutation in a patient with recurrent febrile episodes

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Tumour necrosis factor (TNF) receptor-associated periodic syndrome (TRAPS) is an autosomal dominant hereditary periodic fever syndrome characterised by recurrent, long inflammatory episodes with fever, migratory localized myalgias and skin rash, arthritis, conjunctivitis and abdominal pain, associated with a marked acute phase response. In 1999 its genetic basis was elucidated by means of the description of monoallelic pathogenic mutations in the TNFRSF1A gene, which encodes the TNF receptor type 1 (TNFR1) and maps on 12p13 chromosome. Since then, more than XX different pathogenic TNFRSF1A mutations have been reported, located on exons 2, 3, 4 and 6. Herein, we describe the clinical case and results of genetic tests performed in a Spanish patient who experienced recurrent episodes of fever, arthralgias, and mild abdominal pain and headache.
CASE REPORT: Patient is a 5 year-old girl who was referred to our pediatric rheumatology department due to recurrent febrile episodes, which started during the last year. There was not familial history of a similar disease. The acute episodes lasted 3-4 days, recurred every 2-3 weeks, and the main detected symptoms were fever (up to 40ºC), intense polyarthralgias, abdominal pain and headache. Neither arthritis, myalgias nor skin eruptions were noted. She was repeatedly admitted in the emergency room, showing in all cases an intense acute phase response and negative results for all microbiological tests performed. Due to the potential diagnosis of autoinflammatory disease, genetic tests were performed. There were not detected mutations in the MEFV and NLRP3 gene. However, it was detected the novel and heterozygous nucleotide G in the exon 5 of TNFRSF1A gene, which encodes for®transition c.482 A the missense p.Lys-132-Arg (p.K132R) variant in the TNFR1. Its absence among a panel of 200 Spanish control chromosomes suggest its role as a pathogenic mutations rather a rare polymorphism. However, patient's

parents TNFRSF1A analyses revealed the presence of the p.K132R variant in patient's mother, supporting for the presence of low penetrance.
CONCLUSIONS: This case expands the diversity of TRAPS syndrome by the identification of moderate and atypical febrile episodes, associated to the low penetrance p.K132R mutations, which represent the first and the only known mutation located at exon 5 of TNFRSF1A gene.

P 083
Familial Mediterranean Fever: a 10-year follow-up in Iranian patients

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OBJECTIVE: Familial Mediterranean Fever (FMF) is the most frequent periodic fever that characterized by recurrent fever, abdominal pain, joint pain, skin rash and polyserositis. This disorder is seen sporadic in Iranian family. In this study, we report 10 years follow up and outcome of disease in 85 patients from Iran.
METHODS: In a retrospective study, all referred patients during the last 25 years with a diagnosis of Mediterranean fever Rheumatology Clinic were studied. Following data were registered for all patients: early symptoms, initial laboratory results, follow-up period, drug doses, complications of disease and treatment. Infection, malignancy and rheumatologic diseases ruled out in all patients.
FINDINGS: Out of 96 patients who reffered to rheumatology clinic with FMF diagnosis, 6 patients were excluded (due to incomplete follow up). Totally, 90 patients enrolled in this study including: 47 male (52.2%) and 43 females (47.8%). The mean age of patients was 13.0 (± 4.9) and the range 2.7 to 24.5 years. The mean age of patients at the first presentation was 49.2 (±39.8) months (2 months to 15 years). The period time of symptoms was every 4.1 (±2.1) weeks (range 1 to 8 weeks) before starting treatment. The mean time of follow up was 8.9 (±4.7) years (1 to 17.9 years). Regular and periodic symptoms have been mentioned in 68 patients (75.5%), but in others there are no regular periodic symptoms. Positive family history was recorded in 12.2% of patients, 6% in brothers and sisters and remaining in uncle or grandmothers. Common symptoms of FMF were: fever (92.2%), abdominal pain (84.4%), and joint pain (43.3%). Less common symptoms including chest pain, skin rash, and bone pain were recorded in 20%, 17.8% and 11.1%, respectively. Rare symptoms were vomiting (8.9%), pelvic pain (4.4%), neck pain and tension each one in 2.2% patients, and diarrhea and headache each one in 1.1% of patients.
In laboratory investigations, the mean of hemoglobin, platelets and ESR were 11.5 (±1.4), 304000 (± 102077), and 29.3 (±24.4), respectively. CRP in 20 patients (23.5%) was positive between 12 to 48.
Genetics study was conducted in 21 patients that in 47.7% of patients were normal. Out of 11 patients with abnormal genetic test, 7 patients (63.6%) had a mutation in the M694V gene, 3 patients (27.3%) a mutation in the M726A and 3 patients (27.3%) a mutation in the M680I gene. Two patients (18.2%) had a mutation in both M726A and M680I genes. All patients responded to Colchicine very good and there is no resistance to Colchicine in this study. In this study, 2.2% patients were symptom free with 0.25 mg, 15.5% under 0.5 mg, 74.6% with 1mg, 3.3% and 4.4% with 1.5 and 2 mg daily Colchicine. No serious complication due to treatments, or disease was recorded during follow up period.
CONCLUSION: According to our study, all symptoms and complication of FMF are controlled with proper treatment. There is not any Colchicine resistance or serious complication in our study. The frequent mutation was M694V and M726A genes in our patients, although 47% of patients had no known mutation gens.

P 084
Somatic p.G307V NLRP3 mutation associated with a moderate case of CINCA patient

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INTRODUCTION: Chronic infantile neurologic, cutaneous, and articular (CINCA) syndrome is a cryopyrinopathy associated to mutations in the NLRP3 gene encoding cryopyrin, which plays a critical role in interleukin (IL)-1beta processing.
Conventional analyses of NLRP3 gene detect mutations in about half of CINCA patients, and it remains unclear which gene(s) is/are responsible for the remaining cases. Up to now approximately 60 disease-associated NLRP3 mutations have been described, some of them as somatic, non-germline mutations. A severe CINCA case with the p.G307V NLRP3 mutation was recently reported.
CASE REPORT: A 9 year-old girl was referred to our hospital with a diagnosis of CINCA syndrome based on an early-onset urticarial generalized non pruritic skin rash, fever (<38ºC), painful knee arthropathy with enlargement of left patella from her 5º birthday, and headache and papyledema due to intracranial hypertension diagnosed at 7 years.
At the age of 11 years-old, her symptoms persisted and a proliferation in tibial physis was observed. Anakinra treatment was then started, and cutaneous lesions, headache and musculoskeletal pain disappeared. To avoid daily drug administration, at 14 years old she was switched to Canakinumab, remaining asymptomatic. She is now in a good condition, in spite of non painful knee arthropathy.
A first conventional genetic study did not find any NLRP3 mutation. However, a new analysis based on PCR-cloning and sequencing showed the presence of a de novo, heterozygous somatic p.G307V NLRP3 mutation.
CONCLUSIONS: Somatic NLRP3 mosaicisms could be the molecular basis of some patients diagnosed as CINCA syndrome without mutations in conventional analyses.
The p.G307V mutation here described has been recently reported in an unfortunate case of severe CINCA syndrome, who exhibited an incomplete response to IL-1 blockade, in contrast to our patient.
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P 085
Progressive Osseous Heteroplasia as distinct clinical entity from Fibrodysplasia Ossificans Progressiva

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BACKGROUND: Progressive Osseous Heteroplasia (POH) is a recently described clinical entity characterized by dermal ossification beginning in childhood and subsequent progressive ossification of subcutaneous fat, skeletal muscle and deep connective tissues. There are some clinical features There are clinical features may allow distinction from the Fibrodysplasia Ossificans Progressiva (FOP) as presence of cutaneous ossification, absence of congenital malformations of skeleton, absence of tumor-like swellings, asymmetric mosaic distribution, absence of predictable regional patterns of heterotopic calcification and predominance of heterotopic ossification intramembranous rather than endocrondral.
OBJECTIVE: Describe and compare the clinical and radiological features of two cases of FOP HOP and five follow-up for the Pediatric Rheumatology Unit of our service
METHODS: We conducted a review of medical records of patients diagnosed with FOP and POH followed by our service. Clinical data were collected functional limitation, congenital skeletal malformations, early papular rash, type of calcification, ossification following trauma, alterations of Ca/P metabolism, radiologic pattern and treatments received.
RESULTS: Study results are summarized in **Table 1**. Unlike the FOP, POH patients had no significant functional limitation, or congenital malformations, or ossification after trauma. Both patients with POH presented with early papular rash, skin, subcutaneous and muscular ossification, but the pattern of calcification was fibrillar with unlike FOP patients had a gross pattern.
CONCLUSIONS: The POH and FOP are similar and little known clinical entities. The POH can be distinguished from FOP by absence of congenital malformations of the first toe, asymmetric distribution of calcified plaques and evolution of topographic pattern, lowest clinical and radiological progression and therefore, lack of need for treatment bisphosphonates. In our series we found differences in the presence of cutaneous calcification, but it is necessary to analyze more cases.

P 086
MRP8/14 Complex: useful marker in a 10-year-old patient with oligosymptomatic fever of unknown origin

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BACKGROUND: Systemic onset Juvenile Idiopathic Arthritis (SoJIA) is an important differential diagnosis of Fever of Unknown Origin (FUO) in children. Characteristic signs of active arthritis often develop later in the course of the disease and make early diagnosis difficult. Serum levels of Myeloid-Related Proteins 8 and 14 (MRP8/14) complex have been suggested to be an excellent diagnostic tool to allow early discrimination between SoJIA and other causes of FUO.

CASE REPORT: A 10-year-old girl is admitted to hospital because of quotidian fever of more than ten days. She reports no other symptoms apart from slight myalgias and arthralgias of wrists during the first days of the illness.
The physical examination is normal. Initial laboratory findings show 20.600/mcl leukocytes with 88% of Neutrophils, ESR 52 mm, CRP 215 mg/l and Ferritin 1362 ng/ml. An extensive diagnostic work up including repeated body fluid cultures and serology, bone marrow aspirate and imaging studies does not reveal any pathology.
Empiric antibiotic therapy with Cefotaxime and Clarithromicin during 14 days does not improve her condition. By the third week she presents an evanescent salmon coloured rash during fever spikes. The suspicion of SoJIA is raised but she does not fulfil the ILAR diagnostic criteria.
In order to support the suspected diagnosis of SoJIA we determine the serum level of MRP8/14 complex. With 7130 ng/ml serum level is highly elevated.
After starting therapy with oral prednisone in dose of 2 mg/kg/day the fever remits after one day, CRP and ESG return to normal after a week and Ferritin normalizes after three weeks of treatment.
Corticoid therapy is tapered off over a three month period. Four month after first symptoms the patient is asymptomatic apart from mild iatrogenic Cushing.
DISCUSSION: Recently it was shown that serum MRP8/14 complex can discriminate between SoJIA and other possible causes of FUO. In a study with 60 patients with SoJIA and 148 patients with other causes of FUO (Frosch et al, Arthritis and Rheumatism, 2008) the mean value for SoJIA was 14.920±4.030 ng/ml. Our patient had levels well above mean values of other differential diagnosis of FUO as reported in the literature (proven bacterial infection 3.720±870, Kawasaki diseases 3.630±480, NOMID 2830±580) . Values of above 7000 ng/ml are considered very suggestive of SoJIA (personal communication Dr. Frosch, University of Muenster) supporting the suspected diagnosis of SoJIA though the patient did not fulfil the ILAR criteria for SoJIA .
Serum MRP8/14 levels may reflect MRP concentration in skin and synovia (Foell et al, Arthritis and Rheumatism, 2004). The slightly lower levels of our patient compared to mean values in SoJIA as reported in the mentioned study might be due to a very oligosymptomatic course without arthritis. The early diagnosis and initiation of treatment before appearance of overt arthritic signs might have prevented a more severe disease course.
CONCLUSION: Mean serum levels of MRP8/14 in a subset of patients with SoJIA who present initially without arthritis have to be established. In these patients SoJIA MRP8/14 complex in serum could be a very useful laboratory marker to establish early diagnosis and to enable prompt adequate treatment.
ACKNOWLEDGMENTS: The author thanks Dr. Michael Frosch and Staff of the laboratory of Paediatric Rheumatology/Immunology at University of Muenster, Muenster, Germany for measuring MRP8/14 complex serum levels.

P 087
Circulating levels of vaspin and omentin, two novel adipokines, in juvenile idiopathic arthritis

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BACKGROUND: Adipokines are associated with the pathophysiology of obesity and metabolic syndrome, and have gained recent attention also in inflammatory diseases such as rheumatoid arthritis (RA). Vaspin and omentin are two novel adipokines, and their clear role is still not defined. Vaspin is a member of the serine protease inhibitor family with insulin-sensitizing effects. Omentin is a fat depot-specific secretory protein synthesized by visceral adipose stromal vascular cells. It has been identified in other tissues including the adipose tissue of patients with Crohn disease. In a recent study elevated levels of vaspin and reduced levels of omentin have been demonstrated in the synovial fluid of RA patients. To our knowledge they have not been studied in juvenile idiopathic arthritis (JIA).
OBJECTIVE: To investigate the serum levels of two novel inflammatory adipokines, vaspin and omentin, in JIA. As controls we took a group of patients with Kawasaki disease (KD) and a group of healthy subjects.
METHODS: Serum concentrations of vaspin and omentin were measured by ELISA in a sample of 41 children with JIA (M=7, F=34, mean age 6.81±3.84 years), as well as in 21 with KD (M=16, F=5, mean age 3.98±3.04 years) and 14 healthy controls (M=7, F=6, mean age 8.84±4.79 years). In patients with JIA, body mass index SD score (BMI-SDS) was calculated, and number of active joints, use of DMARDs, and ESR and CRP levels were also determined. Statistical analyses was perfomed with non parametric tests (Mann-Whitney and ANOVA).
RESULTS: Elevated levels of omentin were found in patients with JIA (mean 8.52±3.06 ng/mL) compared to healthy controls (mean 6.12±1.92 ng/mL; p=0.01), and in KD (mean 7.83±2.13 ng/mL) compared to healthy controls (p=0.02). There was not a significant difference in omentin levels between JIA and KD patients (p= 0.36). Vaspin levels were not different in healthy subjects (mean 3.78±4.08 ng/mL) compared to patients with JIA (mean 2.70±2.73 ng/mL; p=0.27) nor compared to patients with KD (2.30±3.23 ng/mL; mean p=0.24). There was not a significant difference in vaspin levels between JIA and KD patients (p= 0.6). In JIA patients, levels of adipokines did not show a significant correlation with BMI-SDS (omentin p=0.6, vaspin p=0.57), ESR (omentin p=0.09, vaspin p=0.23), or CRP (omentin p=0.42, vaspin p=0.59). JIA patients with active disease had higher levels of omentin compared to patients in clinical remission (p=0.02), while vaspin did not show a significant correlation with disease activity. Use of DMARDs was not correlated with serum levels of the adipokines (omentin p=0.27, vaspin p=0.83).
CONCLUSIONS: Our study shows that omentin serum levels are increased in patients with JIA and KD when compared to controls. Moreover, in JIA we also found a significant correlation between omentin levels and presence of active arthritis. This is only a preliminary study and further research is ongoing in order to validate these findings and elucidate more the role of adipokines.

P 088
HMGB-1 and TNF-alpha mRNA Expressions in patients with juvenile idiopathic arthritis

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BACKGROUND: Although the use of glucocorticoids and immunosuppressants brought a substantial improvement in treatment of Juvenile Idiopathic Arthritis (JIA), about 60% of patients do not benefit. The development of TNF-alpha inhibiting therapy has dramatically improved patient outcomes. Nevertheless, there are unresponsive patients, indicating a considerable need for novel therapeutics that are independent of TNF activity. Emerging targets for treatment are alarmins, a family of multifunctional intracellular proteins with strong pro-inflammatory activity. In the context of JIA, among the alarmins, particularly interesting are high mobility group box 1 (HMGB-1), that induce endothelial cytokine expression, cause epithelial barrier dysfunction, and activate macrophages to release pro-inflammatory mediators, including TNF, IL-1α, IL-6, and macrophage inflammatory protein-1α
OBJECTIVES: We aim to investigate the TNF-alpha and HMGB-1 gene expressions in patients affected by JIA in treatment with anti- TNF-alpha drugs.
METHODS: 22 Italian (7M/15F) JIA patients who are followed at our Unit in Messina are included in this study. 14 patients present polyarticular JIA: 11 with Etanercept treatment, 3 with Adalimumab treatment. 8 patients have oligoarticular JIA: 6 with Etanercept treatment, 2 with Adalimumab treatment. All patients were in Methotrexate treatment, except for 3 patients (2 polyarticular JIA and 1 oligoarticular JIA) only in Etanercept therapy. Total RNA was extracted from whole blood, by using a commercially available kit. After quantification mRNA was reverse transcribed into cDNA and used to quantitate the amount of TNF-alpha and HMGB-1 (TaqMan probes) by Real-Time RT-PCR method using the SDS 7300 Applied Biosystems instrument. Beta-actin was also determined as endogenous control. The results for the target gene were expressed as n-fold difference relative to the endogenous control gene (relative expression levels). ACR Pedi responses were assessed throughout the study. Laboratory assessment of inflammation (VES and CRP) were used in this study.
RESULTS: The polyarticular JIA patients with ACR Pedi 60 showed significant reduced HMGB-1 mRNA expression (5,5+/-0,3; p<0,05) than ACR Pedi 30 patients (7+/-0,5). Not significant difference was demonstrated by TNF-alpha mRNA expression (ACR Pedi 60: 5,1+/-0,5 vs ACR Pedi 30: 5,3+/-0,3). The oligoarticular JIA patients with ACR Pedi 60 showed significant reduced HMGB-1 (3,7+/-1,2; p<0,01) and TNF-alpha (4,8+/-0,3; p<0,01) mRNA expressions than ACR Pedi 30 patients (respectively 6,9+/-0,4 and 6,75+/-0,1). The laboratory inflammation assay were negative in all patients.
CONCLUSIONS: The JIA patients with better disease control (ACR Pedi 60) have significant reduced TNF-alpha and HMGB-1 mRNA expressions. The present study supports the hypothesis that HMGB1 is an important treatment target, , indicating a research for novel therapeutics that are independent of TNF activity
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P 089
Resistin levels in juvenile idiopathic artrhritis: associations with disease characteristics and long-term prognosis

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Juvenile idiopathic arhritis (JIA) is the most frequent inflammatory joint disease in children. Humane resistin is an adipokine, which promotes inflammation via induction of a cytokine cascade. Elevated levels of resistin have been found in

inflammatory / autoimmune diseases. Resistin level in JIA patients has not been studied earlier.
OBJECTIVES: To determine the level of resistin in patients with JIA and to assess whether it is associated with JIA subtype characteristics, disease activity and predicts long-term prognosis.
METHODS: Blood samples were obtained from 131 Estonian children with JIA (75 girls and 56 boys, mean age 10.5 ± 4.4 years). In 8 patients with acute joint effusion, matching sample of synovial fluid was also collected. 21 patients were prospectively followed up after 10 years. Resistin levels were analysed using an ELISA technique. Clinical disease characteristics, inflammatory and immunological parameters were recorded.
RESULTS: The mean resistin level in the circulation was 16.8±2 ng/ml and it was 400-folds higher in the synovial fluid (6976±3984 ng/ml). The levels of resistin were similar between boys and girls (20±4 ng/ml vs.14±1 ng/ml, respectively). Patients with systemic arthritis (n = 7) displayed significantly higher (p = 0.03) resistin levels (59±29 ng/ml) than those with oligoarthritis (n = 68; 13±1 ng/ml). No significant difference was found regarding resistin levels between groups according to their RF, ANA and HLAB27 status. A positive correlation was found between resistin levels at start and after 10 years of follow-up in the total study group and in boys as well (rho = 0.549, p = 0.014 and rho = 0.717, p = 0.043, respectively). Resistin level at the disease start correlated with CRP value (rho = 0.349, p=0.0003). Patients with persistently active disease (n = 5) had significantly higher resistin levels in comparison with those in complete remission (n =14) at 10 years (14±1 ng/ml vs. 8±1 ng/ml; p = 0.043). The patients with detectable ultrasound changes at 10 years showed a significant positive correlation between resistin level and neutrophil count (rho=0.675, p=0.012).
CONCLUSIONS: Our results suggest that resistin level in JIA patients reflects the magnitude of inflammation in systemic arthritis and locally in the joints being associated with disease activity. The level of resistin is in correlation with disease activity in long-term follow-up.

P 090

Long-term anti-TNF therapy safety outcomes – results from biology therapy register of JIA patients in Slovakia

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BACKGROUND: When evaluating the efficacy of biological therapy with anti-TNF-α medications, special attention is given to assessment of the risk of infection, malignancy and occurrence of other immunity-related diseases as consequence of inhibition of TNF-alpha physiological function.
OBJECTIVES: Evaluation of the safety records from biology therapy register for juvenile idiopathic arthritis (REBIJIA) patients treated with recombinant TNF-α receptor (etanercept).
METHODS: Records of 59 paediatric patients, 36 females and 23 males, 12 years old on average, treated with recombinant TNF-α receptor (etanercept) were entered into register between November 2003 and March 2010.
Penetration of particular forms according ILAR criteria was 54% sero-negative polyarthritis, 29% extended oligoarticular form, 7% enthesitis-related arthritis, 7% persistent oligoarticular form, 3% sero-positive polyarthritis. Average therapy duration was 3 years (0.4 – 5.4 years), 154 patient-years in total. 73% patients were treated for 2 years or more. Efficacy and safety parameters were evaluated every 3 months after etanercept therapy initiation (dose 0.8 mg/kg/per week). Safety outcomes: incidence of serious adverse events, malignancies and other immunity-related disease – intercurrent infections and changes in auto-antibody profile.
RESULTS: In 5 children etanercept therapy was discontinued because of the adverse events . Serious adverse event – macroscopic haematuria due to urinary bladder hypervascularisation was observed in 1 female patient. Other immunity mediated diseases developed in 4 patients (1x M. Crohn, 1x Sjögren's syndrome with vasculitis, 1x autoimmunity thrombocytopenic purpura, 1x Henoch-Schönlein purpura). Serious infection was observed in 3 cases (0.019 infection/patient-years. The change in frequency of common upper respiratory tract infections (2.5 infections per year during first year of therapy vs 1.7 infection in the following period) was not statistically significant. Change in auto-antibody profile without development of clinical symptoms of other autoimmune disease was observed in 5 patients. Among those induction of ANA production was found in 4 children and anti dsDNA was observed in 1 patient. There was no occurrence of malignant proliferation in the entire cohort.
CONCLUSIONS: Proper indication and close monitoring of the patient throughout the course of therapy seems to be paramount for the elimination of the risks of infectious and non-infectious complications during the anti-TNF therapy. Etanercept therapy proved to be effective in treatment of the primary autoimmune disease without increasing the frequency of adverse events.

P 091

Efficacy of add-on treatments of tacrolimus and methotrexate for patients with deteriorated articular manifestation of systemic-onset juvenile idiopathic arthritis during tocilizumab treatment

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Systemic-onset juvenile idiopathic arthritis (sJIA) is a chronic inflammatory multisystem disease characterized by prolonged systemic and synovial inflammation. We reported that tocilizumab (a humanized anti-IL-6 receptor antibody, TCZ) was safe and effective in the clinical management of refractory sJIA (1). Most of the patients became free from clinical symptoms and signs of inflammation and the side effects of the long-term. high doses of corticosteroids along with TCZ treatment. However, in some patients there still remained articular manifestation and/or high levels of serum metalloproteinase 3 (MMP-3) and the progression of joint damage were observed despite the improvement of systemic inflammation during TCZ therapy.
OBJECTIVE: We evaluated the add-on treatment of tacrolimus and methotrexate (MTX) in patients with deterioration in articular manifestation of sJIA.
METHOD: 76 patients satisfying the WHO/ILAR criteria for sJIA were treated with tocilizumab (8 mg/kg every 2 weeks). For 16 patients who showed improvement of systemic inflammation but still had progressive joint damages with high levels of MMP-3, weekly oral MTX (10 mg/BSA/week) was added on. If joint damages were still progressive, then, oral tacrolimus was further added on. Disease activity was assessed by determining joint manifestations, inflammatory markers, MMP-3 and fibrin degradation product E (FDP-E).
RESULTS: Among a total of 76 s-JIA patients treated with TCZ, 16 patients remained articular manifestation despite the improved in systemic inflammation during TCZ treatment for 2 to 4 years. MTX was additionally administered for these 16 patients, and 7 patients were responded. However, other 9 patients still had progressive joint damages and, thus, tacrolimus were added on to tocilizumab and MTX. The joint symptoms and damages were improved in 6 patients, but 3 showed partial improvement. The decreases of serum MMP-3 and FDP-E were observed from 530.1 ng/mL to 62.7 ng/mL and 153 ng/mL to 79.0 ng/mL within 24 weeks in these 6 patients, respectively. The rest, 3 patients, improved in both systemic inflammation and joint damages, but they still continue the combination therapy with these three medications because of short treatment period with less than 3 months.
CONCLUSION: Add-on therapy with MTX alone or MTX plus tacrolimus to TCZ will be an alternative treatment for patients with sJIA who respond inadequately to TCZ.
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P 092

Assessment of quantiferon as a screening tool prior to initiation of infliximab: a single centre's perspective

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BACKGROUND: Patients with autoimmune diseases and latent tuberculosis infection (LTBI) are at risk of developing catastrophic TB disease following infliximab treatment. Quantiferon-TB gold in-Tube (QTB), an interferon gamma releasing assay, has proven a more accurate screening tool than tuberculin skin test (TST) in adult populations.
OBJECTIVES: To assess the utility and validity of QTB in children, prior to treatment with infliximab.
METHODS: Retrospective cohort of patients started on infliximab following introduction of QTB as a screening tool according to the NICE guidelines. Patients' data were collected using the hospital's electronic medical data system, systemic review of medical records and personal communication with responsible clinician.
RESULTS: Twenty three patients (12 females and 11 males) were included in the study. A chest radiograph (CXR) and QTB was performed prior to infliximab. Fourteen patients had a recorded negative TST result. Underlying diseases included Juvenile Idioathic Arthritis (JIA) 34%, uveitis (5%), Juvenile Dermatomyositis (JDM) 26%, vasculitis 9%, systemic onset (So)JIA 17% and Inflammatory bowel disease (IBD) 9%. Five patients were on methotrexate (15mg/m2/week), and the remaining were on methotrexate and steroids (mean prednisolone dose 0.8mg/kg/day). One patient had a positive QTB while two had indeterminate results. Their CXRs were not suggestive of TB and TST's were negative. All three were on methotrexate and steroids. The patient with the positive QTB received 6 months anti TB treatment following which QTB became negative. The patients with indeterminate results were started on infliximab and had regular clinical assessment for TB disease. Repeat QTB was negative in one while remained indeterminate in the other. None of our 23 patients developed TB.

CONCLUSION: QTB is a useful screen tool for LTBI. There was poor agreement between TST and QTB in the indeterminate or positive cases, and good in the negative ones. Our yield of indeterminate results is lower compared to previous studies (8.5% versus 21%). Indeterminate results warrant careful assessment and re-evaluation, but should not preclude from initiation of anti TNF treatment.

P 093

Takayasu arteritis: clinical features and treatment outcome in 16 pediatric patients

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BACKGROUND: Takayasu arteritis (TA) is a rare granulomatous vasculitis involving the aorta and its major branches. Inadequately controlled disease leads to vascular insufficiency, potentially resulting in claudication of the extremities and inadequate vital organ perfusion. The condition typically affects women of childbearing age, and it is particularly rare in prepubertal children. Optimum monitoring and therapy in children are not defined; generally data obtained in adult series form the basis for treatment plans in children.
OBJECTIVE: To describe clinical features and to asses the efficacy of anti-tumor necrosis factor to reach and sustain remission in pediatric patients with TA.
METHODS: Retrospective study of 16 pediatric patients with TA, evaluated and treated at a single tertiary care children's hospital between November 1992 and April 2010. All patients met both ACR and EULAR/PRINTO/PRES criteria for the diagnosis of TA.
RESULTS: Sixteen patients (14 female) were followed up for a mean of 4.9 years (range 0.08-10.5 years). The mean age of disease onset was 11.9 years (range 3.3-17 years) with a mean delay between first clinical manifestation attributable to the disease and diagnosis of TA of 12.5 months. The most common presenting feature of TA was asymmetric hypertension (81%), with a difference of >10mmHg in systolic blood pressure between limbs, primarily between the arms (77%). Sixty-nine percent of patients had vascular signs of turbulent or decreased blood flow, with bruits and/or diminished or abolished pulses. Headache was observed in 45% of patients. Considering both angiographic and MRA modalities, stenosis was the most frequent vascular lesion (88%), followed by dilatation (19%), occlusion (6%) and aneurysm (6%). Fifty percent of patients had thickening of multiple vessels. The sites of arterial involvement were similar to those seen in other series (1), though the patterns did not typically conform to those described in the Japanese literature (2) and none of our patients presented pulmonary or coronary lesions. The majority of patients (81%) were treated with corticosteroids in combination with immunosuppressive agents as first line therapy, mostly methotrexate (13/16). Seven patients were treated with anti-TNF therapy after a mean of 2 years of incompletely controlled illness (range 0.3-4.8 years). In 50% of our patients, sustained control of active disease was achieved with aggressive immunosuppressive treatment. TNF inhibitors were most reliably effective, with 5/7 patients reaching substained remission. Three patients achieved sustained remissions with steroids and methotrexate alone. No patients died.
CONCLUSION: In this series of children with TA, the largest reported from a single center in a developed country, aggressive therapy aimed at normalizing laboratory tests and preventing clinical or angiographic evidence of disease progression could achieve sustained remissions in more than 50% of pediatric patients after an average 5 year followup.
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P 094

Refractory vasculitic ulcer in adolescent suffering from Systemic Lupus Erythematosus treated successfully with hyperbaric oxygen therapy

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BACKGROUND AND OBJECTIVE: We describe the case of a teenager suffering from Systemic Lupus Erythematosus(SLE),with digital ulcer resistant to conventional therapy, treated successfully with Hyperbaric Oxygen(HBO) Therapy.
METHODS: A 14 year old girl came to our observation for the presence since about 3 months of persistent fever(38°C),weight loss,headache,asthenia.Physical examination reveals rash on the face, livedo reticularis,acrocyanosis at the first and second finger of the left foot, arthritis in knees and ankles. Blood tests show: anemia (Hb 10.5gr/dl), leukocitopenia (3300/mmc) with lymphopenia (30%), increased inflammatory indexes (CRP 1,44mg/dl, ESR 53mm/1°h) increase serum IgG (2270 mg/dl), lengthening of prothrombin time (57.5sec), serum iron (16 µg/dl) and reduced levels of C3 (70mg/dl) and C4(9mg/dl). Urinalysis excludes renal involvement and instrumental examinations (chest radiography, abdominal ultrasound, echocardiography) deny the presence of serositis and other signs of disease. Even echocolordoppler of lower limbs and capillaroscopy are negative.Diagnosis of SLE is considered and confirmed, according to the diagnostic criteria laid down by American College of Rheumatology, for the presence of ANA (1:1280 homogeneous), anti-DNA(107 IU/ml), anti-Sm(129 AU/mL), anti-Sm/RNP(120 AU/ mL), anti-lupus anticoagulant (1.48)and antibodies cardiolipin (25 U/mL).Patient was discharged with the following therapy:prednisone 60mg (1.5 mg/kg/day); ranitidine (4mg/kg/die); vitamin D3 and calcium carbonate; hydroxychloroquine (5mg/kg/die); anti-aggregating platelet therapy (acetyl salicylic acid, (3mg/kg/die). After 2 weeks of therapy there is an improvement in symptoms with normalization of biochemical indices of inflammation but a worsening of peripheral cyanosis,with the appearance of an intensely painful and infected ischemic ulcer on the plantar surface of the second finger of the left foot. Echocolordoppler and capillaroscopy are again practiced resulting both negative and a local ulcer treatment is started with medications and cleaning performed by a consultant surgeon.Ulcer, oval form, evolves in a pejorative sense at a distance of 1 month after onset, reaching a maximum diameter of about 1cm. For this reason, and because of the deepening of the lesion and the risk of impairment osteo-tendinous, it is decided to associate with immunosuppressive therapy a course of HBO, protocol which provides for 5 weekly sessions of 90 minutes at a pressure of 2.6 atmospheres absolute.
RESULTS: After a week of therapy cyanosis disappears,while the ulcer heals after 16 sessions **(fig.1)**.HBO is tolerated by the patient running in total 32 sessions without presenting any side effects. From the interruption of hyperbaric therapy, there were no relapses in 22 months.After 4 weeks from the beginning of therapy, daily dosage of prednisone is reduced of 5mg every 15 days; once reached 20mg/day, it is reduced further of 2.5mg every 4 weeks until the current dose of 10mg/day(0,15mg/kg/day). Immunosuppressive therapy is well tolerated by the patient, blood tests are normal and there were not new flares of disease until now.
CONCLUSION: Our case demonstrates the usefulness and effectiveness of this treatment in healing infected ischemic lesions. The lack of serious side effects and relatively low cost makes this treatment beneficial for patients with ischemic vasculitic ulcers, but further studies are needed.
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P 095

Fibroblast growth factor (FGF23) serum levels in Juvenile onset Systemic Lupus Erythematosus (JSLE): A possible link with renal involvement

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BACKGROUND: Phosphatonins are new hormones involved in the regulation of phosphate homeostasis, vitamin D metabolism and bone mineralization. FGF23, the master phosphatonin, acts through FGF receptor 1 present in target tissues, kidney, vessels and heart. FGF23 levels are high in chronic kidney disease pts and an association between serum FGF23 levels and increased mortality independently of established risk factors has been reported. In addition, FGF23 contributes to the development of cardiovascular damage in several diseases. Previous reports have shown that JSLE is associated with an increased risk of atherosclerotic changes and related cardiovascular disease. Endothelial dysfunction, caused by autoantibodies, ICC and cytokines play a role in vascular injury. Moreover, renal disease in JSLE either as presenting symptoms or as complication is related to poor outcome.
OBJECTIVES: 1.To evaluate the serum level of intact FGF23 in JSLE pts. 2.To correlate FGF23 values to lipid profile (total cholesterol, LDL, HDL, tryglicerides), renal function (serum creatinine, creatinine clearance, proteinuria, microalbuminuria), renal biopsy results in pts with renal disease and cardiac data.
PATIENTS AND METHODS: 53 pts (46F 7M, mean age 13.3±5.6) with SLE onset <18 yrs, entered randomly in the study. 12/53 had signs of renal disease at onset and 13 at different time from disease onset. Corticosteroids were the first drug in all pts, then hydroxychloroquine, azathioprine, cyclophosphamide, and Cellcept (MMF); 3 pts with refractory disease received Rituximab. At study entry the disease was under controls with Hydroxychloroquine in 28/53 while the remaining were given a low dose of prednisone and MMF or azathioprine. One pts was on dialysis due to renal failure. All pts with glomerulonephritis (GN) underwent renal

biopsy within the first 6 mths from onset: 4 WHO IIA, 6 IIB, 10 III, 5 IV. 35 sex and age matched subjects acted as controls. The serum intact FGF23 concentration was measured with an ELISA assay (Immunotopics Inc. San Clemente, CA, USA).
RESULTS: FGF23 serum levels resulted significantly higher in SLE pts than in controls (t-student:67.1±40SD vs 5±3.2SD pg/ml). By Mann-Whitney U Test, pts with GN had serum FGF23 values significantly higher than those without (45.3±20 vs 13,77±9.2 SD pg/ml; p=0.0001). By Ancova analysis pts with severe renal disease (WHO III-IV) had higher levels when compared to WHO IIA-IIB (52,5±21 and 58,5±15 pg/ml respectively vs 13.7±9 and 35±10 pg/ml p=0.004). No significant correlation was found among serum FGF23 levels, lipid profile and cardiac function. A trend characterized by an inverse correlation between FGF23 and HDL was found (r-0.07;p=n.s.).
CONCLUSIONS: Serum FGF23 is higher in JSLE pts and seems to correlate with renal damage. It may be a helpful biomarker for assessing the risk of renal damage and useful in pts with early kidney disease in whom FGF23 levels firstly increase. Data in a larger cohort of pts are needed to define the role of FGF23 in renal disease JSLE pts.
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P 096
In vitro up-regulation of chemokines and inflammatory mediators by synthetic peptides in Kawasaki disease

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BACKGROUND: Kawasaki disease (KD) pathogenesis is largely unknown, but chemokines, that orchestrate the migration of leukocytes in the context of inflammation, and many other inflammatory mediators have been implicated.
AIM: To characterize the expression induced by acute KD sera of the following chemokines and inflammatory mediators: CXCL12/SDF1, CXCL11/I-TAC, PAI-1, MIP1alpha, IL-8, TLR-4, cPLA2alpha, iPLA2beta, iPLA2gamma, sPLA2-IIA, PGAM1, S100A8, S100A9.
METHODS: We have co-cultured acute-phase sera from individual KD Italian patients with PBMC from healthy controls, further adding to each co-colture system either nothing, a novel recombinant 28kD antigen called p28 (Streptococcus sanguinis variant) that we previously found to be KD-specific and to specifically up-regulate the intracellular expression of the same chemokines tested, or one of four synthetic peptides, two of which from the same p28 antigen, one from S100A8, and one complement fH domain 9 variant (C->R). mRNA was extracted from the rinsed PBMC pellets and real time PCR was performed after the method of Masuda S et al (FEBS J 2005;272:655-72), by evaluating the relative expression/GADPH.
RESULTS: p28 recombinant antigen, and its epitope 1 (synthesized as YDVLP-PAMPRDDEYSAHTDRRYAS) up-regulated the expression of most of the molecules tested. CXCL11/I-TAC (a ligand of CXCR3 previously involved in autoimmune diseases, and an angiogenesis related chemokine) relative expression increased 50- fold after the addition of this synthetic peptide. Other significant up-regulations were found for TLR-4, iPLA2gamma, sPLA2-IIA, PGAM1, and MIP1alpha. S100A expressions were surprisingly not changed, while PAI-1 was down-regulated by that same peptide in 7/7 samples .
CONCLUSION: The study of mRNA up- or down-regulation used in this system might help in knowledge advancement in KD pathogenesis and in finding novel targets for therapy. We are currently testing more acute samples, as well as others form febrile controls and subacute/convalescent KD in order to validate and expand these findings.

P 097
Anti-Cyclic Citrullinated Peptide (Anti-CCP) antibodies in Iranian children with Juvenile Idiopathic Arthritis (JIA)

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OBJECTIVE: Anti- Cyclic Citrullinated Peptide (Anti-CCP) Antibodies have been detected in 70% of adult patients with Rhematoid Arthritis (AR) and children with polyarticular IgM-RF JIA. Our objective was to determine the prevalence of Anti CCP Antibodies in Iranian children with Juvenile Idiopathic Arthritis (JIA), and if they can be used to identify patients with a more destructive course of disease.
METHODS: Serum samples of 61 Iranian children with JIA were collected on their active course of disease and were analyzed by a commercially available anti-CCP ELISA. The children were followed for two years. Correlations between anti-CCP and disease characteristics, medication, and radiological damage were also determined.
RESULTS: 47.5% of patients with JIA exhibited anti-ccp antibodies with no significant differences between polyarthritis, oligoarthritis, or systemic onset types. Anti-CCP antibodies was positive in 54.5% of children with IgM-RF-positive JIA patients and 45.5% of other types of JIA (p>0.05).
CONCLUSION: The overall prevalence of anti-CCP antibodies in Iranian children with JIA is lower than adults with AR. However, IgM-RF-positive patients with polyarticular JIA have more these antibodies.

P 098
Prevalence and clinical associations of autoantibodies in Juvenile Idiopathic Arthritis

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BACKGROUND: The reported prevalence of anti-nuclear autoantibodies (ANAs) in juvenile idiopathic arthritis (JIA) has varied between studies, however there is evidence for an association with the oligoarticular subtype and the presence of uveitis. Additionally, whilst several studies have reported ANAs in JIA, the specific autoantigen target has not yet been recognised.
OBJECTIVES: The aims of this study were to determine the frequency and immunofluorescence (IIF) pattern of ANAs in a large prospective cohort of JIA patients with different subtypes, and investigate JIA specific autoantigen targets.
METHODS: Plasma samples from 325 JIA patients recruited to the Childhood Arthritis Prospective Study (CAPS) were screened for autoantibodies by IIF on HEp2 cells, all positive results had a titre of at least 1/40. Samples were also analysed by immunoprecipitation (IPP) using radiolabelled K562 cell extract and SDS-PAGE. Results were compared for different subtypes of JIA and/or the presence of uveitis as recorded in the CAPS database. Probabilities were calculated using the Pearson Chi-Squared test.
RESULTS: 191 of the 325 children (58.8%) were ANA positive, most often (84.3%) at high titre (161/191 > 1/160) and predominantly with a homogeneous pattern (84.8%). ANAs were most prevalent in persistent oligoarthritis (63.4%), extended oligoarthritis (72.2%) and polyarthritis (67.5%) subgroups whereas a positive ANA was less common in either the systemic (29.4%) or enthesitis-related subgroups (15.4%). 81.4% of children recorded as ever having uveitis (n=35) were ANA positive in comparison to 57.3% of children recorded as never having uveitis (n=149), (p=0.003). This association was more significant when comparing the presence of a homogeneous pattern on ANA with uveitis (74.4% with uveitis vs 48.1% without uveitis, p=0.001). IPP on all samples resulted in the presence of strong unidentified bands for 46 samples, of which 31 were also positive on IIF, however there was no common autoantigen target for either the ANA-positive or ANA-negative IPP positive groups. Seven patients with uveitis had IPP bands, although these were at varying molecular weights.
CONCLUSIONS: Our preliminary results show that a significant number of JIA patients are ANA positive, with a significant association between uveitis and a positive ANA, particularly with the homogeneus pattern. Our immunoprecipitation studies did not identify any common autoantigen targets, or determine a bio-marker for patients at greater risk of uveitis or any clinical subgroup of JIA. Our studies are now ongoing to determine the autoantigenic targets responsible for the strong ANA pattern seen on IIF.

P 099
Safety and efficacy of influenza vaccination in children with juvenile idiopathic arthritis

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OBJECTIVE: To assess safety and efficacy of annual 2008/09 influenza vaccination in children with juvenile idiopathic arthritis (JIA).
METHODS: Thirty one children with stabile JIA were included in the study group (10 male/21 female, mean age 11.0, range 3-18); 15 with persistent oligoarthritis, 4 with psoriatic arthritis, 4 with enthesitis related arthritis, 3 with extended oligoarthritis, 3 with polyarthritis RF negative and 2 with systemic JIA. Nine were

without therapy, 9 were receiving only NSAID, 8 methothrexate, 7 low dose systemic steroids, 3 leflunomide, 2 sulfasalazine and 6 anti TNFα treatment. Patients were followed for 6 variables according to ACR pediatric core set before, one and six months after vaccination. The control group consisted of 14 children who were evaluated at the cardiology outpatient clinic. Children in both groups were followed for adverse events and infections 6 months after influenza vaccination. Parents received specific instructions when and how to take oral and nasal swabs at home in case of acute infection. Children in both groups were tested for autoantibodies including antinuclear antibodies (ANA), antibodies against extractable nuclear antigens (anti-ENA), anti-neutrophil cytoplasmic antibodies (ANCA), anticardiolipin antibodies (aCL), anti-beta2-glycoprotein I antibodies (aβ2-GPI) and lupus anticoagulant (LA). Antibody titers against the three vaccinal influenza viruses were measured before and after the vaccination. Blood samples were taken from each participant before annual influenza vaccination, one month and six months after the vaccination.
RESULTS: Eleven children (35%) in JIA and 5 (36%) in the control group reported short term adverse events, mainly pain at the injection site, one week after vaccination. Deterioration for more than 30% in at least 3 variables was observed one month after the vaccination in 3 patients (10%) and 6 months after the vaccination in 6 patients (19%). Before the vaccination 4 (13%) JIA patients and none of the controls were positive for ANA, none in either group were positive for anti-ENA, 3 (10%) were positive for aCL in JIA and 3 (21%) in controls, 1 (3%) for aβ2-GPI and LA in JIA and none in the control group. All participants were negative for ANCA. One month after the vaccination 20 (65%) children in JIA and 13 (93%) in the control group showed no changes in the levels of autoantibodies. After 6 months there were no changes in autoantibodies in 19 (61%) JIA children and in 10 (71%) controls. Significant changes were found only for aCL antibodies in JIA group: one month following vaccination 6 (20%) children were positive for aCL and after 6 months 10 (32%) were positive for aCL. Infections in the JIA group didn't have any impact on aCL autoantibodies. Six months after the vaccination protective antibodies against at least two vaccinal influenza viruses were present in all children of both study groups. Protective titers against all 3 vaccinal influenza viruses 6 months following vaccination were found as follows: 79% in children in the control group, 78% in children without any therapy or only with NSAID, 83% in children receiving DMARDs and 83% in children receiving antiTNF-α agents.
CONCLUSION: Influenza vaccination in the majority of our children with stabile JIA was generally considered safe. It was also effective in children with JIA treated with antiTNF-α agents. Nevertheless, 6 (19%) children with JIA experienced flare of the disease 6 months after they had been vaccinated.

P 100
Familial Mediterranean fever cases accompanied with central nervous system diseases

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Familial mediterranean fever (FMF) is a monogenic autoinflammatory syndrome characterized by attacks of fever, serositis and elevated acute phase reactants. Mutations in the gene causing FMF have been associated with various vasculitic and inflammatory disease. We present four FMF patients with central nervous system involvement, in the form of vasculitis or demyelinating disease.
All patients met the clinical diagnostic criteria for FMF. Two of them were homozygous for M694V and two other patients were heterozygous for M694V and V726A, respectively.
The first patient with demyelinating disease is seventeen year old girl and have been diagnosed as FMF six years ago. She presented with severe headache, dizziness, blurred vision and vertigo. Cranial MRG revealed multiple demyelinating plaques in left cerebellar hemisphere, left periventricular and right subcortical area of the brain. She is on colchicine therapy and heterozygous for V726A. Second patient with demyelinating disease is 9 year old girl and has been followed with diagnosis of FMF since 7 year of age. She is on colchicine therapy and heterozygous for M694V. She presented with headache, ataxia, double vision, vertigo. Cranial MRG revealed multiple cerebellar, callosal plaques. Spinal MRG revealed also multiple plaques located on anterior, lateral or posterior parts of spinal cord. Both patients have a positive oligoclonal band test on cerebrospinal fluid examination.
One of the patients with central nervous system vasculitis presented at the age of 9, with central 7th cranial nerve palsy and mild ataxia, CNS vasculitis was demonstrated on CT-angiography. Earlier, she was diagnosed as FMF and mutation analysis revealed that she was homozygous for M694V.
Next patient had the diagnosis of thalassemia. He developed left hemiparesis at the age of 7. MR angiography revealed vasculitic changes, especially prominent on right middle cerebral artery. Pulse methlyprednisolone and cyclophosphamide treatment were started. Later he was diagnosed as FMF and mutation analysis revealed homozygosity for M694V.
We suggest that the increased inflammatory milieu in FMF patients may predispose them to develop CNS vasculitis or CNS demyelinating disease at an earlier age.

P 101
Trace elements in juvenile idiopathic arthritis

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BACKGROUND: Trace elements play a key role in many physiological processes, the following being potentially the most relevant: arthritis/inflammation, immune support, antioxidant, e.g.(1)
OBJECTIVES: We evaluated the serum concentrations of trace elements patients with juvenile idiopathic arthritis (JIA).
METHODS: In this study, the plasma levels of Boron (B), Aluminium (Al), Zinc (Zn), Nickel (Ni), Copper (Cu), Chrome (Cr), Selenium (Se) and Vanadium (V) in 23 patients with juvenile idiopathic arthritis (JIA group), and the plasma levels of these trace elements in 14 healthy children (control group) were measured by using inductively coupled plasma mass spectrometry.
RESULTS: Serum Zn and Se and B concentrations in children with JIA were lower than in healthy children and unlike, Cu, Al, Ni, Cr, V concentrations in children were higher than in healthy children.
CONCLUSION: The plasma levels of some trace elements in patients with juvenile idiopathic arthritis may be different from healthy children. The causes of these differences and the relations between trace elements levels and the clinical severity of JIA may be necessary further investigations.
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P 102
The turnover of synovial T cells in persistent oligoarticular Juvenile Idiopathic Arthritis is higher than in T cells in the peripheral blood

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INTRODUCTION: Juvenile idiopathic arthritis (JIA) summarizes a group of inflammatory diseases of childhood. The etiology remains still unclear. In JIA T cells have been demonstrated to play key roles in the pathogenesis. T-cell proliferation in JIA may be different in the peripheral blood (PB) and the synovial fluid (SF). The aim of this study is to demonstrate the turnover of T-cells in the PB and SF of patients with persistent oligoarticular JIA (oJIA) compared to controls.
PATIENTS AND METHODS: Matched pairs of samples were investigated derived from PB and synovial fluid SF of 9 patients with persistent oJIA. The cells from PB and SF were determined by flow cytometry.
RESULTS: The majority of the PBMC and IAMC were in phase G0/G1, with fewer than 1% in S phase. In the SF the percentage of cells in the S phase is higher than in the PB. The percentage of cells in the S phase in SF is equal to the result in the control group. In conclusion the turnover of synovial T- cells in persistent oJIA is higher than in the PB.

P 103
Clonotypic archetypes in the T cell repertoire mark persistent oligoarticular Juvenile Idiopathic Arthritis

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BACKGROUND: Juvenile Idiopathic Arthritis (JIA) is characterized by chronic inflammation. Diagnostic markers for JIA have not been established yet. T cells are supposed to play an important role in the pathogenesis of JIA. The aim of this study was to demonstrate a profile of a limited T cell repertoire in the peripheral blood (PB) and the synovial fluid (SF) of JIA patients with persistent oligoarthritis (oJIA).
MATERIAL AND METHODS: Paired samples from PB and SF of 9 patients with oJIA were -chain variability ofbanalyzed for their T cell repertoire based on the the T cell receptor (TCR). Multicolour flow cytometry was performed using a panel of TCR Vbeta and CD4 or CD8 specific monoclonal antibodies.
RESULTS: The CD4/CD8 ratio was inconspicuous in both compartments. Comparing CD4 and CD8 cells differences were observed in both compartments with predominance of Vbeta2, 5.1 and 17 in PB and V beta2 and 5.1 in the SF CD4 cells. In CD8 cells Vbeta 2, 3, 13.1 and 13.2 were dominant in the PB and Vbeta1, 2, 12

and 13.2 in the SF. Double positive T cells present significantly Vbeta13.1 in PB mononuclear cells and in SF.
CONCLUSION: Expression patterns of Vbeta chains suggest oligoclonal T cell expansion of Vbeta families differing in PB and SF in patients with persistent oJIA. Further studies are necessary to evaluate, if these patterns characterize persistent oJIA.

P 104
Functional analysis of the complement system in oligoarticular Juvenile Idiopathic Arthritis

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OBJECTIVE: Juvenile idiopathic arthritis (JIA) summarizes a group of chronic joint diseases in childhood. The role of the complement sytem in the pathogenesis of JIA is unclear. The aim of this study was to evaluate the contribution of the complement system in the pathogenesis of oligoarticular JIA.
MATERIAL AND METHODS: Serum of the peripheral blood and the synovial fluid were investigated for activity of the classical pathway (CP), the mannose binding lectin (MBL) pathway and the alternative pathway (AP) of the complement system.
RESULTS: A total of 12 samples from PB from two girls and two samples from SF from two joints of one girl (four and five years old) with oligoarticular JIA were investigated in a longitudinal observation from the timepoint of the diagnosis of JIA. The differences between the complement activity in the PB and in the SF were extremly statistically significant (CP and MBL : $p < 0.0001$; AP: < 0.0087). The results for CP and the MBL pathway were considered to be pathologic.
CONCLUSION: The AP is the main contributor in the pathogenesis of oligoarticular JIA. Anti C5 therapy may be an option to avoid the creation of the membrane attack complex.

P 105
Characterisation of synovial fluid and peripheral blood TH17 cells in JIA

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Characterisation of synovial fluid and peripheral blood TH17 cells in JIA: a pilot study
BACKGROUND: Juvenile idiopathic arthritis (JIA) is the most common rheumatologic disease of childhood, the treatment of which includes the use of anti-inflammatory and immunomodulatory therapies. IL-17 producing cells (TH17 cells) are believed to be the major inducers of severe autoimmune tissue inflammation and destruction(1). In RA, IL-17 is responsible for osteoclastogenesis(2), the promotion of cartilage and bone resorption and destruction and the generation, attraction and expansion of further TH17 cells which sustain joint inflammation(3). Few studies have analysed the immune response within active joints in JIA(4).
OBJECTIVES: To determine if analysis of T cells (particularly TH17 cells) in the peripheral blood and synovial fluid of JIA patients will provide biomarkers which reflect disease activity and predict natural history accurately such that treatment decisions and outcomes for JIA patients can be improved.
METHODS: Thirty children with JIA were enrolled in this pilot study. The frequency, phenotype and function of T lymphocytes in peripheral blood and synovial fluid were characterized using flow cytometry.
RESULTS: The percentages of memory T helper and IL-17-producing T cells (Th17) were increased in synovial fluid compared with matching blood samples. There was a further increase of Th17 cells in patients with polyarthritis, whereas enthesitis-related arthritis patients showed an increase in Th1 cells. All IL-17-producing cells were CD4+CD45R0+CCR6+, the majority expressed CD161 but less than 10% expressed CCR4. A significant proportion of Th17 cells produced IL-22 and IFNγ, but almost none produced IL-10. We found a negative correlation between the expression of CD27 and the production of IL-17 ($r=-0.4$).
CONCLUSIONS: Contrary to studies in adult RA, our results suggest that peripheral blood does not reflect processes ongoing in active joints in JIA. Furthermore, the enrichment of IL-17 producing cells especially in more severe subtypes of JIA supports the hypothesis that these cells contribute to inflammation and tissue damage.
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P 106
Evidence of immunodominant epitopes, epitope switching, and the role of IgM autoantibodies in Acute Rheumatic Fever in children

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Acute Rheumatic Fever (ARF) is a sequelae of group A streptococcal infection that can cause irreversible damage to heart valves. In the United States, Hawaii has the highest consistent prevalence rate of ARF and most of the affected children are of Polynesian descent. It is felt that antibodies and T cell responses against group A strep cross-react to host tissues are thought to play an important role in the disease process.
OBJECTIVES: Using translational research, we first characterized the serum antibody responses to overlapping human cardiac myosin peptides in ARF subjects and identified immunodominant epitopes using ELISA. We then studied the longitudinal responses in ARF subjects and demonstrated epitope spreading using this assay.
In the second part we used a multiplex immunoassay to study the predominant IgM and IgG immune responses toward cardiac and valve proteins namely myosin, elastin, collagen I, collagen II, collagen IV, laminin, fibronectin, lysoganglioside, tubulin and N-acetyl glucosamine.
METHODS: Sera were obtained from 51 ARF subjects, 25 age matched controls, and 21 subjects with GAS pharyngitis. Antibody responses were measured using ELISA and multiplex immunoassay. Paired t-test, Kruskal Wallis test and random effects multiple linear regression analysis were used.
Results: Within the ARF population, we identified immunodominant epitopes in the S2 and LMM subregion of human cardiac myosin as S2-1, 4, 8 and 11 and LMM-7, 16, 26 and 33. We showed an epitope spreading phenomenon to peptides S2-22, 27, 28 and 29, late in the onset of disease.
The multiplex immunoassay showed significant IgM specific responses toward human cardiac myosin ($p<0.03$), Collagen I ($p<0.02$), Elastin ($p<0.04$), and N-acetyl glucosamine ($p<0.03$), and none of these antigens showed significant IgG responses.
CONCLUSION: The immunodominant epitopes corresponded to the disease specific epitopes identified by Ellis et al. (JID 2010) in the rod region of S2. We showed that epitope spreading occurred toward the head region/C-terminal end of the human cardiac myosin molecule. This spreading occurred on the opposite end of the S2 subfragment of human cardiac myosin as the immunodominant region. There appeared to be significant IgM responses to valve and cardiac proteins that were not seen with IgG. This result may implicate the importance of IgM autoantibodies in the understanding of ARF and Rheumatic heart disease.

P 107
Tubulointerstitial nephritis in a patient with Autoimmune Lymphoproliferative Syndrome

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Autoimmune lymphoproliferative syndrome (ALPS) is characterized by chronic lymphadenopathy, splenomegaly, autoimmune cytopenia and an increased risk of lymphomas due to impaired apoptosis of activated lymphocytes. The diagnosis is suspected by the clinical presentation and confirmed by elevated number of double negative T-cells (DNT-cells CD3+CD4-CD8-).
The genetic defect in apoptosis is known in 85-90% of the patients with ALPS. Germline and somatic FAS mutations are the most frequent causes but mutations in FAS ligand, caspase 8 and caspase 10 can be involved.
Usually ALPS has a characteristic phenotype and has only in exceptional cases been associated with renal disease.
We present a patient with tubulointerstitial nephritis who later developed symptoms of connective tissue disorder and eventually showed a clear ALPS phenotype.
A previously healthy 2½ year old girl presented with swelling of cervical lymph nodes and anemia (hemoglobin 8.6 g/dL). Excision of a lymph node showed un-

specific hyperplasia. At the age of 5½ years the child was readmitted with fever, vomiting, and hypertension. Creatinine was elevated at 134 μmol/l, urea at 20.4 mmol/l, and ESR of more than 140 mm/h. There was no prior drug exposure and no skin rash. Viral and streptococcal antibodies, ANA , anti-dsDNA, MPO-ANCA, Pr3-ANCA, anti-GBM, complement C3c og C4 were all negative. Ultrasound of the kidneys showed enlarged kidneys and a renal biopsy confirmed the diagnosis severe tubulointerstitial nephritis (TIN) showing small-vessel vasculitis but no abnormalities in the glomeruli. Ocular examination showed no sign of uveitis. The child responded rapidly to prednisolon 1 mg/kg/d which was slowly tapered after 2 weeks and renal remission was achieved a month later.

The anemia responded to the corticosteroid and normalized to 10.7 g/dL within 11 days of treatment but aggravated 3 months later with signs of hemolysis (hemoglobin 9.6 g/dL) and the child had hypergammaglobulinemia. Severe splenomegaly and chronic lymphadenopathy supervened and the diagnosis ALPS was confirmed by an elevated number of DNT-cells being 28% of lymphocytes (normal <2%).

To our knowledge this is the first case of combined ALPS and TIN. Six cases of ALPS and glomerulonephritis have been reported. In five of these cases the clinical presentation is not described. Kanegane et al present a 12 months old child who showed signs of lymphadenopathy. 4 months later the renal symptoms started and at the age of 6 years ALPS was suspected. The patient did not have an increased number of DNT cells but the diagnosis ALPS was genetically confirmed by a FAS gene mutation.

There remain unanswered questions regarding the genetics in ALPS and how the impaired apoptosis of activated lymphocytes affects the phenotype. More clinical trials are needed to develop the understanding of the disease further.

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P 108

Plasma B Lymphocyte Stimulator levels in pediatric systemic lupus erythematosus and its association with disease activity

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BACKGROUND: B-lymphocyte stimulator (Blys), a member of the tumor necrosis factor family, is a key factor in B-cell maturation, survival, and function. During the last years, there is growing evidence that Blys plays a central role in the pathogenesis of systemic lupus erythematosus (SLE). However, so far, almost all studies have focused on the adult population and data on pediatric-onset SLE (pSLE) are limited.

OBJECTIVES: To determine the plasma Blys levels in patients with pSLE and to assess its correlation with disease activity.

MATERIAL-METHOD: Twenty-seven patients with pSLE (22 girls), aged 8-20 3.52 years) were studied. Sixteen children with±years (mean age: 12.83 juvenile idiopathic arthritis (JIA), 35 with other autoimmune diseases (celiac disease, type 1 diabetes mellitus, thyroiditis,) and 24 healthy children, of the same age, were used as the control groups. SLE disease activity was assessed by the European Consensus Lupus Activity Measurement (ECLAM). Fifty-two blood samples were collected from the patients with pSLE (34 samples corresponded to ECLAM score 1-10 and 18 to ECLAM score 0). Single blood samples were taken from the controls. Plasma Blys levels were measured by ELISA, following the manufacturer's instructions (Quantikine Human BAFF/BLyS, R&D Systems, Minneapolis).

RESULTS: Blys levels were found to be significantly higher in patients with pSLE compared to the three control groups (SLE: 1877.8 ± 32.15, JIA: 82.8 ± 4.8, other autoimmune diseases: 87.9 ± 6.5, healthy children: 79.6 ± 3.7pg/ml, p <0.0001). In patients with pSLE, Blys level was positively correlated with ECLAM score (r=0.345, p=0.02) and anti-dsDNA levels (r= 0.354, p=0.0097) and negatively correlated with C3 level (r= -0.518, p<0.0001) and C4 level (r= -0.5828, p< 0.0001).

CONCLUSIONS: In this study, BLyS levels were found to be significantly higher in pSLE patients compared to those with other autoimmune diseases and healthy children, suggesting Blys involvement in the pathogenesis of pSEL. In addition, Blys association with disease activity indicates that Blys may be included among other disease activity markers and considered as a potential therapeutic target in pSLE

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P 109

Different clinical features of Turkish Kawasaki patients followed by a single referral center

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INTRODUCTION: Kawasaki Disease (KD) is a vasculitis of young children with marked geographic/ethnic differences in its epidemiology. We have aimed to review the main characteristics of KD in Turkish children and review our treatment approach.

METHODS: Medical files of patients diagnosed as suspected KD between March 2007-March 2010 were overviewed by a working group in the department of Pediatrics at Hacettepe University Medical School. 38 patients were evaluated by working group between March 2007-March 2010. 28 out of 38 patients had prolonged fever (lasting more than five days) and fulfilled at least four criteria and therefore confirmed as KD.

RESULTS: 28 patients (12 boys, 16 girls) were diagnosed as KD. The age range of the patients were 7 months-9 years (mean and median values were 32 months and 24 months, respectively). All patients had prolonged fever and the mean duration of fever was 9.2 days. Percentage of other criteria were as follows; changes in extremities 78.6%, polymorphous exanthem 75%, bilateral bulbar conjunctival injection without edema 67.9%, changes in lips and oral cavity 92.9%, cervical lymphadenopathy 75%. 20 out of 28 patients (71.4%) had periungual peeling of fingers or toes. Periungual peeling of fingers or toes started 10.9±6.6 days after fever onset (median 8.5 days). 50% of patients had periungual peeling within seven days duration after fever onset.

All patients had increased erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Mean ESR and CRP were 64,1 mm/h and 9,7 mg/dl, respectively.

11 out of 28 patients (39.2%) had coronary artery (CA) involvement. Patients were divided into three groups according to changes in CAs. Group 1, without CA changes (n=17), group 2 (n=8) with small CA dilatation (<5 mm), group 3 (n=3) with CA aneurysm. Only one patient had giant aneursym (>8 mm) with thrombosis.

Coronary artery involvement have started relatively early after fever onset. Coronary artery involvement have been detected 12.2 days after fever onset, at an average (minimum: 5 days, maximum: 33 days, median: 8 days). 54.5% of the patients have diagnosed CA aneurysm in a duration of eight days after first fever peak.

7.1% of the patients (2/28) did not respond to the first dose of IVIG. Second dose of IVIG was administered either for persistent ESR and CRP elevation or persistent dilatation of coronary arteries.

DISCUSSION: This single center study suggests certain differences in the presentation of KD among Turkish children. Periungual peeling of fingers or toes and coronary artery changes start relatively in early period. More than half of the patients have CA changes diagnosed within eight days after fever onset. In addition to these differences, the response to IVIG was exceptionally good. This study suggests certain differences of KD patients followed by a single referral center in Turkey.

P 110

International consensus conference on PFAPA syndrome: evaluation of a new set of classification criteria

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INTRODUCTION: PFAPA syndrome is characterized by periodic fever, associated with pharyngitis, cervical adenitis and/or aphthous stomatitis and belongs to the auto-inflammatory diseases. Diagnostic criteria are based on clinical features and the exclusion of other periodic fever syndromes. An analysis of a large cohort of patients has shown weaknesses for these criteria and there is a lack of international consensus. An International Conference was held in Morges in November 2008 to propose a new set of classification criteria based on a consensus among experts in the field.

OBJECTIVE: We aimed to verify the applicability of the new set of classification criteria.

PATIENTS & METHODS: 80 patients diagnosed with PFAPA syndrome from 3 centers (Genoa, Lausanne and Geneva) for pediatric rheumatology were included in the study. A detailed description of the clinical and laboratory features was obtained. The new classification criteria and the actual diagnostic criteria were applied to the patients.

RESULTS: Only 40/80 patients (50%) fulfilled all criteria of the new classification. 31 patients were excluded because they didn't meet one of the 7 diagnostic criteria, 7 because of 2 criteria, and one because of 3 criteria. When we applied the current criteria to the same patients, 11/80 patients (13.7%) needed to be excluded. 8/80 patients (10%) were excluded from both sets. Exclusion was related only to some of the criteria. Number of patients for each not fulfilled criterion (new set of criteria/actual criteria): age (1/6), symptoms between episodes (2/2), delayed growth (4/1), main symptoms (21/0), periodicity, length of fever, interval between episodes, and length of disease (20/0). The application of some of the new criteria

was not easy, as they were both very restrictive and needed precise information from the patients.
CONCLUSION: Our work has shown that the new set of classification criteria can be applied to patients suspected for PFAPA syndrome, but it seems to be more restrictive than the actual diagnostic criteria. A further work of validation needs to be done in order to determine if this new set of classification criteria allow a good discrimination between PFAPA patients and other causes of recurrent fever syndromes.

P 111
Microalbuminuria and oxidative stress in patients with familial Mediterranean fever

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BACKGROUND: Familial Mediterranean fever (FMF) is an autosomal recessive disease characterized by attacks of fever and serositis. Renal amyloidosis is the most important complication of the disease for the prognosis. Some studies have indicated oxidative system abnormalities in patients with FMF.
OBJECTIVES: We aim to investigate the urinary microalbumin (MA) level, which is a sensitive marker of renal involvement in early stages of the disease in our patients with FMF, and oxidative system changes in some patients with or without proteinuria.
METHODS: 51 Italian (29M/22F) FMF patients followed at our Unit are included in this study. 37 FMF patients were <18 years, 14 were adults (patients age: range 4-72 years). Diagnosis was based on Tel-Hashomer criteria. All patients had received regular colchicine therapy and none showed renal amyloidosis. In 2009 twice early, renal function (serum creatinine and creatinine clearance), 24 hour urinary protein (adult patients: normal values <200 mg/24h; paediatric patients: normal values <4mg/mq/h) and MA (normal values <30 microg/min) levels were evaluated in every patient without fever attack . Plasma malondialdehyde (MDA) concentrations, indicators of lipid peroxidation, were measured by HPLC in 14 FMF patients versus 30 controls.
RESULTS: All patients had normal renal function. 6 (12%) patients had increased MA and 3 of these patients had even elevated proteinuria (mean 9,04±3,4mg/mq/h). Comparison of subgroups (with and without increased MA) in terms of all parameters (gene mutations, age, age at diagnosis, duration of delay in treatment and serum amyloid A levels) showed no difference. Plasma MDA concentrations were elevated in FMF patients with MA (mean 0,36± 0,04 nmol/ml) compared to FMF patients without MA (mean 0,29±0,06) and controls (0,24±0,05). After increase of colchicine dosage (from 1 mg to 1,5 mg/day), MA, proteinuria and MDA decreased significantly until normal level.
CONCLUSIONS: We suggest measurement of MA with regular intervals in order to establish renal injury earlier. Our preliminary data suggest that there is an increase of reactive oxygen species in patients with FMF, especially when the disease is not held in check by therapy and MA is increased.
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P 112
Association between fractalkine gene polymorphism and Familial Mediterranean Fever

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INTRODUCTION: Chemokines are known to regulate cell migration and adhesion. CX3CL1 (also called fractalkine) is a unique membrane-bound chemokine that has dual functions for cells expressing its receptor CX3CR1: a potent chemotactic factor in its soluble form and a type of efficient cell adhesion molecule in its membrane-bound form. The polymorphism of CX3CR1 gene modulates fractalkine affinity to its receptror, which influences the risk of development and progression of various diseases. Interestingly, the V249I and T280M genetic polymorphisms influence CX3CR1 expression and function. We investigated whether these polymorphisms are associated with Familial Mediterrenean Fever(FMF)
METHODS: DNA was prepared from whole blood of 112 patients with FMF and 60 healthy children by a standard salting-out procedure. Two polymorphisms, V249I and T280M, were analyzed by multiplex polymerase chain reaction-sequence-specific primers. MEFV gene analysis were studied in all patients. Twelve mutations were analyzed by reverse hybridization after multiplex PCR amplification of DNA samples
RESULTS: Mean age of patients was 9,93±4,9 years. Distribution of age and gender were similar between the groups. About 36.4% were heterozygous for the V249I CX3CR1 polymorphism, 17.7% were heterozygous for the T280M CX3CR1 polymorphism There was no significant difference in the frequencies of V249I and T280M between patients and control subjects Frequency of heterozygote V249I polymorphysm were significantly lower in M694V homozygote patients. There was no significant association between genetic and clinical findings.
CONCLUSION: Our results show that these CX3CR1 gene polymorphisms are not different between patients with FMF and controls. V249I polymorphism was found to be significantly less frequent in M694V homozygote patients. Changes in the activity of this interaction may have a role in the pathogenesis of FMF.

P 113
Role of biological agents in auto-inflammatory disease in children

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BACKGROUND: Biological agents (BA) have recently completed the treatment options in auto-inflammatory diseases (AID) in children with the aim to improve the outcome. TNF-α blocking agents have been the first BA successfully used in children. However, other biological agents targeting cytokines including IL-1 and IL-6 have been shown to be effective (anti-IL-1/6), especially in AID like systemic onset juvenile arthritis (SoJIA) or cryopyrine-associated periodic syndrome (CAPS). In Switzerland, Etanercept has been approved for the treatment of JIA since 2000 and Canakinumab for the treatment of paediatric CAPS since 2009.
OBJECTIVES: Evaluation of the use of biological agents in AID in Western Switzerland.
METHODS: We selected all patients with AID seen in the Réseau Romand de Rhumatologie Pédiatrique (Lausanne, Geneva, Aigle, Sion, and Neuchâtel) who were treated with the following BA: anti-TNF-α (Etanercept, Infliximab, Adalimumab) and Abatacept, and anti-IL-1/6 (Anakinra, Canakinumab, Tocilizumab). We looked at minor and major adverse events and the activity of the disease before and after treatment with BA and with special regards on anti-IL-1/6.
RESULTS: Among 921 children and adolescents followed between 2004 and 2010, we selected 85 patients with AID (PFAPA: 40, FMF: 6, HyperIgD: 1, CAPS: 3, SoJIA: 34). Only patients with CAPS and SoJIA were treated with BA. They had a mean age of 9 years (3-22) and F: M ratio of 1.6:1. 7 patients were treated with one BA, 6 patients with 2 different BAs and 3 with 3 BAs.
3 patients with CAPS were treated with anti-IL-1 and responded very well. 13 SoJIA patients were treated with BA (anti-TNF-α: 8, Abatacept: 1, anti-IL-1/6: 8). 4 patients treated by anti-TNF-α were switched to anti-IL-1/6 because of lack of response to treatment **(cf Table 1)**. We did not have any serious adverse events and no serious infections.
CONCLUSIONS: Patients with SoJIA and CAPS clearly benefit from treatment with BA. General tolerance was good. In the CAPS group the response to IL-1 was excellent. In SoJIA, 3/4 patients, switched from anti-TNF-α to anti-IL-1/6 for lack of therapeutic response, did not respond well to the second medication. These patients seem to represent a population relatively resistant to treatment with BA. Due to the low number of patients in our cohort, the response to BA in SoJIA patients non-responder to anti- TNF-α agents should be further studied.

P 114
Profiling blood cells and inflammatory mediators in Periodic Fever, Aphthous Stomatitis, Pharyngitis and Adenitis (PFAPA) syndrome

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BACKGROUND: During recent years the periodic fever, aphthous stomatitis, pharyngitis and adenitis (PFAPA) syndrome has been considered an autoinflammatory disease. The etiology of PFAPA syndrome is unknown. To further advance the pathophysiological understanding of the disease, experimental investigations at the cellular and molecular level are required.
AIM: This study aimed to profile levels of blood cells and serum cytokines during afebrile and febrile phases of PFAPA syndrome to advance pathophysiological understanding of this pediatric disease.
METHODS: A cohort of ten patients with a median age of 4.9 years experiencing 'typical PFAPA' episodes participated in this study. Controls to each patient were recruited. Blood cells and serum cytokines were analyzed by complete blood cell count (CBC) analysis and multiplex ELISA.
RESULTS: Oscillations in the concentration of blood cells during the afebrile and febrile phases of typical PFAPA syndrome were observed; novel findings include increased monocytes and decreased eosinophils during a febrile episode and increased thrombocytes in the afebrile interval. Relatively modest levels of pro-inflammatory cytokines were present in sera. IFN-gamma induced cytokine IP10/CXCL10 was increased after the onset of fever while T cell-associated cytokines IL7 and IL17 were suppressed during afebrile and febrile periods.
CONCLUSIONS: Identification of dysregulated blood cells and serum cytokines is an initial step towards the identification of biomarkers of PFAPA disease and/or players in disease pathogenesis. Future investigations are required to conclusively discern which mediators are associated specifically with PFAPA syndrome.

P 115
Evidence of activated innate and adaptive immunity in juvenile idiopathic arthritis

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BACKGROUND: There is an awareness that mainly innate and possibly the adaptive immune system is involved in disease mechanisms of juvenile idiopathic arthritis (JIA), but so far detailed knowledge of immunological processes is limited. Here we have investigated the humoral immune response and the involvement of innate immune signals in JIA.
OBJECTIVES: To study B cell hyper reactivity and Fc and complement pathways in JIA.
METHODS: Twenty-six patients with JIA, in a flare of disease, were grouped as having polyarticular or oligoarticular disease. Twenty-one healthy age-matched controls were recruited. Peripheral blood samples were collected at inclusion. Antibody and complement levels were analyzed according to routine methods. Fc receptor and complement receptor (CR) expression on monocytes and B cells were studied by flow cytometry.
RESULTS: We demonstrate a significant increased proportion of CD14+ monocytes in JIA patients, regardless of the number of active joints. Patients with polyarticular JIA expressed higher levels of activating Fc receptors for IgG (FcgR), as well as CR type 1 (CR1) on monocytes. In addition, we found enhanced CR1 expression on B cells compared to age-matched controls. The increased receptor expressions correlated with enhanced immunoglobulin (IgM, IgG) and complement levels in the JIA patients.
CONCLUSIONS: In an active phase of JIA we found an important monocyte-related alteration of FcγR and CR, suggesting a strong contribution of innate immunity to disease pathology. The results also imply a polyclonal B cell activation with increased antibody levels and enhanced CR expression in active JIA. These findings support the newly reports in JIA on upregulated Fc and CR genes (1,2).
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P 116
CD4+CD161+ cells with Th1 or Th17/Th1 profile accumulate in the synovial fluid of patients with oligo- and polyarticular juvenile idiopathic arthritis

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BACKGROUND: Following the discovery of Th17 cells, increased levels of IL-17A, as well as the presence of Th17 cells and expression of their transcription factor RORC in the synovial fluid (SF) of JIA children have been reported.
OBJECTIVES: To investigate phenotype and function of CD4+ T cells in synovial fluid (SF) of affected joints from children with juvenile idiopathic arthritis (JIA) and to establish a possible link with disease activity parameters.
METHODS: CD4+ T cells of peripheral blood (PB) and SF of 37 JIA and PB from 15 healthy children were analyzed for exression of CXCR3, CCR6, and IL-17A by intracellular cytokinegCD161, and for production of IFN- production assays (flow cytometry on cultured cells and on T-clones). RORC transcription marker was evaluated by RT-PCR. Spectratyping and clonotypic analyses on different T cell subsets were performed.
RESULTS: Numbers of CD4+CD161+, showing either a Th1 or a Th17/Th1 phenotype were higher in SF than in PB from JIA children. The few Th17 cells from SF of JIA spontaneously shifted in vitro to Th1 cells, whereas Th17 cells from PB of healthy children did it only in presence of SF, this effect being neutralized by blocking IL-12 activity. Spectratyping and clonotypic analyses showed a similar skewing of the TCR-BV repertoire in both SF-derived CD161+Th17 and CD161+Th1 cells from the same JIA patient. The frequencies of CD4+CD161+ cells, particularly of those showing the Th17/Th1 phenotype, in SF of JIA positively correlated with levels of erythrocyte sedimentation rate and C-reactive protein.
CONCLUSIONS: These findings suggest that a shifting of CD4+CD161+Th17 cells into Th17/Th1 or Th1 cells in the SF from affected joints of JIA can occur, and indicate that the accumulation of these latter correlates with parameters of inflammation, thus supporting the hypothesis that these cells play a role in disease activity.

P 117
Biological and immunological characteristics of bone marrow and pulpa derived mesenchymal stroma cells in children with juvenile idiopathic arthritis

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Human multipotent mesenchymal stromal cells (MSC) can be expanded ex vivo for clinical use.Their potent immunomodulatory properties make them potentially suitable for the treatment of clinical inflammatory conditions. Autologous MSC have been proposed as an alternative treatment for patients with autoimmune disease (AID) and their use is currently under investigation in patients with Crohn's disease. Before contemplating clinical studies in JIA, the biological and immunological characteristics of MSC derived from patients need to be determined.A comparative analysis was performed of the phenotypical and functional properties of bone marrow (BM)as well as dental pulpa derived ex vivo expanded MSC from children with juvenile idiopathic arthritis(JIA).MSC from healthy pediatric donors were used as controls.We analyzed MSC from dental pulpa (DP)in relation to those derived from BM to explore the possibility of developing a less invasive method to obtain research material from patients.As MSC may functionally be modulated by pharmacologic immune-suppressive agents, we additionally investigated MSC from patients and controls co-incubated with drugs commonly used in the treatment of JIA. BM and pulpa from deciduous teeth were obtained according to an ethical committee approved protocol. MSC were expanded according to standardized protocol 1.The adherent cells were analyzed by flow cytometric analysis (positive: CD73, CD90, CD105; negative: CD3, CD31, CD34, CD45, CD86 HLA-DR). MSC underwent differentiation into adipose and osteogenic lineages according to published methodology 1. The capacity of MSC to suppress T cell proliferation was measured by 3H-thymidine incorporation following PHA stimulation of PBMC with increasing ratios of MSC to PBMC (1:80 to 1:5). Cytokine production (IL-1β, IL-10, TNF-α,IFN-γ) in the supernatant of these cultures was measured by ELISA. These experiments were also performed in the presence of various concentrations of immune suppressive drugs equivalent to therapeutic doses (i.e. dexamethasone, adalimumab® and indomethacin).Expansion potential, morphology and phenotype showed no differences between patient (BM n=12; DP n=4) and control derived MSC (BM n=8; DP n=9). However,DP derived MSC in both patient and control material showed variable differentiation as compared to BM derived MSC (also in paired samples).MSC from JIA and healthy controls suppressed T cell proliferation in a dose dependent manner. No differences in immune modulatory capacity were evident between JIA and controls.In contrast to differentiation, immune modulation including cytokine production by DP derived MSC was identical to that observed when using BM derived MSC. The addition of dexamethasone in culture has an immunosuppressive effect,which can be augmented by the addition of MSC. The observed suppression at 1:5 ratio of MSC to PBMC was significantly (p<0,05) reduced by the addition of indomethacin. Adalimumab had no effect even though TNF-α was no longer measurable in the culture supernatants.We describe for the first time that MSC derived from children with JIA exhibit the same phenotype, proliferation and differentiation potential and immune modulatory effect compared to healthy aged matched controls. DP derived MSC offer a good alternative source for future fundamental research into the immune modulatory function of MSC in children. These results suggest that autologous MSC can be used in clinical prospective studies in pediatric patients, to determine the role of MSC in controlling resistent AID.(1)Haematologica 2003; 88: 845-852

P 118
Transient Peripheral Neuropathy (PN) in a JIA patient during Thalidomide treatment

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BACKGROUND: Thalidomide is an immunomodulating agent; although its action mechanisms are not fully understood, many authors have described its anti-inflammatory and immunosuppressive properties with Peripheral Neuropathy (PN) as a significant side effect in a range from 25,2 % (2) to 75 % (3), which may limit its clinical use.
METHODS: We describe a patient with JIA at systemic onset, partial responding to etanercept, who presented a good control of articular symptoms after thalidomide, but showed PN after 16 months of therapy with unexpected remission of this complication, proved by electrophysiological test.
RESULTS: Our patient, boy, 21 years old, 66.9 kg, 161 cm, is affected by JIA, diagnosed at the age of 7 years. Since he presented many acute phases of illness, though on therapy with immunosuppressant (methotrexate 10 mg/m2/week),steroid and NSAID, in 2001 we introduced an anti-TNF drug (etanercept 0.5 mg/kg/twice a week) while reducing progressively steroid dose. However the patient showed still

numerous articular acute phases. We decided to associate thalidomide (100 mg/die). After two months, the boy showed an improvement of the articular symptoms. After six months JIA was in remission. After 16 months of thalidomide therapy, he presented electrophysiological PN, without clinical signs;we decided to stop the thalidomide therapy. Now, after 5 years of thalidomide suspension, no acute phases of JIA were observed and an electrophysiological normalization of PN was confirmed.
CONCLUSIONS: Our data show that thalidomide can be administered in children with resistant forms of JIA, but a long-term administration can significantly increase the risk of neurotoxicity (1). It is related to length of therapy (4), the daily dose (no neuropathy if < or = 25 mg/ day)(2), individual susceptibilities with possible genetic predisposition (5). Thalidomide is also associated with different type of neuronal damage. In children axonopathy is more frequent than ganglionopathy and this is probably related to a higher rate of reversibility than in adult age.
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P 119
Abatacept for severe anti TNF-alpha refractory JIA-associated uveitis: a case report

M G Alpigiani, P Salvati, M Vannati, S Callegari, F Trovato, R Rossi, S Gamba, R Lorini

Chronic anterior uveitis in JIA can be severe and common immunosuppressive therapies may not be sufficient to control uveitis.
Concerning biological drugs, anti TNF-alpha agents such as infliximab and adalimumab have been proposed. But the percentage of success is different in case series and no controlled trials have yet been published. Abatacept, a selective T-cell costimulation modulator has been shown to be a valid alternative to anti TNF-alpha agents in patients with refractory autoimmune uveitis (Angeles-Han S. 2008).
We report on a girl aged 20 years, affected since one year by a severe form of poliarticular JIA. She received immunosuppressive therapy (Methotrexate, Azathioprine, etc...), associated with oral steroids, with no articular benefit. When Enbrel plus Methotrexate was started she got into remission. After one year of this therapy, she presented uveitis in both eyes, so oral steroids were started again. She obtained only partial ocular improvement, even when she received Infliximab associated with Methotrexate. Meantime she underwent cataract surgery because of visus reduction. After one year, Infliximab was suspended because of an adverse reaction (dyspnea and rash) and Adalimumab (0.7mg/kg subcutaneous/14 days) associated with Methotrexate was started, with no side effects and an improvement of uveitis and arthritis. After about 3 years, because of ocular and articular flares, Adalimumab was suspended and Abatacept (750 mg at time 0, 750 mg after 2 weeks, 750 mg after 4 weeks and, then, 750 mg monthly) was started, with no side effects and a partial improvement of uveitis and arthritis.
During the last ten years, anti TNF-alpha agents have been really useful to improve JIA outcome but the percentage of success changes considerably in chronic anterior uveitis. Side effects and poor visual outcome are still quite common in severe, refractory uveitis.
Abatacept may represent an effective and safe treatment for patients with severe anti TNF-alpha refractory uveitis but further research and long term follow up are needed.

P 120
The role of musculoskeletal ultrasound in children with pain in the upper LIMBS

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BACKGROUND AND OBJECTIVE: Because upper limb pain as initial presentation of different pediatric diseases may lead to misdiagnosis of juvenile idiopathic arthritis (JIA), the purpose of this study was to evaluate prospectively the use of ultrasonography (US) as an adjunct tool to clinical history for the early diagnosis in children with complains of the upper limbs.
METHODS: Prospective study with clinical follow-up for six months. Twenty patients were assessed clinically and underwent US scanning (Mode B and power-Doppler technique). The US imaging variables were assessed according to the OMERACT RA-US definitions.
RESULTS: Of 22 patient studied 15 children complained only tenderness without swelling and limitation; in this group we found US findings in 9 patients but in 6 patients there was no evidence of US abnormalities. The 7 remaining patients presented joint swelling in physical examination with US findings too. The most frequent US finding was joint effusion (the wrist and elbow joints commonly). Other findings: tenosynovitis of the flexor tendons of fingers, ganglion cysts, bone lesions and cellulitis. Clinical diagnosis of JIA was confirmed in 9 patients within 6 months of follow-up with basal US examination that evidenced abnormalities in 7 of these patients. Other unexpected diagnoses were Kawasaki disease (1) and leukaemia (1) at last follow-up.
CONCLUSION: In addition to clinical history, US as a complementary screening test let us confirm early diagnosis of JIA and rule out quickly mechanical problems.
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P 121
Outcome of children with Coeliac Disease (CD) and Juvenile Idiopathic Arthritis (JIA)

M G Alpigiani, P Salvati, M Vannati, R Rossi, A Calcagno, E Zaninoni, S Callegari, R Lorini

Coeliac disease (CD) is an enteropathy caused by sensitivity to gluten that affects about 1% of the European population (Branski D 1998). Many studies both in adults and, more recently, in children, have reported an association between CD and various autoimmune diseases, including JIA. Recently, we have investigated the risk of developing CD after JIA diagnosis (Alpigiani M.G. 2008). In our study the incidence of CD was evaluated in a cohort of 108 consecutive children (37 males, 71 females) diagnosed with JIA at our institution between 1992 and 2004. One girl with CD diagnosis made before JIA onset, was considered as a "prevalent case" and was not tested for EMA and tTGA. Two patients had positive immunological tests and jejunal biopsy, 3.5 and 4.6 years after JIA diagnosis, respectively. Neither had intestinal, haematological or other clinical symptoms of CD and were prescribed a gluten free diet. The prevalence of CD was 0,9 % at JIA diagnosis and 2,8 % at the end of the study.
Outcome of three patients with CD and JIA **(table 1)**:
the patient number 1 had many arthritis flares even if she was treated with Enbrel, methotrexate and corticosteroids;
the patient number 2 had one flare after 4 years of gluten-free diet and was treated with intraarticular corticosteroid with complete remission;
the patient number 3 had an improvement of JIA symptoms after gluten-free diet; lost to follow-up at 18 years of age.
Our data show that a gluten free diet does not always improve JIA symptoms. Even, patient number
1 had JIA onset after 22 months of gluten-free diet.

P 122
Osteonecrosis of the femoral heads in rheumatic diseases with juvenile onset: comparative results of radiological and morphological data

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BACKGROUND: Destructive changes of the hip are one of the leading causes of disability of patients with juvenile onset of different rheumatic diseases. Causes and mechanisms of the development of this complication are not well known.
OBJECTIVES: We have implemented a comprehensive radiologic and morphologic study of two patients with this disorder for better understanding of the nature of abnormalities occuring in osteonecrosis of the femoral heads.
METHODS: We've examined 2 female patients, 17 and 19 years old, with systemic juvenile idiopathic arthritis (sJIA) and systemic lupus erythematosus with

disease duration 13 and 6 years. Both of them underwent hip replacement, because of osteonecrosis of the femoral head. Changes in femoral heads were studied with conventional radiography (Ro), computed tomography (CT), magnetic resonance imaging (MRI) as well as morphologically. Subsequent comparative analysis of radiological and morphological data was done.
RESULTS: These two patients had distinction in anamnesis and clinical picture of hip damage: in patient with sJIA – very active arthritis persist 10 years; in patient with SLE – without preceded coxitis, suddenly manifested damage of hip then lasted 1.5 years. In spite of these differences, both of them had the similar changes on Ro and CT images – marked joint space narrowing, picture of osteonecrosis with femoral head deformation, erosions and realignment of bone structure with fragmentation. Areas with enhanced heterogeneous MR-signal (T1-, T2- weighted) were consistent with zones between osseus fragments on CT images. Zones with heterogeneous MR-signal were characterized by diverse changes in cartilaginous and bone tissues at morphologic examination. Furthermore, areas with erosions and fissures in hyaline cartilage of articular surface, cysts, sites of the bone without hyaline cartilage with sclerosis, necrosis of trabecular bone were revealed in patient with sJIA. In patient with SLE, irregular thicken of articular cartilage had been observed within the whole surface of the femoral head, as well as subchondral necrotic osseus area at the burden surface of the femoral head. Changes in the central parts of the femoral heads on MRI and CT images were slight whereas histologically founded diminished of bone trabeculae, their thinning that is typical for osteoporosis.
CONCLUSIONS: These data reveal that similar radiographic manifestation of osteonecrosis of the femoral head in children with different rheumatic diseases have various morphological changes and data of radiologic and morphologic examinations were not always correlate with each other. This may be ex-plained by different pathogenesis of femoral osteonecrosis in patients with SLE and sJIA. Further research is necessary in this field.

P 123
Changes in the immunegenicity profiles of patients with childhood systemic autoinmunes diseases treated with biological therapies

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INTRODUCTION: It has been described in adults that the use of biological therapies, particularly anti-TNF receptors, are associated to modifications in the immunological profile. Moreover, it has been demonstrated in adults, an increase of the prevalence of positive antinuclear antibodies (ANA) between 10 and 12%, and anti-DNA antibodies in a 12% of patients treated with Infliximab; an also significant increase of the positive titers of AAN in patients treated with Adalimumab or Etanercept (11%). Regarding to this last one, it has been also described an increase of positive titers of anti-DNA and anti-cardiolipin antibodies. The aim of the present study is to review the evolution of the immunological profile in patients with childhood rheumatic systemic diseases (CRSD).
MATERIAL AND METHODS: Medical records of our cohort of 78 patients from 1999 to 2009 who underwent 100 biological therapies due to CRSD diseases were reviewed. Analytical tests were collected in the moment of diagnosis, at the beginning of treatment, and in the 3rd and 6th months of treatment. Only cases with complete analytical testing up to 15 days after the designed day were analyzed.
RESULTS: Patient's diagnoses were as follow: 90 Juvenil Idiopathic Arthritis (JIA), 2 Systemic Lupus Erythematosus (SLE), 2 Wegener granulomatosis (WG), 2 autoinflammatory syndromes (AS) and a single case of dermatomyositis (DM). The followed up treatments were: 32 Etanercept (ETN), 15 Infliximab (IFM), 15 Adalimumab (ADM), 10 Anakinra (ANK), 3 Rituximab (RTM), 2 Canakinumab (CAN) and a single treatment with Tocilizumab (TZB).
Anti-DNA profile evolution: 4/26 showed a titer increase (15,3%): 3 patients, that were previously negative, with JIA (2 with ETN and 1 with IFM) and one with SLE y RTM; 22/26 remained negative (84,6%).
AAN profile evolution: 17/49 showed an titer increase (34,6%): 15 patients with JIA (ETN in 8, IFM in 4, ANK in 2 and TZM in 1), 1 patient with SLE and RTM and 1 patient with WG and IFM; 25/49 did not show modifications (51,1%) and 7/49 showed a titer decrement (14,3%).
There was a statistically significant increment of the proportion of positive titers of AAN after 3 and 6 months of biological therapy respect to the baseline ($p<0,05$ chi square). This phenomenon was not observed with the anti-DNA profile. The titers or proportion of positive extractable nuclear antigen antibodies (aENAs) and Rheumatoid factor (RF) did not show significant modifications in the studied cohort.
CONCLUSION: It seems that exposure to biological therapies, especially anti-TNF is capable to induce the increase of titers of ANAs and anti-DNA antibodies in one third and one fifth respectively in patients with CRSD, however we do not observed clinical outcomes related to those changes. The prevalence of significant modifications of the inmunogenicity profile is higher than the reported in adult population. We consider that the confirmation of our outcomes requires the serial determination of these signs in a protocol-scheduled way in all patients treated with these therapies.

P 124
Juvenile idiopathic arthritis associated with autoimmune cholangitis

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BACKGROUND: Hepatic disorder in patients with juvenile idiopathic arthritis (JIA) can not be only an extra-articular manifestation of this illness but also due to autoimmune liver disease. We report a case of JIA who developed autoimmune hepatic disease sharing features of autoimmune hepatitis and cholangitis
CASE REPORT: A 13-year old girl with JIA diagnosed at the age of 18 months presented with high aminotransferases (AST 305 IU/L, ALT 229 IU/L).She was on indometacin, methrotrexate and etanercept. Methrotrexate was first discontinued, second indometacin and finally etanercept with no improvement.
Additional tests: IgG 1950 mg/dL. GSR, CRP, WBC, haemoglobin, platelets, electrolytes, ceruloplasmin, alpha1antitrypsin and clotting test: normal. Hepatitis and Epstein-Barr antibodies: negative. Smooth muscle antibody(ASMA)1:160, ANCA 1:20. ANA, Anti-LKM-1, antidouble stranded DNA and anti-Sm: negative.
Abdominal ultrasound was normal. Liver biopsy showed well preserved lobular architecture with widened portal tracts corresponding to lymphocytic infiltration, mainly due to plasmatic cells. Some eosinophylic cells were also found. Periductal regions exhibited areas of focal inflammation and isolated epithelial lesions.
She was diagnosed of autoimmune liver disease with overlap syndrome. Azathioprine and prednisone were started and liver function tests were normal 3 months later. Etanercept was necessary to control of JIA activity.
One year later, abdominal ultrasound showed dilation and thickening of bile ducts. Aminotransferases level increased, predominantly cholestatic enzyme pattern with elevated serum gamma glutamyl transferase. She received ursodeoxycholic acid and prednisone while the anti TNF was withdrawn. However, due to arthritis flare, Adalimumab was added. Afterwards, she showed progressive improvement and both clinical and liver function tests have been normal during last year
COMMENT: Autoimmune hepatitis and cholangitis have been reported in some patients with JIA. Whether these diseases share a similar pathogenic mechanism has not been defined. It is difficult to rule out if they are triggered by anti TNF therapy. There is no consensus for therapy in autoimmune cholangitis. We have evidence of one year follow-up with normal liver function in our patient treated with Azatioprine, low dose of prednisone and Anti-TNF.

P 125
Chronic arthritis as clinical presentation of Acute Lymphoblastic Leukemia

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BACKGROUND: Musculoeskeletal pain is a common symptom in patients with hematological malignancies. But chronic arthritis has been only referred in small series. The diagnosis of Juvenile Idiopathic Arthritis (JIA) needs the exclusion of other possible causes. Magnetic Resonance (MRI) is a sensitive technique to show bone marrow infiltration. It is controversial if patients with chronic arthritis as first clinical presentation should be considered affected by Acute Lymphoblastic Leukemia (ALL) with better prognosis.
OBJECTIVES: Reinforce the importance of malignancies in the differential diagnosis in patients with chronic arthritis.
METHODS: Presentation of a multicentric series with 5 patients referred to Pediatric Rheumatology.
RESULTS: Patient 1: 8 years old female. Brother died of ALL 2 years before. Limping for 3 months. Left ankle inflamed. Normal labs. Synovial thickening in US. MRI suggestive of malignancy, confirmed by bone marrow biopsy (BMB). In remission 2 years after treatment.
Patient 2: 7 years old female. Articular pain and asthenia for 2 months. Elbows, shoulder, knees and hips limited and inflamed. Slightly increased LDH. Multifocal bone marrow infiltration in MRI. ALL diagnosed with BMB. Treatment recently completed.
Patient 3: 26 months old female. Limping for 1'5 months. Hip, knee and ankle limited and synovial liquid increased in US. Normal labs. Findings in MRI made the indication for BMB and ALL confirmed. In remission 2 years after treatment.
Patient 4: 9 years old male. Mother diagnosed of JIA. Arthritis in elbow for 2 month. Normal labs. Synovial thickening in US. Blasts found in synovial liquid in the arthrocentesis. Follow up lost.
Patient 5: 9 years old female. Poliarticular presentation for 6 months that included leg and ATM growth alteration. Normal labs before a cytopenia presented at the same time as a viral infection. Bone marrow signal was pathological in MRI and BMB confirmed ALL. Currently under treatment.
Conclusions: Malignancy, specially ALL, should be excluded before making the diagnosis of JIA. Atypical findings in clinical presentation (night pain, asthenia) or in laboratory results (increased LDH or uric acid, cytopenias) could indicate a bone

marrow biopsy. Otherwise a MRI can offer signs suggestive of malignancy. Further studies are needed to confirm if such presentation has prognostic importance in patients with ALL.
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P 126
Juvenile Idiopathic Arthritis (JIA) in Omani paediatric population

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BACKGROUND: Juvenile idiopathic arthritis is the most common rheumatic disease of children which begins before 16 years of age. It is also one of the more frequent chronic illnesses of childhood causes long-term disabilities.
OBJECTIVE: To determine the clinical features and outcome of Juvenile Idiopathic Arthritis in 56 children seen in Royal Hospital. This is the first review of juvenile idiopathic arthritis in Omani paediatric population.
METHOD: We retrospectively reviewed medical records of 56 patients with juvenile idiopathic arthritis treated in Royal hospital over 7 years period (from 2002-2009).
RESULTS: 56 patients (40 female and 16 male).Mean age at onset of the disease was 5.9 years (range 7mo-16y).Mean age at diagnosis was 7.0 years (range 2y-16y). Mean disease duration at the time of diagnosis was 2.5y (range2 wk-3y). All patients were diagnosed according to the International League of Associations for Rheumatology (ILAR) 1997 classification. The most common subtype was polyarthritis rheumatoid factor negative 41%, followed by oligoarthritis 27% and systemic arthritis 18%. Other forms notably, polyarthitis RF positive 7%, enthesitis –related arthritis 3.5%, and psoriatic arthritis3.5% were less frequent in this study. The most common drug used was non steroid anti-inflammatory drugs, followed by glucocorticoids. Diseases Modifying Anti-Rheumatic Drugs was used in 54% of patients and biologic agents in 28%. Complete remission was observed in 26% of patients, 10% of patients had joint deformity and 12% of patients loss follow up. Mortality was (n=1) because of chicken-pox pneumonitis.
CONCLUSION: Our results showed that polyarthritis (RF) negative was the most common subtype of juvenile idiopathic arthritis compare to systemic arthritis which was the most common subtype in Saudi Arabia and Kuwait1-2. However oligoarthritis is the most common subtype in European white population3. Larger prospective, multicentre study is required to find the incidence of JIA in Oman.
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P 127
Functional limitation in JIA: A matter of pain or disease severity?

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BACKGROUND: Children with JIA are often unable to fully participate in physical and social activities but it is unclear how this compares with other childhood rheumatic disease populations with comparable disease severity.
OBJECTIVES: To evaluate whether children with JIA have greater activity limitations than children with other rheumatic conditions and determine whether functional limitation differences are partly explained by differences in pain and/or disease severity.
METHODS: Children in this study were part of a larger ongoing study to evaluate pain and functional limitations in children with JIA. Forty children with JIA and 15 children with other rheumatic conditions (systemic lupus erythematosus, juvenile dermatomyositis, polychondritis, sarcoidosis, scleroderma), aged 8-18 years, were recruited from a pediatric rheumatology clinic. Children completed baseline questionnaires assessing functional limitations (Child Activity Limitations Questionnaire),health-related quality of life (PedsQL 4.0), and pain (5-point categorical pain rating scale). Diagnoses and disease severity ratings (0-3) were obtained from the attending pediatric rheumatologist.
RESULTS: Both groups had mild to moderate physician-rated disease severity (M=1.40/3 general sample versus M=1.37/3 JIA sample), but were significantly different in reported pain severity (M=2.07/5 general sample versus M=3.10/5 JIA sample, t(42)=2.83, p<.01). Children with JIA on average reported greater than threefold more activity limitations than their counterparts with non-JIA rheumatic conditions and had significantly lower health-related quality of life scores (M=64.70/100 versus 76.44/100, t(42)=2.27, p=.03). Significant group differences in activity limitations remained after adjusting for disease severity, but were eliminated after controlling for differences in reported pain (see Figure).
CONCLUSIONS: Children with JIA may have greater functional limitations compared to children with other rheumatic conditions despite having comparable disease severity. However, the greater functional limitations reported in children with JIA appears to be largely explained by higher reported levels of pain compared to children with other rheumatic diagnoses.

P 128
Juvenile idiopathic arthritis on biologic treatment: new onset adverse events. A retrospective study

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INTRODUCTION: The treatment of rheumathologic systemic diseases in patients on the pediatric age, especially Juvenile Idiopathic Arthritis (JIA), has lead to a substantial improvement in the control of symptoms, secuelae progression and early resume to daily activities. The experience with this medication on adults obligates to an extensive surveillance for the promptly detection of adverse events. The objective of this study is to describe de new onset adverse effects on our patient cohort.
METHODS AND MATERIALS: A review of clinical records was made, that includes 66 patients with JIA diagnosis who had recieved a total of 90 biological treatments. Epidemiological and clinical data was collected at the moment of diagnosis as was any adverse event not related to the disease progression. The data was ordered according to the JIA categories and the treatment given specifically: Etanercept (ETN), Infliximab (IFM), Adalimumab (ADM), Anakinra (ANK), Rituximab (RTM), Tocilizumab (TZM) and Canakinumab (CAN). The new onset of events is presented as an incidence in the time of follow-up, based on treatment and JIA category.
RESULTS: Sixty two percent of the patients were females. The JIA categories distribution was as follows: Systemic 21(31,8%), Oligoarticular 16(24,2%), Polyarticular 13 (19,7%), Psoriatic 6(9,1%), Enthesitis related 5 (7,6%) and undifferentiated disease 5 (7,6%). We found uveitis in 7 cases (10,6%), of this group six patients had oligoarticular JIA and one polyarticular JIA.
The total number of given treatments and their follow-up time is described above: ETN 36(40,0%), 1088,6 months; IFM 22(24,4%), 1011,4; ADM 17(18,9%), 411,9; ANK 10(11,1%), 259,0; CAN 2(2,2%), 6,0; RTX 2(2,2%), 14,3 y TZM 1(1,1%) 4,3. A hundred and eighteen adverse events were reported: Polyarticular JIA 38(32,2%), Oligoarticular JIA 31(26,3%), Systemic JIA 30(25,4%), Enthesitis-related and undifferentiated forms both with 8(6,8%) and in Psloriatic JIA 3(2,5%). Among the most relevant adverse events we had a case of Macrophagic Activation Syndrome (MAS), one of toxic hepatitis to ANK, Salmonellosis in a patient with ETN, Herpes Zoster infection with IFM and two cases of Varicella in patients with ETN.
DISCUSSION: The new onset of events in our series does not differ from the expected findings compared to other reports in the pediatric age. The small number of patients that received RTM and TZM explains the disproportionate incidence of adverse events in this group when compared to other biologics. We consider that there is a great perspective of usage of these drugs, therefore it is important to have a national registry of adverse events with information and prevention purposes.

P 129
A systemic Juvenile Idiopathic Arthritis (JIAs) Cohort analysis

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BACKGROUND: Juvenile Idiopathic Arthritis (JIA) is one of the most common rheumatic conditions of childhood. It´s expressed in a wide clinic range. There are seven clinical subtypes of JIA, between 10 and 15% of this children belong to subtype of JIAs. In this subtype we can find the most severe patients. On the one hand because of the joint affection and on the other hand because of its side effects due to the persistent inflammatory activity (growth retardation, severe osteoporosis and amyloidosis). Given that the clinical patterns and cytokine profiles (where IL-6 and IL-1 play a specific roll), JIAs represents a very different category than the others of JIA subtypes.

OBJECTIVE: To assess the epidemiologic, clinical and evolution characteristic of patients diagnosed with JIAs according to ILAR Classification. (Edmonton 2001)
PATIENTS AND METHODS: Descriptive, longitudinal and retrospective study of patients of the Rheumatology Pediatric Unit of the Hospital Ramón y Cajal.
RESULTS: We reviewed 23 clinical reports of patients (currently under follow up).13 boys and 10 girls. They have been classified in historic (>18 years) and recent (<18) according to the age. The current mean age was 18 years and 5 months (rank 2-32). The mean age at diagnosis was 8.25 years (rank 1.5-16 years).
The mean time between the symptoms onset and the diagnosis was 11 months (rank 1-27months). The mean time of the disease´s progress to present is 9 years and 2 months (1 month-30 years). Country of origin: 19 Spanish and 4 foreign (Colombia, Peru, Poland and Irak). Comorbidity: psychomotor retardation (2), atopic dermatitis (2), congenital cardiophaty (1), Guillén Barré (1), epilepsy (1), asthma (1) and demyelization disease (1).
The clinical patterns on the first 6 months were: 1.Systemic: fever (100%), rash (82%), lynphadenopathy (36.4%), hepatosplenomegaly (18.2%), serositis (18.2%), Macrophage activation syndrome (MAS) (4.5%). 2. Joint manifestations: inflammatory polyarthralgia (45.5%) and arthritis (77%) (2 monoarthritis, 4 oligoarthritis and 11 polyarthritis).
EVOLUTION: Monocyclic course (recent diagnose): 9%; polycyclic (systemic and joint disease with remission intervals): 36.6%; recurrent course (chronic polyarthritis): 54.5%. During the evolution a 100% of the patients developed polyarthritis. Joints affected mainly were: knees and wrists (85%), ankles (80%), hands and elbows (65%), hips (38.8%) and cervical spine (33.3%).
COMPLICATIONS: Structural injury (50%), osteoporosis (60%), growth retardation (45.5%), sexual maturation delayed (9%), ophthalmologic affection (22%), MAS (9%) and amiloidosis (4.5%), amyloidosis 5.5% (1 case).
TREATMENT: NSAID (100%), corticosteroids (oral: 100%, intravenous 23%, intra articular 36%), Methotrexate (95.44%), Azathioprine (9%), Cyclosporine (9%) and Biological Therapies (54.54%): anti-TNF (etanercept (7), infliximab (3), adalimumab (2)), anti IL1 (anakinra (11), canakinumab (4), anti iL6 (tocilizumab (2))
CONCLUSIONS: The JIAs patients with persistent inflammation drive to a destructive polyarthritis with severe functional disability and derive into serious complications such a MAS or amyloidosis. For this reasons, early diagnosis and treatment is fundamental in this patients. AIJs patients had a better control of the disease activity with antagonist of IL-1 and IL-6 than others categories patients.

P 130
Ultrasonography and Color Doppler of Gluteal Enthesitis in Juvenile Idiopathic Arthritis

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INTRODUCTION: Enthesitis implies inflammation at the insertion of a tendon, ligament, capsule or fascia to bone1. The clinical finding of enthesitis is tenderness1 and there are no other objective criteria of enthesitis. Some insertions, like the proximal insertion of the Gluteus medius muscle and fascia, are deeply situated which makes clinical examination and diagnosis difficult2-3. Enthesitis is the most common cause of JIA patients being classified into more than one subgroup3.
The aim of this study was to evaluate the usefulness of ultrasonography (US) and Doppler-US of the proximal insertion of the Gluteus medius muscle and fascia for diagnosis of enthesitis.
MATERIAL AND METHODS: Thirty-eight consecutive JIA patients, 23 girls and 15 boys between 8 and 18 years (mean and median 13 years), with bilateral pain at the proximal insertion of Gluteus medius (n=76) at Crista iliaca were examined clinically, and with Doppler-US (GE logiq 9, 12-5 MHz transducer). Thirty-eight healthy age- and sex-matched controls were examined with Doppler-US.
On the US image the thickness (mm) and the echogenicity of the proximal insertion of the Gluteus medius muscle and fascia were evaluated and a semi-quantitative evaluation of the color Doppler flow was performed.
RESULTS: Our data indicates that the bilateral proximal insertions of Gluteus medius was significantly thicker and more hypoechoic in the JIA patients compared to the healthy controls. No significant difference was found between the left and right side in the same individual. Doppler flow was rare in both patients and controls, possibly due to the deep location of the insertion. The results of US examinations are presented in **table 1.**
CONCLUSION: US seems to be a valuable tool to define enthesitis of the proximal insertion of the Gluteus medius muscle. US is quick (< 5 minutes), cheap, non-invasive, well suited for repetitive assessment and can be used bedside combined with clinical assessment of pain. In this study US seems to add valuable information in diagnosing enthesitis. Further research of the application of US in the pediatric population and comparison of US with MRI is needed before firm conclusions of the clinical value of US can be drawn.
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P 131
Course and complications of uveitis in children

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Uveitis is a complex multifactorial autoimmune disease of eyes, characterized by the inflammation of the uveal tract and retina, degeneration of the retina and development of blindness in genetically predisposed patients (M.J. Mattapallil et al., 2008).
The autoimmune forms of uveitis may appear either as a solitary disease or as a part of the systemic autoinflammatory process, e.g. under the Behçet\'s disease, juvenile idiopathic arthritis, HLA-B 27 association uveitis under the Reiter's disease, spondylarthritis, inflammatory diseases of the intestine, sarcoidosis.
Extraction of this group of uveitis, differential diagnostics and policy making of the treatment in cooperation with an oculist is an actual problem nowadays.
The anterior uveitis is, on the one hand, the most often and, on the other hand, the most important problem connected with extraarticulatory manifestation of the juvenile idiopathic arthritis.
The objective of this research was to trace the frequency of the development of uveitis' complications, terms of their appearance in patients with different rheumatologic diseases depending on initial symptomatology.
The methods of observation and analysis were used.
The group of children with the uveitis who were being treated in the pediatric department №3 of SPbSPMA since 2007 to 2009 has been analysed. In general there were 35 children including 31 children with juvenile idiopathic arthritis, 1 with a systemic vasculitis, 1 with HLA-B27 association spondyloarthropathy, 1 with a systemic scleroderma and 1 male child with Crohn\'s disease.
THE FOLLOWING RESULTS HAVE BEEN RECEIVED: 82.87% of children of the sample are female and 17.13% are male children.
The uveitis in the beginning of the disease was observed in 48,6% of cases and in 31,4% of cases it appeared during next 2 years since the beginning of the disease. For 20% other cases terms of uveitis' appearance varied from 3 to 12 years since the beginning of the disease.
65,7% of children had different complications of uveitis. 47,8% of children with complications had uveitis since the very beginning of the disease and 30,4% of children with complications acquired uveitis during 2 years since the beginning of the disease.
The course of the uveitis in 34,3% of cases is hard-to-control, recurrent with often exacerbations in spite of the fact that all children got methotrexate and cyclosporine therapy. 77,73% of these children suffer from uveitis since the very beginning of the disease.
At the moment of analysis 42,86% of patients are in condition of medicamental remission, 40,0% of them having the uveitis since the beginning of the disease.
All children got active hormonally-cytostatic therapy that included pulse-therapy with methylprednisolone, cyclosporine A, methotrexate, sulfasalazine. Metho-trexate is a medicine of the first row. In 2 hard cases, when traditional medicines were ineffective, Infliximab was successfully applied.
CONCLUSIONS: 80% of uveitis develop within 2 years since the beginning of the disease.
In 1/3 of the cases despite of the active hormonally-cytostatic therapy the uveitis has hard-to-control course.
The development of the uveitis within 2 years is a indicator of negative prediction.
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P 132
Handwriting difficulties in juvenile idiopathic arthritis: a pilot study

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BACKGROUND: In juvenile idiopathic arthritis (JIA) precocious involvement of the hand and wrist is commonly described and is among the early signs of poor outcome [1]. Children with JIA and arthritis of the upper extremity often report that they experience difficulties in handwriting.
OBJECTIVES: The aim of the current study was to describe handwriting limitations that occur in elementary school children with JIA and to look for possible correlations with hand function and writing performance. For a maximal understanding, the findings were compared with those of a group of matched controls.
METHODS: Following a cross-sectional approach 15 children with JIA and reported handwriting problems were included together with 15 healthy matched controls. Children were matched regarding gender, handedness and school level. Signs of arthritis or tenosynovitis, handwriting, perceived handwriting difficulties, pain and hand function (grip force and ROM of wrist and finger joints) were assessed.
RESULTS: The study group consisted of 8 children with rheumatoid factor negative polyarthritis and 7 children with extended oligoarthritis, all of them under optimal medical regime and with overall mild disease activity. Median age: 11.3 years (IQR 9.3 - 11.8); Median disease duration: 3.3 years (IQR 1.8 - 7); Median number of joints with arthritis: 3 (IQR 1 - 6). At study inclusion 73 % of the children had no clinical signs of arthritis nor tenosynovitis in any joint of the dominant upper extremity while all had shown arthritis of an upper extremity joint at one point during the disease course. Overall the children with JIA performed well during a short-term handwriting test but the number of letters they wrote per minute decreased significantly during five minutes of performance compared to healthy controls. The JIA children did report difficulties due to pain during handwriting and limitation in sustaining handwriting for a longer period of time. At physical examination only minor hand impairments were found and these did not correlate with observed handwriting difficulties. Children with JIA had high pain scores on a 100-mm Visual Analogues Scale (VAS-pain) after handwriting tasks. Comparing the VAS-pain between the groups before (patients: mean ± SD: 17.7±17.8 mm; control: 6.8±13.2 mm) and after the handwriting task (patients: 51.9±24.6 mm; controls: 33.2±27.4 mm) indicated that JIA children showed significantly higher pain scores than the healthy controls (p=0.008).
CONCLUSIONS: This pilot study shows that children with JIA and reported handwriting difficulties experience these limitations mainly through pain and the inability to sustain handwriting for a longer period of time. No correlations could be found with hand function. Handwriting difficulties were often reported and observed in children without clinical signs of active arthritis nor tenosynovitis in upper extremity joints, therefore more attention for hand function evaluation and rehabilitation is needed.
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P 133
Juvenile psoriatic arthritis - a category in the gap between clinic and classification

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Juvenile psoriatic arthritis (jPsA) – a category in the gap between clinic and classification
The ILAR criteria define jPsA as arthritis and psoriasis or arthritis and 2 of the following: dactylitis, nail pitting or onycholysis, psoriasis in a first degree relative. In contrast to the former criteria (Lambert 1976, Southwood 1989) ILAR excludes not only patients with systemic or RF positive disease but also most children with a HLA B 27 related arthritis. Results: We have followed 79 children with arthritis and psoriasis. Joint pattern during the first 6 months was oligoarticular in 49 patients, 15 children showed asymmetric arthritis of 5 to 9 joints and 15 patients had symmetric polyarthritis of > 9 joints. Further rheumatologic features were iridocyclitis in 8 patients (5 chronic, 3 acute), enthesopathies in 16 and sacroiliitis in 13 patients. We found antinuclear antibodies in 32 patients (40%), 25 patients (34%) were HLA B 27 positive. According to course we defined the following subgroups:
· Oligoarthritis, early onset: 17 patients, 12 girls, 5 boys
· Asymmetric arthritis, onset at school age: 48 patients, 17 girls, 31 boys
· RF-negative symmetric polyarthritis: 11 patients, 8 girls, 3 boys
· RF-positive polyarthritis: 3 girls
With the exclusions of ILAR criteria 17 patients with asymmetric arthritis of late onset have to be excluded. One girl because her father suffers from ankylosing spondylitis and 16 boys who are HLA B 27 positive. The 3 girls with RF positive disease will also be excluded. This means that 20 patients = 25% with arthritis and psoriasis will not fulfill the ILAR criteria for jPsA.
CONCLUSION: The ILAR classification criteria strongly differentiate between the categories in order to have comparable patient groups for studies. This results in a high number of JIA patients with undifferentiated arthritis. For jPsA this is relevant because we lose the important group who suffer from psoriatic spondyloarthropathy, a well defined disease in adult rheumatology. Thus remains an unsolved conflict for longterm studies and in transition of juvenile patients into adulthood.

P 134
A follow-up study of patients with Juvenile Idiopathic Arthritis who discontinued Etanercept due to disease remission, using the Juvenile Arthritis Disease Activity Score

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BACKGROUND: Sporadic data regarding the discontinuation of anti-Tumor Necrosis Factor (anti-TNF) therapy due to disease remission in adults with Rheumatoid Arthritis and a report in patients with Juvenile Idiopathic Arthritis (JIA) have recently appeared. However, in contrast to adults, the disease course in JIA is qualitatively assessed and compared to baseline.
OBJECTIVES: Assessment of the post-Etanercept (ET) era in patients with JIA who discontinued the drug due to disease remission, using a recently developed tool that scores the disease activity.
METHODS: Eleven patients (F/M 9/2, median age 9.2 years), with either a polyarthritis (9) or an oligoarthritis (2) course were followed-up for 12.25-27 months after ET withdrawal. The median treatment period was 36 months. The Juvenile Arthritis Disease Activity Score (JADAS) was used to rank the JIA activity at the time of ET initiation and discontinuation and at the disease flare thereafter.
RESULTS: All 11 patients flared during the follow-up period. Compared to the time of ET introduction, JADAS was significantly reduced at discontinuation as well as at the time of the flare (26.3 to 0 and to 9.5 respectively, p<0.001).The median remission off ET lasted 3 months. The flares were controlled with methotrexate ± cyclosporine A (n=10) and methotrexate plus anti-TNF in the remaining one.
CONCLUSIONS: All patients after the ET withdrawal flared but they had a lower disease activity score compared to baseline. Flares were mostly controlled by the administration of 1 or 2 DMARDs. JADAS was a useful and handy tool for assessing and following-up the JIA activity over the disease course.
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P 135
Functional ability in children with juvenile idiopathic arthrits

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INTRODUCTION: Juvenile idiopathic arthritis (JIA) is a chronic disease associated with decreased functional capacity and potentially long-term consequences. The establishment of early prognostic factors could help in prevention of damage and improve quality of life.
AIM OF THE STUDY: To assess functional status of patients with JIA, compare with clinical and laboratory variables, therapy applied and determine factors associated with unfavorable functional ability.
PATIENTS AND METHODS: The study included 87 pts., seen at the tertiary care referral hospital, average age 14 yrs. (F 69%, M 31%), mean disease duration 6.7 yrs. (range 2.0-18.9), median follow up duration 4 yrs. The patient's distribution according to ILAR subtypes was polyarticular (36.8%), sJIA (14.9%), oligoarticular persisted and extended (35.6%) and ERA (12.6%). 67.8% pts. were treated with methotrexate and etanercept was introduced in 52.8% pts. during the period of observation. Disease activity was assessed by clinical, laboratory parameters (ESR, CRP) and physician\'s global assessment (PGA). Functional ability was evaluated by Steinbrocker functional class and CHAQ.

RESULTS: An overall decreasing of the DI over baseline was observed (0.54 vs. 0.38, p<0.05). By the Steinbrocker classification of the functional capacity, two-third of patients were in class I (58, 67.8%) at baseline and this number significantly increased to 76 (87.4%), (p<0.001) over time. A significant decrease number of patients in class II were found. The patients with sJIA had the most severe limitation in functional ability, while patients with persisted oJIA had mildest disability (0,86 vs. 0,18). When compared patients without to those with wrist arthritis significantly lower CHAQ DI was found in the former group (0.16 vs. 0.56, p<0.01). Similarly, CHAQ DI was significantly higher in the patients with coxitis compared to those without coxitis (0.71 vs. 0.17, p<0.001). CHAQ disability index significantly correlated with the majority of clinical and laboratory parameters of disease activity, PGA and parent\'s/patient\'s assessment at the end of a follow-up (p<0.01). The similar findings were observed at baseline.
CONCLUSION: Functional disability is influenced by disease activity and severity as well. Systemic onset, polyarthritis, involvement of wrist and hip are predictors of unfavorable functional ability. Our results demonstrated improvement of functional status in children with JIA which could be addressed to new therapeutic options, notably biologic drugs.

P 136
90K Immunostimulatory Glycoprotein evaluation in children with Juvenile Idiopathic Arthritis: preliminary RESULTS

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BACKGROUND: 90K is an immuno-stimulant serum glycoprotein who belongs to the scavenger receptor cysteine-rich (SRCR) protein super family, whose members are implicated in different mechanism of immune response and host defence function. Although 90K is found in the serum of all healthy individuals, its concentration in the serum of patients with various types of cancer, viral infections and autoimmune disorders is frequently increased.
OBJECTIVE: Juvenile idiopathic arthritis (JIA) is an autoimmune disorder characterized by a clinically heterogeneous group of arthritis of unknown cause and several immunological abnormalities. The aim of this study was to evaluate serum 90K glycoprotein in a group of children with JIA.
METHODS: We tested 90 K protein in 20 newly diagnosed JIA children, according to ILAR criteria, who had been referred to the Rheumatologic Unit, Department of Paediatrics, University of Chieti, Italy. There were 8 males and 12 females, with a mean age of 7.7±4.9 years: 12 with oligoarthritis; 5 with polyarthritis and 3 with systemic onset JIA. Fifteen sex- and age-matched healthy controls (6M/9F; mean age 9.9±4.6 years) were also evaluated. Serum 90K was determined by immunosorbent ELISA. Inflammatory status (ESR, CRP and Hb, TNF-alpha, IL1, IL6) and other outcome measures (VAS, CHAQ, number of joints affected) were also evaluated in all children.
RESULTS: As expected, at the time of diagnosis, children with JIA had significantly increased values of inflammatory markers and reduced Hb levels. They also had significantly increased values of 90K than healthy controls (188.54±68.03 vs. 116.25±57.14 ng/ml, p=0.002).
Moreover, serum 90K levels were significantly related to the increase in ESR values (r=0.395, p=0.023) and CRP (r=0.427, p=0.012), and inversely correlated with Hb values (r=-0.463, p=0.006).
CONCLUSIONS: To our knowledge, this is the first evaluation of 90K in JIA. Increased levels of this glycoprotein were observed in the serum of children with JIA compared to healthy controls, with significant relation to inflammatory markers. Even if the role of 90K in JIA is completely unknown, our findings may suggest a possible implication for the 90K glycoprotein in the inflammatory response of JIA.

P 137
Limping child protocols - are they adequate?

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BACKGROUND: Limp is a common complaint in children, often self limiting and trauma related but may be the presentation of serious potentially life threatening pathology, as well as a common presenting feature of juvenile idiopathic arthritis (JIA). Children may present to various specialties and hospital departments which often use protocols to facilitate screening for serious pathology and direct management. The literature reports differing protocols invariably focussed on sepsis, malignancy and orthopaedic hip problems.
OBJECTIVES: To describe limping child protocols currently in use in paediatric departments in the North East of England and paediatric rheumatology national training centres across the UK.
METHODS: Email requests to access existing limping child protocols were sent to all paediatric departments in the North East of England (n=9) and all UK paediatric rheumatology training centres (n=8). Using a piloted proforma the protocols were analysed qualitatively in terms of content and evidence source. This was deemed an audit of clinical practice and exempted from ethical approval.
RESULTS: 14 out of the 17 centres responded (82%), and 50% of the responders had a limping child protocol (2 paediatric rheumatology grid training centres & 5 North East of England paediatric departments). **See table** for summary of their content:
CONCLUSIONS: Limping child protocols clearly differ within the UK in terms of their content, clinical focus and evidence base. Although history taking and examination form the basis of clinical assessment, guidance was not detailed in most protocols and where given, was focussed on septic arthritis. There was variation in content regarding investigations with the focus being on detection of infection and hip problems, with scant reference to 'clinical prediction rules' for septic arthritis(1). Paediatric rheumatologists had not contributed to most protocols. Referral to rheumatology / consideration of JIA was infrequently mentioned, which may contribute to the reported delay in access to care for children with JIA. This study highlights the need for evidence based, consensus derived protocol to improve management of these children.
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P 138
Tocilizumab improves systemic and laboratory features of Systemic Juvenile Idiopathic Arthritis: 12-week data from the Phase 3 TENDER Trial

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BACKGROUND: Systemic juvenile idiopathic arthritis (sJIA) is characterised by chronic arthritis associated with systemic symptoms and/or features such as spiking fever, rash, hepatosplenomegaly, lymphadenopathy and serositis. Characteristic laboratory features include marked elevations of acute-phase proteins, microcytic anaemia, thrombocytosis, leucocytosis and subclinical coagulation activation. A vast body of evidence suggests that increased interleukin-6 (IL-6) production plays a role in sJIA pathogenesis.
OBJECTIVE: To evaluate the effect of the IL-6 receptor inhibitor tocilizumab (TCZ) on systemic and laboratory features of patients with active sJIA in the 12-week, double-blind, placebo-controlled part of the global phase 3 TENDER trial.
METHODS: Patients (2-17 years of age) with active sJIA of ≥6 months' duration and inadequate response to previous non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids (CS) were randomly assigned (2:1) to receive TCZ every 2 weeks (8 mg/kg for patients ≥30 kg body weight; 12 mg/kg for patients <30 kg) or placebo (control). Stable doses of NSAIDs and methotrexate were continued; CS tapering was allowed at weeks 6 and 8. Patients who qualified for rescue therapy received standard of care, were offered open-label TCZ and were considered non-responders. The primary end point was the proportion of patients with JIA ACR 30 response and absence of fever at week 12. All other end points presented herein were secondary except for the 2 exploratory end points: the proportion of patients with normal levels of serum amyloid A (SAA) and with serum ferritin at week 12 after having abnormal values at baseline. Post hoc analysis included the proportion of patients whose D-dimer levels dropped from elevated (at baseline) to normal (at week 12).
RESULTS: A total of 112 patients (37 controls, 75 TCZ), mean age 9.6 years, were included in the intent-to-treat analysis. Baseline characteristics were similar between groups. Efficacy at week 12: significantly more TCZ patients than controls reached the primary end point (JIA ACR 30 response and absence of fever: 85% vs 24%, p<.0001). Of patients with fever and/or rash at baseline, significantly more TCZ patients than controls were afebrile at week 12 **(Table)**. Mean improvement from baseline to week 12 in pain score (Visual Analogue Scale) was significantly greater in TCZ patients than in controls **(Table)**. At week 12, significantly more TCZ patients than controls experienced normalisation of laboratory parameters, including acute-phase proteins (C-reactive protein, SAA), serum ferritin, haemoglobin (Hb) levels, platelet/white blood cell counts and the coagulation activation marker D-dimer (Table). Notably, an increase in Hb level was observed as early as 6 weeks after TCZ initiation **(Table)**. Safety: four serious adverse events were reported by week 12 (in 3 TCZ patients)—angio-oedema and urticaria in one patient, varicella and bacterial arthritis—all of which resolved without sequelae.
CONCLUSIONS: These findings demonstrate that 12-week TCZ treatment in patients with sJIA refractory to NSAIDs and CS is well tolerated and rapidly effective on the characteristic systemic and laboratory features of sJIA.

P 139
Subclinical synovitis detected by ultrasound in patients with oligo-articular JIA in clinical remission

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OBJECTIVE: To investigate, the frequency of ultrasound (US) subclinical synovitis, in patients with oligoarticular JIA considered to be in clinical remission, that have had at least one of the knees involved in the past.
METHODS: The clinician established the clinical remission following the previous preliminary criteria(1): no joints with activity; no systemic symptoms; no uveitis; normal CRP or ESR and physician global assessment indicating no disease activity. Data regarding treatment, both at the present and in the past, were collected. The sonographist was blind for all clinical data, with the exception that the patients fulfilled the clinical criteria to be enrolled in the study. High resolution ultrasound and Power Doppler exam were performed in the two knees of all patients. The whole knee was study including the suprapatellar bursa, medial recess, lateral recess, infrapatellar area and posterior aspect of the knee. Synovial effusion and synovial hyperplasia were scored following two different methods (OMERACT/EULAR definitions and Kakati measurements (2)).
RESULTS: Eleven patients were included. The median period on remission was 10 months (range 9-15). The US study showed that 3 patients had synovial fluid/hypertrophy in the suprapatellar bursa; one patient had synovitis at the medial recess of the opposite knee. In one patient only the lateral recess showed US signs of active synovitis. In summary, 4/11 patients (36%) had synovitis when evaluated by US.
CONCLUSION: Although the clinical criteria of remission for JIA are quite stringent there is not a direct correlation with US findings. The data suggest that US evaluation should be included in the follow-up of oligoarticular JIA arthritis and taken into account before considering a patient in complete remission.
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P 140
Pregnancy in women of childbearing age affected by Juvenile Idiopathic Arthritis (JIA)

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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 JIA patients (Chakravarty EF 2003)
We report on five cases of women affected by JIA with a median age of 30,1; median age at onset of 6,8; median age at first delivery of 25,6. **(table 1)**
In all cases, pregnancy was associated with remission of disease activity, however a post partum flare appeared after 3 pregnancies (pt 1-4-5) and in the first year post-partum. The six 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.
As reported for pregnant patients affected by RA (Dolhain RJEM 2010), in our cases pregnancy was associated with a remission of disease in 5/5 patients and flare in post-partum period in 3/5 patients (the number 3 patient has a baby of 2 months only), probably depending on increased levels of serum alpha 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, progesterone 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.
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.

P 141
Temporomandibular joint changes in Juvenile Idiopathic Arthritis patients with TMJ symptoms or abnormal TMJ status

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BACKGROUND: Regular orthodontic and radiological evaluation of the temporomandibular joint (TMJ) is recommended to recognize TMJ involvement in juvenile idiopathic arthritis (JIA) (1).
OBJECTIVES: To examine the TMJ involvement using clinical and radiological evaluation in children with JIA suffering from TMJ symptoms or with abnormal TMJ status.
METHODS: In 7/2007-4/2010, 66 children (46 girls, 20 boys, mean age 10.4; range 2-18) of the 305 children with JIA followed-up at the Paediatric Rheumatology OPD, complained TMJ symptoms or had abnormal status in TMJs in the standard examination by the pediatric rheumatologist. Therefore they were examined also at the Orthodontic department in Oulu University Hospital.
The mean duration of JIA (oligoarthitis 36, seronegative 23 and seropositive 1 polyarthritis, systemic arthritis 3, enthesitis related arthritis 3) was 5 years (0,5-15years). Orthodontic examination was performed in all children and orthopantomogram (OPG) in 61. Condylar changes were graded 0-3 (no changes, mild =erosions, moderate = flattening, severe = flattening with erosion or absence of condylar head).
RESULTS: 18 children had acute and 48 children chronic TMJ symptoms or findings. The most common TMJ symptoms were tiredness or stiffness (n=23), sounds (n=21), pain on mouth opening or other jaw movements (n=12), TMJ or facial pain (n=10), difficulties in mouth opening (n=10), and TMJ subluxation (n=5). TMJ symptoms were missing in 39,7% (n=25) of the patients. The most common finding was asymmetry during maximal opening or during protrusion 39,7% (n=40).
The patients with acute TMJ symptoms or findings had almost as much (73%, 11/15) and as severe (mild 4, moderate 3, severe 3) radiological TMJ involvements as the patients with chronic symptoms or findings [83% (40/48), mild 6, moderate 17, severe 19]. Patients with findings but no symptoms had TMJ involvement in 76%. The early onset of JIA (<4 years) was a risk factor for severe TMJ changes. Severe condylar changes were found in 48% of early onset JIA patients (n=27) but only in 26% of the late onset (>4 years) (n=34) .
CONCLUSION: There is a high prevalence of severe radiological TMJ changes in JIA patients with TMJ symtoms or clinical findings. It is cruzial to detect TMJ inflammation in early phase, before major radiological or orthodontic changes have occured. Therefore a regular evaluation of asymptomatic patients, especially children with early onset JIA (<4years), is needed.
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P 142
Is Intraarticular Corticosteroid Injection (IAC) an effective therapy for Temporomandibular Joint (TMJ) Involvement in JIA?

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BACKGROUND: TMJ involvement is a common and often undiagnosed complication of all subtypes of JIA and can lead to jaw dysfunction, impairment of mandible growth evolving in facial asymmetry or micrognatia.
OBJECTIVE: to evaluate the efficacy of IAC in TMJ and identify possible clinical and radiological factors which can affect the result of the procedure.
METHODS: All patients with JIA followed at the Paediatric Rheumatology Unit of Padova undergoing IAC of TMJ between 2005 and 2009 were included in the study. TMJ involvement was diagnosed by clinical examination (maximal incisal opening =MIO, pain, jaw asymmetry on mouth opening, morning stiffness and crepitus) and by Magnetic Resonance Imaging (MRI) according to the grading scale by Cahill (1). All patients were injected with triamcinolone acetonide by an expert maxillo-facial surgeon and were prospectively assessed after the procedure according to the routine follow up. Clinical variables, concomitant systemic treatment and MRI findings were included in the univariate and multivariate analysis in order to identify possible predictors of result.
RESULTS: 22 patients (mean age 9.2 years, 20 F) were included in the study, 15 had persistent and 7 extended oligoarticular JIA. Five pts underwent bilateral TMJ IAC and 17 unilateral. Before IAC mean MIO was 3.4 cm (median 3.5, range 2.0-5.0 cm), morning stiffness was reported by 9 pts, 6 had pain at rest, 11 pain at mastication and 6 had both, 8 patients presented crepitus. MRI was performed in 19 patients and a severe involvement (grade 3-3a and 4-4a) was shown in 15 TM

joints, mild (grade 1-2) in 23. After IAC we observed a significant improvement of MIO (mean 4.1, median 4.0, range 3.1-5.0 cm, p<0.001), morning stiffness (1 patient, p=0.008) and pain at rest (p<0.05). Best MIO increase was showed in patients with persistent oligoarticular JIA and without contemporary IAC in other joints. After IAC no significant difference was noted on pain at mastication, jaw asymmetry and presence of crepitus. No association between outcome and clinical variables such as age at procedure, systemic treatments and MRI findings (joint effusion, meniscus alteration, bone edema or erosion) or grading was observed.
Conclusions: IAC is effective in reducing pain and improving mouth opening particularly in patients with milder disease but is not reliable in arresting the condyle alterations that lead to mandible growth impairment. Early diagnosis and systemic and orthodontic treatment are recommended for reducing functional and aesthetic complications.
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P 143
Systemic Juvenile Idiopathic Arthritis: a heterogeneous disease

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BACKGROUND: Systemic juvenile idiopathic arthritis is characterized by systemic features such as spiking fever, skin rash, hepatosplenomegaly and serositis. The course of the disease is variable which affects the outcome of the disease.
AIM: To analyze the course of our systemic JIA patients and the response to treatment.
PATIENTS AND METHODS: 40 patients who were diagnosed as systemic JIA according to ILAR criteria were analysed retrospectively. These patients were stratified into three groups: 1. Monocyclic: defined as patients who have had only one attack and have resolved with treatment; policyclic: those who have had more than one attack predominated by fever; and chronic persistant polyarticular course: those who have progressed into a polyarticular course with waning fever. Patient outcome was assessed by ACR50 as previously defined. MEFV mutations were checked in most of groups 1 and 2.
RESULTS: 40 (17F,23M, median age 9 years (3-25)) patients were enrolled into the study. The median duration of disease was 33.5 months(10-206). Two of the patients were late referrals to our center (newly diagnosed) and died shortly due to MAS and were not included in the following analysis. The course of the disease were as follows: 10 (26%) monocyclic, 12 (31%) polycyclic and 16 (43%) chronic persistant polyarticular. The number of joints affected at the time of diagnosis in the monocylic group were less than the chronic persistant polyarticular(p<0.05). The thrombocyte count at diagnosis in the monocyclic group was higher than the chronic persistant polyarticular group (p<0.05). All of the patients classified as chronic persistant polyarticular were given anti-TNF therapy whereas only 30% of polycyclic group received this treatment. In the chronic persistant polyarticular group 50% of patients had an ACR50 response to the anti-TNF therapy while none of the polycyclics reached ACR 30. All of the three patiets resistant to anti-TNF responded well to anti-IL-1 therapy in polycyclic group. Overall ten patients were diagnosed as MAS.
DISCUSSION: Systemic JIA patients display a heterogeneous course. This single center study suggests that a number of features at presentation may help in predicting the course of the study. We also suggest that antiTNF treatment may be helpful in those with a polyarticular course whereas in the others anti-IL1 treatment should be the first biologic to be considered.

P 144
Status of vaccination coverage in children with juvenile idiopathic arthritis (JIA) followed at a pediatric tertiary-care center

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BACKGROUND: Immunization is recognized as being one of the most efficient ways to prevent mortality, morbidity and complications related to infectious diseases in children. Recent studies reported on the safety and efficacy of single vaccines in patients with juvenile idiopathic arthritis (JIA). However, no data on vaccination coverage rate is available in JIA patients. Factors such as the presence of chronic disease, fear of inducing flare of disease and treatment with immunosuppressive medication may impact on the vaccination schedule of this population.
OBJECTIVES: To evaluate the vaccination coverage rate of patients with JIA followed at a pediatric tertiary-care center and to determine the coverage rate for individual vaccine required as per the Quebec Public Health guidelines.
METHODS: The Division of Rheumatology at the Montreal Children's Hospital (MCH) follows actively a cohort of 356 patients with JIA. During the period from August 1st 2008 to March 31st 2009, all consecutive JIA patients coming for their scheduled visit were included if they were between 2 and 18 years old and if they had an available written immunization record. Demographic data, ILAR disease subtype, active joint count and medications used since diagnosis were retrospectively collected for each patient. Descriptive statistics were used to evaluate the proportion of children with complete vaccination status according to the Quebec Public Health guidelines at 2.5, 10 years and at the last visit to the clinic.
RESULTS: During the study period, 301 JIA patients were evaluated in the outpatient clinic. A total of 200 patients were included, 69% were girls. Mean age of the cohort was 11.4 years, with a median age at diagnosis of 4.8 years (0.5-16.6 years). The diagnosis at onset was oligoarthritis in 51.5% of the children, rheumatoid factor (RF) negative polyarthritis in 20.5%, RF positive polyarthritis in 1.5%, systemic in 6%, psoriatic in 6%, ERA in 7.5%, and undifferentiated in 7%. Over time, NSAIDs were used in 99 % of patients, methotrexate in 51%, steroids in 10.5%, and biologics agents in 7.5%. Vaccination coverage rates at 2.5, 10 years and at the last clinic visit for each vaccine are shown in the table, as well as the proportion of patients with complete vaccination status.
CONCLUSION: Despite overall good vaccination coverage rate of single vaccines, only 61% of our cohort has a complete vaccination status at the last clinic visit. Further analysis is required to determine factors that may influence vaccination such as age at diagnosis, activity of the disease and medication use. A limitation to our study was the inability to include all JIA patients. The children with no available immunization record may be less well vaccinated, thus the coverage rate may have been overestimated in this cohort. Further studies need to be done to explore the reasons underlying incomplete vaccination status in the JIA population, both from a parental and a physician perspective. Measures to optimize vaccination coverage, such as catch-up vaccination, should be implanted when possible.

P 145
Time-interval between onset of symptoms and diagnosis of Juvenile Idiopathic Arthritis: evaluation of 416 patients over two decades

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BACKGROUND: The timely diagnosis of Juvenile Idiopathic Arthritis (JIA) allows the administration of early treatment in order to alter the disease course, to control the disease activity and to prevent the development of damage.
OBJECTIVES: To evaluate the time-interval between onset of symptoms and diagnosis (Lag Time, LT) of JIA and to investigate factors that influences the LT and the impact of delayed diagnosis on the disease outcome.
METHODS: Four hundred sixteen patients with JIA were enrolled. The disease onset was during 1989-1998 in 183 (Group A) and during 1999-2008 in 233 of the 416 patients (Group B). The LT, the demographics and the disease course pre- and post-diagnosis were recorded.
RESULTS: LT>6mo was more frequent in group A than in group B (49/183 vs.39/233, p=0.013). The shortest LT was found in patients with Systemic JIA (p<0.001), whereas the longest one in patients with Enthesitis Related Arthritis (p=0.03). A LT>6mo was associated with an older age at disease onset (8.0 vs.5.3 yrs, p=0.03) and the presence of damage at diagnosis (p<0.001), whereas a LT≤6mo with the disease remission off medication (p=0.003).
CONCLUSIONS: The LT decreased over time and was influenced by JIA subtype and patients' age at the disease onset. A longer LT was associated with the presence of disease damage at diagnosis, while a shorter one with a disease remission off medication.
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Evaluation of the role of bone mass determinants in prediction of bone strength in patients with Juvenile Idiopathic Arthritis (JIA): bone status assessment using pQCT, DXA and QUS

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BACKGROUND: Despite the current more effective drugs, pts with JIA have a low bone mass. The main reasons are the disease activity, medication, reduced physical activity and unbalanced nutrition. From recent studies, using peripheral quantitative computed tomography (pQCT) emerged that abnormalities in bone geometry and a reduction in muscle cross sectional area and muscle force, are the major responsible of bone loss in JIA.
AIM: To evaluate bone status in a cohort of pts affected with
METHODS: One hundred and thirty-nine pts with JIA (median age 16.2 years, range 8.9 to 21.1 years: 101 oligoarticular, 29 polyarticular, and 9 systemic onset), after informed consent, entered the study. In all pts, peripheral quantitative computed tomography (pQCT), dual energy X-ray absorptiometry (DXA) at lumbar spine 2-4, and digit broadband ultrasound attenuation (cBUA) were performed. The data obtained were compared with 62 age- and sex- matched healthy subjects.
RESULTS: Patients with JIA showed a reduced spine Bone Mineral Apparent Density (BMAD) SDS in comparison to controls ($p<0.01$). These results were confirmed when the subjects were divided into JIA subtypes: systemic onset showed more impaired parameters than polyarticular and oligoarticular onset ($p<0.005$). Spine BMAD SDS significantly correlated with JIA onset type ($p<0.05$), age at JIA onset ($p<0.005$), flares ($p<0.01$), sex ($p<0.01$), and corticosteroids exposure ($p<0.01$). Also digit quantitative ultrasound (QUS), broadband ultrasound attenuation (BUA), speed of sound (SoS; $p<0.005$), volumetric cortical bone mineral density (cBMD; $p<0.001$), stress-strain index (SSI; $p<0.05$), muscle cross-sectional area (mCSA; $p<0.005$) were reduced in comparison to controls. Otherwise, the fat area was increased in JIA patients ($p<0.001$). These results were confirmed also when the subjects were divided into JIA subtypes; systemic onset showed more impaired parameters than polyarticular and oligoarticular ($p<0.001$).
CONCLUSIONS: Children with JIA have decreased skeletal size, muscle mass, cortical bone density, cortical bone geometry, and muscle strength. These patients have also a higher bone fat mass. Not surprisingly, these bone abnormalities are more pronounced in pts with greater disease severity. To reduce the risk of impaired bone mass, a close monitoring of BMD, a better control of disease activity, physical activity, and a dietary intake of calcium and vitamin D are advocated.
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P 147

Circulating COMP in young persons with or without juvenile idiopathic arthritis

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PURPOSE: Cartilage oligomeric matrix protein (COMP) is a structural protein in hyaline cartilage. Elevated serum levels can be the result of joint cartilage degradation, de-novo synthesis, and/or deficient clearance. Thus, raised serum COMP may hypothetically reflect ongoing tissue damage as well as tissue repair or normal anabolism. The present study was done to investigate serum COMP in young persons in relation to markers of inflammation (CRP) and growth (IGF-1).
METHODS: Serum COMP and IGF-1 were analysed by immunoassays (AnaMar Medical AB; Siemens Healthcare Diagnostics Ltd) in sera from 96 persons <19 years of age who had undergone allergy tests (IgE antibodies) with negative results and CRP <10mg/L (=referents). 43 sera from patients with juvenile idiopathic arthritis (JIA) were also analysed regarding serum COMP. All results were subgrouped according to age and sex >and the JIA patients also<. JIA patients were also subgrouped regarding type of disease.
RESULTS: Average COMP levels were significantly lower in persons aged 16-18 years (comparable to adult levels) than in children <16 years. COMP was significantly lower in the JIA group compared to referents. IGF-1 levels correlated with age, but not with COMP (apart from patients with IGF-1 >g/L).m400
DISCUSSION: In contrast to adult rheumatoid arthritis patients, where circulating COMP is often raised, we report that COMP is on average lower in children with JIA compared to referents. Others have shown that IGF-1 is lowered in JIA (Allen et al, Ann Rheum Dis 1991;50;602), which is intriguing considering that COMP gene expression is upregulated by IGF-1 (Hua & Stogiannidis, Acta Biochim Biophys Sin 2006;38:677). Further, it is known and that serum COMP rises in children treated with growth hormone (Bjarnason et al, J Clin Endocrinol Metab 2004;89:5156). We hypothesize that a rise in serum COMP due to articular cartilage erosion can be masked by reduced IGF1-mediated COMP production in active inflammatory disease. The clinical utility of serum COMP measurements may possibly be enhanced by relating the results to IGF-1 levels and CRP.

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Relationship between inflammatory markers, oxidant-antioxidant status and intima media thickness in children with Juvenile Idiopathic Arthritis

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BACKGROUND: Chronic inflammatory diseases are associated with early atherosclerotic cardiovascular complications. In juvenile idiopathic arthritis (JIA) the early onset of systemic inflammation might induce these alterations even in childhood.
OBJECTIVES: The aim of our study was to evaluate the relationship between carotid intima-media thickness (cIMT), inflammatory markers and oxidant status in JIA prepubertal children and to detect the effects of 12 months of therapy.
METHODS: In 38 JIA prepubertal children (12M/26 F, mean age 7±2 years) inflammatory markers (CRP, ESR), proinflammatory cytokines (TNF-α,), lipid profile and blooda, IL-1b, IL-6), oxidative stress (PGF-2gINF- pressure (BP) were evaluated and compared with 40 healthy controls (18/22F, mean age 6±2); all patients underwent carotid ultrasound performed with high-resolution B-mode ultrasonographies of carotid arteries with a linear 14 mHz transducer (Philips Sonos). Ultrasonographies were performed by a single reader unaware of the patients status.
RESULTS: JIA children showed higher levels of inflammatory markers, citokynes, lipid profile, blood pressure and oxidative markers when compared to healthy controls; cIMT was also significantly increased in JIA subjects ($p=0.0003$).
All JIA patients showed significant improvement of all parameters, including cIMT ($p=0.001$) after 12 months of therapy. Patients treated with etanercept had worse laboratory and US values at the beginning of our study but reached the same improvement of other patients in terms of all parameters after 12 months of treatment.
CONCLUSIONS: Early changes in inflammatory markers, lipid profile and oxidant-antioxidant status leading to increased cIMT are already present in JIA prepubertal children. All parameters including cIMT show substantial improvement after one year of therapy especially in children treated with etanercept.

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Validation of the Juvenile Arthritis Disease Activity Score (JADAS) based on C-reactive protein in a population-based Nordic cohort of juvenile idiopathic arthritis

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BACKGROUND: Juvenile Arthritis Disease Activity Score (JADAS) is a recently developed composite tool for scoring disease activity in juvenile idiopathic arthritis (JIA). JADAS consists of four items; the joint count, the erythrocyte sedimentation rate (ESR) as an inflammatory marker, the physician and the patient's/parent's global assessment. C-reactive protein (CRP) is often a more available test and has been suggested as an alternative inflammatory marker to ESR (1).
OBJECTIVES: The aim of the study was to validate and compare the CRP versus the ESR as an inflammatory marker in JADAS in a cohort of Nordic children with JIA in a near population-based setting.
MATERIALS AND METHODS: Five hundred fourteen consecutive cases of JIA from defined geographical areas of Denmark, Finland, Sweden and Norway with disease onset in 1997 to 2000 were included. Clinical data and disease activity measures were registered at regular follow-up visits from six to 147 months after onset. To calculate the JADAS, CRP was "normalized" to a value in the range 0-10 in a similar method as ESR, as described by Consolaro et al (1). Cut-off for CRP

was <10mg/ml and for ESR <20mm/H. Spearman's rank order correlation rho was used to evaluate the correlations between CRP and ESR, and the JADAS27 based on CRP and ESR.
RESULTS: Of the 514 children 66% were girls, 51% had oligoarticular disease six months after onset and 3% were rheumatoid factor positive. The first visit, when both CRP and ESR were taken, was chosen for analysis. Correlation between corresponding CRP and ESR values from each visit was moderate (r= 0.57). There was a high correlation between JADAS27-CRP versus JADAS27-ESR (r=0.98). Bland-Altman plot of JADAS7-CRP versus JADAS27-ESR showed a high level of agreement (mean difference of 0.046 (CI -0.012 to 0.104)).
CONCLUSIONS: JADAS based on CRP showed a high correlation with JADAS based on ESR in a multi-center Nordic cohort of juvenile idiopathic arthritis, which indicates that CRP can be used as an alternative to ESR. Further analyses on predictive value and responsiveness to change of the JADAS-CRP are planned.
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P 150
Functional status in severe JIA: an assessment in a Tertiary Pediatric Rheumatology Reference Centre

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BACKGROUND: Studies on functional outcomes of patients with juvenile idiopathic arthritis (JIA) over the last 10 years have revealed a diversity of CHAQ scores with median values ranging from 0 to 0.8.The frequency of patients with severe functional disturbance reportedly varies between 3.3 and 4%.Comparison between studies is difficult because of differences in composition of JIA cohorts, in disease duration and therapy.Most published cohorts have a limited proportion of systemic JIA and spondylarthritis patients,and in addition a reduced proportion of patients receiving biotherapy.
OBJECTIVE: To investigate the functional status of children with difficult to treat JIA of all subtypes,comprising an important number of patients receiving biotherapies,and to relate their functional status to subjective and objective measures of disease activity.
METHODS: 95 consecutively JIA patients seen in a Pediatric Rheumatology reference center between November 2008 and March 2009,were enrolled in this observational cross-sectional study.Outcome measures included CHAQ, physician's VAS overall disease activity,parent's VAS global wellbeing and pain,numbers of active and limited joints;criteria for minimal and inactive disease were applied. Non-parametrical tests were used.
RESULTS: Our cohort comprised 26% systemic JIA,29% polyarticular JIA,22% spondylarthritis and 23% oligoarticular JIA with median disease duration of 3.5 years (2 month-16.5 yrs).Treatment comprised NSAIDs (56%),MTX (23%),corticosteroids (21%) and biotherapy (45%).Criteria for inactive disease and minimal disease activity were met by 31 % and 47% of patients respectively.The median value of CHAQ score was 0.375 (range 0-3).The majority of patients had no or mild functional disability (61%),overall well being impairment (63%),and pain (55%).Conversely,10% of patients reported severe functional disability and impaired wellbeing,19% experienced severe pain.Within JIA subgroups,spondylarthropathy patients had significantly worse scores for CHAQ,VAS wellbeing and pain.CHAQ correlated with objective and subjective measures of disease activity in altogether JIA patients,and with VAS scores overall wellbeing and pain in every JIA subgroup.Patients with prolonged disease (>6 years) presented better scores for CHAQ, VAS wellbeing and pain.Patients with biotherapy reported better scores for CHAQ,wellbeing and pain despite no difference in number active joints nor the physician's global VAS,compared to patients without biotherapy.
CONCLUSION: In the present cohort,despite the high proportion of severe JIA,CHAQ values are in the lower range of those recently reported,a fact that may be related at least in part to new therapeutic approaches,including biotherapies. However,functional ability still remains a challenge for an important proportion of JIA patients.Spondylarthritis patients presented high impairment in functional ability,pain and wellbeing,justifying more attention for this JIA subtype in future studies.The constant interrelation found between functional disability and overall wellbeing underlines the importance of improving functional ability through appropriate therapies to improve patient's quality of life.

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Assessment of disease activity in juvenile idiopathic arthritis

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BACKGROUND: Recently Juvenile idiopathic Arthritis (JIA) Disease Activity Score (JADAS) was developed to measure disease activity. There is still discussion what additional measures should be included in such score.
OBJECTIVES: To determine associations between JADAS and clinical and laboratory findings.
Methods. Data from 34 patients with JIA were recorded from one visit, including JADAS, joint assessment, morning stiffness, Childhood Health Assessment Questionnaire (CHAQ), C-reactive protein, antinuclear antibodies, rheumatoid factor (RF), degree of radiologic and ultrasonographic changes. Correlation of the JADAS with above mentioned measures was examined. Physican's, parent's and patient's 10-cm VAS was statisticaly analysed. Pearson's and Spearman's correlations, T-test was performed using Windows Excel 2007 and SPSS 14.
RESULTS: For the JADAS the strongest correlation was with patient's VAS for wellbeing and active joint count; moderate with physician's VAS for disease activity, parent's VAS for wellbeing, patient's VAS for pain, CHAQ, morning stiffness, radiologic changes; week with RF. There where no statistical differencies between physician's, parent's and patient's VAS measures (p>0,5).
CONCLUSIONS: 1. Active joint count and patient's VAS are the most important measures in assessing disease acitivity. 2. CHAQ, morning stiffness, radiologic changes are also important in assessing disease activity and some of them could be included in disease activity score. 3.There where no statistical differencies between different VAS, but there where tendency for the parents to overrate child's disease activity 2 times more than patients.
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P 152
Outcome in Juvenile Idiopathic Arthritis (JIA). Earlier biologic drugs treatment could be effective in preventing clinical and radiological progression of juvenile idiopathic arthritis

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BACKGROUND: Juvenile idiopathic arthritis is the commonest inflammatory rheumatic disease of childhood worldwide(1). Modern therapies aim to avoid uncontrolled local and systemic chronic inflammation which leads to joint and end-organ damage(2). Biologic drugs could reach that goal when previous treatments (e.g. MTX) failed but, to date, few data exist on their long-term impact on disease outcome.
OBJECTIVES: To evaluate the relationship between selected clinico-therapeutic features of JIA and disease outcome.
METHODS: This is a monocentric IRB-approved retrospective study. We enrolled patients affected by JIA fulfilling ILAR criteria referring to our center from 1995 to 2009. Medical charts were reviewed for physical, laboratory and imaging findings and for antirheumatic treatment at onset, throughout the follow-up and at last medical examination. Primary outcome was established to be the presence at the end of follow-up of at least one of the following features: ongoing active disease, radiographic changes, functional disability and extra-articular complications. Data were analyzed with univariate analysis. Results. The cohort consisted of 100 patients (75 females and 25 males; ratio, 3:1), with a mean age at diagnosis of 5.2 years (range, 1 to 15 years) and distributed as follows: 40 persistent oligoarthritis, 21 extended oligo, 24 RF– poly, 2 RF+ poly, 6 SoJIA, 1 ERA, 1 psoriatic, 5 undifferentiated. The mean follow-up was 3.2 years (range, 1 to 19 years). 34 patients received biologic drugs, 56 were treated with MTX. At univariate analysis a longer therapy with MTX (17.6 vs 11.2 months; p=0.0297) was associated with an unfavorable primary outcome while presence of at least one course with any biologic drug was associated with the following outcome variables: functional disability (47% vs 9%, p<0.0001); radiographic changes (29% vs 12%, p=0.0330) and extra-articular complications (59% vs 36%, p=0.0321). JIA in patients undergoing biologics treatment had a longer mean duration (13.5 vs 3.6 years) and involved on the average more joints (polyarticular course in 76.5% vs 47.0%). In this subgroup of patients delayed introduction of these drugs seemed to predict poor outcome considered as: functional disability (13.6 vs 6.8 years; p=0.0331) and radiographic changes (15.7 vs 7.7 years; p=0.0240). Similarly a postponed start of MTX (5.8 vs 2.3 years; p=NS) and a higher cumulative number of affected joints (12 vs 6.8 joints; p=0.0280) were associated with radiographic damage.

CONCLUSIONS: In our study biologic drugs and longer MTX therapy were associated with poor JIA prognosis, possibly because the "need" for the most aggressive approach often marks a refractory long-standing polyarticular disease. Most interestingly earlier introduction of biologics showed a tendency to protect from functional disability and radiographic changes at the end of follow-up. Furthermore the "disease-modifying" role of MTX seems to be confirmed by the negative radiographic effects of a 2.5 year lag before its commencement. The cumulative number of active joints appears to account for the local radiographic burden of JIA (whereas joint counts assess instantaneous disease activity). The small size of our series didn't allow us to perform multivariate analysis. These preliminary results warrant further investigation.

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Juvenile idiopathic arthritis, rheumatoid factor positive polyarticular form: retrospective multicentre study about 26 patients

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Juvenile idiopathic arthritis is an inflammatory arthritis of unknown cause which begins before the age of 16. Rheumatoid factor positive polyarthritis is the rarest and the most severe form, involving early erosive disease.
Our retrospective multicentre study reports 26 patients with rheumatoid factor positive polyarticular form.
Methotrexate was used as the first disease-modifying antirheumatic drug (DMARD) for 90% of the patients with 2/3 of responders. This treatment was modified with the introduction of an anti-TNF agent, etanercept, in 2/3 of the cases.
A combination of etanercept and methotrexate for the second-line treatment is common.
After an average follow-up of 3,9 years, half of the patients are in clinical remission and the other half are non-controlled. Erosive radiographic damage is almost constant.
Early prognostic factors such as the IgM rheumatoid factor and anti-CCP antibodies, were suggested.
Thus, rheumatoid arthritis shows similar clinical signs and functional disability.
Clinical description and management could be consensual with rheumatologist.

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Should we measure long term morbidity in Juvenile Idiopathic Arhritis (JIA) in terms of functional disability? Comparison between a measure of functional status and a valid instrument for damage

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INTRODUCTION: Long-term morbidity in JIA should be assessed by a damage instrument aimed to evaluate irreversible components of the disease instead of the current measurement of functional disability, which is highly influenced by reversible factors.
OBJECTIVE: To compare the measurement obtained by an instrument of functional status with those obtained with a vaild damage tool in the assessment of long term morbidity in children with JIA.
METHODS: Cross sectional study of patients with JIA according with ILAR criteria. Functional status evaluated by the Childhood Health Assessment Questionnaire (CHAQ) and damage assessed with the Juvenile Arthritis Damage index (JADI); were correlated (Spearman's Rho) with several measures of disease damage such as the number of joints with limited range of motion, Poznanski radiological index, Steinbrocker´s functional class and two VAS for the evaluation of disease damage by the attending physician and the parents.
RESULTS: A total of 310 patients (244 females) were included with JIA according with LAR., with a mean age at diagnosis of 4.3±3.3 years and a mean disease duration of 7.9±3.3 years . The following table show the correlations obtained for both instruments:
CONCLUSIONS: The functional status measured with the CHAQ correlate fairly to moderate with several measures of disease damage; however the correlation obtained with the JADI was higher. Long term morbidity in JIA patients should be evaluated measuring damage with valid tools such as the JADI , instead of the traditional measurement of functional disability with the CHAQ.

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Discontinuation of etanercept after successful treatment in patients with juvenile idiopathic arthritis

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OBJECTIVE: To analyze the evolution of patients with Juvenile Idiopathic Arthritis (JIA) after discontinuation of etanercept (ETN) and the clinical response to reintroduction of the drug in those who relapsed.
METHODS: During 2004 to 2009 therapy with ETN was discontinued in 26 patients with JIA due to inactive disease including 11 patients with enthesitis-related arthritis, 7 rheumatoid factor negative polyarthritis, 2 systemic JIA and polyarticular involvement, 1 psoriatic arthritis and 1 with persistent oligoarticular arthritis. In 14 patients the withdrawal of the drug was performed abruptly, and in 12 in a progressive way either by reducing the dose or by increasing the interval between doses. ETN was restarted on all patients who relapsed.
RESULTS: The duration of therapy with ETN was 19±8.4 (9.6-38.5) months. The disease persisted inactive during 14.7±8.6 (1-36) months before ETN was interrupted.
Eighteen cases (69%) relapsed at 5.8±5.3 (0.6-15.9) months after drug discontinuation, whereas in the other 8 (31%) patients the disease remained inactive for an average time of 21±14.7 (5-44.5) months.
The survival curve shows that 50% of the patients continued to have inactive disease at 6 months and 39% at 12 months after drug discontinuation. No significant differences were observed in the time to relapse between the group in whom the drug was tapered and the group in whom ETN was discontinued abruptly (11 vs 14 months, p=0.48). Similarly, no association was found between the duration of inactive disease prior to drug withdrawal and the time to relapse (p=0.23). Patients who relapsed were started again on ETN and all responded satisfactorily.
CONCLUSIONS: • Most JIA patients (69%) relapsed after ETN discontinuation.
• The probability of remaining symptom-free at 6 months was 50%.
• The response to re-introduction of treatment was satisfactory.
• Low doses of ETN may suffice to maintain remission.

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Predictors of clinically inactive disease at one year in 60 patients with polyarticular juvenile idiopathic arthritis receiving very early disease-modifying or biologic drug therapy. ACUTE-JIA study.*

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BACKGROUND: In very early polyarticular JIA, in a randomized clinical trial we compared the efficacy of methotrexate alone (MTX) to that of two combination therapies; infliximab plus methotrexate (TNF); and a synthetic combination with the DMARDs methotrexate, sulfasalazine, and hydroxychloroquine (COMBO).[1] Data on predictive factors for favorable response was collected alongside the efficacy and safety analysis.
OBJECTIVES: To detect predictors at baseline and during drug therapy for clinically inactive disease at one year.
METHODS: Randomized, open-label, clinical trial with 60 DMARD-naïve patients aged 4-15 years. Predictors and confounding factors were explored by Cox regression model using 95% CIs for hazard ratios (HR).
RESULTS: Of 60 patients, 22 (37%) had ANA, 13 (22%) were HLA-B27 positive, and one (2%) RF positive. At baseline mean (± SE) duration of JIA was 0.10 ± 0.02 years, age 9.6±0.4 years, ESR 36±4 mm/hr, active joints 18±1, physician's global 55±2 mm, and CHAQ 0.763±0.082. At baseline, positive ANA (HR 3.0, 95% CI 1.3-6.6) and lower patient's global assessment by visual analogue scale (VAS; HR 0.98, 95% CI 0.96-0.99) predicted faster achievement of inactive disease. On therapy, those on TNF achieved inactivity four times faster than those on MTX (HR 4.5, 95% CI 1.6-12.5) and - just above the level of significance- two times faster than those on COMBO (HR 2.3, 95% CI 1.0-5.7), but MTX and COMBO were comparable. Combining the predictors at baseline and on therapy, best predictors of inactive disease were: inactive disease at 24 weeks (HR 5.0, 95% CI 1.9-13.1), at 6 weeks (HR 6.1, 95% CI 1.4-26.1), and at 12 weeks (HR 3.7, 95% CI 1.2-11.5). In these models, both positive ANA and lower patient VAS were significant.
CONCLUSIONS: In patients with early polyarticular JIA, baseline predictors of clinically inactive disease were positive ANA and lower patient VAS. Drug therapy was a strong predictor; those commencing early infliximab plus methotrexate achieved inactivity faster than those commencing single methotrexate. Inactivity at early stage of disease was the strongest predictor for inactive disease at one year.
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P 157
Abatacept for refractory juvenile idiopathic arthritis-associated uveitis: two case reports

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INTRODUCTION: Chronic anterior uveitis is one of the most serious manifestations of juvenile idiopathic arthritis (JIA) with the risk of sight-threatening ocular complications.
METHOD: We describe 2 patients with JIA-related uveitis refractory to anti-TNF-α agents who were treated with abatacept.
RESULTS: Ts, 11 years old, suffered from oligoarticular JIA and unilateral chronic anterior uveitis since the age of 3 years. Despite topical treatment, methotrexate and TNF-α antagonists (infliximab and adalimumab), the disease remained active and visual acuity decreased. In November 2008 Abatacept was started. After 14 months, arthritis and uveitis remained inactive, with normal laboratory indexes. Ophthalmic drops could be stopped and abatacept infusions have been spaced every 7 weeks.
Ch, aged of 9 years, had oligoarticular JIA and uveitis since the age of 3 years. Arthritis and uveitis remained active with sigh-threatening ocular complications despite topical treatment, systemic steroids, methotrexate, azathioprine and the three TNF-α antagonists. In June 2009 abatacept was started. After 5 infusions, arthritis was inactive, visual acuity had improved and the laboratory inflammatory indexes have normalized. After 10 months, abatacept infusions were given every 6 weeks. No infusion reactions or other drug-related adverse events were reported.
CONCLUSION: Our two case reports and the previous seven [1;2] suggest that abatacept may represent an effective and safe treatment for patients with JIA-related uveitis refractory to methotrexate and anti-TNF-α. Nevertheless prospective studies are needed to confirm these preliminary findings.
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P 158
Tocilizumab in patients with Systemic Juvenile Idiopathic Arthritis (sJIA): 12-week Pharmacokinetic (PK) and Pharmacodynamic (PD) data from the Phase 3 TENDER Trial

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BACKGROUND: Tocilizumab (TCZ) is a recombinant humanised monoclonal antibody targeting both the soluble and membrane-expressed interleukin 6 receptor (sIL-6R, mIL-6R), thereby inhibiting IL-6 signaling and ameliorating symptoms of diseases in which IL-6 plays a pathologic role such as with rheumatoid arthritis (RA) and systemic juvenile (sJIA). Studies in RA patients demonstrated that TCZ administration is associated with an increase in serum levels of IL-6 (presumably due to inhibition of IL-6R-mediated clearance) and with an increase in sIL-6R complex (due to the formation of TCZ/sIL-6R complexes).
OBJECTIVE: To evaluate the pharmacokinetics/pharmacodynamics (PK/PD) of TCZ in patients with sJIA during the 12-week, randomised, double-blind, placebo-controlled, parallel group part of the global phase 3 TENDER trial.
METHODS: Patients in the TENDER trial were randomly assigned (2:1) to receive intravenous (IV) TCZ (8 mg/kg for patients ≥30 kg body weight; 12 mg/kg for patients <30 kg) or placebo (control) given once every 2 weeks for 12 weeks (stable doses of NSAIDs and MTX were continued; CS tapering was allowed from week 6). Sparse PK (TCZ) and PD (IL-6, sIL-6R) samples were collected from all patients before and after each IV administration; TCZ, IL-6 and sIL-6R levels were measured by enzyme-linked immunosorbent assay. Population PK analysis was performed, individual PK parameters (AUC2weeks, Cmin and Cmax) at week 12 were derived and PD parameters were summarised descriptively.
RESULTS: PK: 75 patients were included in the PK analysis (group 1: TCZ 8 mg/kg, n=37; group 2: TCZ 12 mg/kg, n=38). Mean ± SD age was 13.5±2.9 y and 6.6±3.3 y for groups 1 and 2, respectively; mean ± SD body weight was 49.7±20.1 kg and 20.1±5.9 kg, respectively. Mean observed serum TCZ concentration-time profiles were superimposed for the two TCZ dose groups; the PK profile generally trended upward until week 10 and stabilised between weeks 10 to 12 (10% difference); an approximate 3-fold increase in mean TCZ pre-dose concentration was observed between week 2 (22.8 μg/ml) and week 12 (69.5 μg/ml). Mean AUC2weeks, Cmin, and Cmax at week 12 were similar between the two TCZ dose groups (Table), and no clear effect of body weight on PK parameters was observed. PD: 112 patients were included in the PD analysis (75 patients in groups 1 and 2 combined, 37 controls). In patients receiving TCZ, mean IL-6 and sIL-6R levels increased rapidly by week 2; mean IL-6 levels declined subsequently through week 12 (although mean levels did not reach baseline level by week 12); and mean sIL-6R complex levels continued to increase toward a plateau at week 12. PD profiles were generally similar between the two TCZ dose groups. Conversely, in control patients, IL-6 and sIL-6R levels remained relatively unchanged throughout the study period.
CONCLUSIONS: These findings from the TENDER trial in patients with sJIA show similar PK/PD profile for the two evaluated TCZ doses (8 mg/kg for patients ≥30 kg; 12 mg/kg for patients <30 kg), demonstrating the appropriateness of the selected body weight dosing algorithm and confirming the previously reported effect of TCZ on IL-6 and IL-6R levels.

P 159
Epidemiology of acute rheumatic fever in Abruzzo, Italy, 1999-2009

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BACKGROUND: Acute rheumatic fever (ARF) results from an autoimmune response to group A Streptococcus infection. Despite a declining incidence in developing economies, ARF remains a leading cause of acquired heart disease worldwide.
OBJECTIVES: The aim of this study was to investigate the incidence of acute rheumatic fever (ARF) in the pediatric population of Abruzzo, Italy, in the last 10 years.
METHODS: A retrospective study was conducted at the Department of Pediatrics of Chieti, Italy, to identify patients <18 years with a diagnosis of ARF from January 1st 1999 through December 31st 2009. Patients' age, sex, date and age at presentation and major Jones criteria fulfilled were recorded. Echocardiographic findings both at presentation and at follow up were noted.
RESULTS: We identified 88 ARF patients (52 males, 36 females, median age 8,7 ± 4,1 years); 40 patients (45,4%) experienced acute carditis and 36 patients (40,9%) had residual chronic rheumatic heart disease (RHD). Major Jones criteria at presentation were arthritis in 51 (57,9%), carditis in 40 (45,4%), chorea in 5 (5,7%), erythema marginatum in 10 (11,3%) and subcutaneous nodules in 4 (4.5%). The overall mean incidence rate was 3.5/100000. The lowest incidence rate (1.4/100000) was observed in 2003 while the highest was in 2008 (6.1/100000) with an increasing trend in the last five years.
CONCLUSION: Our data are similar to previous studies that have reported, in developed countries, ARF incidence rates <10/100000. The high proportion of RHD found in this study underline the need for an effective surveillance.

P 160
Fabry disease: a diagnostic algorithm for rheumatologists

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BACKGROUND: Fabry disease is an inherited disorder of lipid metabolism caused by deficient activity of the lysosomal enzyme α-galactosidase A. The progressive storage of undegraded substrate affects a variety of cell types, including vascular endothelial, nerve, renal and cardiac cells, and results in a wide array of signs and symptoms.
Burning peripheral pain with triggered crises of excruciating pain generally presents in childhood and points to Fabry small fibre neuropathy. The limb pain may initially be the only manifestation in young Fabry patients, or be part of a cluster of initially harmless-looking symptoms. Gastrointestinal complaints, angiokeratoma, corneal deposits, hypohidrosis and exercise intolerance are other common early manifestations.
Diagnosis is often delayed by a decade or more which is of great concern as the disease progresses to life-threatening complications involving the kidneys, heart and/or brain.
OBJECTIVES, METHODS: A survey using a case-based scenario was conducted among 360 rheumatologists and paediatricians clinically managing patients with rheumatologic conditions. Participants were asked to list the differential diagnosis for a hypothetical patient in a three-level process with additional signs and symptoms suggestive of Fabry disease given at each level. Based on the results of this survey, as well as literature and registry derived information on the presentation of Fabry disease, the International Musculoskeletal Working Group on Lysosomal Storage Disorders developed a practical diagnostic algorithm.
RESULTS: Based on the initial information, only 1 of the 120 paediatric rheumatologists and paediatricians considered Fabry disease in the differential diagnosis,

while 13% of the adult rheumatologists suspected Fabry disease. A slightly higher level of suspicion (4 and 17%, respectively) was detected after providing additional signs and symptoms typically seen in young Fabry patients. A further, although modest, increase of the percentages (to 6 and 22%, respectively) was found at the third level of information, indicating an overall limited awareness of this differential diagnosis among rheumatologists. A diagnostic algorithm was therefore developed with burning pain in hands and feet in conjunction with attacks of excruciating pain as the leading symptom, especially in the absence of clinical and laboratory markers of joint inflammation.
CONCLUSIONS: The rheumatologist may encounter undiagnosed Fabry patients displaying musculoskeletal symptoms, including limb pain. In fact, they are in an excellent position to recognize the early hallmarks and consider diagnostic testing. While the awareness of this important differential diagnosis seems to be limited, at this point a decision-support tool as an aid for diagnosis of patients with Fabry disease was developed to increase recognition of the disease.

P 161
Musculo-skeletal pain in children: an epidemiological study

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BACKGROUND: Musculo-skeletal complaints are quite common in children and can be due to non-inflammatory conditions such as growing pain or benign joint hypermobility syndrome (BJHS). Affected children often undergo several and sometimes invasive procedures which may delay the diagnosis.
OBJECTIVES: Aim of the study was to evaluate the prevalence and clinical features of musculo-skeletal complaints among healthy schoolchildren and to analyze possible risk factors for the development of arthralgia/ myalgia in paediatric age.
METHODS: Healthy schoolchildren, aged 8-13 years, attending four schools in the city of Padua, were invited to take part in the study. Both parents and children gave informed written consent. Clinical history from all participating subjects was collected and included family history of musculo-skeletal conditions, sport activities and sites of musculo-skeletal symptoms. All children underwent a general and rheumatologic examination with particular focus on the presence of generalized joint hypermobility (defined as a Beighton's score > o = 4/9), weight, height, body mass index (BMI) and pubertal stage.
RESULTS: 289 schoolchildren, 143 females and 146 males (F:M=1:1) entered the study; 208 were in pre-pubertal stage, 81 were pubertal. Musculo-skeletal complaints occurred in 88 (30.4%): in 38 (13.1%) they were associated with generalized hypermobility, while in 50 (17.3%) they occurred alone. The most common involved sites (91% of subjects) were the lower limbs and the spine. The higher frequency of symptoms was recorded in 9 year old females and in 10 year old males. Subjects with symptoms were more frequently pre-pubertal than pubertal (83% vs 17%) and males were more frequently affected than females, especially in pre-pubertal age, (42.6% vs 27%, p 0.019). Symptomatic children showed a higher frequency of generalized joint hypermobility than the asymptomatic ones (p 0.05) while pre-pubertal males had a significantly higher BMI than pre-pubertal females (p= 0.003). Sport activities, with or without articular overloading, was not a significant risk factor for the occurrence of musculo-skeletal pain.
CONCLUSIONS: Children presenting with non inflammatory musculo-skeletal pain should be always evaluated for the presence of generalized hypermobility. Pubertal stage plays an important role in the pathophysiology of this condition.
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P 162
Primary and secondary failure of biological therapy: a review on a pediatric cohort with autinmune rheumatic diseases

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INTRODUCTION: Although their great contribution to the management of rheumatic diseases of childhood (RDC), biological therapy is always tested for the need of change that could be motivated by intolerance, allergic reactions, increased rate of infections, onset of opportunistic infections or inefficiency. The purpose of this work is to review the failures of biological therapies, their causality, and the outcome after the modification of the drug.
METHODS AND MATERIALS: We made a review of 78 medical records of patients with RDC, with a total of 100 biological treatments (BT) between 1999 and 2009. A categorization was made based on the first drug administered and diagnosis (OA-JIA: Oligoarticular Juvenil Idiopathic Arthritis, PA: Polyarticular, Sys: Systemic, U: Undifferentiated, Ps: Psoriatic and Er: Entesitis Related; SLE, Wegener, etc), and the type of failure, based on the time of effectiveness posted in the drug information tab for each treatment.
RESULTS: Adalimumab (ADM): 17 cases of JIA (6 OA, 5 PA, 4 Sys, and 2 U). Five cases presented uveitis (all OA). In one case we suspended biological treatment due to clinical remission and 2 for secondary failure, of these two, one patient (PA) change to RTM and the other (Sys) to Anakinra (ANK), both with a favorable outcome in follow up reviews. One case of toxicity that change to RTM with good results was recorded.
Etanercept (ETN): 40 patients, 36 of the were JIA (10 OA, 8 PA, 11 Sys, 5 Ps, and 1 U). Four cases presented uveitis (3 OA and 1 PA). There was 6 suspensions of the drug for clinical remission and 9 for secondary failure, from the latest group 4 patients change to ANK (three of them with good outcome), three to ADM (two with good outcome and the other one with a second secondary failure) and 2 to IFM (one with good outcome and the other with a second secondary failure). There was only one suspension for toxicity that was changed to IFM with new toxicity.
Infliximab (IFM): 24 patients. Twenty two of them, cases of JIA (6 OA, 6 PA, 2 Sys, 1 Ps, 5 ER y 2 U), one Behçet and a case of WG. One case presented uveitis (OA). There were 3 suspensions for clinical remission (1 OA, 1 PA y 1 ER) and 5 for toxicity, from the latest 3 patients change to ETN, two to ADM, and one to RTM with good outcome, while one patient change to ADM showing recurrence of toxicity. In 6 cases the treatment was suspended for secondary failure, from them one change to RTM and 4 to ETN with good outcome. In one case we change to ADM with recurrence of the secondary failure.
Anakinra: 11 patients; 9 with the diagnosis of Sys-JIA, one U-JIA and one case of CINCA syndrome. There was one suspension due to toxicity that was changed to TZM with good outcome. There were no records of primary or secondary failures.
Rituximab: 5 patients (1 PA, 1 OA, 2 SLE y 1 WG). We suspend the drug in one of the cases of SLE for serious infections during the treatment.
Tocilizumab: 1 case of Sys JIA.
Canakinumab: 2 cases of Sys-JIA.
There were no reports of primary failures in our series.
CONCLUSION: Our results suggest that when the modification of the treatment is secondary to inefficacy, those drugs with different biologic target are more effective than those of the same family. This phenomenon analysis should be done on greater population to establish the factors that could predict the success or the failure of a therapy change.

P 163
Facial cutaneous necrosis as clinical relapse in an infant with probable catastrophic antiphospholipid syndrome - is there a role for rituximab therapy?

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BACKGROUND: The antiphospholipid syndrome (APS) is an acquired thrombophilic disorder characterized by the presence of auto-antibodies to a variety of phospholipids and phospholipid-binding proteins. Clinical manifestations range from being asymptomatic to having imminently life-threatening events. Catastrophic antiphospholipid syndrome (CAPS) occurs in <1% of patients with APS and is defined by multiple small-vessel occlusions that lead to multiple-organ failure and is associated with high morbidity and mortality rates. Current first-line combined treatment regimens have decreased mortality rates from >50% before 2001 to 33% currently. Rituximab, a chimeric anti-CD20 monoclonal antibody, eliminates autoreactive B cells, reduces antiphospholipid antibody serum levels, improves the clinical features of APS, and has shown promise in the management of catastrophic antiphospholipid syndrome.
CASE REPORT: We report the case of a 3-month-old boy who presented to us with digital necrosis (skin biopsy demonstrated multiple small-vessel thromboses without signs of vasculitis) and pulmonary hemorrhage (hemosiderin-laden macrophages in bronchoalveolar lavage) one month after cardiac surgery for correction of coarctation of the aorta. There was no evidence of infection, nor a family history of coagulation disorders. Autoantibodies were positive for anti-β2 glycoprotein I only. He was diagnosed as probable CAPS and treated with anticoagulation, high-dose steroids, immunoglobulins, exchange transfusion and cyclophosphamide, as well as iloprost and bosentan as vasodilators for his ischemia; he showed an excellent initial clinical response, however the patient deteriorated clinically within two weeks and the subsequent use of a 4-week course of rituximab (375 mg/m2) resulted in a sustained clinical and immunological response. Six months after rituximab therapy

he represented with facial cutaneous necrosis whilst being on anticoagulation and bosentan therapy; anti-β2 glycoprotein I titres remained negative. Again he was treated with high-dose steroids and a second 4-week course of rituximab with excellent response. Currently, at the age of 18 months he remains asymptomatic in good clinical state.
CONCLUSIONS: This is the youngest patient with probable CAPS and the second patient who was successfully treated with a immunomoduladory regimen including rituximab. Clinical relapse six months after the use of anti-CD20 and a good response to a second four week course of this drug supports the hypothesis that autoreactive B lymphocytes play an important role in the pathogenesis of this disease. Rituximab should be considered in the management of APS and CAPS. To achieve a sustained clinical response repeated 6-monthly administration of this drug might be required.

P 164
Increase of minor adverse events in a pediatric population on biologic therapy for rheumatologic autoimmune diseases

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INTRODUCTION: The use of biological therapies (anti-TNF, anti CD20, anti-IL1R, and anti-IL-6) represents an important progress in thebanti-IL1 treatment of rheumatologic autoimmune diseases. Their pharmacological activity induces an immunosuppression state that enhances the risk of having an infectious disease. Although these effects are being studied in several centers that use these therapies, there is only few records on pediatric population. The purpose of this report is to compare the incidence of minor infections with the general population.
METHODS: A review of 79 medical records of patients in the pediatric age with rheumatologic diagnosis (JIA, SLE, WG, CINCA syndrome, Behçet and dermatomyositis) and whom received biological therapies before the 25 years old. There was made an incidence comparison of minor adverse events (those that motivated a non-urgent consult, not requiring hospitalization and the absence of fever for more than 3 days) with the monthly incidence of consults in a control group, available in the epidemiology webpage of the MSC (Spain). We exclude the ER visits, healthy child visits, administrative and vaccination consults.
RESULTS: There were a total of 78 biological treatments between April 2002 and December 2009. The patients with more than one therapy were counted as different patients for the records of adverse events. The treatments were Etanercept(32), Infliximab(15), Adalimumab(15), Anakinra(10), Rituximab(3), Canakinumab(2) and Tocilizumab(1). The total time of follow up was 2104,2 months. We obtain data from general population available in the Spain National Survey in the website www.msc.es. The increase in the incidence of an adverse event risk was 63,2% by month for a hundred of treated patients. The comparison between average incidence by age group is shown in the table
CONCLUSION: There is an increase of the average adverse events on the group with rheumatologic diseases who received biological treatment compare with the general population. We cannot assume that this increase is provoked by the treatments alone, given the chronic nature of the diseases and the previous damage to the immunity of the patients. We suggest a comparison with a similar population without biological treatment.

P 165
Tocilizumab in Pediatric Relapsing Polychondritis

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BACKGROUND: Relapsing polychondritis (RP) is a very rare systemic disease in childhood. Respiratory tract chondritis is considered ominous and portends a poor prognosis. There is no standardized therapeutic protocol for RP, thus an individual approach, directed by clinical severity, is necessary. We report the use of Tocilizumab in a child with severe disease, that improved in the first infusion her clinical and laboratorial parameters, after failing innumerous previous treatments.
OBJECTIVE: To report a severe pediatric RP case, with five years follow-up that failed to cyclophosphamide, mycofenolate mofetil and two anti-TNFs therapy, maintaining prednisolone doses around 1mg/Kg/day. Tocilizumab after the first infusion lowered the sedimentation rate and her clinical manifestations after 5 years of severe desease.
METHOD: Case report of a rare rheumatic disease that fantastically improved with Tocilizumab.
CONCLUSION: Tocilizumab may be a good option to treat severe and refactory RP cases.
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P 166
Gastrointestinal and cardiovascular adverse events of NSAIDS in children clinical trials (RCTs): a systematic review

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BACKGROUND: Non steroidal anti-inflammatory drugs (NSAIDs) are widely used in children for both acute and chronic conditions. Despite a number of studies in the literature show that gastrointestinal (GI) and cardiovascular (CV) side effects are associated with NSAIDs, the incidence in the paediatric age is unknown. This study is part of the Safety Of non-Steroidal anti-inflammatory drugs (SOS) project, funded by European Commission in 2008.
OBJECTIVES: To evaluate GI and CV safety of NSAIDs in children, by a review of published paediatric RCTs and to identify main gaps of the analyzed studies.
METHODS: Relevant RCTs, identified through references of all meta-analyses of RCTs focused on NSAIDs GI and CV safety, were searched in four databases: Medline, ISI, SCOPUS, Cochrane. Eligibility criteria for inclusion were: RCTs on NSAIDs published in English between 1983 and 2008 and consideration of GI and/or CV adverse events (AEs) in the trials. Each RCT was evaluated for quality assessment (Jadad scale), indications, planned follow-up and power to observe AEs.
RESULTS: One hundred and six paediatric RCTs were examined. Mean follow-up planned was 3 days (IQR 1-14 days). Most of them concerned ibuprofen (44) and indomethacin (39). The most common indications were patent ductus arteriosus and pain after surgery; only four concerned chronic diseases (3 juvenile idiopathic arthritis, 1 cystic fibrosis).
The median Jadad score was 10 (IQR 8-11). Only 11 RCTs included treatment groups of more than 100 subjects (95% probability to observe an adverse event of incidence 3%). More than 50% did not provide definition of the outcomes for safety nor details of the methods used for AEs retrieval. In the 106 trials the following AEs were reported: no CV side effects; one case of complicated peptic ulcer and two cases of lower GI bleeding in RCTs evaluating indomethacin in the treatment of patent ductus arteriosus; four episodes of non major GI bleeding in a trial concerning ibuprofen for the treatment of fever. Due to the poor representation of RCTs of acceptable methodological quality, the estimation of risk and event rates associated with the use of NSAIDs was not possible because it would lead to consider in most cases data from only one trial, often of limited size and with limited power for the detection of AEs.
CONCLUSIONS: The systematic review of the literature shows a big lack of knowledge about NSAIDs safety in children, especially in terms of long term follow-up and chronic use. Further high quality studies are needed to determine incidence of AEs and risk estimates.
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P 167
Rhachialgia as opening symptom of Neuroblastoma: a case report

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BACKGROUND: Rhachialgia is not a very common symptom in children. If it is present and associated with systemic symptoms, it may be due to important infectious and neoplastic diseases.
OBJECTS AND METHODS: We describe the case of a little boy of 3 years old came to our observation for rhachialgia, lameness and fever (38.5 °C), not responsive to common nonsteroidal anti-inflammatory drugs (NSAIDs). Symptomatology following to a fall began about a month prior to admission. On that occasion, a radiograph of the spine was negative. Physical examination shows deteriorated general condition, pale skin, lameness, stiffness of the lumbar spine, lower limb in analgesic flexion, pain on mobilization of both hips, difficulty in moving from supine to sitting. Blood-chemical tests show: hemoglobin (Hb) 11.5 g/dl; red blood cells (RBC) 4400000/ µl; white blood cells (WBC) 11400/µl (N 55%; L35%); platelet count (PLT) 317000/µl; hematocrit (Htc) 33.6%; renal and hepatic functional indexes are normal; serology (CMV, EBV, Bartonella) is negative and blood culture is sterile, but inflammatory indexes are increased (erythrocyte sedimentation rate 120 mm/1 h; C-reactive protein 85.5 mg/dl). Chest X-ray and ultrasound of the abdomen are negative, but the ultrasonography of the hips shows intra-articular effusion bilaterally.After 3 days since his admission, despite the anti-inflammatory therapy undertaken, we observe to the worsening of clinical condition
of the patient with increased body temperature. In suspicion of spondylodiscitis, a bone scintigraphy is scheduled, blood tests are performed again and antibiotic therapy is started.
RESULTS: Blood tests show: Hb 10.4 g/dl; RBC 3930000/µl, WBC 9600/µl (N60%, L 30%), Htc 30%; PLT 356000/µl; serum iron 34 µg/dl; ferritin 411 ng/ml; transferrin 233 mg/dl, erythrocyte sedimentation rate (ESR) 87 mm/1h; C-reactive protein (CRP) 112 mg/dl; lactic dehydrogenase (LDH) 915 U/l. Bone scintigraphy, performed with technetium-99m methylene-diphosphonate (Tc-99m MDP), highlights areas of photonic defect in the sixth and twelfth thoracic vertebra **(Figure 1)** that the computed tomography(CT) turns out to be areas of considerable rarefaction of the spongy bone of the vertebral bodies. Bone marrow aspirate is then performated showing the presence of rosettes of tumor cells. In suspicion of Neuroblastoma, we perform the assay of urinary catabolites of catecholamines (vanillymandelic acid 18.1 mg/24h; homovanillic acid 18.5 mg/24h) that they are higher than the standard. The patient is then transferred to the oncology department to complete the staging of the disease and to define and undertake a specific chemotherapy.
CONCLUSIONS: Neuroblastoma, a neoplasm of the sympathetic nervous system, is the second most common extracranial malignant tumor of childhood and the most common solid tumor of infancy. It represents over 7% of malignancies in individuals younger than 15 years and about 15% of all cancer deaths in children. It occurs slightly more frequently in boys than girls (ratio 1.2:1). The incidence peaks at age 0 to 4 years, with a median age of 23 months. Neuroblastoma is difficult to diagnose because it has a wide and diverse spectrum of clinical manifestations, depending on the primary tumor and the presence or absence of metastases or paraneoplastic syndromes.
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P 168
A 12-year-old boy with recurrent painful knee swelling

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A 12-year-old sporting boy presented with a 3 months history of pain and swelling of right knee. Physical examination was totally unremarkable except for presence of knee effusion then also confirmed by ultrasonography and Magnetic Resonance Imaging (MRI). History and clinical features were consistent with Juvenile Idiopathic Arthritis (JIA) diagnosis; a two months therapy with non-steroidal anti-inflammatory drug failed, so a steroids knee injection with triamcinolone esacetonide was performed then repeated three months later. The patient completely recovered, but one year later he presented right knee effusion again. Physical examination revealed joint enlargement with decreased range of motion. A radiograph showed multiple radiopaque, round, loose bodies within the joint. **(Figure 1)** Radiological findings were consistent with diagnosis of synovial chondromatosis then confirmed by histological findings after synoviectomy. Synovial chondromatosis is an uncommon, monoarticular, proliferative disease of the synovium that usually affects large joints. The disorder is characterized by the presence in the synovial space of multiple highly cellular cartilaginous nodules, that results from metaplasia of the synovial tissue. As the disease progresses, the cartilaginous nodules become partially calcified, the synovium thickens, and the joint surfaces may become eroded. When calcification of nodules occurs, radiographs reveal radiopaque loose bodies within the joint. Initially MRI can be negative, because in the phase of unmineralized synovial chondromatosis, the signal intensity of the nodules may resemble sinovial fluid. Malignant transformation has been reported.
Clinical manifestations of synovial chondromatosis can be suggest a monoarticular JIA diagnosis; a standard X-ray should be periodically performed in the follow-up of recurrent monoarticular arthritis.
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Congenital self-healing histiocytosis with eye and liver involvement

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A female presented at birth with congenital multiple purpuric lesions distributed over the trunk, limbs and face. The mucous membranes, palms and soles were spared. Laboratory values showed slight reduction of haemoglobin level, with normal blood count, immunoglobulins level, inflammatory indeces, clotting tests. Autoimmune markers were negative. Chest radiography was normal. Abdominal ultrasonography revealed hypoechogenic small round lesions with blurred borders with hyperechogenic micro spots. Congenital infections were ruled out.
At one month of age the patient developed right progressive ocular redness; keratitis and iridocyclitis of unknown origin in the right eye were diagnosed; local antibiotic and corticosteroid therapy was therefore started, with slightly improvement. Laboratory tests showed an elevation of inflammatory markers (ESR 71 mm/h, CRP 8,35 mg/dl).
Biomicroscopy of the right eye showed normal cornea; there were posterior synechiae with fibroid deposits on the anterior lens capsule and moderate anterior chamber flare, without cells. No mydriatic response was observed after instillation of tropicamide 1% eye drops in the right eye. Biomicroscopy of the left eye was normal. Fundus examination was prevented in the right eye by the posterior synechiae. B-scan echography showed small dots and linear areas of low reflective mobile vitreous opacities in the right eye, without retinal alterations. These findings were consistent with a previously unreported uveal and vitreous involvement by Self Healing Langerhans Cell Histiocytosis (SHLCH).
A brain sonography and a radiographic skeletal survey showed no anormalities.
Bone marrow aspirate showed high cellularity with prevalence of myelocytes (M/E = 7/1) and 5% of eosinophils. There was no elevation in histiocytic cells number (1%) but all histiocytes had an erythrophagocytic aspect. Immunohistochemistry revealed 0.1% of cells CD1a + CD4 + CD14+.
A skin biopsy revealed a massive infiltration of eosinophils, lymphocytes (CD43 positive) and histiocytic cells principally in the dermis. Immunohistochemistry demonstrated that histiocytic cells were positive for S-100 protein, CD1a and CD56 antigens. These findings confirmed the diagnosis of Langerhans Cell Histiocytosis (LCH).
For ocular involvement, a treatment with atropine 1% eye drops twice a day was then introduced, with slight absorption of the fibroid deposits on the anterior lens capsule, and slow improvement of the mydriasis. After one month visual evoked potentials were normal as well as fundus examination.
At a 2-months follow up the patient did not show any ocular or cutaneous involvement; liver involvement, although largely improved, persisted at ultrasound evaluation.
We have described a case of SHLCH with spontaneous resolution. The most common presentation is multiple red-brown macules, papules, and nodules noted at birth or shortly thereafter that become spontaneously involute in a healthy infant who remains symptoms free. Skin biopsy with immunohistochemical study is required to confirm the diagnosis. SHLCH is most appropriately classified as an entity within the LCH disease spectrum; it is usually a benign disease but there are reports of systemic involvement and relapses. Long-term follow up is mandatory in order to assess potential relapses and/or development of malignant LCH.
There is a single report in literature, describing a case of SHLCH with ocular manifestations, as exudative retinopathy. Our case is the first reporting simultaneous uveal and vitreal involvement.

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Camptodactyly-Arthropathy-Coxa Vara-Pericarditis (CACP) Syndrome with severe costrictive pericarditis

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INTRODUCTION: The camptodactyly-arthropathy-coxa vara-pericarditis syndrome (CACP) is a rare disorder of which only 30 cases have been described since 1995, most patients being of North African origin. It is characterized by congenital or early-onset camptodactyly and childhood-onset non-inflammatory arthropathy associated with synovial hyperplasia. Some patients have progressive coxa vara deformity and/or noninflammatory pericardial effusion. CACP is autosomal recessive inherited and the gene is located on chromosome 1q25-31. Histopathologically, there is pronounced hyperplasia of synovium with multinucleated giant cells.
CASE REPORT: We present an eight-years-old boy from Guinea who arrived to Spain two weeks prior his admission in our hospital. Past medical history consisted of recurrent malaria episodes likely being P. falciparum. Over the last 12 months he complained about increased abdominal distension and weight loss. His grandfather suffered from camptodactility, the parents were non consanguineous.
On clinical examination he was apyrexial, slim and muscle wasted, there was marked abdominal distension with marked hepatosplenomegaly and ascitis. Articular involvement included camptodactyly of both hands and feet **(picture 1)**, arthritis of his elbows, wrists, and knees **(picture 2)**. There was no respiratory distress. A thick blood film confirmed P.falciparum infection with a low parasitaemia for which he was treated with quinidine and clindamicin resulting in a transitorily clinical improvement. A full blood count, acute phase proteins as well as the renal and hepatic profile were normal. Cardiomegaly was detected on thorax radiography **(picture 3)** and pericardial effusion with signs of constriction was confirmed by echocardiography. Pericardiocentesis showed few lymphocytes, cultures were negative for mycobacteria, parasites and fungi, pericardial biopsy demonstrated markedly thickened pericardium with fibrosis. An autoimmune screening including RF, ANA and HLA B 27 were negatives.
A skeletal survey showed bilateral short femoral neck and generalized osteopenia without articular destruction. MRI confirmed synovial effusion without bone erosions.
His management consisted of daily prednisolone 2mg/kg and weekly methotrexate (15mg/m2) with little improvement of the pericardial effusion and articular mobility. He underwent a pericardiectomy resulting into prompt improvement of his cardiac function, hepatosplenomegaly and ascitis. Currently he is clinically stable and receives physiotherapy as part of his rehabilitation.
CONCLUSION: CACP is a rare and difficult to diagnose syndrome since articular symptoms can mimic inflammatory arthritis not responding to conventional treatment. Management is mainly supportive. Pericardiectomy appears to be an effective treatment option for non-inflammatory pericarditis which occurs in up to 30%.

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Transition clinic for adolescents and young adults with childhood onset rheumatic diseases: a ten-year Italian experience

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BACKGROUND: Despite new antirheumatic drugs, a high percentage of pts with infantile rheumatic diseases (RD) have either active or reactivated disease in adolescence and young adult life still requiring medical support. As there are many differences between paediatric and adult health care, a Clinic dedicated to transition is required to face their medical, psychosocial and educational-vocational needs. In 2000, the first Italian outpatient clinic for adolescents and young adults was founded at the Rheumatology Unit of Florence University.
OBJECTIVES: 1. To care for children with RD during the transition from childhood to adult life.
2. To equip young people with the appropriate knowledge and skills to cope with this change.
3. To support patients in all the needs related to a chronic rheumatic disease.
PATIENTS: Among 545 pts (F 359, M 186, median age 21 yrs, median age at disease onset 7.2 yrs (range 1-15), followed at the young-adult outpatient clinic: 264 (48%) were affected by JIA, 134 oligo, 60 polyarticular, 15 systemic, and 55 Enthesitis related arthritis (B27 positive or negative), 42 (8%) had SLE, 18 (3%) Scleroderma (localised and systemic), 51 (9%) musculoskeletal non inflammatory syndromes, 35 (6%) Raynaud phenomenon or undifferentiated connective tissue diseases, and 20 (3%) Dermatomyositis and vasculitis, while 115 (23%) other diseases. All patients have been followed with periodic evaluation of general health status, disease activity and possible complications, efficacy and safety of therapy, adherence to therapy, and psychological problems.
RESULTS: The experience achieved over 10 years has recognized as more frequent issues: 1. Active or reactivated disease 2. Non adherence to therapy 3. Eye disorders (uveitis, cataract, glaucoma) 4. Maxillo facial abnormalities (condilar dysplasia, jaw shortness) 5.Osteopenia/osteoporosis, 6. psychological disorders (anxiety, depression, socialization difficulties 7. Sexuality related problems (contraception, pregnancy) 8. School performance 9. Working troubles.
CONCLUSIONS: Transition from paediatric to adult rheumatology care is a critical component of comprehensive care for adolescents and young adults with RD. Lacking good quality services, there is a high risk to loose the benefits acquired in childhood, and disease worsening. One of the main concern is to identify when young pts with chronic RD should move from paediatric to adult centred care in order to guarantee a future cooperation between doctor and patient, and to facilitate therapeutic compliance. Improving transition care for youth with childhood-onset rheumatic diseases requires collaboration between paediatric and adult rheumatologists, and between rheumatologists and primary care providers. Providers of transition care must recognize that young adults with rheumatic diseases present complex medical and psychological needs.
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Rheumatic complaints as a presenting symptom in patients with genetic-metabolic diseases

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Pediatric non inflammatory arthropathy may present with symptoms or signs suggesting connective tissue diseases. A group of these conditions is represented by storage disease family, like mucopolysaccharidoses, some glycogenosis or skeletal disorders like spondyloepiphyseal dysplasia.
We report six patients diagnosed with genetic-metabolic diseases, who were referred to Pediatric Rheumatology Unit for symptoms suggesting a rheumatic disease.
1. GG, 7 years-old boy first admitted in our department for suspected polimyositis. After an episode of upper respiratory tract infection, he presented myalgia and important asthenia. Laboratory tests revealed elevation of transaminases, creatinphosphokinasis and lactate dehydrogenase; the parameters of inflammation were slightly raised. After 2 weeks there was a resolution of symptoms, with normalization of flogosis parameters and persistent alteration of enzyme values. Physical examination was normal. Molecular tests for dystrophinopathies was negative. Muscular biopsy was performed and led to make a diagnosis of Mc Ardle disease.
2. DN, 6 years old girl, was admitted to our unit for the suspect of Sjogren Syndrome. She presented dry eyes and submandibular lymphadenopathy. Physical examination revealed multiple dental caries, peg-shaped teeth, thin and sparse hair. Laboratory tests were normal, quantitative pilocarpine iontophoresis showed decrease sweat production. Genetic evaluation confirmed the hypothesis of ectodermal dysplasia.
3. CE, 12 years-old girl presented functional limitation of hands, wrists, hips, ankle and temporomandibular joint with bilateral valgus hallux. The parameters of inflammation were slightly raised. Juvenile idiopathic arthritis was diagnosed and methotrexate therapy (15 mg/mq) was started without improvement. The patient was screened for genetic-metabolic disease. Skeletal radiography revealed alterations suggesting the diagnosis of progressive pseudorheumatoid arthropathy.
4. CA, 4 years-old boy, was admitted to our unit for the hypothesis of juvenile idiopathic arthritis. Physical examination showed limitation of all joints, with normal inflammatory parameters. Metabolical screening led to diagnose mucopolysaccharidosis, confirmed by deficiency of the lysosomal enzyme iduronate-2-sulfatase.
5. CF, 12 years old girl, with history of early puberty and psoriasis, presented a clinical suspect of spondyloarthropathy. Family history revealed psoriasis. She presented chronic back pain and coxalgia. 99-TC scintigraphy and MRI were normal, but skeletal radiography showed tipical alterations of spondyloepiphyseal dysplasia.
6. LA, 10 years old girl. First admitted with diagnosis of scleroderma. Laboratory work up was normal as well as instrumental investigations. Genetic evaluation led to make a diagnosis of Dunnigan Syndrome.
These case reports reveal the importance of metabolic screening and genetic evaluation for patients with musculoskeletal symptoms, with normal physical examination and inflammatory parameters.

P 173
Clinical manifestations of Down's Arthropathy

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BACKGROUND: Down's syndrome is the most common congenital cause of developmental disability in Ireland with a birth prevalence of 1 in 547 live births, the highest in Europe1. The arthropathy of Down syndrome has an estimated prevalence of 8.7/1000 which is 6 times higher than JIA (Juvenile Idiopathic Arthritis) in the general population2. Despite this, there is a lack of awareness of the risk of arthritis in these children amongst relevant caring health professionals. Delayed diagnosis and poor recognition of the disease can lead to significant impairment3.
OBJECTIVES: To determine the clinical manifestations and therapeutic interventions used in the management of children with Down's arthropathy.
METHODS: A retrospective chart review of all patients attending our centre since it's establishment in 2006.
RESULTS: A total of seven patients (male=2, female =5) were identified. The age at diagnosis ranged from 5 to 15 years (mean 8.9 years). The average delay in diagnosis from onset of symptoms was 2.1 years. Polyarticular disease was noted in six with the remaining 1 patient having an extended oligoarticular course.
Joint contractures were present in all with polyarticular disease, 2 of whom also had joint subluxations. No radiographic evidence of erosive joint disease was noted. Intra-articular steroid joint injections, NSAIDs and methotrexate were the mainstay of treatments to date.
CONCLUSIONS: The arthropathy of Down syndrome can cause significant disability in a vulnerable group of patients. Awareness needs to be increased among those caring for children with Down syndrome in order to facilitate earlier diagnoses and potentially better outcomes.
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P 174
Splenomegaly and pancytopenia: a case report of Autoimmune Lympho-Proliferative Syndrome

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BACKGROUND: Autoimmune lymphoproliferative syndrome (ALPS) is a rare disease characterized by lymphadenopathy, hepatosplenomegaly and multilineage cytopenias (due to autoimmunity and/or splenic sequestration) and susceptibility to malignancy.
The underlying mechanism is a disorder of lymphocyte apoptosis with an elevated percentage (>1%) of CD3+CD4-CD8- TCRαβ double negative Tcells (DNT) in peripheral blood and lymphoid tissue. Most patients have a mutation in the fas gene or fas signaling pathway.
CASE REPORT: We present the case of a 14 year-old boy referred for an incidental finding of pancytopenia, without systemic symptoms. On physical examination there was skin pallor and splenomegaly measuring 10cm below the costal margin, and no lymphadenopathy or hepatomegaly.
Laboratory tests showed pancytopenia, high reticulocyte count and LDH, but negative Coombs test; there was also hypergammaglobulinema with high serum IgA and IgD.
Viral serologies, bone marrow aspirate and bone biopsy were normal. Spleen aspirate showed sinusoidal dilation, congestion, leukostasis and small aggregations of hystiocytes.
Autoimmunity markers were negative and α1 anti-trypsin deficiency and storage diseases were also excluded. Further investigations were done for a differential diagnosis of ALPS: peripheral blood flow citometry showed an elevated percentage of DNT cells (5%), in vitro apoptosis studies revealed resistance to fas-induced apoptosis, and an heterozygote mutation of the fas gene was also detected, confirming the hypothesis of ALPS.
Medication with steroids was started (deflazacort 1,5mg/kg/day), which lead to improvement of both the cytopenias and spleen size.
DISCUSSION: Although rare, ALPS should be considered as a cause for lymphadenopathy and/ or splenomegaly and cytopenias without systemic symptoms, after excluding the most frequent causes.
An early diagnosis and treatment may avoid unnecessary studies and medications, and has important prognostic value.

P 175
Macrophage activation syndrome / hemophagocytic lymphohistiocytosis secondary to rheumatic diseases or primary immunodeficiency in a tertiary pediatric hospital

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BACKGROUND: Macrophage activation syndrome (MAS), also called hemophagocytic lymphohistiocytosis (HLH), is characterized by cytopenias, multiple organ dysfunction, coagulopathy and macrophages activation due to exaggerated release of inflammatory cytokines. This syndrome may be inherited (primary) or secondary to rheumatic diseases (RD) and primary immunodeficiency (PID), with rare reports considering both populations(1,2,3).
OBJECTIVES: To evaluate the prevalence and to describe clinical and laboratory data, prognosis and therapies and evolutions of MAS/HLH in a large pediatric population of RD and PID.
METHODS: MAS was diagnosed according to recent guidelines for systemic juvenile idiopathic arthritis (sJIA) (Ravelli et al., 2005) and juvenile systemic lupus erythematosus (JSLE) (Parodi et al., 2009). Diagnosis of sJIA and JSLE were established according to ILAR and ACR criteria, respectively. HLH for PID was diagnosed according to Janka & Schneider 2004 criterion and PID according to IUIS update 2009.
RESULTS: From 1983 to 2009, 5367 patients were followed at the Pediatric Rheumatology Unit and MAS was observed in 10/251 (3.9%) sJIA and in 11/263 (4.1%) JSLE patients. All sJIA patients had high fever, hepatosplenomegaly, lymphadenopathy, encephalopathy, pancytopenia, increased liver enzymes and hypofibrinogenemia; high levels of serum ferritin (>10.000 ng/ml) was observed in 5/8 and bone marrow aspirate showed activated macrophage with erythrophagocytosis in 7/10. All of our JSLE patients had cytopenias; macrophage hemophagocytosis in bone marrow aspirate was observed in 3/11 patients and hyperferritinemia in 5/11. Treatment of MAS included intravenous methylprednisolone, intravenous immunoglobulin and/or cyclosporine. Death due to MAS complications was evidenced in 4/11 JSLE and 5/10 sJIA. In addition, during 30 years of the Pediatric Allergy and Immunology Unit, 338 had diagnosis of PID. Of note, 20 HLH episodes were detected in 12 patients (3.6%): Chédiak-Higashi syndrome (n=6), Griscelli syndrome (n=2), HLH associated to EBV infection (n=2), common variable immunodeficiency associated with JSLE (n=1) and one patient was under investigation for a severe hereditary HLH. Clinical and laboratory findings were similar to MAS associated to RD. Treatment in HLH patients included corticosteroids, etoposide, anti-thymocitic globulin and/or intravenous immunoglobulin. Death was observed in all patients with Chédiak Higashi and Griscelli syndromes.
CONCLUSIONS: MAS/HLH is a rare and under recognized syndrome in RD and PID, with high mortality rates, mainly when associated to PID. This study reinforces the importance of diagnosis suspicion and the need for aggressive treatment for better prognosis of patients.
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Mucopolysaccharidosis (MPS)Type I and VI: evalutation of clinical criteria for early diagnosis of mild form

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BACKGROUND: Clinical presentation of attenuated mucopolysaccharidosis type I and VI is heterogeneous in time of onset and in clinical features. A delay in diagnosis is common due to the non specific presenting symptoms and signs. The progressive storage of GAGs in these mild cases leads also to a multisystemic irreversible damage. Many of the presenting features are musculoskeletal manifestations.
OBJECTIVES: The Aim of this pilot study is to contribute to an early diagnosis of the mild forms of MPS I and VI in a pediatric population.

METHODS: We reviewed all published clinical studies and recorded all the different symptoms and signs at presentation.
RESULTS: According to frequency of the clinical presenting features, we distinguished 6 major criteria: fixed flexion deformity fingers, carpal tunnel syndrome, skeletal abnormalities (spatulate ribs/clow fingers/beaked vertebrae), cervical cord compression, corneal clouding, hydrocephaly; and 12 minor criteria: joint stiffness, femoral head dysplasia, thickening of the aortic and/or mitral valves, recurrent ENT symptoms and/or recurrent respiratory infections, hearing difficulty, hepatomegaly, umbilical and/or inguinal hernias, delayed cognitive and/or psychomotor development, coarse facial features, obstructive sleep apnea syndrome, grouth retardation, cardiac dysrhythmias, for the diagnosis of mild form of MPS I and VI. Patients with at least one major criterion or two minor criteria are considered as potentially affected by MPS I or VI. In these cases the quick quantification of GAGs levels in urine samples is indicated. The presence of GAGs excess in urine requires confirmation of the diagnosis via demonstration of the lysosomal enzymatic activity defect in cultured fibroblasts, leukocytes, serum or plasma. The condition sine qua non for uGAGs value is the family history of lysosomal storage. To identify the clinical criteria for early diagnosis of MPS I and VI in pediatric population aged 0-16 yrs, we evaluated the sensitivity of the diagnostic criteria in childhood affected by MPS I and VI and the specificity of diagnostic criteria in childhood affected by rheumatic disease.
CONCLUSION: Our preliminary results validate the clinical criteria for early diagnosis of mild form of MPS I and VI.

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Immunization status of children with rheumatic diseases: can the pediatric rheumatologist help to improve?

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BACKGROUND: There are limited data on safety and immunogenicity of vaccines in children and adolescents with rheumatic diseases and frequently these patients do not receive adequate age-recommended vaccines.
OBJECTIVE: To assess the immunization status and possible causes of delayed immunization in children and adolescents with rheumatic diseases, evaluating the impact of physician specific intervention for missing vaccines.
METHODS: We performed a descriptive study based on interviews with patients/parents, review of charts and immunization cards of patients with rheumatic diseases receiving care in a Brazilian Pediatric Rheumatology Center from April/08 to March/09. For patients with delayed immunization, specific vaccine prescription was made by the pediatric rheumatologist and the new immunization status was recorded after 6 months.
RESULTS: Two hundred and seven patients (58% women; median age: 10.9y) were enrolled: 86 juvenile idiopathic arthritis (JIA); 30 systemic lupus erythematosus (SLE); 21 juvenile dermatomyositis (JDM); 10 scleroderma; 20 vasculitis; 10 antiphospholipid antibody syndrome (APS); 6 mixed connective tissue disease (MCTD); 24 with other rheumatic diseases. Prior to intervention, vaccines of the routine Brazilian childhood immunization schedule had been received among these children as follows: tuberculosis (BCGId): 100%; mumps, measles and rubella (MMR): 98.1%; poliomyelitis (Sabin): 95.2%; tetanus, pertussis and diphtheria: 92.8%; hepatitis B: 89.4%; and yellow fever: 85%. With respect to the routine schedule 90/207 (43.5%) enrolled patients had missed at least one dose of any vaccine. Delayed immunization occurred, respectively, in 43%, 70%, 42.9%, 60%, 40%, and 66.7% of the patients with JIA, SLE, JDM, scleroderma, vasculitis and MCTD. The proportions of non-routinely scheduled (special) vaccines received amongst the 207 children were: hepatitis A (9.6%); influenza (24%); meningitis (10.6%); pneumococcal (15%), and 52.8% for varicella (38/72 susceptible patients). In 20.8% of patients vaccination was contraindicated by the physician: 88.4% for yellow fever and 11.6% for MMR. Delayed immunization caused by family/patient fear or omission occurred in 28.9%. Specific prescription for the missing vaccines were given to 41/60 patients (68.3%) with incomplete immunization. The complete updated vaccination was verified after 6 months in 75.6% of these children.
CONCLUSION: The frequency of delayed immunization in pediatric patients with rheumatic diseases is high and worrying. Specific vaccine prescription should be given during the follow-up with the aim of reducing the mortality associated with preventable infections in these patients.
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P 178
Sacroiliitis in adolescents presenting with chronic low back pain

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BACKGROUND: Sacroiliitis can be the initial manifestation of juvenile spondyloarthropathy but identifying this condition can be challenging. Clinical evaluation of low back pain and the sacroiliac joint can be unreliable.
OBJECTIVE: This case series outlines the clinical features at presentation of adolescents with sacroiliitis and demonstrates the importance of MRI in diagnosis.
METHODS: Data was collected retrospectively on patients attending a tertiary centre for sacroiliac joint MRI. Case notes of those with positive findings were analysed further to establish clinical features at presentation including duration of symptoms, distribution of pain and family history. Information on subsequent management was also recorded.
RESULTS: Four patients (1 female, 3 male), age range 12 to 15 years, presenting between December 2008 and April 2010 were diagnosed with sacroiliitis based on MRI findings. Duration of symptoms ranged from 8 weeks to 6 years. Symptoms included low back pain with morning stiffness, pain at night and improvement in pain with movement. All had signs of sacroiliac tenderness. Two out of four patients had peripheral joint arthritis. In all patients there was a history of inflammatory arthritis in a parent. MRI findings included joint space widening, periarticular oedema and erosions. Signal enhancement post contrast with gadolinium was a significant finding. One patient with significant bilateral sacroiliitis on MRI had a normal scan reported 9 months previously. Subsequent management included physiotherapy in all patients; three out of four required methotrexate as second line treatment and one patient achieved symptom control following commencement of biologic therapy (etanercept).
CONCLUSIONS: Sacroiliitis is difficult to diagnose clinically and physical signs are unreliable. This case series suggests further investigation with sacroiliac joint MRI should be considered in adolescents with significant features of lower back pain with morning stiffness, especially with a positive family history of inflammatory arthritis. First line treatment is with physiotherapy but some patients will require methotrexate or etanercept for symptom control.
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P 179
Juvenile Systemic Lupus Erythematosus and Castleman's disease: a case report

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INTRODUCTION: Castleman\'s disease (CD, angiofollicular lymph node hyperplasia) is a lymphoproliferative disorder of uncertain etiology first described in 1956 by Benjamin Castleman. CD is rare in pediatric population. Castleman\'s disease has two clinical forms: unicentric and multicentric. Multicentric CD has been associated with autoimmune diseases. We present a child with systemic lupus erythematosus and Castleman\'s disease.
Case report.11 years old Omani boy presented with intermittent low grade fever, anorexia, weight loss, skin rash, arthralgia and generalized lymphadenopathy. Clinical examination revealed pallor, generalized lymphadenopathy (cervical, axilla, inguinal) measure1.5-2 cm firm, non tender. No organomegally. Cardiopulmonary examination was normal. Laboratory tests showed: high erythrocyte sediments rate 35mm/hr, and C-reactive protein 18mg/L. High immunoglobulin G= 19.7g/L (6.5-16 g/L). Antinuclear antibody and anti-double stranded DNA was initially negative. Test for tuberculosis, brucellosis, Ebstain barr virus, human immunode-

ficiency virus and human herpesvirus-8 were all negative. Computer tomographic scan of neck, chest, abdomen and pelvis showed extensive lymphadenopathy largest in axilla and mediastinum measures 22x15 cm. Axillary lymph node biopsy showed follicular hyperplasia with prominent vascular proliferation mostly in the interfollicular regions. Vascular channels were seen entering the centre of the follicles. The interfollicular region showed lymphocytes, plasmacytoid monocytes and occasional plasma cells. No granuloma or necrosis was seen **(figure 1)**. Immunohistochemistry showed positive CD3, CD20, CD 21 and CD3. The diagnosis of Castelman\'s disease, hyaline vascular type was made. Few months later he developed autoimmune hemolytic anemia, and cytopenia. Laboratory tests showed: positive antinuclear antibody (1:1000) and anti-double stranded DNA antibody. Low complements, C3 = 448mg/dl (790-1520 mg/dl) and C4 =73 mg/dl (160-380 mg/dl). Urine analysis was normal. Our patient fulfilled 4 out of 11 diagnostic criteria of systemic lupus erythematosus. He was treated with rituximab 375mg/m2 with a good clinical and radiological response. He is doing well now with low dose of prednisolone 5mg/day and hydroxychloroquine 200mg/day.

CONCLUSION: Castleman\'s disease of hyaline vascular type has overlapping signs and symptoms with SLE. Systemic lupus erythematosus patient may have histological feature of castleman\'s disease.

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Pediatric Systemic Lupus Erythematosus: clinical features and system involvement in two different age groups

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Pediatric Systemic Lupus Erithematosus: Clinical features and System involvement in two different age groups. Hospital Luis Calvo Mackenna y Clínica Alemana Santiago, Santiago, Chile.

INTRODUCTION: Pediatric Systemic Lupus Erithematosus (SLEp) is an autoimmune disease with variable clinical features and characteristic serological abnormalities. It affects patients up to 16 years of age.

OBJECTIVES: To analyze the main clinical features, autoimmune serology and organ involvement of pediatric lupus in pre pubertal and post pubertal patients. METHODS The files of 41 patients with SLEp between the years 2000 and 2009 were analyzed retrospectively. Patients were divided into two groups based on age at disease onset: Group A, children less than 11 years old (pre-pubertal) and Group B children between 11 and 16 years old (post-pubertal). Clinical presentation, laboratory features and organ involvement were compared between each group.

RESULTS: Twelve patients had SLEp onset before their 11th birthday and 29 were diagnosed between 11 and 16 years of age. In Group A, the age of onset ranged from 7 to 10 years 11 months (mean 8.7, median 9) and in Group B from 11 to 16 years (mean 12.8, median 12). There were 10 females (83%) and 2 males (17%) in Group A and 24 females (83%) and 5 males (17%) males in Group B. There were differences in the frequency of the various clinical manifestations, laboratory features and organ involvement between the two groups. Nevertheless, none of them were statistically significant. The most common manifestations at disease onset were mucocutaneous, musculoesqueletal and fever. There was a higher prevalence of mucocutaneous involvement in Group B (62% vs 50%), but there was no difference in the other parametes. There was a higher frequency of renal and hematological abnormalities in Group B; with no difference in the frequency of neurological compromise. Renal biopsy was performed in 8 patients from Group A and 27 from Group B. More severe renal involvement, grouped in Class IV & V, was present in 37% of Group A patients versus 47% of Group B. An elevated ESR at disease onset was more frequent in Group B. Complement fractions C3 and C4 were reduced in more than 50% of patients in both Groups. Leukopenia and thrombocytopenia were only observed in the post pubertal group and there was no difference in the frequency of anemia among the groups. All of our patients had positive antinuclear antibodies. Although not statistically significant, there was a higher frequency of Anti ds DNA and anti SM antibodies in Group B. Antiphospholipid antibodies were only present in Group B.

CONCLUSIONS: We found no differences in gender distribution, clinical manifestations or laboratory features among the two groups. Group B, had a higher frequency of renal and histological compromise. Although no significant, this findings showed a trend towards more severe renal involvement in post pubertal patients.

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Recurrent cranial nerve VI palsy as a rare initial presentation of systemic lupus erythematosus

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Systemic lupus erythematosus (SLE), a chronic multisystem autoimmune disease of unknown etiology, most commonly affects the skin and the musculoskeletal system. Neurologic manifestations are well recognized with a variety of focal and diffuse neuropsychiatric symptoms preceding or following the diagnosis of SLE. However, isolated cranial neuropathy is rarely reported. A 17-year-old Caucasian girl was referred to us with recurrent facial paralysis six times since 11 year old. She suffered intermittent right knee pain and morning stiffness over 7 years. Also, she had bilateral hand swelling and Raynaud's phenomenon. She had no dry mouth and dry eyes. The family history was noncontributory. The physical examination showed livedo reticularis on the lower and upper extremities. She had effusion on left knee, arthralgia on right shoulder and hip. Her capilloroscopic examination was abnormal (increased tortuosity). Laboratory investigations revealed a white blood cell of 5,2X109/L with normal differential, absolute lymphocyte count 2000/mm3, hemoglobin 11.7 g/dl, hematocrit 35%, platelets 79X109/L, and normal C-reactive protein, but erythrocyte sedimentation rate was 60 mm/hour. Urine analyses were normal. 24-hour urine protein collections were 1,2mg/m2/hour. Serological tests were all negative. Her thyroid function tests were normal. The antinuclear antibody (ANA) was positive at a titer of 1:1280 showing a speckled pattern and anti- extractable nuclear antigen (ENA) antibodies were positive for SSA/anti-Ro and anti-double stranded DNA. Her anti-Sm, rheumatoid factor, antineutrophil cytoplasmic antigen (ANCA) and all anti-phospholipid antibodies were negative. The diagnosis of definite SLE was made based on the American College of Rheumatology (ACR) SLE classification criteria. The patient was started on hydroxychloroquine 200 mg orally bid and aspirin 100 mg/day with her symptoms were no recurrence. This case highlights a rare presentation of SLE.

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Acute hemichorea as presenting manifestation of systemic lupus erythematosus (SLE)

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BACKGROUND: Chorea is a rare manifestation of SLE, a chronic, autoimmune, inflammatory disease that can affect every organ system of the body. Four of the eleven specific criteria (malar rash, discoid rash, photosensitivity, oral ulcers, arthritis, sierositis, kidney involvement, neurological manifestations, positive ANA, hematologic and immunologic disorders) are necessary for the diagnosis.

Case report. A 12 years old girl was admitted to our hospital because of a one month history of arthralgia affecting the small joints, associated to choreiform movements involving right extremities. Her past medical history was not relevant. On admission to hospital she was mentally slow, markedly irritable. Examination showed her cardiorespiratory and gastrointestinal systems to be normal. Neurological examination showed unilateral choreiform movements of the extremities but no other neurological abnormalities. Sydenham chorea was suspected. Laboratory findings included lymphocytopenia, increased inflammatory parameters, low concentration of complement, hypergammaglobulinemia. Her antinuclear antibody titre, test for antidsDNA and anticardiolipin antibodies were positive. Also antiphospholipid antibodies were present. Her electroencephalogram showed only non-specific slowing and brain MRI scan was normal. The electrocardiogram, chest x ray, and cardiac evaluations were all normal. Brain SPECT with 99mTc-labeled ECD has been used to assess regional cerebral blood flow, which always has a strong correlation with changes in glucose metabolism: it showed increased perfusion of left striatum.

She was successfully treated with intravenous pulse methylprednisolone therapy, followed by oral steroids

CONCLUSIONS: Our patient fulfilled the revised criteria of the American Rheumatism Association for SLE, in whom chorea was the presenting feature of the disease. In conclusion, this case confirms a direct link between antiphospholipid antibodies and the development of chorea and the useful treatment with steroids. Based on our experience, SPECT scanning can play an increasingly important role in evaluating neurological conditions in patients with SLE.

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Cross cultural validation of a novel quality of life scale for pediatric lupus – update on international recruitment, translation, adaptation and validation

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BACKGROUND: Health-related quality of life (HRQOL) is an important clinical outcome in pediatric systemic lupus erythematosus (SLE). We developed \"Simple Measure of the Impact of Lupus Erythematosus in Youngsters\" (SMILEY©), a novel, brief, valid and reliable health-related quality of life (HRQOL) tool for children with systemic lupus erythematosus (SLE). SMILEY© has parallel child/parent reports with 5 faces-scale responses and percentage scores. Higher scores mean better HRQOL. The 4 domains of SMILEY© are: Effect on Self, Limitations, Burden of SLE and Social. SMILEY© is valid in US-English. We are currently conducting cross-cultural validation of SMILEY worldwide.
PURPOSE: Objective of our study is to conduct cross-cultural adaptation and validation of SMILEY© worldwide. In this abstract we will report updates on international recruitment, translation, adaptation and validation of SMILEY©.
METHODS: Centers worldwide are invited for participation in this study. Cross-cultural adaptation for each language comprises translation, back-translation and review by expert. For validation, children 2-18 years with SLE and parents will complete the appropriate SMILEY© translation, Pediatric Quality of Life Inventory Generic/Rheumatology scales, and Childhood Health Assessment Questionnaire. We will obtain data on demographics, comorbidity, medications, and SLE–related parameters. Subjects will complete another copy of SMILEY© and return in 10 days to assess test-retest reliability. At 3-month intervals, subjects will complete SMILEY© and physicians will assess their disease activity. We are determining validity, reliability, and responsiveness to change in disease activity.
RESULTS: 54 centers worldwide are participating (37 have ethics committee approval; 33 are enrolling) and are part of the International SMILEY collaborative group (participants are listed under **Table 1**). Translation and adaptation of the following 21 SMILEY© versions are complete (table1): Arabic, Chinese (Mandarin), Danish, Dutch, English for UK, French, German, German for Austria, Greek, Hebrew, Hindi, Italian, Japanese, Portuguese for Brazil, Serbian, Slovene, Spanish for Argentina, Spanish for Mexico, Spanish for Spain, Spanish for US and Puerto Rico, and Turkish. Currently, we are translating and adapting SMILEY© into Czech, English for Australia, German for Switzerland,Hungarian, Malayali, Romanian, Spanish for Costa Rica, Spanish for Colombia, and Spanish for Venezuela. We intend to translate SMILEY© into English for Ireland and other languages. We are in the process of validating the following translations of SMILEY©: Arabic, Chinese (Mandarin), Danish, Dutch, English for UK, French, Hindi, Italian, Japanese, Portuguese for Brazil, Slovene, Spanish for Argentina, Spanish for Mexico, Spanish for Spain, Spanish for US and Puerto Rico, and Turkish (Table 1).
Preliminary data analysis from Spanish (Spain-presented EULAR 2009), Portuguese (Brazil) and Italian versions (unpublished) showed SMILEY© to be valid. A preliminary analysis of across five countries (Argentina, Brazil, Italy, Netherlands and Spain) showed that SMILEY© performed uniformly.
CONCLUSION: Cross-cultural validation of SMILEY© will enable uniform assessment of HRQOL, an important outcome to consider while evaluating treatment success. Currently this international project is ongoing and we are actively recruiting other centers.

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Rituximab Improving Arthritis in a patient with Juvenile Systemic Lupus Erythematous

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BACKGROUND: Arthritis is one of juvenile systemic lupus eritematous (jSLE) manifestations. It is usually of short duration, but sometimes persistent and rarely results in permanent deformity.
Rituximab is used for lupus nephritis, and showed an excellent response in a patient with a persistent deforming arthritis, with subcutaneous nodules, refractory to the conventional therapy.
OBJECTIVE: To report a case of persistent and refractory arthritis in a patient with jLES, that improved and maintained remission after 35 months of the use of rituximab.
METHOD: Chart review and case report of a jLES patient with severe deforming arthritis, that failed to innumerous therapeutic options (ciclofosfamide, micofenolate mofetil, methotrexate, azathioprine), with difficult corticosteroid tapering that improved in the first month after 2 doses of rituximab, sustaining remission for over 35 months.
CONCLUSION: Rituximab may be effective for persistent arthritis in jLES.
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Mycophenolate mofetil use in refractory Juvenile Systemic Lupus Erythematosus

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BACKGROUND: The optimal immunosuppressive treatment in patients with systemic lupus erythematosus (SLE) remains controversial. Mycophenolate mofetil (MMF) has proved to be an efficacious and safe therapy in adult lupus nephritis. Recently, this drug has been suggested as a possible new alternative treatment for juvenile-SLE, especially in cases of lupus nephritis refractory to treatment with corticosteroids, cyclophosphamide azathioprine, methotrexate and/or cyclosporine. In this review we describe our experience with six children diagnosed with SLE and treated with MMF.
OBJECTIVES: To report the clinical experience of a single center in the use of Mycophenolate mofetil (MMF) in refractory juvenile systemic lupus erythematosus (SLE).
METHODS: Chart review of refractory juvenile SLE.treated with MMF in the pediatric rheumatology outpatient clinic of Santa Maria Hospital.
RESULTS: Six children with juvenile SLE (five girls and one boy) with a mean age of 13.8 years (range 10-16) were treated with MMF at a dose of 0.5 to 2.5g/dl daily for a period of 6 to 29 months (mean 17.5±11.6). Patients were followed for 5.2±2.2 years. The average disease duration was of 3.5±2.1 years at the beginning of the MMF treatment. All patients had kidney involvement; three of them had concomitant severe central nervous system involvement and two antiphospholipid syndrome. Five patients were biopsy-proven severe lupus nephritis (three with class IV and two with class V). One patient had thrombotic thrombocytopenic purpura associated to SLE. All patients were previously treated with high dose steroids, four of them started ciclophosphamide (CYC) pulses and one received rituximab (RTX). Five patients began MMF as induction therapy in renal involvement and only one as maintenance therapy. MMF was effective in reducing disease activity and as a steroid-sparing agent in half of the patients. The responders experienced a marked reduction in SLEDAI score, in anti-dsDNA antibody titers and in serum complements levels. One patient stopped MMF therapy due to gastrointestinal intolerance and another one reduced the dose due to leucopenia.
CONCLUSION: MMF appeared to be effective and safe in controlling disease activity in some refractory juvenile SLE. It also showed a significant steroid sparing effect.
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Simple Measure of Impact of Lupus Erythematosus in Youngsters (SMILEY©): Methodology and preliminary validation in Portuguese

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BACKGROUND: Simple Measure of the Impact of Lupus Erythematosus in Youngsters (SMILEY©) is a novel health-related quality of life (HRQOL) assessment tool for pediatric systemic lupus erythematosus (SLE), valid in US-English.

The 26-item SMILEY© has parallel child and parent reports with 5 faces-response-scale for better comprehension. Scores for 24 items are reported as percentages. Higher scores indicate better HRQOL. The first two items on global assessments of quality of life (QOL) and lupus status are not included in the final score. We are reporting preliminary data on cross-cultural validation and reliability of SMILEY© in Portuguese (Brazil).
PURPOSE: To perform adaptation and cross-cultural validation of the SMILEY© in Portuguese.
METHODS: SMILEY© was translated (forward and back) to Portuguese, reviewed and adapted by Brazilian pediatric rheumatologists. In this multi-center cross-sectional study, children (4-18 years) and parents completed child/parent reports of the Portuguese-SMILEY© and Portuguese Pediatric Quality of Life Inventory (PedsQL™) Generic and Rheumatology scales. Parents also completed the Childhood Health Assessment Questionnaire (CHAQ). Physicians completed the SLE disease activity index (SLEDAI), Physician's Global Assessment of disease activity (PGA) and Systemic Lupus Erythematosus International Collaborating Clinics ACR Damage Index (SDI). Correlations between the child/parent SMILEY© with corresponding reports of the above scales and the first two global ratings were determined by the Spearman Rank (r) test. Internal consistency was determined by Crohnbach's alpha. Subjects completed SMILEY© ten days later and returned the forms to determine test-retest reliability. Spearman Rank (r) and intraclass correlations (ICC) were calculated between the initial and the retest results.
RESULTS: Forty-five children (36 girls) with SLE had mean age 13±3 years (n=45); SLE duration 40±31 months (1-116); median SLEDAI 2(0-36); median PGA 0(0-3, n=44) and median SDI 0(0-4). The mean score for child SMILEY© was 69±16; parent SMILEY© was 65±17. Subjects found SMILEY© relevant and easy to understand and completed SMILEY© in 10-15 minutes. Moderate to strong correlations were seen between SMILEY© child/parent reports with other scales **(Table 1)**. Cronbach's alpha was 0.9 for both child/parent SMILEY© reports. Spearman correlation between child and parent total SMILEY© score was 0.3 (n=39). Spearman correlations and ICC between initial and retest scores for child and parents SMILEY© reports were ≥ 0.7 ($p<0.0001$).
CONCLUSION: On preliminary evaluation, Portuguese SMILEY© for Brazil is a brief, easily understood, valid and reliable pediatric SLE-specific HRQOL scale. We are expanding our sample and collecting follow-up data to determine responsiveness of SMILEY© to change in disease activity.

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Spondyloenchondrodysplasia with Systemic Lupus Erythematosus: a report of three cases

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Spondyloenchondrodysplasia (SPENCD) is defined by the presence of radiolucent spondylar and metaphyseal lesions that represent persistance of islands of chondroid tissue within bone. Immune dysregulation with autoimmunity could be a part of this disease in some of the patients. We herein report 3 SPENCD patients diagnosed as systemic lupus erythematosus (SLE).
Two siblings were admitted to our hospital due to short stature. They were diagnosed as SPENCD with clinical and radiological findings. Older sister of 16 years of age was referred to our clinic due to recurrent arthritis of PIP joints.Laboratory findings indicated leukopenia, hypocomplementemia and positive ANA, anti-dsDNA antibody. She had proteinuria of 615mg/day. Kidney biopsy was performed and revealed class V membranous lupus nephritis.
Her brother, at age 5 also, admitted to our clinic due to arthritis of his knee. He had microscopic hematuria. His kidney biopsy revealed class IV-S diffuse proliferative nephritis.
Third patient was born to consanguineous parents. She was followed up as hereditary spastic paraplegia in another center and diagnosed as SPENCD at age of 15. She was referred to our clinic due to erythromelalgia. She had leukopenia, hypocomplementemia and ANA, anti-DNA positivity. Kidney biopsy was performed due to 770 mg/day proteinuria and revealed class IV-S diffuse proliferative lupus nephritis.
Arthralgia and arthritis should not be overlooked in SPENCD patients. These patients deserve a meticulous investigations in regards to SLE and lupus nephritis.

P 188
Disease patterns in Vietnamese children with SLE

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BACKGROUND: Incidence and disease pattern of juvenile SLE (jSLE) is described to differ among ethnic groups.
OBJECTIVE: Our objectives were to describe disease patterns in a consecutive referral based cohort of 45 native Vietnamese jSLE children and to do a 6-month renal follow up on severe nephritis cases.
MATERIAL: 45 children (f/m = 4/1) referred to the Ho Chi Minh City Children's Hospital No.1 over a 12-month period in 2009. In 29 Lupus Nephritis (LN) patients two renal biopsies were performed, the first at onset and the second after initial induction therapy (n = 15). CNS involvement or LN ISN (International Society of Nephrology) class IV or worse were treated with i.v. methylprednisolone and low dose i.v. cyclophosphamide (max. 0.5 g/dose) followed by maintenance therapy with azathioprine and oral prednisolone. All other cases or cases with mild LN were treated with systemic steroids only.
RESULTS: Mean age at diagnosis was 12.8 y (SD=2.5). 37 (82%) fulfilled criteria for LN, of whom 29 had a renal biopsy, 20 ISN Class IV, 8 ISN Class III, 1 complex presentation of ISN Class III/ V. At diagnosis high SLEDAI and ECLAM scores were recorded, mean (SD)=23.8 (11.6) and 6 (2.3) receptively. Decreased Haemoglobin (g/dL) mean (SD)=8.5 (2.1), positive Coombs test in 30 of 36 tested (83%), increased plasma Creatinine (unit) mean (SD)=0.98 (1.2) and ESR mean (SD)=83.6 (37.4) were the most outstanding biochemical findings. LN was more prevalent in the children <12 y of age at diagnosis (Fisher's Exact Test p=0.06 (ns)). Patient age at diagnosis was positively correlated to the SLEDAI (p=0.034) and ECLAM (p=0.022). At 6 month follow-up 15 patients were in complete remission, 5 were in partial remission, 6 had stable disease, 3 had relapsed, 3 had evolving disease, 2 had ongoing resistant disease and 4 had died. Seven patients were lost to follow-up. The second renal biopsy showed improved ISN class in 13 of 15; in 2 cases it remained unchanged.
CONCLUSION: The study was suggestive of distinct SLE patterns in Vietnamese children characterized by a strikingly high prevalence of Coombs positive anaemia, high prevalence of LN and very high SLEDAI scores at the time of diagnosis.

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Predictors of outcome in Juvenile Polyarteritis Nodosa: a multicenter study

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BACKGROUND: Polyarteritis nodosa (PAN) is a necrotizing vasculitis, seldom reported in childhood and adolescence.The disease is more frequent in Asian populations but has been reported in all ethnical groups.
AIMS: To describe the clinical features, at onset and during the disease course, and look for possible predictive factors related with outcome or persistent damage in a cohort of Italian patients with paediatric onset PAN.
METHOD: A retrospective data collection of demographic, clinical and therapeutic characteristics of patients with definite diagnosis of PAN from 8 Paediatric Rheumatology Units and one Transition Unit, was performed. Correlation between symptoms and internal organs involvement at onset and during the disease course and final outcome or persistent damage was made.
RESULTS: Data from 50 patients (21 M, 29 F), all Caucasians, were collected. All pts fulfilled the EULAR/PRES criteria for the diagnosis of PAN. The mean age at onset was 7.9 yrs (range 2-16 yrs) and the mean follow up 6.2 yrs (range 0.3-16.4 yrs). At onset, skin involvement and systemic symptoms were the most common findings being present in 36/50 pts (72%); nodules were the main cutaneous manifestation (40%), fever was the most frequent systemic symptom (66%). Other early clinical manifestations were musculo-skeletal symptoms (54%), renal (12%), CNS involvement (10%), peripheral nervous system (6%), cardiac involvement (6%), and gastrointestinal manifestations (4%). All patients were treated with corticosteroids either oral or IV, 16 pts (32%) received azathioprine, 20 pts cyclophosphamide (15 pts oral and 5 IV), 9 (18%) thalidomide, 7 (14%) IVIG, 5 (10%) methotrexate, 4 (8%) mycophenolate mofetil and 2 (4%) biological agents (etanercept and infliximab). At the last follow up visit, 25 pts (50%) were in remission off therapy, 17 (34%) were under control on immunosuppressive medication and 6 (12%) had

persistent relapsing course. Two patients deceased because of ischemic cerebral infarction. At onset, the presence of renal involvement and fatigue significantly correlated with a bad outcome. CNS involvement, as seizures and paralysis, and nephrogenic hypertension, during the disease course, significantly correlated with the development of persistent damage.
CONCLUSION: The present study shows that in Caucasian children, PAN is quite severe despite the use of immunosuppressive treatments. Renal and CNS involvement seem to be the main factors affecting the final outcome.
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P 190
Risk of subclinical atherosclerosis and Kawasaki Disease (KD): e-tracking study in a Sicilian population

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Patients with Kawasaki Disease (KD) may have an increased risk for early atherosclerosis. Arterial stiffness (AS) has recently recognized as a predictor of atherosclerosis. AIM of this study was to evaluate AS in a populations of KD patients (pts). The study was performed by means of E-tracking, a system measuring changes in arterial diameter synchronized with the ECG signal and permitting evaluation of pulse wave propagation velocity in a point of the vascular system.
METHODS: 31 children who had suffered from KD and 20-age- and sex-matched healthy controls were enrolled. In each subject, E-tracking was performed in both common carortid arteries.The following parameters were calculated: 1) Stiffness index, 2) Pulse wave velocity, 3) Elastic modulus, and arterial compliance. In addition, intima-media thickness (IMT) was measured.
RESULTS: Kawasaki patients' age at examination was 5 years; the mean time interval between the disease onset and the testing time was 3.5 years. Coronary involvement was recognized in 6 pts. All KD pts show a significant AS compromise as expressed by increase in stiffness index, pulse wave velocity and elastic modulus, as well as by arterial compliance decrease. IMT was normal. Arterial stiffness was related to severity of Kawasaki disease (duration of fever, second infusion of IVIG).
CONCLUSION: Pts with KD show a clear arterial stiffening. This report is the first one describing changes in AS revealed by E-tracking in pts with KD; we suggest that E-tracking study could be more sensitive than IMT in revealing arterial damage in KD

P 191
Childhood polyarteritis nodosa (cPAN) in a 7-month -d girl

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cPAN is a rare vasculitis, characterized by necrotizing inflammation of medium/small-sized arteries. Average age of presentation is 8.81±3.55 years.
A previously healthy 7 month-old girl presented with mild acute gastroenteritis-like symptoms. Three days after she was admitted for suspected sepsis, due to fever, dehydration and lethargy. Four days later, left III-nerve palsy and left hemiparesis emerged.
Brain-MRI showed areas of signal hyperintensity in the right pons and left mesencephalon, suggestive of abscesses.
Her condition worsened progressively, maintaining intermittent fever, despite the several antimicrobials instituted. Arterial hypertension emerged.
Blood, urine, stool and CSF studies to identify bacteria, fungae, viruses and parasites where negative. Urinalysis, renal function and immunological studies were normal. Echocardiogram showed no lesions.
After three weeks, she underwent emergent exploratory laparotomy and required segmental enterectomy due to ileal stenosis. Pathology examination revealed necrotizing inflammation of medium and small-sized arteries.
cPAN EULAR/PRINTO/PRES classification criteria where met, and IV methylprednisolone pulses followed by maintenance prednisolone were started. Rapid improvement of general condition with regression of fever and acute inflammatory markers occurred.
Follow-up brain angioMRI showed residual lesions and no vascular changes.
The patient was discharged with near-resolution of neurological deficits.
Two months after, the disease relapsed with left hemiparesis and abnormal eye movements, but no imaging changes. Monthly cyclophsphamide was started for 6 months, followed by azathioprine.
She remains stable more than one year after initial presentation, with mild neurological deficits.
The authors intend to review cPAN diagnostic criteria as well as to discuss the challenges in the management of these patients, especially in an age group where this entity is exceedingly rare.

P 192
Nailfold capillary changes in children with Henoch-Schönlein purpura

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BACKGROUND: Architecture and morphology of the microvascular network can be observed in vivo by nailfold videocapillaroscopy (NVC) and very little capillaroscopic data can be collected with regard to children with Henoch-Schönlein purpura (HSp).
OBJECTIVES: To investigate by NVC the capillary changes in children with HSp at the disease onset and after a 6-month-period.
PATIENTS AND METHODS: Thirty-one patients (17 males, 14 females; mean age: 7,5 +/- 3,4 years; age range: 3-16 years; all with palpable purpuric lesions, 21 with arthralgia, 14 with abdominal and 6 with renal involvement) underwent NVC evaluation through a videomicroscope at the disease onset and after 6 months. Twenty sex/age-matched controls were also examined. All NVC variables of architecture (skin transparency, density, length, focal absence of capillaries, neoangiogenesis, haemorrhages) and morphology (tortuosity, bizarre shape, enlargement and edema of capillaries) were statistically examined in combination with laboratory/clinical data and outcome.
RESULTS: Architectural and morphological changes recorded at the disease onset were statistically significant in comparison with controls ($p< 0,01$). At 6 months edema was still observed in all patients. There was no significant correlation between NVC abnormalities, laboratory/clinical data and outcome.
CONCLUSIONS: NVC can be a simple non-invasive technique for the in vivo assessment of the capillaries in the acute phase of HSp. The persistence of edema could suggest an incomplete disease resolution at the microvascular level.

P 193
ANCA induced neutrophil microparticles: effect on endothelial cell activation and angiogenesis

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BACKGROUND: Antineutrophil cytoplasmic antibodies (ANCA) have been implicated in the pathogenesis of ANCA associated vasculitis (AAV), but the molecular mechanisms by which these autoantibodies contribute to vasculitis are still being explored. Neutrophil microparticles (NMPs) are increased in the plasma of patients with AAV(1)and could contribute to vascular injury but have yet to be studied in this context.
OBJECTIVE: To examine the hypothesis that ANCA stimulation of neutrophils results in neutrophil microparticle (NMP) release in vitro. The functional effects of NMPs on endothelial cells were also studied.
METHODS: Neutrophils were primed with 2ng/ml tumour necrosis factor (TNF-alpha) for 15 minutes and then treated with 200µg/ml ANCA/normal IgG, 12.5µg/ml chimeric IgG1 or IgG3 PR3-ANCA/control chimeric antibody for 60 minutes. NMPs were recovered from supernatants by ultracentrifugation and identified using flow cytometry as AnnexinV+ particles co-expressing MPO, PR3, CD18 or CD11b. NMP were then incubated with HUVEC to examine the surface expression of ICAM-1 using flow cytometry. Lastly, a matrigel assay was employed to examine the effect of NMP on HUVEC angiogenesis.
RESULTS: Neutrophil TNF-alpha priming alone or with control IgG had a minimal effect on NMP release. In contrast, ANCA stimulation of primed neutrophils resulted in release of AnV+ MPO+ NMPs ($p<0.01$), and AnV+ CD11b+ NMPs ($p<0.05$). These NMPs caused upregulation of ICAM-1 on HUVEC ($p=0.014$), and inhibited HUVEC angiogenesis in matrigel ($p=0.03$). Chimeric IgG1 or IgG3 PR3-ANCA had a similar effect on NMP release as polyclonal human ANCA, and these NMPs again exhibited similar ability to activate HUVEC and inhibit of angiogenesis in matrigel. There was no difference in the effect of either the chimeric IgG1 and IgG3 PR3-ANCA in any of these experiments.
CONCLUSION: We show for the first time that NMPs are released from primed neutrophils upon stimulation with ANCA, and exert potent pleiotropic effects on

HUVEC. Thus NMPs could play an important primary role in the pathogenesis of vascular injury in AAV and we are currently undertaking further studies to investigate the mechanism of NMP induced endothelial dysfunction.
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P 194
Evidence for persistent endothelial injury in years after Kawasaki Disease

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BACKGROUND: Male Japanese patients who had Kawasaki Disease (KD) with coronary artery abnormalities (CAA) are at risk of premature atherosclerosis. The risks following KD for those without CAA remain uncertain.
AIMS: To test the hypothesis that endothelial injury persists for years after KD irrespective of conventional cardiovascular risk factors (CRF).
METHODS: Patients with KD >12 months previously were studied. Healthy siblings of KD cases were controls. Subjects underwent echocardiography, BP measurement, and blood tests for conventional and non-conventional CRF including lipids, hs-CRP, circulating endothelial cells (CECs), hs-CRP, serum amyloid A, plasma TNF-α, IL1β, 6, 8, 10, VEGF, MCP-1, soluble adhesion molecules (sAM), pulse wave velocity (PWV), and carotid intima medial thickness (cIMT).
RESULTS: 30 KD patients (17M), age 13.45 yrs (4.9-23.1 yrs) with age at KD onset 1.23 yrs (0.2-11.3 yrs), were studied 9.45 yrs (1.9-22 yrs) after KD. 12/30 had CAA at first presentation. 2 patients had persistent coronary abnormalities on echocardiography at the time of study: 1 patient with giant CAA, and one patient with regressed CAA but luminal irregularity. There were 19 controls (9M) aged 16.0 yrs (4.9-22.8 yrs). Overall CECs were higher in the KD patients irrespective of CAA status (median 88 /ml) versus controls (8/ml), $p<0.0001$. Those with CAA at presentation had higher CECs than those without ($p=0.05$), but those without CAA also had higher CECs than controls ($p=0.003$). MCP-1 was higher in KD with CAA than controls ($p=0.04$). There were no differences in lipids, BP, carotid-femoral PWV, cIMT, hs-CRP, SAA, sAM, or any other cytokine.
CONCLUSION: Elevated CECs provide evidence for persistent endothelial injury years after KD, not explained by conventional CRF, and occurring prior to structural arterial injury. This was true for those with CAA, but also for those with no CAA at presentation. These data
provide a rationale for targeted primary prevention of premature cardiovascular morbidity for all patients following KD.

P 195
The addition of glucocorticoids to initial IVIG therapy in children with Kawasaki Disease

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BACKGROUND: Treatment of Kawasaki disease with intravenous immunoglobulin and aspirin reduces the risk of coronary artery abnormality. Although glucocorticoids have been reported to be beneficial in patients with KD who fail to respond to IVIG, it remains unknown whether they have a role in initial therapy. Coronary artery abnormalities not improve in some children and some patients have persistant fever despite IVIG therapy. In the other hands, several studies including a randomised controlled trial, have shown that the addition of glucocorticoids to initial IVIG therapy was beneficial in patients with KD. The aim of this study was to determine whether the addition of corticosteroids to intravenous immunoglobulin (IVIG) might improve outcomes in Kawasaki disease (KD).
METHODS: A total of 54 patients who full filed criteria for Kawasaki disease were randomly assigned to either an IVIG (Control group n=36) or an IVIG pulse intravenous methylprednisolone (case group n=18).
RESULTS: The duration of fever and duration of hospitalization after treatment in the case group were shorter than in the control group ($p=0.008$, $p=0.018$). Erythrocyte sedimentation rate and C-reactive protein decreased more rapidly in the case group than in the control group ($p=0.038$, $p=0.046$). The two groups had similar rate of retreatment with IVIG and improve coronary artery abnormality ($p=0.77$, $p=0.2$).
Conclusion:The comparison of case and control groups demonstrated that addition of corticosteroid therapy dose not significantly improve coronary artery abnormality but improve clinical course in children with Kawasaki disease.

P 196
Juvenile Amyopathic Dermatomyositis in a 5-year-old girl

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BACKGROUND: Amyopathic Dermatomyositis is defined as the hallmark cutaneous manifestation of the Dermatomyositis confirmed by a biopsy and with no evidence of muscular inflammation for at least 6 months. In adults it is a rare condition and malignancies should be always considered. In children it is more unusual and the prognosis reported is better, specially after 2 years since the skin changes first appeared. The low risk of long-term complications and calcifications can allow the avoidance of systemic treatments.
OBJECTIVES: Reinforce that pediatric patients with Amyopathic Dermatomyositis have excellent prognosis in absence of treatment.
METHODS: Case report of a patient diagnosed and followed in a multidisciplinary unit.
RESULTS: A 5 years old girl presented with asymptomatic papules on the dorsal aspects of the distal interphalangeal and metacarpophalangeal joints of the hands and in the extensor surfaces of knees and elbows. A rush on both upper eyelids was also noticed. The girl was healthy and active, she denied fever, myalgias, althralgias, weakness, neurological, digestive or respiratory problems. Except for the skin, the physical exploration was completely normal, Childhood Myositis Assessment Scale (CMAS) 50/52. Nailfold capillaroscopy showed decreased density, megacapillaries and tortuosity. No inflammation marker were increased and muscular enzymes were in normal limits. Negative autoantibodies. Thigh MRI with no sign of muscular implication. Skin biopsy was consistent with Dermatomyositis. After more than 2 years of follow up there has been no clinical changes, exploration and laboratory has been always unaltered, and no calcifications observed. She has been unresponsive to topical treatments and we have never used systemic medication.
CONCLUSIONS: Gottron's papules and heliotrope rash are the classical manifestations of Dermatomyositis. Normal exploration, muscular enzymes, inflammatory markers and MRI could exclude myositis without more aggressive techniques (electromyography or muscular biopsy) in pediatric patients. Side effects of the medication used in the treatment of Juvenile Dermatomyositis can be more harmful than the disease itself. Follow-up will confirm such a good prognosis.
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P 197
"Persistent skin lesions, muscle weakness and faltering growth: Striking features of an uncommon disease"

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A 9 year-old boy presented with an eighteen month history of faltering growth, recurrent respiratory tract infections, persistent "apthous" ulcer on his tongue and "warts" on his fingertips and soles.
He is the second offspring of a healthy unrelated Sri-Lankan couple and past medical history was unremarkable. Baseline immunology and infectious disease screen was negative. On close questioning he had reduced energy levels, poor appetite and dysphagia on solids. His growth parameters were below the 5th centile, he had sustained central muscle weakness, a heliotrope rash on his eyelids, and extruding calcinosis on his palms and soles, nail beds and tongue.
He was clinically diagnosed with juvenile dermatomyositis and underwent investigations to define the disease severity. Muscle biopsy confirmed the diagnosis.
The patient was treated with steroids and methotrexate and surgical excision of the calcinosis on his tongue.
Discussion:
JDM is a rare autoimmune disease in childhood. It affects 1-4/106 children per year and females are affected twice as often. Median age at presentation is 7 years (0-16) and it is more frequent in Caucasians. Calcinosis is seen in 14 % of children at presentation while 30% of patients will develop it in the course of their disease. Its occurrence has been linked with delayed diagnosis or inadequate treatment. Re-

cently, the presence of specific anti p-140 auto-antibodies has been associated with calcinosis in JDM patients. It presents as a firm nodular dystrophic calcification of previously injured areas and is mainly seen in extremities. Lesions may resolve or extrude towards the skin emptying 'milky' material. Treatment options include pamidronate, anti-TNF agents and surgical excision when pressure phenomena or disfigurement are present.

P 198
Juvenile dermatomyositis: a retrospective study of 74 cases

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BACKGROUND: Juvenile dermatomyositis is a rare inflammatory disease. Its treatment is not standardized.
AIM: To describe the presentation and course of children with juvenile dermatomyositis.
METHODS: Retrospective study of children with definite or probable juvenile dermatomyositis diagnosed according to the criteria of Bohan and Peter and followed-up between 1993 and 2009 in the pediatric rheumatology and the dermatology department of Necker's hospital.
RESULTS: 74 patients (49 girls, 25 boys) were included. The median age at diagnosis was 7.06 ± 3.67 year. Mean follow-up was 57 months (3-137). The most frequent skin signs were heliotrope rash (65%), erythema of the extension side of the limbs (62%), Gottron's papules (57%) and malar rash (57%). At diagnosis proximal muscle weakness, swallowing dysfunction and/or voice changes, abdominal pain, arthritis and mild fever were present in 100%, 26%, 24%, 17.5% and 12% of patients respectively. Four patients demonstrated no increase in CPK, ALT, AST or LDH levels. Initial nailfold capillaroscopy, muscle biopsies, electromyogram and muscle magnetic resonance imaging were abnormal in 7/7, 29/32, 30/37, and 13/16 patients respectively. First line treatment was corticosteroids (daily oral regimen: 51 patients, IV methylprednisolone pulses: 22 patients) either alone (60 patients) either in association with immunosuppressive drugs (13 patients). One patient have only immunosuppressive drug. Among patients followed-up for > 3 years, the course was chronic, monophasic, and polyphasic in 62%, 35% and 3% of the patients. The median time to remission was 11 months. Life threatening complications occurred in 7/74 patients and required plasmapheresis in 2/7. No dermatomyositis related death occurred. Calcinosis and lipodystrophy developed in 32% and 9.5% of the patients with a mean delay from onset disease of 2.3 years and 3.9 years and we were not able to find any predictive factor of their occurrence. Treatment related complications (osteoporosis, arterial hypertension, cataract and growth retardation) occurred in 60% of the patients. The incidence of calcinosis, lipodystrophy, treatment-related complications, rate of patients with chronic/polyphasic course and delay to have first remission did not significantly differ between the patients who received methylprednisolone pulses and those who did not.
CONCLUSION: Juvenile dermatomyositis is a heterogeneous and often severe disease. Further studies are needed to assess the indications and efficacy of methylprednisolone pulses.

P 199
Juvenile-onset clinically amyopathic dermatomyositis: a retrospective study of 9 cases

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BACKGROUND: Juvenile-onset clinically amyopathic dermatomyositis has been reported in less than 60 patients with a short mean follow-up <4 years.
AIM: To describe the presentation, complications and outcomes of juvenile-onset amyopathic dermatomyositis.
Methods: Retrospective monocenter study of clinically juvenile-onset amyopathic dermatomyositis defined as cutaneous manifestations suggestive of classical DM occurring for 6 months or longer with no clinical evidence of proximal muscle weakness and no serum muscle enzyme abnormalities in patients followed-up between 1993 and 2009 in the department of Dermatology center at Necker\'s hospital.
RESULTS: 9 patients (8 girls, 1 boy) were included. The median age at diagnosis was 9.5 ± 3 years. All the patients presented with heliotrope rash and Gottron's papules associated with at least 2 other skin involvement: erythema of the extension side of the limbs (7 patients), malar rash (4 patients), periungual telangiectasia (7 patients). 3/9 patients underwent a skin biopsie which revealed basal membrane's vacuolation and blood vessels with thickened wall, surrounded by inflammatory infiltrate in the dermis. At diagnosis no muscle involvement was present, but joint manifestations were found in 5 patients. ESR, muscle enzyme assays, EMG (n=5), and muscle MRI (n=2) were normal. ANA titers > 1/160 were found in 6/9 patients. Mean follow-up was 5.5 years (1-10). Progression to classical dermatomyositis and to sclerodermatomysitis occurred in 2 patients 7 and 1 years respectively after the onset of skin disease. Localized calcinosis was present in one other patient at diagnosis and regressed spontaneously within two years. No other complications especially severe vasculopathy or malignancy occurred. Six patients received hydroxychloroquine in association with topical steroids (n=2) or non-steroidal anti-inflammatory (n=1) patient.Three patients have only photoprotective measures and only one patient needed systemic corticosteroids for persistent arthritis under non-steroidal anti-inflammatory.
CONCLUSION: Juvenile-onset amyopathic dermatomyositis has usually a good prognosis without aggressive treatment. However, muscle involvement may occur many years after the diagnosis, and long-term prospective studies are needed to better assess the natural history of the disease.

P 200
Two Cases of Juvenile Dermatomyositis with Lipodystrophy

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Acquired lipodystrophy is recognized as a rare complication of autoimmune diseases, especially in juvenile dermatomyositis (JDM), which can predict abnormal glucose and fat metabolism in the body, including mesangial proliferative glomerular nephritis. Autoimmune disease complicated by LD is rarely reported in Chinese. Herein we describe two cases of juvenile dermatomyositis with lipodystrophy in Chinese children in order to further understand the clinical features of this complication.

P 201
Applications of magnetic resonance imaging of muscles in juvenile dermatomyositis and polymyositis in China

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OBJECTIVE: To investigate the significance of magnetic resonance (MR) imaging of muscles in the early diagnosis of juvenile dermatomyositis and polymyositis (JDM/PM).
METHODS: Investigations were carried out on 36 children with confirmed JDM/PM in the active stage, and 12 children with acute benign myositis; 14 children with complicated juvenile idiopathic arthritis and muscular injuries were also included as the control group. MR scanning was carried out on both thighs and muscle groups on the buttocks of these children (the thickness was 5 mm and the interval between layers was 1 mm; coronal plane T1 weighting [T1WI], T2 weighting [T2WI], and short time inversion recovery T2 [STIR]). Twenty-seven children had muscle biopsies. The functions of the MR examinations, muscle biopsies, and detection of six kinds of major creatases (AST, ALT, CK, CKMB, LDH, and HBDH) in the active stage of JDM/PM were analyzed.
RESULTS: Among the 36 children, 18 were males and 18 were females. The children were 2~13 years of age, and the average age was 7.1±3.5 years. Thirty of the 36 cases were confirmed to be JDM (83.3%) and 6 of the 36 cases were confirmed to be JPM (16.7%). MR examinations were carried out on 36 JDM/PM children in the active stage. Thirty-five of the 36 cases suffered from extensive involvement of multiple groups of muscles; 5 cases were accompanied by myofascitis, 3 cases were accompanied by inflammation of subcutaneous connective tissues, and 1 case was accompanied by skin involvement. Seven children with JDM were subjected to MR re-examination on muscles during the convalescence stage. It was found that four cases had become normal and patching focal abnormal high signals were only found in a few muscle groups in 3 cases. Twenty-seven of the 36 cases were subjected to muscle biopsies; among them, 14 cases suffered from inflammatory cell infiltration and typical changes in myofibrosis. The 36 cases underwent creatase examinations during the active stage, with the following results: AST>40 IU/L in 18 cases; ALT>40 IU/L in 16 cases; CK>220 IU/L in 15 cases; CKMB>40 IU/L in 12 cases; LDH>300 IU/L in 20 cases; and HBDH>260 IU/L in 19 cases. Statistical analysis showed that the sensitivity of MR was higher in achieving a diagnosis

compared to muscle biopsy and examinations of 6 major creatases (P<0.01). In the control group, 33% of the children had acute benign myositis, and the representations in MR were long focal T2 signals in the muscles of both lower extremities with a uniform distribution; 67% of the children had normal MR examinations. Two-thirds of the children that had systemic juvenile idiopathic arthritis had long focal T2 signals in the muscles with a uniform distribution; the MR examinations showed muscular atrophy in the pauci-arthritis and polyarthritis cases.
CONCLUSION: Major representations on MR examinations fn muscles in children with JDM/PM in the active stage were patching, stripes, or lamellar abnormal signals on T2WI. The lesions in the STIR sequences were even more apparent, with extensive involvement of multiple muscular groups. The scope of abnormal signals in muscle groups in the proximal end was wide and the intensity was higher. Lesions in multiple muscle groups and adjacent tissues can be generally reflected, and the resolution of STIR is higher. MR is a sensitive, reliable, and non-invasive examination for the diagnosis of JDM/PM which can be used to monitor pathologic activities and direct treatments.
Key words: dermatomyositis; polymyositis; magnetic resonance imaging; muscles; diagnosis; children; China

P 202
The diagnostics problems in primary Sjögren's syndrome in children

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Primary Sjögren's syndrome occuring in childhood is a rare disease. The accurate frequency is unknown. Clinical symptoms are atypical and mostly occur as an isolated disorder. Secondary Sjőgren's syndrome is generally associasted with SLE or MCTD.
We would like to present 2 children with primary Sjögren's syndrome. 7 years old girl with recurent chronic lymphadenitis and 17 years old boy with hyperthermia as the first symptom of primary Sjögren's syndrome. Diagnosis was based on immunological serum tests and histopathological examination of salivary gland.

P 203
Chronic recurrent multifocal osteomyelitis (CRMO): a review of imaging findings in 21 patients

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BACKGROUND: CRMO is a rare inflammatory bone disease of unknown aetiology occurring mainly in children and adolescents. It may be difficult to distinguish CRMO from other bone diseases such as bacterial osteomyelitis or primary bone tumours. Diagnosis of CRMO is often delayed.
OBJECTIVE: To review typical and atypical imaging patterns in order to prevent misdiagnosis and therefore, to avoid unnecessary invasive procedures or prolonged antibiotic therapy.
MATERIALS AND METHODS: We retrospectively reviewed clinical and imaging (X rays, CT, scintigraphy and MRI) findings of 21 children with CRMO. Diagnosis was based on the following criteria: (1) age under 18 years, (2) two different sites (at least) of bone involvement or one site associated to a fluctuating course with at least 2 recurrent episodes of pain and (3) surgical biopsy to exclude infectious and tumoral processes.
RESULTS (N=21): The sex ratio was 2/1 (14 girls and 7 boys) and the age range 3-18 years.
The disease was multifocal in 17 patients.
Appendicular skeleton was involved in 19 patients: tibia, femur, humerus and radius were primarily affected, mainly at the metaphyseal sites. Involvement of epiphysis or diaphysis was rare.
Axial skeleton, mostly clavicle and spine, was involved in 8 patients.
Radiographs and CT demonstrated the typical pattern of combined osteolysis and osteosclerosis in half of the study group. In the other half, osteosclerosis only or osteolysis was present. Hyperostosis was a common finding.
MRI showed in all patients bone marrow oedema and adjacent soft tissue edema was frequent. No abcess formation was seen.
Whole-body-MRI (STIR sequences) was always more contributive than scintigraphy to detect metaphyseal abnormalities.
CONCLUSION: Imaging patterns in CRMO are quite characteristic. However, atypical features deserve attention and whole-body-MRI seems very pertinent to detect silent lesions.

P 204
Treatment with antagonists IL-1 In those patients with autoinflammatory syndromes

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BACKGROUND: Autoinflammatory syndromes are genetically based diseases currently known and characterized by recurrent febrile episodes associated with systemic symptoms. In recent years it has raised the role of different cytokines in their pathogenesis, such as IL-1, which is a therapeutic target for the treatment of these diseases generally do not respond to conventional therapy.
OBJECTIVE: To evaluate the efficacy and safety of treatment with antagonists of IL-1 in patients with Autoinflammatory syndromes (familial Mediterranean fever-FMF-, hypergammaglobulinemia D periodic fever syndrome-HIDS-, cryopyrin associated periodic syndromes –CAPS, tumor necrosis Factor receptor associated periodic syndrome-TRAPS-).
PATIENTS AND METHODS: Design: Retrospective observational study. Population: we identified a total of 29 patients with autoinflammatory syndrome confirmed genetically and assigned to the Pediatric Rheumatology Service of the Hospital La Fe de Valencia (Spain), of which eight (27%) patients (6 males and 2 females) began treatment with antagonist IL-1 (3 HIDS, 2TRAPS, 1CAPS y 2 FMF). All received steroids prior to the commencement of therapy with antagonists of IL-1. There was a treatment failure to colchicine and methotrexate in patients with FMF. A HIDS patients received etanercept with failure to it. In 7 (87%) patients underwent treatment with anakinra at doses of 2-3 mg / kg / day. However, in patients with a diagnosis of CAPS (Muckle Wells syndrome) was conducted canakinumab treatment at doses of 2 mg / kg / day. Clinical variables include: age at diagnosis, age at onset and duration of treatment, number and duration of annual attacks of the same before and after the start with the antagonist of IL-1 and observed adverse effects during treatment.
RESULTS: Participants had a mean age at diagnosis of 9.64 years (2-20) and mean age at baseline of 10.57 years (2-21). The average duration of treatment during the study period was 11.57 months (1-30). The main clinical variables are shown in **Figure 1**. It can be seen in 5 (71%) patients there was a marked improvement with a decrease in the number of episodes per year and the duration thereof, and 4 (57%) patients had no attacks during therapy antagonist of IL-1. In one patient remained the same number of annual attacks, however the duration and severity of them was lower. One patient with FMF who had an associated cutaneous PAN, the latter worse treatment with anakinra what motivated his suspension. Complications were seen in 3 (42%) patients, the most frequent upper respiratory infections uncomplicated. One patient with TRAPS was not included in the analysis of data due to recent onset of treatment with anakinra.
CONCLUSIONS: Antagonists of IL-1 have been shown effective and safe in treating the majority of our patients with autoinflammatory syndrome, thus documenting a significant reduction in the number and duration of attacks, as well as the absence of serious side effects, so consider that could constitute an adequate therapeutic alternative, although we believe that further studies would be needed with a larger number of patients.

P 205
Chronic recurrent multi-focal osteomyelitis: diagnosis and treatment in 15 paediatric cases

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BACKGROUND: Chronic recurrent multi-focal osteomyelitis (CRMO) is a non-infectious inflammatory osteitis predominantly affecting children and adolescents. Diagnosis is often difficult as initial symptoms and clinical course can vary widely. CRMO can result in significant morbidity. Treatment regimes are varied but bisphosphonate therapy with pamidronate is proving effective at reducing pain and improving bone remodelling in some patients.
OBJECTIVES: To determine the route to diagnosis, the clinical course and the effectiveness of treatment in patients with CRMO.
METHOD: The clinical, radiological and laboratory data of 15 patients identified with CRMO between 2000 and 2009 were reviewed.
RESULTS: Median age at diagnosis: 9.6 years (range 3-15); 6 were male, 9 female. Median follow-up: 2 years. Sites of bony involvement: clavicle(8), proximal tibia(4),distal femur(2), vertebrae(2), ankle(2) and rib(1). 2 patients had skin changes. All had x-ray and MRI studies. 11 underwent diagnostic bone biopsy. All had extensive microbiological investigations with no organism identified. The clinical course varied – 4 patients had a single episode of osteitis, 5 experienced one recurrence and 6 had more than two relapses. 8 patients suffered chronic persistent inflammation and pain lasting over one year. All patients were initially treated with intravenous antibiotics (IVAB) for presumed infectious osteomyelitis; 9 had more

than one course of IVAB before diagnosis. Non-steroidal anti-inflammatory drugs (NSAIDs) were used in 7 patients; 2 received NSAIDs alone. 2 patients received oral prednisolone; 1 IV methyl prednisolone, 4 sulphasalazine and 4 methotrexate. 5 received bisphosphonates (pamidronate) and have shown significant improvement in function and reduction of pain.
CONCLUSIONS: CRMO is a diagnosis of exclusion often resulting in delay of appropriate treatment. We highlight the importance of an early biopsy in confirming the disease. Pamidronate was potentially effective in the management of 5 patients.
REFERENCES: Miettunen et al; Dramatic pain relief and resolution of bone inflammation following pamidronate in 9 patients with CRMO. Ped Rheum 2009,7(2)
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P 206
Clinical characteristics and treatment outcome in Danish PFAPA patients

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BACKGROUND: PFAPA is an idiopathic systemic fever syndrome characterised by periodic fever, aphthous stomatitis, pharyngitis and cervical adenitis. It was initially described in 1987 and diagnostic criteria were outlined in 1989 (1).
OBJECTIVES: The aim was to describe PFAPA through a retrospective review of the medical records of patients seen in the pediatric rheumatology clinic.
METHODS: A retrospective review of the medical records of patients diagnosed with PFAPA who had their first visit to our centre during the period January 1999 - January 2010. For each of the 28 patients a questionnaire was completed including gender, ethnicity, age at onset of symptoms, clinical manifestations, EuroFever diagnostic criteria, treatment and outcome.
RESULTS: The study population consisted of 28 patients (19 males: 9 females), 27 Caucasian and 1 Asian, 24 fulfilled the EuroFever diagnostic criteria. The remaining four patients did not due to only vague records of the characteristic symptoms and in one patient the growth chart was missing. The median age at onset of symptoms was 33 months, range 6 to 160 months. The mean fever duration was 4.5 days (95% CI = 3.93; 5.07) and the mean duration of the asymptomatic intervals was 30.6 days (95% CI = 25.87; 35.35). A seasonal variation in the frequency of the fever episodes was seen in 43 % of the patients, two thirds had more frequent episodes during autumn and winter and the last third more frequently during spring and summer.
All patients were completely asymptomatic during the intervals between fever episodes. Concomitant with the fever the patients had characteristic symptoms (pharyngitis, cervical adenitis and aphthous stomatitis) associated. The distribution is illustrated in **table 1**. Furthermore, 27 patients had other symptoms associated with the fever episodes in the form of headache, stomachache, arthralgias, tiredness, rash, vomiting or diarrhea. Eleven patients had prodromal symptoms before the fever episodes in the form of headache, tiredness or pain in extremities. Normal growth was seen in 27 patients.
The time from onset of symptoms to the diagnosis was defined varied from 2 to 160 months, with a median value of 30.25 months. However, the duration of the diagnostic delay declined significantly during the study period (r= -0.7512).
Twenty-three patients were treated with oral prednisolone (dosage: 1-2 mg/kg/day), administered at the start of the fever and for 1-3 days. Prednisolone caused an immediate reduction in the fever in 82.6 %. However, the duration of the asymptomatic interval was shortened in 73.9 % after the treatment. It was not possible to estimate an exact value for the reduction from the medical records. Tonsillectomy was performed in 16 patients. The cessation of fever episodes was observed in 62.5 % (10/16) after the operation. For 3 patients this was not the case and for the last 3 patients the post-op status was not known. A spontaneous resolution of fever episodes was seen in three patients during follow-up at our centre which appeared after 3 to 7 years of fever episodes.
CONCLUSIONS: Although PFAPA was first described more than 20 years ago and the diagnostic process in our material was shortened over time, the considerably long diagnostic delay of PFAPA gives rise to concern, indicating a need for greater awareness of the disease so the diagnosis can be made earlier.
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P 207
Anti IL1 treatment for FMF patients resistant to colchicine: reasoning treatment from laboratory experience

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BACKGROUND: Familial Mediterranean Fever(FMF) is a recessively inherited autoinflammatory disorder characterized by recurrent attacks of fever and serositis. Although colchicine is the standart therapy for preventing attacks and suppressing inflammation, about %5-10 of the compliant patients are colchicine resistant.
AIM: We report the effect of antiTNF (etanercept) and antiIL1 (anakinra) treatment in 5 cases resistant to colchicine therapy.
MATERIALS AND PATIENTS: Five patients (3F,2M) who were experiencing at least two attacks per month and had consistently elevated CRP levels despite regular colchicine therapy were given either etanercept or anakinra. The median age was 16 (11-19) years. FMF mutations were as follows: 3 M694V/M694V, M680I/M694V and M680I/M680I. Three patients were given 0.8 mg/kg/week etanercept initially. The median follow up with etanercept was 3 months. These patients were subsequently switched to anakinra for better control. Two patients received anakinra as the initial biologic treament. Anakinra was given at a dose of 1 mg/kg/day. The median follow up with anakinra was 5.5 months.
RESULTS: Although etanercept lowered the number of attacks (3-4 attacks per month to 2 attacks per month) attacks still recurred and acute phase reactants remained high in two. All three patients were switched to anakinra. In two patients anakinra completely resolved clinical and laboratory findings. The other three patients have just been switched to anakinra in the last 1-3 months; as for now anakinra has already reduced the number of attacks (to 1 attack per month) and lowered the acute phase reactants.
CONCLUSION: In this small series biologic treament, anakinra in particular, was succesful in suppressing inflammation and decreasing the number of attacks in FMF. This may be explained by the role of pyrin in the regulation of IL-1 b activation.

P 208
Periodic fever syndromes in Eastern and Central European countries: results of a multinational survey

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INTRODUCTION: Periodic fever syndromes are rare diseases. Studies published so far were mainly conducted in Mediterranean and western European countries and in USA. To our knowledge, no published study has reported the frequency of periodic fever syndromes in Eastern and Central European (ECE) countries.
AIM: To establish the burden of periodic fever syndromes in ECE countries.
METHODS: Two different strategies were used to collect data on patients with periodic fever syndromes from ECE countries: i) the Eurofever survey: a secured web-based questionnaire among the pediatric rheumatology centers included in the Paediatric Rheumatology International Trials Organization (PRINTO), and ii) collection of data with the structured questionnaire sent by e-mail to the pediatric immunologists included in the J project and other physicians working in the field of pediatric rheumatology and/or immunology in ECE countries. The structured questionnaire included information on the number of patients with genetically confirmed or suspected periodic fever syndromes, the number of patients with other autoinflammatory diseases and availability of genetic testing for periodic fever syndromes in ECE countries.
RESULTS: All together we received data from 37 physicians from 35 centers (response rate for both surveys together was 51%) in 14 ECE countries including Albania, Bosnia and Herzegovina, Bulgaria, Croatia, Czech Republic, Hungary, Latvia, Lithuania, Macedonia, Poland, Romania, Serbia, Slovakia and Slovenia. All together there were 11 patients reported with genetically confirmed familial

Mediterranean fever (FMF), 14 with genetically confirmed mevalonate-kinase deficiency (MKD), 11 with genetically confirmed tumor necrosis factor (TNF) receptor associated periodic syndrome (TRAPS) and 4 with genetically confirmed chronic infantile neurological cutaneous and articular syndrome (CINCA). Significantly higher numbers were reported for suspected cases which were not genetically tested. All together there were 49 suspected FMF patients reported, 24 suspected MVK, 16 suspected TRAPS, 7 suspected CINCA and 2 suspected Muckle-Wells syndrome (MWS) patients.
CONCLUSIONS: The number of genetically confirmed patients with periodic fever syndromes in ECE countries is very low. In order to identify more patients in the future, it is important to organize educational programs for increasing the knowledge on these diseases and to establish a network for genetic testing for periodic fever syndromes in ECE countries.

P 209
Vitamin D and bone mineral density in health and disease. Is vitamin D analogue treatment option in JIA?

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BACKGROUND: Low bone mineral density (BMD) and vitamin D levels in JIA and healthy children are often undiagnosed condition. Recent data indicated potential of vitamin D hormone forms to benefit different autoimmune diseases. We evaluated vitamin D levels and BMD in healthy children and influence of alfacalcidol, vitamin D analogue, on BMD and disease activity in JIA patients.
METHODS: We have analyzed 25(OH)D3 (vitamin D) levels, calcium metabolism parameters and lumbar BMD (DXA) in 40 JIA patients and 35 healthy aged mached volunteers. JIA patients treatment regime remained unchanged while alfacalcidol 1mcg/day during 3 months followed with 0.5 mcg/day next three months and 0.25mcg/day during last six months was added during one year follow up. In JIA patients ACR Pedi 30,50 and 70 response was evaluated before and after alfacalcidol treatment.
RESULTS: JIA patients mean age was 14,7±4,22 and disease duration 6,59± 2,76. Prior MTX therapy duration was 3,34 (1-7.24) with average dose 12,5 mg/m2/week and steroid cumulative therapy duration 2.29 (0.3-7.0) with average dose 16.04 mg/day. We have found significantly lower BMD in JIA patients compared to controls (BMD 0.835±0.27 vs. 0.985 ± 0.108) as well as Z score to –0.98±1.48 vs. –0.005±0.36 ($p<0.01$, Man Whitney U test). Alfacalcidol treatment have significantly improved BMD in JIA patients (BMD 0.896±0.37 and Z score to –0.45±1.02; $p<0.05$). Vitamin D levels were under optimal level (30 ng/ml) in both groups. JIA patients have had significantly lower concentrations then healthy controls 6.03±3.01 ng/ml and lower vitamin D level correlated with disease severity (chi square for indenpendency 37.4 df=2, $p<0.01$). Improvement of 73,15%, 58,4% and 43,2% in ACR Pedi 30,50 or 70, respectively, was achieved in JIA patients. We did not find any change in serum calcium, ionized calcium, alkaline phosphatase or phosphorus levels, as well as urine calcium in both groups.
CONCLUSION: Our results indicate that both healthy children and JIA patients have low 25(OH)D3 levels and impaired BMD. Low 25(OH)D3 levels correlate with disease severity in JIA and treatment with vitamin D analogue could improve BMD and disease outcome.

P 211
Prevalence of Mutations in Mefv Gene in Slovenian Children with Henöch-Schonlein Purpura and in Apparently Healthy Population

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INTRODUCTION: Henoch-Schönlein purpura (HSP) is a small vessel vasculitis caused by deposition of IgA immune complexes. Familial Mediterranean fever (FMF) is a periodic fever syndrome and belongs to a group of hereditary autoinflammatory diseases. It is caused by mutations in MEFV gene on chromosome 16 and is rare among people living in other regions than Mediterranean basin. Studies showed that HSP is more prevalent in patients with FMF and mutations in MEFV gene were found to be more common in patients with HSP than in healthy population.
Objective of our research was to investigate the prevalence of MEFV mutations in Slovenian population, to determine if these mutations present a risk factor for HSP in Slovenian children and to evaluate the association of the presence of MEFV mutations with clinical and laboratory characteristics of HSP patients.
MATERIAL & METHODS: In the groups of 105 apparently healthy controls and 102 patients with HSP exons 2 and 10 of the MEFV gene were sequenced and screened for the presence of most often described mutations in the MEFV gene. Clinical and laboratory data were collected for patients with HSP. Data were analyzed by Student t test, chi-squared test of Fisher's exact test (SPSS 13.0) where appropriate. A p value <0.05 was considered statistically significant.
RESULTS: The difference in prevalence of single mutation in apparently healthy participants and patients with HSP was not statistically significant (7/105 vs 6/102, p= 0.8271). None of the healthy participants or patients with HSP was found to have two mutations in the MEFV gene. HSP patients with MEFV mutation were younger than patients without mutation at the time of HSP diagnosis, but the difference was not statistically significant (5,8±2,6 years vs 7,1±3,9 years, p= 0.111).
CONCLUSION: Our study demonstrated that MEFV mutations are present also in apparently healthy Slovenian population. We found no statistically significant difference in the frequency of MEFV mutations between healthy Slovenian population and patients with HSP. These results are in contrast to previously published studies from other Mediterranean countries, where the presence of MEFV mutation presents a risk factor for development of HSP.

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Interleukin-1 targeting drugs in Familial Mediterranean Fever

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INTRODUCTION: Familial Mediterranean fever (FMF) is an autosomal recessive autoinflammatory disorder common in Mediterranean populations. FMF is associated to mutations of the MEFV gene, which encodes Pyrin. Functional studies suggest that Pyrin is implicated in the maturation and secretion of IL-1beta. Daily Colchicine is the gold standard for therapy in this disease, however 10% of patients may not respond or develop serious side effects. IL-1 receptor antagonists may therefore represent a new approach to treat difficult FMF patients. Anakinra is an IL-1R antagonist that competitively inhibits binding of IL-1a and IL-1b to the IL-1 receptor. Single case reports suggest that Anakinra may be efficient for the treatment of FMF but clear indications for the use of Anakinra in FMF patients are not yet established.
AIMS: To evaluate and discuss clinical situations that lead to the use of Anakinra in FMF patients.
METHODS: Electronic mailing lists of French pediatric and adult rheumatologists-societies were used to call for FMF-patients (confirmed by carriage of 2 MEFV-mutations) who received interleukin-1 signnlling targetting drugs.
RESULTS: Two adults and five pediatric patients were identified. The indication for the use of Anakinra (daily injections of 1mg/kg/d in children and 100mg/day in adults) or Canakinumab (2mg/kg/month) were: Case 1 and 2 - Frequent and severe FMF episodes hindering the quality of life in spite of optimal Colchicine treatment. Case 3 and 4 – Frequent FMF episodes and elevated serum amyloid A levels despite Colchicine treatment. Case 5 - Colchicine induced neuromyositis. Case 6- FMF associated to severe Henoch-Schoenlein vasculitis in spite of Colchicine plus steroids treatment. Case 7 – An atypical FMF phenotype marked by episodes of severe myositis (protracted febrile myalgia syndrome) in patient who was not compliant to Colchicine treatment. In all cases Anakinra was well tolerated and allowed sustained remission.
CONCLUSION: This report points out that in some rare difficult FMF-patients the availibility of a treatment alternative to Colchicine is necessary. The reported cases indicate that Anakinra (and other IL-1 blockers) may provide important benefit. However, treatment modalities (treatment of FMF episodes only versus continous treatment), safety and efficacy of interleukin-1 targeting drugs in FMF patients need to be evaluated in controlled trials.

P 213
Syndrome-related Arthritis

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It is well known that many children with genetic syndromes, such as trisomy 21 , have an increased risk of developing arthritis. Although there are some case series in the literature describing the arthropathy of Trisomy 21, few other large case series that include patients with other genetic syndromes have been published. It is also recognised that for various reasons, arthritis in these children, who are often mentally and physically handicapped, is under recognised and probably under treated. We undertook a chart review of patients with arthritis from three centres two in Europe and one in the united states, to try to better understand the characteristics of these diseases in this subgroup of patients.

METHODS: A retrospective chart review was undertaken of all patients with arthritis and genetic syndromes in Leuven, Belgum. The following data were collected: Age, Sex, Syndrome, Age at onset, age at diagnosis, type of arthritis, number of joints involved, symmetrical or asymmetrical involvement, associated conditions, management and response to therapy.
RESULTS: Eleven patients with syndrome related arthritis were identified form Leuven. Of these, five were patients with Trisomy 21. Other syndromes included Cohen Syndrome, Di-George syndrome, Coffin-Siris Syndrome, p-18 deletion, Schimke Syndrome and SPENCD.
Trisomy 21 was the most common genetic abnormality.
Children tended to have Polyarticular, ANA negative disease
The incidence of other disorders of the immune system was high.
Patients tended to present later in childhood.
There was a very high rate of radiographic progression in this population
Therapy was fairly conservative, probably reflecting caution in using strong immunosupression in this vulnerable group. A lower level of functioning and lower functional expectations may play a role in this finding.
A summary of the clinical characteristics of each individual syndrome is given.
CONCLUSION: Children with Syndrome related arthritis present late, have a number of associated problems and tend to be treated conservatively, despite radiographic progression.

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Neutrophils Gene expression profile in systemic Juvenile Idiopathic Arthritis (sJIA) patients treated successfully with Anakinra

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BACKGROUND: Inflammatory cytokines such as interleukin (IL)-6 and IL-1 have been shown to mediate the pathogenesis of systemic juvenile idiopathic arthritis (sJIA), which is now generally regarded as a family member of autoinflammatory diseases. Biologics to block IL-6 or IL-1 (tocilizumab and anakinra respectively) are proven to be effective in sJIA patients that are refractory to standard therapy. In this pilot prospective study, we examined polymorphonuclear neutrophils (PMN) of sJIA patients for mRNA expression as these cells are particularly important in autoinflammatory diseases.
OBJECTIVE: To determine changes in neutrophil gene expression profile from sJIA patients after successful treatment with anakinra.
METHODS: We performed gene expression profiling using DNA microarray on PMN isolated from eight paired blood samples ("before" and "after" treatment), obtained from sJIA patients that responded well to anakinra. Unsupervised hierarchical clustering and significance analysis were performed. Differentially expressed genes were annotated and grouped into biologically meaningful networks. Quantitative real-time PCR was performed on selected genes to verify the analysis of the microarray experiment.
RESULTS: Unsupervised hierarchical Cluster analysis revealed small intraindividual differences and larger interindividual differences, supporting our use of paired comparisons. In all paired samples, expression of 104 genes were significantly upregulated and 45 genes were downregulated after treatment ($p<0.01$). Among the downregulated genes is mitogen-activated protein kinase kinase 6 (MAP2K6), a specific upstream activator of the p38 MAP kinase signalling pathway that is involved in inflammatory responses. Among differentially expressed genes are previously described genes in active JIA (S100A8, CCL4), while many others are novel.
CONCLUSION: Neutrophils from sJIA patients examined for the first time, showed significant changes in gene expression following anakinra treatment, in innate immune pathways and the p38 signalling pathway.

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Usefulness of autoantibodies against inner ear antigens for the diagnosis

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BACKGROUND: Autoimmune inner ear disease is an uncommon entity in the young [1,2]; the diagnosis is usually made by excluding all other known causes of inner ear damage and by the positive response to corticosteroid administration.
OBJECTIVES: We tested the capability of Western blot immunoassay for heat shock protein-70 (hsp-70, a 68-KD antigen expressed in mammalian inner ear extract), cell-density-enhanced protein tyrosine phosphatase-1 (DEP-1/CD148, expressed on the sensory epithelia of the inner ear and on endothelial cells), connexin 26 (Cx26, a component of gap junction channels in the epidermis and in the stria vascularis of the cochlea), reovirus, and a specific Cogan peptide for predicting an autoimmune pathogenesis of the idiopathic deafness in a paediatric population.
METHODS: Between 2008 and 2010, six patients (5 females, 1 male, aged between 2 and 15 years) with sudden, bilateral, asymmetric and rapidly progressive sensorineural hearing loss of unknown origin were evaluated at the Rheumatology Unit of the A. Meyer Children\'s Hospital of Florence. All children had been previously studied with a complete otoneurological and ophthalmologic examination, and appropriate imaging and laboratory studies to exclude other inner-ear disorders. The 6 patient samples were analysed by Western blot for HSP70, DEP-1/CD148, Cx26, reovirus, and Cogan peptide.
RESULTS: Among 6 patients, 5 showed at least 1 reactive band, however only one of them was positive for HSP70. Four of the positive patients were treated with high doses of oral steroids and 3 of them experienced an improvement on audiograms and associated symptoms within 6 weeks, one patient started the steroid only recently. One positive girl refused corticosteroid treatment. The seronegative patient spontaneously recovered.
Conclusions our results suggest that Western blot immunoassay-positive results may help to discriminate the autoimmune sudden deafness from idiopathic cases in children [3].
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Human induced CD4+CD25+FOXP3+ regulatory T cells suppress effector immune responses *in vitro*, but not *in vivo*

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BACKGROUND: Regulatory T cells (Treg) are important to maintain immune homeostasis. Presence of Treg correlates with a favorable disease course in Juvenile Idiopathic Arthritis (JIA) patients. A distinction within the Treg population can be made between naturally occurring Treg (nTreg), which are derived from the thymus, and peripherally induced Treg (iTreg). Induction of Treg in the periphery is a promising way to modulate diseases like JIA, since it is easier to obtain high numbers of cells. However, the functionality of activation-induced CD4+CD25+FOXP3+ Treg has been highly debated in the last few years. Furthermore, in vivo induction of Treg by TCR or co-stimulation could induce a cytokine storm. Therefore, it is important to carefully monitor iTreg functionality.
OBJECTIVES: In this study, we tested whether human iTreg suppress immune responses *in vitro*, and *in vivo* in a humanized mouse model of xenogeneic Graft versus Host Disease (x-GvHD).
METHODS: CD4+CD25- T cells were isolated from human PBMC and cultured with aCD3/aCD28 with or without IL2 and TGFb to obtain iTreg. CD4+CD25high T to obtain nTreg.bcells were cultured with aCD3/aCD28, IL2 and TGF Supernatant was taken for Luminex analysis and cells were stained for Treg markers. Suppression assays were performed to determine suppressive chain-/- mice were sub-lethally irradiated andgcapacity. RAG-/- injected with clodronate liposomes to deplete phagocyting cells. Next, human PBMC were injected with or without iTreg or nTreg from the same human donor. Mice were scored for x-GvHD during 9 weeks.
RESULTS AND CONCLUSIONS: We show here that Induced Treg FOXP3 expression levels and suppressive capacity in vitro were comparable to nTreg. As expected, nTreg efficiently prevented acute x-GvHD. However, in contrast with nTreg, iTreg did not suppress disease. Our results show that polyclonally induced Treg display no suppressive capacity in x-GvHD, due to a quick loss of FOXP3 in vivo. This underscores the importance to use humanized mouse models for validation of data regarding iTreg function obtained in in vitro assays, before proceeding to application in patients.

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How frequently does etanercept induce a state of remission or near-remission of joint inflammation in children with Juvenile Idiopathic Arthritis?

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BACKGROUND: The biologic agent etanercept (ETN) is currently the medication of first choice in children with polyarticular juvenile idiopathic arthritis (JIA) who are refractory or intolerant to methotrexate. The results obtained thus far with this drug in therapeutic trials and clinical practice have increased the expectations of the therapeutic benefit, with the achievement of clinical remission being now the main goal of treatment for most pediatric rheumatologists.
OBJECTIVE: The aim of the present study was to evaluate the proportion of patients treated with ETN at the study unit who reached a state of complete remission (CR) or near remission (NR) of synovitis in the affected joints.
METHODS: The study was conducted through the retrospective evaluation of clinical charts of all consecutive patients who were started with ETN at the study unit between 2002 and 2009. Achievement of CR or NR of joint inflammation was assessed in all patients at last follow-up visit while the patient was still on ETN therapy or at the time of ETN discontinuation. CR was defined as a count of joints with active disease = 0. NR was defined as a count of joints with active disease = 1.
RESULTS: A total of 165 patients were given ETN in the study period. The ILAR category was systemic arthritis in 28 patients, persistent oligoarthritis in 12 patients, extended oligoarthritis in 63 patients, rheumatoid factor (RF)-negative polyarthritis in 38 patients, RF-positive polyarthritis in 9 patients, psoriatic arthritis in 6 patients, enthesitis-related arthritis in 8 patients, and undifferentiated arthritis in 1 patient. Disease duration ranged from 4 months to 20.9 years (mean 5.7 years, median 4.6 years). Ten patients had not yet received the first visit after ETN start or were lost to follow-up. In the remaining 155 patients, treatment duration ranged from 2 months to 10 years (mean 2.4 years; median 1.7 years). Concurrent treatment included MTX in 67.4% of patients, systemic corticosteroids in 11.5% of patients, and intraarticular corticosteroids in 21.6% of patients. At last follow-up visit, 92 (59.3%) patients had CR, 22 (14.2%) patients had NR, and 41 (26.5%) patients still had active synovitis. The table shows the frequency of outcomes at last follow-up visit in the whole patients and by ILAR category.
CONCLUSIONS: Our study shows that ETN is able to induce complete remission or near remission of joint inflammation in the majority of JIA patients. As found in other series, ETN is distinctly less effective in the systemic subtype.

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High frequency of subclinical synovitis, as detected by ultrasound, in juvenile idiopathic arthritis patients with clinically-defined inactive disease

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BACKGROUND: In children with juvenile idiopathic arthritis (JIA), it is unclear whether clinically-defined remission couples with absence of synovitis on imaging studies. Subclinical synovitis, as detected with US, has been found to be common in JIA.
OBJECTIVES: To investigate the frequency of US-detected subclinical synovitis in JIA patients with clinically-defined inactive disease (ID) and the role of US abnormalities in predicting a subsequent flare of synovitis.
METHODS: The clinician established the presence of ID (active joint count =0, physician's global assessment on a 0-10 cm visual analog scale <0.5, and negative acute phase reactants) in 28 consecutive JIA patients. On the same day, a sonographer scanned independently 52 joints in each patient for synovial hyperplasia (SH), synovial fluid (SF), power Doppler signal (PDS), and tenosynovitis (TS). Based of the subsequent disease course, patients were classified having persistent ID or a relapse of arthritis (defined as a recurrence of clinically-defined active synovitis in 1 or more joints).
RESULTS: The frequency of SH, SF, PDS, and TS in the 28 patients with ID was 75%, 71.4%, 32.1%, and 14.3%, respectively. Following the diagnosis of ID, 21 patients had persistent ID after a median of 12 months, whereas 7 patients experienced a relapse of arthritis a after a median of 6 months. The frequency of US abnormalities at the time of the diagnosis of ID in the 7 patients who had a subsequent disease flare was 100% for SH, 87.5% for SF, 14.3% for PDS, and 28.6% for TS.
CONCLUSION: JIA patients with clinically-defined ID had a high frequency of US-detected synovial abnormalities, namely SH and SF. Of the US features, SH and SF may have a greater role in predicting a future relapse of synovitis.

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Familial Mediterranean fever and liver involvement: a case series from the French Reference Centre for Auto-inflammatory diseases

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We report a case series of 6 paediatric patients with familial Mediterranean fever (FMF) and liver involvement.
First: P. B. from the age of 4 months presented recurrent FMF attacks. During three episodes lab tests revealed liver enzymes abnormality (tenfold the normal ranges). Genetic analysis confirmed MEFV homozygosity.
Second: E. B. had typical FMF since 1 year. At 18 months, marked elevation of liver enzymes during attacks lead to a liver biopsy showing hepatic fibrosis, minimal steatosis and inflammatory infiltrate.
Third: A.Y., at 4, was referred for prolonged fever, fatigue, hepatosplenomegaly, pancytopenia and severe hepatic cytolysis. Liver biopsy showed a predominantly lymphocytic inflammatory infiltrate and fibrosis. Autoimmune hepatitis was first suspected and he received methylprednisolone and azathioprine. A full-blown picture of macrophage activation syndrome (MAS) was confirmed retrospectively and FMF diagnosis was then confirmed (M694V homozygote).
Fourth: A.W. had recurrent episodes of fever, abdominal pain, purpura, and arthralgias starting at 3 years. FMF was rapidly confirmed (M694V homozygote). Severe attacks of Henoch-Schönlein purpura appeared, in spite of colchicine treatment with slight elevation of liver enzymes and cholestasis. Anakinra treatment allowed clinical remission but liver enzymes remained elevated. The ultrasound revealed marked steatosis and initial fibrosis.
Fifth: S. B. had liver transplantation at 3 years, after fulminant HAV hepatitis. Afterward, he had recurrent elevations of liver enzymes, with repeated liver biopsies interpreted as alloimmune hepatitis or acute rejection. Genetic test were performed due to recurrent FMF attacks, and showed compound heterozygosity (M694V E148Q).
Sixth: C.B. presented typical FMF since the age of 1 year. Her genotype was a complex allele in MEFV gene (I692 del/V726A+E148Q). An abdominal ultrasound at 6 years, in the context of a general assessment before anti-IL-1 treatment, showed hepatic steatosis.
Only few studies investigated liver involvement in FMF. At our knowledge there's only one case report of hepatitis in a paediatric FMF patient. FMF may involve the liver more frequently than previously thought. Increased liver enzymes, steatosis and fibrosis seem the most frequent but other type of disease may occur (such as MAS). The mechanism is unclear and the outcome needs to be defined by prospective follow-up.

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To explore the use of the PedsQL Subjective Questionnaire to assess levels of fatigue in children with Juvenile Dermatomyositis

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BACKGROUND: Fatigue is one of the regularly reported clinical features of Juvenile Dermatomyositis (JDM), however there is no standardised method of assessing the degree of fatigue. The PedsQL Fatigue score (FS) is a self reported questionnaire and a Visual Analogue Scale (FVAS) which has been developed to measure fatigue in children with paediatric inflammatory diseases. Great Ormond Street Hospital has a specialist service for children with JDM and the FS and FVAS were used to assess whether they were an effective measure of disease related fatigue.
OBJECTIVES: To establish if the PedsQL FS measures fatigue in children with JDM compared to clinical outcome measures of active JDM including muscle strength and function.
METHODS: All children attending the JDM clinic were routinely assessed using the Childhood Myositis Assessment Score (CMAS), manual muscle testing score (MMT8), parental VAS score of general wellbeing (PaVAS), physicians VAS of disease activity (PVAS), 6 minute walk test (6MWT) and Childhood Health Assessment Questionnaire (CHAQ). The PedsQL questionnaire was given out separately to both parents and children and includes a fatigue VAS (FVAS), a pain VAS as well as specific questions about cognitive fatigue, physical activity and sleep. The data was analysed using SPSS v16.0.
RESULTS: The patient cohort comprised of 52 children (39 F: 13 M). The mean age was 11.92 years (range 3-19). The mean disease duration was 9.42 years (range 0.2-13yrs)
The PedsQL FS (both parent and child) showed statistical significance with pain VAS, Pa VAS and CHAQ however did not show significance with the objective markers; MMT8 and CMAS. The child and parent FVAS shows statistically significant results with the pain VAS, MMT8 and the CHAQ. Additionally, the child FVAS statistically shows a correlation with the CMAS. Neither the PedsQL FS or FVAS showed any statistical correlation with the 6MWT or the PVAS.
Spearman's Correlation

Pain VAS CMAS MMT8 PaVAS PVAS 6MWT CHAQ
Parent FS
Correlation -.632** .222 .286 -.427** -.029 .129 -.406**
Sig (2- tailed) .000 .162 .060 .006 .868 .490 .008
Child FS
Correlation -.648** .087 .144 -.445** .029 .137 -.411**
Sig (2- tailed) .000 .577 .363 .005 .876 .478 .009
Parent FVAS
Correlation .550** -.303 -.313* .280 .110 -.280 .417**
Sig (2- tailed) .000 .057 .041 .085 .537 .134 .007
Child FVAS
Correlation .535** -.304* -.415** .311 .004 -.324 .545**
Sig (2- tailed) .000 .044 .006 .054 .984 .086 .000
CONCLUSIONS: It appears that the PedsQL FS does not fully objectively measure fatigue but combined with the FVAS may be a reasonable tool for assessing fatigue in JDM. It is also recognised that psychological and psychosocial factors play a role in patient self reported fatigue and that further research is required into this area.

P 221
Effect of Different Variants of TNFRSF1A Gene on Health-Related Quality of Life (HRQOL) in Children

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INTRODUCTION: The Child Health Questionnaire (CHQ) is a self-administered instrument designed to capture the physical, emotional and social components of health status of children. It comprises 15 health concepts exploring either physical and psychosocial domains. Higher scores in the scales indicate better HRQOL.
AIM: To analyze the effect of different mutations of TNFRSF1A gene on the quality of life of children with recurrent fever in comparison to healthy controls.
METHODS: The national language version of the parental administered 50-item version of the Child Health Questionnaire (CHQ-PF 50) was used to assess the health related quality of life in …. Patients wirth structural mutations (cysteine or T50M) and … with low-penetrance R92Q mutation.
The questionnaire was proposed at the moment of the first evaluation in the Centre and at the last follow-up. An international sample of 3315 healthy children (52.2% female), with a mean (SD) age of 11.2 (3.8) years constituted the healthy control group.
RESULTS: TNFRSF1A structural mutations were associated with a severe impairment in both physical summary (PhS) and psychosocial summary (PsS) score in respect to healthy controls ($p<0.001$). Structural mutations have a major impact on most of the items described to asses health related quality of life. The most impaired CHQ health concepts were those related to physical domains, such as global health, physical functioning and bodily pain/discomfort ($p<0.001$). However, several items related to psychosocial domains, such as general heath perception, parental impact emotional, family activities and family impact time were also variably impaired. Conversely, the impact of disease activity was less severe in patients carrying R92Q mutation. Notably, the most affected concepts in respect to healthy controls were those associated to global health perception (global health, general health perception and parental impact emotional).
A significant amelioration of was observed after long-term treatment (mean follow-up 36 months, range 14-56 months) with Anakinra in 5 pediatric patients.
CONCLUSIONS: The less severe effect of the R92Q mutations was confirmed by the milder impact of the disease on many aspects of health-related quality of life, that was much more severely affected in patients with structural TNFRSF1A mutations

P 222
Tuberculosis in children with SLE from Cape Town, South Africa

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INTRODUCTION: Patients with SLE are at increased risk from infectious diseases and have a higher morbidity and mortality from infections than the general population. In addition, immunosuppressive and immunomodulatory therapies used in the treatment of SLE exacerbates the risk of and complications from infection. The Western Cape region of South Africa has a particularly high incidence of tuberculosis.
AIM: We report a series of 3 patients who contracted tuberculosis at various stages of their disease and treatment at the Red Cross Children's Hospital in Cape Town.
RESULTS: Three cases of TB were diagnosed from a cohort of 26 Paediatric SLE patients at our hospital (11%). The most prominent symptom at presentation in all three was weight loss. All the patients had been treated with Prednisone, Cyclophosphamide and Azathioprine. one also had 4 doses of Rituximab. The patient who had Rituximab early on in her course developed TB after 7 months. She was also the patient with the most complicated course, requiring 21 months of treatment due to recurrence, despite recurrent repeated culture evidence that the organism was sensitive to Rifampicin and Isoniazid. None of the patients had previous TB contacts or evidence of TB exposure at presentation with SLE. Only one patient had a positive PPD upon presentation with TB. In 2 cases TB was confirmed by culture. None of the patients had INH prophylaxis prior to developing TB.
DISCUSSION: Patients with pSLE in the Western Cape are at risk for infection with mycobacterium tuberculosis. In addition to the disordered immunity of SLE,immunosuppressive therapy is likely to play a role in their susceptibilty to infection. The most severe and complicated case of TB, with the earliest onset, was possibly related to Rituximab exposure. This association has not previously been reported in children with pSLE. INH prophylaxis should be strongly considered in areas where TB has a high incidence.

P 223
Efficacy and safety of treatment with Infliximab in patients with early Oligo- and Polyarticular Juvenile Idiopathic Arthritis

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OBJECTIVE: To evaluate the efficacy and safety of adalimumab in patients with Juvenile idiopathic arthritis (JIA).
METHODS: 28 children (21 girls, 7 boys) diagnosed with different subtypes of JIA participated in the study. 14 patients had polyarthritis; 8 – oligoarthritis, 6 - enthesitis related arthritis. The average age was 9.4±2.3 years; disease duration was 4.2±2.9 years. Before adalimumab therapy 5 patients received methotrexate, 9 patients - methotrexate in combination with cyclosporine, 5 children received oral glucocorticoids, and 12 - infliximab. Adalimumab was administrated to all patients by subcutaneous injection at dose 40 mg every 2 weeks during 9 months. Adalimumab use was approved by the Local Ethics Committee. The efficacy of the therapy was measured by DAS28 score and ACR-pedi criteria.
RESULTS: Before adalimumab therapy the number of active joints was 3.6±3.2, ESR - 29±19,1 mm/h, CRP level – 2.1±1.4 mg/%, CHAQ – 1.4±0.8. 5 (28) patients had a very active disease (DAS28 > .1), 19 (28) had moderate disease (5,1>DAS28>3,2), 4 (28) patients had low disease activity (3,2>DAS 28>2,8). After 28 weeks ESR, CRP levels normalized in 78% patients, only 3 patients had active joints, CHAQ was 0,15±0,09 ($p<0,001$). After 40weeks of adalimumab therapy the remission was reported in 69% (11 of 16) patients (DAS28 <2.8), good effect was obtained in 5 (16) of patients (DAS28 <3.2). ACR-pedi70 response had been achieved in 7 (16) patients, ACR-pedi50 response- in 11 (16) patients. Adalimumab wasn`t discontinued due to inefficacy and secondary inefficacy. Severe reactions requiring treatment discontinuation weren`t observed.
CONCLUSION: Thus, our results indicate that adalimumab results in earlier clinical improvement for children with JIA refractory to methotrexate, cyclosporine, infliximab.

P 224
Yersinia pseudotuberculosis infection disrupts the intestinal barrier and enables systemic translocation of Yersinia and bacteria from the gut flora in mice

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INTRODUCTION: Reactive arthritis is associated to specific urogenital or enteropathogenic bacteria including the enteropathogen Y. pseudotuberculosis. In patients with arthritis, bacterial antigens seem to proliferate throughout the body.

Yersinia antigens and Yersinia DNA have been detected in the joints of patients. However, how the bacteria manage to translocate from the gut is currently poorly understood.
AIMS: Here we investigate the effect of Y. pseudotuberculosis on the intestinal permeability and bacterial translocation ex vivo and in vivo in a mouse model.
MATERIALS AND METHODS: Translocation of nonmetabolizable fluorescein-isothiocyanate-labelled dextran (4kDa or 40 kDa), as well as translocation of heat killed fluorescent E. Coli through Peyer's patches (PP) and PP-free ileum from C57BL6 mice was studied ex vivo using Ussing chambers. For in vivo experiments, mice were intragastrically infected with 1x107CFU Y. pseudotuberculosis. Serum concentrations of nonmetabolizable 40 kDa Dextran and bacterial counts of Y. pseudotuberculosis and commensal bacteria in PP and spleens were measured at day 1, 2 and 5.
RESULTS: Ex vivo, Y. pseudotuberculosis increases the paracellular, transcellular permeability and translocation of E. coli through Peyer's patches and ileum. A similar increase of the intestinal permeability was found in vivo after oral infection. Furthermore, at day 2 of infection systemic translocation was found not only for Y. pseudotuberculosis but also for bacteria from the gut flora.
CONCLUSIONS: These results show ex vivo and in vivo that Y. pseudotuberculosis disrupts the intestinal barrier function and provide a mechanistic of how Yersinia may arrive in the joints. Furthermore, the fact that Yersinia infection also enables the translocation of commensal gut bacteria opens the possibility that Yersinia-associated reactive arthritis to may be triggered by bacteria other than Yersinia.

P 225
Physiotherapy management of children with hypermobility: a review of an out patient self management exercise programme

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BACKGROUND: The recognition of hypermobility in the paediatric population has increased and common complaints associated with this are pain and fatigue. Great Ormond Street Hospital UK, has implemented a self management exercise programme, which is specific and progressive to key muscle groups. It utilises open chain exercises with high repetitions (30) and low weights (0.5-2.5kg), in order to manage these patients from an outpatient-based clinic.
OBJECTIVES: To establish whether this specific muscle training programme can be effectively used in the paediatric hypermobile population, to increase muscle strength, decrease pain and improve overall function.
METHOD: A retrospective case note review of children who had attended the hypermobility out-patient service between Nov 2009 and March 2010 was completed (comparing 1st and 2nd appointments between these dates). Assessments of muscle strength, school attendance and Childhood Health Assessment Questionnaire (CHAQ), parental visual analogue scale (VAS) of general well being and pain VAS were collected on all children. All children were provided with an exercise programme at the initial assessment, based on 4-5 key exercises, focusing on increasing repetitions and weights. An excel database was used to compile findings.
RESULTS: Data from 20 children (10Male:10Female) who had already been diagnosed with hypermobility (beighton score of >4/9), was collected. The mean age was 11 years (range 5-16 years). The primary complaints within the cohort were of pain and fatigue longer than 6 months in duration. School attendance for all but one patient was 100%.
On initial assessment the mean muscle strength score was 3.5/5 (oxford manual muscle score) in hip abductors, hip extensors and inner range quadriceps (range 2.5-5) and 7.25/10 repetitions for plantar flexors (range 2-10). At 8-12 week follow up, all children were completing 30 repetitions and using an average weight of 1.5kg (range 0.5-2.5kg). There was an average increase in muscle strength of hip abductors (60%), hip extensors (70%), inner range quadriceps (55%) and plantar flexors (40%).
The average score of the CHAQ on assessment was 1.15/3, pain VAS was 4.6/10cm and parental VAS of general well being 3.9/10cm (10=most unwell).There was a 60% decrease in the score of CHAQ between visits. Pain and parental VAS diminished by 55% and 45% respectively. All parents reported an improvement in fatigue.
CONCLUSION: The use of a specific progressive muscle strengthening programme using open chain exercise, with high repetitions and low weights has been shown to increase muscle strength, improve overall function and decrease pain in children with hypermobility. It is therefore considered to be an effective method of managing hypermobile children with in an outpatient clinic.

P 226
Pain, fatigue and poor school attendance in young patients with Chronic Musculoskeletal Pain related to Hypermobility

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BACKGROUND: The debilitating impact of pain on children and adolescents' daily functioning has been well established in chronic pain research. Recent studies have further focused on the way in which pain levels correlate with school impairment. Researchers have yielded mixed results, fostering a need for further investigative studies.
OBJECTIVES: To investigate the relationship between pain variables, fatigue and physical functioning related to school attendance in a cohort of children with hypermobility.
METHODS: Children who attended a multidisciplinary musculoskeletal pain assessment clinic in 2009 completed a range of measures including visual analogue score relating to pain and general well-being, function, muscle strength and the Childhood Health Assessment Questionnaire (CHAQ) and these were correlated with school attendance and reported reasons for non-school attendance.
RESULTS: Results were collected on 200 children whose age ranged from 5–16 years (mean 8.47years). 40%were male. In this cohort 28% reported missing at least 1 day a week from school due to symptoms related to their hypermobility. This is significantly higher than the national average of 7.4%. Of those missing school 81% reported pain and 64% reported fatigue as the reason for not attending. Missing school strongly correlated with objective measures of muscle weakness (Pearson Correlation .993, p <.005) however there was no statistically significant correlation with the CHAQ score or the pain VAS.
CONCLUSIONS: Parents report the main reasons for reduced school attendance are pain and fatigue however this does not correlate to the intensity of pain reported. Though loss of muscle strength is positively associated with poor school attendance, reduced levels of general function were not. More research is required to fully explore the multiple reasons behind the poor school attendance including symptom coping strategies and parental anxiety in relation to children and adolescents with hypermobility.

P 227
Efficacy of TNF-alpha inhibitor treatment of Juvenile Idiopathic Arthritis in eastern Denmark – preliminary results

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OBJECTIVE: To evaluate efficacy of treatment with TNF-α inhibitors in Juvenile Idiopathic Arthritis (JIA).
METHOD: Children with JIA in eastern Denmark with insufficient effect of or severe adverse events to MTX treated with TNF-α inhibitor.
In the present data, the majority of patients began TNF-α inhibitor treatment with Etanercept. A minority began treatment with Adalimumab or Infliximab, and these drugs were furthermore used in Etanercept failures. The patients have been followed with visits approximately every 3-month and scored according to the Pediatric ACR-criteria.
Patients with insufficient effect or severe adverse effects to one of the TNF-α inhibitors were changed to another TNF-α inhibitor. These patients were registered as having not achieved ACR 30/50/70 at the following visits.
The results from patients that did not achieve the full 3 years of treatment because of lack of time, where included in the results. If single ACR-criteria were missing, data have been carried forward, if it was present at the last visit.
RESULTS: 113 patients were treated with Etanercept. 42 patients with Infliximab and 71 patients with Adalimumab. 20 patients were treated with Etanercept for the full 3-year period, 2 patients with Infliximab, 2 patients with Adalimumab. 62 patients in the Etanercept group did not achieve the full 3-year treatment because of the lack of time, 28 patients from the Infliximab group and 58 patients in the Adalimumab group. 31 patients in the Etanercept group were changed to other treatment, due to lack of effect or severe AE, 12 patients in the Infliximab group and 11 patients in the Adalimumab group. ACR 30, ACR 50 and ACR 70 results are shown in graph 1,2,3. Each TNF-a inhibitor is shown separately.
DISCUSSION AND CONCLUSION: Etanercept seems to be superior compared to adalimumab and infliximab. Both the immediate effect and the long-term effect were greater in this group.
The efficacy of Infliximab and Adalimumab were surprisingly low. One reason could be that a large part of JIA patients treated with these drugs were Etanercept non-responders. Other explanations could be that we register patients that drop out of treatment, because of lack of efficacy or severe adverse events, as not reaching ACR 30/50/70 and lastly that some patients did have relatively few symptoms at initiation of the TNF-α inhibitor, thus the comparative ACR30/50/70 will not show as strong an effect.
For all three TNF-α inhibitors we found decreasing efficacy over time.
The current data however are preliminary and before any definite conclusion the data has to be studied intensively.

P 228
Intravenous ibandronate injections for osteoporosis treatment in children with rheumatic diseases

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OBJECTIVE: To evaluate the efficacy and safety of intravenous ibandronate injections for osteoporosis treatment in children with rheumatic diseases
PATIENTS AND METHODS: 21 children (7 boys and 14 girls) with rheumatic diseases and osteoporosis were enrolled in the study: 9 children with juvenile idiopathic arthritis, 4 - with arthritis related spondylitis, 4 - with systemic lupus erythematosus, 2 - with systemic sclerosis, 1 -with dermatomyositis and 1 - with juvenile polyarteritis. Mean age of patients was 14,5 (14;16) years, disease duration was 4,5 (3; 6,5) years. All children were treated with combined immunosuppressive therapy. 18 children were treated with steroids. All children were given intravenous ibandronate injections (2 mg every 2 months) with calcium (500 mg) and vitamin D (400 IU). The main outcome measures were changes in lumbar spine (Z-score index examined by dual-energy X-ray densitometry) and serum C-telopeptide level (a marker of bone resorption). The duration of treatment by ibandronate was 12 months.
RESULTS: Prior to treatment all patients had abnormally low bone mineral density (z-score index -4,5 SD), 14 patients had vertebral fractures. Post-treatment z-score index increased to -3,5 SD (p<0,05), no new vertebral fractures were reported. At 1 year serum C-telopeptide level increased significantly (from 14,25 to 10,9 nmol/ml, p <0,01). Treatment-related flu-like illness was reported in 1 patient. 4 patients had transient hypocalciemia.
CONCLUSIONS: Ibandronate may be safe and useful for osteoporosis treatment in children with rheumatic diseases.

P 229
Decreased pain threshold in Juvenile Idiopathic Arthritis: a cross-Ssctional study

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BACKGROUND: Pain is a primary symptom in juvenile idiopathic arthritis (JIA). Some children even report severe pain despite low disease activity. Dealing with this group of patients is a challenge for the health care system. Recent studies in this area are scarce, and more knowledge is needed to improve the treatment of pain in these children.
OBJECTIVES: To assess the pain threshold in JIA compared with a healthy control group in a cross-sectional study.
METHODS: We included 58 children with JIA born 1995 to 2000 admitted to the pediatric rheumatology clinic. 91 age and sex-matched healthy school children served as a control group. The instrument used for testing was a digital pressure algometer and the pain threshold was measured on 17 symmetric, anatomically predefined joint- or bone-related spots. Prior to testing, all children were asked to complete three short questionnaires (Pain Coping Questionnaire, Functional Disability Inventory, Pediatric Quality of Life Inventory Scale) and to rate their current pain on a VAS. Furthermore, parents were asked to complete a parent version of the CHAQ. Clinical data were registered on children with JIA.
RESULTS: The proportion of females was higher in both groups (JIA: 72.4%; controls: 60.4%) and the age distributions were similar (mean age JIA: 11.95 years ± 1.77; controls: 12.24 years ± 1.93). Among the JIA patients oligoarticular onset (22 children = 38%) and polyarticular onset (20 children = 34%) were the most common subtypes, and the average disease duration was 68.93 months ± 44.79. The pain threshold was significantly lower among children with JIA (mean range for the anatomical area with the lowest threshold was 0.59±0.36, and 1.78±1.03 for the area with the highest threshold) when compared with the healthy control group (mean range: 0.80±0.39 to 2.40±0.98, respectively) in all areas measured, including negative control areas that are normally unaffected in JIA (p=0.0001 to 0.005). These results remained the same after adjusting for active joints in children with JIA. Overall, pain threshold was substantially higher in males than in females in both groups (p<0.0001), but we found no difference between age groups in 15 of 17 areas. The interaction effect of gender and the two groups on the level of pain threshold did not reach statistical significance; neither did the interaction effect of age groups and the two groups. Furthermore, we found no correlation between current pain experience, disease duration, and pain threshold.
CONCLUSIONS: Children with JIA had a substantially lower pain threshold even in areas usually unaffected by arthritis. These findings suggest that JIA alters the pain perception and causes decreased pain threshold. Earlier and more aggressive treatment of pain symptoms in these children may prevent future alteration of the nervous system, but further studies in this area are needed.

P 230
Glucocorticoid receptor gene polymorphism and juvenile idiopathic arthritis

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BACKGROUND: The glucocorticoid receptor (GCR) gene has been suggested as one of candidate genes to contribute to juvenile idiopathic arthritis (JIA) course and prognosis. The purpose of this study is to investigate the polymorphism of BclI glucocorticoid receptor gene in JIA patients and the gene's role in susceptibility to juvenile idiopathic arthritis and associations with JIA activity, course and bone mineralization.
METHODS: One hundred and twenty two Caucasian JIA children and 143 healthy ethnically matched controls were studied. We checked markers of clinical and laboratorial activity: morning stiffness, Ritchie Arthicular Index (RAI), swollen joints count (SJC), tender joints count (TJC), physician's visual-analog scale (VAS), hemoglobin level (Hb), leucocytes (L) and platelets (Pl) number, Westergren erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), albumin levels, DAS and DAS28. Bone mineralization was detected by dual-energy X-ray absorptiometry (DXA) of lumbar spine L1-L4 (densitometry Hologic QDR 4500C with reference pediatric database). Assessment of bone metabolism included osteocalcine, C-terminal telopeptides (CTT), parathyroid hormone (PTH), total and ionized calcium, inorganic phosphate and total alkaline phosphatase (TAP). BclI polymorphism was genotyped by polymerase chain reaction restriction fragment length polymorphism.
RESULTS: No association with GCR polymorphism was revealed with JIA patients and controls. In JIA girls, G allele presence was associated with an unfavorable arthritis course, a younger age of onset of arthritis (0.0017), and higher inflammatory activity. The higher inflammatory activity was demonstrated by: increased time of morning stiffness (p=0.02), VAS (p=0.014), RAI (p=0.048), DAS (p=0.035), DAS28 (p=0.05), Pl (p=0.003), L (p=0.046), CRP (p=0.01) and bone metabolism disturbances: decreased BA (p=0.0001), BMC (p=0.00007), BMD (0.005) and Z score (p=0.002), higher levels of osteocalcine (p=0.03), CTT (p=0.036), TAP activity (p=0.01) and Ca++(p=0.017). In JIA boys there were nothing significant disturbances due to polymorphic genotypes and alleles.
CONCLUSIONS: The allele G and genotype GG of the GCR may be one of the molecular patterns to contribute to unfavorable arthritis course and low bone mineral density in JIA.

P 231
Bone metabolic molecular markers and juvenile idiopathic arthritis

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BACKGROUND: The system of vitamin D and its active metabolites involve in immunologic regulation, calcium and phosphorus absorption, bone mineralization and calcium-phosphorus homeostasis. Biologic effects of vitamin D depend on functional activity of its receptor. Today several single nucleotide polymorphism were detected in vitamin D receptor gene (VDR), which involved in VDR functional activity. Multiply interactions between VDR gene polymorphism and immunological, oncology and bone mineralization disturbances were shown in previous studies. Also part of juvenile idiopathic arthritis (JIA) patients have signs of collagenopathy and we suppose about role of collagen genes polymorphism in JIA pathogenesis.
OBJECTIVES: The aim of our study was to detect an association between such molecular markers as TAGI and CDX2 vitamin D receptor gene polymorphism, alpha 1 chain of collagen type 1 (COL1A1) gene Sp1-binding site polymorphism and PCOL2 polymorphism and JIA course and bone mineralization in JIA patients.
METHODS: We included 192 children with JIA, 81 boys and 111 girls. The mean age was 11.22±4.43 years.
In all children we detected clinical and laboratorial arthritis activity parameters, such as the time of morning stiffness, visual activity score (VAS), Ritchie arthicular index (RAI), tender and swollen joints count, DAS, DAS28, Shteinbroker index, C-reactive protein (CRP), albumin, α2- and γ-globulins, platelets and leucocytes count, erythrocyte sedimentation rate (ESR).

Bone mineralization of lumbar spine (L1-L4) was detected by dual-energy X-ray absorbtiometry with pediatric referral database. Low bone mineral density for chronological age was detected in 22,7% children, 18,5% of girls and 29,3 of boys.
Bone metabolic markers, such as total Ca, Ca++, phosphorus, Ca/P and Ca++/P ratios, total alkaline phosphatase, osteocalcine, C-terminal telopeptides and parathyroid hormone also were detected in our patients.
Molecular testing of studied molecular markers was carried out by PCR-RFLP.
RESULTS: Girls with GG genotype of Sp1 COL1A1 polymorphism had lower ESR (p=0.01), platelets (p=0.03), higher Hb (p<0.05) and Ca/P ratio (p=0.03) compare to girls carrying T allele (GT and TT genotypes). Boys with GG genotype had lower RAI (p=0.04), VAS (p=0.02) and DAS (p=0.04) than boys carrying T allele. Girls with GG genotype of the PCOL2 COL1A1 polymorphism had lower Ca/P (p<0.05) and Ca++/P ratios (p<0.05) compare with girls, carrying T allele (GT and TT genotypes). Boys with GG genotype had lower albumin (p<0.05) and higher platelets (p=0.04), PTH (p<0.05) and γ-globulins (p=0.03) than boys carrying T allele.
We didn't reveal differences in polymorphic TagI and Cdx2 alleles and genotypes distribution of VDR gene between children with normal and low BMD. Girls with TT genotype of TagI VDR had lower BA (p=0,05), BMC (p=0,044), BMD (p=0,05) compare with girls, carry C allele (genotypes TC and CC). Boys with GG genotype of Cdx2 had lower Ca (p=0,003), albumin (p=0,044) and higher CRP (p=0,048) and α2-globulins (p=0,016) than girls carry allele A (genotype GA and AA). Girls with GG genotype of same gene had higher ESR (p=0,03), Ca/P relation (p=0,03) and PTH (p=0,026). In our study we've revealed association between polymorphic genotypes of VDR gene and inflammatory activity, low bone mineralization.
CONCLUSIONS: We have detected differences in bone mineralization, methabolism and course in JIA children with polymorphic genotypes.

P 232

Use of adalimumab in juvenile idiopathic arthritis-associated refractory uveitis: efficacy in ocular disease – a retrospective case series

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BACKGROUND: Juvenile idiopathic arthritis (JIA) – associated uveitis is a potentially sight-threatening complication occurring in 8-30% of children with JIA. [1] In a proportion of patients, uveitis is refractory to topical and systemic steroids and first line immunomodulatory treatment. Adalimumab, a fully-humanised monoclonal antibody to tumour necrosis factor (TNF)-α, has been used to treat uveitis in JIA although no controlled trials have been performed to date.
OBJECTIVE: To assess the efficacy of adalimumab in treatment of JIA-associated refractory uveitis.
METHODS: To assess efficacy a retrospective review of the case notes was performed in patients with JIA-associated uveitis refractory to steroids who were treated with adalimumab for 15 months or more. Data including visual acuity, markers of ocular inflammation, joint inflammation and concomitant medications were recorded on a set proforma in the clinics at least every 3 months. Side effects and adverse events were also noted routinely.
RESULTS: Eight patients (5 female, median age 9.5 years at commencement of adalimumab) from a single regional centre were included. All received fortnightly doses of subcutaneous adalimumab (20 or 40mg dependent on weight). Six patients had previously received an anti-TNF agent (five infliximab, one etanercept) and were changed to adalimumab because of failure to control uveitis and/or arthritis. Seven continued on maintenance methotrexate (MTX) and six also received mycophenolate mofetil (MMF) in addition to MTX during part or all of the study period. Of 16 eyes, 31% had visual acuity of 6/15 or worse prior to starting adalimumab. This had decreased to 6% at 12 months following commencement of the medication. Using Standardised Uveitis Nomenclature (SUN) criteria [2] for anterior chamber cells, at 12 months after starting adalimumab, 44% of eyes (n=16) had improved, 25% had stable inflammation and 6% had worsened while 25% had no inflammation at any time. Improvements were seen in all eyes with vitreous haze and cystic macular oedema by follow-up 6 months after starting adalimumab. Two patients during adalimumab therapy required courses of oral steroids for uveitis and one patient for arthritis. One eye received orbital floor injection of steroids and one patient required intra-articular steroid injections for worsening arthritis. Due to varicella zoster infection, adalimumab was temporarily stopped in one patient. Three patients reported injection site reactions, in one case lasting up to one week.
CONCLUSIONS: In this group of children with refractory JIA-associated uveitis, use of adalimumab was associated with improvement in visual acuity and improving or stable ocular inflammation. However, it did not completely obviate the need for systemic or periocular steroid treatment. Prospective randomised controlled trials are required to help determine which subset of patients may benefit from adalimumab and the duration of treatment.

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P 233

Subtype specific association of IL23R with Juvenile Psoriatic Arthritis and ERAP1 with Enthesitis Related Arthritis (ERA)

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ABSTRACT: Background: There is now strong evidence supporting the hypothesis of common autoimmune susceptibility loci. There is also evidence to support clustering of loci in diseases that share similar clinical phenotypes e.g. Ankylosing spondylitis (AS), psoriasis (Ps), psoriatic arthritis (PsA) and they appear to have some overlapping susceptibility loci such as IL23R and ERAP1.
Juvenile idiopathic arthritis (JIA) is an umbrella term for all chronic childhood arthropathies and can be classified into 7 subtypes on the basis of features present in the first 6 months of disease. It includes the enthesitis related arthritis (ERA) subtype which displays symptoms similar to AS and juvenile onset psoriatic arthritis which has similarities to psoriatic arthritis and psoriasis. We therefore hypothesized that the two well-established susceptibility loci IL23R and ERAP1 could also confer susceptibility to these JIA subtypes, to this end the most associated SNP within each of these genes have been selected for genotyping across all JIA and also analysed stratified for each subtype.
METHODS: SNPs in IL23R (rs1129026) and ERAP1 (rs30187) were genotyped in JIA cases (n=1054) and healthy controls (n=2390). The numbers genotyped per ILAR subgroup were: Systemic onset (n=165), persistent oligoarthritis (n=276), extended oligoarthritis (n=143), Rheumatoid factor (RF) negative polyarticular JIA (n=208), RF positive polyarticular JIA (n=67), enthesitis related JIA (n=64), psoriatic JIA (n=74) and unclassified (n=57).Genotype and allele frequencies were compared between all JIA cases and controls using the Cochrane-Armitage trend test implemented in PLINK and allelic odds ratios (ORs) and their 95% confidence intervals (CIs) calculated. Stratified analysis by subtype was performed.
RESULTS: Neither the SNP in the IL23R gene, rs1129026, nor the SNP in the ERAP1 gene, rs30187, were significantly associated (p<0.05) with the total JIA dataset. Stratification by subtype found that the IL23R SNP showed significant association in the psoriatic arthritis subtype (ptrend=0.04 OR 0.4 95% CI 0.16-0.98) and a trend towards association in the enthesitis related subtype (ptrend=0.15 OR 0.52 95% CI 0.21-1.28). The enthesitis related arthritis (ERA) subtype showed strong association with ERAP1 SNP (ptrend=0.004 OR 1.69 95% CI 1.17-2.43).
CONCLUSIONS: We present evidence for subtype specific association of the IL23R gene with juvenile psoriatic arthritis and ERAP1 gene with ERA. The findings will require validation in independent JIA datasets. These results suggest distinct pathogenic pathways in these subtypes.
ACKNOWLEDGEMENTS: Childhood arthritis prospective study (CAPS), UKRAG consortium and BSPAR study group

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Development and initial validation of the Patient's/Parent's Acceptable Symptom State for Juvenile Idiopathic Arthritis: a new ambitious target for disease management

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BACKGROUND: The patient's and parent's acceptable symptom state (PASS) constitute the symptom threshold beyond which patients and parents consider juvenile idiopathic arthritis (JIA) patients' health status as satisfactory. The PASS represents an ambitious target for disease management.
OBJECTIVE: To develop and validate the patient's (PASS-Child) and parent's (PASS-Parent) acceptable symptom state for the whole JIA and for select disease categories.
METHODS: 578 parents and 340 patients completed a multidimensional questionnaire (the JAMAR), which includes the Juvenile Arthritis Functionality Scale (JAFS) (score 0-30), the Pediatric Rheumatology Quality of Life Scale (PRQL) (score 0-30) and the other traditional JIA outcome measures, and stated whether they considered the status of the patient satisfactory or not. Patients were classified into the main 3 ILAR categories of JIA (oligoarthritis, polyarthritis, and systemic arthritis) based on their clinical features and number of affected joints during disease course. Patients with enthesitis-related arthritis, psoriatic arthritis or undif-

ferentiated arthritis were classified as oligoarthritis or polyarthritis depending on whether they had less or more than 5 affected joints, respectively.
PASS-Child and PASS-Parent thresholds were computed targeting the 75th percentile of cumulative distribution in children and parents who declared themselves as satisfied with the outcome of the illness. PASS-Child and PASS-Parent were validated by analyzing the proportion of patients who were judged by the patients themselves or the parents in remission, flare or continued activity.
RESULTS: 269 (68%) children and 474 (66%) parents reported being satisfied with illness outcome. The table shows the PASS-Child and the PASS-Parent for the whole JIA and the different ILAR categories.
Among patients judged in remission, flare or continued activity by the patients, the percentage of those in PASS-Patient was 92, 37 and 41% ($p<0.0001$). Among patients judged in remission, flare or continued activity by the parents, the percentage of those in PASS-Parent was 97, 46 and 37% ($p<0.0001$).
CONCLUSION: We identified the symptom threshold beyond which children with JIA and their parents consider the child's health status as satisfactory. The PASS demonstrated good validity by discriminating strongly between patients in remission or active disease. The PASS-Child and PASS-parents should be included among the clinical measures used to asses the therapeutic response in future JIA clinical trials.

P 235
Effectiveness of Dexamethasone Iontophoresis in Temporomandibular Joint (TMJ)-Arthritis in Juvenile Idiopathic Arthritis (JIA)

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BACKGROUND: TMJ-arthritis is common in JIA and the best treatment approach is unknown. The effectiveness of dexamethasone iontophoresis, a non-invasive method of transdermal steroid administration, has not been evaluated for TMJ-arthritis in JIA.
OBJECTIVE: Evaluate the effectiveness of dexamethasone iontophoresis for the treatment of TMJ-arthritis in JIA.
METHODS: Medical records of all JIA patients who underwent TMJ iontophoresis at Cincinnati Children's Hospital from 1997-2010 were reviewed. Effectiveness was assessed by comparing primary outcomes (i.e. inter-incisor distance and lateral translation) and secondary outcomes (pain, clicking and crepitus) before and after treatment using two-sided paired t-test.
RESULTS: There were 28 JIA patients (all subtypes; median age ± IQR = 12±8 years) who received TMJ iontophoresis. At baseline (median ± IQR) the number of active joints was 3±4 and ESR was 5±7. Medications included methotrexate (29%), biologics (25%) and NSAIDS (53%), with no clinically relevant medication-change during the treatment period. Iontophoresis was done using a standard dose of dexamethasone (6 mg) per TMJ per session (average number of sessions = 8, 45% bilateral). Statistically significant improvement was observed in the inter-incisor distance and right lateral translation (**see Table 1**). Improvement in TMJ pain (70%), clicking (80%) and crepitus (40%) were noted in those who initially presented with these findings. Side effects reported were transient and included site erythema (46%) and metallic taste (27%). Imaging with MRI was available only in select number of patients and thus not useful as study endpoint.
CONCLUSION: Dexamethasone iontophoresis appears to be effective in the management of TMJ-arthritis in JIA. Because of its ease of use and relative lack of side effects, it may be a good initial therapy for TMJ-arthritis and thus warrants prospective evaluation with focus on durability of response, imaging outcomes and optimization of treatment protocol.

P 236
An analysis of the costs and treatment success of etanercept in Juvenile Idiopathic Arthritis

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OBJECTIVE: To analyze and report the costs and effects of etanercept therapy in patients with Juvenile Idiopathic Arthritis (JIA).
METHODS: Forty-nine JIA patients were evaluated by means of the JIA core set at start of etanercept, and after 3, 15 and 27 months of therapy. At the same time points parents of the patients were asked to complete the Health Utility Index mark 3 (HUI3). Direct medical costs were collected during one year before and 27 months after start of etanercept and associated with gain in utility.
RESULTS: Mean total direct medical costs after start etanercept were on average 12,318 euro per patient per year compared to 3,695 euro in the year before start. The cost analysis showed that three quarters of total direct medical costs originated from etanercept itself. Other direct medical costs, such as costs concerning hospitalization and concomitant medication, decreased compared to the costs in the period before start of etanercept. Especially a great reduction in frequency of visits to the outpatient clinic was seen. Utility was 0.53 before start of etanercept, according to the multi-attribute utility function of the HUI3 on a scale from 0 (dead) to 1 (perfect health). After 27 months utility was 0.78, which is a utility gain of 0.25. In accordance, also all JIA core set response variables improved significantly over 27 months of etanercept treatment.
CONCLUSIONS: Although the costs of etanercept therapy are substantial, the gain in utility is even more impressive. Considering that these JIA patients were previously refractory to conventional treatment, and at risk for long-time disability and pain, costs are justifiable.

P 237
Long term follow-up of patients with PFAPA syndrome followed in two tertiary national referral Centers

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INTRODUCTION: PFAPA syndrome is a common cause of periodic fever during early childhood. Few information are available on the long term follow-up of this condition.
Aim of the study is to describe the long term-follow up of patients fulfilling PFAPA criteria not carrying mutations in MVK, MEVF and TNFRSF1A genes or with a low risk of being affected by a monogenic periodic fever.
PATIENTS AND METHODS: PFAPA patients referred to the paediatic reumatology centers of two national referral centers were enrolled from 2002 to 2010. Diagnosis was made according to current clinical criteria (Thomas et al 1999). Monogenic periodic fevers were excluded by mean of genetic analysis or, from 2008 onwards, on the basis of a low risk at the "Gaslini diagnostic score" (www.printo.it/periodicfever). Baseline clinical informations were collected at the first visit and at last follow-up.
RESULTS: The data on 157 consecutive PFAPA patients (54% males, 46% female) were collected. The mean age at onset of the disease was 20 months (range: 1 month – 5 years). The mean follow-up was 4,6 years (range: 6 months – 8 years). In 48 patients (31%) the disease resolved spontaneusly during the follow-up period (mean duration of disease: 3,7 years). 42 patients (27%) reported an improvement of the disease (reduction of fever episodes from baseline higher that 30%). In 25 patients (16%) disease course didn't change in term of frequency and severity of fever attacks, while in 7 patients (4%) fever episodes recurred more frequently during the last 12 months of follow-up. In 35 patients (22%) tonsillectomy completely resolved the fever attacks. However in 11 patients tonsillectomy did not change the course of the disease, while in 2 patients it just reduced the frequency of fever episodes.
CONCLUSIONS: This long-term follow-up study confirms the general good prognosis of PFAPA syndrome. The surgical treatment is generally effective in resolving fever attacks. However in a relevant group of patients (up to 20%) fever attacks still persist, even after surgical treatment. The study of this latter cohort of patients may unravel new monogenic autoinflammatory disorders.

P 238
Clinical Characteristics of children carrying yhe hypomorphic V198M mutation of NLRP3 gene

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INTRODUCTION: The V198M mutation is described as a possible hypomorphic variant of the NLPR3 gene. The impact of this mutation in childhood is still largely unknown.
Aim of this study: to analyse the prevalence of V198M mutation in children with a clinical history suggestive for CAPS and to describe the clinical and laboratory findings of patients carrying this mutation.
METHODS: From 2002 the molecular analysis of the NPLR3 gene was performed in 259 patients with a clinical history suggestive for CAPS. In order to estimate the pravalence of the mutations of this gene in the healty population 98 healthy individuals were also analyzed for the same mutation.
RESULTS: The V198M mutation was found in 6 screened patients: four were heterozygous for the mutation only. In one patient with a typical MWS phenotype the

V198M variant was associated with the D303N mutation of the same gene. In a latter patient a low-penetrance mutation of TNFRSF1A gene (P46L) was also found. Out of the 4 patients heterozygous for the V198M mutation, only two displayed a story of periodic fever associated with urticarial rash, arthralgia and transient arthritis, associated with elevation of acute phase reactants and responding to steroid treatment at demand. In other two patients the clinical picture was mild and uniquely characterized by urticarial rash and arthralgia, often induced by cold, but not associated with elevation of acute phase reactants. The patients carrying the P46L mutation of TNFRSF1A gene presented periodic fever with athralgia and headache, not associated with elevation of acute phase reactants.
Treatment with IL-1 blockers (Anakinra at the staring dosage of 1 mg/kg) was used in 2 patients, one heterozygous for V198M and one compound heterozygous for V198M and D303D, with a rapid a complete control of the clinical manifestations.
None of the healthy individuals screened for the V198M mutation turned out to be positive.
CONCLUSIONS: This study confirm in childhood the low-penetrance of the V198M mutation of the NLPR3 gene. However a minority of these patients may present a clinical phenotype consisting with a CAPS, thus requiring treatment with IL-1 blockers.

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Behçet's disease in the differential diagnosis of multiple sclerosis: a pediatric case

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A 14-year-old girl was admitted to pediatric neurology department with headache, vertigo, and lomber pain. She was first admitted to another center one year ago with headache and brain magnetic resonance imaging (MRI) showed a 2 cm-demyelinating plaque in the frontal lobe. Then, she was diagnosed as "multiple sclerosis (MS)" and was given steroid therapy. Repeated MRI demostrated that the demyelinating plaque remained unchanged and active. CSF IgG index was 0.85 and oligoclonal band was negative. ESR was 45 mm/h, ANA (-), ANCA (-), C3 and C4 were in normal ranges. She was thought to have the second MS attack and given pulse steroid therapy. She was consulted to pediatric rheumatology because of high acute phase reactants and lomber pain. Her past medical history revealed recurrent oral and genital aftous lesions. Her mother had recurrent oral-genital ulcers, acneiform skin lesions and artthralgia. The HLA B51 was positive both in patient and mother. The mother was consulted to adult rheumatology and was diagnosed as "Behçet's disease". Patergy test was negative under steroid therapy and ophtalmologic examination was normal. Plain X-rays revealed sacroiliitis and spondilitis, MRI also confirmed these findings. She was diagnosed as "Behçet's disease". Methotrexate and sulphasalazine were added to steroid therapy.
This case was presented to keep in mind Behçet's disease in the differential diagnosis of multiple sclerosis.

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Characteristics of children with Juvenile Dermatomyositis in the UK and Ireland: a comparison of children with onset of symptoms before or after their fifth birthday

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BACKGROUND: Juvenile Dermatomyositis (JDM) is the most common of the childhood idiopathic inflammatory myopathies. Experts in the field have previously suggested that a young age of onset may be associated with poor prognosis.1 Using data from the UK and Ireland Juvenile Dermatomyositis Research Group (JDRG) cohort study we compared children at presentation and at follow up 2 years later by grouping them according to age of symptom onset.
METHODS: Data were collected on children with a diagnosis of probable or definite JDM from the JDRG cohort study. To minimise use of retrospective data, only patients with less than 12mths between diagnosis and registration were included in this analysis. Using data from time of entry to the registry and at 21-36 months later, we compared demographic and clinical features of children who were <5 years old at disease onset with those who were ≥5 years old.
RESULTS: 157 patients were included with a median time between symptom onset and diagnosis of 4 months. 35% were in the younger group with onset of symptoms before their 5th birthday. 77.7% were white, 8.3% black, 6.4% were Indian or Pakistani and 7.6% were of other ethnicity. 38.2% of the younger group were male as opposed to 25.5% of the older group. At presentation there was a trend towards increased arthritis and generalised oedema in the younger group and increased Raynauds and alopecia in over 5s. None of the younger group had arthritis or contractures at 2 year follow up. 2 patients in the older group had arthritis at follow up and 5 had contractures.
Values for CHAQ, CMAS, PGA and parental VAS were similar at follow up for both groups. There was no difference between the groups regarding the presence of rash or number of children still on steroids at follow up. Children in the younger group were more likely to have received cyclophosphamide or anti-TNF therapy although this difference did not reach statistical significance.
DISCUSSION: Our data suggest that there are differences at presentation for patients presenting with JDM at a younger age. In our cohort they include a larger proportion of children who receive cyclophosphamide or anti-TNF therapy. There was no evidence that patients with a young age of onset had a worse outcome at follow up 2 years later than older children: this may reflect the more intensive treatment that they received.
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Vaccinations in pediatric patients receiving DMARDs, glucocorticosteroids or biological therapy: a systematic literature review

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BACKGROUND: The safety and immunogenicity of vaccinations in pediatric patients receiving immunosuppressive therapy have not been systematically reviewed.
OBJECTIVES: To evaluate the safety and immunogenicity of vaccinations in pediatric patients treated with biological therapy, disease-modifying antirheumatic drugs (DMARDs) or glucocorticosteroids (GC).
METHODS: A systematic literature search in Medline (Pubmed) and EULAR/ACR abstracts from 2008/2009 was conducted using several terms for all biologicals, DMARDs and corticosteroids currently used as immunosuppressive drugs. These terms were combined with various terms for vaccination, safety and immunogenicity. Papers were included based on relevance. Experts added additional papers. Studies on patients with malignancy, immunodeficiency or transplantation were excluded. A panel of 13 European experts in the field appraised methodological quality and extracted data using predefined criteria.
RESULTS: 45 papers and 15 abstracts were included on anti-TNFα (25), MTX (18), GC (10), rituximab (6), anti-Il-1 (1), anti-Il-6 (1), and other DMARDs (10) The majority of studies were performed in adult RA and SLE patients, 8 studies included JIA patients.
Most studies were on the influenza (23) and pneumococcal (10) vaccines. MTX lowers responses to T-cell independent polysaccharide pneumococcal vaccine, whereas studies on the effect of anti-TNF blockers on immunogenicity are contradicting. In general, the protection rate after vaccination seems to be similar to patients without anti-TNF blockers. Anti-CD20 therapy generally reduces the responses.
The number of studies on live attenuated vaccines in combination with immunosuppressive therapy was very limited. 6 studies were available on live attenuated vaccines (4 MMR, 1 varicella, 1 yellow fever). During MTX treatment (mean dose ≤15mg/m2/week) MMR vaccination was safe in 55 patients, and varicella vaccination in 25 patients. During anti-TNFα treatment, booster vaccinations of MMR (n=5) and yellow fever (n=17) did not induce severe adverse events or disease flares. In general, GC >2 mg/kg or 20 mg/day for >2 weeks are considered sufficiently immunosuppressive to raise concern about the safety of vaccination with live-virus vaccines. Data on safety and immunogenicity when treating with high dose GC were scarce. Until more data are available, live attenuated vaccines should be avoided in patients on high dose DMARDS, high dose GC or biologicals whenever possible.
CONCLUSIONS: During the use of high dose DMARDs, high dose corticosteroids or biologicals non-live vaccines are safe, whereas live-attenuated vaccines should be avoided whenever possible until more data are available (grade D). Immunogenicity may be reduced in particular in patients on rituximab. Vaccines ideally should be administered before starting on B-cell depleting biological therapy (grade C-D).

P 242
Effects of Methotrexate (MTX) treatment on cytokine profile and gene expression in Juvenile Idiopathic Arthritis (JIA)

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**contributed equally to this work*

BACKGROUND: Methotrexate (MTX) is the primary disease modifying therapy for children with juvenile idiopathic arthritis (JIA), inducing remission in ~65% of cases although the mechanism of action of MTX remains unclear. Where MTX fails selecting the appropriate subsequent biologic therapy is important. In the SPARKS Childhood Arthritis Response to Medication Study (CHARMS) we have studied cytokine profiles and gene expression before and after MTX therapy to further understand MTX response. Our previous work used gene expression array analysis to compare the transcriptome before and after MTX therapy.
METHODS: JIA patients were from the SPARKS CHARM study with response to MTX defined using ACR criteria. Blood samples from JIA patients were taken pre and at 6 months of MTX therapy were stored as serum or peripheral blood mononuclear cells (PBMC). A multiplex assay was used to measure serum cytokines pre and post MTX treatment. Multi-colour flow cytometry was performed on PBMC samples for characterisation of cellular composition and intracellular cytokines. RT-PCR was used on PBMC to validate gene expression changes pre-post MTX treatment found in initial gene expression array analysis for six genes of biological interest.
RESULTS: Cytokine profiling showed that the serum concentration of IL-6 fell after MTX in responders and this was greatest in children with ACR-Ped70 response, irrespective of clinical subtype. Interestingly levels of the transcription factor PPARa, known to inhibit IL-6 production, were altered by MTX. RT-PCR was found to validate gene expression changes observed by Affymetrix gene expression array in ACR-Ped70 patients including upregulation of the transporter SLC16A7 after MTX treatment.
CONCLUSIONS: In this study, cytokine profiling has identified the proinflammatory IL-6 as a potential novel candidate to measure MTX response in JIA. For patients who fail to respond, this type of analysis may inform the choice of an appropriate alternative drug such as biologic agents.
ACKNOWLEDGEMENTS: This study was supported by SPARKS UK, the Big Lottery Fund and the Arthritis Research Campaign.

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Endothelial injury and repair in childhood primary angiitis of the central nervous system

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BACKGROUND: Primary angiitis of the central nervous system in children (cPACNS) is an inflammatory vasculitis that affects the CNS vessels in the absence of systemic vasculitis. There are no robust clinical or radiological predictors of disease progression that can be used to inform therapeutic decisions to prevent permanent neurological sequelae. An emerging paradigm relating to vascular health is the concept of the balance between endothelial injury and repair. Vascular injury is associated with the detachment of whole circulating endothelial cells (CECs), and in response there is a repair response mediated by migration of endothelial progenitor cells (EPCs) from the bone marrow to sites of injury. Nothing is known about the balance of endothelial injury and repair in cPACNS, and how perturbations in this balance might contribute to disease progression.
OBJECTIVE: To describe the relationship of CECs and EPC number and function to clinical and/or radiological disease progression in cPACNS.
METHODS: 30 children, 16M, 14F; age 10 (1.2-16.1) years old with cPACNS were studied and compared with 25 healthy child controls; age 7.8 (3-15)years old. Ten patients with non inflammatory CNS pathology(age 8.1, range 2-13 years old) served as an additional disease control group: the diagnoses in these patients were arteriovenous malformation, fibro-muscular dysplasia and moyamoya arteriopathy. Two groups of cPACNS patients were then classified according to radiological and/or clinical progression, or non progression at >6 months from diagnosis. CECs were isolated using immunomagnetic bead extraction. EPCs were detected using flow cytometry and were defined as peripheral blood mononuclear cells (PBMCs) triple positive for CD34/CD133/CD144 and CD34/CD133/VEGFR2. For patients presenting acutely, cells were additionally cultured in endothelial cell growth medium, the endothelial-like phenotype was confirmed, and the colony forming unit (CFU) capacity in tissue culture monolayers was determined. Vasculogenic function of EPCs was further quantified by their ability to incorporate into human umbilical endothelial cell (HUVEC) vascular structures in matrigel. All data were expressed as median and range unless otherwise stated.
RESULTS: 7/30 patients had progressive cPACNS. CEC count in this group was significantly raised at 232/ml (56–1152) compared to 40/ml (0–200) in 23/30 with non-progressive disease (p=0.001); 32/ml (0–152) in child controls (p=0.003); and 24/ml (16–141) in patients with non-inflammatory cerebrovascular pathology (p=0.001). EPCs were also significantly raised in patients with progressive cPACNS compared to child controls: CD34/CD133/CD144 EPCs p=0.005; CD34/CD133/VEGFR2 EPCs p=0.03; and patients with non progressive disease: CD34/CD133/CD144, p=0.008; CD34/CD133/VEGFR2 EPCs, p=0.005. Compared to healthy child controls EPC-CFU were significantly reduced in children with acute presentation of cPACNS, p=0.01. In addition, the number of EPC that incorporated into a vascular network formed by HUVEC was reduced in children with acute cPACNS, versus healthy child controls, p=0.001.
CONCLUSION: CECs can be used to track vascular injury due to cPACNS and differentiate progressive versus non-progressive cerebral vasculitis. However, vasculogenic function of EPCs is impaired in children with acute cPACNS despite increased EPC numbers in peripheral blood. This unfavourable balance of endothelial injury and repair is likely to contribute to the severe cerebrovascular injury associated with disease progression.

P 244
Microparticle mediated thrombin generation: a novel mechanism of thrombotic propensity associated with systemic vasculitis of the young

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BACKGROUND: Thrombo-embolic disease is an increasingly recognized feature of primary systemic vasculitis (PSV). However, the pathogenesis of hypercoagulability in PSV is poorly understood, and conventional prothrombotic markers are frequently negative or normal. Microparticles (MPs) are cellular or platelet membrane fragments rich in phosphatidylserine (PS), and therefore are potentially important thrombotic protagonists. Platelet MPs and MPs from other cellular sources are increased in PSV, but their contribution to pathological thrombosis in this context is unknown.
OBJECTIVE: Assess the functional pro-coagulant activity of released plasma MPs in children with PSV.
METHODS: Children with a diagnosis of PSV with or without thrombotic episodes were studied during periods of active or inactive disease as measured by the Birmingham Vasculitis Activity Score (BVAS). Disease activity assessment was additionally supported by evidence of endothelial injury (raised Circulating Endothelial Cells, CECs). Healthy controls were also studied. Conventional risk factors for thrombosis including protein C, protein S, antithrombin III, factor V Leiden, prothrombin gene G20210A, methylene tetrahydrofolate reductase (MTHFR C677T) mutations, presence of anticardiolipin antibodies and lupus anticoagulant were assessed. Annexin V+ MPs were isolated from platelet poor plasma and quantified using flow cytometry. MP pellets were then re-suspended in normal pooled MP-free plasma (MPFP), and their thrombin generating capacity was quantified using a fluorometric thrombin generation assay (TGA), measuring three parameters: peak thrombin (nM), rate (nM/min) and the area under the curve (AUC). Data were expressed as median and range unless otherwise stated.
RESULTS: 18 children, 6M, 12F; age 10 (1.2-16.1) years, with PSV were studied. There were 11/18 children with active PSV (Polyarteritis Nodosa, PAN n=6; Kawasaki Disease, KD n=3; Wegener's granulomatosis, WG n=1; Churg Strauss Syndrome, CSS n=1), with BVAS 7/63 (5-20/63), and CECs 240 (112-1600) cells/ml. This group exhibited a significantly higher peak thrombin of 145.85, (80.4-189.2 nM) compared to 7 children with inactive PSV (PAN n=2,WG n=3, unclassified n=1, Behçet's disease n=1) BVAS=0/63 in all, CECs 46, range 40-112 cells/ml), median peak thrombin 53.6 nM (45-131.4), p=0.002; and healthy controls, peak thrombin 45 nM (24-60), p=0.001. The rate of thrombin generation as well at the AUC were also higher in children with active vasculitis compared with those with inactive disease (p=0.001), or healthy controls (p=0.002). Children (n=8/18) with thrombotic events (pulmonary embolism n=1; cerebral arterial infarction n=3; cerebral sinovenous thrombosis n=1; myocardial infarction n=1; digital infarction n=1; thrombotic peripheral gangrene n=1) had significantly higher peak thrombin, p=0.0184 and AUC, p=0.0175 compared to 10/18 children with PSV without thrombosis. The peak thrombin generated correlated significantly with the total number of plasma MPs, R2=0.42, p=0.005. Five children (2 of which had a thrombotic event) were found to be heterozygous for MTHFR C677T mutations and one child was positive for anticardiolipin antibodies.
CONCLUSIONS: Enhanced MP-mediated thrombin generation was demonstrated in children with active PSV with significantly higher levels in those with thrombotic events. MP-mediated thrombin generation provides a novel mechanism which, combined with endothelial injury, could account for the excessive pathological thrombosis observed in patients with systemic vasculitis.

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In vitro skewing of naïve human CD4+ T cells, does not result in clearly differentiated helper T cell subsets

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BACKGROUND: CD4+ T cells play a major role in the pathogenesis of Juvenile Idiopathic Arthritis, as others and we have documented a role for regulatory and effector T cells in the perpetuation of the disease. Yet still many questions remain what determines the fate of human naïve T cells upon encounter with the environment. Naïve CD4+ T lymphocytes have the potential to differentiate and produce a range of cytokines crucial for appropriate immune responses. The mechanism of maturation of T lymphocytes into distinct T helper subsets, like Th1, Th2, and Th17, is not completely understood, but it is clear that cytokines play a dominant role in most *in vitro* experimental conditions for murine T cells. Here, we differentiated human naïve T cells into mature helper T cells, and used different combinations of cytokines in the environment of the cell to skew cells towards different T helper subsets. We investigated the in vitro differentiation and cytokine production of human naïve T cells. In this study, we aimed to establish whether human T cells, similar to murine T cells, can be differentiated *in vitro* into distinct T helper subsets.
OBJECTIVES: In this study, we aimed to establish whether human T cells, similar to murine T cells, can be differentiated in vitro into distinct T helper subsets.
METHODS: Naive T cells were obtained from fresh peripheral blood of healthy human donors by CD4+ MACS enrichment, followed by FACS-sorting of naïve CD4+CD27+CD45RO- cells. The cells were labelled with CFSE (0.5 mM on day 1-3, 3mM on day 4-7), stimulated with antiCD3/anti-CD28 beads, and skewed into different helper T cells subsets by adding different cytokine combinations in the media. The cells where incubated for 7 days.
Cytokine expression was quantified using flow cytometry on days 1, 2, 3, 4, 5 and 7.
RESULTS AND CONCLUSIONS: We show that it is difficult to differentiate naïve human CD4+ T cells into clearly distinct mature helper T cell phenotypes. Thus, widely used protocols for skewing of naïve CD4+ T cells do work for murine cells, but not as well for naïve human CD4+T cells. More studies are crucial to analyse what determines the fate of human CD4+T cells *in vitro* and *in vivo* in an inflammatory or anti-inflammatory environment.

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The place of the interleukin-1-receptor antagonist Anakinra in the treatment of systemic-onset juvenile idiopathic arthritis (SoJIA)

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Systemic onset juvenile idiopathic arthritis (SoJIA) is a debilitating childhood disease presenting with fever, skin rash and arthritis. The current therapy, consisting mainly of corticosteroids, can be inefficient in treating SoJIA and is often accompanied by many serious adverse events. Anakinra, an interleukin-1 receptor antagonist, is not registered for use in SoJIA. We reviewed the published and presented data of 140 children with SoJIA treated with Anakinra. Anakinra has shown to be a very efficient medicine in reducing symptoms even in these therapy resistant SoJIA patients with poor outcome. The systemic symptoms improved in almost all patients mostly within hours or days and had a low recurrence rate. So a statement about the effectiveness of Anakinra in an individual patient can often be made quite quickly. In about two thirds of the patients arthritis responded as well. Disease remission with Anakinra seemed to be better in patients with systemic symptoms, less active joints and a shorter disease duration. Use of steroids could, in most cases, be reduced or even stopped. If relapse did occur, this was mostly within a period of about six months. Withdrawal rates after a first beneficial response were between 7 and 31% with secondary inefficacy and intolerance as main reasons. Serious adverse events are minimal. In our opinion Anakinra should surely be started in a SoJIA patient before a trial of TNFα-blockade and maybe even before administration of corticosteroids. The optimal starting dose of Anakinra in SoJIA patients is likely to be 2 mg/kg/day and not 1 mg/kg/day.

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Anti-C1Q, Anti-Nucleosome and Anti-dsDNA Antibodies in Juvenile Systemic Lupus Erythematosus patients

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BACKGROUND: Anti-C1q antibodies have been described in up to 65% of adult systemic lupus erythematosus (SLE) patients associated to disease activity, especially nephritis 1,2. We previously studied the anti-C1q and nucleosome antibodies in juvenile SLE (JSLE) patients 1,2. However, to our knowledge, the concomitant evaluation of these antibodies, including double strand-DNA (dsDNA), was not carried out in pediatric lupus population.
OBJECTIVES: To evaluate the prevalance of anti-C1q, anti-nucleosome and anti-dsDNA antibodies in JSLE and controls; to establish a comparison between the sensitivity, specificity, positive and negative predictive values of the three autoantibodies and to evaluate the possible association of these antibodies with disease activity and lupus nephritis.
METHODS: Sixty-two JSLE (ACR criteria) and 34 age and gender matched healthy controls were analyzed for the presence of anti-C1q (Inova Diagnostics, San Diego, USA), anti-nucleosome (Inova Diagnostics, San Diego, USA) and anti-dsDNA antibodies (The Binding Site, Birmingham, UK). All antibodies were measured in duplicated samples by enzymatically amplified two-site two-step sandwich-type (ELISA) immunoassay.
RESULTS: The mean current age was similar in JSLE patients and controls (14.6±3.86 vs. 13.6±2.93 years, p=0.14). The female gender was similar in both groups (83% vs. 79%, p=0.58). The age at JSLE onset ranged from 3 to 16 years. A higher frequency of anti-C1q, anti-nucleosome and anti-dsDNA antibodies was observed in JSLE compared to controls (20% vs. 0%, p=0.0037; 48% vs. 0%, p<0.0001 and 69% vs. 3%, p<0.0001, respectively). The median of anti-C1q, anti-nucleosome and anti-dsDNA were also significantly higher in JSLE patients versus controls [9.6(5.5-127) vs. 7.5(5-20) Units, p=0.0006; 18(1.9-212) vs. 3.2(1.7-17)Units, p<0.0001; 111(6-741) vs. 14(6-33)UI/ml, p<0.0001; respectively]. Importantly, the sensitivity for anti-C1q, anti-nucleosome and anti-dsDNA was 21% (CI 11-33%), 49% (CI 36-62%) and 70% (CI 57-81%). Additionally, specificity was 100% (CI 88-100%), 100% (CI 88-100%) and 97% (CI 83-99%) for these antibodies, respectively. Positive predictive value was 100% (CI 75-100%), 100% (CI 88-100%) and 97% (CI 87-99%) and negative predictive value was 39% (CI 28-50%), 50% (CI 37-62%) and 62% (CI 47-76%) for these antibodies, respectively. Interestingly, a positive correlation was found between anti-dsDNA levels and both anti-C1q (r=0.51, CI 0.29-0.68, p<0.0001) and anti-nucleosome (r=0.87, CI 0.79-0.92, p<0.0001) levels. No differences were observed in JSLE patients with and without nephritis in the frequencies of anti-C1q (26% vs. 8%, p=0.26), anti-nucleosome (48% vs. 50%, p=1.00) and anti-dsDNA antibodies (72% vs. 58%, p=0.3). Moreover, the frequencies of these three antibodies were similar in JSLE patients with SLEDAI≥4 versus SLEDAI<4 (p>0.05).
CONCLUSION: Although anti-C1q and anti-nucleosome auto-antibodies had a lower sensitivity compared to anti-dsDNA, the exceedingly high specificity of both antibodies could help in JSLE diagnosis, especially in those patients with negative anti-dsDNA.
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Safety and Immunogenicity of Influenza Vaccine (FluVac) in patients with Juvenile Systemic Lupus Erythematosus (JSLE)

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BACKGROUND: The FluVac is highly effective in general population. However there have been concerns about safety and immunogenicity of this vaccine in patients with SLE.
OBJECTIVE: To evaluate safety and immunogenicity of FluVac in JSLE.
PATIENTS AND METHODS: Twenty-six JSLE patients (10-18 years; mean SLEDAI score of 5.8), were immunized with trivalent split FluVac (A/Solomon Islands/3/2006, A/Brisbane/10/2007, B/Florida/2006), licensed for the 2008 Winter season in the South Hemisphere (Sanofi Pasteur SA/ Butantan Institute Brazil). All but one patient were receiving prednisone (mean dose 12.2mg/day), and 17 were also receiving other drugs (methotrexate/leflunomide:4; azathioprine:12; mycophenolate mofetil:3). Influenza antibodies were measured before and 4-6 weeks

after vaccination using hemagglutination inhibition (HAI) test according to standard World Health Organization procedure. Immune response (seroconversion) was defined as a 4-fold or greater rise in HAI antibodies and seroprotection rate was considered when HAI titers were at least 1:40. Local symptoms at the injection site and systemic symptoms were assessed by diary. The SLEDAI score, erythrocyte sedimentation rate (ESR), anti-dsDNA and anti-cardiolipin antibodies where evaluated before and 4-6 weeks after vaccination.
RESULTS: All patients responded to at least 2 FluVac strains. Seroprotection rates after vaccination were 92% to A/H1N1, 73% to A/H3N2 and 100% to B-strain. Seroconversion rates were 91% to A/H1N1, 60% to A/H3N2 and 45% to B-strain. Use of medications did not interfere in seroprotection or seroconversion rates. No significant differences were found in SLEDAI score, ESR, or antibody titers against dsDNA and cardiolipin 4-6 weeks after vaccination. Local symptoms at the injection site (tenderness and/or redness) were described in 5/26 patients; 1 patient had a quickly reversible lipothymia five minutes after receiving the vaccine and 2 patients developed cough and rinorrhea without fever, one and nine days after receiving the vaccine.
CONCLUSION: Trivalent split influenza vaccine seems to be safe and immunogenic in patients with JSLE.
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The beneficial effect of Mesenchymal Stem Cell Therapy in Arthritis

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BACKGROUND: Mesenchymal Stem Cells (MSC) are adult stem cells which are mainly present in bone marrow and fat. The cell is a fine candidate for treatment of juvenile idiopathic arthritis since it has strong immunosuppressive activities in vitro as well as in vivo and can be expanded easily to quantities needed.1
OBJECTIVES: To find out if injection of MSC is feasible as a therapy in established arthritis in a non-collagen arthritis animal model. Are the MSC migrating and how is the immunosuppressive mechanism of MSC in arthritis.
METHODS: We performed a study using proteoglycan induced arthritis in Balb/c mice. The arthritic mice were assigned to 5 groups: 1 control-group (PBS) and 4 treatment-groups (MSC 1x or 2x intraperitoneal [ip] or intra-articular [ia]). Ten days after 2nd PG-antigen injection, treatment was started and if planned again after 4 weeks. Dosages were 5×106 ip and 1×10 6 cells ia. Arthritis was scored 2 times a week by 2 independent observers according to a scoringsystem with a maximum of 16. Bioluminescence imaging was performed with luciferase genemarked MSC via different routes: ip, iv, ic and ia. Serum was taken at the end of the study of all mice and post-mortem spleens, inguinal and popliteal lymhpnodes were extracted.
RESULTS: Intraperitoneal injection of 5* 106 MSC in mice with established arthritis resulted in a decrease in the arthritis score, while in control mice a marked increase was seen. There was no significant benefit in repeating the intraperitoneal injection of MSC after 4 weeks. Intraarticular injection of 1* 106 MSC in the right knee on the other hand only worked well if it was repeated after 4 weeks. Histology of the knee joints showed comparable results. Bioluminescence imaging (BLI) showed that the ip administered MSC were present in the peritoneal cavity for up to 5 weeks, but at no point seen outside the peritoneal cavity. The ia administered MSC also stayed at the site of injection. The iv injected MSC in mice were not seen after 1 week, nor did MSC injected in the left ventricle show any specific homing. Pro-inflammatory populations (IFNγ+ and IL-17+ CD4+T-cells) were lower in the treated group than in the control group. On the other hand, antiinflammatory IL-10-producing lymphocytes were more largely present in the treated group. The inguinal and popliteal lymph nodes showed no significant differences in relative numbers of activated CD4+ T-cells, IL17-positive or Fox-P3 positive regulatory T-cells. Serum cytokine levels measured at the end of the study showed no significant differences in the serum levels of cytokines (IL-1ß, IL4, IL6, IL10, IL17, IFNγ and TNFα) between healthy mice, untreated arthritic controls, or the treatment groups.
CONCLUSION: The use of MSC in established proteoglycan induced arthritis is effective both clinically and histologically when a minimal cumulative dose of 2 million cells was given. The MSC were visible for weeks at the site of location in ip and ia treated mice for weeks but specific migration was not seen. Neither was this the case in ic or iv treated mice. Proinflammatory splenocytes were lower and IL-10 producing T-cells were higher in the treated groups compared to the control group.
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Cogan Syndrome: a rare but severe vasculitis in pediatric age

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BACKGROUND: Cogan syndrome (CS) is a vasculitis characterized by systemic, ocular and vestibuloauditory symptoms. Only a few pediatric patients have been reported in literature so far and few information is available as far as disease course and outcome.
OBJECTIVES: We describe three caucasian children (1M, 2F) with CS and compare them with the data of the literature.
METHODS: We reviewed the clinical records of patients with defined diagnosis of CS followed at two Pediatric Rheumatology Institutions and patients with pediatric-onset CS from a database search in Medline. Data collected included clinical features, ocular and ENT evaluations at onset and during the disease course, laboratory variables, treatment and outcome.
RESULTS: During the period 1990-2009, three patients with definite diagnosis of CS have been followed in our units and 20 more patients have been reported in 16 publications. In the whole cohort of 23 cases, the mean age at onset was 11.6 years (range 4-18) and the F:M ratio was 2:1. Half of the patients had systemic symptoms at onset such as fever (30%), or musculoskeletal pain (26%), 78% had ocular symptoms such as red eye, often with photophobia (57%), as presenting signs of interstitial keratitis (26%), episcleritis (9%) or uveitis (4%), conjunctivitis (17%), and visual loss (4%). Audiovestibular symptoms were present in 74% of the patients, most of them (65%) had sensory neural hearing loss (SNHL) and 35% vestibular dysfunction such as vertigo, vomiting or ataxia. Cardiac involvement, mainly aortic insufficiency, and skin rash were found in 22% and 13% of the patients, respectively. Treatment consisted in corticosteroids (83%), methotrexate (30%), cyclophosphamide or MMF (4%). After a mean 4 year follow-up, 35% of the patients were in complete remission with no organ damage, the remaining reported residual deafness or SNHL (35%), irreversible cardiac complications (13%), vestibular dysfunction (4%), ocular damage (4%), or chronic hepatitis (4%). Only one patient died one year after disease onset for subaracnoid hemorrhage.
CONCLUSIONS: Cogan syndrome is a rare, severe and, probably, under diagnosed vasculitis of the pediatric age. In older children with systemic symptoms, red eye, vertigo and/or hearing loss CS should be always considered in the differential diagnosis since a prompt treatment may prevent irreversible organ damage.
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P 251
Ineffectiveness of tumor necrosis Alpha inhibition in association with Bisphosphonates for the treatment of Cherubism

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BACKGROUND: Cherubism is a rare genetic disorder characterized by swelling of jaw, secondary to multilocular cysts composed of fibrotic stromal and osteoclast-like cells. It has its onset in early childhood, and clinical manifestations usually stabilize around puberty. Diagnosis is based on family history and clinical findings, although a genetic defect has been demonstrated. Medical treatment is unsatisfactory and is mainly based on surgical procedures. Animal models and *in vitro* findings have suggested that massive bone resorption by osteoclasts and TNF-alpha activation play a major role in the disease pathogenesis.

OBJECTIVES AND METHODS: We describe the case of a girl affected with cherubism and treated with alendronate and adalimumab.
RESULTS: A 5 year-old girl came to our attention for progressive swelling of the cheeks, that occurred since she was 3 years old, upward gaze, and poor decidual dentition. The mother had the same diagnosis, and had been subjected to multiple maxillo-facial surgeries for cosmetic reasons throughout her life. Physical examination and laboratory tests were otherwise normal. X-rays of the jaw showed bone fibrous dysplasia. CT scan showed thick jaw cortex, multilocular cysts, bulging and blown appearance of jaw. A therapeutic trial with oral alendronate (35 mg/week) and subcutaneous adalimumab (24 mg/sq.meter/2wks) was started. Treatment was well tolerated, but after 9 months, clinical examination and CT scan did not show any improvement.
CONCLUSIONS: To our knowledge this is the first report of treatment of cherubism with a TNF-alpha antagonist. Despite hopes based on experimental evidence, treatment of cherubism with anti-TNF and alendronate was not effective in our patient.
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P 252
Methotrexate does not exert immunomodulatory effects on regulatory T cells but on effector T cells

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BACKGROUND: Methotrexate (MTX) is the most commonly used anti-rheumatic drug in juvenile idiopathic arthritis (JIA). MTX induces "remission on medication" in 70% of patients and continuous "remission off medication" in up to 50% of patients (1). MTX is unique in the realm of anti-rheumatic drugs since it is currently the only drug that appears capable of establishing immune tolerance in JIA. In spite of this, it is unclear which immunomodulatory mechanisms enable MTX to achieve sustained remission. We thus examined the immunomodulatory effects that MTX exerts on two major players in immune tolerance – regulatory (Tregs) and effector (Teffs) T cells.
MATERIALS AND METHODS: Peripheral blood mononuclear cells (PBMCs) from 20 extended oligoarticular and polyarticular JIA patients were isolated before MTX start, 3 and 6 months after MTX start. We analyzed frequency and phenotype of Tregs by flow cytometry. The function of Tregs was evaluated in CFSE-suppression assays. Proliferation of Teffs was examined in proliferation assays in the presence of anti-CD3. Teff cytokine production was measured ex vivo with flow cytometry upon PMA-ionomycin stimulation and in 4-5 day-culture supernatants with the luminex technique.
RESULTS: The frequency of FoxP3+ Tregs and the FoxP3 content per cell did not change upon MTX start. Suppressive capacity of Tregs appeared to be lower 6 months after MTX start compared to 3 months after MTX and prior to MTX start. In cross-over experiments, however, suppressive capacity of Tregs from all time points was equal. Teffs after MTX start proliferated significantly more in comparison to Teffs prior to MTX upon stimulation with anti-CD3. We observed an increase in IFNγ production by flow cytometry and luminex and an increase in TNFα and IL-10 production by luminex only. IL-17 production decreased in supernatants of Teff cultures.
CONCLUSIONS: MTX does not exert its immunomodulatory actions on Tregs. Instead, we observe changes in Teffs upon the start of therapy. Strikingly, we show that Teffs after MTX start demonstrate increased proliferation upon general stimulation. We will further explore the effect of MTX on Teff proliferation upon antigen-specific stimulation with HSP60 self-antigens as well as cytokine production of Teffs in cultures upon general and antigen-specific stimulation.
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Primary immunodeficiencies in Juvenile Systemic Lupus Erythematosus patients

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BACKGROUND: Three groups of PIDs have been described as associated with SLE or lupus-like manifestations: i) homozygous deficiency of early components of the classical Complement pathway (1); ii) partial or selective immunoglobulin deficiency, mainly IgA (2), seldom IgG2 (3) and IgM deficiency (4); and iii) Chronic Granulomatous Disease (CGD), affecting both patients and female carriers of the X-linked CGD allele (5).
OBJECTIVES: To evaluate the frequency of complement and antibody primary immunodeficiencies (PIDs) in Juvenile Systemic Lupus Erythematosus (JSLE) patients and to compare lupus patients with and without PID regarding demographic data, clinical features, disease activity and damage, treatment and occurrence of infections.
METHODS: Seventy-two JSLE (ACR criteria) patients (1 to 16 yrs at diagnosis) were analyzed for early components of the classical complement pathway (C1q, C1r/C1s, C4, C2, C3) and immunoglobulin levels (IgG, IgA, IgM, IgE, and IgG2 subclass). Statistical analysis was carried out according to Fisher´s exact test, Mann-Whitney test and Backward Stepwise multivariate analysis.
RESULTS: Nineteen patients (26%) had underlying PID. Complement PIDs were: 5 cases of C2 deficiency and 2 of C4 deficiency, and 2 cases with complete C1q deficiency. All PID patients had normal C3 levels. Immunoglobulin deficiencies were: 4 cases with IgG2 deficiency (<20mg%), 3 with IgA deficiency (<7mg%), and 3 with IgM deficiency (<35mg%). One IgA deficient patient also presented C4 and C2 deficiencies. A gender bias was observed, since 54% of the boys (7/13) and 20% (12/59) of the girls presented an underlying PID (p=0.032; RR: 3.25; CI: 1.25–8.46). The 2 cases of infantile SLE (age at onset <2 years) were both males (one with C1q deficiency and other with IgM deficiency). A higher frequency of severe sepsis was observed in the PIDs group (31% vs 7.5%; p=0.017; RR: 4.2; CI: 1.32–13.2). Specific lupus clinical features (cutaneous-mucosal, neuropsychiatric, cardiopulmonary, renal and hematological manifestations and antiphospholipid syndrome) were uniformly alike in patients with and without PIDs. The median of the cumulative damage related to SLE (SLICC/ACR-DI) was significantly higher in immunodeficient subjects [1(0-5) vs 0 (0-3); p=0.0075]. Logistic regression showed that male gender (odds ratio=4.7; 95% CI=1.2–19.2; p=0.034) and SLICC/ACR-DI (odds ratio=2.5; 95% CI=1.13–4.8; p=0.007) were independent risk factors for PID (Nagelkerke R2=0.26).
CONCLUSIONS: An exceedingly high frequency of antibody and complement deficiency was observed amongst JSLE patients, suggesting that these immunologic defects may contribute to the disease development. Our results command that these two groups of PIDs should be systematically investigated in early onset lupus.
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P 254
The role of Vasoactive Intestinal Peptide Receptor Type One in pathogenesis of oligoarticular Juvenile Idiopathic Arthritis

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BACKGROUND: Vasoactive intestinal peptide (VIP) has been previously reported to have an anti-inflammatory role in vitro and in animal models(1). By gene expression profiling we have shown the type one receptor (VIPR1) is expressed at increased levels in synovial fluid mononuclear cells (SFMC) from children with persistent compared to extended oligoarticular JIA(2). The role of VIPR1 in oligoarticular JIA and its severity are currently not understood.
OBJECTIVE: Determine the expression pattern of VIPRI in SFMC and the mechanism by which it exerts it effect in oligoarticular JIA.
METHODS: Expression of VIPR1 mRNA and protein was analyzed by quantitative RT-PCR and western blotting, on sorted (CD3+CD4+, CD3+CD4-, CD14+ and CD19+) and unsorted healthy peripheral blood mononuclear cells (PBMC) and patient SFMC.

RESULTS: Expression of VIPR1 mRNA is differentially distributed between cell types. VIPR1 is enriched in CD4 T lymphocytes and CD14+ monocytes. In oligoarticular JIA synovial fluid (SF) samples VIPR1 mRNA expression is significantly lower than in healthy PBMC. Data from sorted cells showed that the greatest reduction in VIPR1 expression was in the CD4 T cell population.
Investigation of VIPR1 protein expression showed a band ~4kDa smaller in samples isolated from patient SF compared to the protein size seen in samples from healthy PBMC. This suggests either expression of a splice variant or atypical post-translational modifications of VIPR1 under inflammatory conditions.
CONCLUSION: This work shows a reduction of VIPR1 mRNA expression in oligo JIA SF. Additionally it suggests a possible change in transcription and/or post-translational modifications under inflammatory conditions compared to healthy conditions.
An understanding of the expression and function of VIPR1 could help to explain the pathogenesis of childhood arthritis, and lead to the development of novel therapeutic targets and biomarkers with which to predict disease course and outcome.
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Prospective evaluation by Nailfold Capillaroscopy (NFC) in children and adolescents with juvenile dermatomyositis

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BACKGROUND: Nailfold capillaroscopy (NFC) represents the best method to analyse microvascular abnormalities in autoimmune rheumatic diseases, and is also useful to evaluate disease activity and follow-up in dermatomyositis.
OBJECTIVE: To evaluate prospectively the value of the nailfold capillaroscopy in the follow-up of activity of dermatomyositis.
METHODS: This prospective study included 30 juvenile dermatomyositis patients (Bohan and Peter criteria) evaluated by clinical examination (skin abnormalities and muscle weakness) and laboratory exams (muscle enzymes and acute phase reactants). Concomitantly we also performed a nailfold capillaroscopy by using an optical microscope with a magnification of 10 and 16 fold.
RESULTS: Twenty out of 30 patients (66.6%) were girls with a mean age of 10.4 years and mean follow-up time of 3.4 years. In the first evaluation 22 of 26 nailfold capillaroscopy (84.6%) performed during the active phase exhibited scleroderma pattern and all 4 tests performed during remission were normal. Therefore, in 26 of 30 patients (86.6%) the clinical and laboratory data were associated with the capillaroscopy findings. In prospective evaluation 15 of 18 patients (83.3%) who had disease activity remained with scleroderma pattern at the nailfold capillaroscopy and 10 of 12 (83.3%) exams performed during remission were normal or showed improvement of the scleroderma pattern. Therefore, in 25 of 30 patients (83.3%) the nailfold capillaroscopy was also associated with disease activity.
CONCLUSIONS: Nailfold capillaroscopy is a non-invasive examination that is associated with disease activity and may be a useful tool for the disease follow-up.

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Th17 cells that undergo plasticity to a Th1 phenotype in human autoimmune arthritis can be detected by the expression of CD161 within the inflamed joint

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BACKGROUND: Th17 cells (secreting interleukin-17 (IL-17)) have been identified as key players in murine models of autoimmune arthritis. In JIA, we have shown that a high frequency of synovial Th17 cells is linked with a more severe disease course1 But the source and fate of these highly pro-inflammatory cells is still unclear
OBJECTIVES: We tested the hypothesis that Th17 cells within the joint undergo plasticity to a Th1 phenotype and can be detected by the expression of CD161, a recently identified Th17 marker2.
METHODS: Th17 cells from healthy donors were purified using a cytokine capture assay and driven to a Th1 phenotype by the addition of IL-12. CD161 and cytokine expression was assessed after 6 days of culture. Synovial Th17 and CD161± Th1 cells were sorted and RORC2 mRNA expression and T cell receptor (TRBV18) sequence analysis was performed,
RESULTS: Th17 cells maintained expression of CD161 even after conversion to a Th1 phenotype (82+/-5%,n=3), confirming that CD161 tracks Th17 ancestry in vitro. Consistent with this, synovial CD161+Th1 cells had significantly higher levels of the Th17 transcription factor, RORC2 than in CD161- cells ($p<0.05$, paired t test) and 10% of the unique TCR sequences from synovial Th17 cells were shared with CD161+ Th1 cells but there was no overlap with CD161- cells.
CONCLUSIONS: Several murine studies have highlighted the importance of T cell plasticity in autoimmune disease. To our knowledge our study is the first to show evidence of Th17 plasticity towards a Th1 phenotype in humans, directly ex-vivo. As CD161+ Th1 cells make up a large proportion of the synovial inflammatory infiltrate, we predict that therapies targeting Th17 induction will have a significant impact on the T cell influx into the joint.
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KN is an Arthritis Research UK Clinical Fellow (ref 17998).

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Response to Recombinant IL1Ra (Anakinra) in two Brazilian patients with a New Autoinflammatory Syndrome: deficiency of Interleukin-1 Receptor Antagonist (DIRA)

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BACKGROUND: Deficiency of Interleukin-1-Receptor Antagonist (DIRA) was described in 2009 and it is caused by mutations on IL1RN, encoding the interleukin-1-receptor antagonist (IL1Ra) 1,2. DIRA is clinically characterized by early-onset of pustular dermatitis and multifocal aseptic osteomyelitis and treatment of choice is the recombinant IL1Ra anakinra 1.
OBJECTIVE: To describe the response to treatment in the first two Brazilian cases of DIRA.
RESULTS: Patient 1 is a 22 month-old girl that was born to consanguineous parents. She was noted to have disseminated pustular cutaneous lesions just after birth. Laboratory exams showed hemoglobin 7.9 g/dl, white blood cell count 21.300 cells/mm3, platelet count 681.000 cells/mm3, erythrocyte sedimentation rate (ESR) 51mm1st/hour and C-reactive protein (CRP) 54mg/dl. At the age of one month, she presented acute aseptic osteomyelitis in left clavicle and right 7th and 9th costal archs and did not respond to several courses of broad spectrum antibiotics. Prednisolone and acitretin were started with a partial response. At the age of 8 months, mutational screening of IL1RN was performed and identified a homozygous in-frame deletion (15bp). Both parents are heterozygous for the same mutation. Anakinra was initiated with an impressive improvement of the cutaneous findings. She presented a marked decrease of ESR, CRP, platelets and leukocytes count and increase of hemoglobin concentration. Three months later, the patient had a new mild skin flare that resolved after adjustment of anakinra dose.
Patient 2 is a 2.5 year-old girl that developed a respiratory discomfort in the first hours of life and a neonatal-onset of pustular cutaneous lesions. Laboratory exams showed Hb 7g/dl, WBC count 24.100 cells/mm3, platelet count 853.000 cells/mm3, ESR 47mm1st/hour and CRP 21mg/dl. At 2 months of age, patient presented radial and ribs osteomyelitis and lytic lesions of thoracic vertebral bodies. Several antibiotics courses did not change the clinical picture. Since the age of 5 months, she had presented hypoxemia and dyspnea crises and CT scan showed interstitial lung disease. Moreover, a severe and persistent anemia led to seven blood transfusions until now. DNA sequencing revealed the same deletion on IL1RN as patient 1 and both parents are heterozygous for the deletion. Anakinra was started at the age of 15 months with a remarkable improvement of inflammatory markers. No new bone or lung flares have been observed since then.
Real time PCR revealed that both patients had a higher IL1RN expression compared to other 3 DIRA patients. The expression is comparable to the observed in heterozygous carriers. Although these patients express the protein, the 15 bp deletion causes a loss of 5 amino acids, modifying the tertiary structure of the protein and probably its function.
CONCLUSION: We report herein two rare cases of a new AS named DIRA. These patients presented the same deletion on IL1RN gene, causing severe cutaneous and bone manifestations, that dramatically improved with anakinra. The clinical and genetic findings suggest that other gene(s) and/or environmental factors should be modulating their phenotypes.
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Validation of the new Pediatric criteria for the diagnosis of Familial Mediterranean fever: data from a mixed population of 100 children from the French Reference Center for Auto-Inflammatory Disorders

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BACKGROUND: FMF is the most frequent inherited periodic fever syndrome due to recessive mutations in the MEFV gene on chromosome 16p13.3. As genetic testing may not help all diagnoses of FMF the availability of reliable tools for clinical diagnosis is still critical. The most commonly used criteria are those of Tel Hashomer established in Jewish adult population. Recently a Turkish group has suggested new criteria for diagnosis of FMF in children
OBJECTIVES: We aimed to validate the new pediatric criteria for diagnosis of familial Mediterranean fever (FMF) in a mixed population of 100 French patients
METHODS: The study group included 100 FMF children from the French reference center for auto-inflammatory disorders. FMF diagnoses were made on clinical expert advices then confirmed by mutation analyses in the MEFV gene. Routine genetic screening included exon 2 and 10 most frequent mutations using PCR and sequencing techniques reported elsewhere. A control group of 40 patients with unexplained recurrent fevers was reviewed in parallel. Both groups of patients were assessed for both the Tel Hashomer criteria and the new pediatric criteria published by Yalcinkaya et al. The severity of FMF was assessed by the pediatric modified score of Pras et al. All patients (and/or parents) gave informed consents for genetic analyses
RESULTS: Our FMF group included 100 patients, SR M/F (54/46), 70% were Sephardic Jews, 11% North Africans, and 9% of Turkish origin. The median age at first symptom was 2,5 years (1,5 month – 13,1 years). Mean Pras severity score was 8 and was not influenced neither by the genotype (p=0.46) nor by the ethnicity (p=0.28) The control group included 28 PFAPA patients and 12 with unexplained recurrent fevers, SR M/F 25/15, median age at first symptoms 2 years. 65% were Caucasian Europeans, 20% were North Africans and 5% were Sephardic Jews Comparison between Tel Hashomer criteria versus Yalcinkaya's criteria in both groups gave a sensitivity of 99% versus 100% a specificity of 45% versus 50%, a positive predictive value (PPV) 81.8% versus 83.3%, and a negative predictive value (NPV) of 94, 7% versus 100%. However, when we used at least 3 Yalcinkaya's criteria we obtained a sensitivity of 77% and a specificity of 95% with a PPV 97.3% of and a NPV of 62,3%. The number of mutations in the MEFV gene did not modify results for both sets of criteria.
CONCLUSION: The new pediatric Turkish criteria did not give higher contribution for FMF diagnosis than the Tel-Hashomer criteria in our mixed population of French children. However, if needed, we could recommend to apply them with at least 3 criteria what slightly decreases their sensitivity but markedly increases their specificity.

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Rheumatologic manifestations in a large cohort of patients with Chronic Granulomatous Disease

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BACKGROUND: CGD is a rare inherited phagocytic disorder resulting in an increased susceptibility to infections and inflammatory and autoimmune complications that might be severe.
OBJECTIVE: To describe non infectious inflammatory flares in a large cohort of pediatric patients with CGD, with particular regards to rheumatologic manifestations.
METHODS: Medical records of patients diagnosed with CGD in Necker Hospital between April 1968 and June 2009 and registered in the French National Registry of PID (CEREDIH) database were retrospectively reviewed.
RESULTS: A total of 98 patients were analysed. Sixty-eight patients (69.4%) presented at least one inflammatory flare. 53% of patients had an X-linked CGD (XL) and 11.2% an autosomic recessive CGD (AR). A total of 221 inflammatory flares were analysed. The overall median age of the first inflammatory flare was 3.25 years (range 0.87-8.87). The incidence rate of inflammatory flares/person-year was 0.15. The autoimmune manifestations were found in 2.6% of inflammatory flares and included arthritis (4 patients, 3 XL and 1 AR), discoid lupus (3 patients, XL). leucocytoclastic vasculitis (2 patients, XL), dermatomyositis (1 patient, XL). These disorders were the predominant inflammatory pattern in 5 patients, and associated with other inflammatory manifestations (gastrointestinal and/or ocular) in 5 patients. Autoimmune features were also found in XL-CGD female carriers, and included: Systemic Lupus Erythematosus (4 women), discoid lupus (7 women, in 3 cases associated with recurrent oral aphtae), arthritis and autoimmune hepatitis (1 woman), recurrent oral apthae and photosensitivity (1 woman).
A global inflammatory assessment has been performed. Other inflammatory manifestations included the gastrointestinal tract (colitis, Crohn-like disease) (70.3% of flares) , the urogenital tract (granuloma) (8.9%), lungs (chronic disease) (8.3%) and eyes (chorioretinitis) (2.1%). Other granulomatous features (notably cutaneous) were found in 7.8% of patients. Granuloma was found on 50% of the 42 biopsies. Fifty-two patients received anti-inflammatory drugs: 20 required steroids only and 32 in association with non-steroidal or anti-TNF therapy. No patients received HSCT for severe inflammation. Risk of developing an inflammatory complication was higher in patients with XL-CGD than in patients with AR-CGD (RR=2.40 [1.40-4.14]), while no difference was found for infections (Poisson regression analysis).
A total of 95 patients had at least one infection (a total of 558 infections). The median age at first infection was significantly lower in XL-CGD (0.31 years [0.09-1.14]) than in AR-CGD (3.18 years [0.18-4.81]) ($p<0.05$). The number of inflammatory flares was significantly associated with the number of infections (OR=1.04 [1.01-1.08]). One out of 17 deaths was due to inflammatory complications. The mortality risk was found significantly correlated with the number of infectious episodes ($p<0.01$), unlike the inflammatory flares.
CONCLUSIONS: The prevalence of inflammatory complications in CGD is high and can be responsible of important morbidity. Patients with XL-CGD have a higher risk of developing inflammatory complications than patients with AR-CGD. Rheumatologic manifestations can be part of the wide spectrum of CGD. Although this is not a classical asssociation, the underlying disease should be considered in patients presenting a particular clinical context, including other inflammatory and/or infectious manifestations, as well as in CGD female carriers.

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The role of damage-associated molecular pattern (DAMP) molecules in juvenile systemic lupus erythematosus (JSLE)

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INTRODUCTION: Adaptive immune responses in the pathogenesis of SLE have been the focus of immunological research for many years. More recently, it has been discovered that the innate immune system senses and responds to a pathogen-associated molecular pattern (PAMPs) and is also able to detect damage-associated molecular patterns (DAMPs) also known as alarmins. In this way, a new accent has been placed on the role of innate immunity in SLE
AIM: To explore the involvement of alarmins (HMGB-1, S100A12, and RAGE) in the pathogenesis of juvenile SLE.
PATIENTS AND METHODS: We harvested peripheral blood mononuclear cells from the 17 children with SLE (13 girls, 4 boys, age 8,7 ± 2,35) at the diagnosis, before any therapy was introduced, as well as from the 18 healthy age- and sex-matched controls. Serum concentrations of alarmins were determined using ELISA kits: RAGE (R&D Systems, Minneapolis (MN), USA), S100A12/EN-RAGE (CycLex Co., Nagano, Japan), and HMGB1 (Shino-Test Corporation, Tokyo, Japan). For gene expression, we separated peripheral blood mononuclear cells (PBMC) by centrifugation in Fycoll gradient and isolated RNA by 6100 PrepStation. RNA was reversely transcribed by High Capacity RNA-to-cDNA Kit and cDNA was amplified in ABI PRISM 7000 real-time platform using specific TaqMan Gene Expression Assays (Applied Biosystems, Foster City (CA), USA). Glyceraldehyde 3-phosphate dehydrogenase (GAPDH) was used as endogenous control. The study was approved by the Ethics Committee of the Zagreb University School of Medicine
RESULTS: The serum levels of HMGB-1 protein was significantly higher in the SLE children compared with healthy controls (median 7.1 ng/ml vs 6.1 ng/ml, interquartile range 6.3 to 11.8 vs 5.1 to 6.4) ($p<0.05$), while no significant correlation was found in the gene expression between the groups. There was no significant correlation between the HMGB-1 levels and standard laboratory tests commonly used to evaluate the disease activity. Unexpectedly, there was no significant difference in gene expression and serum S100A12 and RAGE levels between the healthy and the SLE children.
CONCLUSION: Increased circulating protein level of HMGB-1 confirmed its role in JSLE and its potential use as disease activity marker. Although more data are needed to get a good insight, we believe that the present results provide a useful foundation for further studies.

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HMGB-1, S100A12, and RAGE as biomarkers of systemic juvenile idiopathic arthritis

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INTRODUCTION: Systemic juvenile idiopathic arthritis (sJIA) is chronic childhood arthritis of unknown cause. Novel studies seem to point to deregulation of the innate immune system as the primary pathophysiological mechanism.
AIM: Assessment of HMGB-1, S100A12, and RAGE protein and mRNA levels in children with sJIA
PATIENTS AND METHODS: Peripheral blood was collected from the 15 children (6 girls, 9 boys, age 10.1 ± 4.5 years) with the sJIA, at onset of disease, and 20 healthy children (11 girls, 9 boys, age 7.6 ± 5.0 years). The study was approved by the Ethics Committee of the Zagreb University School of Medicine. Protein levels of HMGB-1, S100A12, and RAGE were determined by ELISA kits (RAGE (R&D Systems, Minneapolis (MN), USA), S100A12/EN-RAGE (CycLex Co., Nagano, Japan), and HMGB1 (Shino-Test Corporation, Tokyo, Japan) and gene expression by qPCR.
RESULTS: Serum levels of HMGB-1 and S100A12 were significantly higher in children with sJIA than in control children ($P<0.05$), while RAGE was lower in the sJIA group ($P=0.04$). Serum concentrations of HMGB-1 and S100A12 were significantly correlated with several common laboratory indicators of the disease activity. The expression of the S100A12 gene in PBMC paralleled the serum levels of the S100A12 protein, while the expression the HMGB-1 in children with sJIA was inverse to the respective protein levels, being lower in the sJIA group ($P=0.004$) than in the controls. To confirm whether those differences in gene expression could be used as disease markers we performed ROC curve analysis and found significant discrimination for HMGB-1 (area under curve (AUC)=0.868, $P<0.001$) and S100A12 (AUC=0.823, $P<0.001$).
CONCLUSION: Increased circulating protein levels of HMGB-1 and S100A12 confirmed their role in sJIA and their potential use as disease activity markers.

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Paediatric Autoimmune Neuropsychiatric Disease Associated with Streptococcal infection (PANDAS) and movement disorders

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BACKGROUND: Until the 1990s, Sydenham's chorea was considered to be the only neurological sequel of streptococcal infection. However, during an outbreak of GAHBS (Group A β-Hemolytic Streptococcus) infection in Rhode Island, there were many reports of affected children developing sudden onset tics and psychiatric disorders1. Subsequently, the clinical phenotype of post-streptococcal tics and obsessive-compulsive disorder was described, and the term PANDAS (Paediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal infections) was coined2.
Based on the proposed etiopathogenesis of PANDAS, these patients were started to be treated with antibiotics to reduce exacerbations of the neuropsychiatric symptoms after further GAHBS infections. So far, guidelines limit antibiotics for the treatment of acute streptococcal infections as diagnosed by a positive throat culture or rapid streptococcal test3. The prophylactic use of antibiotics in the management of children in the PANDAS subgroup is still controversial, but at present, they are not indicated.
OBJECTIVES: We wished I) to assess whether there was association between remission and antibiotic treatment in the PANDAS and movement disorders other than PANDAS subgroups in our cohort of children and II) to assess persistence of movement disorders in the first year of follow-up.
METHODS: In our retrospectively evaluation we included, so far, 12 patients with PANDAS according with the diagnostic criteria described by Swedo et al6, and 12 children with movement disorders (tic disorders, Sydenham's chorea, Tourette's syndrome) not fulfilling criteria for PANDAS. For the present abstract we included patients with at least one year of follow-up.
We should have completed data for a total of 50 patients in the next two months.
RESULTS: In the PANDAS subgroup the mean age at onset was 6.4 years (range 4-10), with 9 M and 3 F. In the movement disorders subgroup the mean age at onset was 7 years (range 3-13), with 7 M and 5 F.
We found that, in the PANDAS subgroup, 3 out of the 12 children (25%) achieved remission at 1 year of follow-up. Of these three, one was on antibiotic treatment. None of the three patients were taking symptomatic therapy. Seven out of 8 patients (87.5%) on antibiotics had no remission at one year. In the control group remission rate was 25%. One out of 4 patients (25%) that were on antibiotics achieved remission. This patient was also on valproic acid therapy.
The antibiotics used were benzilpenicilline or amoxicilline.
CONCLUSIONS: In our cohort we did not observe an association between antibiotic therapy and tics remission in patients with PANDAS, as shown by the fact that 87.5% of children taking antibiotics had no remission at one year.
We will update our database adding more data to the present results for a total of 50 children, and we are planning to evaluate some biological markers in our cohort of patients.
Further studies are needed to clarify the need of antibiotics in PANDAS patients.
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P 263
CD30 displays an immune regulating role on human CD4+ T

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BACKGROUND: The presence of CD30 on CD4+CD25+ Treg is related to a more favourable disease course in Juvenile Idiopathic Arthritis (JIA). Although a regulatory role of this cell surface receptor is confirmed by various murine auto-immune disease models, the mechanism of regulation is far from clear.
OBJECTIVE: In this study, we aim to assess whether CD30 has a functional role in modulating CD4+ T cell phenotype, proliferation and cytokine production in vitro.
METHODS: Jurkat cells were used to test CD30 stimulation reagent efficiency. Following, CD30 was knocked down or stimulated in cultures of PBMCs from healthy donors. After 2 or 3 days of culture, cells were analysed by flowcytometry for expression of CD25, CD30, CD153 and FOXP3. True count beads were used to determine absolute cell numbers. Cytokine content in supernatants was analysed using a Multiplex Immuno Assay.
RESULTS: In this study, we show a significant decrease in both CD25 and FOXP3 expression on CD30 knockdown CD4+ T cells and a decrease of total cell numbers. However, CD30 stimulation for 1 hour did not affect CD25 and FOXP3 expression.
CONCLUSION: This study provides more clues for an immune modulating role of CD30 on CD4+ T cells. Further investigation is needed to reveal CD30 function. In the end, this may prove CD30 as a target to restore the balance between regulatory T cells and effector T cells in JIA.
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P 264
Results of arthroscopy and synovial biopsy in pediatric chronic knee monoarthritis

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BACKGROUND: Chronic knee monoarthritis (CKMA) – very geterogenous group of knee damage with different causes, courses and outcomes. Infection, malignancy, trauma, onset of juvenile idiopathic arthritis and spondiloarthropathy could appear as CKMA. To establish the exact diagnosis different means of joint visualization, such as X-ray, ultrasonography, CT scan, MRI and arthroscopy usually are performed.
OBJECTIVES: The aim of our study was to evaluate patients with CKMA, compare results of different means of joint visualization and assess synovial morphology in CKMA.
METHODS: we included 23 children with CKMA, 11 boys and 12 girls. Knee X-ray, ultrasound, CT scan and MRI was performed a lot of our patients. Knee

arthroscopy with sinovial biopsy from 4 standard points of knee was performed in all patients. During arthroscopy synovial hyperemia, degree and type of synovial hyperplasia and anatomical changes was evaluated. In synovial samples we assessed degree and type of cell infiltration, deposition of Ig A, M, G, fibrinogen and complement by immunohistochemistry assay.
RESULTS: The mean age of our patients was 11.37±4.4 years. The mean CKMA duration was 2.55±3.0 years. Routine laboratorial examination has not revealed inflammatory activity. Progressive arthritis course was in 5/23 and 18/23 had relapsing course. X-ray stages were: 0 stage 13/23, I stage 9/23 and II stage 1/23. Infection such a trigger suspected in 3/23, trauma in 6/23 and both triggers in 1/23. Morning stiffness had only 4/23 and all of them transformed in future in oligoarthicular subset of JIA. X-ray examination has revealed periarthicular osteoporosis 1/18, fibrous cortical defect 2/18, swelling of knee soft tissue 1/18 and 14/18 had no changes. Ultrasonography has revealed only joint effusion in all examined patients. CT scan MRI has revealed 1 case of osteochondritis dissecans, 5 cases of synovitis, 2 cases of suspected traumatic damage, 1 suspected cases of anomaly of menisci and 3 cases of chondromalacia. In arthroscopy 21/23 patients has chronic synovitis, 2/23 had pigmented villous-nodular synovitis without evidence of any suspected non-inflammatory conditions. Intensity of synovial hyperemia were: I grade-3/23, II grade-6/23, III grade-12/23, IV grade-2/23, intensity of synovial hyperplasia were: I grade 2/23, II grade-4/23, III grade-10/23, IV grade-7/23. We observed 2 types of synovial proliferation: villous-20/23 and mixed-3/23. Evidence of secondary to inflammation cartilage elasticity loss was detected in 11/23 without structural changes. Histological changes were: predominantly lymphoid cell infiltration with Ig G deposition. In small amount of patients there were mild Ig A and fibrinogen depositions.
Synovial hyperplasia degree has high positive correlation with synovial hyperemia ($r=0.77$, $p<0.001$). X-ray progression has positive correlation with synovial hyperplasia degree ($r=0.54$, $p<0,001$) but not with synovial hyperemia degree. Also X-ray progression positively correlated with inflammatory activity markers, such as ESR ($r=0.45$, $p<0.05$) and platelets count ($r=0.44$, $p<0.05$). No correlation between X-ray stage and CKMA duration observed. Synovial hyperplasia and hyperemia degree had no correlation with as well CKMA duration as markers of inflammatory activity.
CONCLUSIONS: CKMA is a group of chronic arthritis, which is characterized by prevalence of chronic local inflammation (synovial hyperplasia, cell infiltration) above systemic inflammatory markers.

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Chronic Recurrent Multifocal Osteomyelitis in children
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BACKGROUND: Chronic recurrent multifocal osteomyelitis (CRMO) is a rare condition characterized by a chronic non-suppurative inflammation involving multiple sites (1). It has previously been described having a resemblance with the adult SAPHO (Synovitis, Acne, Pustolosis, Hyperostitis, Osteitis) syndrome (1).
CRMO primarily affects the bones, but extra skeletal lesions, such as pustulosis, acne, uveitis and inflammatory bowel disease, have been described.
The incidence of CRMO is estimated to be 1:1.000.000 (1,2).
OBJECTIVE: To describe the patients, that have passed through our center since 2004 up till now.
METHODS: All patients were included upon their first visit to our pediatric rheumatology center. They were followed up upon their next visits. Among other things follow up included radiology findings, blood tests and a questionnaire about symptoms, filled out by the physician upon follow up.
RESULTS: We included 20 patients. 13 girls and 7 boys. All the patients complained of pain from their bones. Some had constant pain, others often or sometimes. There was no significant finding in the blood work, including ESR, CRP, ANA and RF.
Radiologically the findings varied between lytic, sclerotic, and mixed lytic/sclerotic lesions. Most of the findings were described in the lower limbs.
CONCLUSION: CRMO is a rare condition. We have discovered 20 cases in 6 years, which corresponds quite well with the estimated incidence.
The most common symptom is bone pain, which was present in all the patients.
MR is the best imaging tool available and should be used to assess the efficacy of the treatment.
Biopsy of the lesions is recommended, especially from a differential diagnostic point of view. Particularly to exclude osteomyelitis.
NSAID is the first drug of choice. If there is relapse, there has been success using steroids, mtx, and TNF-α antagonist.
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P 266
Functional Status in Severe JIA: an assessment in a Tertiary Pediatric Rheumatology Reference Centre
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BACKGROUND: Studies on functional outcomes of patients with juvenile idiopathic arthritis (JIA) over the last 10 years have revealed a diversity of CHAQ scores with median values ranging from 0 to 0.8.The frequency of patients with severe functional disturbance reportedly varies between 3.3 and 4%.Comparison between studies is difficult because of differences in composition of JIA cohorts, in disease duration and therapy.Most published cohorts have a limited proportion of systemic JIA and spondylarthritis patients, and in addition a reduced proportion of patients receiving biotherapy.
OBJECTIVE: To investigate the functional status of children with difficult to treat JIA of all subtypes, comprising an important number of patients receiving biotherapies, and to relate their functional status to subjective and objective measures of disease activity.
METHODS: 95 consecutively JIA patients seen in a Pediatric Rheumatology reference center between November 2008 and March 2009, were enrolled in this observational cross-sectional study.Outcome measures included CHAQ, physician's VAS overall disease activity, parent's VAS global wellbeing and pain, numbers of active and limited joints;criteria for minimal and inactive disease were applied. Non-parametrical tests were used.
RESULTS: Our cohort comprised 26% systemic JIA, 29% polyarticular JIA, 22% spondylarthritis and 23% oligoarticular JIA with median disease duration of 3.5 years (2 month-16.5 yrs).Treatment comprised NSAIDs (56%), MTX (23%), corticosteroids (21%) and biotherapy (45%).Criteria for inactive disease and minimal disease activity were met by 31 % and 47% of patients respectively. The median value of CHAQ score was 0.375 (range 0-3).The majority of patients had no or mild functional disability (61%), overall well being impairment (63%), and pain (55%).Conversely, 10% of patients reported severe functional disability and impaired wellbeing, 19% experienced severe pain.Within JIA subgroups, spondylarthropathy patients had significantly worse scores for CHAQ, VAS wellbeing and pain.CHAQ correlated with objective and subjective measures of disease activity in altogether JIA patients, and with VAS scores overall wellbeing and pain in every JIA subgroup.Patients with prolonged disease (>6 years) presented better scores for CHAQ, VAS wellbeing and pain.Patients with biotherapy reported better scores for CHAQ, wellbeing and pain despite no difference in number active joints nor the physician's global VAS, compared to patients without biotherapy.
CONCLUSION: In the present cohort, despite the high proportion of severe JIA, CHAQ values are in the lower range of those recently reported, a fact that may be related at least in part to new therapeutic approaches, including biotherapies.However, functional ability still remains a challenge for an important proportion of JIA patients.Spondylarthritis patients presented high impairment in functional ability, pain and wellbeing, justifying more attention for this JIA subtype in future studies. The constant interrelation found between functional disability and overall wellbeing underlines the importance of improving functional ability through appropriate therapies to improve patient's quality of life.

P 267
Efficacy of Single and Multiple Intraarticular Corticosteroid Injections in children with Juvenile Idiopathic Arthritis
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BACKGROUND: Intraarticular corticosteroid injections (IACI) are widely used in the treatment of children with juvenile idiopathic arthritis (JIA). However, the therapeutic role of multiple IACI is still unclear and controversial.
OBJECTIVE: To investigate the efficacy of IACI in single and multiple joints in children with JIA and to seek for predictors of relapse of synovitis.
METHODS: The clinical charts of 440 consecutive patients who received their first IACI at the study centres between 2002 and 2008 and had a follow-up ≥ 6 months after the IACI were reviewed. A total of 974 joints were injected. Corticosteroid preparation was triamcinolone hexacetonide for large joints and methylprednisolone acetate for small joints. Patients were divided in 3 groups based on the number of injected joints: 1) 1 joint; 2) 2 joints; 3) > 2 joints. Outcome of IACI was examined by looking at: 1) frequency of remission of synovitis at 6 and 12 months; 2) duration of remission until relapse of synovitis or last-follow-up visit with sustained remission; 3) survival analysis, with relapse of synovitis as end-

point. Remission of synovitis was defined as absence of all clinical signs of joint inflammation. Relapse of synovitis was defined as recurrence of inflammation in injected joints that required a new IACI or the start of systemic therapy. Predictors included sex, ILAR category, onset age, age and disease duration at IACI, number and type of injected joints, general anesthesia, ANA status, ESR, CRP, and simultaneous DMARD or biologic therapy.
Results. The frequency of remission of synovitis at 6 months was 58.1%, 40.2%, and 41.5% for group 1, 2 and 3, respectively. The frequency of remission of synovitis at 12 months was 40.6%, 23.4%, and 29.7% for group 1, 2 and 3, respectively. The mean duration of remission after IACI was 1.29, 1.14, and 1.16 years for group 1, 2 and 3, respectively. Survival analysis is shown in the **figure**. In the Cox model, the strongest predictors of relapse of synovitis were increased CRP, negative ANA, and IACI in the ankle.
CONCLUSION: As expected, patients who received IACI in a single joint had a higher probability of having remission of joint synovitis. However, on average, duration of remission was similar among patients who underwent IACI in single and multiple joints. Survival curve analysis showed that patients who received multiple IACI and had sustained remission for 1 year tended to have subsequently the same probability of relapse of patients who were injected in a single joint. These findings suggest that multiple IACI are a suitable and effective therapeutic option for children with JIA. Patients who had increased CRP, were ANA-negative, and underwent IACI in the ankle joint were less likely to experience sustained remission of synovitis.

P 268
Vaccinations in pediatric autoimmune and autoinflammatory diseases: a systematic literature review

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BACKGROUND: The safety and immunogenicity of vaccinations in pediatric autoimmune and autoinflammatory diseases are often debated.
OBJECTIVES: To construct recommendations for vaccination of pediatric patients with autoimmune and/or autoinflammatory diseases (AiD) using currently available evidence.
METHODS: A systematic literature review in Medline (Pubmed) and EULAR/ACR abstracts from 2008/2009 was conducted using various terms for vaccination, AiD, safety and immunogenicity. Experts added relevant papers. Papers were selected based on relevance. A panel of 13 European experts in the field were invited by EULAR to grade methodological quality and extracted data using predefined criteria.
RESULTS: 122 papers and 21 abstracts were included. The majority of papers considered influenza (44) or pneumococcal (20) vaccination. With regard to the live-attenuated vaccines, studies were available for varicella (1), measles-mumps-rubella (12), bacillus Calmette-Guérin (9) and yellow fever (1). There were no studies on hepatitis A, Japanese encephalitis, tick-borne encephalitis, typhoid fever, human papillomavirus (HPV), oral polio, and pneumococcal (polysaccharide or conjugate) vaccination in the pediatric AiD population. 10 studies were performed in JIA patients, 1 in pediatric SLE, 9 in Kawasaki Disease (KD) and the majority in adult RA and SLE patients.
Considering composite vaccines, it is recommended to adhere to national guidelines for the meningococcal serogroup C conjugate, Hib , pneumococcal, hepatitis A and B, DTaP, HPV, Japanese encephalitis, tick-borne encephalitis, typhoid fever, rabies and cholera vaccination (Grade C-D).
Seasonal influenza vaccination is recommended (Grade D). Patients on anti-CD20 therapy must receive tetanus specific immunoglobulines when indicated, since rituximab lowers responses to tetanus toxoid (Grade D).
Non-live vaccines can be administered during the use of DMARDs and TNF blocking agents, although responses can be reduced. Most studies were performed in adult RA and SLE patients (Grade C-D). Live attenuated vaccines should not be given when using biologicals, high dose glucocorticoids or high dose DMARDS, until more data are available. These vaccines can be considered in patients on low dose MTX (≤15mg/m2) in stable disease (Grade C). For all other patients, national guidelines can be followed.
CONCLUSIONS: Composite vaccines are safe and immunogenitic, although immunogenicity may be reduced when using anti-TNFalpha or anti-CD20 therapy. Live-attenuated vaccines in pediatric AiD patients on biological should be avoided when possible, but can be considered when using low dose MTX in stable disease.

P 269
Introducing a new approach into clinical care of children with Juvenile Idiopathic Arthritis: The Juvenile Arthritis Multidimensional Assessment Report (JAMAR)

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BACKGROUND: In recent years, there has been an increasing interest in parent/patient-reported outcomes (PROs) in juvenile idiopathic arthritis (JIA). Incorporation of these measures in patient assessment is deemed important as they reflect the parents' and children's perception of the disease course and the effectiveness of therapeutic interventions. Although several measures of single PROs have been developed, to date a clinical measure that groups all PROs used in the assessment of children with JIA does not exist. Such measure would provide a physician with a thorough and systematic overview of the patient status to be scanned at the start of the visit. This would facilitate focus on matters that require attention, leading to more efficient and effective clinical care. Objective. To develop and test a new multidimensional questionnaire incorporating all main PROs to be used in the assessment of children with juvenile idiopathic arthritis (JIA) in standard clinical care.
METHODS: The Juvenile Arthritis Multidimensional Assessment Report (JAMAR) includes 14 parent/patient-centered measures that assess well-being, pain, functional status, health-related quality of life, morning stiffness, disease activity, disease status and course, joint disease, side effects of medications, therapeutic compliance, and satisfaction with illness outcome. The JAMAR is proposed for use as both proxy-report and patient self-report, with the suggested age range of 7-18 years for use as self-report. From March 2007 to September 2009, the questionnaire was completed by the parents of 618 children with JIA in 1814 visits and by 332 children in 749 visits.
RESULTS: The JAMAR was found to be feasible and to possess face and content validity. All parents and children reported that the questionnaire was simple and easy to understand. Completion and scoring appeared to be quick, requiring 5-10 minutes. In the study patients, the JAMAR provided a thorough information about recent medical history and current health status. Parent proxy-reported and children self-reported data were remarkably concordant. Regular use of the questionnaires enables keeping a flow sheet to monitor patient's health status and response to therapy. Individual measures included in the JAMAR data can be used to compute a simple parent/patient-centered disease activity score. The figure shows the graphic representation of the time course of disease activity of a 5-year old girl with JIA, depicted through the calculation of the Juvenile Arthritis Parent Activity Score (JAPAS)-4, entirely based on JAMAR data, and of the Juvenile Arthritis Disease Activity Score (JADAS)-10 at all visits. Notably, both scores captured well the relapsing-remitting course of the patient and revealed a strikingly parallel course.
CONCLUSION: The JAMAR opens a new avenue toward the introduction of regular quantitative patient assessment in pediatric rheumatology practice. This new questionnaire may help to enhance the quality of care of children with JIA.

P 270
Prevalence of extracutaneous events in the Juvenile localized Scleroderma

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BACKGROUND: Localized scleroderma is a disorder characterized by cutaneous induration, but it can affect the subcutaneous tissue, muscle and even bone, plus the fact that there has been an association with other connective tissue, led to consider a sclerosing inflammatory autoimmune disease.
OBJECTIVE: To determine the prevalence of extracutaneous manifestations and autoantibody positivity in juvenile localized scleroderma (JLS).
PATIENTS AND METHODS: Design: Retrospective observational study. Population: We included 13 patients (8 women and 5 men) in pediatric age assigned to the Pediatric Rheumatology Unit of Hospital La Fe de Valencia, and JLS diagnosis confirmed by histological examination in 12 (92%) patients. Clinical variables include: age, diagnosis, subtype of JLS, type of collagen disease associated, laboratory abnormalities (leukopenia, lymphopenia, elevated CPK, hypergammaglobulinemia) autoantibodies positivity, abnormalities in respiratory function tests (RFT), echocardiogram, capillaroscopy and the presence of Raynaud's phenomenon and extracutaneous manifestations.
RESULTS: The subjects of study had a mean age at diagnosis of 8.46 years (2-16), and were classified into subtypes: 9 (69%) had plaque morphea, 3 (23%) linear morphea and 1 (8%) generalized morphea. The main clinical and analytical variables are shown in **Figure 1**. As shown, nine (69%) patients in our study showed musculoskeletal manifestations (46% myalgia, 31% arthritis) and 4(31%) tendon retractions. Of the four (31%) patients with Raynaud's phenomenon, 50% had an associated collagen disease. The ANA were positive in 9 (69%) patients, of whom

only 33% associated systemic autoimmune disease (22% mixed connective tissue disease and 11% polyarticular JIA). Of the laboratory and functional findings 23% of our patients had leuko-lymphopenia (<4000 total leukocyte and/or <1500 lymphocytes total), 31% elevated CPK (> 145 IU/L), 54% hypergammaglobulinemia (IgG >1200 mg/dL) and 31% change in diffusing capacity. Of these patients had associated collagen disease, 100%, 50%, 43% and 50% respectively. Only unspecific alterations objectified capillaroscopy 3 (23%) patients, of whom had associated systemic autoimmune disease in 2 of 3 cases.
CONCLUSIONS: The results of our study show a high prevalence of extracutaneous manifestations in the JLS, the most common musculoskeletal disorders and a high percentage of positivity for ANA, suggesting an association the JLS with autoimmune disorders, what consistent with previously reported studies.

P 271
Hereditary angioedema. A condition to remember

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Hereditary angio-oedema (HAE) is a rare disease caused by mutations in SERPING1 causing quantitative (type I) or qualitative (type II) deficiency of complement C1 inhibitor (C1 inhibitor). The low C1 inhibitor concentration permits activation of the kallikrein-kinin, complement, fibrinolytic and coagulation systems releasing vasoactive plasma kinins. Because of the rarity and variety of clinical manifestations, it was also assumed that the disease was underdiagnosed and mistreated with potential fatal consequences.
We described 3 patients 2 boys and 1 girl aged 4 -16 years referred to the Pediatric Rheumatology Unit of Federico II University of Naples because frequent painful swellings involving joints. One patient had positive family history (the mother had the same manifestations), one patient had abdominal pain attacks. The parameters of inflammation and antinuclear antibodies were normal in all patients, level of complement C4 was decreased in all patients, whereas C1q level was normal. Functional C1-INH was decreased in 2 patients and 0% (normal value > 70%) in 1 patient and her symptomatic mother. Functional C1-INH level of the asymptomatic parents of one patient was normal, the mother of the other boy had decreased level, without clinical manifestations.
The complete, classical HAE triad of symptoms includes laryngeal and peripheral oedema in combination with abdominal pain. A recent survey indicates that predominant joint involvement is a rare disease manifestation (1). HAE (OMIM 106100) is inherited as an autosomal dominant trait with incomplete penetrance. When new patients are diagnosed, it is very important to perform a systematic genealogical and biochemical study of first-degree family members to reveal eventual additional cases. Genetic testing is not necessary to confirm the diagnosis. Early diagnosis is the cornerstone of successful management of HAE. Treatment requires adequate professional experience and lifelong follow-up. HAE is an important differential diagnosis for recurrent painful swellings of extremities in pediatric patients as our cases.
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P 272
The first familial syndrome of camptodactyly, arthropathy, coxa vara, pericarditis in a Hungarian family

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BACKGROUND: The camptodactyly, arthritis, coxa vara, pericarditis syndrome is inherited as an autosomal recessive disorder caused by a defective gene on chromosome 1q25-31.It is characterized by congenital camptodactyly and childhood onset of noninflammatory synovial hyperplasia.
OBJECTIVE: The authors present the clinical and radiographic features of camptodadactyly-arthropathy-coxa-vara-pericarditis (CACP) syndrome in a Hungarian family. They present the clinical and radiological differentiation of CACP syndrome from juvenile idiopathic arthritis.
METHOD: CASE REPORT: Results: The brothers were born in Hungary. There was no history of consanguinity or unusual genetic conditions in either parents. They were ten and sixteen years old and were seen by us for flexed fingers, swelling and contractures in most of their joints (knees, ankles, wrists).They received steroidal, non steroidal therapy, methotrexat without success. The lack of clinical signs of inflammation, normal erythrocyte sedimentation rate, C-reactive protein and full blood, absent inflammatory changes in the synovium, lack of cells in the synovial fluid, and the radiological features, the non erosive arthropathy with large joint effusions, help us to differentiate the symptoms from JIA.
CONCLUSIONS: However the familial arthropathy associated with congenital flexion deformity of the fingers was described by Jacobs in 1965, there are only a few reported cases, much more sporadically occurring cases. JIA is a diagnosis of exclusion and there are a number of disease entities affecting the joints that may present in similar way. The CACP differentiation from JIA is clinically important, for the different management of the two conditions and because of the possible severe side effects of JIA treatment.
Although the gene has not been identified it has been mapped to chromosome 1q25-31.
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P 273
Disease patterns in Vietnamese children with SLE

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BACKGROUND: Incidence and disease pattern of juvenile SLE (jSLE) is described to differ among ethnic groups.
OBJECTIVE: Our objectives were to describe disease patterns in a consecutive referral based cohort of 45 native Vietnamese jSLE children and to do a 6-month renal follow up on severe nephritis cases.
MATERIAL: 45 children (f/m = 4/1) referred to the Ho Chi Minh City Children's Hospital No.1 over a 12-month period in 2009. In 29 Lupus Nephritis (LN) patients two renal biopsies were performed, the first at onset and the second after initial induction therapy (n = 15). CNS involvement or LN ISN (International Society of Nephrology) class IV or worse were treated with i.v. methylprednisolone and low dose i.v. cyclophosphamide (max. 0.5 g/dose) followed by maintenance therapy with azathioprine and oral prednisolone. All other cases or cases with mild LN were treated with systemic steroids only.
RESULTS: Mean age at diagnosis was 12.8 y (SD=2.5). 37 (82%) fulfilled criteria for LN, of whom 29 had a renal biopsy, 20 ISN Class IV, 8 ISN Class III, 1 complex presentation of ISN Class III/ V. At diagnosis high SLEDAI and ECLAM scores were recorded, mean (SD) = 23.8 (11.6) and 6 (2.3) receptively. Decreased Haemoglobin (g/dL) mean (SD) = 8.5 (2.1), positive Coombs test in 30 of 36 tested (83%), increased plasma Creatinine (unit) mean (SD) = 0.98 (1.2) and ESR mean (SD) = 83.6 (37.4) were the most outstanding biochemical findings. LN was more prevalent in the children <12 y of age at diagnosis (Fisher's Exact Test p=0.06 (ns)). Patient age at diagnosis was positively correlated to the SLEDAI (p=0.034) and ECLAM (p=0.022). At 6 month follow-up 15 patients were in complete remission, 5 were in partial remission, 6 had stable disease, 3 had relapsed, 3 had evolving disease, 2 had ongoing resistant disease and 4 had died. Seven patients were lost to follow-up. The second renal biopsy showed improved ISN class in 13 of 15; in 2 cases it remained unchanged.
CONCLUSION: The study was suggestive of distinct SLE patterns in Vietnamese children characterized by a strikingly high prevalence of Coombs positive anaemia, high prevalence of LN and very high SLEDAI scores at the time of diagnosis.

P 274
Prevention of flare recurrences in childhood refractory chronic uveitis: an open-label prospective, comparative, multi-centre, cohort study of Adalimumab versus Infliximab

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OBJECTIVE: To compare the efficacy and safety of Adalimumab versus Infliximab in an open-label prospective, comparative, multi-centre, cohort study of childhood non-infectious chronic uveitis.
METHODS: 33 patients (22 F, 11 M; median age: 9,17 years) with refractory vision threatening non-infectious uveitis, were enrolled, over 28 months, to receive, for at least 1 year, Infliximab (5 mg/kg at weeks 0, 2, 6 and then every 6–8 weeks) or Adalimumab (24 mg/sq.mt, every 2 weeks). Primary outcome was to assess, once remission was achieved, the time of a first relapse during time treatment. Time to remission, time to steroid discontinuation and the number relapses, were also considered.

RESULTS: 16 children (12 with Juvenile Idiopathic Arthritis [JIA], 3 with idiopathic uveitis, 1 with Behçet's disease) were recruited in the Adalimumab cohort; 17 children (10 with JIA, 5 with idiopathic uveitis, 1 with early-onset sarcoidosis, 1 with Behçet's disease) into the Infliximab group. Cox-regression analysis did not show statistical significant differences between the two groups with regard to time to achieve remission, and time to steroid discontinuation, whilst showed a higher probability of uveitis remission on Adalimumab during the time of treatment entered for each cohort (Mantel-Cox $\chi 2$ 6.83, $p<0.001$). At 40 months follow-up, 9/15 children on Adalimumab (60%) compared to 3/16 children on Infliximab (18.8%) were still on remission on therapy ($p<0.02$).
CONCLUSION: Even if limited to a relatively small group, our study suggests that, at 3 year treatment, Adalimumab is more efficacious than Infliximab in maintaining remission of chronic childhood uveitis.

P 275
An atypical presentation of Kikuchi-Fujimoto Disease associated with a transient increase of lupus specific autoantibodies: case report and literature review

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CASE REPORT: A 16-year-old boy with an unusual presentation of Kikuchi-Fujimoto disease (KFD) is described. The patient presented with fever, weight loss and severe abdominal pain secondary to extensive necrotizing retroperitoneal and mesenteric lymphadenopathy. Work up for infections and malignant disorders was negative. While in hospital, the patient developed a pericardial effusion and cotton wool spots on the retina. Despite autoantibodies being initially negative, the patient developed positive ANA, anti-Sm and anti-RNP antibodies during the course of his illness, which suggested systemic lupus erythematosus as a possible etiology. However, the patient started to improve spontaneously and no immunosuppressive therapy was initiated. Full remission was achieved 8weeks after initial presentation. Interestingly, all previously positive autoantibodies became negative 5months after initial presentation. Nine months after initial presentation, the patient remains in remission without any treatment with no clinical or serological evidence of autoimmune disease.
DISCUSSION: We hypothesize that the transient elevation of autoantibodies was triggered by extensive lymph node necrosis and may have contributed to other organ involvement (retinal vasculitis and pericarditis). KFD can present as severe necrotizing abdominal lymphadenitis and mimic several features of systemic lupus erythematosus.

P 276
PFAPA syndrome: single centre experience

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INTRODUCTION: PFAPA syndrome (Periodic Fever, Aphthous stomatitis, Pharyngitis and Adenitis) is an idiopathic autoinflammatory disease with the first manifestation often before 5 years of age.
AIM: To describe clinical and laboratory characteristics of the patient's cohort with PFAPA syndrome in Czech Republic.
METHODS: Clinical data from 82 patients were analysed using the PFAPA questionnaire. Laboratory parameters (C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), white blood count (WBC) has been evaluated in febrile and afebrile period.
RESULTS: 42 boys and 40 girls with PFAPA syndrome were diagnosed between years 2004 – 2010. Median age of the first manifestation was 18 months, median interval between attacks was 4 weeks and fever duration was 3.5 days. Fever was associated with pharyngitis/tonsilitis (90%), cervical adenitis (77%) and aphthous stomatitis (45%).
All patients had high levels of routine inflammatory parameters such as CRP (median 63.4; range 11.6-237.4 mg/l), ESR (median 30.5; range 9-60/h), and leukocytosis (median 13.8; range 2.6-19.9.109/l) with subsequent normalisation in afebrile time period. All children had negative mevalonic acid in urine.
Corticosteroid therapy was successful in febrile attack in 81% and tonsilectomy in 90% of children.
CONCLUSIONS: PFAPA syndrome appears to be relatively common cause of recurrent fever in early childhood in Czech Republic. The diagnosis was made after careful clinical exclusion of hereditary fevers and other systemic diseases or immune deficiencies. To our knowledge, we have the follow-up of the largest cohort of patients with PFAPA syndrome in Europe.
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P 277
Severe atipical Henoch-Schonlein Purpura with elements of Microscopic Polyangitis

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BACKGROUND: Clasificafication, even with new diagnostic criteria, and diagnosis of Henoch-Schonlein purpura (HSP) or microscopic polyangitis (mPAN) can be difficult in some patients.
AIM: We present case of HSP with early appearance of long lasting necrotic purpuric skin changes and nephritis resistant to steroid therapy hard to differentially diagnose to microscopic polyangitis.
RESULTS: Girl I.N., age 5 years, two weeks after moderate respiratory infection developed purpuric skin changes with elements of necrotic purpura at lower limbs and gluteal region. She also had oedema and pain in talocrural joints and was diagnosed as HSP and symptomatic therapy was commenced. Few weeks later, laboratory findings have showed microhematuria and secondary nephrotic syndroma. She was hospitalised and treated with corticosteroids, diuretics, antihypertensive and immunoglobulin therapy. Extremity oedema vanished but ulcerative-necrotic vacuities persisted and due to persistent proteinuria (2g/24h) kidney biopsy was performed showing non-specific diffuse mesangium proliferation with rare crescent and IgA imunofluorescent deposits. Laboratory findings were: ESR=30/58 LDH=1250 CRP=2.99 IgA=1.18 IgM=0.45 IgG=2.85 C3=2.14 C4=0.213 anti-SS-A (Ro) anti-SS-B (La) antiPR3 (cANCA) anti-MPO (pANCA) ANA and dsDNA were negative, but RF screen was positive. She was treated with methyl-prednisolon boluses and azathioprine, but with limited response. She still had proteinuria and ulcerative-necrotic vacuities. Biopsy of skin changes has showed microscopic vacuities with predominant perivascular infiltrates indicating possible diagnosis of microscopic polyangiitis. More over, coagulation parameters were changed: PT=10,5 s, APTT=22,2 , D-Dimer=90 ng/ml, extremely low Protein S, AT III=67, P chrom=257%, APCR V=3,08. Since, vasculitic and kidney disease progressed she was treated with steroid and cyclophosphamide pulses followed with tapering dose of steroids and antihypertensive therapy. After six months proteinuria disappeared and skin changes were reduced.
CONCLUSION: Clear diagnosis of type of vasculitis in this patient could not be established. In mPAN high sensitivity marker - ANCA are positive but in 80% of patients, kidney biopsy finding (even typical for HSP) can be seen in both vasculitides but steroid resistant disease and skin biopsy finding favour mPAN diagnosis.

P 278
PFAPA syndrome and increased levels of IgD-a distinct clinical phenotype?

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BACKGROUND: PFAPA syndrome is characterized by episodes of periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis. Previous reports suggested that high levels of serum immunoglobulin D (IgD) are observed in children with PFAPA and perhaps are associated with a distinct clinical phenotype.
OBJECTIVE: Analyze whether there were any clinical differences between children with PFAPA syndrome and high serum levels of IgD and those with normal levels of IgD.
METHODS: Single centre retrospective case series note review of children with recurrent fevers meeting the criteria for PFAPA syndrome. Two groups were identified according to the presence of high serum levels of IgD or not (normal 0-100 IU/L). History, physical examination findings, therapy, immunological, serological studies and genetic testing for mutations in the MVK gene, and other routinely tested periodic fever genes were reviewed. Differences in frequencies of symptoms and response to therapy were evaluated by using the Fisher exact test and differences between average values of continuous variables were evaluated by using the Mann-Whitney U test.
RESULTS: Twenty five children, 12 female, with a median of 7.4 (range 1.8-13.5) years old at presentation were identified. Five of these children were documented to have increased levels of serum IgD with a median of 124 (range 100-345) IU/L. There were no significant differences between the children with PFAPA and high IgD compared to those with PFAPA and normal levels of IgD, in respect to attack frequency (P=0.8), duration (P=0.28) or attack precipitants (P=1). The pattern of symptoms was similar between the two groups with the exception of gastrointestinal symptoms being reported significantly more frequently in those with high levels of IgD than those with normal levels (P=0.037). None of the children with high IgD tested positive for MVK, MEFV or TNFRSF1A mutations. In addition there were

no differences in the treatment responses to corticosteroids (P=0.47), tonsillectomy (P=0.99) or antibiotic courses (P=1.0) between the two groups.
CONCLUSIONS: With the exception of increased frequency of gastrointestinal symptoms there appeared to be no differences in the symptoms and treatment responses between children with PFAPA and high levels of IgD and children with PFAPA and normal IgD.

P 279
Early functional impairment and structural changes predict long-term damage in children with Polyarticular Juvenile Idiopathic Arthritis

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BACKGROUND: Juvenile idiopathic arthritis (JIA) is a heterogeneous condition whose clinical course varies widely and is difficult to predict. Predicting outcome in JIA is crucial for its optimal clinical management. It would be desirable to distinguish patients with a high likelihood of untoward outcome so as to best manage the course of their disease and treat them with appropriately aggressive therapy at an early stage. This is important as new therapies that can be effective in the most severe and refractory forms of JIA are now available
OBJECTIVE: To search for early predictors of long-term damage and remission in children with polyarticular JIA.
METHODS: 130 children with polyarticular-course JIA and wrist involvement who underwent a bilateral hand-wrist radiographs within 2 years after disease onset from January 1986 to December 2004 were included in the study. All but 1 patients had received MTX therapy, whereas 22 patients had received biologic agents. Long-term outcome was assessed as follows: 1) Radiographic damage at 5 years, scored with the adapted Sharp-van der Heijde (aSH) method. 2) Damage at last-follow-up visit (5-21 years after baseline) defined as the presence of 1 or more of the following 5 criteria: a) CHAQ score >0.625; b) restricted joint count >7; c) Juvenile Arthritis Damage Index-Articular score >2; d) Poznanski score of radiographic damage <-2; e) Steinbrocker functional class II-IV. 3) Remission at last follow-up visit, defined according to Wallace criteria. Radiographic damage at 5 years was defined as an aSH score above the minimal clinically important difference between 2 readers. For outcome 2), score threshold of measures a) to c) was set at the third quartile of score distribution. Predictors included sex, ILAR category, disease duration at baseline, and baseline value and baseline-1 year change in joint counts, CHAQ score, radiographic scores (aSH and Poznanski scores), and acute phase reactants. Predictor analyses included univariate and multivariate tests.
RESULTS: Outcome predictors in multivariate models were as follows: 1) Radiographic damage at 5 years was predicted by ESR >67 mm/h (OR 11.7) and abnormal aSH score in >1 joints at baseline (OR 8.2), and by baseline-1 year change in restricted joint counts >3 (OR 7.2). 2) Damage at last follow-up visit was predicted by age >5.4 years (OR 5.4) and CHAQ score >0.625 (OR 4.1) at baseline, and by baseline-1 year change in restricted joint counts >1 (OR 3.6). 3) No predictors were identified for remission at last follow-up visit.
CONCLUSION: We found that early functional and structural damage predicted strongly long-term disease damage. This underscores the need of prescribing precociously an aggressive therapy, including biologic medications, to JIA patients who develop functional impairment or signs of radiographic damage early in the disease course.

P 280
TNF-blocking agents in Juvenile Psoriatic Arthritis: are they effective?

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BACKGROUND: In adult-onset Psoriatic Arthritis (PsA) anti-TNF therapies seem highly effective and safe. Many studies have been done to the efficacy and safety of anti-TNF blocking agents in JIA patients with a poly-articular course. Until now no research has focused on Juvenile PsA (JPsA) only.
OBJECTIVES: To evaluate the effectiveness of TNF-blocking agents in JPsA.
METHODS: This study is embedded in the ABC-register, a since 1999 prospective ongoing multicentre, observational study of all Dutch juvenile idiopathic arthritis (JIA) patients using biological agents. At start of treatment, after three, six, 15 months and thereafter yearly variables of the JIA disease activity score; physician's global (VAS), Childhood Health Assessment Questionnaire (CHAQ), including global assessment of wellbeing (VAS), number of active and limited joints and ESR, are retrieved. Response of arthritis was assessed by the ACR paediatric criteria, and inactive disease in accordance with the Wallace criteria.
RESULTS: Included were 18 patients diagnosed as JPsA subtype, and 2 JIA patients with other subtypes who developed psoriatic skin lesions during treatment: 70% female, 85% polyarticular course, median age at onset of arthritis 11.1 (range 3.3-14.6) years, median follow-up since start of anti-TNF-alpha agents 27 (range 3-80) months. Nineteen patients started etanercept, one adalumimab. After 3 months of treatment 83% of JPsA patients achieved ACR30 response, increasing to 100% after 15 months. Sixty-seven percent of the patients reaching 39 months of follow-up (n=6) reached inactive disease.
The ACR responses and inactive disease in the JPsA patients, in all JIA patients and in non-systemic JIA patients is shown in **Figure 1.**
There was no discontinuation because of inefficacy. Six patients discontinued treatment after good clinical response. However, 5 flared again and restarted treatment after which all achieved good clinical response. During treatment 4 patients developed de novo psoriasis; in only 4 of the 9 patients the pre-existing psoriatic skin lesions improved.
CONCLUSION: Anti-TNF-alpha therapy in JPsA seems effective to treat arthritis. During treatment the psoriatic skin lesions improved in a minority of the patients, and 4 patients developed de novo psoriatic skin lesions. In most patients the arthritis flared after discontinuation of treatment, emphasizing the need to investigate optimal duration of therapy.
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University Medical Centre Groningen, Beatrix Children's Hospital, Groningen
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P 281
Adolescents with Juvenile Idiopathic Arthritis currently followed in a tertiary care hospital have a better psychosocial well-being than healthy adolescents

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BACKGROUND: Assessment of health-related quality of life (HRQL) is increasingly recognized as a fundamental component of the clinical evaluation of children with pediatric rheumatic diseases (PRD). It has been suggested that measurement of HRQL be incorporated into routine pediatric rheumatology care. Several studies have investigated the HRQL of children with PRD. However, comparison with healthy children has seldom been attempted.
OBJECTIVE: To compare the health-related quality of life (HRQL) of children with juvenile idiopathic arthritis (JIA) and healthy children.
METHODS: 472 parents of children with JIA, 232 children with JIA, 801 parents of healthy children, and 796 healthy children completed independently the Pediatric Rheumatology Quality of Life scale (PRQL). Children with JIA and healthy children who completed the questionnaire were aged >7-8 years.
RESULTS: As expected, both parents of children with JIA and JIA children provided worse rating on the physical health (PhH) subscale of the PRQL than did parents of healthy children ($p<0.0001$) or healthy children ($p=0.0002$), respectively. However, scores on the psychosocial health (PsH) subscale were comparable between parents of JIA patients and parents of healthy children ($p=0.34$), and were much worse for healthy children than for children with JIA ($p<0.0001$). Stratification of children by age (<10 years, 10-13 years, >13 years) showed that proxy- and self-reported scores on the PsH subscale were much worse for healthy children older than 13 years than for the other age groups. These differences were not related to sex or JIA severity. The **figure** shows the comparison of the frequency of abnormal values in the 10 items of the PRQL as self-reported by adolescents with JIA (continuous line) and healthy adolescents (dotted line). Items 1 to 5 refer to the PhH, whereas items 6 to 10 refer to the PsH.
CONCLUSION: To our knowledge, our study is the first to show that psychosocial functioning of adolescents with JIA is better than that of healthy adolescents. This phenomenon may depend, at least partially, on most of the JIA patients attending our clinics for follow-up visits having well-controlled disease with little or no disease activity or disability. This observation deserves further exploration in different populations.
REFERENCES: 1) Filocamo et al. A new short and simple health-related quality of life measurement for paediatric rheumatic diseases: initial validation in juvenile idiopathic arthritis. Rheumatology 2010

P 282
Effectiveness of etanercept in children with Enthesitis Related Arthritis

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BACKGROUND: Etanercept has proven to be effective in children with systemic and polyarticular Juvenile Idiopathic Arthritis (JIA). Experience with etanercept in the treatment of children with the Enthesitis Related Arthritis (ERA) subtype is limited to case-reports and small series, mostly retrospective and including other TNF-alpha antagonists.
OBJECTIVES: To evaluate the effectiveness of etanercept in JIA-patients with ERA subtype.
METHODS: This study is embedded in the ABC-register, a since 1999 prospective ongoing multicentre, observational study of all Dutch JIA patients using biological agents with until now more than 300 JIA-patients included. Patient and disease characteristics are collected at baseline. At start of treatment, after three, six, 15 months and thereafter yearly variables of the JIA disease activity score; physician's global (VAS), Childhood Health Assessment Questionnaire (CHAQ), including global assessment of wellbeing (VAS), number of active and limited joints and ESR, are retrieved. Response of arthritis was assessed by the ACR paediatric criteria, and inactive disease in accordance with the Wallace criteria.
RESULTS: In our register 14 patients with ERA-subtype are included; 79% male, presence of enthesitis in 86% (mostly the Achilles tendon), presence of SI-joint tenderness and/or inflammatory lumbosacral pain in 57% and HLA-B27 positivity in 79%. None had (symptomatic) anterior uveitis. Median age at onset ERA was 10.4 years (range 2.3-17.0 years), median disease duration at start etanercept 3.3 years (range 0.8-11.8 years), with a median follow-up since start etanercept of 3.8 years (range 0.5-9.2 years).
After 3 months of etanercept treatment 86% achieved ACR30 response, increasing to 91% at 15 months of treatment. Of the patients reaching 27 months (n=6) and 39 months of follow-up (n=4), all showed ACR
pedi70 responses and inactive disease was reached resp. in 67% and 50%.
The ACR responses and inactive disease in the ERA patients, in all JIA patients and in non-systemic JIA patients is shown in **Figure 1.**
One patient temporarily discontinued etanercept due to an episode of fever. None discontinued due to inefficacy. One patient withdrew etanercept after 4.2 years of treatment because remission was reached. However, flared after 1.5 year and needed to restart etanercept with again a good clinical response.
CONCLUSION: Etanercept in enthesitis related arthritis seems very effective, with 91% achieving ACR pedi 30 response after 15 months of treatment, and up to 67% of the patients reaching inactive disease.
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University Medical Centre Groningen, Beatrix Children's Hospital, Groningen
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Haga Hospital, Juliana Children's Hospital, The Hague
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P 283
An International Consensus Survey of the Diagnostic Criteria for Macrophage Activation Syndrome in Systemic Juvenile Idiopathic Arthritis

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BACKGROUND: Macrophage activation syndrome (MAS) is a potentially life-threatening complication of systemic juvenile idiopathic arthritis (sJIA) Because MAS is a serious condition that can follow a rapidly fatal course, prompt recognition of its clinical and laboratory features and immediate therapeutic intervention are critical. However, diagnosis of MAS can be difficult and hard to distinguish from sepsis-like syndromes. In addition, subclinical forms of MAS in SJIA underscore the importance of establishing criteria sensitive enough to identify MAS from routine disease flare.
OBJECTIVE: To select the clinical, laboratory and histopathologic features that are more suitable as diagnostic criteria for sJIA-associated MAS through an international Delphi questionnaire survey.
METHODS: All members of the Paediatric Rheumatology International Trials Organisation (PRINTO), the Childhood Arthritis & Rheumatology Research Alliance (CARRA), and the Pediatric Rheumatology Collaborative Study Group (PRCSG) were submitted a questionnaire that listed the 28 most typical features of MAS and were first asked to select the 10 features that they deemed most important in the diagnosis of the syndrome, and then to rank order the 10 selected features by assigning 10 to the most important, and end with 1 as the least important.
RESULTS: A total of 232 pediatric rheumatologists participated in the survey. The table shows, in order of frequency, the features selected by more than 50% of respondents. Results are reported for all respondents and for respondents divided by geographic area. Falling platelet count, hyperferritinemia, evidence of hemophagocytosis in the bone marrow, falling leukocyte count, and persistent fever were the 5 most frequently selected features. Only evidence of hemophagocytosis in the bone marrow, hyperferritinemia, and persistent fever reached a median rank >7. Overall, investigators from Europe and other parts of the world tended to give more weight to clinical manifestations than North American investigators, whereas North American investigators appeared to rely more on laboratory abnormalities than investigators from Europe and other parts of the world.
CONCLUSIONS: We identified the features of MAS that were agreed upon by the majority of international pediatric rheumatologists. The ability of each feature to discriminate MAS from potentially "confusable" conditions and the optimal diagnostic threshold for laboratory tests will be assessed through a large-scale data collection, which is ongoing. Altogether, these processes will lead to the development of a new and robust set of criteria for MAS complicating SJIA

P 284
Antinuclear antibody positive patients should be grouped as a separate category in the classification of juvenile idiopathic arthritis

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OBJECTIVE: We hypothesized that in the International League of Associations for Rheumatology (ILAR) classification of juvenile idiopathic arthritis (JIA), patients with similar characteristics are classified into different categories. We sought to investigate whether ANA-positive patients belonging to the ILAR categories of oligoarthritis, rheumatoid factor (RF)-negative polyarthritis, psoriatic arthritis, and undifferentiated arthritis share homogeneous features and to compare these features with those of ANA-negative patients in the same categories.
METHODS: We identified all JIA patients who were followed up during a 22-year period. ANA positivity was defined as ≥ 2 positive results at a titer of ≥ 1:160. Demographic and clinical features were recorded retrospectively and compared among ANA-positive and ANA-negative patients. Statistics include univariate, multivariate, multiple correspondence, and cluster analysis.
RESULTS: A total of 1219 patients fulfilled the ILAR criteria for JIA. The ILAR category was systemic arthritis in 149 patients (12.2%), oligoarthritis in 649 patients (53.2%), RF-positive polyarthritis in 26 patients (2.1%), RF-negative polyarthritis in 223 patients (18.3%), enthesitis related arthritis in 73 patients (6.0%), psoriatic arthritis in 37 patients (3.0%), and undifferentiated arthritis in 62 patients (5.1%). Of the 649 patients with oligoarthritis, 433 had the persistent subtype and 195 had the extended subtype; 21 patients could not be sub-classified in the course type due to a disease duration of less than 6 months. Patients with systemic arthritis, RF-positive polyarthritis and enthesitis-related arthritis were excluded from the study. The remaining 971 patients belonging to the ILAR categories of oligoarthritis, RF-negative polyarthritis, psoriatic arthritis, and undifferentiated arthritis were combined and classified according to their ANA status as follows: 711 (73.2%) were ANA positive, 149 (15.3%) were ANA negative, and 111 (11.4%) had a doubtful ANA status. Patients with a doubtful ANA status were excluded from the analysis. The number of ANA determinations per patient in the 860 patients who had the ANA status specified ranged from 2 to 20 (mean 5.4); the total number of determinations was 4610. All ANA-positive patients were similar in terms of age at disease presentation, female-to-male ratio, and frequency of asymmetric arthritis and iridocyclitis. Compared with ANA-positive patients, ANA-negative patients were older at disease presentation and had a lesser female prevalence, a lower frequency of iridocyclitis and asymmetric arthritis, a greater number of affected joints over time, and a different pattern of arthritis. The close relationship between the presence of ANA and younger age at disease presentation, female predilection, asymmetric arthritis, and development of iridocyclitis was confirmed by multivariate, multiple correspondence, and cluster analysis. The figure shows the 2-dimensional scatterplot of multiple correspondence analysis. This analysis led to the identification of 2 patient groups with distinct characteristics: the circle identifies the interrelated variables that define the ANA-positive patient profile.
CONCLUSION: Our findings substantiate the hypothesis that ANA-positive patients classified into different JIA categories by current ILAR criteria constitute a homogeneous patient population, irrespective of the course of joint disease or the presence of psoriatic features.

P 285
Odontostomatologic involvement in Juvenile Localized Scleroderma of the face

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BACKGROUND: Juvenile Localized scleroderma (JLS) is the most frequent form of scleroderma in childhood. The linear facial subtype (known also as scleroderma en coup de sabre and Parry-Romberg syndrome) can lead to significant aesthetical and functional abnormalities. Despite their quite frequent clinical observation, the odontostomatologic complications are not thoroughly described in the literature.
OBJECTIVE: Aim of the study was to describe the clinical features and prevalence of the most frequent odontostomatologic complications of JLS of the face and to propose clinical and radiologic criteria for the follow-up and the management of these complications.
METHODS: We performed a cross-sectional, multicenter study involving a multidisciplinary team formed by pediatric rheumatologists, dentists and radiologists. Selected patients with a diagnosis of JLS of the face underwent a comprehensive rheumatologic evaluation, dental examination (intraoral and gnatologic examination, orthodontic casts, photographs), conventional radiology (orthopantomography, frontal and lateral skull teleradiography) and Cone Beam Computed Tomography (CBCT). An odonto-maxillo-facial score (OMF-score), based on four clinical-instrumental parameters, including facial anomalies (soft tissues and bone), dental abnormalities, asymmetry and malocclusion, was applied.
RESULTS: 16 patients, 9 F, 7 M, aged 6.5–21.9 years, were investigated. The mean disease duration was 7.7 years (range 1.4–18.5), 62,5% had extracutaneous complications, 87,5% were in clinical remission. All patients reported at least one odontostomatologic complication. The main alterations were: overgrowth tendency of the lower third of the face (81,8%), malocclusion (75%), gnatologic alterations (66,7%), dental anomalies (62,5%), skeletal asymmetry (50%), bone involvement (50%), slight quantitative reduction of the soft tissues on the affected side (43,7%) and TMJ involvement (18,7%). According to the OMF-score, the odontostomatologic involvement was mild in 25% of the patients, moderate in 56% and severe in 19%. No correlation was found between degree of odontostomatologic involvement and disease duration.
CONCLUSIONS: A moderate-to-severe odontostomatologic involve-ment was found in the majority of the patients with JLS of the face. CBCT could replace conventional radiology in the dental and maxillofacial practice and may represent a new technique for disease assessment and monitoring. Including this emerging technique, we propose a multistep clinical-radiological protocol to standardize the management of the odontostomatologic complications of JLS.

P 286
Quality of life in patients with Juvenile Arthritis: Infliximab might make a difference

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Relevancy. Juvenile arthritis (JA) leads to premature impairment of pediatric physical health, psychological and social limitations, that considerably worsen health related quality-of-life of patients. That is why improvement of health related quality-of-life (HRQOL) is one of the main aims of treatment of patients with juvenile arthritis.
AIM: Evaluate influence of infliximab therapy on HRQOL of children with different forms of JA.
Patients and methods There were examined 97 children (2 - 18 years, median age 6,29±4,08 years, 68 girls, 29 boys) 37 - with oligoarticular JIA, 31-with polyarticular JIA, 15-with systemic JIA and 14 – with Juvenile Enthesitis related arthritis. 65 (67%) from 97 children were treated with infliximab for more than a year in the dose of 6 mg/kg. Evaluation of HRQOL was performed by the questionnaires PedsQL Generic Core Scale (PedsQL GCS), PedsQL Rheumatology Module (PedsQL RM) and CHAQ.
RESULTS: HRQOL of children with JA before the conducted therapy in all scales of PedsQL GCS was considerably lower in comparison with population norm (p<0,001). To week 54 of infliximab therapy there was detected statistically reliable increase of HRQOL values in all scales of self and proxy-report of PedsQL RM and PedsQL GCS (p<0,001). By CHAQ disability index decreased reliably from 1,43 to 0,28, pain level by VAS - from 7,23 to 0,6, Evaluation of health state by VAS increased from 7,58 to 2,53. To the year of receiving the therapy by self report HRQOL differed from population norm only by the scale of social functioning (p<0,01), and by proxy report HRQOL was lower only by the scales of emotional and social functioning (p<0,001).
CONCLUSION: Infliximab administration in pediatric rheumatologic practice increases physical, psychological, social adaptation of patients, allows changing diagnosis of such a severe disabling disease, as JA, stopping steadily progressing disease course and preventing severe disability in such tender age.

P 287
Different patterns of response to Anakinra treatment in Systemic onset Juvenile Idiopathic Arthritis

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BACKGROUND: Anakinra has shown promising results in the treatment of Systemic onset Juvenile Idiopathic Arthritis (SoJIA). There have been reports of different response rates from USA, France and Italy.
AIMS: To access efficacy and safety of anakinra treatment in a cohort of patients with SoJIA with followup period of 12 months.
METHODS: SoJIA patients treated with anakinra (2mg/kg/day) were monitored clinically and biochemically before starting anakinra, at 3, 6 and 12 months of treatment and for adverse effects.
Outcome measures included normalization of acute phase markers and systemic features, ACR pedi 50 improvement, steroid reduction and ability to use anakinra as monotherapy.
RESULTS: 20 SoJIA patients were treated with anakinra. Median age at start of treatment was 8.1years (range 10months-16.5years). The most frequent prior treatments were prednisolone (19/20), methotrexate (18/20) and anti-TNF-α (12/20). Steroids were reduced in most patients (14/20), but monotherapy was achieved in only one.
Sustained efficacy (as defined by reaching ACR pedi 50 improvement, no systemic symptoms and normal SAA/CRP) was seen in 10/20, 7 of which are still on anakinra (1 has not yet reached 12 months of therapy); there was loss of efficacy in 3 patients after a median of 11months* (range 6-13months); 5/20 patients had no response and 5/20 showed partial responses **(table)**.
Median duration of anakinra treatment was 14months (range 0.5-53months). Adverse events included mild injection site reactions (13/20), pain on administration (2/20), and infections (2/20), 1 of which (partial responder) had to stop treatment.
CONCLUSION: IL-1 inhibition with anakinra was associated with substantial efficacy in 50% of patients in this SoJIA cohort, with a good safety profile. Efficacy was not sustained after a median of 11months in 3 patients (15%).

P 288
Nutritional status related to Vitamin D in children and adolescents with Systemic Lupus Erythematosus

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BACKGROUND: The vitamin D deficiency has been related to the development of autoimmune diseases. There are only a few studies in the literature evaluating the nutritional status related to vitamin D in pediatric patients with rheumatic diseases.
OBJETIVES: To evaluate the levels of 25(OH)D3 and correlate with disease activity, use of medications (chloroquine and glucocorticoids), calcium and vitamin D intake, bone mineral density and parathormone (PTH) levels.
METHODS: Determination of 25(OH)D3 and PTH was performed during the spring in 30 children and adolescents with Systemic Lupus Erythematosus according to the Hochberg classification criteria (1997), with or without disease activity, any clinical manifestation, in use of any medication, minimal disease evolution of 6 months and compared to 30 healthy individuals age and gender matched who were not on any medication and with no calcium metabolism impairment. Vitamin D normal levels were considered between 20 – 32 ng/mL.
RESULTS: We found significant different levels of 25(OH)D3 between patients and controls (mean 18.79 ng/mL and 27.18 ng/mL respectively – p<0.001). 15 (50%) of patients and 6 (20%) of controls had low levels of 25(OH)D3. There was no association between PTH levels in patients and controls (mean of 35.86 pg/mL and 31.26 pg/mL respectively – p=0.268). Only one patient with low level of vitamin D presented with hyperparathyroidism. We found no association between

disease activity when considered SLEDAI >1 and low levels of vitamin D with a mean concentration of 12.05 ng/mL (4.61–19.79) in a total of 10 (33%) patients (p=0.705). Considering a SLEDAI >4 there was no association between disease activity and low vitamin D levels (p=0.439) with a mean concentration of 13.27 ng/mL (6.04–19.79) in a total of 6 (20%) patients (p=0.439). 11 (37%) patients have been taken vitamin D supplementation and 5 (17%) had low levels of vitamin D. 7 patients (23%) presented a bone mineral density under -2.0 SD and mean levels of 25(OH)D3 of 14.70 ng/mL (9.61–19.88) with no association between them (p=0.456).
CONCLUSION: The patients presented with serum levels of vitamin D significantly lower than the controls, however those values did not correlate with disease activity, higher levels of parathormone and bone mineral density alterations.
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P 289
Fibrodysplasia Ossificans Progressiva in South African children

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INTRODUCTION: Fibrodysplasia Ossificans Progressiva (FOP) [OMIM 135100] is an uncommon genetic disorder in which progressive ossification of connective tissue leads to severe musculoskeletal disability. This disease presents in young children, initially with painful , hard swellings on th back and neck leading to progressive limitation of the spine and upper limbs initially, followed eventually by complete immbobilisation of all joints in adulthood. The nature of its presentation means that it is highly likely that a number of these patients will present to paediatric rheumatologists.
FOP is an autosomal dominant trait and the majority of affected persons represent new mutations for the determinant gene, ACVR1. The protein product of this gene is a trans-membrane receptor with functions in the bone morphogenetic protein (BMP) signalling pathway.
Although FOP has a worldwide distribution, there are only a few reports of affected persons of indigenous African stock. Four were documented in South Africa, and from the literature only three more can be identified in other countries in sub-Saharan Africa. This paucity of reports probably reflects the difficulty with diagnosis and compromised survival in disadvantaged circumstances rather than any actual discrepancy in mutation rate.
METHODS: We have recently studied and documented six affected individuals in the African (Xhosa and Zulu) community.
RESULTS: Two were initially reported in childhood almost three decades ago [2] and four are young children. All have the typical features of heterotopic ossification (in an embryonal pattern from dorsal to ventral and from cranial to caudal) as well as the characteristic deformity of the big toe. In one patient delay in diagnosis resulted in unnecessary and harmful biopsies, which exacerbated and stimulated heterotopic bone formation.
CONCLUSION: FOP is a devastating condition with no known cure, but early diagnosis is essential to prevent unnecessary and directly harmful special investigations. A number of these patients will present to paediatric rheumatologists and orthopedic surgeons. The pathogenesis of FOP offers fascinating insights into the function of Bone Morphogenic Proteins and bone metabolism.

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Multiple organ dysfunction syndrome in Juvenile Systemic Lupus Erythematosus patients

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BACKGROUND: Multiple organ dysfunction syndrome(MODS) is a important factor associated with high mortality in children admitted in pediatric intensive care unit(PICU) 1. Patients with juvenile systemic lupus erythematosus(JSLE) admitted in PICU often present several causes of hospitalization as disease activity, infections and MODS with high mortality rates 2,3. However, there are few studies evaluating MODS in such patients.
OBJECTIVES: To analyze MODS in a population of JSLE in the PICU of a tertiary University Hospital
METHODS: From January 1994 to June 2009,58 JSLE patients(ACR criteria) were hospitalized in PICU of our University Hospital and were studied. At admission in ICU, MODS was evaluated according to Goldstein4 sepsis definition and Wilkinson5 criteria. Goldstein assessed five organs and systems(cardiovascular, respiratory, renal, hematological and neurological) and Wilkinson evaluated six organs and systems(cardiovascular, respiratory, renal, hematological, neurological and gastrointestinal).Pediatric Risk of Mortality(PRISM) was also analyzed.6 Clinical and laboratorial features necessary to fulfill criteria and PRISM, disease activity (SLEDAI-2K)7, cumulative damage (SLICC-ACR/DI)8 and treatment were also collected in the first 72 hours after hospital admission.
RESULTS: Wilkinson and Goldstein criteria were performed in 48 patients and PRISM in 36. Death was observed in 18/48(37.5%) patients. JSLE patients fulfilled a median of two affected organs and systems according to both. These patients were divided in two groups: survivors and death. Of note, the median of Wilkinson and Goldstein criteria were significantly higher in those who died versus survived [3.0(1-4) vs.1.0 (0-3), p=0.001; 3.0(1-5) vs.1.5(0-4), p=0.004; respectively].Compromised cardiovascular system (present in 22 cases) showed the most strongly association with death in both evaluations (p=0.007). The median of PRISM score was significantly higher in those who died versus survived [14.5 (2-33) vs.4.5 (0-23), p=0.002]. Presence of sepsis (p=0.045), severe sepsis (p=0.002) and septic shock (p=<0.0001) were also considered risk factors for death outcome. In contract, systemic inflammatory response syndrome was similar in both groups (p=0.14). No differences were evidenced in the median of SLEDAI-2K and SLICC-ACR/DI in those who died versus survived [21.0 (2-39) vs. 20.0 (0-42), p=0.733; 1.0 (0-3) vs. 0 (0-3), p=0.801; respectively].
CONCLUSIONS: This study suggests that JSLE patients admitted on ICU with MODS by severe infectious are more susceptible to death, particularly in the presence of compromised cardiovascular system.
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P 291
Ultrasonographic measurement of the femoral cartilage thickness in Juvenile Idiopathic Arthritis patients with unilateral knee involvement

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BACKGROUND: Knee is the most commonly affected joint in patients with juvenile idiopathic arthritis (JIA). Loss of cartilage may be an early feature of joint destruction and may also predispose to early degenerative joint disease in late periods of life. Ultrasound is a validated technique to measure the femoral cartilage thickness.
OBJECTIVE: To explore sonographically whether there is difference in cartilage thickness measurements between the affected vs. unaffected knee joints in a group of oligoarticular JIA patients with unilateral knee involvement.
METHODS: Thirty-one JIA patients (17 F, 14 M; mean age 9.38±3.84 years) were enrolled. Patients with extended oligoarticular JIA and patients with involvement of both knees were excluded. Ultrasonographic measurements were performed axially with 5-10 MHz and 8-16 MHz linear probes (Diasus Dynamic Imaging) while both knees were kept in maximum flexion. Three thickness values were recorded from each knee; mid-condylar (lateral), mid-intercondylar and mid-condylar (medial). Each of the three measurements was compared with the contralateral side (affected side vs. unaffected side).
RESULTS: Mean disease duration of the patients was 30.22±30.88 months. Femoral cartilage thicknesses were found to be similar between the compared knee joints (all p values > 0.05).
CONCLUSIONS: In the light of our results, we may conclude that knee joint involvement does not cause early cartilage loss in patients with JIA. Future studies recruiting larger group of subjects with longer disease duration may provide further data whether the thickness of knee joint cartilage also remains similar in later periods of the disease.

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Long-term follow up of Hyper IgD syndrome: a national collaborative study

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INTRODUCTION: Hyper-IgD syndrome (HIDS) is an autosomal recessive disease caused by mutation in the MVK gene.
AIM: To analyze the long term follow-up of a group of children and young adults affected by HIDS
PATIENTS & METHODS: The first 10 exons of MVK genes were analyzed in 720 consecutive patients with periodic fever by means of denaturing high-performance liquid chromatography (DHPLC) and DNA sequencing. 40 patients carried 2 mutations of the MVK gene. Detailed clinical information were collected at the time of molecular analysis and last follow-up through a standardized questionnaire. Spontaneous disease course was classified as follows: i) resolution (no episodes in the last 6 months), ii) improvement (reduction of more then 30% of fever episodes) iii) stationarity iv) worsening (increase frequency of fever episodes or appearance of new major clinical manifestation).The Child Health Questionnaire (CHQ-PF 50) was used to assess the health related quality of life
RESULTS: The mean age of disease onset was 0.7 yrs (range1 months-3 yrs). At baseline, mean duration of fever episode was 4.7 days. The clinical features associated to fever episodes were abdominal pain (97.5%), cervical lymphadenopaty (97.5%) with pain (80%), diarrhea (77.5%), erythematous pharingitis (75%), vomiting (65%) and aphtous stomatitis (57.5%).
So far, data on follow-up are available for 24 patients. The mean follow-up time was 13.8 yrs (range 2.3-38.2 yrs). Steroid on demand was effective in treating fever episodes. Ten patients showed a significant spontaneous reduction of the frequency of fever episodes. In the remaining 14 patients the frequency of fever episodes was stable (7 patients) or increased (7 patients). In this latter group, a complete resolution was achieved after introduction of Anakinra (2 patients) and tonsillectomy (1 patient). One patients improved after Anakinra, 2 after tonsillectomy. Two patient did not respond to Etanercept. Health–related quality of life at follow-up was generally affected when compared to a cohort of healthy age-matched individuals .
CONCLUSIONS: Even if a relevant percentage of HIDS patient show a spontaneous amelioration of the disease, most of them display a tendency towards a persistence of fever episodes that affect their quality of life.

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Validation of the newly developed pediatric criteria for the diagnosis of Familiar Mediterranean fever in a large pediatric cohort of western European children with periodic fever

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INTRODUCTION: FMF belong to the group of the periodic fever and is caused by mutations in the MEFV gene. Despite the possibility of a molecular characterization the diagnosis of the disease is mainly based on clinical criteria. Several diagnostic criteria have been developed, but none of them are specific for the pediatric age. A new set of criteria for the diagnosis of FMF in children were recently proposed (Yalçinkaya et al., Rheumatology 2009;48(4): 395).
AIM: To verify in a pediatric cohort of Caucasian patients with periodic fever the sensitivity and specificity of the new pediatric criteria in comparison to Tel-Hashomers'.
PATIENTS & METHODS: Detailed clinical information on 389 pediatric patients (mean age 8,5 yrs; SD±8,3) with periodic fever were collected. All patients were screened for mutations of MVK, TNFRSF1A and MEFV genes. For each patient Tel Hashomer criteria and new pediatric FMF criteria were applied.
RESULTS: 106 children carried mutations of MEFV gene (40 were homozygous or compound heterozygous, 66 with a single mutation), 38 patients displayed two mutations of MVK gene. Structural mutations of TNFRSF1A gene were found in 12 patients, whereas 18 patients displayed low-penetrance (R92Q or P46L) TNFRSF1A mutations. 215 patients were negative to all three genes.
All patients (100%) carrying two mutations of MEFV gene and 49 heterozygous individuals (74%) were positive for Tel-Hashomer criteria. The same criteria were also positive in 135 (63%) of genetically negative and 71 % of individuals affected by other monogenic periodic fevers, with an overall specificity of 33.2%.
Conversely, the new pediatric criteria were positive in 33/40 (82,5%) patients carrying two MEFV mutations and in 27/66 (41%) heterozygous patients, whereas its overall specificity was 76 %.
Six out of the 7 patients carrying two MEVF mutations that did not satisfied the new pediatric criteria carried low penetrance mutations and generally displayed a mild phenotype.
CONCLUSIONS: Pediatric FMF criteria show an higher specificity when compared to Tel-Hashomer criteria.

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Sensitivity and Specificity of Diagnostic Guidelines for Macrophage Activation Syndrome (MAS) or Hemophagocytic Lymphohistiocytosis in children with Systemic JIA-Associated MAS

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BACKGROUND: Diagnosis of macrophage activations syndrome (MAS) in systemic juvenile idiopathic arthritis (sJIA) may be challenging because it may mimic the clinical features of the underlying disease or be confused with an infectious complication. However, the diagnostic value of the preliminary diagnostic guidelines for MAS complicating SJIA (1) or the diagnostic guidelines for hemophagocytic lymphohistiocytosis (HLH) (2) has seldom been examined.
OBJECTIVE: To investigate the sensitivity and specificity of diagnostic guidelines for SJIA-associated MAS and HLH in patients with SJIA who developed MAS.
METHODS: 24 children with SJIA who had MAS (diagnosed and treated as such by the attending physician) were included in the study. The control groups with a potentially "confusable" condition included 105 patients with active SJIA without MAS and 25 patients with a systemic febrile infection. Diagnostic guidelines for MAS and HLH were applied to MAS and control patients. Frequency of fulfilment of MAS and HLH diagnostic guidelines in patients with MAS and control patients was compared. Furthermore, sensitivity and specificity of guidelines in discriminating MAS from control patients was assessed.
RESULTS: The table shows the comparison of the frequency of fulfilment of diagnostic guidelines in patient samples.
The sensitivity and specificity in discriminating patients with sJIA-associated MAS from the control group (active JIA + infectious diseases) was 79.2 and 95, respectively, for MAS guidelines, and 11.8 and 100, respectively, for HLH guidelines. Among the features non included in the MAS guidelines, the best performances in terms of sensitivity and specificity were provided by hyperferritinemia, hypertriglyceridemia, and lactic dehydrogenase increase.
CONCLUSIONS: The diagnostic guidelines for MAS revealed strong sensitivity and specificity in the diagnosis of MAS complicating sJIA, whereas HLH guidelines were highly specific, but lacked sensitivity. Sensitivity of HLH was mostly hampered by the excessive stringent threshold for cytopenia, the requirement of histopathologic confirmation of hemophagocytosis, and the inclusion of 2 laboratory parameters (NK cell activity and soluble CD25) that are not routinely assessed in patients with MAS. We have identified some laboratory features of MAS not included in current guidelines that deserve consideration in future diagnostic criteria.
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Efficacy of infliximab treatment in patients with early and long-standing juvenile idiopathic arthritis

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TNFalpha has a key role in cell recruitment, proliferation and death, expression of adhesion molecules and immune responses. In juvenile idiopathic arthritis (JIA), TNFalpha is involved in matrix degradation and osteoclastogenesis. TNFalpha antagonists, in combination with methotrexate, reduce bone erosions and thinning of cartilage. Infliximab slows progression of joint damage in recently diagnosed JIA. Patients with early and long-standing JIA treated with infliximab have now shown improvement in ACR scores, inflammation and disability for up to 2 years. The efficacy, safety, and quality of life benefits of infliximab suggest using it possibly earlier than today, even in clinically moderate JIA.
OBJECTIVE: To determine the efficacy and safety of infliximab (IFX) therapy during 2 years\' follow-up in patients with early and long-standing juvenile idiopathic arthritis (JIA).
METHODS: 95 (56 with early and 39 with long-standing JIA) patients received IFX 6-7 mg/kg q8wks. IFX therapy was initiated in patients who had active disease despite ongoing treatment with combinations of DMARDs. During treatment, evaluation of efficacy was defined by the American College of Rheumatology pediatric criteria, 30% 50%, 70% and 90% improvement and remission.
RESULTS: After 30 weeks 100%, 95.5% and 84.1% early JIA patients achieved

ACR-Pedi 50, 70 and 90 improvements rates were respectively; in patients with long-standing JIA improvements rates were 94.8%, 89.7% and 69.2% respectively. At day 365 the results of the treatment suggest that all of the patients with early JIA and 95% patients with long-standing JIA achieved at least 50% response. At 30 week after baseline, patients with early JIA experienced more improvement in tender joint counts, VAS scale, physician\'s global assessment, CHAQ, CRP-level and ESR count than patients long-standing JIA ($p<0.05$). 47 patients received 15 infusions of IFX. After 2 years ACR-Pedi 70 and 90 response and stable remission was recorded in 100%, 96% and 96% (26/27) of the patients with early JIA, respectively. The proportions of patients with long-standing JIA achieving ACR-Pedi-50/70/90 response criteria and remission were 100%, 90%, 80% and 75% (15/20). As much as 24.2% of the patients discontinued due to an adverse event, mainly lack of efficacy (18 patients) and hypersensitivity reactions (5 patients). During the course of IFX treatment infusion reactions occurred in 18.9% (18/95) of patients, acute respiratory viral infection was observed in 4 patients, bronchitis in 2 and herpes labialis in 1. Neither an increase in infection rates nor tuberculosis cases were observed in patients who participated in this study.
CONCLUSIONS: The results of this analysis suggest that using IFX as initial treatment for patients with recent onset JIA is more effective than reserving it for patients with long-standing JIA, with more improvement in tender joint counts, VAS scale, physician\'s global assessment, CHAQ, CRP-level and ESR count.
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P 296
Impact of gene mutations on disease severity scores in patients with Familial Mediterraian fever: preliminary results

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BACKGROUND: There is no validated severity score assessment tool for childhood FMF. Numerous genotype–phenotype correlation studies in FMF patients suggest that patients carrying certain mutations are prone to have a more severe disease.
AIM: To test the effect of the type of FMF mutation on disease severity scores in pediatric FMF patients.
MATERIALS & METHODS: 258 children with a clinical diagnosis of FMF included to the study. Disease severity scores were calculated using the Sheba Medical Center score modified for children as previously suggested. Genetic analysis was performed using polymerase chain reaction and restriction endonuclease digestion methods to detect the presence of the eight FMF gene mutations (M694V, M680I, V726A, M694I, E148Q, R761H, A744S and T267I, R202Q). Mutations were grouped into three based on the presence of homozygote, heterozygote and compound heterozygote mutations. In addition, mutations were further grouped into four classes based on well known geno-phenotypic associations (class I: homozygote or compound heterozygote mutations of M694V, M680I, M694I; class II: homozygote or compound heterozygote mutations of V7726A, E148Q; class III: all the other compound heterozygote mutations; class IV: all heterozygote mutations).
RESULTS: According to the score, 59 (22.9%) were mild, 81 (31.4%) were moderate, 118 (45.7%) were severe. Of the patients, 84 (32.6%) were homozygote, 85 (32.9%) were heterozygote and 89 (34.5%) were compound heterozygote. The frequency of homozygote mutations significantly increased while the disease severity trended towards more severe form 18.6%, 28.4%, 42.4%, respectively (p for trend=0.015). Furthermore, there was a positive correlation between the homozygote mutation and the severe form of FMF ($p=0.02$, $r=0.19$). The second grouping of the mutations based on geno-phenotypic associations failed to demonstrate any significant relationship with the disease severity.
CONCLUSION: Current severity scoring indices for FMF are inadequate for the pediatric population as well known geno-phenotypic severity associations did not correlate with the disease scores. Homozygote mutation might be -a marker- or a component of disease severity scoring system. Further studies are warranted to investigate this association in larger populations. There is an urgent need to develop an evidence based severity assessment tool for childhood FMF.

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Wegener's granulomatosis: clinical features and outcome in 5 Czech children

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BACKGROUND: Wegener's granulomatosis (WG) is a rare primary systemic vasculitis affecting small vessels with characteristic features of non-specific granulomatous inflammation affecting preferentially respiratory tract and kidneys. Wide variety of clinical severity has been reported in both children and adults, though there are no controlled studies available in children.
OBJECTIVES: To describe clinical and laboratory features and disease outcome in a small cohort of paediatric patients with WG.
METHODS: Retrospective chart review of the main clinical characteristics of children with WG followed in the Unit since 2006 to 2010.
RESULTS: Five cases of childhood WG were identified, all girls, 4 Caucasian, 1 Romani. Their main demographic and clinical characteristics are summarised in the **Table** where main features of active vasculitis are listed. In 3 patients disease control was achieved with combined medication (patients 1, 2, 3) but only in patient 3 remission has been maintained off treatment. Apart from corticosteroids (CS) used in various schemes in all patients other treatments included MTX, CP, AZA, MMF and in the 2 most severe cases (4,5) also rituximab. Of 2 patients with both lung and kidney involvement patient 1 has achieved and maintains remission on medication while patient 5 has had persistently active disease with recurrent flares and significant damage (avascular necrosis, hypertensive retinopathy, cataract). Although 3/5 patients have had limited disease, subglottic stenosis in patient 4 led to an episode of prolonged airway obstruction and brain ischemia resulting in apalic syndrome.
CONCLUSIONS: This small case series demonstrates heterogeneity of disease outcomes and underlines the need for unified outcome measures that would enable large collaborative studies in order to identify high-risk patients and the best effective treatment strategies.

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Arthropathy in Nephropathic Cystinosis, an under-recognised disorder?

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BACKGROUND: Nephropathic cystinosis is a rare multi-system disorder characterised by lysosomal cystine accumulation affecting 1 in 100,000 live births. Renal osteodystrophy, and later onset crystal arthropathy are already recognised in cystinosis1,2. The clinical and imaging features of unique younger onset, destructive arthropathy is described.
METHODS: All children in Scotland with cystinosis are cared for in a single centre. Comparison of cases with and without arthropathy was made by review of the case notes, imaging and examination of these children.
CASE CHARACTERISTICS: From the Scottish population of one million children eleven have cystinosis, of whom four have significant arthropathy. The **table** gives the characteristics of the eleven patients. Adherence to standard treatments with cystine depleting therapy, electrolyte supplementation and growth hormone is challenging for these patients, but was not judged to be different in the group with or without arthropathy by their regular clinician. Of those with arthropathy poorer adherence to treatment appeared to be associated with a more destructive disease course. None had biochemical rickets after the initial presentation period.
The arthropathy presented in all cases with progressive large joint, lower limb pain, stiffness and limp. All demonstrated quadriceps wasting, genu valgus, and pes planus. Three had swollen knees. Variable short-term pain relief was achieved with NSAIDs, intra-articular steroids, orthotics and physiotherapy. Immunosuppression given after renal transplantation, and a trial of methotrexate in the child with synovitis, did not alter symptoms or the progressive nature of this arthropathy. One underwent tibial osteostomies with no clear benefit, but surgery was complicated by osteomyelitis.
Plain radiographs showed consistent features in all affected patients. Imaging showed a spectrum of severity within individual patients, which progressed over time, and also across the group. Lesions in the metadiaphyseal and epiphyseal regions were common, as were erosive changes within the joints. MR imaging in three children confirmed irregular cortical surfaces in two, mild synovial thickening and enhancement in one. The radiological features did not support a diagnosis of crystal arthropathy or rickets. Synovial fluid obtained from two was not clearly supportive of a crystal arthropathy. Synovial biopsy obtained from one showed only a non-specific inflammatory infiltrate.
DISCUSSION: This is the first description of a destructive, early onset, predominantly lower limb, large joint arthropathy characterised by early onset growth plate

defects, and non-inflammatory erosive disease in nephropathic cystinosis unresponsive to various treatment approaches. The association with non-adherance to cystinosis treatment is unclear. This arthropathy has distinctly different characteristics from both renal osteodystrophy described in cystinosis patients,1 and the crystal induced synovitis of predominantly upper limbs reported in adolescent onset intermediate cystinosis2. The aetiology is unclear. It affects a high proportion of the Scottish children with nephropathic cystinosis. Given the rarity of cystinosis, and limited published material available we would welcome reports of similar findings from other centres to facilitate research into reducing the high morbidity suggested by this cohort.
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P 299
Anakinra for the treatment of TNF receptor associated periodic syndrome

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INTRODUCTION: Treatment of TNF receptor associated periodic syndrome (TRAPS) remains challenging. High dose steroids have many adverse effects, other immunosupressants lack efficacy, and many patients respond to etanercept poorly or only for a limited period. Anecdotal experience has suggested that anakinra is an effective treatment for TRAPS in some patients.
AIMS: To assess efficacy and safety of anakinra in a cohort of patients with TRAPS.
METHODS: Patients with TRAPS were treated with anakinra 100 mg daily and were monitored clinically and biochemically and for adverse effects. Outcome measures included steroid reduction, ability to use anakinra as monotherapy and its effect on amyloidosis.
RESULTS: 19 TRAPS patients were treated with anakinra (13F/6M, 3 children, 16 adults). Median age at start of treatment was 34.4years (range 8.8-76.6).
The most frequent prior treatments were prednisolone (9/19), etanercept (6/19) and colchicine (6/19), but the range included azathioprine, ciclosporin, thalidomide, chlorambucil, mycophenolate mofetil and moxifloxacin. Anakinra was used first-line in two cases.
Twelve different mutations in TNFRSF1A were identified. None of the 3 patients with the R92Q variant responded to anakinra, but 12/16 of the others achieved complete clinical and biochemical responses that enabled steroids to be withdrawn in all except the 2 who required immunosuppression for renal transplantation. One patient had a partial clinical and biochemical response, and 3 responded well clinically but had persistently elevated SAA and CRP concentrations. Median duration of anakinra treatment duration was 21.5 months (range 0.8-74months). Adverse events included mild injection site reactions (5/19), pain on administration (1/19), and infections (2/19), none of which required discontinuation of the therapy.
Amyloidosis was present in 7/19 patients of whom, 5 were nephrotic and 2 had undergone renal transplantation; to date there has been regression of amyloid and improvement in organ function in 4 cases.
CONCLUSION: These data suggest that anakinra is highly efficacious and safe for the treatment of non-R92Q associated TRAPS.

P 300
Anakinra – a review of the experience in an Irish tertiary paediatric centre

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BACKGROUND: Anakinra is an Interleukin-1 Receptor Antagonist that has been used in the treatment of rheumatological disorders in adults. Its application in a paediatric population is relatively new, but good treatment responses and tolerability have been reported.
Objectives: This study is a case series of seven Irish paediatric patients that have been treated with Anakinra for different presentations, including Juvenile Idiopathic Arthritis, CINCA Syndrome and Periodic Fever Syndrome.
Methods: The study is designed as a retrospective chart review of up to one year into treatment. Patient demographics and previous treatments were analysed, as were clinical and inflammatory markers of disease activity pre and post initiation of Anakinra.
RESULTS: All 7 patients tolerated Anakinra well, 5 of the 7 patients having had rapid response to therapy and subsequently remained in remission. Of the other two patients, one initially responded but then had flare of disease activity and the other had a poor response to therapy from initiation. They were subsequently started on Tocilizumab. Both patients had a dramatic response to the Interleukin-6 RA after a single dose.
CONCLUSIONS: Previous reports have emphasized the inflammatory nature of autoimmune disease, being either Interleukin-1 or Interleukin-6 driven. The present case series certainly helps support this hypothesis. Current research is looking to clarify the underlying pathophysiology of autoimmune diseases to enable physicians to start more targeted therapy. Anakinra has proven to be a safe drug, but dosage regimes for paediatric patients remain empiric. Further research is needed to evaluate safe and effective dosing.
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P 301
Disappearance of left ventricular hypertrabeculation/noncompaction after anti IL-1 therapy in a patient with autoinflammatory disease

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Left ventricular noncompaction (LVNC), also known as left ventricular hypertrabeculation, is an uncommon, unclassified type of cardiomyopathy in children, characterized by the presence of numerous prominent trabeculations and deep intratrabecular recesses which communicate with the left ventricular cavity. This disease has a very bad prognosis. Autoinflammatory diseases are a group of monogenic inflammatory diseases with an early onset in childhood. They are characterized by periodic or recurrent episodes of systemic inflammation causing fever, accompanied by rash, serositis, lymphadenopathy, arthritis, and other clinical manifestations. More recently IL-1 blocking therapies are used successfully to treat this new group of immune-mediated inflammatory conditions. Emerging evidence suggests that the balance between IL-1 agonists and antagonists plays an essential role in a variety of cardiovascular conditions.
We report the case of a 12-year-old girl who experienced periodic fever and painful cutaneous lesions, with splenomegaly and high inflammation index by the age of 19 days. At 2 years, a cutaneous biopsy was performed, and an unspecific vasculitic aspect was found; corticosteroid therapy was started with discrete control on the symptoms, but after 10 months of therapy, fever and cutaneous lesions reappeared, associated to mucositis and, later, to arthralgias.
At the age of 8 years, because of a severe bilateral hypoacusia, the diagnosis of CINCA syndrome was suspected. The mutation research of CIAS1 gene was negative (it is positive only in 60% of patients). A month later, a preoperative ECG was done, showing a severe left ventricular hypertrophy. Echocardiographically, she showed an enlarged poorly contracting left ventricle (E.F.= 30%) with LVNC involving the lateral and apical wall. (previous echocardiograms were normal). A heart failure therapy was started (ACE inhibitors, b-blockers, digitalis, diuretics and ASA). Several echocardiograms were repeated in the succeeding months, all of them confirming the diagnosis of LVNC and showing a pump function improvement. An year later, according to literature positive results on utilization of Anakinra (anti-IL1 monoclonal antibody) in autoinflammatory diseases, the therapy was started (1 mg/Kg/die, increased up to 2,5 mg/kg/die) with clinical and laboratory parameters improvement. After 5 months of daily Anakinra administration, surprisingly, LVNC could no longer be detected echocardiographically.

In conclusion, acquired LVNC has been only occasionally reported, although it may disappear in single cases, an association between the anti-IL1 monoclonal antibody therapy and the LVNC complete remission could be presumed. In fact increased IL-1 mRNA levels were found in endomyocardial biopsies from patients with idiopathic dilated cardiomyopathy and IL-1Ra administration had beneficial effects in experimental models of inflammatory cardiomyopathy (1). This case report raises the possibility that IL-1 inhibitors may be clinically useful agents in patients with acquired LVNC.

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Switching anti-TNF therapy in JIA – outcome and results of six Brazilian patients

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BACKGROUND: Juvenile idiopathic arthritis (JIA) is the most common childhood rheumatic disease. In recent years biological agents are used early in JIA, and the switch of them in refractory cases is very common. The main representative agent is the anti TNF α, responsible for neutralizing the action of TNF-α, a pro inflammatory cytokine through its connection with soluble form or membrane receptor. Some patients still remain with active disease with these drugs.
Objectives: To evaluate the outcome of JIA patients who switched anti-TNF therapy by another of the same class in a single center in Brazil.
METHODS: Medical records of six female JIA patients (3 soJIA ,1 FR+ poly, 1 FR – poly), who have switched anti-TNF therapy were analyzed. Disease activity improvement was observed according to the following criteria : decrease in the number of active joints, decrease in inflammatory laboratory tests, improvement of uveitis and fever. Five patients switched due to the lack of efficacy of the previous anti-TNF and the last one had anaphylaxis with the first Anti-TNF.
RESULTS: The 3 poly JIA kept remission after the switch, and the 3 so JIA remained with active disease.
CONCLUSIONS: Switching anti-TNF therapy was very effective in polyarticular JIA, but with no improvement in so JIA, as shown on previous studies. For polyarticular JIA, switching anti-TNF therapy is a good therapeutic option.
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Macrophage Activating Syndrome complicating Wegener Granulomatosis: treatment with plasma exchange

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Wegener Granulomatosis (WG) is a rare systemic granulomatous necrotizing vasculitis in children. We present a seven year of girl admitted to our hospital with skin and upper respiratory tract involvement. She presented with fever, noduler vascular lesions on her face, limbs and hemorrhagic ulserated lesion on her nose and hard palate. The biopsy of these lesions showed necrotizing granulomatous inflammation that was consistent with WG. At admission she had severe lymphopenia (absolute lymphocyte number was 200 /mm^3) which was interpreted as a possible primary or secondary lymphopenia. Her ANCA levels were negative. Her paranasal computed tomography showed pansinusitis that was consistent with WG but her chest CT and urinary examination was normal. Her lesions progressed and C reactive protein remained high in spite of conventional treatment with pulse and oral steroids and cylophosfamide. Subsequently, she developed an unusual fever and pancytopenia. Bone marrow aspiration showed hemophagocytosis. Other labaratory parameters confirmed the diagnosis of macrophage activating syndrome and pulse steroids, cyclosporine was started and she was given IVIG. Because of resistance to treatment and acute deterioration, she was started on plasma exchange which resulted in improvement of her laboratory features and regression of clinical features of WG.
We suggest that plasma exchange can be considered as alternative treatment in resistant WG patients and MAS even if ANCA is negative.

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Pulmonary involvement in 3 SLE cases

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INTRODUCTION: Systemic Lupus Erytematosis is a chronic disease affecting multiple systems especially renal, skin and central nervous system. Respiratory system involvement includes pleurite, pneumonitis, infectious pnömonia, pulmonary hemorrhage, pulmonary embolia pulmonar hypertension and pneumotorax. The aim of our study is to present tree SLE cases with pulmonary involvement and their treatment.
MATERIALS: We evaluated tree cases with pulmonary involvement, among the 38 cases diagnosed by the diagnostic criteria of American Rheumatology Association , treated in Ege University Medical Faculty Pediatric Nephrology Clinic, between 1986- 2009.
RESULTS: Case 1: 17 years old girl suffered from respiratory distress, fatigue and weakness. She had hemolytic anemia, hypocomplementenemia, ANA (1/5110) and Anti ds DNA positivity. Due to pulmonary embolia she admitted to Intensive Care Unit with the need of mechanic ventilation and given to cyclophosphamide and methyl prednisolone. By the third months of treatment, she had remission and from now on , has no problem.
Case 2: 16 years old girl came to hospital via malar rash, photosensitivity and artritis in wrist and ankle. She had diagnosed as SLE with the findings of high sedimentation,hemolytic anemia, neutropenia and high ANA, dsDNA. She died though following in Intensive Care Unit, due to massively pulmonar hemorrhage and failure suddenly coming after cough.
Case 3:15 years old girl diagnosed as SLE, having of fatigue, malar rash , hemolytic anemia, high ANA and ds DNA and proteinüria in another centre. She came with dispnea and respiratory distress in the 15th week of following time. She had mechanical ventilator care owing to interstitial lung and pleural effusion. Intermittant plasmapheresis and one dose of rituximab were given to her. She died from sudden massive pulmonary hemorrhage.
In juvenile lupus cases, pulmonary involvement is quite rare and lethal. Although the rapid and correct intervention, it can be fatal.

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Treatment of Systemic Juvenile Idiopathic Arthritis (JIAs). Where are we?

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INTRODUCTION: JIA is a heterogeneous group of chronic arthropathy and the systemic category represents 10-20% of all cases. AIJs, because of its clinical patterns (fever, rash, serositis, lymphadenopathy, and polyarthritis), absence of autoimmunity and cytokines profile (where the IL1 and IL6 play a critical role), is a clinical category very different from the rest of the subtypes of JIA. The therapeutic strategy should attempt to control both articular and extra-articular manifestations. Due to the peculiarities of this group, the treatment differs significantly to those used in other patients with JIA. There are new biological therapies, not yet approved by the FDA for this entity, that are showing high effectivity rates.
OBJECTIVES: To evaluate the treatment regimens administered to patients diagnosed in AIJs Pediatric Rheumatology Unit of Hospital Ramón y Cajal and the response to them.
METHODS: An observational, descriptive and transversal study of AIJs patients being monitored in our Pediatric Rheumatology Unit.
RESULTS: 23 patients are currently followed up in our unit. With an average age of 17(2-32 years). 15/23 patients from the national scope. The mean follow-up in our unit is 6.4 years (0.5-22 years). The **table** shows the treatments used:
Of the patients who were administered anti-TNF, only 1 maintains remission (whith Adalimumab). The rest has required replacement of anti-TNF by Anakinra with a historical rate of response to treatment of 66.6% (7/11). Among patients treated with Anakinra, 4 required to shift to other therapies: 1 cyclosporine for developement of MAS, 2 tocilizumab (1 for development of renal amyloidosis and other for local reactions at the injection site), and 1 Canakinumab with an excellent clinical response (ACRp 70).
One patient who received an antagonist of IL-6 (8 infusions) remains in remission for 6 months after withdrawal. The other patient is inactive with treatment.

The four patients with anti IL1 ß (Canakinumab) after 1 to 12 months of treatment have made a good clinical response, achieving suspend oral corticosteroids in one of them. We have obtained a good clinical response (ACRp 50-90).
Surgical treatment: 2 patients with longstanding disease have required bilateral hip prosthesis, 2 bilateral knee prostheses, 1 wrist synovectomy, 1 synoviorthesis knee and one reconstructive surgery with abductor tenotomy and biceps lengthening at the knee.
CONCLUSIONS: 1.- The treatment of systemic JIA is complex and requires a deep etiopathogenic knowledge of the disease and the current therapeutic options.
2.- The new biologic drugs have greatly improved the prognosis of AIJs and offer the possibility of achieving the objective of complete remission without sequelae.
3.- We would like to highlight the importance of biological therapies data bases in childhood arthritis for the control of the efficacy and safety in the medium and long term.

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Takayasu's arteritis: follow-up of a clinical case

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BACKROUND: Takayasu's arteritis (TA) is a chronic idiopathic granulomatous arteritis, which involves the aorta and its main branches. The diagnosis is based on clinical findings and is confirmed by radiologic imaging techniques. To date the first line treatment are corticoids, but most patients require immunosuoppressive medication such as Cyclophosphamide, Methotrexate and Azathioprine. Recent investigations show evidence of good response to Myophenolate mofetil. In later stages, percutaneous transluminal angioplasty can become necessary.
CLINICAL CASE: The patient here presented is a six years old girl, diagnosed at the age of four years with Takayasu's arteritis. At present she shows severe stenosis of abdominal aorta, as well as of right renal artery and left ventricular hypertrophy. Treatment for hypertension was started along with corticoids and Mycophenolate mofetil. Initially good response was elicited and soon Methotrexate was added to the treatment in order to permit corticoid withdrawal.
Six months later, percutaneous angioplasty was performed, placing a vascular stent in the right renal artery. One year after this intervention, functional abolition of right kidney was found due to stent obstruction and therefore the patient underwent right nephrectomy.
CONCLUSION: In light of this case, knowledge and awareness by the pediatrician of Takayasu's arteritis is vital to allow an early diagnosis and treatment of the patient.
Mycophenolate mofetil is a medication with a favorable profile compared to other immunosuppressors, in terms of security and efficacy. There are no relevant renal or hepatic side effects and its easy oral administration makes it a very suitable medication for outpatient treatment.
Angioplasty is a secure and effective treatment of renal hypertension in children but unfortunately there is a high percentage of recurrence of stenosis, despite a correctly placed stent.