ORAL PRESENTATIONS

O1
2.1 Long-term safety and efficacy of tocilizumab in children with systemic juvenile idiopathic arthritis (JIA)
S Yokota1, T Imagawa1, T Miyamae1, K Kasai1, M Mori1, N Nishimoto2 and T Kishimoto2
1Yokohama City University, Yokohama, Kanagawa, Japan
2Osaka University, Suita, Osaka, Japan

Objectives: To evaluate long-term safety and efficacy of tocilizumab in treatment of children with systemic JIA.

Methods: Patients with systemic JIA fulfilled WHO/ILAR criteria were enrolled in a long-term extension study immediately after completion of phase II and III trials of tocilizumab. Tocilizumab was intravenously administered at a dose of 8 mg/kg every 2 weeks. Efficacy was assessed every 6 weeks using ACR Pedi 30 Criteria for Improvement.

Results: Sixty-seven patients (29 boys and 38 girls) were included in this analysis. Median age was 8 years and median disease duration was 3.8 years. At the time of analysis, 9 patients had discontinued tocilizumab treatment, 4 due to AEs, 4 due to development of anti-tocilizumab antibodies and 1 due to lack of efficacy. Median duration of tocilizumab treatment was 146 weeks. The most frequent AEs were upper respiratory tract infections and gastroenteritis. The incidence rate of serious infections was 10.7 per 100 patient-years. No deaths, malignancies, or autoimmune diseases were observed. ACR Pedi 30, 50 and 70 Improvement Criteria were achieved in 100%, 98% and 93% at Week 96. All patients were treated with oral corticosteroids at the registration and 72% were able to reduce corticosteroid dose by more than 50% at Week 96. Fourteen patients became steroid-free during the study.

Conclusion: The long-term extension study demonstrated sustained clinical improvement and a favourable risk-benefit profile for tocilizumab treatment in children with systemic JIA. Even medication-off status will be expected.

O2
2.2 A phase II trial with canakinumab, a new IL-1β blocking monoclonal antibody (ACZ885), to evaluate preliminary dosing, safety and efficacy profile in children with systemic Juvenile Idiopathic arthritis (sJIA)
N Ruperto1, P Quartier2, N Wulfraat3, P Woo4, A Loy1, R Mouy3, B Bader-Meunier2, B Prakken3, E Noseda5, C Rordorf5 and Martini for the Paediatric Rheumatology International Trials Organisation (PRINTO) A1
1IRCCS G. Gaslini, Pediatria II – PRINTO, Largo Gaslini, Genova, Italy
2Hospital Necker Enfants Malades, Unité d’Immunologie, Hematologie et Rhumatologie Pediatrique, Paris, France
3Dept. pediatric immunology, University Medical Center Utrecht, Utrecht, Netherlands
4Centre of Paediatric and Adolescent Rheumatology, The Windyke Institute, London, UK
5Novartis Pharma AG, Basel, Switzerland

Objectives: Phase II trial to evaluate dosing and interval range, preliminary efficacy, safety, immunogenicity, and pharmacokinetics of subcutaneous (s.c.) canakinumab in patients with active sJIA.

Methods: 19 children 4–19 years old, with fever, at least 2 active joints, CRP > 50 mg/L and steroids ≤ 0.4 mg/kg, were enrolled in a staggered dose escalation study. Patients received a single sc injection of canakinumab in the dose range 0.5–9 mg/kg, followed by an observation period and re-dosing upon relapse. Dose escalation was based on safety and efficacy review of each cohort. Response was measured according to modified ACR pediatric criteria, (at least 3/6 variables improved by ≥ 30% with no more than one variable worsening by >30% and no fever). Relapse was defined as reappearance of fever and CRP > 30 mg/L, and/or ACR pediatric flare criteria.

Results: 11/19 patients responded to canakinumab. At Day 15 post first dose all the 11 responders achieved at least an ACR Pediatric 50. In 4 cases inactive disease status was reached (no joints with active arthritis, no fever, normal CRP and no disease activity according to physician’s assessment). Time to relapse after first dose ranged from 23 days to >200 days. The injections were well tolerated and no immunogenicity developed. One serious adverse event (gastritis with ulcer bleeding) was reported.
Conclusion: In this dose-escalation trial canakinumab was efficacious and provided improvement in sign and symptoms of sJIA with an acceptable safety profile.

O3

2.3 Long-term efficacy and safety of infliximab plus methotrexate for the treatment of polyarticular course juvenile rheumatoid arthritis (JRA): Findings from an open-label treatment extension

N Ruperto,1 DJ Lovell,2 P Cuttica,3 P Wu,4 G Espada,5 C Wouters,6 ED Silverman,2 Z Balogh,4 M Henrickson,15 J Davidson,8 I Foeldvari,9 L Imundo,10 G Simonini,11 J Oppermann,12 YK Shen,13 S Visvanathan,13, A Fasanmade,13, A Mendelsohn,13, A Martini,1 EH Giannini8 and for the Paediatric Rheumatology International Trials Organisation (PRINTO) and the Paediatric Rheumatology Collaborative Study Group (PRCSG Study)

1IRCCS G Gaslini, Pediatria II – PRINTO, Genova, Italy
2Cincinnati Children’s Hosp Med Center, Cincinnati, USA
3Hosp de Pediatra Dr Pedron de Elizalde, Buenos Aires, Argentina
4Great Ormond St Hosp, London, UK
5Hosp de Ninos Ricardo Gutierrez, Buenos Aires, Argentina
6U Hosp Gathuisberg, Leuven, Belgium
7Hosp for Sick Children, Toronto, Canada
8Royal Liverpool Childrens NHS Trust, Liverpool, UK
9Eilbek Clinic, Hamburg, Germany
10Columbia/NY Presbyterian Hosp, New York, USA
11U Florence, Firenze, Italy
12Kinderklinik, Cottbus, Germany
13Centocor R & D, Inc, Malvern, USA
14National Inst Rheuma & Physiotherapy, Budapest, Hungary
15Children’s Hospital, Oklahoma City, USA

Pediatric Rheumatology 2008, 6(Suppl 1):O3

We report long-term safety & efficacy of infliximab (IFX)+ methotrexate (MTX) treatment in JRA patients. In an international, multicenter, randomized, double-blind study, 122 children w/active polyarticular JRA despite prior MTX therapy received MTX plus a 3-dose induction (wks 0, 2, 6) of IFX 3 mg/kg through wk 44, or placebo (PBO) for 14 wks followed by IFX 6 mg/kg (wks 14, 16, 20, & then q8 wks) through wk 44. Patients completing treatment through wk 44 were eligible to enter an open-label extension (OLE) of IFX 3 mg/kg, beginning at wk 52 & continuing q8 wks through wk 196. All patients continued with concomitant MTX. Physicians could increase or decrease the IFX dose by ≤1.5 mg/kg/infusion q8 wks, up to 6 mg/kg or down to 3 mg/kg, based on clinical response. Primary endpoint was the proportion of patients meeting ACR-Pedi-30, defined as improvement of ≥30% in ≥3 of 6 core variables, & ≤30% of the remaining variables worsened by >30%. Remission was defined as 0 joints with active arthritis, normal ESR, & physician’s global assessment ≤10 mm on a 10-cm visual analog scale. 78/122 (63.9%) children entered the OLE. The mean(SD) IFX dose at wk 196 was 4.4(1.6) mg/kg. IFX was well-tolerated:14.1% of patients discontinued due to adverse events (AE) from wks 52–204. The distribution/types of AE were similar to those in the first 52 wks & no new safety issues were reported. Among the 36 study patients by wk 204, ACR-Pedi-30/50/70/90 responses were 91.7%(33/36), 83.3%(30/36), 69.4%(25/36), & 50%(18/36), respectively. 39%(14/36) of patients achieved remission. From wk 52 through wk 216, 36.6%(26/71) of patients were positive for IFX antibodies; 57.7%(15/26) of these had an infusion reaction. Continuous IFX+MTX administered up to 4 yrs was safe & effective in JRA patients, although accompanied by a high rate of patient discontinuation, which included subjects in remission.

O4

2.4 Magnetic resonance imaging, ultrasonography and conventional radiography in the assessment of bone erosions in juvenile idiopathic arthritis

C Malattia1, MB Damasio1, F Magnaguagno1, A Pistorio1, M Valle1, C Martinoli2, S Viola1, A Buoncompagni1, A Loy1, A Raveli2, P Tomà1 and A Martini3
1Istituto G. Gaslini, Genova, Italy
2DICIM and Universita` di Genova, Genova, Italy
3Istituto G. Gaslini e Universita` di Genova, Genova, Italy

Pediatric Rheumatology 2008, 6(Suppl 1):O4

Objective: To compare magnetic resonance imaging (MRI), conventional radiography and ultrasonography in identifying bone erosions in patients with Juvenile Idiopathic Arthritis (JIA). To determine the validity and reliability of an MRI scale in detecting and grading joint damage.

Methods: In twenty-six JIA patients the clinically more affected wrist was studied with MRI, radiography and ultrasonography, coupled with standard clinical assessment and biochemical analysis. MRI images were assessed independently by 2 readers according to an appositely devised scoring system.

Results: Twenty-five out of 26 patients (96.1%), had one or more erosions as detected by MRI, while conventional radiography and ultrasonography revealed erosions in 13/26 (50%) and 12/24 (50%) patients respectively. The ability of MRI to detect erosive changes was significant higher with respect to conventional radiography (P0 = 0.003) and ultrasonography (P0 = 0.0003) in the group of patients with < 4 years disease duration. Ultrasonography and conventional radiography were of equivalent value for the detection of destructive changes. Wrist MRI score correlated highly with radiographic erosion score (rS = 0.82) and with wrist limited range of motion score (rS = 0.69). The inter-reader intraclass correlation coefficient (ICC) for MRI score was excellent (0.97); intra-reader ICCs were good for both investigators (0.97 and 0.79).

Conclusion: MRI seems to represent a powerful tool to disclose early structural damage in JIA. Preliminary results in terms of reliability, and construct validity of our MRI scale appear promising, however its suitability is yet to be tested in large-scale longitudinal studies in view of its further application in both clinical and research context.

O5

2.5 Mesenchymal Stem Cell Therapy has significant clinical effect in proteoglycan induced arthritis

JF Swart2, MJG Backer3, F Hofhuis3, W de Jager1, BJ Prakken1, W Kuis1, ACM Martens1 and NM Wulffraat1
1Department of Pediatric Immunology, Wilhelmina Children’s Hospital/UMC Utrecht, Utrecht, Netherlands
2VU University Medical Center, Amsterdam, Netherlands
3Department of Immunology, UMC Utrecht, Utrecht, Netherlands
Introduction: 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 [1, 2].

Methods: We performed a study with 104 Balb/c mice with 55 as donors of MSC. The 49 mice that were induced twice with human proteoglycan for the development of PGIA were randomly assigned to 5 groups: 1 control-group (PBS) and 4 treatment-groups (MSC once or twice intra-articular [ia] or intra-artericular [ia]). Ten days after 2nd PG-antigen injection, treatment was started and if planned again after 4 weeks. Dosages were $5 \times 10^6$ ip and $1 \times 10^6$ cells ia. MSC used were syngeneic and passaged twice. Arthritis was scored 2 times a week by 2 independent observers according to a scoringsystem with a maximum of 16.

Results: Arthritis-score was on average 1.3 (0.8–2.0) just before start of the treatment and increased to 6.0 in the control group towards the end of the experiment (day 67). At day 67 arthritis-scores were significantly lower in both ip-groups (1.0 and 0.5) and in the repeated ia-group (2.0). Furthermore in both ip-groups arthritis-scores decreased after treatment and stabilized until day 67.

Conclusion: High dose MSC systemically administered (ip) has good clinical effect on established arthritis. Arthritis score not only stabilized but even diminished after injection of ip MSC. Ip injection of MSC once was as good as twice; this was not true for the ia injection.

References

O6
3.4 Physical activity in adolescents with juvenile idiopathic arthritis
OTHM Lelieveld, W Armbrust, MA van Leeuwen, N Duppen, JHB Geertzen, PJJ Sauer and E van Weert
University Medical Center Groningen, Groningen, Netherlands

Background: The beneficial effects of physical activity (PA) on normal growth and development of children and adolescents have been widely recognised. We explore physical activity (PA) in adolescents with JIA in comparison with a healthy population.

Materials and methods: Patients eligible for this study were patients attending an adolescent JIA outpatient clinic. Total energy expenditure (TEE), Activity-related energy expenditure (AEE), Physical activity level (PAL) and Physical activity pattern (PAP) were assessed with a 3-day activity diary. Reference data were collected from healthy Dutch Secondary School Children.

Results: Thirty patients and 106 controls were included; mean (± SD) age in years was 17.0 (± 0.6) and 16.7 (± 0.9), respectively. TEE, AEE and PAL were significantly lower in the JIA group (Table 1) compared to the normal population. The JIA group spent more time in bed and less time on moderate to vigorous PA. 23% of the JIA patients met public health recommendations to perform daily one hour or more of moderate to vigorous PA, compared to 66% in the reference group.

Conclusion: Adolescents with JIA have low PA levels and are therefore at risk of losing the benefits of PA. Interventions by paediatric rheumatologists are needed to increase PA levels in patients with JIA.

Table 1 (abstract O6)

<table>
<thead>
<tr>
<th></th>
<th>JIA (mean ± SD)</th>
<th>Controls (mean ± SD)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TEE (mega joule.day$^{-1}$)</td>
<td>12.17 (± 3.38)</td>
<td>14.48 (± 3.38)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>AEE (mega joule.day$^{-1}$)</td>
<td>3.99 (± 2.20)</td>
<td>6.12 (± 2.58)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>PAL (TEE/8MRp)</td>
<td>1.74 (± 0.29)</td>
<td>2.09 (± 0.39)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

O7
3.5 Comparison of functional ability in juvenile idiopathic arthritis, juvenile dermatomyositis, juvenile systemic lupus erythematosus and healthy controls.

An analysis of the PRINTO database
G Filocamo, S Meiorin, C Saad-Magalhães, A Pistorio, A Ravelli, E Cortis, D Mihaylova, M Alessio, O Arguedas, S Garay, A Martini, N Ruperto and for the Paediatric Rheumatology International Trials Organisation (PRINTO)
IRCCS Istituto G. Gaslini, Genoa, Italy

Pediatric Rheumatology 2008, 6(Suppl 1):O7

Objective: To assess and compare functional ability, as measured by the Childhood Health Assessment Questionnaire (C-HAQ), in juvenile idiopathic arthritis (JIA), juvenile dermatomyositis (JDM), juvenile systemic lupus erythematosus (JSLE) and healthy controls.

Methods: Patients with active JIA, JDM and JSLE, C-HAQ availability and less than 18 years were compared to healthy children. All patients were also evaluated for demographic and disease activity parameters at baseline and after 6 months.

Results: 4,624 subjects (613 JIA, 277 JDM, 531 JSLE, and 3,203 healthy children) were included. Baseline functional disability was higher in patients with JDM (mean ± SD C-HAQ 1.7 ± 0.9), followed by JIA (1.2 ± 0.8 JIA), and JSLE (0.8 ± 0.9) and healthy control (0.1 ± 0.3). The C-HAQ score correlated moderately with the physical well being scale of the Child Health Questionnaire (CHQ PhS) for all 3 diseases and with the number of active joints in JIA, and with the Disease Activity Score (DAS) in JDM and poorly with JSLE disease activity variables. Common predictors of persistence of poor functional ability (C-HAQ ≥1.27, ≥1, ≥0.25 for JIA, JDM and JSLE respectively) were poor baseline C-HAQ and younger age at onset; other predictors were ANA negativity, and low CHQ-PhS for JIA, higher JSLE disease activity, and poor CHQ PhS and longer disease duration for JDM.

Conclusion: Baseline functional ability was poorer in active JDM than in JIA, and JSLE. A poor baseline C-HAQ and younger age at onset are predictors of persistence of poor functional ability despite treatment in either JIA, JDM and JSLE.

O8
4.4 Different phenotype of anaemia in systemic juvenile idiopathic arthritis (s-JIA) compared to anaemia in other subtypes of JIA
CH Hinze, N Fall, MG Barnes, S Croswell, K Jennings, S Thornton, RA Colbert, DN Glass and AA Grom
Cincinnati Children’s Hospital Medical Center, Cincinnati, OH, USA
**Table I (abstract O8)**

<table>
<thead>
<tr>
<th>Disease Category</th>
<th>N (flow data available)</th>
<th>Hb in g/dL</th>
<th>CD34+ (% of PBMC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. JIA (Hb &lt; 11 g/dL)</td>
<td>18 (5)</td>
<td>9.4 ± 1.0*</td>
<td>0.20 ± 0.12*</td>
</tr>
<tr>
<td>II. Other JIA (Hb &lt; 11 g/dL)</td>
<td>21 (8)</td>
<td>10.5 ± 0.4*</td>
<td>0.08 ± 0.03*</td>
</tr>
<tr>
<td>III. S-JIA (Hb &gt; 11 g/dL)</td>
<td>3 (3)</td>
<td>11.9 ± 1.0*</td>
<td>0.09 ± 0.07*</td>
</tr>
<tr>
<td>IV. Other JIA (Hb &gt; 11 g/dL)</td>
<td>14 (5)</td>
<td>12.7 ± 1.0*</td>
<td>0.08 ± 0.05*</td>
</tr>
<tr>
<td>P value (ANOVA)</td>
<td></td>
<td>1.65 × 10^-6</td>
<td></td>
</tr>
</tbody>
</table>

*Values are represented as mean ± standard deviation. Comparison of CD34+ count via T test: I vs. II: p = 0.008, I vs. III.: p = 0.19, I vs. IV: p = 0.000001, I vs. III.: p = 0.65, II vs. IV: p = 0.93, III vs. IV: 0.74.*
restricted joints and a progressive resisted strengthening programme (high repetitions and low resistance weights) completed into the full range of movement of most joints. Gait re-education and balance training were also included.

**Results:** Six children (5 M, 1 F) were included, 2 sibling pairs (2 M and 1 M, 1 F). 5/6 had initially been diagnosed with arthritis by their local hospital and one diagnosed with EDS. All had significant difficulties with walking and 3 required crutches. All had severe fixed flexion deformities (FFD) at the hips, 4 had FFD at knees and 2 hyperextension. All demonstrated extremely weak muscles especially hip abductors, hip extensors, inner range quadriceps and planter flexors. All had very poor balance. Following treatment over 3 months (combination of IP and OP treatment) all had significantly improved the FFD in hips and knees and increased the muscle strength in all groups. Balance had increased in all and gait improved; though I still remained on crutches at school.

**Conclusion:** Physiotherapy can significantly improve the muscle function and quality of life for children with SED.

---

**O11**

7.1 Transgenic overexpression of CREM alpha in murine T cells results in an anergic phenotype with enhanced IL17 production

RL Lippe¹, KS Sturm¹, JR Roth¹ and KT Tenbrock²

¹Inst of Immunology and Dept. of Pediatrics, University of Muenster, Germany
²Div of Pediatric Allergology and Immunology, Dept. of Pediatrics, University of Aachen, Germany

**Pediatric Rheumatology 2008, 6(Suppl 1):O11**

**Background and methods:** The cAMP responsive element modulator CREMa is a transcriptional repressor and putatively important in T cell pathophysiology of Systemic Lupus Erythematosus (SLE). To clarify the relevance of CREMa we overexpressed CREMa under control of the T cell specific CD2 promoter in mice.

**Results:** As expected, overall T cell proliferation in naive T cells as response to different stimuli like anti-CD3 or an allogenic MLR was diminished in CREMa transgenic mice compared to wildtype mice, however–unexpectedly – disease activity in a contact dermatitis model was more severe in transgenic mice. Moreover, when T cells were purified from the lymphnodes of the challenged ears were used for proliferation assays, transgenic T cell showed an enhanced proliferative response. Additionally, T cells from transgenic mice displayed an enhanced IL-17 production.

**Conclusion:** These data suggest that murine T cells with a transgenic overexpression of CREMa show an anergic phenotype in vitro, however when challenged in an in vivo disease model they react in a way, which predisposes to autoimmunity. Thus these T cells partially mimic the phenotype of human SLE T cells and support the relevance of CREMa for the pathophysiology of SLE.

---

**O12**

7.2 Interleukin-17 (IL-17) secreting cells in synovial fluid express the “Th17” master transcription factor RORC and their numbers correlate with CCL20 levels within the joint

K Nistala, P Hunter, E Sala-Soriano, J Diss and LR Wedderburn

Institute of Child Health, UCL, London, UK

**Pediatric Rheumatology 2008, 6(Suppl 1):O12**

**Background:** Th17 cells are a recently characterised, highly proinflammatory subset of T cells. We have shown that Th17 numbers are elevated in JIA synovial fluid and are significantly higher in extended than persistent oligoarthritis patients [1]. Interestingly we noted a high number of synovial T cells which produce both IL17 and interferon gamma (IFNγ). We also demonstrated that Th17 are actively recruited by the CCR6 ligand, CCL20, but the clinical relevance of this remained unclear.

**Methods:** 16 JIA patients had serum and/or synovial fluid samples assayed for CCL20 and corresponding samples of SF mononuclear cells (SFMC) analysed for IL-17 expression. SFMC were sorted by flow cytometry by CCR4 and CCR6 expression and sorted cells were analysed for IL-17 and IFNγ expression by intracellular staining. Sorted cells were analysed for expression of the transcriptional regulator of Th17 cells, RORC variant 2, by Q-PCR.

**Results:** CCL20 levels were elevated in synovial fluid compared to serum (mean 74 pg/ml vs <5 pg/ml) and correlated with Th17 numbers in synovial fluid (r = 0.74, p = 0.0055). IL-17+ CD4 T cells were limited to the CCR6+ fraction while IL-17+ IFNγ+ double positive cells were enriched within the CCR6+CCR4lo fraction. There was a >10 fold increase in RORC2 expression in the CCR6+ compared to CCR4-/CCR6-CD4+ T cells.

**Conclusion:** These results suggest that IL-17 expressing T cells within the joint are bona fide Th17, (RORC+). Elevated levels of CCL20 within the joint may account for the enrichment of both classical Th17 and also the IL-17+ IFNγ+ T cells seen in JIA.

**Reference**


---

**O13**

7.3 Successful use of anakinra, a soluble IL-1 receptor antagonist, in pediatric rheumatic diseases associated macrophage activation syndrome/reactive hemophagocytic lymphohistiocytosis

PM Miettunen, A Jayanthan and A Narendra

University of Calgary, Calgary, Canada

**Pediatric Rheumatology 2008, 6(Suppl 1):O13**

**Background:** Increased interleukin 1 (IL-1) production characterizes macrophage activation syndrome/reactive hemophagocytic lymphohistiocytosis (MAS/rHLH), a potentially lethal complication of pediatric rheumatic diseases. Standard treatment (corticosteroids, cyclosporine, +/- IVig) is not always effective.

**Objective:** To test effectiveness of anakinra, a soluble IL-1 receptor antagonist, in pediatric rheumatology patients who failed to respond to standard MAS/rHLH therapy.

**Methods:** 6 pediatric rheumatology patients (3 F:3 M); mean (range) age 8.14 (0.5–13.3) years, with MAS/rHLH were enrolled (SoJIA n = 4; Churg Strauss vasculitis n = 1; and infant onset ANCA +ve pulmonary renal syndrome n = 1). The infant patient was moribund in ICU. Histioctysis society’s 2004 criteria (HLH2004), including a T-cell activation marker, soluble IL-2
receptor (sIL2r), were used to confirm MAS/rHLH. Subcutaneous anakinra (2 mg/kg/day) was added to existing therapy (high dose IV Methylprednisolone n = 5/6; IVIG n = 6/6, and cyclosporine n = 5/6). HLH2004 specified clinical and laboratory data were collected pre, 48 hours, and 2 weeks after initiation of anakinra; including sIL2r in 3/6 patients.

Results: All patients defervesced within 24 hours of first anakinra dose, and ventilatory and dialysis support was discontinued within 96 hours in the ICU patient. All patients recovered from MAS/rHLH by 2 weeks; 5/6 pts discontinued corticosteroids by 5 weeks. Abnormally elevated baseline sIL2r resolved by 48 hours post first dose of anakinra in all 3 patients tested.

Conclusion: 1) Anakinra, in combination with corticosteroids, IVIG, +/- cyclosporine, was effective in controlling MAS/rHLH in all patients, allowing rapid discontinuation of corticosteroids in 5/6 patients.

2) Elevated baseline sIL2r level normalized rapidly following anakinra, suggesting resolution of abnormal T-cell activation.

O14
7.4 Improvements in individual disease components are sustained with long-term adalimumab therapy for polyarticular Juvenile Idiopathic Arthritis

N Ruperto1, D Lovell2, S Goodman3, A Reiff4, D Nemcová1, P Quartier1, R Jops1, V Gerloni5, J Bohnsack2, L Wagner-Weiner3, Hl Huppertz1, N Olson7, J Medich6, M Mclraith6, A Martini1 and E Giannini2

1PRINTO, Genova, Italy
2PRCSG, Cincinnati, OH, USA
3Arthritis Associates of South Florida, Del Ray Beach, FL, USA
4Children's Hospital of Los Angeles, Los Angeles, CA, USA
5Abbott Laboratories, Parsippany, NJ, USA
6Abbott GmbH and CoKG, Ludwigshafen, Germany

Pediatric Rheumatology 2008, 6(Suppl 1):O14

To control symptoms and prevent increasing disability in children with active polyarticular Juvenile Idiopathic Arthritis (JIA), long-term, effective treatment that controls all aspects of the disease is necessary. Individual ACR Pedi response criteria were analyzed for the 128 patients who entered the open-label extension (OLE) of the Phase III study of adalimumab in the treatment of polyarticular JIA. Measurements of disease activity were performed at each visit, including active joint count (AJC), number of joints with limitation of passive motion (LOM), patient's or parent's assessment of patient's pain (PaP), disability index of the Children's Health Assessment Questionnaire (CHAQ DI), and physician's global assessment of disease activity (PhDA). Observed data were examined for patients who had been treated with adalimumab throughout the study and reached more than 1 year in the OLE (Week 56; 75% of entering patients had data available). Patients entering the study had active polyarticular JIA, with clinically significant joint involvement, limitation of motion, pain, and disability in performing daily living activities. Long-term treatment with adalimumab provided marked improvements in disease activity (Table 1). The established safety profile for adalimumab remained consistent.

Long-term treatment with adalimumab substantially improves multiple aspects of polyarticular JIA.

Table 1 (abstract 14) Improvements in JIA with adalimumab therapy

<table>
<thead>
<tr>
<th></th>
<th>AJC*</th>
<th>LOM**</th>
<th>PaP†</th>
<th>CHAQ DI †</th>
<th>PhDA†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>17</td>
<td>14</td>
<td>49</td>
<td>1.05</td>
<td>57</td>
</tr>
<tr>
<td>Improvement at</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 56 of OLE</td>
<td>90%</td>
<td>70%</td>
<td>74%</td>
<td>83%</td>
<td>84%</td>
</tr>
</tbody>
</table>

*75 joints assessed; **69 joints assessed; †100-mm visual analog scale: greater scores = more active disease/more pain; ‡0 (best) to 3 (worst).

O15
7.5 Safety data from over 1,200 patients-years of methotrexate and/or etanercept treatment in children with polyarticular or systemic juvenile rheumatoid arthritis

EH Giannini1, NT Ilowite2, DJ Lovell1, CA Wallace3, CE Rabinovich4, A Reiff5, G Higgins6, B Gottlieb7, Y Chon8, SW Baumgartner8 and S-L Lin8

1Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA
2Albert Einstein College of Medicine, Bronx, NY, USA
3Children's Hospital of New York Presbyterian, New York, NY, USA
4Duke University Medical Center, Durham, NC, USA
5Childrens Hospital of Los Angeles, Los Angeles, CA, USA
6Ohio State University and Children's Hospital, Columbus, OH, USA
7Schneider Children's Hospital, New Hyde Park, NY, USA
8Amen, Thousand Oaks, CA, USA

Pediatric Rheumatology 2008, 6(Suppl 1):O15

Background: Etanercept has approval for use in children with polyarticular juvenile rheumatoid arthritis (JRA). Here we evaluate the safety of etanercept in children with polyarticular or systemic JRA.

Methods: This 3-year, open-label, non-randomized registry included patients age 2–18, with a diagnosis of polyarticular or systemic JRA. Patients treated with methotrexate (MTX), etanercept (ETN), or methotrexate/etanercept in combination (MTX/ETN) were eligible. Co-administration of non-biologic DMARDs was allowed. MTX was administered at 0.3 to 1 mg/kg/wk and etanercept was administered at 0.4 mg/kg (max 25 mg) twice weekly or 0.8 mg/kg (max 50 mg) weekly.

Results: 602 patients enrolled; 198 received MTX, 105 received ETN, and 299 received MTX/ETN. A total of 33%, 31%, and 35% of patients have completed the 3-year registry for a total of 388, 210, and 610 subject-years of exposure for the MTX, ETN, and MTX/ETN groups, respectively. In the MTX, ETN, and MTX/ETN groups, 18%, 8%, and 19% discontinued due to insufficient therapeutic effect while 2%, 2%, and 0.3% discontinued due to adverse events. The rates of serious adverse events and medically important infections per 100 patient-years were 4.4, 7.6, 5.7 and 1.3, 1.9, and 2.1 for patients receiving MTX, ETN, or MTX/ETN. One case of lupus (MTX) and 2 cases of sepsis (ETN and MTX/ETN) were reported. No cases of lymphoma, malignancy, tuberculosis, or death were reported.

Conclusion: These data suggest etanercept is safe as a long-term, continuous therapy for treatment of JRA. Funded by Immunex, a wholly-owned subsidiary of Amgen Inc., and by Wyeth Pharmaceutical.
O16

7.6 Long-term treatment with glucocorticoids and low bone mass: a longitudinal study in 266 children and adolescents

M Biggioggero1, ML Bianchi1, C Limonta1, S Vai1, L Ghio2, C Colombo2, A Edelfonti2, F Corona2, G Nebbia2, L Morandi2 and A Colombini3

1Istituto Auxologico Italiano, Bone Metabolic Unit, Milan, Italy
2Ospedale Maggiore, Clinica Pediatrica, Milan, Italy
3Istituto Neurologico Besta, Milan, Italy
4Ospedale San Gerardo, Monza, Italy

Pediatric Rheumatology 2008, 6(Suppl 1):O16

Background: Few longitudinal data are available on bone mass changes in children and adolescents treated with glucocorticoids (GCs). The aim of our study is to verify their long-term effects on bone mass.

Materials and methods: 266 patients (3–20 years) on long-term treatment with GCs for chronic diseases were followed with evaluation of bone mineral density (BMD) for at least 3 years (3–14 years).

BMD was measured with DXA at lumbar spine and on total body and expressed as the Z-score. BMAD was calculated.

Results: GCs had a major effect on trabecular bone independently of the disease and age of patients. This effect is dose related: cumulative dose GCs < 10 g = decrease of 23%; 10–30 g = −40%; >30 g = −68%. A significant correlation was found between spine Z-score vs cumulative GCs (p < 0.001).

Bone loss of spine was higher during the first year of GCs and continues during time at a lower degree (16% the first year, 6% second-fifth year, 3.5% over the fifth year).

GCs influenced BMD differently in relation to age at start of therapy and the disease.

83 patients had at least 1 fragility fractures and 33 had more than 1 fracture. A total of 161 fragility fractures occurred in the group.

Conclusion: GCs induce bone loss and fractures in the young and alter the bone accrual. The relationship between BMD and cumulative dose of steroids clearly underline the absolute need to use the minimum effective dose of GCs.

O17

8.3 Disease patterns in Danish Juvenile Dermatomyositis patients

PR Mathiesen1, M Zak1, T Herlin3 and SM Nielsen1

1Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark
2Holbaek County University Hospital, Holbaek, Denmark
3Skejby University Hospital, Aarhus, Denmark

Pediatric Rheumatology 2008, 6(Suppl 1):O17

Purpose:
– Evaluation of the Myositis disease activity assessment tool (MYOACT) and Myositis intention to treat activity index (MITAX) as prognostic tools.

Methods: Hospital records from Danish JDM patients (1977–2005) were reviewed. The parameters of the MYOACT and MITAX were used for the database.

Table 1 (abstract O17) Most frequent symptoms at disease onset

<table>
<thead>
<tr>
<th>Symptom</th>
<th>% of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal muscle weakness</td>
<td>81</td>
</tr>
<tr>
<td>Fatigue</td>
<td>74</td>
</tr>
<tr>
<td>Erythema</td>
<td>74</td>
</tr>
<tr>
<td>Gottrons papules</td>
<td>70</td>
</tr>
<tr>
<td>Heliotrope</td>
<td>57</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>41</td>
</tr>
<tr>
<td>Fever</td>
<td>32</td>
</tr>
<tr>
<td>Arthritis</td>
<td>30</td>
</tr>
<tr>
<td>Weight loss</td>
<td>30</td>
</tr>
</tbody>
</table>

Results: 53 patients were classified as JDM. The female:male ratio was 2:1, the mean age at disease onset was 7.1 years and the mean disease duration was 3.6 years. Most frequent symptoms at disease onset are displayed in Table 1. At the 5-years follow-up 34% were in remission, 30% had ongoing disease and disease-or treatment-induced damage was present in 36%. In the total follow-up period (2–30 years) 3 patients (6%) had died, 68% were in full remission, 13% had ongoing disease and 13% had unknown status.

Conclusion:
– Most patients had a favourable outcome; however irreversible damage was found in 36% at 5-years follow-up;
– Baseline predictors of unfavourable disease outcome could not be identified;
– Due to frequently missing chart data MYOACT and MITAX could not be used as a scoring tool in this retrospective set-up;
– A clinical long-term follow-up study is warranted and now carried out by the authors.

O18

8.4 Novel autoantibodies targeting a p140 protein are a major autoantigen system in juvenile dermatomyositis and a marker of calcinosis

H Gunawardena1, LR Wedderburn2, ZE Betteridge3, H Chinoy4, J North5, RG Cooper6, AV Ramanan6, JE Davidson6 and NJ McHugh1

1Rheumatology Department, Royal National Hospital for Rheumatic Diseases, Bath, UK
2Rheumatology Unit, Institute of Child Health, London, UK
3School for Health, University of Bath, Bath, UK
4Centre for Integrated Genomic Medical Research, University of Manchester, Manchester, UK
5Rheumatic Diseases Centre, Hope Hospital, Salford, UK
6Rheumatology Department, Bristol Royal Hospital for Children, Bristol, UK

Pediatric Rheumatology 2008, 6(Suppl 1):O18

Background: To demonstrate that autoantibodies targeting a p140 protein are a major autoantigen in juvenile dermatomyositis (JDM) and describe the clinical associations in children recruited to the JDM Registry (JDRR).

Methods: 156 children were studied. Serum was screened by immunofluorescence (IF) and radio-immunoprecipitation (IPP) [1]. Immunodepletion was used to establish whether p140 is different to p155/140 also recognised in JDM [1].
Results: 21% of children were positive for anti-p140 on IPP, with a weak non-specific nuclear pattern or negative ANA on IF. No anti-p140 cases were positive for other autoantibody specificities. Immunodepletion confirmed that p140 and p155/140 are different autoantigens. Anti-p140 positives compared to negatives had a similar male:female ratio and age at diagnosis. No significant difference was observed in the type or distribution of rash when comparing anti-p140 positives vs. negatives except for more rash on the trunk in negative cases (p = 0.017). Calcinosis was significantly more frequent in anti-p140 positives (52%) compared to negatives (13%) (p < 0.001, OR 7.1 95% CI 3–16.8). When comparing anti-p140 and anti-p155/140 cases; cutaneous oedema (p = 0.04) and rash over the trunk (p = 0.002) and small joints (p = 0.013) was more frequent in anti-p155/140. Calcinosin in anti-p140 remained a significant feature compared to anti-p155/140 (p = 0.005, OR 6.4 95% CI 2–22).

Conclusion: Anti-p140 found in this cohort is likely to be the same as anti-Mj, described against nuclear matrix protein NXP-2 [2]; further confirmation is required. Anti-p140 is a major autoantibody subset in JDM. Further characterisation of this system will provide insights into the pathophysiology of calcinosis in JDM.

References

O19
8.5 Predictors of long-term outcome of Juvenile Dermatomyositis (JDM): a Multicenter, Multinational Study of 490 patients
C Ferrari1, L Trail1, C Pilkington2, S Maillard2, R Cuttica3, MM Katsicas4, R Russo4, M Bandeira6, V Ferriani6, S Oliveira7, C Saad-Magalhaes7, CA Silva7, V Baca7, R Burgos-Vargas7, E Solis-Vallejo7, M Alessio7, MG Alpigiani8, F Corona9, F Falconi9, V Gerloni9, L Lepore9, S Magni-Manzoni9, F Zulian10, N Ruperto1, A Pistorio1, E Felici1, F Rossi1, E Sala1, A Martin1 and A Ravelli1
1Italian Pediatric Rheumatology Study Group, Italy, Italy
2Great Hormond Street Hospital, London, UK
3Hospital General de Ninos Pedro de Elizalde, Buenos Aires, Argentina
4Hospital Garrahan, Buenos Aires, Argentina
5Hospital Pequeno Principe, Curitiba, Brazil
6Hospital da Universidade, Ribeirao Preto, Brazil
7Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil
8Hospital das Clı ´nicas, Sao Paulo, Brazil
9Hospital Clı ´nicas, Buenos Aires, Argentina
10Hospital Garrahan, Buenos Aires, Argentina
11Hospital General de Mexico, Mexico City, Mexico
12CMN La Raza, Mexico City, Mexico

Background and objective: Little information exists on long-term outcome of JDM. Furthermore, most studies have been conducted in single centres or have involved a few patients. Objective of the study is to identify predictors of a poorer long-term outcome of JDM in a multicenter cohort of patients.

Methods: 490 patients with JDM and disease duration > 2 years seen in 27 centers in 5 countries (Italy, UK, Argentina, Brazil, Mexico) after 1980 were identified. Outcomes included muscle weakness (MMT), continued activity (DAS), cumulative damage (MDI), calcinosis, lipodystrophy, functional impairment (CHAQ), and health-related quality of life (HRQL) impairment (CHQ). Predictors included: continent (Europe vs. Latin America), gender, year of onset, onset age, onset type (acute vs. insidious), onset manifestations, severity of muscle/skin manifestations at onset, and course type (monocyclic, polycyclic, chronic continuous).

Results: Table 1 shows significant predictors for each outcome.

Conclusion: The chronic continuous course predicted all outcomes, which highlights the critical need for treatments and treatment strategies that have the ability to better control disease activity over time.

Table 1 (abstract O19)

<table>
<thead>
<tr>
<th><em>At onset</em></th>
<th>M. weak'ss activity</th>
<th>Cont’d Damage</th>
<th>Funct. Impairm’nt</th>
<th>HRQL Impairm’nt</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>Onset after 2000</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Onset age &lt; 5 yrs</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Onset type</td>
<td>–</td>
<td>+</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Dysphonia*</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Mm/skin severity*</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>Chronic Course</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

O20
9.1 Innate resistance of endothelial cells to the effects of glucocorticoids
P Koenen, K Barczyk, M Wolf, J Roth and D Viemann
University Hospital of Muenster, Institute of Immunology, Muenster, Germany

Glucocorticoids (GCs) represent a mainstay of treatment in most chronic inflammatory diseases. However, many forms of vasculitis relapse after cessation of GC medication or remain primarily unresponsive. Assuming the vasculature and especially endothelial cells (ECs) as origin of the inflammatory process we investigated the effects of GCs on ECs in comparison to monocytes. We treated human micro- and macrovascular ECs as well as human monocytes for 4 h and 16 h with GC or GC + TNF or pretreated ECs with GC followed by TNF stimulation. Testing several genes by quantitative RT-PCR as well as by microarray analysis considering more than 17,000 genes we found no significant gene expression changes in ECs neither with GC alone nor for GC on TNF-induced genes which was in strict contrast to the impressive GC-response of monocytes. We checked that all known GC receptor (GR) subtypes as well as potential cofactors of GC were readily expressed in untreated and inflammatory stimulated ECs. However, in immunofluorescence stainings we surprisingly found that GC treatment failed
to induce a nuclear shift of the GR in ECs in contrast to a substantial shift in steroid-sensitive monocytes.

Summarizing our results indicate that the molecular prerequisites for the implementation of GC effects on gene regulation are not given in ECs in contrast to myeloid cells. The anti-inflammatory effects of GCs in vasculitis might primarily act on infiltrating leucocytes without targeting ECs which may be the molecular basis for symptomatic effects but lack of long-lasting success of GC-treatment in many forms of vasculitis.

O21
9.2 QT interval dispersion in North Indian children with Kawasaki disease
S Ghelani, S Singh and R Manoj Kumar
Post Graduate Institute of Medical Education and Research, Chandigarh, India

Pediatric Rheumatology 2008, 6(Suppl 1):O21

Background: Increased QT interval dispersion is associated with an increased risk for ventricular arrhythmias and sudden cardiac events. We examined the association between increased QT interval dispersion and Kawasaki disease (KD) in children aged 4 1/2 to 12 years and compared the same with matched controls.

Design and patients: The study population consisted of 20 children in convalescent phase of KD and 20 age and sex matched healthy controls. All children with KD had received intravenous immunoglobulin (IVIG) during the acute phase and only 1 had mild events. We examined the association between increased QT interval dispersion and Kawasaki disease (KD) in children aged 4 1/2 to 12 years and compared the same with matched controls.

Results: Of 480 leads obtained (12 per subject) 36 were excluded from analysis (15 because of poor T wave formation and 11 because of presence of U waves). Children with KD had significantly higher QTc dispersion in 12 lead (67.08 ± 17.72 msec compared to 47.63 ± 16.48 msec in controls; p = <0.001) as well as 8 lead (60.51 ± 18.54 msec compared to 42.92 ± 18.03 msec in controls; p = <0.001) analysis.

Conclusion: QT interval dispersion appears to be significantly increased in children with KD. The dispersion is indicative of inhomogenous ventricular repolarization and may represent increased risk for developing ventricular arrhythmia in this population.

O22
9.3 Endothelial progenitor cells and vasculogenic responses to therapy in children with primary systemic vasculitis
LA Clarke¹, Y Hong¹, D Eleftheriou¹, N Klein² and PA Brogan¹
¹Department of Rheumatology, Institute of Child Health, UCL, London, UK
²Department of Infectious Diseases and Microbiology, Institute of Child Health, UCL, London, UK

Pediatric Rheumatology 2008, 6(Suppl 1):O22

Background: Endothelial progenitor cells (EPCs) are involved in vascular repair. This study describes the relationship between EPCs and growth factors influencing EPC mobilisation from the bone marrow in children with primary systemic vasculitis (PSV).

Materials and methods: 20 children (median age 10.6 years (1–16.6); 10 males) with PSV at various stages of disease activity were studied. PSV was classified as: polyarteritis nodosa (n = 10); Wegener’s granulomatosis (n = 6); Kawasaki disease (n = 2); Behçet’s disease (n = 1) and unclassified (n = 1). EPCs were detected using flow cytometry and defined as cells triple-positive for CD34, CD133, and VEGFR2. Growth factors were measured using ELISA in serum (VEGF) or platelet-poor plasma (Angiopoietin-1, Angiopoietin-2). Disease activity was assessed using a modified BVAS scoring system and evaluation of circulating endothelial cells (CECs) [1].

Results: Peripheral blood EPCs were higher in 12 children with active PSV prior to treatment compared to 20 age-matched child controls (p = 0.024). With remission inducing therapy, EPCs declined. Correspondingly VEGF and Angiopoietin-1 and 2 were also significantly elevated at disease onset compared to controls (all p < 0.03); VEGF and Angiopoietin-2 declined significantly with treatment (both p < 0.04).

Conclusion: Our preliminary observations suggest mobilization of EPCs at the time of maximal endothelial injury, which corresponded with the upregulation of growth factors associated with angiogenesis and vasculogenesis. This observation could thus represent an attempt to repair endothelium in response to vasculitic injury, however the function of EPCs in this context remains poorly defined, and is the subject of ongoing work within our group.

Reference

O23
9.4 Autoantibodies in pediatric systemic lupus erythematosus: ethnic grouping, autoantibody clustering and clinical correlations
R Jurenca³,¹ Mj Fritzler³,¹ PN Tyrrell³,¹ LT Hiraki³,¹ SM Benseler¹ and ED Silverman¹
¹The Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada
²Department of Medicine, University of Calgary, Calgary, Alberta, Canada

Pediatric Rheumatology 2008, 6(Suppl 1):O23

Objective: The aims of this study were: 1) to evaluate the spectrum of serum autoantibodies (AA) in pediatric-onset systemic lupus erythematosus (pSLE) with a focus on ethnic differences, 2) to use cluster analysis to identify patients with similar AA patterns and to determine their clinical associations.

Methods: A single center cohort study of all newly diagnosed pSLE patients seen over an 8-year period was performed. Ethnicity, clinical and serological data were available in 156/169 patients (92%). The frequencies of 10 selected AA among ethnic groups were compared. Cluster analysis was used to identify groups of patients with similar AA profiles. Associations of these groups with clinical and laboratory features of pSLE were examined.

Results: Among our 5 ethnic groups, there were differences in the prevalence of anti-U1RNP and anti-Sm antibodies which occurred more frequently in non-Caucasian patients (p < 0.0001, p < 0.01, resp.). Cluster analysis revealed 3 AA clusters. Cluster I consisted of anti-dsDNA antibodies. Cluster 2 consisted of...
anti-dsDNA, anti-chromatin, anti-ribosomal P, anti-U1RNP, anti-Sm, anti-Ro and anti-La AA. Cluster 3 consisted of anti-dsDNA, anti-RNP and anti-Sm AA. The highest proportion of Caucasians was in cluster 1 (p < 0.05) which was characterized by a mild disease with infrequent major organ involvement compared to cluster 2 which had the highest frequency of nephritis, renal failure, serositis and hemolytic anemia, or cluster 3 which was characterized by frequent CNS disease and nephritis.

**Conclusion:** This study demonstrated ethnic differences in AA profiles in pSLE. AA tended to cluster together and the clusters predicted subsequent clinical course.

### O24

#### 12.2 Mevalonate kinase deficiency: Impaired isoprenoid synthesis induces IL-1β production via activation of Rac1

LM Kuijken1, J Frenkel1, HR Waterham2, J Koster2 and PJ Coffer1

1Division of Paediatrics, University Medical Center, Utrecht, Netherlands
2Laboratory for Genetic Metabolic Diseases, Academic Medical Center, Amsterdam, Netherlands

**Pediatric Rheumatology** 2008, 6(Suppl 1):O24

Mevalonate kinase deficiency is an autosomal recessive disorder characterized by recurring episodes of fever and inflammation. Peripheral blood mononuclear cells from mevalonate kinase deficiency patients secrete high levels of IL-1β when stimulated with lipopolysaccharide (LPS) due to the presence of hyperactive caspase-1. The molecular mechanism of mevalonate kinase deficiency-induced caspase-1 activation remains unclear.

We artificially impaired isoprenoid biosynthesis in the monocytic cells (THP-1) with simvastatin, after which cells were stimulated with LPS. Simvastatin-treated THP-1 cells stimulated with LPS demonstrated enhanced release of IL-1β. LPS enhanced transcription of IL-1β, whereas simvastatin enhanced proteolytic activation of IL-1β. This effect was mediated by phosphatidylinositol 3 kinase (PI3K) and protein kinase B (PKB/c-Akt). In addition, simvastatin-induced IL-1β secretion required the small GTPase Rac1. Simvastatin treatment increased the levels of biologically active gTPase-bound Rac1 and inhibition of Rac1 reduced simvastatin-mediated IL-1β secretion. Rac1 functioned upstream of PKB, since Rac1 inhibition abolished the effect of simvastatin on PKB. Simvastatin-mediated activation of the Rac1/PI3K/PKB pathway enhanced IL-1β secretion through activation of caspase-1, since inhibition of both Rac1 and PI3K blocked the release of active caspase-1 subunits. The importance of Rac1 in mevalonate kinase deficiency was confirmed when a specific Rac1 inhibitor was shown to inhibit spontaneous IL-1β release by mononuclear cells from mevalonate kinase deficiency patients.

Together, these results demonstrate that Rac1, PI3K and PKB are involved in simvastatin-induced secretion of IL-1β through regulation of caspase-1 activity and that Rac1 is a potential new therapeutic target in mevalonate kinase deficiency.

### O25

#### 12.3 Long-term follow up of patients with CINCA syndrome: efficacy and tolerability of Anakinra treatment

G Paloni1, M Gattorno2, M Alessio2, D Rigante4, M Cattalini5, F Zulian6 and L Lepore1

1Institute of Child Health IRCCS Burlo Garofolo, University of Trieste, Italy
2Division of Pediatric, ‘G. Gaslini’ Institute for Children, Genoa, Italy
3Department of Pediatrics, Federico II Hospital, Naples
4Department of Pediatric Sciences, Catholic University of Sacred Heart, Rome, Italy
5Department of Rheumatology and Clinical Immunology, Brescia, Italy
6Pediatric Rheumatology Unit, Department of Pediatrics, Padova, Italy

**Pediatric Rheumatology** 2008, 6(Suppl 1):O25

We report the long-term follow up of 15 Italian patients affected by Chronic Infantile Neurological Cutaneous and Articular (CINCA) syndrome (7 males and 8 females, mean age 13, 5 years).

We report the updating of the survey following the introduction of the IL-1 receptor antagonist therapy (Anakinra).

11 patients were treated with subcutaneous injections, at a daily dosage of 1 mg/Kg in children and up to 100 mg in adults.
2 refused the therapy, and the others did not require the treatment due to a mild presentation of the disease so far.

In treated patients fever, rash, articular involvement, conjunctivitis, uveitis disappeared or improved. Laboratory data normalized in most of the cases within the first month. The neurologic symptoms ameliorated, papilledema disappeared in four out of eleven treated patients while dysmorphisms (typical facies) and bone alterations constantly persist.

No further Cinca related signs and symptoms appeared after Anakinra was introduced.

The medication showed very good tolerability: we observed local erythema at the site of injection in 2 out of 11 subjects, and oral aphthosy in another.

The untreated subjects kept presenting all their symptoms of CINCA syndrome and the disease went on with its poor manifestation. We found no differences in the response to Anakinra therapy between CIAS1-mutated and not mutated patients.

In summary, our study demonstrates that a long lasting treatment with Anakinra appears to be safe and highly effective in patients affected by CINCA syndrome.

### O26

#### 12.4 ACZ885 (canakinumab), a new IL-1 beta blocking monoclonal antibody provides long-lasting remission in children with cryopyrin associated periodic syndrome (CAPS)

J Kümmerle-Deschner1, N Blank2, J Roesler3, E Ramos3, N Tzaribachew1, K Graßl1, C Well1, SD Felix3, C Rordoń2 and T Jung2

1Universitätsklinik Tübingen, Kinderklinik I, Hoppe-Seyler-Straße 1, Tübingen, Germany
2Medizinische Klinik 5, Im Neuenheimer Feld 410, Heidelberg, Germany
3Univ.-Klinikum Carl-Gustav-Carus, Kinderklinik, Fetscherstraße 74, Dresden, Germany
4Servicio de Pediatria, Hospital Central de Asturias, C/Julian Claveria, s/n, Oviedo, Spain
5Novartis Pharma AG, Basel, Switzerland

**Pediatric Rheumatology** 2008, 6(Suppl 1):O26

This study was conducted to assess the efficacy, safety, and immunogenicity of canakinumab administered as a subcutaneous
injection to patients with CAPS. Herein we report the results of 5 children (4–13 years) and 2 adolescents (16 and 17 years) enrolled in the study. All had documented NALP-3 gene mutations. Entry criteria were active disease evaluated by moderate to severe symptoms of CAPS (based on a 5-point global physician’s assessment scale) and/or elevated CRP and SAA levels. The children received canakinumab 2 mg/kg, while the 2 adolescents received a dose of 150 mg. Subsequent injections were administered after each relapse. Clinical remission was defined as: physicians global assessment of disease activity absent/minimal, assessment of skin disease absent/minimal, normal serum SAA and CRP levels. Canakinumab improved symptoms in the majority of patients within 1 day, with full clinical remission within 7 days. Two children received subsequent additional intravenous injections (5 mg/kg) to achieve a complete response. The median time to re-dosing due to relapse was 88 days (n = 6) and 63 days (n = 5) after the first and second dose of canakinumab respectively. One patient was discontinued 70 days after the first dose due to pregnancy. Injections were well tolerated and so far no immunogenicity developed. The total exposure time ranged from 70 to 383 days. Adverse events (AE) were mainly upper respiratory tract infections. One serious AE was reported (vertigo). In conclusion, canakinumab was well tolerated and provided long-lasting complete clinical remission in children with CAPS.

**O27**

13.4 High frequency of CNS involvement in linear scleroderma of the face

M Parolin1, R Russo2, F Corona3, SKF de Oliveira4, EM Nowakowska5, F Sztajnbok6, J Chaitow7, G Espada8, M Desjouquieres9, S Ullman10 and F Zulian1

1University of Padua, Padua, Italy
2Hospital de Pediatria Juan P. Garrahan, Buenos Aires, Argentina
3Clinica Pediatria II De Marchi, Milan, Italy
4Instituto de Puericultura e Pediatria Martagao Gesteira, Rio de Janeiro, Brazil
5Institute of Rheumatology, Warsaw, Poland
6Hospital Universitario Pedro Ernesto, Rio de Janeiro, Brazil
7The Children’s Hospital Westmead, Sydney, Australia
8Hospital de Ninos Ricardo Gutierrez, Buenos Aires, Argentina
9Hospital E Herriot, Lyon, France
10Bispebjerg Hospital, Copenhagen, Denmark

**Objective:** To evaluate the prevalence of thrombotic and non-thrombotic clinical manifestations and long-term outcome in a large group of children with positive antiphospholipid antibodies (aPL).

**Methods:** We retrospectively reviewed medical records from January 1997 to November 2007 at University Children’s Hospital Ljubljana for all patients who tested positive for aPL. Testing for aPL was requested by the treating physician given the clinical suspicion of aPL-related manifestations. All patients fulfilled the consensus laboratory criteria for antiphospholipid syndrome.

**Results:** We identified 190 aPL-positive patients and randomly selected 100 patients for detailed evaluation. Sixty-two were girls and 38 boys with mean age at presentation 9.7 years. Twenty-seven (27%) patients had underlying systemic autoimmune disease (SLE 16, JIA 8). Sixty patients presented with one, 14 with two and 13 with three or more aPL-related clinical manifestations. Thromboses occurred in 10 (10%) patients and one patient had recurrent thrombosis. One or more non-thrombotic clinical manifestations were found in 77 (77%) patients including hematological disorders in 27 (thrombocytopenia 20, autoimmune hemolytic anemia 2), neurological disorders in 26 (migraine 15, seizures 3, chorea 2) and skin disorders in 22 patients (livedo reticularis 9, Raynaud’s phenomenon 4). Seventeen infants born to mothers with aPL-positive autoimmune disease had positive aPL and 4 of them exhibited aPL-related clinical manifestations.

**Conclusion:** In our cohort, thrombotic events occurred in 10% of all symptomatic patients with positive aPL evaluated at the tertiary care pediatric hospital. The most common non-thrombotic manifestations found in children with aPL were thrombocytopenia, migraine headache and livedo reticularis.
O29
14.2 Causes of early death in juvenile onset systemic lupus erythematosus (JSLE)
B Bader-Meunier1, A Klein2, A Aggarwal3, R Merino4, R Russo5, F Sztajnbok6, T Avcin7, S Knupp8, R Khubchandani9, S Ozen10, R Cimaz10 and P Quartier1
1Necker Hospital, Paris, France
2Saint Jacques Hospital, Besançon, France
3SGPGI, Lucknow, India
4La Paz Hospital, Madrid, Spain
5Garrahan Hospital, Buenos Aires, Argentina
6Universidade do Estado do Rio de Janeiro, Rio de Janeiro, Brazil
7University children’s hospital, Ljubljana, Slovenia
8Hacettepe university, Ankara, Turkey
9Jakov Hospital, Mumbai, India
10Hospices civils de Lyon, Lyon, France
11IPPMG, Rio Do Janeiro, Brazil

Pediatric Rheumatology 2008, 6(Suppl 1):O29

Purpose: To describe the causes of death occurring within the first month following the diagnosis of JSLE in order to prevent them.

Methods: Retrospective study of causes of early death in JSLE patients during the period 1995–2006 conducted on behalf of Paediatric Rheumatology International Trials Organization (PRINTO). All the patients fulfilled the American College of Rheumatology (ACR) criteria for the diagnosis of SLE, and were diagnosed before 16 years of age.

Results: Death was recorded in 5 girls and 1 boy including three non-Caucasian patients, aged 6 to 16 years. Initial SLE manifestations comprised at least three organ involvement, including at least two major organ involvement: central nervous system (4 patients), kidney (5 patients), pancreas (2 patients), hematopoietic system (3 patients), heart (1 patient), skin (2 patients), and joints (3 patients). Despite administration of oral and pulsed steroids, associated twice with intravenous cyclophosphamide, SLE activity remained uncontrolled in all the patients. Death resulted from SLE organ failure either alone in 2 patients (pancreatitis: 1 patient, neurolupus: 1 patient), either associated with thrombotic event (catastrophic antiphospholipid syndrome: 2 patients, pulmonary thromboembolism: 1 patient with nephrotic syndrome) and/or infection (paravertebral abcess: 1 patient, pneumococcal sepsis: 1 patient).

Conclusion: Despite prompt diagnosis and management, death may occur at presentation of juvenile-onset SLE. Half of them resulted from thromboembolic event in patients with nephrotic syndrome or APL. These features suggest that prompt prophylactic anticoagulation may be beneficial in patients with severe SLE multiorgan involvements associated with risk factors of thromboembolic event.

O30
14.3 Early cardiovascular risk assessment in patients with juvenile idiopathic arthritis
AP Vlahos1, S Alfantaki2, A Bechlioulis3, K Vakalis4, LK Michalis1 and A Siamopoulou1
1University of Ioannina, Ioannina, Greece
2Michaelion Cardiac Centre, University of Ioannina, Ioannina, Greece
3University Hospital of Ioannina, Ioannina, Greece

Pediatric Rheumatology 2008, 6(Suppl 1):O30

Background: Inflammation has emerged as an important factor that contributes to the development of atherosclerosis and is associated with increased cardiovascular risk. Juvenile idiopathic arthritis (JIA) is a chronic inflammatory condition with its origin in childhood. Its adult form, rheumatoid arthritis, has been associated with an excess of cardiovascular disease even after adjustment for traditional risk factors.

Materials and methods: Arterial stiffness indices were measured, noninvasively. Pulse Wave Velocity (PWV) and Augmentation Index (Alx) were calculated using the Shygymocor device (AcCor Medical, Sydney, Australia). Vascular Compliance was determined as a function of both the arterial system’s capacitance (C1) and that of the reflectance or oscillatory (C2) function using the HDI/PulseWave CR-2000 (Hypertension Diagnostics, Inc., Eagen, MN). The cardiac diastolic function was assessed using classic, tissue Doppler and colour M-mode echocardiography.

Results: There were 33 patients with JIA (25 F, 8 M) aged 13 ± 6 years with 6 years mean duration of the disease that were compared with 22 controls (13 ± 5 years) matched for age and gender. Among the indices assessed a significant difference was found regarding the Alx (p = 0.006) and the C1 (p = 0.029) of the patients, indicating increased vascular stiffness compared to controls. There was no difference in the cardiac diastolic function in respect to all indices assessed.

Conclusion: Early manifestations of vascular dysfunction are evident in patients with JIA from childhood. Cardiac diastolic dysfunction appears to be a later finding in this patient group. Since vascular stiffness is an early finding this may necessitate appropriate pharmaceutical and lifestyle intervention.
expressed in activated macrophages were among those more highly expressed in the extended outcome phenotype.

**Conclusion:** Our data suggest that in children with early oligoarthritis, deterioration of disease can be predicted by cell composition or gene expression from synovial fluid cells. If these findings are replicated in a new set of samples, they may represent a major step forward in our understanding of mechanisms governing severity in childhood arthritis.

**O32**

14.5 Rheumatoid Arthritis susceptibility loci; STAT4, TRAF1/C5 and 6q23 region, are also associated with Juvenile Idiopathic Arthritis

A Hinks, A Barton, S Eyre, X Ke, J Worthington and W Thomson

BSPAR Study Group, UKRA Genetics Consortium arc Epidemiology Unit, Manchester, UK

**Pediatric Rheumatology** 2008, 6(Suppl 1):O32

**Background:** Recent genome wide association studies (GWAS) of many complex diseases have successfully identified novel susceptibility loci. An emerging observation is that a number of loci are associated with more than one condition, particularly in the cases of autoimmune diseases.

In view of the shared pathology of adult inflammatory arthritis and juvenile idiopathic arthritis (JIA) we hypothesised that loci identified in GWAS of rheumatoid arthritis (RA) may also have a role in JIA.

**Aims:** To test whether markers at three recently identified RA susceptibility loci, STAT4, TRAF1/C5 and 6q23 region, are also associated with JIA.

**Methods:** Previously associated SNPs for each of the three regions (11 SNPs in total) were selected for investigation. Genotyping was performed using Sequenom MassArray. DNA was available for 855 UK Caucasian JIA cases and 3599 controls. Genotype frequencies were compared between cases and controls using the trend test implemented in PLINK.

**Results:** Strong evidence for association was seen for both STAT4 (strongest effect rs754865 OR 1.24 95% CI 1.1–1.4, ptrend = 0.0008) and TRAF1/C5 (strongest effect rs2900180 OR 1.23 95% CI 1.1–1.38, ptrend = 0.0004). The 6q23 region showed weak evidence for association with JIA (rs6920220 OR 1: 1.19 95% CI 1.01–1.38, ptrend = 0.03). In all cases the associated allele was the same as for RA and the effect sizes were similar.

**Conclusion:** We have identified three novel JIA susceptibility loci. These findings are currently being validated in a North American JIA cohort. Fine mapping and functional studies will be required to elucidate how these polymorphisms contribute to disease.

**O33**

14.6 MRP-Targeting in experimental rheumatoid arthritis allows monitoring of disease activity with optical molecular imaging

M Eisenblätter, T Vogl, C Bremer and J Roth

University Hospital Münster, Münster, NRW, Germany

**Pediatric Rheumatology** 2008, 6(Suppl 1):O33

**Purpose:** Monitoring disease activity of chronic arthritis is still a major challenge in clinical praxis. Activated macrophages play a crucial role during joint inflammation. Expression of myeloid related protein 14 (MRP14) by activated macrophages correlates with disease activity in different forms of arthritis. We analyse the use of Cy5.5-labelled antibodies against MRP14 for monitoring of inflammation activity in experimental model of arthritis using optical molecular imaging.

**Methods:** Anti-MRP14 antibody was coupled to Cy5.5-NHS-ester. Collagen-induced arthritis was analysed in male DBA/1lacj-mice. Fluorochromes (anti-MRP14-Cy5.5 or IgG-Cy5.5 as control) were injected in amounts of 2 nm Cy5.5 per animal at day 25 and Fluorescence Reflectance Imaging (FRI) was performed from day 26 to 30 and signal-to-noise-ratios (SNR) were calculated. For correlation of imaging findings expression of MRP14 was confirmed by immunohistochemistry of inflamed tissue and determination of serum levels of MRP14 by ELISA.

A one-way ANOVA was performed for statistical analysis.

**Results:** Injection of Anti-MRP14-Cy5.5 resulted in SNR which was more than three-fold higher compared to those after IgG-Cy5.5-injection (6359.2 vs. 2087.5, p < 0.01), confirming that the measurable signal was due to probe-to-target-binding. Fluorescence intensity correlated with clinical disease score and MRP14 serum levels: highly symptomatic mouse (clinical score 3/4) vs. asymptomatic mouse (1/4): Fluorescence Intensity 10256 vs. 4459 AU; MRP14 serum level 1450 vs. 83 ng/ml.

**Conclusion:** Anti-MRP14-Cy5.5 combined with FRI allows sensitive and specific detection of inflammatory activity represented by MRP14 expression in vivo. Thus imaging disease activity of inflammatory arthritis at high resolution in living animals is feasible using this approach.

**O34**

15.3 Agreement between parent and adolescent assessment of disability, pain and well-being: results from the Childhood Arthritis Prospective Study (CAPS)

SD Lal1, N Adib1, LR Wedderburn2, J Gardner-Medwin3, H Foster4, A Chieng5, J Davidson3, E Baildam6, W Thomson1 and KL Hyrich1

1University of Manchester, Manchester, UK
2Institute of Child Health, London, UK
3Royal Hospital for Sick Children, Glasgow, UK
4University of Newcastle, Newcastle, UK
5Royal Manchester Children’s Hospital, Manchester, UK
6Royal Liverpool Children’s Hospital, Liverpool, UK

**Pediatric Rheumatology** 2008, 6(Suppl 1):O34

**Background:** Limited data exist regarding agreement between parent and adolescent perceptions of disability, pain and general well being (WB), with some showing discordance in those with severe disease [1], and not others [2]. This analysis studies the agreement between these measures in a cohort of adolescents with inflammatory arthritis (primarily JIA) and explores reasons for discordance.

**Methods:** Subjects were participants in CAPS, which systematically follows children with new inflammatory arthritis. This analysis is limited to 154 parent-adolescent dyads who respectively completed a CHAQ and adolescent CHAQ with 100 mmVAS for pain and WB. Agreement in scores was measured using Bland-Altman plots, with agreement defined as ± 0.25 units (CHAQ), ± 10 mm (Pain VAS) and ± 10 mm (WB VAS). Predictors of discordance were identified using logistic regression.
Results: Median age was 13 years (range 11–19); disease duration 1 year (range 0–5). Median parent/child CHAQ, pain and WB scores were, respectively: 0.13/0.19, 1.1/10 mm, 7/9 mm. Agreement was high for all three measures: CHAQ 85%, pain 73%, WB 70%. Bland and Altman plots showed pain and WB agreement was strongest at the lower end of the scale. Similarly, higher adolescent CHAQ correlated with higher discordance in pain (OR 2.1 (95% CI 1.2, 3.5) and WB (OR 2.2 (95% CI 1.3, 3.7)). There was no association between discordance, age, gender or disease duration.

Conclusion: A parent as proxy to measure disability (CHAQ) in adolescents shows validity across the spectrum of disease. However, disagreement exists in subjective measures of pain and well-being in those with more severe disease.

References

POSTER PRESENTATIONS

P1
Analysis of the classical, alternative, and MBL pathways of the complement system in juvenile idiopathic arthritis
J Brunner, J Scheiring, B Petzelsberger, M Prelog and L-B Zimmerhackl
Department of Pediatrics, Innsbruck Medical University, Innsbruck, Austria

Pediatric Rheumatology 2008, 6(Suppl 1):P1

Introduction: The complement system is involved in the host defence by recognition and elimination of potentially harmful exogenous and endogenous structures from the human body. Activation of complement may also promote inflammatory reactions and cause tissue damage if adequate control is not provided by the complement regulatory proteins. Significant amounts of biologically active products arising from complement activation have been detected in patients with rheumatoid arthritis.

Objective: To investigate the role of complement cascade in juvenile idiopathic arthritis.

Methods: 12 serum samples and 2 samples from synovial fluid were obtained from 2 individuals with juvenile idiopathic arthritis (JIA). The complement kit for assessment of classical, alternative and MBL pathway activity was developed by the EU consortium and prepared centrally at Wieslab (Sweden).

Results: The samples of synovial fluid showed a deficiency in the classical, alternative and MBL pathway of the complement system. The results in the sera were normal.

Conclusion: Complement system might play a major role in the development of joint effusion in JIA.

P2
The Damage Associated Molecular Pattern (DAMP) molecule S100A12 induces pro-inflammatory responses in monocytes via innate immunity signalling pathways
H Wittkowski1, D Viemann1, A Lueken2, K Barczyk3, T Vogl4, J Roth2 and D Foell2
1University Hospital Muenster, Department of Pediatrics, Muenster, Germany
2University Hospital Muenster, Institute of Immunology, Muenster, Germany

Pediatric Rheumatology 2008, 6(Suppl 1):P2

Background: In a previous study, we demonstrated excessive activation of neutrophils leading to high concentrations of S100A12, a member of the damage-associated molecular pattern molecules (DAMP), in systemic-onset juvenile idiopathic arthritis (SOJIA) which is not found in other inflammatory diseases. Binding to the Receptor for Advanced Glycation Endproducts (RAGE) has been shown but exact molecular mechanisms of S100A12 leading to pro-inflammatory responses in immune cells are still lacking.

Methods: We analyzed the S100A12-induced expression pattern in human monocytes by microarray technology. Results were independently confirmed by real-time polymerase chain reaction (PCR) and flow cytometry. Additionally we used different knock down approaches of signalling pathways to identify common inflammatory and ligand-specific effects on gene expression changes.

Results: Functional clustering indicated induction of monocytic properties such as pro-inflammatory activation, chemotaxis, and repression of apoptosis. 43% of 745 S100A12-induced genes are also up-regulated by LPS already indicating a strong overlap. Inhibition revealed TLR-4 and NFB as key signalling pathways.

Conclusion: In terms of gene expression changes S100A12 shows strong overlaps with LPS. Similar to LPS a significant portion of gene expression changes induced by S100A12 are dependent on TLR4 and NF-kB. Additionally, S100A12 activates an at least second strong signalling pathway which might be a RAGE-dependent cascade.

P3
The influencing of environmental and genetics factors on bone metabolism in juvenile idiopathic arthritis children
MM Kostik1, PB Glazkov1, MV Moskalenko2, DN Baranov1, MA Pachomova1, AA Kozyreva3, LA Scheplyagina1 and VL Larionova1
1State Pediatric Medical Academy, Saint-Petersburg, Russian Federation
2Scientific and Research Institute of Hematology and Transfusiology, Saint-Petersburg, Russian Federation
3Federal Center of Heart, Blood and Endocrinology, named by V.A. Almazov, Saint-Petersburg, Russian Federation

Pediatric Rheumatology 2008, 6(Suppl 1):P3

Background: Bone mineralization losses depend on not only inflammatory aggression and complication of arthritis therapy or
presence of whole numbers of genetic factors, influencing on bone metabolism, inflammation, immune system's functions and the therapy effectiveness.

The aim of our study was to research bone metabolism status depending on molecular markers and inflammatory activity in JIA children.

**Materials and methods:** We included 184 JIA children, 77 boys and 112 girls. Bone mineralization was detected by dual-energy X-ray absorptiometry of lumbar spine L₁–L₄. Bone biochemical markers were osteocalcin, C-terminal telopeptides, parathyroid hormone (PTH), Ca, Ca⁺⁺, P, total alkaline phosphatase (TAP) activity. We've detected Apal-, Tagl-, BsmI-restriction length polymorphism assay of vitamin D (VDR) receptor gene, Hind III osteocalcin gene, Sp I type I collagen β2 chain (CollI), BclI glucocorticoid receptor gene (GCR).

**Results:** Low bone mineral density (LBMD) for age was detected when Zscore <−2 SD in 36 children, 18 girls and 18 boys. Girls with LBMD had lower height and weight, earlier age of arthritis onset and higher clinical and paraclinical arthritis activity parameters, higher osteocalcin and lower PTH. Children, who received glucocorticoids had lower BMD-Zscore, Ca in boys and lower BMC, BMD, BMD-Zscore, Ca, P, TAP activity in girls. Boys with normal BMD had frequently GG genotype BclI GCR. We have revealed positive correlation A allele Apal VDR and negative correlation B allele BsmI VDR with BMD.

**Conclusion:** We have detected opposite changes of bone mineralization between boys and girls, due to large numbers of environmental and genetics factors.

**P4**

May antihistone antibodies replace antinuclear antibodies (ANA) as a predictor of uveitis in juvenile idiopathic arthritis?

EB Nordal¹, NT Songstad², B Straume³, L Berntson⁴ and M Rygg⁵

¹Department of Pediatrics, University Hospital of North Norway and Institute of Community Medicine, University of Tromsø, Tromsø, Norway
²Department of Pediatrics, University Hospital of North Norway, Tromsø, Norway
³Institute of Community Medicine, University of Tromsø, Tromsø, Norway
⁴Department of Women’s and Children’s Health, Uppsala University Children’s Hospital, Uppsala, Sweden
⁵Department of Laboratory Medicine, Children’s and Women’s Health, Norwegian University of Science and Technology and Department of Pediatrics, St. Olavs Hospital, Trondheim, Norway

**Background:** Antihistone antibodies (AHA) are an ANA subtype reported to be associated with uveitis in Juvenile idiopathic arthritis (JIA). Enzyme-linked immunoassays (E-ANA) are increasingly used as a more standardized alternative to the immunofluorescense method on Hep-2 cells (IF-ANA). E-ANA, however, show no association with uveitis and should not be used in the diagnostic work-up of JIA.

**Materials and methods:** Sera of 100 children with JIA and 60 healthy children were analyzed for antihistone IgM/IgG (Pharmacia ELIA kit), for E-ANA and IF-ANA. Patients were recruited prospectively and followed at regular intervals from onset of disease in 1997–2004.

**Results:** Of the 100 children with JIA, 16 developed asymptomatic chronic uveitis; mean observation time was seven years. Antihistone IgM/IgG >30 U/ml were found in six of the 100 children with JIA, four of whom developed uveitis, and in one of the controls. However, exploring lower cut-off levels of AHA, we found uveitis in 13 of 44 patients with AHA >8 U/ml. Analyses of predictors for uveitis show that young age at onset of arthritis, AHA >8 U/ml and IF-ANA titer >1/320 carry significantly increased risk of developing uveitis. No significant increased risk is found for the oligoarthritis subtype, female gender, positive E-ANA and IF-ANA titer >1/80.

**Conclusion:** Antihistone IgM/IgG are significantly associated with uveitis in JIA children. AHA at a low cut-off level, show comparable test performance as IF-ANA, in predicting uveitis. As E-ANA replaces IF-ANA in many laboratories, further studies are needed to confirm the value of the AHA in risk stratification for uveitis screening.

**P5**

A juvenile idiopathic arthritis biobank at the Royal Children’s Hospital, Melbourne, Australia.

J Ellis¹, S Macnee², A-L Ponsonby³, J Akkusqa², R Allen² and J Munro³

¹Murdoch Children’s Research Institute, Melbourne, Victoria, Australia
²Royal Children’s Hospital, Melbourne, Victoria, Australia
³Royal Children’s Hospital, Melbourne, Victoria, Australia

**Background:** Juvenile idiopathic arthritis (JIA) is a complex disease determined by both genetic and environmental factors. Whilst prior research has provided preliminary evidence for some factors, most studies have been hindered by small sample sizes and low statistical power. It is clear that to successfully identify causal factors for complex diseases, large sample sizes and comprehensive approaches will be required. To this end, we have established the Victorian JIA Biobank (VJIAB), a collaborative effort between the Royal Children’s Hospital (RCH) and the Murdoch Childrens Research Institute in Melbourne Australia. Our aim is to collect biospecimens and extensive clinical and environmental information on 1000 cases (incident and prevalent, attending RCH Paediatric Rheumatology Clinic) and 1000 controls (healthy children, matched to cases by age and sex, attending RCH for elective surgery).

**Materials and methods:** The VJIAB was initiated in January 2008. A peripheral blood sample is being collected from all participants, from which plasma and mononuclear cells are being banked. An extensive questionnaire that includes over 130 items is also being completed to capture information from both parent and child on such aspects as medical and family history, early life environment (for consideration of the hygiene hypothesis), and sun exposure (for consideration of the role of Vitamin D in the autoimmune process).

**Results and conclusion:** To date, we have recruited 24 cases and matching controls. There are also plans to extend VJIAB to capture cases Australia-wide through the newly established Australian Paediatric Rheumatology Research Network.
P6
Tumor necrosis factor-alpha polymorphism and susceptibility to juvenile idiopathic arthritis
S Bayraktar, O Kasapcopur, N Arisoy, B Batar and M Guven
Istanbul University, Cerrahpasa Medical School, Istanbul, Turkey

Background: Juvenile idiopathic arthritis (JIA) is a complex, multifactorial and chronic inflammatory disease of unknown etiology with considerable variability in which tumor necrosis factor-alpha (TNF-α) plays an important role. Both genetic and environmental factors can contribute to a susceptibility to disease initiation as well as a severity of disease course. TNF-α polymorphisms may be an independent marker of susceptibility and severity of JIA. The aim of this study was to elucidate putative association between the -863 C/A polymorphism in the promoter region of the TNF-α gene and susceptibility to onset and severity of JIA.

Methods: We used PCR-RFLP (polymerase chain reaction – restriction fragment length polymorphism) method to detect the -863 C/A polymorphism. We analyzed DNA samples from 76 patients with JIA and 80 healthy individuals.

Results: The distribution of TNF-α genotypes in cases differed significantly from that in the controls, comparing TNF-α A carriers (CA or AA genotypes) with noncarriers (CC genotype) (OR = 2.49; 95% CI: 1.21–5.14; P = 0.01). However, TNF-α -863 C/A allelic frequencies were not significantly different between cases and controls.

Conclusion: The TNF-α CC genotype was associated with increased risk factor for JIA in a sample of Turkish patients.

P7
Are genetic variants of Caspase-1 and Cryopyrin associated with systemic JIA?
CJ Stock, EM Ogilvie, JM Samuel, M Fife and P Woo
University College London, London, UK

Background: The systemic subtype of juvenile idiopathic arthritis (sJIA) can be the most severe, and unlike other forms of JIA is an autoinflammatory disease. There is evidence for the involvement of IL-1 in sJIA: treatment with the IL-1 receptor agonist, Anakinra, has shown dramatic improvement in some sJIA patients. Additionally we have shown a significant association with members of the IL-1 gene family and sJIA [1]. Caspase-1 is required to cleave IL-1β into its active form and Cryopyrin (NLRP3) is part of the IL-1β inflammasome, required for the activation of caspase-1. Mutations in NLRP3 have been found in patients that have similar clinical features with sJIA, e.g. CINCA. Here we describe a candidate gene association study of CASP1 and NLRP3 in sJIA.

Materials and methods: Publicly available genotyping data and a tagging SNP(tSNP) approach were used to examine SNPs across the CASP1 and NLRP3 genomic regions. A total of 47 tSNPs were genotyped in 130 sJIA patients and 146 healthy controls. Analysis of the genotypes were performed using the software UNPHASED.

Results: There is no evidence of an association between CASP1 and NLRP3 with sJIA.

Conclusion: These results indicate that while members of the IL-1 gene family have been shown to be associated with sJIA, there is no evidence for an association with SNPs in CASP1 or NLRP3.

Reference

P8
Role of Vγ9Vδ2+ γδ T cells in juvenile idiopathic arthritis
M Gerstein1, A Bendersky2, S Padeh1, I Bank2 and Y Berkun1
1Safra Children’s Hospital at SHEBA Medical Center, Tel Aviv, Israel
2Laboratory for Immunoregulation, Tel Aviv, Israel

Introduction: T cells (TC) bearing Vγ9Vδ2+ γδ TC receptor (TCR), are a subset of innate CD4-CD8- TC pro-inflammatory and immunoregulatory TC recognizing non-peptidic phosphorylated mediator isopentenyl pyrophosphate (IPP) in the mevalonate pathway. The role Vγ9Vδ2+ TC has never been explored in JIA joints.

Patients and methods: Mononuclear cells (MC) isolated from synovial fluids (SF) of 47 patients with monoarticular (M, n = 11), pauciarticular (P, n = 19), extended (E, n = 5), polyarticular (Po, n = 2), systemic (S, n = 4), psoriatic (Ps, n = 4), enthesitis related (Sp, n = 2) JIA were dually stained with monoclonal antibodies to CD3 and variable (V) regions of the γδ TCR. Flow cytometry of fresh SFMC and following in vitro 10 days stimulation with 0.5 mg/ml IPP plus 100 IU/ml interleukin-2 (IL-2) was performed.

Results: Vγ9Vδ2+TC constituted 6.8 ± 1.3%, 6.4 ± 0.9%, 4.6 ± 1.0%, 3.8 ± 3.6%, 5.6 ± 1.6%, 6.1 ± 0.1% and 1.3 ± 0.8% of the SF CD3+cells in the M, P, E, Po, Ps, Sp and S JIA types respectively, and were significantly higher in ANA+ (n = 19) than ANA- (n = 22) patients (7.8 ± 0.9% vs 4.1 ± 0.6% p < 0.004, Student T test). IPP and IL-2 activated SFMC showed a greater expansion of Vγ9Vδ2+ TC of ANA+ (n = 12) than ANA- (n = 18) patients (61.2 ± 17.1% vs 31.7 ± 7.6%, p < 0.005) and of patients with M or P (n = 11) relative to S, E or Po (n = 6) JIA (44.9 ± 10.9 vs 16.2 ± 10.5 p < 0.02).

Conclusion: SF Vγ9Vδ2+ TC responses are stronger in M and P than in E, Po, and S JIA and in ANA+ than – patients, suggesting that a potent Vγ9Vδ2+ TC response may augment acute inflammation while limiting progression to chronic and destructive arthritis.

P9
Diagnostic value and clinical significance of antibodies against a modified citrullinated vimentin (anti-MCV) in patients with early juvenile arthritis
SO Salugina1, ES Fedorov1, EN Alexandrova1, AA Novikov1, MV Cherkasova1, AA Baranov1, YA Varlagina2, TN Nikolaeva2 and NA Zubova2
1Institute of Rheumatology RAMS, Moscow, Russian Federation
2Department of Clinical Pathology, Yaroslavl Medical Academy, Yaroslavl, Russian Federation

http://www.ped-rheum.com/supplements/6/S1
Objective: To investigate the diagnostic value and clinical significance of anti-MCV in pts with early JA.

Patients and methods: 85 pts were included in the study (M/F = 36/49) in the age of 1.5–16 years (mean 8.7 ± 4.9 years). Systemic JA – 10 pts (11.8%), poly – 37 (43.5%), oligo-38 (44.7%). Duration of disease was < 6 months. We studied also 54 pts with early RA, 28 pts with undifferentiated arthritis (UA) and 14 healthy children. Anti-MCV was measured in serum by enzyme-linked immunosorbent assay (ELISA) using the cut off value of 25 U/ml. IgM RF and hsCRP by laser nephelometry assay on BN-100 analyser.

Results: Anti-MCV levels were elevated in 23 (27.1%) pts with early JA, in systemic – 2 (20%), poly – 11 (29.7%), oligo-10 (26.3%). In pts with RF positive JA – 5 (100%), in RF negative pts- 7 (17.1%) (p < 0.001). In the control groups: 34/54 (62.9%) adults with early RA (p < 0.001), 14/28 (50%) with UA (p < 0.05), none of the healthy children showed anti-MCV positivity. The median anti-MCV level in JA was 16.8 U/ml (IR: 11.5–26.4), in RF+ pts (M-834.9; IR 539.3–1149.3 U/ml) was higher than in RF-pts (M-14.5; IR:5.7–22.0 U/ml) (p < 0.001). Anti-MCV correlated with parameters of disease activity (hs CRP, ESR), with RF and anti-CCP positivity. Anti-MCV were not associated with ANA.

Conclusion: Determination of anti-MCV levels especially together with RF and anti-CCP in pts with early JA can indicate evolution JRA similar RA in adults. Anti-MCV levels correlated with common parameters of inflammation and acute phase response and may be useful to monitor disease activity.

P10 CD39: a regulatory role in childhood arthritis
H Moncrieffe, K Nistala, P Hunter, Y Kamhihe and L Wedderburn
Institute of Child Health, UCL, London, UK

Background: Human regulatory T cells (T reg) are classically defined as CD4+ CD25hi Foxp3+. There is increasing evidence that T cells may be subject to regulation via the conversion of CD39+ T cells with a memory phenotype, express Foxp3 and have regulatory function. CD39 belongs to a family of ectoenzymes that degrade extracellular ATPase activity and therefore represent an important regulatory mechanism in JIA.

Materials and methods: Mononuclear cells from peripheral blood (PBMC) and synovial fluid (SFMC) of patients with JIA and healthy controls were analysed by 5-colour flow cytometry for expression of Foxp3, CD25 and CD39. FACS sorted cells were assayed for ATPase activity.

Results: CD39 expression was demonstrated on a variety of mononuclear cells in both controls and JIA patients. Increased expression of CD39 was seen on SFMC. Mononuclear cells expressing CD39 showed rapid ATPase activity in vitro. We characterise a proportion of CD39+ T cells with a memory phenotype, express Foxp3 and have regulatory function.

Conclusion: ATPase activity may represent a novel mechanism by which regulation may occur in JIA. CD39+ CD4 cells are enriched in the joint in JIA. CD4+ T cells which express both CD39 and Foxp3 may represent a population with the capability to regulate via multiple mechanisms and therefore be more potent suppressors.

P11 The TRAF1/C5 region is a risk factor for polyarthritis in juvenile idiopathic arthritis
HM Albers1, FAS Kurreeman1, JJ Houwing-Duistermaat1, DMC Brinkman1, SSKamphuis2, HJ Girschick3, C Wouters4, MÁJ van Rossum5, W Verdunyn, REM Toes5, TVJ Huizinga1, MW Schilham1 and R ten Cate1
1Leiden University Medical Center, Leiden, Netherlands
2Erasmus Medical Center – Sophia Children’s Hospital, Rotterdam, Netherlands
3University of Wuerzburg, Wuerzburg, Germany
4University Hospital Gasthuisberg, Leuven, Belgium
5Emma Children’s Hospital AMC, Amsterdam, Netherlands

Background: Juvenile idiopathic arthritis (JIA) is a chronic disorder in which both genetic and environmental factors are involved. Recently we identified the TRAF1/C5 region (located on chromosome 9q33-34) as a risk factor for rheumatoid arthritis (RA) (OR 1.46, 95% CI 1.12–1.90; p = 0.004). The present study the association of the TRAF1/C5 region with the susceptibility to JIA was investigated.

Methods: A case-control association study was performed in 338 Caucasian JIA patients and 511 healthy individuals. We genotyped SNP rs10818488 as a marker for the TRAF1/C5 region.

Results: The A-allele was associated with the susceptibility to Rheumatoid Factor (RF) negative polyarthritis with an 11% increase in allele frequency (OR 1.14, 95% CI 1.09–1.19; p = 0.002). This association was stronger when combining subtypes with a polyarticular phenotype (OR 1.46, 95% CI 1.12–1.90; p = 0.004). In addition, we observed a trend towards an increase in A-allele frequency in patients with extended oligoarthritis versus persistent oligoarthritis (49% and 38% respectively); p = 0.055.

Conclusion: Apart from being a well replicated risk factor for RA, TRAF1/C5 also appears to be a risk factor for the RF negative polyarthritis subtype of JIA and, more generally, seems to be associated with subtypes of JIA characterized by a polyarticular course.


P12 The role of synovial fluid cytokines IL-6, IL-23 and IL-17 in the pathogenesis and persistence of synovial inflammation in JIA patients
V Tzimouli1, M Trachana1, A Taparkou1, P Pratsidou-Gertsis1, S Metsovitis1, G Pardalos1 and F Kanakoudi-Tsakalidou1
1Pediatric Immunology and Rheumatology Referral Center, First Department of Pediatrics, Aristotle University, Thessaloniki, Greece
Objective: Recent data in adult Rheumatoid Arthritis support that the Th17 cell-derived cytokine interleukin 17 (IL-17) in the presence of IL-6 and IL-23 plays a critical role in the pathogenesis of chronic destructive arthritis. Data on synovial fluid (SF) concentrations of IL-17 in JIA pts are sparse. We measured concentrations of the above 3 cytokines and assessed the CD4+CD25 Treg+FoxP3+ (Treg) and CD4+CD25 lowFoxP3- T cell subpopulations in the SF of children with JIA. Findings were correlated with SF sRANKL which expresses the osteoclastic activity in active disease.

Materials and methods: 80 samples of SF obtained from 69 children (4–16 yrs) with JIA (oligo-persistent 35, oligo-extended 15, and poly-19) were studied. All samples derived from knees with active arthritis and hydrarthros. Fifteen more SF samples from children with recent traumatic arthritis were used as controls. ELISA and Flow cytometry were used for assessments.

Results: Synovial fluid concentrations of IL-6, IL-23, IL-17 and ELISA and Flow cytometry were used for assessments. Children with recent traumatic arthritis were used as controls. IL-17 were found in PBMCs supernatants of patients when compared to controls (p < 0.01). An inverse significant correlation was observed between IL-17 levels and % of FOXP3+ cells, (P = 0.016, r = −0.509). ROR γt mRNA levels were also higher in SFMCs of JIA patients as compared to their peripheral counterparts (3-fold), and were lower in the presence of higher FOXP3 levels.

Conclusion: These findings point to a Treg/Th17 balance as one important axis in JIA pathogenesis.

P14
Association between IL2RA and juvenile idiopathic arthritis (JIA) disease severity at first presentation to paediatric rheumatology: results from the Childhood Arthritis Prospective Study (CAPS)

KL Hyrich1, SD Lal1, A Hinks1, LR Wedderburn2, J Gardner-Medwin3, H Foster5, A Chien6, J Davidson3, E Baildam4 and W Thomson1

1University of Manchester, Manchester, UK
2Institute of Child Health, London, UK
3Royal Hospital for Sick Children, Glasgow, UK
4Royal Liverpool Children’s Hospital, Liverpool, UK
5University of Newcastle, Newcastle, UK
6Royal Manchester Children’s Hospital, Manchester, UK

Pediatric Rheumatology 2008, 6(Suppl 1):P14

Background: CAPS was designed to study clinical and genetic predictors of JIA outcome. The gene IL2RA has recently emerged as a JIA susceptibility locus. This study investigates

Table 1 (abstract P14)

<table>
<thead>
<tr>
<th>Gene</th>
<th>N (%)</th>
<th>Median CHAQ score (IQR)</th>
<th>OR CHAQ ≥ 0.75 (95% CI), p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Unadjusted</td>
<td>Adjusted</td>
</tr>
<tr>
<td>rs2104286</td>
<td>185</td>
<td>0.75 (0.13, 1.38)</td>
<td>Ref</td>
</tr>
<tr>
<td>11</td>
<td>119 (64)</td>
<td>0.81 (0.13, 1.38)</td>
<td>1.06 (0.56, 1.99), p = 0.86</td>
</tr>
<tr>
<td>12</td>
<td>58 (31)</td>
<td>0.94 (0.81, 1.38)</td>
<td>6.02 (0.72, 50.42), p = 0.09</td>
</tr>
<tr>
<td>22</td>
<td>8 (4)</td>
<td>0.88 (0.13, 1.44)</td>
<td>0.63 (0.34, 1.18), p = 0.15</td>
</tr>
<tr>
<td>rs11594656</td>
<td>185</td>
<td>0.63 (0.13, 1.07)</td>
<td>3.52 (0.95, 13.02), p = 0.06</td>
</tr>
<tr>
<td>11</td>
<td>100 (54)</td>
<td>1.38 (0.88, 1.88)</td>
<td>Ref</td>
</tr>
</tbody>
</table>
the association between SNPs located within the IL2RA region and disease severity at first presentation to rheumatology.

**Methods:** Demographic and disease features were collected at first presentation to rheumatology. SNPs (rs2104286, rs41295061, rs11594656) were genotyped on a Sequenom MassARRAY platform. Logistic regression, adjusted for ILAR subtype, was used to determine the association between genotype and moderate to severe disability (defined as CHAQ score ≥ 0.75).

**Results:** 185 children with JIA (median age 7.2 years (IQR 3.6, 11.7), 65% female) were included. Median CHAQ score at presentation was 0.75 (IQR 0.13, 1.38). There was a trend towards higher disability with increased number of copies of the rare allele of rs2104286 (Table 1) (OR 8.00 (0.93, 68.79), p = 0.07). An association was also seen between increased disability and homozygosity for the rare allele of rs11594656 (OR 3.37 (0.89–12.75), p = 0.07). There was no association with rs41295061.

**Conclusion:** Children homozygous for the rare allele (rs2104286) a SNP associated with JIA susceptibility, showed a trend towards increased disability. Interestingly, a second SNP in the IL2RA region not previously associated with JIA susceptibility also showed a similar trend. Validation of these results in larger cohorts is required.

**P15**

**Single-nucleotide polymorphisms in the folate pathway are associated with response to methotrexate treatment in juvenile idiopathic arthritis**

MW Heijstek 1, NM Wulfraat 1, Y Eken 1, SMF Pluijm 2, CMA Rademaker 1 and R de Jonge 2

1University Medical Center Utrecht, dept. of pediatric immunology, Utrecht, Netherlands
2Erasmus Medical Center, Rotterdam, USA

**Pediatric Rheumatology 2008, 6(Suppl 1):P15**

**Background:** Insight into factors associated with outcomes of methotrexate (MTX) treatment may contribute to more individualized treatment of juvenile idiopathic arthritis (JIA). In this study, associations of SNPs in genes encoding folate pathway enzymes with MTX efficacy and adverse effects in JIA patients were evaluated.

**Methods:** Genotypes were determined in an observational cohort of 183 JIA patients that had been systematically followed at 3 months intervals. The following SNPs were determined: methylenetetrahydrofolate reductase (MTHFR) 677C>T and 1298A>C, methionine synthase reductase (MTRR) 66A>G, thymidylate synthase (TS) 2R/3R and Reduced Folate Carrier (RFC) 80G>A. MTX efficacy and adverse effects were compared among genotypes during the first year of treatment and at long-term follow up.

**Results:** The MTHFR 1298CC variant was associated with MTX efficacy (OR 3.3, 95%-CI 1.0–10.2) after 3 months, while MTHFR 677T-allele carriers had a lower chance of early good clinical response (OR 0.4, 95%-CI 0.2–0.9). The MTHFR 1298C-allele was also associated with MTX efficacy after long-term follow-up (OR 1.8, 95%-CI 1.0–3.4).

Regarding adverse effects, MTHFR 677TT was associated with liver toxicity in the first year of MTX use (OR 10.4, 95%-CI 2.2–48.6). MTRR 66G-allele carriers were more likely to have gastrointestinal intolerance during the first 3 months of treatment (OR 9.9, 95%-CI 1.3–76.9).

**Conclusion:** Polymorphisms in the MTHFR and MTRR genes are associated with methotrexate efficacy and adverse effects. Genotyping may add in predicting response to MTX treatment in JIA patients.

**P16**

**MTHFR polymorphism and red cell folate levels are not useful as biomarkers of methotrexate efficacy and toxicity in children with juvenile idiopathic arthritis**

J Tukova 1, M Hroch 1 and P Dolezalova 1

1Department of Paediatrics and Adolescent Medicine, 1st Medical School, Charles University, Prague, Czech Republic
2Department of Pharmacology, Medical School, Charles University, Hradec Králové, Czech Republic

**Pediatric Rheumatology 2008, 6(Suppl 1):P16**

**Introduction:** In adults with rheumatoid arthritis several polymorphisms of C677T genotype (CT and TT) were associated with increased toxicity and higher methotrexate (MTX) efficacy. Homozygote CC polymorphism of A1298C genotype was associated with toxicity.

**Aim:** To evaluate usefulness of MTHFR polymorphism and folate concentration assessment for prediction of toxicity and efficacy in children with juvenile idiopathic arthritis (JIA). To test association between MTHFR polymorphism and MTX polyglutamate concentration in erythrocytes (EMTX).

**Patients and methods:** In 46 MTX treated children with JIA C677T and A1298C polymorphisms of MTHFR, red cell folate (<800 nmol/l vs. >800) and erythrocyte EMTX concentration were studied using previously described methods.

**Results:** The prevalence of CT and TT genotype was 37 and 13%, distribution of AC and CC alleles 43 and 9%, respectively. MTX toxicity was noticed in 41% of children (GI complaints, raised transaminases, alopecia). 66% of patients were classified as MTX responders. Folate concentration was below 800 nmol/l in 28%. Presence of neither of MTHFR polymorphisms correlated with side effects (p = 0.71, χ² test), clinical efficacy (p = 0, 18, χ² test), quartiles of EMTX (p = 0, 33) or folate concentration (p = 0, 71).

**Conclusion:** We have not found MTHFR polymorphism assessment helpful as a biomarker for prediction of clinical efficacy or toxicity in children with JIA. We have shown absence of association of MTHFR genotype with efficacy of MTX therapy.

**P17**

**High membrane expression of CD163 by bone marrow cells is not a specific marker of macrophage activation syndrome (MAS)**

C Bracaglia 1, R Devito 2, A Insalaco 1, PS Buonuomo 1, A Campana 1, E Cortis 1 and AG Ugazio 1

1Division of Rheumatology, Department of Pediatric Medicine; IRCCS, Ospedale Pediatrico Bambino Gesù, Rome, Italy
2Division of Pathology, Department of Laboratory; IRCCS, Ospedale Pediatrico Bambino Gesù, Rome, Italy

**Pediatric Rheumatology 2008, 6(Suppl 1):P17**

**Background:** MAS is a life-threatening complication seen predominantly in children with SoJIA, often difficult to recognize because specific diagnostic criteria for MAS have not yet been...
devised. MAS is characterized by an overwhelming inflammatory reaction driven by excessive T cell expansion and hemophagocytic macrophages. Preliminary studies suggest that high sIL-2R \( \alpha \) serum levels and sCD163 might be useful as diagnostic markers for MAS. This study assesses the expression of CD163 and CD68 in bone marrow cells of patients with MAS and especially in those with SoJIA who developed MAS.

**Methods:** Thirteen bone marrow biopsies (BMB) were performed, 7 on patients with MAS secondary to SoJIA, 6 with virus-induced HLH. Fifteen BMB controls were included. Immunohistochemical staining was performed using monoclonal antibodies directed against CD163 and CD68.

**Results:** CD163 immunoreactivity was characterized by a strong, granular cytoplasmic or cytoplasmic and membrane staining pattern. The macrophage marker CD68 showed a granular cytoplasmic pattern. Increased numbers of macrophages were observed in the bone marrow of all MAS and HLH samples. CD163 expression in macrophages was brighter than that of CD68. CD163 expression was similar in MAS associated with SoJIA and in virus induced HLH.

**Conclusion:** Our data demonstrate that CD163 in BMB is restricted to the monocyte/macrophage lineage but is not specific for MAS. Furthermore CD163 is similarly expressed by macrophages from biopsies of both SoJIA and HLH patients. This antibody is a marker of activated macrophages but cannot differentiate patients with MAS from patients with other diseases of the macrophage lineage.

**References**


P18 Lymph act, TCR \( \alpha \beta \), TCR \( \gamma \delta \) cells in peripheral blood in children with juvenile idiopathic arthritis

H Mazur-Zielinska
Department of Pediatrics, Medical University of Silesia, Zabrze, Silesia, Poland

**Abstract withdrawn**

P19 Activated CD27+ and CD27− memory B cells accumulate in the joints of patients with juvenile idiopathic arthritis

H Morbach, N Suffa, P Richl and HJ Girschick
Children’s Hospital, University of Würzburg, Würzburg, Germany

**Abstract withdrawn**

P20 Characterization of B cells in synovial fluid and tissue from patients with JIA

F Ferlito1, A Corcione2, E Traggiai1, A Gregorio3, A Martini1, V Pistoia2 and M Gattorno1

1. UO Pediatria II, G. Gaslini and Laboratory of Immunology of Rheumatic diseases, University of Genoa, Genoa, Italy
2. Laboratory of Oncology, G. Gaslini Institute, Genoa, Italy
3. UO Anatomia Patologica, G. Gaslini Institute, Genoa, Italy

**Aim:** The nature of B cell subsets infiltrating the synovial membrane from JIA patients is poorly defined. To this aim we...
performed an immunophenotypic and functional characterization of B cells in JIA patients.

**Methods:** MNC from synovial fluid (SF) and paired peripheral blood (PB) from 25 JIA patients and 20 age-matched controls were analyzed with multi-colour flow cytometry.

**Results:** SF B cells were found to be significantly enriched in CD27+ switch memory (sm) 1 cells and in the recently identified isotype class switch memory (CD19+CD27+IgG+IgA+) B cells (sm2) compared to paired and healthy PB (P < 0.0001). CCR5, CCR8, and CCR9 expression was significantly higher on SF sm1 and sm2 B cells than on correspondent paired PB B cells (P < 0.001). Naïve (IgD+, CD27-) B cells were significantly reduced in SF compared to paired and control PB (P < 0.0001). Similarly, transitional B cells (CD19+CD24hiCD38loIgMhiIgDlo) were significantly less numerous in SF than in paired PB from JIA patients (P < 0.0001).

Plasma blasts were significantly enriched in SF than in paired PB (P = 0.005). ELISPOT experiments showed significantly higher proportions of CD19+ IgG secreting cells in SF vs paired JIA PB (P = 0.028). Histological analysis of synovial tissue sections demonstrated the presence of lymphoid aggregates containing clusters of CD20+ cells surrounded by CD138+ plasmablasts/demonstrating the presence of lymphoid aggregates containing clusters of CD20+ cells surrounded by CD138+ plasmablasts/plasmacells producing predominantly IgG.

**Conclusion:** These findings support a model whereby memory B cells are selectively attracted through chemokine gradients to the inflamed joints of JIA patients and differentiate locally into plasmablasts/plasmacells in the absence of ectopic follicular structures.

**P22**

**Methotrexate in childhood arthritis: effects on gene expression**

H Moncrieffe1, S Ursu1, A Etheridge1, L Kassoumeri1, A Stansfield1, N Jina2 and L Wedderburn1

1Rheumatology Unit, Institute of Child Health, UCL, London, UK
2Molecular Haematology and Cancer Biology Unit, Institute of Child Health, UCL, London, UK

**Pediatric Rheumatology 2008, 6(Suppl 1):P22**

**Background:** Methotrexate (MTX) is the standard disease modifying therapy for children with juvenile idiopathic arthritis (JIA), inducing remission in ~65% of cases. There are currently no known predictors which classify who will successfully respond to MTX therapy nor those who will remain well following MTX withdrawal. Mechanisms of MTX action in JIA are at present unclear: genetic and gene expression profiling would provide novel insights into the biology of this therapy.

**Materials and methods:** We sampled 11 patients with active poly-arthritic JIA (poly-JIA) prior to and 3–6 months after initiating MTX. Moreover, 11 poly-JIA patients in remission on MTX were sampled prior to and 3–6 months after withdrawal of MTX. Frequency and characteristics of Foxp3+CD4+Treg and effector T cells after 3 months MTX compared to pre-MTX. The quality of the HSP60-response was not altered by MTX. Interestingly, stimulation with anti-CD3 resulted in increased proliferation of CD4+CD25- T reg remained unchanged.

**Results:** MTX-treatment resulted in a decrease of Foxp3+CD4+ Treg (3.7% to 2.8% of CD4+ T cells). Suppressive function of Treg was not altered by MTX. Interestingly, stimulation with anti-CD3 resulted in increased proliferation of CD4+CD25-effector T cells after 3 months MTX compared to pre-MTX. Moreover, proliferative responses to human HSP60 increased after MTX-treatment. The quality of the HSP60-response changed with a less pro-inflammatory cytokine profile in supernatants after MTX-treatment. When JIA-patients in remission on MTX were sampled prior to and 3–6 months after withdrawal of MTX, the frequency of Treg increased (3.2 to 3.8% of CD4+ T cells) but their suppressive function remained unchanged.

**Conclusion:** MTX seems to exert its immune-modulating effects not by affecting Foxp3+ T reg. Instead, we observed changes in effector T cells and HSP60 specific T cells.

**P24**

**Outcome of repeat dosing of sJIA patients with tocilizumab in one UK centre**

P Livermore1, T Woodworth2 and L Hou1

1Great Ormond Street Hospital, London, UK
2Roche, Basel, Switzerland

**Pediatric Rheumatology 2008, 6(Suppl 1):P24**

**Background:** Tocilizumab is effective in treating sJIA in a phase III Japanese study. Before the worldwide pivotal trial, 4 patients were admitted to the compassionate use programme available in 2006 at one UK centre.
Methods: Each patient was assessed clinically before dosing and laboratory markers recorded. The dose was 8 mg/kg fortnightly iv. All had steroids and methotrexate concurrently. The follow up period vary from 1 year to 18 months.

Results: In 3 patients CRP returned to normal after the first dose. 2/4 patients were below 30 kg and only had transient lowering of CRP between doses. Active joint counts decreased partially in 2 and not in the 2 patients with body weight <30 kg after 3 doses. These 2 patients were given 12 mg/kg on the basis that pharmacokinetic modelling predicts underexposure to the drug if given at 8 mg/kg, when the body weight is <30 kg. The higher dose led to improvements in clinical and laboratory markers. All were able to reduce steroid therapy. There were no significant side effects, apart from transient urticarial rash.

None are able to discontinue steroid therapy completely. One has significant growth retardation on 5 mg prednisolone daily. One still had 22 active joints (decreased from 32) after one year with a normal CRP. She is now in remission after a bone marrow allograft.

Conclusion: Multiple dosing of tocilizumab has greatly improved the global disease activity of severe sJIA, but their arthritis requires concurrent steroids and methotrexate. PK/PD strategies to optimize dosing in sJIA may be indicated.

P25 Systemic-onset juvenile rheumatoid arthritis and ANCA-associated glomerulonephritis

A Belot1, B Bader-Meunier2, LH Noel2, AM Prieur2, P Niaudet2, R Salomon2 and P Quartier2

1Hopital Femme Mère Enfant, Lyon, France
2Hopital Necker-Enfants Malades, Paris, France

Pediatric Rheumatology 2008, 6(Suppl 1):P25

Systemic-onset juvenile rheumatoid arthritis (SoJRA) associated renal lesions are unusual, except for amyloidosis or side effects of antirheumatic drugs.

We report on 3 children with SoJRA diagnosed in the first years of life, who presented a perinuclear antineutrophil cytoplasmic antibodies (pANCA) associated glomerulonephritis during the disease course.

ANCA glomerulonephritis was diagnosed after 5, 6 and 1 year follow-up for SoJRA in Patients 1, 2 and 3 respectively.

Treatment and outcome of the kidney lesions were as follows: Pt1 was treated with steroids bolus associated to rituximab then switched for mycophenolate mofetyl (MMF). At the age of 7, he benefited from anakinra for the still ongoing systemic symptoms of the SoJRA with excellent results on both inflammation baseline and proteinuria.

Despite steroids bolus and azathioprine in Pt2, renal lesions led gradually to end stage renal disease (ESRD) when she was 17. She benefited from kidney transplantation and interestingly both systemic symptoms and renal function are well under triple immunosuppressant (MMF, tacrolimus and steroids) with a follow up of 3 years after transplantation.

Pt3 evolved to ESRD despite the use of steroids bolus, cyclophosphamide, cyclosporine and immunoglobulin. She died when she was 16 years, after 4 years of dialysis, from a severe sepsis with digestive occlusion.

ANCA vasculitidis is exceptional in the JRA. Outcome is poor and can lead to ESRD and death. ANCA-associated glomerulonephritis were related to SoJRA with uncontrolled inflammation baseline. These data suggest a common pathogenesis between SoJRA and ANCA glomerulonephritis and underline overlapping syndrome in the pediatric practice.

P26 MEFV mutations in systemic JIA

N Aktaa Ayaz1, Y Bilginer1, E Yilmaz2, M Ergüven2, R Topaloglu1, A Bakkaloglu1 and S Ozen1

1Hacettepe University Medical Faculty, Ankara, Turkey
2Göztepe Education and Research Hospital, Istanbul, Turkey

Pediatric Rheumatology 2008, 6(Suppl 1):P26

Background: Systemic form of juvenile idiopathic arthritis (JIA) is regarded as an autoinflammatory disease. Certain genetic polymorphisms in genes coding inflammatory proteins have been associated with the disease. On the other hand mutations of the MEFV gene cause a monogenic autoinflammatory disease, Familial Mediterranean Fever (FMF).

In a previous study in adult rheumatoid arthritis 3 out of the 25 British patients who developed secondary amyloidosis had a mutation/polymorphism in the MEFV gene.

Aim: To analyse whether mutations in the MEFV gene had an association with systemic JIA.

Patients and methods: MEFV mutations were screened in a total of 32 systemic JIA patients. All had been classified as systemic JIA according to the Durban JIA criteria. None had disease characteristics that met the Tel Hashomer criteria for the diagnosis of FMF.

Results: 2 carrier for M694V and two patients who were homozygote for MEFV mutations. Both of these patients were among the most severe patients in the group. One had an excellent response to etanercept whereas the other was resistant to anti-TNF and other conventional treatments and had only a partial response to thalidomide. Although the number of severe mutations were increased in this small group of patients with systemic JIA the difference with the Turkish population did not reach statistical significance, but the disease causing mutation (M694V) was significantly high in the patients with systemic JIA (p = 0.02).

Conclusion: However, the severe disease course in the aforementioned patients suggest that MEFV mutations may be a modifying genetic factor in systemic JIA.

P27 Efficacy, safety and effect on gene expression profiling of anakinra in systemic-onset juvenile idiopathic arthritis: final results of a randomised, double-blind, placebo-controlled trial (ANAJIS)

P Quartier1, F Allantaz2, R Cima3, P Pillet4, O Richer5, M Desjonesqueres3, A Duquesne3, C Messiaen3, C Bardin5, X Bossuyt4, A Boutten5, J Bienvenu9, V Menoni1, S Sotou-Bere1, B Neven1, N Mahloui1, A Mogenet1, B Kassai1, D Chaussabel1, JM Treluyer1, JL Bresson1, P Landais1 and V Pascual2

1Necker-Enfants Malades, Assistance Publique Hopitaux de Paris, Paris, France
2Baylor Institute, Dallas, USA
3Edouard Herriot, Lyon, France
4Pellegrin, Bordeaux, France
5Hotel Dieu, Paris, France
6University of Leuven, Leuwen, Belgium
7Bichat, Assistance Publique Hopitaux de Paris, Paris, France
8Laboratoire d’Immunologie Lyon sud, Lyon, France

Pediatric Rheumatology 2008, 6(Suppl 1):P27

Systemic-onset juvenile idiopathic arthritis: final results of a randomised, double-blind, placebo-controlled trial (ANAJIS)

P Quartier1, F Allantaz2, R Cima3, P Pillet4, O Richer5, M Desjonesqueres3, A Duquesne3, C Messiaen3, C Bardin5, X Bossuyt4, A Boutten5, J Bienvenu9, V Menoni1, S Sotou-Bere1, B Neven1, N Mahloui1, A Mogenet1, B Kassai1, D Chaussabel1, JM Treluyer1, JL Bresson1, P Landais1 and V Pascual2

1Necker-Enfants Malades, Assistance Publique Hopitaux de Paris, Paris, France
2Baylor Institute, Dallas, USA
3Edouard Herriot, Lyon, France
4Pellegrin, Bordeaux, France
5Hotel Dieu, Paris, France
6University of Leuven, Leuwen, Belgium
7Bichat, Assistance Publique Hopitaux de Paris, Paris, France
8Laboratoire d’Immunologie Lyon sud, Lyon, France

Pediatric Rheumatology 2008, 6(Suppl 1):P27
Purpose: To investigate efficacy and safety of anakinra in systemic-onset juvenile idiopathic arthritis patients. To assess treatment effect on gene expression profiling, immune response to anti-pneumococcal Pneumo23 vaccine, serum amyloid A level, serum ferritin level and the percentage of glycosylated ferritin.

Methods: Multicenter randomized double-blind trial. The primary objective was to compare the efficacy of a one-month treatment with anakinra to a placebo between 2 groups of 12 patients each. Response was defined by 30% improvement of pediatric ACR core-set criteria for JIA, resolution of fever and systemic symptoms and normalization or a decrease of at least 50% of both CRP and first hour ESR compared to baseline. Intention-to-treat analysis. Secondary objectives included tolerance and efficacy assessment over 12 months and treatment effect on blood gene expression profiling.

Results: At one month, there was a significant difference in the response rate between patients treated with anakinra (8/12) and placebo (1/12). During the double-blind phase, the number of adverse events, mainly pain to injections, was similar between both groups. Ten patients from the placebo group switched to anakinra at Month 1 and 9 were responders at month 2. Eight patients discontinued anakinra before Month 12: painful injections during the double-blind phase (2 patients, both on placebo), ileo-colic symptoms leading to the diagnosis of Crohn’s disease (1 patient), transient hepatic cytolyis (one case), lack of efficacy or a disease flare (4 cases). Gene expression profile analyses showed a set of gene pathways dysregulated in SOJIA whose expression dramatically changed upon anakinra treatment.

P28 Gene expression in active systemic JIA after anti-IL1 and anti-IL6R treatment
EM Ogilvie, JM Samuel and P Woo
University College London, London, UK

Introduction: We have previously found specific genes upregulated in PBMCs of active sJIA [1]. Biologics to block IL-1 and IL-6 signalling have both been shown to be effective in early clinical trials. In this study we examine the expression before and after anti-IL1 and anti IL-6R treatment in PBMCs and their constitutive cell types; using gene expression analysis to further understand the disease pathways.

Methods: PBMCs were collected before and after treatment from patients that responded to treatment: two patients were treated with tocilizumab, one with anakinra and another with an experimental anti-IL1 antibody (Novartis). A proportion of PBMCs were reserved and positive selection of B cells, T cells and monocytes performed on the rest. RNA was extracted and hybridised to Affymetrix U133 Plus 2.0 arrays. Pairwise significance analysis was performed using LIMMA.

Results: In the B cell population we found 1902 genes differentially expressed after anti-IL1 treatment and 165 after anti-IL6R treatment. While genes involved in transcriptional regulation and the immune response were differentially expressed after both treatments there were only 24 genes that were common to both lists including TCL1A and CD69. Differential expression unique to the anti-IL1 blockade included downregulation of complement-mediated immunity genes e.g. CD55. Other genes downregulated after anti-IL1 include IL12RB2, and CREB1. Genes upregulated after anti-IL6R treatment include CEBPδ and BTLA. We are currently characterising gene expression in the remaining cell types.

Conclusion: We have found that the majority of changes in gene expression in B cells differ according to the specific cytokine modulation.

Reference

P29 Early effects of Anakinra in corticosteroid naive SOJIA patients
NM Wulffraat, W de Jager, B Prakken and W Kuis
University Medical Center Utrecht, Department Pediatric Immunology, Utrecht, Netherlands

Pediatric Rheumatology 2008, 6(Suppl 1):P29

Interleukin-1R antagonist (anakinra) induces disease remission in about 50% of corticosteroid (CS) resistant cases of systemic onset JIA (SOJIA) [1, 2]. Clinicians debate whether etanercept should still be tried first before giving anakinra to such patients. Another, more challenging, issue is to start anakinra even in CS naïve SOJIA patients. We here report our first experiences of such an approach in 7 patients with SOJIA. Four patients had recent onset SOJIA (3 weeks to 3 months) with classical spiking fever, exanthema and arthritis, 3 had a recent flare. They were all treated with indomethacin for at least 2 weeks without effect. There were no signs of haemophagocytosis. Anakinra was started (2 mg/kg sc daily) as an in-patient procedure to monitor for disease progression. Disease activity was monitored at 0, 24, 72 hr and 3 weeks. Fever and exanthema disappeared within 24 hours, arthritis within 3 days. One child had a recurrence of arthritis without fever or exanthema after 2 weeks. The mean values at t = 72 hrs: CRP decreased from 178 to 33, ESR from 120 to 94, ferritin from 1260 to 375. In 3 of 5 tested NK cell function restored within 72 hr. Current follow up of 3 weeks anakinra showed persistent remission in 6/7 without the use of CS.

Based on these short term results we would like to propose a RCT (PRINTO) to define the place of anakinra with a read-out of disease activity and prednisone use.

References

P30 Anakinra in systemic juvenile idiopathic arthritis (soJIA) non responsive to antiTNF
I Pontikaki, V Gerloni, M Gattinara and F Fantini
Unit of Pediatric Rheumatology, Gaetano Pini Institute, Chair of Rheumatology, University of Milan, Milan, Italy
DMARDS and TNF inhibitors. Pediatric patients were evaluated with MTX at the dose of 100 mg daily (>50 kg) or at the dose of 2–5 mg/kg daily (<50 kg). All patients failed previous DMARDs and TNF inhibitors. Paediatric patients were evaluated according to the ACR30 paediatric criteria. Adults were evaluated according to EULAR criteria (DAS). We also considered clinical parameters as fever, rash, adenopathy and organomegaly.

**Results:** Median age 16 years (9.4–47.2); median duration of the disease 14.5 years (0.5–44.3); mean duration of therapy 1 year (0.08–4.3). 11/16 patients (69%) were responders. 5/16 patients (31%) suspended for adverse events and/or inefficacy. The most important adverse event was the intensive pain on the injection site and a severe cutaneous reaction. Responders reduced or suspended prednisone and NSAIDS. Systemic symptoms like spiking fever and rash had an immediate improvement. In 3 patients Anakinra was efficacious in renal amyloidosis as well.

**Conclusion:** Anakinra plus MTX showed a good efficacy and safety in short and medium term treatment of long lasting refractory systemic JIA. A controlled multicenter clinical trial is needed.

**Objective:** To evaluate efficacy and safety of Anakinra in SJIA non responsive to anti-TNF.

**Introduction:** TNF-inhibitors have demonstrated a favourable benefit-to-risk profile. Intolerance, lost of efficacy or adverse events led to other options as the antagonist of the IL-1 receptor (Anakinra), in SJIA.

206 pts were treated with TNF inhibitors; 45 patients (22%) were affected by SJIA.

**Methods:** Sixteen patients affected by SJIA (12 F, 4 M) were switched to Anakinra. Patients received Anakinra (in association with MTX) at the dose of 100 mg daily (>50 kg) or at the dose of 1–2 mg/kg daily (<50 kg). All patients failed previous DMARDs and TNF inhibitors. Paediatric patients were evaluated according to the ACR30 paediatric criteria. Adults were evaluated according to EULAR criteria (DAS). We also considered clinical parameters as fever, rash, adenopathy and organomegaly.

**Results:** Median age 16 years (9.4–47.2); median duration of the disease 14.5 years (0.5–44.3); mean duration of therapy 1 year (0.08–4.3). 11/16 patients (69%) were responders. 5/16 patients (31%) suspended for adverse events and/or inefficacy. The most important adverse event was the intensive pain on the injection site and a severe cutaneous reaction. Responders reduced or suspended prednisone and NSAIDS. Systemic symptoms like spiking fever and rash had an immediate improvement. In 3 patients Anakinra was efficacious in renal amyloidosis as well.

**Conclusion:** Anakinra plus MTX showed a good efficacy and safety in short and medium term treatment of long lasting refractory systemic JIA. A controlled multicenter clinical trial is needed.

**P31**

**A phenotypic shift after initiation of IL-1 receptor blockade in a boy with systemic juvenile arthritis**

C Scott, CH Wouters and F de Zegher
University Hospital Leuven, Leuven, Belgium

**Case presentation:** A boy with systemic juvenile arthritis (sJIA) for 7 years, treated with prednisone 1 mg/kg/day, NSAIDS, Methotrexate and TNF-α antagonism, presented at age 15 with severe incapacitating back pain.

Clinically, a cachectic and stunted boy, weight and height SD scores were −5.05 and −3.65 respectively. He had fever, anaemia, splenomegaly and polyarthritis. There was complete immobility and severe pain of his lumbar spine. X-rays revealed compression fractures of all lumbar vertebrae. Bone mass densitometry confirmed severe osteoporosis (Z-score −4.5 SD). ESR: 33. Hb: 7.4 g/dl, CRP 112 mg/dl.

IL-1 receptor antagonism resulted in a rapid major improvement. Within a few weeks, there was no fever, no arthritis, no splenomegaly, with normal CRP, ESR and Haemoglobin.

Body composition changed dramatically; weight increasing by 10 kg (SDS −2.9) and body fat fraction (DEXA) from 17% to 35%, despite weaning steroids from 1 to 0.3 mg/kg/day. Bone Z-score improved to −3.3 SD.

**Discussion:** The present case illustrates the striking effectiveness of IL-1 receptor antagonism in a patient with severe refractory sJIA, and steroid dependency (with devastating side effects, esp on bone mineralization). IL1-ra has been associated with obesity in adults [1, 2]. IL1 receptor antagonism was associated with an important change of body composition in this patient. It remains to be clarified how the interplay between inflammation, IL-1 blockade and corticosteroid therapy impacts on body composition and fat metabolism.

**References**


**P32**

**Experience of one UK site presenting a closer examination of safety and efficacy of Anakinra (Kineret®) in systemic juvenile idiopathic arthritis**

P Livermore and P Woon
Great Ormond Street Children’s Hospital, London, UK

**Background:** It has been postulated by Pascual and others that Anakinra works only early in systemic JIA (sJIA) and mainly on systemic features. This paper specifically examines the interval between the age of onset and time of starting Anakinra for responders and non-responders, and considers those with active systemic features versus persistent arthritis and their response to Anakinra.

**Methods:** 10 patients (3–17 yrs) with sJIA were enrolled onto a 12 week study at our institution. All patients fulfilled the ILAR classification for sJIA. Out of the 10 patients, 9 had failed anti-TNF. All patients received Anakinra at 2 mg/kg/day subcutaneously with their current therapy, except anti-TNF. Responders met Definition of Improvement (DOI) criteria by >30% improvement in at least 3 of the 6 JIA core set criteria with no more than 1 criteria worsening by >30% as well as their serum SAA/CRP returning to normal. Systemic features were documented.

**Results:** Of 10 subjects, 8 completed 12 weeks, 1 dropped out due to lack of efficacy and 1 due to non-compliance. Duration of JIA before starting Anakinra was 1–9 yrs, responders have median duration of 2 yrs of JIA and non-responders median duration of 6.5 yrs. The non-responders had no systemic features at the start of Anakinra, whilst 3 out of 4 responders had fever at initiation of treatment and improved in all.

**Conclusion:** Out of the 8 patients, the 4 responders started Anakinra a median of two years into their sJIA. This group’s persistent systemic feature also improved. These findings support the hypothesis by Pascual.

**P33**

**Macrophage activation syndrome with systemic onset juvenile idiopathic arthritis (SOJIA) in Chinese children**

C Li, X He, W Kuang, T Han, Y Zhou, J Zhang and X Tan
Beijing Children’s Hospital, Beijing, PR China

**P33**

**Background:** Macrophage activation syndrome (MAS) is a complication of systemic onset JIA (SOJIA), which is characterized by fever, hepatosplenomegaly, lymphadenopathy, pancytopenia, liver dysfunction, pulmonary damage and CNS dysfunction. We did the study to analyze the clinical features, treatment, outcome of MAS with SOJIA.

**Materials and methods:** Review of cases of MAS from a prospectively collected database of children with SOJIA in Beijing Children’s Hospital from the year of 2003 to 2007.

**Results:** 42 patients were diagnosed MAS with SOJIA from 159 SOJIA cases. The duration prior to MAS is 11 months. High fever, hepatosplenomegaly, pancytopenia, liver dysfunction were in all cases. Bleeding was in 12. 45% had CNS dysfunction. 24% were with ARDS. 2 suffered from renal damage. The lab. tests revealed elevated enzyme and ferritin, decreased value of ESR, album, CBC and fibrinogen in all. Bone marrow examination supported the diagnosis with definite haemophagocytosis in 42 cases. Lymph node biopsy was done for one case and found out it was filled of activated macrophage. In the treatment, thirteen only received high dose steroids (four of thirteen died), twenty-one got high dose steroids plus cyclosporine (four died), five were steroids plus cyclosporine and etoposide (none died). The causes of death were ARDS and CNS involvement.

**Conclusion:** MAS is a rare and potentially fatal complication of SOJIA. Most of our patients were male. Bone marrow studies support the diagnosis. CNS involvement and ARDS are poor prognostic signs. Early diagnosis and aggressive therapy is essential.

**P34**

**The TLR4 ligands MRP8 and MRP14 in the diagnosis and pathogenesis of systemic onset juvenile idiopathic arthritis**

M Frosch¹,², D Viemann¹,², H Wittkowski¹,², D Foell¹,², T Vogl¹,², K Barczyk¹,², N Wulffraat¹,² and J Roth¹,²

1University of Muenster, Muenster, Germany
2University of Utrecht, Utrecht, Netherlands

**Background:** Fever of unknown origin (FUO) is a diagnostic challenge in children, especially differentiation of systemic onset juvenile idiopathic arthritis (SOJIA), an autoimmune inflammatory syndrome associated with uncontrolled activation of phagocytes. In this study, we analyzed the relevance of myeloid related proteins 8 and 14 (MRP8, MRP14), two endogenous activators of toll-like receptor 4, for early diagnosis and pathogenesis of SOJIA.

**Materials and methods:** Serum concentrations of MRP8/MRP14 were analysed in 60 SOJIA patients, in 85 patients with severe infections, in 40 patients with acute lymphoblastic leukaemia (ALL), 5 patients with acute myeloblastic leukemia (AML) and in 50 healthy controls. In addition, we investigated the link between interleukin-1ß and MRP8/MRP14 in SOJIA.

**Results:** MRP8/MRP14 serum concentrations were significantly (p < 0.001) elevated in patients with active SOJIA (mean 14,920 ± 4,030 ng/ml) and distinguished them with high specificity from healthy controls (340 ± 70 ng/ml), patients with severe infections (2,640 ± 720 ng/ml), ALL (650 ± 280 ng/ml) and AML (840 ± 940 ng/ml). MRP8/14 in serum of SOJIA is a strong inducer of interleukin-1ß expression in phagocytes.

**Conclusion:** The analysis of MRP8/14 in serum is an excellent diagnostic tool for the initial diagnosis of SOJIA. MRP8/14 and IL-1 represent a novel positive feedback mechanism activating phagocytes via major signalling pathways of innate immunity during the pathogenesis of SOJIA.

**P35**

**Adverse events during anti-TNF therapy in 269 patients with juvenile idiopathic arthritis**

M Tarkiainen¹, P Tynjälä¹, P Vähäsalö² and P Lahdenne¹

¹Hospital for Children and Adolescents, Helsinki University Central Hospital, Helsinki, Finland
²Oulu University Hospital, Oulu, Finland

**Background:** Patients with juvenile idiopathic arthritis (JIA), non-responsive to disease-modifying anti-rheumatic drugs (DMARDs) are treated with anti-TNF agents. The aim of this study was to evaluate the occurrence of adverse events (AEs) in these refractory patients.

**Patients and methods:** In three tertiary centers patient charts were reviewed, and for each anti-TNF drug the severity and type of AEs were specified. Of 269 patients, 97% were on concomitant DMARDs at anti-TNF onset. Their mean age was 5.4 years (SD ± 3.8) at disease onset and 10.5 years (SD ± 3.9) at anti-TNF onset.

**Results:** The total drug exposure was 665 years; etanercept exposure was 354 years, infliximab 287, and adalimumab 24. Of altogether 1057 AEs, 49 (5%) were considered as serious (Table 1). A total of 509 (49%) infections occurred, of which 291 (57%) were upper respiratory tract infections. Dermatological problems were documented in 57 (21%) patients, and hypersensitivity reactions (consisting infusion and injection site reactions) in 52 (19%). Neither malignancies nor tuberculosis appeared, although one patient had a mycobacterium avium pneumonia during adalimumab therapy.

**Conclusion:** Infections were the most common AEs in patients with JIA receiving anti-TNF therapy, but the rate of serious infections seemed to be low.

**Table 1 (abstract P35) AEs and SAEs per patient-year during anti-TNF therapy**

<table>
<thead>
<tr>
<th>Category</th>
<th>Etanercept</th>
<th>Infliximab</th>
<th>Adalimumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>AEs</td>
<td>1.40</td>
<td>1.51</td>
<td>2.34</td>
</tr>
<tr>
<td>SAEs</td>
<td>0.09</td>
<td>0.06</td>
<td>0.08</td>
</tr>
<tr>
<td>All infections</td>
<td>0.79</td>
<td>0.74</td>
<td>0.66</td>
</tr>
<tr>
<td>Upper respiratory</td>
<td>0.47</td>
<td>0.40</td>
<td>0.33</td>
</tr>
<tr>
<td>Serious infections</td>
<td>0.04</td>
<td>0.02</td>
<td>0.04</td>
</tr>
<tr>
<td>Hypersensitivity reactions</td>
<td>0.03</td>
<td>0.23</td>
<td>0.29</td>
</tr>
</tbody>
</table>
P36

Anti-tumour necrosis factor (anti-TNF) in the treatment of juvenile idiopathic arthritis-associated uveitis
C Rivarola1,2, C Hovhanessian1, A Duquesne1 and R Cimaz1
1Hôpital Femme Mère Enfant, Bron, France
2Hôpital Cochin, Paris, France

Pediatric Rheumatology 2008, 6(Suppl 1):P36

Introduction: Chronic uveitis is associated with JIA in about 15–30% of cases. Treatment with anti-TNF agents is very effective in JIA, but their efficacy for uveitis is controversial. We present here the preliminary results of a retrospective case series of uveitis associated of JIA and treated by different anti-TNF.

Objective: To evaluate the efficacy of TNF inhibitors in JIA-associated uveitis, as well as report the cases of uveitis associated with the use of anti-TNF.

Methods: The data of 16 patients with JIA and uveitis receiving anti-TNF were collected retrospectively in three French centers.

Results: Of the 16 patients, 10 were treated with etanercept (62.5%), 1 with adalimumab (6.25%), and 5 (31.2%) with infliximab. Notably, two cases of uveitis were associated with use of etanercept. In 5 patients (31.2%) the anti-TNF was changed because of lack of efficacy and/or side effects to another one (in 4/5 adalimumab). Ten patients had a complicated uveitis (cataract in 5). The number of relapses of uveitis was 4 ± 1.35 with the first anti-TNF, and 1.3 ± 1.5 with the second one. Remission of uveitis was obtained in 4 cases, 3 of them with adalimumab and one case with etanercept.

Conclusion: Anti-TNF agents have a favourable effect in JIA-associated uveitis, but adalimumab and perhaps infliximab may be more effective than etanercept, during which treatment uveitis may even develop.

P37

Efficacy and safety of anti-TNF agents in patients with enthesitis related arthritis
P Tynjälä1, V Honkanen1, K Aalto1 and T Levälampi2
1Hospital for Children and Adolescents, Helsinki, Finland
2Rheumatism Foundation Hospital, Heinola, Finland

Pediatric Rheumatology 2008, 6(Suppl 1):P37

Background: Approximately 5–15% of patients with juvenile idiopathic arthritis belong to a subcategory of enthesitis related arthritis (ERA), which is strongly associated with HLA-B27 and male gender. Recent investigations have suggested markedly low discontinuation rates of anti-tumour necrosis factor (anti-TNF) agents in those with ERA, in whom reports on long-term efficacy and safety of anti-TNFs are still few.

Patients and methods: Based on Finnish register on biologic agents (ROB-FIN) in children, assessment of efficacy was available in 12 male patients with ERA, mean age being 13.6 years at anti-TNF onset (range 8.9–17.3), mean duration of ERA 2.6 years (range 0.2–6.3), and mean follow-up on anti-TNFs 18.5 months (range 6.0–70). All patients were receiving their first course of anti-TNF agents; 7 infliximab, 4 etanercept, and 1 adalimumab.

Results: At 3 months, 100% achieved ACR Pediatric 30% improvement (ACR Pedi 30), 83% ACR Pedi 50, 83% ACR Pedi 70, and 17% ACR Pedi 100. At 6 months, these rates were 100%, 100%, 83%, and 17%; and at 12 months 100%, 100%, 83%, and 17%. Three patients achieved ARC Pedi 70 at 24 months, and one also at 60 and at 70 months. No-one discontinued anti-TNFs due to adverse events (AEs) or inefficacy. Two patients, one on etanercept and another on infliximab, discontinued the therapy due to clinical remission at 70 and 26 months, respectively. The former relapsed within 6 weeks. Per 100 patient-years, 7.7 AEs and 0.45 serious AEs occurred.

Conclusion: Anti-TNF agents seem to be safe and highly effective in ERA.

P38

DNase I levels in JIA – influence of anti-TNF (etanercept) therapy
J Vojinovic1, J Basic1, G Susic2, T Jevtovic-Stoimenov2, N Damjanov2 and D Pavlovic1
1Ped Rheumatol, Faculty of Medicine, Nis, Serbia
2Institute of Rheumatology, Belgrade, Serbia

Pediatric Rheumatology 2008, 6(Suppl 1):P38

Background: Failure to efficiently degrade the DNA of apoptotic cells activates innate immunity causing chronic arthritis. If deficient, Dnase I could lead to accumulation of undigested DNA which induce activation of phagocytes and production of proinflammatory cytokines, notably TNF.

Methods: The study was performed in 25 JIA patients who donated paired serum samples prior and one year after continuous etanercept therapy. Basic clinical data (six core set variables defined in ACR PEDI outcome score) were recorded along with alkaline Dnase serum levels using the method where acid soluble nucleotides are determined spectrophotometrically at 260 nm. Treatment schedule of etanercept was 0, 4 mg/kg body weight subcutaneously twice weekly.

Results: JIA patients mean age was 14.7 ± 4.22 and disease duration is 6.59 ± 2.76. Disease type distribution was 8% systemic, 28% polyarticular RF–, 25% polyarticular RF+, 17% ERA and 21% extended oligoarticular JIA. Summary of data results prior and after anti TNFz therapy: ESR 26.88 vs. 15.52 (p < 0.01); patientVAS 40.24 vs. 24.40 (p < 0.05); physicianVAS 38.08 vs. 10.32 (p < 0.01); CHAQ 0.674 vs. 0.375 (p < 0.01); LOM 15.52 vs. 11.68 (NS); AA 9.24 vs. 2.64 (p < 0.01). DNasel levels were significantly lower prior (2.934 U/l) compared to values after one year therapy (4.184 U/l; p < 0.01). We have found correlation between DNasel levels and AA (r = –0.993 p < 0.5) and other clinical outcome variables prior and after therapy.

Conclusion: JIA patients with active disease have decreased DNase I levels. Our results indicate significant increase of DNasel in the sera of JIA patients after one year of anti TNFz therapy which was associated to the disease clinical improvement.

P39

Open label multicenter study of once weekly Etanercept 0.8 mg/kg in active polyarticular Juvenile idiopathic arthritis (JIA)
G HornRot2, K Minden2, I Foeldvari3, J Kummerle-Deschner4, A Thon5, H Girschick6 and H Hupertz7
1Asklepios Clinic, Sankt Augustin, Germany
2Charite, Berlin, Germany
Pediatric Rheumatology 2008, 6(Suppl 1):P39

**Background:** In Europe Etanercept is licensed for the treatment of resistant polyarticular JIA at a dosage of 0.4 mg/kg bw. twice weekly in children older than 4 years.

**Objectives:** To evaluate the safety and efficacy of Etanercept once weekly 0.8 mg/kg up to 50 mg in a formal trial.

**Methods:** At each study site an independent ethics committee approved the protocol, and each patient’s parent gave written informed consent (EudraCT No. 2007-000255-34). 20 patients 4 to 17 years old were included and received 0.8 mg/kg bw. of etanercept subcutaneously once weekly for 12 weeks “Active” polyarticular disease was defined by the presence of five or more active joints. PedACR30/50/70 criteria were calculated. Safety assessments were based on adverse events (AE) reported.

**Results:** 15 of 20 JIA patients, 16 girls and 4 boys, mean age 12.9 years, disease duration 4.1 years, already have completed the 12 week study period. The mean dosage was 0.80 ± 0.04 mg/kg Etanercept. Concomitant treatments were kept stable 3 months before and throughout the study and consisted of NSAID (n = 20), prednisone (n = 4), methotrexate (n = 12), leflunomide (n = 2), sulfsalazine (n = 1). A PedACR 30/50/70 response was reached by 8 weeks and 92%/92%/79% after 12 weeks of treatment. There were 33 AEs but no SAE: 9 minor infections 12 injection site reactions and 12 other AEs. There was no drop out.

**Conclusion:** These data indicate that once weekly application of Etanercept at double dosage of 0.8 mg/kg bodyweight up to 50 mg per injection is safe and efficacious in polyarticular JIA patients.

---

**P40**

**When and how to stop etanercept after successful treatment of patients with juvenile idiopathic arthritis**

FHM Prince1, M Twilt2, SCM Simon1, MAJ van Rossum3, W Armbrust4, EPAH Hoppenreij5, SSM Kamphuis1, M van Santen-Hoeuff6, Y Koopman-Keemink7, N Wulffraat8, R ten Cate2 and LWA van Suijlekom-Smit1

1Erasmus MC Sophia Children’s Hospital, Rotterdam, Netherlands
2Leiden University Medical Centre, Leiden, Netherlands
3AMC Emma Children’s Hospital, Amsterdam, Netherlands
4UMCG Beatrice Children’s Hospital, Groningen, Netherlands
5Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands
6Academic Hospital Maastricht, Maastricht, Netherlands
7Hagaziekhuis Juliana Children’s Hospital, Den Haag, Netherlands
8Utrecht MC Wilhelmina Children’s Hospital, Utrecht, Netherlands

**Objective:** The aim of etanercept therapy in juvenile idiopathic arthritis (JIA) is to achieve disease remission. However, little is known about when or how to stop etanercept when this aim is reached. Our objective was to describe characteristics and disease course of JIA patients who discontinued etanercept because of a sustained good clinical response.

**Methods:** The “Arthritis and Biologicals in Children” (ABC)-project is the Dutch national register on biologicals in JIA, in which data are collected prospectively. All patients from this register who discontinued etanercept because of a good clinical response were selected. For evaluation of the disease course we used the criteria for clinical remission on medication and off medication by Wallace et al.

**Results:** Of the 210 patients in the ABC-register, 17 patients discontinued etanercept because of a good clinical response. After discontinuation nine patients (53%), with a mean follow-up of 1.4 years, did not develop a disease flare. They showed a longer mean period of clinical remission on medication (1.9 vs. 0.3 years, p < 0.01) and used etanercept longer (3.7 vs. 2.4 years, p = 0.16) compared to patients who flared. Three out of the 17 patients discontinued etanercept instantaneously and flared within one year, all other patients tapered the etanercept dose before discontinuation. All seven patients who resumed etanercept use after flaring recovered soon.

**Conclusion:** Patients who meet the clinical remission criteria on etanercept for a longer period have a better chance of retaining remission after etanercept discontinuation. Tapering of etanercept dose before discontinuation is favourable.

---

**P41**

**Switching from a first to a second tumour necrosis factor (TNF) alpha antagonist in patients with juvenile idiopathic arthritis**

H Schmeling1 and G Horneff2

1Hospital for Sick Children, Toronto, Canada
2Asklepios Klinik, Sankt Augustin, Germany

**Background:** Etanercept has been the only TNF antagonist licensed for treatment of resistant polyarticular juvenile idiopathic arthritis (JIA) and Adalimumab recently became the second one. Our objective was to evaluate efficacy and safety after switching from Etanercept to Adalimumab in JIA patients.

**Methods:** Prospective data were obtained using the database of the German Etanercept Registry. Reasons for switching to Adalimumab were recorded. Efficacy was assessed using the PedACR30/50/70 criteria. Safety assessments were based on the reporting of adverse events (AE).

**Results:** A total of 33 patients initially treated with Etanercept were switched to Adalimumab after a mean of 25.9 months (range 3–87 months). Reasons for discontinuation of Etanercept were inefficacy (n = 23, 65.8%), uveitis (n = 6, 17.1%), intolerance (n = 3, 8.6%) and patients’ request (n = 6, 17.1%). Follow up data on Adalimumab were obtained from 12 patients for a range of 2 to 26 months (mean 10.9 months). The maximum response rate of the PedACR30/50/70 on Etanercept was 82.4%/73.5%/67.6%. The last documented response rate on Etanercept showed a decrease to 47.1%/35.3%/29.4% (PedACR30/50/70). After switching to Adalimumab a maximum PedACR30/50/70 of 75%/66.7%/50% compared to start of Etanercept and 33.3%/33.3%/25% compared to start of Adalimumab was reached. Treatment on both drugs was safe with no report of serious AE.

**Conclusion:** Although a number of patients have reached a good PedACR response rate on Etanercept, treatment was unsatisfied and therefore it was switched to Adalimumab.
According to the PedACR, only minor improvement was observed after switching to Adalimumab.

**P42**

**Juvenile Psoriatic Arthritis (JPsA) clinical features and outcome of 119 patients**

Y Butbul Aviel, PN Tyrrell, BM Feldman, RM Laxer, RK Saurenmann, L Spiegel, B Cameron, S Tse and ED Silverman

Division of Rheumatology, The Hospital for Sick Children, Department of Pediatrics, University of Toronto, Toronto, Ontario, Canada

*Pediatric Rheumatology* 2008, 6(Suppl 1):P42

**Objective:** To determine the long-term outcome of a single center cohort of children with JPsA.

**Methods:** Clinical records of 122 patients meeting the Vancouver or ILAR criteria for JPsA were reviewed. Patients were divided into 4 groups depending on their clinical features: a) Oligoarticular, b) RF(+) polyarticular, c) RF(+) polyarticular and d) JIA (enthesitis related arthritis (ERA). Patient characteristics and clinical features at onset and during follow-up were determined.

**Results:** The cohort consisted of 119 patients, 59 (49.6%) had oligoarticular course, 54 (47.8%) were RF(−) and 4 (3.3%) RF(+) ERA. The cohort consisted of 119 patients, 54 (47.8%) were RF(−) and 4 (3.3%) RF(+) ERA. At diagnosis patients with ERA were older as compared to patients with oligoarticular and polyarticular course (11.6 ± 2.2 years vs 7.7 ± 4.3 years and 7.1 ± 4.5 years respectively p = 0.001). Patients with polyarticular course had more MCP, PIP and wrist involvement when compared to patients with oligoarticular course and with ERA (p < 0.001 for all). Patients with ERA had significantly more hip and sacroiliac involvement compared to the other groups (p < 0.001 for both). Nail changes were seen in 66 patients (57%) and was associated with DIP involvement at presentation (p = 0.0034).

**Outcome:** Time to first inactive disease period on not off therapy was significantly longer among patients with polyarticular disease when compared to the oligoarticular and the ERA groups (p = 0.0016 and p = 0.48 respectively). Patients with polyarticular had more contracture during follow-up when compared to patients with oligoarticular and with ERA (p = 0.01).

**Conclusion:** Patients with JPsA compromised from three distinct group of patients. Most patients with JPsA will achieve inactive disease and only minority will have long lasting contracture.

**P43**

**Mandibular condyle destruction in juvenile idiopathic arthritis (JIA)**

M Zak1,2, D Falkenström1, Ij Christensen1, NV Hermann1, S Nielsen1, FK Pedersen1 and S Kreiborg1

1 State University Hospital, Righospitalet, Copenhagen, Denmark 2University of Copenhagen, Copenhagen, Denmark

*Pediatric Rheumatology* 2008, 6(Suppl 1):P43

**Aim:** Assessment of destruction of the mandibular condyle in relation to clinical baseline data and disease progression in JIA.

**Materials and methods:** 293 consecutive patients (f = 198; m = 95) diagnosed 1995–2006 participated. Median JIA onset age was 6 1/2 yrs for girls and 8 yrs for boys. ILAR classification: persistent-oligoarticular (p-oligo) 26%, extended-oligoarticular (e-oligo) 24%, polyarticularRF- (poly−) 22%, polyarticularRF+ (poly+) 1%, enthesitis-associated (ERA) 16%, psoriatic (ps) 6% and systemic (sys) 5%. Disease course, uveitis, ANA, IgM-RF and HLA-B27 was recorded. Due to small numbers sys, poly+ and ps were excluded from subtype analysis. Patients with poly− and e-oligo were regarded as polyarticular course. Orthopantomography was done in all. 79% had 2 or more radiographs. Condylar morphology grading was: 0 = normal; 1 = erosions of the surface; 2 = flattening; 3 = total destruction.

**Results and discussion:** At the first examination, 28% had radiographic TMJ changes (1:29%; 2:66%; 3:5%). During the observation period, additional 7% developed TMJ changes, increasing the total frequency to 35%. 10 pt. with condylar lesions showed progression during the observation period. TMJ changes were significantly associated with ANA+. No other baseline associations were observed. In logistic regression models for TMJ changes, the following independent variables contributed significantly to the equation: ANA+ (p = 0.01), ILAR subtype (p = 0.009), and age (p = 0.02) at first examination. The OR for polyarticular course vs. ERA was 4.6 (95% CI: 1.7–12.5) and p-oligo vs. ERA 2.9 (95% CI: 1.0–8.0).

**Conclusion:** A lower frequency of mandibular condyle destruction in JIA than reported in several previous studies was found. Progression of changes was mild to moderate. The data suggest that condyle destruction in JIA is associated with ILAR subtype, age at disease onset and ANA+.

**P44**

**Efficacy of a second TNF blocker, when the first one failed, in patients with juvenile idiopathic arthritis (JIA)**

A Salmajo1, A Lurati2, I Pontikaki1, V Gerloni1, M Gattinara1, B Beruzzi1 and F Fantini1

1 Gaetano Pini Institute Chair of Rheumatology, Milan, Italy 2Fornaroli Hospital Rheumatology Unit, Magenta, Italy

*Pediatric Rheumatology* 2008, 6(Suppl 1):P44

**Objectives:** To determine the efficacy of a second treatment with a different TNF blocker in JIA when the first one failed.

**Methods:** All JIA patients prospectively followed at our Centre, who failed a first TNF blocker and switched to a second one were enrolled. For each patient the DAS, ACR Ped30, ACR20, ACR50 and ACR70 responses were evaluated at baseline and after a period ranging from 3 to 6 months of each treatment.

**Results:** Out of 60 JIA patients enrolled, 40 (37 f, 3 m) were evaluated: 10 systemic arthritis, 2 persistent oligoarthritis, 11 extended oligoarthritis, 9 RF negative polyarthritis, 4 RF positive polyarthritis, 1 ERA (enthesitis related arthritis), 3 psoriatic arthritis. With a standard Chi square model, we didn’t find a significant difference in the ACR and DAS response rates between the first and the second anti TNF treatment (p > 0.1). Stratifying the population for the type of the shift (Etanercept to Infliximab/Adalimumab, Infliximab to Etanercept/Adalimumab) we didn’t find a significant difference in the ACR and DAS response rates between the first and the second anti TNF treatment (p > 0.1). Our data show that failure of an anti-TNF therapy in patients with JIA does not preclude a response to a second anti-TNF agent of a different class.
P45
Relationship between delayed menarche and bone density in patients affected by juvenile idiopathic arthritis
A Lurati1, A Salmaso2, B Teruzzi2, V Gerloni2, M Gattinara2 and F Fantini2
1Fornari Hospital Rheumatology Unit, Magenta, Italy
2Gaetano Pini Institute Chair of Rheumatology, Milan, Italy

Pediatric Rheumatology 2008, 6(Suppl 1):P45

The aim of our study was to prospectively evaluate bone density in adolescents females with JIA, and to correlate the results with puberty. Lumbar spine (L2–L4) areal bone mineral density (aBMD) (assessed by Dual X-ray Absorbiometry, DXA) was monitored every 6–12 months in a group of 38 girls with JIA. The evaluated bone density accrual during the peripubertal time as well as absolute and relative (Z-score) aBMD in relationship with age at menarche, JIA subset, disease activity, corticosteroid and methotrexate treatment was assessed. Height, body mass index, Bone Mass Content values were also collected. Volumetric BMD evaluated with a geometric correction formula has been calculated and compared to aBMD.

Patients were divided into two groups:
– group I included girls with menarche age within normal limits for italian standards;
– group II included girls with delayed menarche. The BMD values and Z scores in group I were not significantly different to normal population. The BMD values and Z scores in group II were significantly decreased when compared to the normal population (p < 0.001). With a multivariate analysis only age at menarche seemed independently related to peripubertal mineralization (p = 0.025, r between −0.65 and −0.75). With a binary logistic analysis only disease activity (ESR and Hgb values) seems independently related to a menarche delay (1.24 ± 0.4 for each mm/h). Our data show a critical role for disease activity in determination of a regular pubertal onset and an optimal bone density achievement.

P46
Time to treatment as an important factor for the response to methotrexate in juvenile idiopathic arthritis
HM Albers1, JAM Wessels1, RJH van der Straaten1, DMC Brinkman1, LWA Suijlekom-Smit2, SSM Kamphuis2, HJ Girschick2, C Wouters2, MW Schilham1, S le Cessie1, TWJ Huizinga1, R ten Cate1 and HJ Guchelaar1
1Leiden University Medical Center, Leiden, Netherlands
2Erasmus Medical Center-Sophia Children’s Hospital, Rotterdam, Netherlands
3University of Wuerzburg, Wuerzburg, Germany
4University Hospital Gasthuisberg, Leuven, Belgium

Pediatric Rheumatology 2008, 6(Suppl 1):P46

Objective: Methotrexate (MTX) is the most commonly used disease modifying antirheumatic drug (DMARD) in juvenile idiopathic arthritis (JIA), especially in polyarticular arthritis. At present no reliable prediction of individual response to MTX can be made. Identification of factors that influence the response to MTX could be helpful in realizing the optimal treatment for each individual patient.

Materials and methods: A cohort of 118 JIA patients that were treated with MTX was studied retrospectively. Clinical parameters and genotypic data of 6 single nucleotide polymorphisms (SNP) in 5 genes related to the mechanism of action of MTX were compared between MTX responders and non-responders using a multivariate regression analysis.

Results: The time-to-start-MTX (time from diagnosis to start MTX treatment), the starting dosage and the baseline physician’s global assessment were significantly related to the response to MTX at 6 months after initiation in a multivariate regression analysis. No effect of the starting dose on the response to MTX was found when correcting for different treatment strategies in different subtypes. The baseline physician’s global assessment was directly related to the time-to-start-MTX. Subgroup analyses showed that time-to-start-MTX was consistently significantly associated with response to MTX. A non significant trend towards an increased probability to respond was seen when the time-to-start-MTX was ≤1 years.

Conclusion: In children with JIA, the time-to-start-MTX appears to be an important factor for the MTX response. In this study we show that an early MTX treatment (≤ 1 year) is associated with an increased efficacy of MTX on short term.

P47
Infliximab to treat chronic uveitis in juvenile idiopathic arthritis (JIA)
C Bracaglia, PS Buonuomo, S Caminiti, A Insalaco, A Campana and E Cortis
Division of Rheumatology, Department of Pediatric Medicine, IRCCS Ospedale Pediatrico Bambino Gesù, Rome, Italy

Pediatric Rheumatology 2008, 6(Suppl 1):P47

Background: Uveitis occurs in 10%–15% of patients with JIA and is still one of the most frequent causes of acquired blindness in the developed world. Female sex, oligoarticular onset, serum antinuclear antibodies (ANA) and early onset of uveitis seem to increase the development of chronic uveitis. If topical treatment fails, second-line agents may be used, but not all patients respond. Infliximab has been reported to be effective in some of these cases. This study aims to assess the response and side effects associated with infliximab in JIA patients with uveitis.

Methods: Fourteen patients, (3 male and 11 female) aged from 6 to 26 years, were treated with infliximab between January 2005 and April 2008. Mean age at the beginning of therapy was 9 years and 8 months. All patients received also methotrexate (15 mg/mq weekly). Infliximab was administered at 5 mg/kg dose at 0, 2, 4, 6 weeks and then every two months. Uveitis activity was evaluated as number of anterior chamber cells every month.

Results: Infliximab was well tolerated and no immediate adverse effects were recorded. Three patients achieved a complete remission of uveits for more than one year and stopped anti-TNF treatment. Eight patients showed a good response with improvement of inflammatory ocular activity and decreased episodes of uveitis. Those patients are still on infliximab. Two patients were unresponsive to the drug after one year.

Conclusion: In our experience infliximab was effective in 85% of patients and none developed any serious systemic adverse events attributable to infliximab.
P48
Use of Intravenous Immunoglobulin Therapy in a paediatric rheumatology service
SM Saladi and AG Cleary
Royal Liverpool Children’s NHS Trust, Liverpool, UK

Pediatric Rheumatology 2008, 6(Suppl 1):P48

Background: Intravenous Immunoglobulin (IVIG) is widely used in paediatric inflammatory disease. The Department of Health, UK recently produced guidelines for IVIG use and a demand management plan in response to global IVIG shortages, recommending use in “selected” patients with juvenile dermatomyositis (JDM), as a “last resort” in systemic juvenile idiopathic arthritis (sJIA), and use not supported in juvenile systemic lupus erythematosus (JSLE) and vasculitis.

In this context, we have retrospectively audited use of IVIG in a UK centre.

Materials and methods: A pilot analysis of children treated with IVIG in the previous 2 years.

Results: 4 patients were male and 6 were female. The diseases were: sJIA (4), JDMS (3), JSLE (1) and polyarteritis nodosa (2). This represented approximately 50% of the total sJIA cohort and 75% of the JDMS cohort presenting during the study period. 9/10 had inadequate response to high dose pulse intravenous and oral steroid therapy along with first line disease modifying agents. The other patient received IVIG post stem cell transplant for sJIA.

Conclusion: IVIG is a valuable adjunct in a broad spectrum of paediatric inflammatory disease and we believe it should remain a treatment option in selected cases with partial response to standard first line therapies.

Reference

P50
Growth retardation in patients with juvenile idiopathic arthritis and growth hormone therapy
I Nikishina and A Shapovalenko
Institute of Rheumatology of RAMS, Moscow, Russian Federation

Pediatric Rheumatology 2008, 6(Suppl 1):P50

Objective: To identify patient characteristics, that predict the growth retardation and to assess the risk/benefits proportion of growth hormone (GH) treatment in JIA patients.

Methods: Study cohort was presented by 170 JIA patients (47 boys, 123 girls, mean age 12.1, disease duration 5.1 yrs). Annual growth parameters were studied in relation with premorbid and disease related factors. 30 prepubertal patients, having the most significant delay of growing were randomized in 2 groups. 15 patients were received recombinant GH 0.05–0.07 mg/kg within 4–18 months; other 15 patients were as control.

Results: Fifteen were females, 22 were males. Mean age was 14.2 ± 5.3 years. Mean follow up after initiation of etanercept was 12.7 ± 10.9 months. Seven patients had an initial PPD score above 10 mm. All received concomitant isoniazid treatment. Except one patient with a very severe course of systemic JIA under aggressive immunosuppressive therapy, all had normal examinations and X-rays. This one patient had a consolidation and cavitation at his right superioposterior lung zones. He is on antituberculosis treatment now without any overt clinical features of Tbc.

Conclusion: With proper initial evaluation anti-TNF treatment is safe even in countries where Tbc is moderate frequency. A 9-month isoniazid treatment is suggested for children with a PPD of >10 mm.
patients. A significant response to GH treatment compared with control group was seen in all children. The median height velocity was 3.1 cm per 3 months (4–12.5 cm/1 year). We observed the disease increasing activity in 8/15 patients under GH therapy. Other complications from GH-therapy were not marked.

**Conclusion:** We conclude that disease activity and genetic factors are the most important reasons of growth retardation in JIA patients. Recombinant GH may be of benefit in severe growth retardation therapy, but can promote disease activity.

**P51**

Sleep, fatigue and quality of life in juvenile idiopathic arthritis (JIA) and Juvenile Dermatomyositis (JDM)

Y Butbul Avie, R Stremler, J Stinson, R Schneider, RM Laxer, L Spiegel, B Cameron, ED Silverman and BM Feldman

Division of Rheumatology, The Hospital for Sick Children, Departments of Pediatrics, Medicine, HPME and PHS, University of Toronto, Toronto, Ontario, Canada

**Pediatric Rheumatology 2008, 6(Suppl 1):P51**

**Objective:** To determine the prevalence of abnormal sleep in JIA and JDM and its relationship to pain, dysfunction, disease activity and medications.

**Materials and methods:** 155 patients (115 – JIA, 40 – JDM) were randomly sampled and were mailed questionnaires. Sleep was assessed by Sleep Self – Report (SSR) and Children’s Sleep Habits Questionnaires (CSHQ). Fatigue, pain and function was assessed by PedsQL. Disease activity was assessed by VAS. Joint counts were self reported.

**Results:** 81% responded. 44% reported abnormal sleep (CSHQ > 41); there were no differences between disease groups.

Sleep self report was highly correlated with PedsQL fatigue ($R^2 = 0.31, \ p < 0.0001$).

Fatigue was highly correlated with quality of life ($R^2 = 0.6, \ p < 0.0001$).

The worse pain intensity in the last week was correlated to sleep disturbance ($R^2 = 0.1, \ p = 0.0005$).

Fatigue was related to prednisone and methotrexate use as reported by patients and parents.

**Conclusion:** Sleep disturbance and fatigue are prevalent among children with different rheumatic diseases. Sleep disturbance and fatigue are strongly related to increases in pain and decreases in quality of life. Strategies aimed at improving sleep should be studied as possible ways of improving quality of life for children with rheumatic illness.

**P52**

Illness representation in adolescents with juvenile idiopathic arthritis

OTHM Lelieveld, W Armbrust, MA van Leeuwen and E van Weert

University Medical Center Groningen, Groningen, Netherlands

**Pediatric Rheumatology 2008, 6(Suppl 1):P52**

**Background:** The Common Sense Model (CSM) conceptualizes a patient as a problem solver creating representations of their disease which may affect coping style and disease outcome [1]. The aim of the study was to explore illness representations in adolescents with JIA.

**Materials and methods:** Adolescents from a JIA transition clinic were asked to complete the revised Illness Perception Questionnaire (IPQ-R) [2]. Representations were rated by answering 4 to 6 questions per component on a 5-point Likert scale (ranging from strongly disagree to strongly agree).

**Results:** Thirty-five patients with JIA participated, 14 boys and 21 girls (mean age in years (SD): 17.1 (±0.7); mean disease duration in years (SD): 8.4 (±5.0). Nineteen patients had active disease, 11 were under disease control with medication, 9 patients were in clinical remission on medication and 6 patients were in remission. Representations (Min-max score) and Mean (± sd) 1. Timeline acute/chronic (6–30): 21.9 (3.9). 2. Timeline cyclical (4–20): 13.1 (3.2). 3. Consequences (6–30), 14.2 (3.3). 4. Personal control (6–30), 20.2 (2.7). 5. Treatment control (5–25), 18.8 (1.7). 6. Illness coherence (5–25), 20.1 (2.7).

**Conclusion:** Adolescents with JIA have a coherent understanding of their disease. Patients perceive JIA as a chronic disease which can be influenced by their own action and by medical treatment. Patients perceive JIA as a disease which gives hardly any feelings of stress and anxiety and as having little impact on their life. Further research is needed how illness representations affect coping strategies and outcome.

**References**


**P53**

Hip arthritis in the TNF-Blockade era: an unresolved issue?

C Scott, C Wouters and P Moens

University Hospital Leuven, Leuven, Belgium

**Pediatric Rheumatology 2008, 6(Suppl 1):P53**

**Background:** Hip involvement is a major cause of morbidity in patients with JIA. TNF-antagonists have improved the control of JIA.

**Methods:** We report on the evolution of hip arthritis in a series of 15 JIA (7 m/8 f; 9 sJIA, 4 pJIA, 2 oejJIA) patients treated with TNF-antagonists add-on MTX. Clinical disease activity, medication, hip x ray and MRI images were recorded.

**Results:** Median disease duration at start of TNF blockade was 51 months (14–108). Follow-up under TNF-blockade was 42 months (11–107). Ten patients had hip involvement at start. Eight (7 sJIA, 1 oejJIA) showed progressive hip disease (PHD) during TNF blockade. In patients with PHD active joint count decreased from 10 to 2.5. Systemic inflammation decreased (ESR 48.5 to 22.5). Steroid dose decreased from 0.315 mg/kg/d at start to 0.155 mg/kg/d. In 4, steroid tapering was impossible necessitating alternative therapy. Hip imaging in 8 PHD children showed cartilage destruction, erosions and sclerosis (7) osteonecrosis of the femoral head (6), AVN (1), extensive osteophyte formation (1).

**Discussion:** In this cohort of 15 patients treated with TNF blockade, 8 patients had progressive hip disease despite better control of arthritic and systemic inflammation in the majority of
them. Our findings suggest that the risk of progressive hip disease and damage may not be sufficiently abrogated by TNF blockade. Hip disease may progress despite a good general response and requires special vigilance especially in patients who do not show an optimal response to TNF antagonism.

P54
Arthritis in Down’s syndrome is still being missed
M Cruikshank1, A Tunc2, J Walsh3, P Galea3, J Davidson2 and J Gardner-Medwin2
1 Royal Hospital for Sick Children, Edinburgh, UK
2 Royal Hospital for Sick Children, Glasgow, UK
3 Royal Alexandra Hospital, Paisley, UK

Background: Children with Down’s syndrome are known to develop inflammatory arthritis with a prevalence thought to be greater than the general population [1]. Despite this, the diagnosis is still being overlooked leading to delayed treatment and poor outcomes.

Cases: We describe 8 cases, 4 females with an age range of 4.2–15.6 (mean 9.3) years at diagnosis. Time from symptom onset to diagnosis ranged from 0.9–8.7 (mean 3.3) years, despite attending up to 16 (mean 6.2) clinics with documented symptoms and signs of arthritis. Misdiagnoses included developmental delay, soft tissue injury, hypermobility, multiple epiphyseal dysplasia and behavioural problems. All had a clear clinical diagnosis of polyarticular arthritis and four where non-weight bearing at first contact with paediatric rheumatology. Two patients had psoriasis. One patient had psoriatic nail changes. Five had a family history of rheumatological disease. All were antinuclear antibody negative. All were treated with intraarticular steroid injections. All were offered methotrexate and five clinically responded. Of the three who did not tolerate methotrexate, two were offered and improved with etanercept.

Conclusion: Diagnosis of arthritis in children with Down’s syndrome is still significantly delayed compared to other children presenting with inflammatory arthritis. In our cohort, response to treatment was similar to children with juvenile idiopathic arthritis (JIA). Current evidence suggests response to treatment in JIA is optimal when commenced early. Many of this cohort had significant joint damage and disability by time of diagnosis. Delays in diagnosis are contributing to unnecessary disability in this group of children.

Reference

P55
Evaluation of the power of six clustering features in identifying a homogeneous disease subset in juvenile idiopathic arthritis (JIA)
A Magnani1, S Oliveira2, E Castelli3, O Arguedas4, N Ullmann1, S Pedezolli1, S Magni Manzoni1, A Pistorio1, N Ruperto1, A Martini1 and A Ravelli1
1IRCCS G Gaslini, Genova, Italy
2Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil
3IRCCS Pol San Matteo, Pavia, Italy
4Hospital Nacional de Ninos Herrera, San Jose, Costa Rica
5Hospital General de Ninos P. Elizalde, Buenos Aires, Argentina

Table 1 (abstract P55)

<table>
<thead>
<tr>
<th>Measure</th>
<th>ANA Pos</th>
<th>ANA Neg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean onset age (years)</td>
<td>3.9</td>
<td>6.8</td>
</tr>
<tr>
<td>Patients with onset age &lt; 6 years (%)</td>
<td>81.3</td>
<td>45.9</td>
</tr>
<tr>
<td>Females (%)</td>
<td>80.0</td>
<td>68.8</td>
</tr>
<tr>
<td>Asymmetric arthritis at 6 months (%)</td>
<td>78.4</td>
<td>63.2</td>
</tr>
<tr>
<td>Iridocyclitis (%)</td>
<td>25.4</td>
<td>1.9</td>
</tr>
</tbody>
</table>

P56
Multicentric Castleman’s Disease (CD) in juvenile idiopathic arthritis (JIA) treated with etanercept: coincidence or causal relationship?
L Rossi, G Martini, L Sainati and F Zulian
Department of Paediatrics, Padova, Italy

Pediatric Rheumatology 2008, 6(Suppl 1):P56

Association of CD and RA is widely described in adults, but has never been reported in children with JIA. We report a 13 years old girl with a 6 years history of polyarticular JIA treated with Methotrexate (MTX) since diagnosis and after 2 years, in April 2004, started on etanercept. On this treatment, patient presented important clinical improvement which allowed steroids withdrawal and progressive reduction of MTX. In June 2007 recurrent attacks of migraine appeared with negative EEG and cerebral MRI. In November headache became continuous and after one month morning palpbral oedema and right chest pain appeared, followed by vomiting which lead to hospitalisation in January 2008. Noticeable elements on
physical examination were: systolic hypertension, papilledema, palpebral and peripheral oedema, generalized lymphadenopathy and hepatomegaly. Relevant lab tests were: Hb 11.6 g/dL, ESR 67 mm/h, CRP 21.6 mg/L, hematuria, nephrotic proteinuria. Viral, bacterial and fungal infections were ruled out. Cerebral MRI showed right emisphere and right tentorial dural thickening (pachymeningitis). CT and ultrasound confirmed the presence of enlarged mediastinal and axillary lymph nodes, pericardial and pleural effusion, bilateral renal enlargement and ascites. Plasmocytosis was found on bone marrow aspirate. Axillary lymph node biopsy was consistent with CD.

To our knowledge this the first report of the combination of two conditions rarely associated with RA, multicentric CD and pachymeningitis, in a child with JIA in remission under treatment with etanercept. This raises the question whether anti TNF-α therapy might contribute to lymphoproliferation possibly via dysregulation of cytokines network.

Reference

P57
HLA-B27 predicts a more extended disease with increasing age at onset in boys with juvenile idiopathic arthritis
L Berntson1, M Damgård2, B Andersson-Gäre3, T Herlin4, S Nielsen5, E Nordahl6, M Rygg7, M Zak8 and A Fasth9
1Department of Women’s and Children’s Health, Uppsala University Children’s Hospital, Uppsala, Sweden
2Department of Pediatrics, Falun Hospital, Falun, Sweden
3Department of Pediatrics, Ryhov County Hospital, Jönköping, Sweden
4Department of Pediatrics, Århus University Hospital, Skejby, Denmark
5University Clinic of Pediatrics II, Rigshospitalet, Copenhagen, Denmark
6Institute of Clinical Medicine/Institute of Community Medicine, University of Tromsø, and Department of Pediatrics, University Hospital of North Norway, Tromsø, Norway
7Department of Laboratory Medicine, Children’s and Women’s Health, Faculty of Medicine, Norwegian University of Science and Technology, Trondheim, Norway
8Department of Pediatrics, St. Olavs Hospita, Trondheim, Norway
9Department of Pediatrics, Göteborg University, Göteborg, Sweden

P58
Does unity of Familial Mediterranean fever with juvenile idiopathic arthritis affect the outcome?
R Topaloglu, N Akty Ayaz, E Demirkaya, Y Bilginer, F Ozaltin, A Duzova, S Ozen, N Besbas and A Bakkaloglu
Hacettepe University Medical Faculty, Ankara, Turkey

P59
Association between inflammatory status and intima-media-thickness in children with juvenile idiopathic arthritis: preliminary data
L Breda, D Di Marzio, A Scarinci, M Nozzi, K Falasca and F Chiarelli
University of Chieti, Chieti, Italy

P60
Atherosclerosis as a cardiovascular disease has been found even in fetal period. However, information about risk factors of pre-clinical atherosclerosis in childhood has been limited [1].
Studies in childhood showed higher intima-media thickness (IMT) in children with chronic diseases such as type 1 diabetes [2], while no data are reported about juvenile idiopathic arthritis (JIA). Hence, this study was aimed to find out signs of atherosclerosis and the relationship with markers of systemic inflammation in children with JIA.

**Materials and methods:** Carotid IMT was measured using high-resolution B-mode ultrasound in 21 JIA prepubertal children (8 M/13 F, mean age 8 ± 2 and mean duration of illness of 2 yrs), and 9 age- and sex-matched healthy controls. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were used to measure systemic inflammation. Lipid profile was assessed in all patients.

**Results:** JIA children had an increased IMT (p = 0.008) compared to healthy subjects; they also had higher levels of ESR and CRP (p = 0.001 and p = 0.05 respectively).

No statistically significant differences between left and right carotid artery IMT were found (p > 0.05).

There were no significant correlation between IMT and markers of systemic inflammation or lipid levels probably due to the small sample size of this preliminary investigation.

**Conclusion:** Children with JIA have increased carotid artery IMT indicating the presence of early carotid structural changes. This is consistent with hypotheses of a role to systemic inflammation in the pathogenesis of atherosclerosis in children.

More data are needed to confirm our results.

**References**


**P60**

**Performance of IFN-γ release assays for detection of tuberculosis infection in juvenile JIA children in biological therapy**

L Assante, M Bocchino, M Alessio, R Ambrosio, A Sanduzzi and A Guarino

1Department of Pediatrics Federico II University, Naples, Italy

2Division of Respiratory Medicine, Federico II University, Naples, Italy

**Pediatric Rheumatology** 2008, 6(Suppl 1):P60

Severe TB has recently been described in association with TNF-α blocker therapy. Furthermore conventional tuberculin skin test (TST) may give false-negative results in patients receiving biological therapy. New in vitro test, based on the detection of IFN-γ release by T-cell stimulated with M. tuberculosis specific antigens (IGRA), are available for LTBI diagnosis, promising to be more sensitive and specific than TST. Nevertheless no sufficient evidence on IGRA performance are available in children. The performance of two commercially available IGRAs, ELISPOT-TB (TS-TB) and Quantiferon-TB gold in-Tube (QFT-GIT), were evaluated in comparison with TST in children with rheumatic diseases. In children with positive result clinical and radiological evidence of TB was sought. Nineteen children with JIA were enrolled since November 2006 (median age 13.5 years; range 2–18). Seventeen children were on long term etanercept therapy plus methotrexate (15 mg/m²/week). I on infliximab and I received adalimumab plus prednisone (0.2 mg/Kg/die). Five children (26%) showed positive TS-TB, QFT-GIT and TST were negative in all children. Both QFT-GIT and TS-TB showed a high percentage of indeterminate results (21% and 16% respectively). None of the 5 patients positive at TS-TB developed active disease, as judged by clinical and radiological findings, at least in a median follow-up period of 16 months (range 9–17 months). Our data suggest that high rate of positive results by TS-TB is expression of non-specific immune reactivity in rheumatic children.

**P61**

**Anti-cyclic citrullinated peptide: its prevalence and clinical significance in a South African cohort with juvenile idiopathic arthritis**

BJ Mistry, G Faller and M Tikly

1Chris Han Baragwanath Hospital, Johannesburg, Gauteng province, South Africa

2University of Witwatersrand, Johannesburg, Gauteng province, South Africa

**Pediatric Rheumatology** 2008, 6(Suppl 1):P61

**Background:** Anti-cyclic citrullinated peptide (anti-CCP) antibodies are a highly specific serological marker for adult-onset rheumatoid arthritis, present early in the course of the disease, and are a marker of erosive disease.

**Objective:** To assess the prevalence and clinical significance of anti-CCP antibodies in a cohort of children with juvenile idiopathic arthritis (JIA).

**Methods:** A retrospective review of the records of children with JIA attending a paediatric rheumatology clinic at Chris Han Baragwanath Hospital was undertaken. Anti-CCP antibodies were tested using an enzyme linked immunosorbent assay (EliA CCP).

**Results:** Records of 52 patients (54% males, 46% females) were reviewed. The mean (SD) age and follow-up period were 10.69 (3.81) and 2.3 (1.7) years, respectively. The majority of the children (83%) were Black. The subtypes of JIA were as follows: systemic 21%, polyarticular 50%, oligoarticular 19%, enthesitis-related arthritis 2%, psoriatic 2% and other 6%. Anti-CCP antibodies were present in the sera of 8 of 28 patients tested (29%). They were detected exclusively in patients with the polyarticular subtype of JIA. IgM RF was positive in 14 (29.17%) of the total cohort, but not exclusively in patients with the polyarticular subtype of JIA. The overall concordance between the 2 tests was fair (Kappa statistic = 0.39).

**Conclusion:** Anti-CCP antibodies are present in a high proportion of patients with JIA, and in the polyarticular JIA subtype. They appear to be a better marker of this subtype than IgM RF. The concordance between anti-CCP antibodies and IgM RF in our patients with JIA is fair.

**P62**

**Macrophage activation syndrome: a potentially fatal complication of rheumatic disorders**

V Ziaee and MH Moradinejad

Children’s Medical Center, Tehran University of Medical sciences, Tehran, Iran

**Pediatric Rheumatology** 2008, 6(Suppl 1):
**Methods:** Retrospective review of cases of MAS from the charts of 120 patients with juvenile rheumatoid arthritis and systemic lupus erythematosus (SLE), were reviewed collected data base of 5 children with MAS from 1998 to 2007, in Children’s Medical Center, In Tehran University.

**Results:** Totally 120 patients evaluated in this study including 108 JIA and 12 SLE. Five patients (4 girls and 1 boy) were considered to have evidence of MAS (incidence rate 4.2%). This rate for all JIA patients was 3.7% and for SoJIA, SLE and juvenile idiopathic arthritis (JIA) and polyarticular RF negative JIA was 8.2%, 16.7% and 2.8%, respectively. Mean age of MAS onset was 4.9 years, and duration of rheumatologic disease prior to MAS, 22 months. Four cases (80%) had abnormal liver function during the disease course, and coagulopathy. Bone marrow examination supported the diagnosis with definite haemophagocytosis in four cases (80%). The mortality rate was 40%.

**Conclusion:** Incidence of MAS in our JIA patients was about other studies, but the mortality rate was higher than other reports. Although MAS is a rare complication, because it is potentially fatal it must be considered in each childhood rheumatic disorders with sudden changes in general condition and decrease peripheral cells.

**References**


**P63**

**Measles, Mumps, Rubella serology in juvenile idiopathic arthritis**

MW Heijstek1, GAM Berbers2, PGM van Gageldonk2, CSP Uiterwaal3 and NM Wulffraat2

1 University Medical Center Utrecht, Utrecht, Netherlands
2 Laboratory for Infectious Diseases and Screening, National Institute of Public Health and the Environment, Bilthoven, Netherlands
3 Julius Centre for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, Netherlands

**Background:** Macrophage activation syndrome (MAS) is a rare complication of childhood with rheumatic disease. This syndrome has been reported in association with many rheumatic diseases, especially systemic juvenile rheumatoid arthritis (SoJIA). The aim of this study was evaluation the rate, symptoms and outcome of MAS during 10 years.

**Methods:** Measles, Mumps, Rubella vaccination in Juvenile Idiopathic Arthritis (JIA) patients. Mumps, Rubella (MMR) vaccination in Juvenile Idiopathic Arthritis (JIA) patients. To assess the efficacy of live attenuated Measles, Mumps, Rubella vaccination in Juvenile Idiopathic Arthritis (JIA) patients.

**Results:** In the group with no vaccinations, MMR seroprevalence and IgG-levels were significantly lower in JIA patients (measles 63% vs. 92%, mumps 39% vs. 92%, rubella 65% vs. 95%). This was probably due to higher natural infection rates in HC, since the majority of HC without vaccination were born in the period before introduction of MMR vaccination. These differences diminished after vaccination, although the overall seroprevalence of mumps and rubella remained lower in JIA (p < 0.001). MMR seroprevalence and IgG levels were significantly lower in systemic JIA patients. 95 patients using methotrexate had MMR serology comparable to patients without methotrexate.

**Conclusion:** Differences in MMR seroprevalence between JIA patients and healthy controls disappear after increasing vaccinations, indicating that JIA patients are able to generate a serological response to MMR vaccination comparable to healthy controls. MMR serology is lowest in systemic JIA patients. Methotrexate does not influence MMR serology.

**P64**

**The therapeutic value of low-energy laser (LLLT) for enthesitis in children with juvenile spondyloarthropathies**

M Harjacek, T Kelava and L Lamot
Children’s Hospital Zagreb, Zagreb, Croatia

**Background:** Children with juvenile spondyloarthropathy (jSpA), classified as enthesitis-related arthritis (ErA), under the ILAR classification, usually experience both arthritis and enthesitis. Therapeutic value of low-energy lasers (LLLT) for enthesitis has not been systematically studied in children with JIA.

**Patients and methods:** In this pilot study we report 20 children with jSpA, diagnosed based on both ESSG and ILAR criteria, which we treated, in addition to standard NSAID therapy, with LLLT. We used gallium-aluminium-arsenide (Ga-Al-As) continued laser (Iskra Medical, Slovenia). The usual location of treatment was AC joints, infrapatellar and/or Achilles’ tendon insertions. The effects of therapy were determined using the 100 mm VAS scale for pain reported by patient, before, and 1 month after the therapy. Usual therapy consisted of 10-minute sessions on 10 consecutive days.

**Results:** There were 12 girls and 8 boys, medium age 11.4 yrs. (range 7–17). The mean VAS before the therapy was 6.1 (range 4–8) and one month after the therapy was 1.3 (range 0–4). The usual dose used was between 2.5–3 J/m² based on localization of enthesitis.

**Conclusion:** The biostimulating effect of LLLT is in its anti-inflammatory, analgesic and anti-edematous effect on tissues. It seems that Ga-Al-As laser therapy is a valuable addition to the standard treatment modalities currently used for pain and inflammation treatment of enthesitis in children with jSpA. New patient enrolment and the correlation with six core outcome variables is underway.

**References**


P65
Methotrexate shows the same efficacy and safety in the real world in all subtypes of JIA as in the controlled trial
I Foedvari and A Wierk
Hamburger Zentrum fuer Kinder- und Jugendrheumatologie, Hamburg, Germany

Pediatric Rheumatology 2008, 6(Suppl 1):P65

Background: Methotrexate (MTX) is the mostly used second line agent to treat Juvenile idiopathic arthritis (JIA). This study presents a retrospective data evaluation.

Objectives: To prove the efficacy and safety of MTX in all subtypes of JIA in a retrospective cohort.

Methods: Single center open-label evaluation of the efficacy and safety of MTX treatment in patients with JIA where treatment was initiated between 31st of March 2005 and 31st of December 2007.

Results: 105 patients were MTX initiated aged between 1 to 17 years. 61 of them were female (58%). The mean treatment duration was 13.9 months. The mean MTX dose was 14.7 mg/m2/week. The response to therapy is shown in table 1, response occurred at months 3 and stayed stable over the observation period. Adverse effects (AE) were reported by 41% of the patients, which were evenly distributed over the observation period. One severe AE occurred, one patient died with ALL.

Discussion: In this real world retrospective study of all JIA subtypes MTX appears to be a safe and effective drug.

Table 1 (abstract P65)

<table>
<thead>
<tr>
<th></th>
<th>baseline</th>
<th>At 3 months</th>
<th>At 6 months</th>
<th>At 12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHAQ-pain subscale</td>
<td>0.886</td>
<td>0.466</td>
<td>0.386</td>
<td>0.338</td>
</tr>
<tr>
<td>CHAQ-disability subscale</td>
<td>0.76</td>
<td>0.491</td>
<td>0.425</td>
<td>0.343</td>
</tr>
<tr>
<td>CHAQ-severity subscale</td>
<td>0.398</td>
<td>0.248</td>
<td>0.184</td>
<td>0.207</td>
</tr>
<tr>
<td>Number of swollen joints</td>
<td>2.4</td>
<td>0.8</td>
<td>0.6</td>
<td>0.4</td>
</tr>
<tr>
<td>Number of tender joints</td>
<td>2.6</td>
<td>1.4</td>
<td>1.1</td>
<td>0.8</td>
</tr>
<tr>
<td>Number of joints with LROM</td>
<td>3.3</td>
<td>2.8</td>
<td>2.4</td>
<td>2.4</td>
</tr>
<tr>
<td>Physician global (VAS)</td>
<td>2.4</td>
<td>1.1</td>
<td>0.8</td>
<td>0.6</td>
</tr>
<tr>
<td>Elevated CRP</td>
<td>45.7%</td>
<td>14.3%</td>
<td>12.5%</td>
<td>42.9%</td>
</tr>
<tr>
<td>Elevated Sedimentation rate</td>
<td>43.8%</td>
<td>17.5%</td>
<td>21.1%</td>
<td>42.1%</td>
</tr>
</tbody>
</table>

P66
Bone mass predictors in a large cohort of children with juvenile idiopathic arthritis (JIA)
FF Falcini1, CS Capannini1, TG Tonini1, NF Nacci1, SG Simonini2, CR Cimaz1 and SS Stagi2
1Department of BioMedicine, Division of Rheumatology, Transition Unit, University of Florence, Florence, Italy
2Department of Paediatrics, Rheumatology and Endocrinology Units, University of Florence, Florence, Italy

Pediatric Rheumatology 2008, 6(Suppl 1):P66

Purpose: Low bone mass has been reported in children with JIA. We wanted to assess areal bone mineral density (BMD) in our cohort of patients and correlate the results with clinical data.

Methods: The study population included 162 pts (113 F and 49 M, mean age 10.6 ± 3.1 yrs) affected with JIA: 77 oligoarticular, 48 polyarticular RF-, 15 systemic, and 22 enthesitis-related arthritis (ERA) onset. All patients underwent bone mass evaluation by DXA at lumbar spine (L2–L4). DXA values were correlated with JIA category, age at onset, disease duration, ESR, CRP, flare rate, and medications. Age- and sex-specific reference values from an age-matched healthy population were used to calculate z-scores. Two-way analysis of variance was used to determine whether the DXA z-score correlated with disease category, medications, age at onset, disease duration.

Results: The whole group of JIA pts showed lower DXA z-scores (systemic p = 0.0012; oligoarticular p = 0.0072; polyarticular p = 0.0002), except ERA (p = NS) when compared to controls. DXA z-scores significantly correlated with JIA subtype: systemic had lower z-score than oligoarticular (p = 0.015) and ERA (p = 0.001), while polyarticular pts had lower z-score in comparison to ERA (p = 0.009).

In the group with oligoarticular onset, patients treated with MTX plus corticosteroids had a higher z-score than those treated with only corticosteroids (p = 0.024).

Conclusion: JIA patients, in particular with polyarticular and systemic onset show a lower DXA z-score in comparison to controls while in ERA DXA values are comparable to controls. Together with sex, disease duration seems the main factor modifying DXA value.

P67
The value of antibodies against mutated citrullinated vimentin in juvenile idiopathic arthritis
D Guseinova1, A Lazareva1, R Shantere2, D Berzinja3, O Rasnachs1 and V Stanevicha1
1Riga Stradinsh University, Riga, Latvia
2Children’s Clinical University Hospital, Riga, Latvia

Pediatric Rheumatology 2008, 6(Suppl 1):P67

Background: Antibodies against cyclic citrullinated peptid (anti-CCP) and mutated citrullinated vimentin (anti-MCV) have been extensively studied as an early diagnostic and prognostic markers in rheumatoid arthritis (RA), however there is little data available on the role of anti-MCV in Juvenile idiopathic arthritis (JIA).

Objectives: To detect significance of anti-MCV in children with JIA.

Materials and methods: We analysed 41 patients with newly diagnosed JIA (25 RF negative polyartarthritis, 10 oligoarthritis, 5 undifferentiated and 1 psoriatic arthritis). To evaluate disease activity, clinical (disease type, number of active and inactive joints) and laboratory (CRP, ESR, TNF alfa, ANA titer, HLA B 27 antigen) data were recorded. The level of anti-MCV in the sera of JIA patients and 21 controls (healthy children with no family history of any rheumatological disease) was measured using ELISA method (Orgenetic Diagnostica, GbmH, Germany). For statistical analysis we used T test and Mann Whitney test.

Results: Although mean anti-MCV level in the JIA group was higher (3.73 U/ml, range 2–10 U/ml), then in the control group
(3.14 U/ml, range 2–9 U/ml), these results are not statistically significant (p > 0.05). Evaluating disease activity, we found a positive correlation of anti-MCV with CRP (p < 0.05) and serum amyloid A (SAA) (p < 0.01) level. SAA has a positive predictive value for anti-MCV.

**Conclusion:** Anti-MCV can’t serve as an early JIA diagnosing marker. There is a direct correlation between anti-MCV level and acute inflammatory markers and anti-MCV can be used as a disease activity marker.

**References**

**P68**

Etanercept therapy in JIA: impact on the need for intra-articular steroid injections
CE Pain, AG Cleary and Heath Jill
Royal Liverpool Children’s Hospital, Liverpool, UK

**Pediatric Rheumatology 2008, 6(Suppl 1):P68**

**Background:** In the UK etanercept is licensed for use in children with JIA age 4–17 years with active polyarticular disease which has not fully responded to or the child has been intolerant to methotrexate [1]. Studies have shown that the annual cost of treatment with the addition of etanercept is only slightly higher than prior costs because of reduced inpatient and outpatient costs of treatment with the addition of etanercept is only slightly higher than prior costs because of reduced inpatient and outpatient visits, reduction in need for other treatments and reduction in loss of parental earnings [2]. The aim of this pilot study is to confirm that the cost of etanercept in a UK cohort is off-set by the reduction in intra-articular steroid injections.

**Materials and methods:** A pilot study was undertaken by random selection of 18 cases from the local etanercept database. The following information was obtained by case note analysis: age, sex, ILAR classification and joint injection episodes for 12 months pre and post commencement of etanercept.

**Results:** The mean age at start date of etanercept was 9.3 years (range was 2.4 years to 16 years). 14 (78%) were girls and 42 (22%) were boys. The diagnosis was polyarticular (n = 7), extended oligoarticular (n = 8), persistent oligoarticular (n = 1), enthesitis related (n = 1) and unclassified (n = 1). Pre etanercept there were 25 joint injection episodes in 15 patients and 9 episodes post-etanercept, representing a reduction of 64%.

**Conclusion:** This pilot study showed a reduction in the need for intra-articular steroid injections post etanercept. We are extending this analysis to our entire cohort and calculating the cost implications.

**References**

**P69**

The role of antibodies to mutated citrullinated vimentin (anti-MCV) in juvenile idiopathic arthritis patients
L Lamot1, A Tesija Kuna2, M Zirovic2, AM Simundic2, E Topic2 and M Harjacek1
1Children’s Hospital Zagreb, Zagreb, Croatia
2Clinical Institute of Chemistry School of Medicine University of Zagreb, Sestre milosrdnice University Hospital, Zagreb, Croatia

**Pediatric Rheumatology 2008, 6(Suppl 1):P69**

**Background:** Anti-MCV antibodies (Ab) have high sensitivity and prognostic value in patients with RA. We attempt to correlate positive anti-MCV Ab in different subtypes of JIA patients with six core outcome variables.

**Patients and methods:** Anti-MCV Ab and Anti-CCP Ab were tested by ELISA (Orgentec, Germany) in sera from 57 JIA, and 14 control patients (12 patients with SLE, 1 with MCTD and 1 with synovial cyst). (16 boys, 41 girls). The mean age was 11.2 years (range 2.5–18.0), and mean disease duration was 3.4 years (SD ± 2.9). Cut off value ≥ 20 U/mL was considered positive.

**Results:** Positive anti-MCV Ab were detected in only 3/58 (5.2%) JIA patients, and were significantly elevated in two RF positive polyarthritis patients, and slightly elevated in 1/19 (5.3%) patients with enthesitis-related arthritis (ErA). Among all patients, anti-CCP Ab were positive only in one anti-MCV positive polyarticular JIA patient. Anti-MCV and RF positivity correlated statistically (r = 0.504, P = 0.028) in ErA, while no association between anti-MCV Ab and six core outcome variables was observed in this, or other JIA subtypes. Unexpectedly, anti-MCV was detected in 3/12 (25%) SLE patients (2 low positive and 1 significantly positive), and in 1 patient with MCTD. All of these patients were both RF and anti-CCP negative.

**Conclusion:** In contrast to RA, anti-MCV antibodies are not specific for JIA. However, within JIA patients, significantly elevated levels are almost exclusively found in two RF positive, polyarticular patients.

**References**

**P70**

Thalidomide: efficacy and side effects in juvenile idiopathic arthritis (JIA)
MG Alpigiani1, Doria Lamba L2, M Haupt1, A Calcagno1, E Poggi1, P Salvati1 and R Lorini1
1Institute G. Gaslini, Department of Pediatrics, University of Genova, Genova, Liguria, Italy
2Institute G. Gaslini, Pediatric Neuropsychiatry Unit, University of Genova, Genova, Liguria, Italy
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, 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.

Results: Our patient, boy, 19 years old, 63.5 kg (50 centile), 161 cm, (3 centile), 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 3 years of thalidomide suspension, no acute phases of JIA were observed and an electrophysiological improvement of PN was confirmed.

Conclusion: 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]. A regular follow-up every 3 months is necessary to identify and monitor possible side effects.

Reference

P71
Rituximab in ANA positive polyarticular juvenile idiopathic arthritis (JIA) with uveitis
EM Baildam and S Saladi
Royal Liverpool Children's Hospital, Mersey, UK

Pediatric Rheumatology 2008, 6(Suppl 1):P71

We report the case of a 15 year old girl with an 8 year history of difficult to control polyarticular ANA +ve, RF -ve, JIA with severe right sided uveitis treated with Rituximab based on the NICE approved regime for adult rheumatoid arthritis. She presented at the age of 7 years with a 6 week history of painful arthritis involving both ankles, knees, left elbow and left middle PIP joints. Subsequently there was progression to include wrists, TMJs, with erosive disease in both hips and ankles, and intermittent wheelchair use. She was treated with 15–20 mg/m2 of Methotrexate, tried on full dose Etanercept for 12 months, then Infliximab for 6 months, followed by Adalimumab for 6 months. Ciclosporine was added for a 3 DMARD approach but stopped due to hypertension. Throughout she always required additional multiple intra-articular steroid injections and methylenpridinolone infusions (and topical Pred Forte eye drops) to maintain her in reasonable remission. After much consideration she was treated with Rituximab 1 gm by intravenous infusion repeated 2 weeks later and sub-cutaneous methotrexate continued. Since then she has remained in arthritis free remission for 7 months but her uveitis is unchanged in severity. CHAQ scores fell from 1.5 pre-treatment to 0.4 post treatment and active joint counts fell from 5 to 0. Rituximab may be useful in polyarticular JIA resistant to anti-TNF therapy and we recommend a drug trial for this small group of patients.

References
2. TA126 Rheumatoid arthritis (refractory) – rituximab: Guidance NICE 22.08.07.

P72
Features of enthesitis related arthritis in Turkish children
K Akkus, N Aktay Ayaz, L Ozcanlar, E Demirkaya, R Topaloglu, A Bakkaloglu and S Ozen
Hacettepe University Medical Faculty, Ankara, Turkey

Pediatric Rheumatology 2008, 6(Suppl 1):P72

Background: In the ILAR criteria the category enthesitis related arthritis (ERA) best describes juvenile ankylosing spondylitis.

Aim: To evaluate the features of patients who met the ERA criteria in an eastern European background.

Patients and methods: Forty-five patients with ERA were enrolled to the study. Clinical data and laboratory data were assessed. Ultrasonographic examination was performed in 36 patients.

Results: There were 4 female and 41 male patients. Mean age of the patients was 14.1 ± 2.31 years. Mean age of the diagnosis was 12, 6 ± 2, 21 years. Arthritis was present in 97% and median number of swollen joints was 1. Sacroileitis was present in 2/3 of the patients. In 68.9% of the patients HLA B27 was positive and 55.6% of the patients had elevated acute phase response. MEVF mutations were present in nine. Uveitis was present in 8.9%. Family history was present in 26.7%. Enthesitis was reported in 42.2% during physical examination. Ultrasonographic evaluation showed enthesis and synovial effusion in half of these patients. In only one of these the physical examination had missed the enthesis. Furthermore tendinitis and bursitis was detected in 11.1% and salazopyrin (71.1%) were the first choice of treatment. Furthermore tendinitis and bursitis was detected in 11.1% and salazopyrin (71.1%) were the first choice of treatment.

Conclusion: In our population HLA-B27 was less frequent and In the ILAR criteria the category enthesitis related arthritis (ERA) best describes juvenile ankylosing spondylitis. In our population HLA-B27 was less frequent and In the ILAR criteria the category enthesitis related arthritis (ERA) best describes juvenile ankylosing spondylitis. In our population HLA-B27 was less frequent and 13.9%, respectively. Nonsteroid anti-inflammatory drugs (97%) and 13.9%, respectively. Nonsteroid anti-inflammatory drugs (97%) and in Turkish children.

P73
Juvenile idiopathic arthritis (JIA) and early diagnosis of temporomandibular joint (TMJ) disorders
MG Alpigiani1, F Baldi1, A Calcagno1, P Salvati1, R Servetto2 and R Lorini1
1Institute G. Gaslini, Department of Pediatrics, University of Genova, Genova, Italy

Pediatric Rheumatology 2008, 6(Suppl 1):P73

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.

Results: Our patient, boy, 19 years old, 63.5 kg (50 centile), 161 cm, (3 centile), 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 3 years of thalidomide suspension, no acute phases of JIA were observed and an electrophysiological improvement of PN was confirmed.

Conclusion: 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]. A regular follow-up every 3 months is necessary to identify and monitor possible side effects.

Reference
P74 Clinical significance of anti-cyclic citrullinated peptide antibodies in patients with juvenile rheumatoid arthritis

Li Bo, Ye Zhizho, Guo Fenlia and Li Jianso
Department of Rheumatology, Xiangmihu Branch of Shenzhen Fourth People’s Hospital, Shenzhen, Guangdong 518040, PR China

Pediatric Rheumatology 2008, 6(Suppl 1):P74

Background: Anti-cyclic citrullinated peptide antibodies (anti-CCP Abs) are considered to be specific for rheumatoid arthritis (RA), but there are few data on anti-CCP Abs and its relationship with the disease activity in patients with juvenile rheumatoid arthritis (JRA). The aim of this study was to explore the sensitivity and specificity of anti-CCP Abs in JRA.

Materials and methods: Serum samples obtained from 37 JRA patients (33 girls and 4 boys, with a mean age of 12.31 ± 3.29 years) and 20 healthy controls (matched for age and sex ratio with JRA patients) were assayed for anti-CCP Abs using ELISA method. The relationship between anti-CCP Abs and disease activity were also analyzed.

Results: Prevalence of anti-CCP Abs was 8.1% (3/37) in JRA patients. In 20 normal subjects, no one was found anti-CCP Abs positive. The sensitivity of anti-CCP Abs was 8.1%, the specificity was 100%. Disease activity score (DAS28) showed no significant difference between anti-CCP Abs-positive group and anti-CCP Abs-negative group.

Conclusion: Prevalence of anti-CCP Abs was very low in patients with JIA. It was not very helpful for diagnosis of JIA and estimating its disease activity. Therefore it is not necessary for anti-CCP Abs be tested routinely in patients with JIA.

P75 Collaboration in long term follow-up of juvenile idiopathic arthritis

JP Larbre, A Duquesne, D Gheta, C Rambaud-Lequin, R Cimaz, P Cochat and G Llorca
Hospices Civils de Lyon, Lyon, France

Pediatric Rheumatology 2008, 6(Suppl 1):P75

Objective: Since many patients with juvenile idiopathic arthritis (JIA) are lost to follow-up in adulthood, we have started a transition clinic with further follow-up, in order to assess the outcome of adults who had JIA during childhood and who still have active inflammatory arthritis.

Methods: 18 patients (13 female, 5 male) seen since the year 1998 and regularly followed at the rheumatology clinic are included.

Results: The mean age is 29 years; the mean duration of disease is 22 years. 8 were polyarticular in onset (all rheumatoid factor negative): joint erosions are noted in 4, hip replacement in 2, amyloidosis in 1 (renal graft); 5 are on methotrexate, 3 on etanercept; functional impairment is evident in 1/8, seven are employed.

Conclusion: Studies of the outcome of JIA at adult age with persistent inflammatory symptoms are few. This cohort emphasizes the need of prolonged treatment with methotrexate and anti TNF in cases of active disease. However, overall prognosis looks relatively good in term of work ability.

P76 Adalimumab and severe uveitis in juvenile idiopathic arthritis (JIA) therapy

MG Alpigiani1, A Çalcagno1, R De Marco2, M Haupt1, P Salvati1, E Poggi1 and R Lorini1
1Institute G. Gaslini, Department of Pediatrics, University of Genova, Genova, Liguria, Italy
2Institute G. Gaslini, Department of Ophthalmology, University of Genova, Genova, Liguria, Italy

Pediatric Rheumatology 2008, 6(Suppl 1):P76

Background: Chronic anterior uveitis in JIA can be severe and common immunosuppressive therapies may not be sufficient to control uveitis. Concerning biological drugs, Enbrel is usually ineffective, Infliximab is partially effective and is frequently associated with side effects requiring drug suspension, while Adalimumab, a TNF competitor, can be successful.

Methods: We report on a girl aged 17 years, affected since one year by a severe form of polyarticular JIA. She received immunosuppressive therapy (Methotrexate, Azathioprine, etc.), associated with oral steroids, with no articular benefit.

Results: 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 with visus reduction. After one
year, Infliximab was suspended because of an adverse reaction (dyspnea and rash) and Adalimumab (0.7 mg/kg subcutaneous/14 days) associated with Methotrexate was started, with no side effects. Fourteen months later there are no flare for uveitis and/or arthritis. Following SUN criteria [1] we demonstrated ocular clinical improvement, not withstanding the presence of signs of cataract and glaucoma.

**Conclusion:** During the last ten years, biological drugs have been really useful to improve JIA outcome. In 2006 Biester S et al [2] showed Adalimumab efficacy in controlling arthritis and uveitis, with acceptable side effects, but further research is needed.

**References**

**P77**
**Time of onset of iridocyclitis (IC) in children with juvenile idiopathic arthritis (JIA)**
S Verazza1, M Allegra1, B Lattanzi1, S Dalpra1, S Magni-Manzonii2, A Pistorio1, S Oliveira2, E Castell2, O Arguedas3, A Martinì and A Ravelli1
1IRCCS G. Gaslini, Genoa, Italy
2Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil
3Hospital General de Ninos P. Elizalde, Buenos Aires, Argentina
4Hospital Nacional de Ninos Herrera, San José, Costa Rica
5IRCSS Pol. San Matteo, Pavia, Italy

*Pediatric Rheumatology* 2008, 6(Suppl 1):P77

**Background:** IC is one of the most important extra-articular complications of JIA. However, little information exists on the time of onset of IC during the disease course.

**Objective:** To evaluate the frequency of IC onset over time in JIA patients who developed this complication.

**Methods:** 1050 JIA patients seen between 1985 and 2007 were identified. 172 patients (16.4%) had IC. 6 patients with psoriatic arthritis, 1 (0.6%) systemic arthritis. Of the 160 patients, 108 (67.5%) had oligoarthritis, 36 (22.5%) RF-negative polyarthritis, 9 (5.6%) undifferentiated arthritis, 6 (3.8%) psoriatic arthritis, 1 (0.6%) systemic arthritis.

Of the 158 patients who had ANA tested, 144 (91.1%) were positive (1:160), 8 (5.1%) low-positive (≤ 1:80) or doubtful, 6 (3.8%) negative.

**Results:** The cumulative proportion of patients who developed IC over time is shown in figure 1 and table I.

**Figure 1 (abstract P77)**

![](image)

**Table 1 (abstract P77)**

<table>
<thead>
<tr>
<th>Time (years)</th>
<th>0–1</th>
<th>1–2</th>
<th>2–3</th>
<th>3–4</th>
<th>4–5</th>
<th>5–6</th>
<th>6–7</th>
<th>7–8</th>
<th>8–14</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cumulative%</td>
<td>48.1</td>
<td>68.1</td>
<td>78.7</td>
<td>84.3</td>
<td>87.5</td>
<td>91.9</td>
<td>94.4</td>
<td>96.9</td>
<td>100</td>
</tr>
</tbody>
</table>

**Conclusion:** Of 160 patients who had IC, half developed this complication in the first year, 2/3 in the first 2 years, 4/5 in the first 3 years, and only 5.6% after 7 years. This suggests that risk of IC onset is greatest in the first 3 years of disease and that the optimal time for reducing the frequency of ophthalmologic visits is 7 years after onset.

**P78**
**Clinical and articular presentation of juvenile idiopathic arthritis**
R Ravichandran, N Vasanthy, Panchapakesa Rajendran C, J Sasikala, S Rukmangatharajan, Seeralia Boopathy K and R Kirthi
*Madras Medical College, Chennai, Tamilnadu, India*

*Pediatric Rheumatology* 2008, 6(Suppl 1):P78

**Aim:** To analyse the clinical and articular features of children with juvenile idiopathic arthritis (JIA) at the time of presentation as per ILAR criteria.

**Materials and methods:** 84 children with JIA who attended between January 2007 – December 2007, fulfilling the ILAR criteria were analysed prospectively.

**Results:** Male-44. Female-40. Age distribution 0–5 yrs-6, 6–10 yrs-19, 11–16 yrs-37, above 17 yrs-25 children were less than 10 yrs.

Sex distribution shows 21 males in ERA, 18 females in polyarticular and 13 males, 14 females in systemic onset.

JIA subtypes shows systemic onset 27(32%), Oligoarticular persistent 9(11%), extended 1(1%), Poly articular RF negative 10 (12%), RF positive 12(14%), Enthesitis related arthritis 23 (27%) and Psoriatic arthritis 2(2%).

Joints commonly affected are knee 119(71%), ankle 92(55%), wrist 70(42%), PIP 56(33%), elbow 54(32%), MCP 48(29%), shoulder 32(19%), MTP 32(19%), hip 26 (15%), sacroiliac joints 25(15%), cervical spine 16(19%), DIP 6(4%) and TMJ 2(1%).

**Conclusion:** Systemic arthritis is the commonest subtype in our study.

Females were commonly affected in poly articular, males in ERA and both sexes equally affected in systemic onset.

Majority of the children were above 10 yrs.

Joints commonly affected are knee, ankle, wrist, PIP and elbow.

Less commonly affected are DIP and TMJ joints.

**P79**
**Efficacy of oral versus subcutaneous methotrexate in children with juvenile idiopathic arthritis**
N Tzaribachev1, S Hahn7, M Eichner7, J Schedel8, A Brandt8 and J Kuenemmerle-Deschner1
1University Children’s Hospital, Pediatric Rheumatology, Tuebingen, Germany
2University of Tuebingen, Medical Biometry, Tuebingen, Germany
3University Medical Clinic, Interdisciplinary Rheumatology-INDIRA, Tuebingen, Germany

The cumulative proportion of patients who developed IC before arthritis onset and 2 patients in whom signs of cataract and glaucoma.
**P79**

**Background:** Therapy of juvenile idiopathic arthritis (JIA) is based on, among various other treatments, methotrexate (MTX). Pharmacokinetic data indicate a lower drug resorption rate when applied orally (po) versus subcutaneous (sc) administration.

**Objectives:** We aimed to compare the effects of po and sc applied MTX on the JIA-disease course.

**Methods:** According to MTX-administration route, children were divided into four groups: sc, po, switching from po to sc and from sc to po. Based on joint counts (pain, swelling and limited range of motion), patient’s and physician’s visual analogue scale for disease activity (VAS) and erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP), a combined overall disease activity score (entitled Co-score, CoS) was generated for each patient. Statistically paired T-test and ANCOVA were applied.

**Results:** For the sc group, the ESR-CoS improved on average by 2.24 units (CI: 1.57–2.91; p < 0.0001) and the CRP-CoS by 1.61 units (CI: 0.87–2.35; p < 0.0002). In the po group, the ESR-CoS improved by 2.37 units (CI: 1.7–3.04; p < 0.0001) and the CRP-CoS by 2.16 units (CI: 1.48–2.85; p < 0.0001). In the po to sc switcher group, both scores showed insignificant improvement during the po phase (p > 0.05). After the change to sc administration, both scores significantly improved (p < 0.0007 and p < 0.0005 respectively). In the sc to po group, data from only four patients were analyzable and therefore, statistically irrelevant.

**Conclusion:** Considering data from adult rheumatoid arthritis studies and MTX pharmacokinetics, our results support to some extent sc MTX-administration in children, at least at treatment initiation, emphasizing the need of prospective investigations.

**References**

---

**P81**

**Enthesitis related arthritis as the early stage of juvenile spondyloarthritis**

L Ruthkowska-Sak, E Musiej-Nowakowska, M Wierzbowska, I Slowinska and B Lisowska

**Institute of Rheumatology, Warsaw, Poland**

**Background:** Peripheral enthesitis related arthritis (ERA) are the major clinical features in the juvenile onset spondyloarthropathies (JSpA).

**Objectives:** To analyze the clinical characteristic of a population of patients with JSpA who presented ERA as their only clinical symptoms as the onset of the disease.

**Methods:** We have studied a group of 80 children diagnosed with JSpA following the ILAR criteria, selecting only those who expressed ERA as initial symptoms of the disease.

**Results:** 41% patients with a mean age of 13 years (range 6–18 years) proved to have ERA. The mean disease duration was 4.1 years (range 0.2–9 years). They had enthesitis most frequent in Achilles tendon and plantar fascia – 33% patients; dactylitis – 30% patients and enthesitis of the site of attachment of the patellar tendon to the tibial tubercle – 6%.

76.8% patients presented arthritis involving peripheral joints and additionally 6.6% of them presented axial skeleton distribution.

**Conclusion:** ERA are most frequently and characteristic initial clinical features of spondyloarthriti.

---

**P80**

**Bone mineral density in patients with Juvenile Rheumatoid Arthritis**

Ye Zhizho, Li Bo, Li Jianso, Guo Fenlia and Zhuang Junhan

**Department of Rheumatology, Xiangmihu Branch of Shenzhen Fourth People’s Hospital, Shenzhen, Guangdong 518040, PR China**

**Pediatric Rheumatology** 2008, 6(Suppl 1):P80

**Background:** There is increasing in bone metabolism in patients with rheumatic disorders, but there are few data on bone mineral density (BMD) and its relationship with disease-related variables in patients with juvenile rheumatoid arthritis (JRA). The aim of this study was to investigate BMD in Chinese patients with JRA and to evaluate its relationship with disease-related variables.

**Materials and methods:** BMD indexes were tested by Osteospace quantitative ultrasound instruments at calcaneus. Clinical and serologic manifestations of patients with JRA were tested and recorded.

**Results:** There were 37 patients with JRA (33 girls and 4 boys, with a mean age of 12.31 ± 3.29 years) and 20 healthy controls (matched for age and sex ratio with JRA patients) were consecutively recruited in this study between 2005 and 2007. BMD of the calcaneus in the patients with JRA was significantly lower than that in healthy controls (0.71 ± 0.13 g/cm² vs (0.97 ± 0.18) g/cm², P < 0.05). Although with the increasing of cumulative dose of steroids, BMD decreased, but there was no significant correlation between cumulative dose of steroids and BMD.

**Conclusion:** BMD was significantly lower in JRA patients compared with healthy controls. Although cumulative dose of steroids and disease appeared to have some influence on BMD, none disease-related variables were independently correlated with BMD.

---

**P82**

**The using of arthroscopy and synovial biopsy in chronic knee monoarthritis in children**

IA Chicova, VV Avramenko and MM Kostik

**State Pediatric Medical Academy, Saint-Petersburg, Russian Federation**

**Pediatric Rheumatology** 2008, 6(Suppl 1):P82

The knee damage in children may be a sign of many diseases. They include bone and joint infections, neoplastic disorders, trauma and arthritis. The aim of our study was to detect diseases which causing with knee damage and to reveal arthropscopic and synovial histological changes.

We included in our study 29 children with chronic knee monoarthritis (CKMA), 15 girls and 14 boys with duration knee monoarthritis symptoms > 6 weeks. Most of the patients were...
examined with arthrosonography and MRI. Arthroscopy with synovial biopsy was performed on 10 children (2 with tuberculosis infection and 8 with CKMA unknown origin).

Five CKMA boys transformed in juvenile spondloarthropathy (3 had psoriatic arthritis). Juvenile rheumatoid arthritis was diagnosed in 6 children (4 F: 2 M), all girls were ANA-positive and developed oligoarthritis and one also had uveitis. There were 3 cases of tuberculosis arthritis without primary lung damage. Another cases included knee osteoarthritis, Borrelia burgdorferi infection, angiodyplasia of knee, posttraumatic arthritis with meniscus damage, osteochondritis dissecans and Hoffa disease.

The largest group consisted of children with chronic villous proliferate synovitis (6 F: 2 M) unknown origin was revealed by arthroscopy and synovial biopsy. Chlamydia infection was detected in synovial fluid and membrane in 2 children.

Synovial histology was determined as focal hypertrophy of synovial membrane with mononuclear cell infiltration in half patients as signs of neoangiogenesis in another part. This form of CKMA was torpid.

CKMA is very heterogenous; some of them need in arthroscopy with synovial biopsy.

P83 Ocular threat in juvenile idiopathic arthritis (JIA)
I Marville1,2,3, C Terada1, P Quartier1, Bui Quoc E1, B Bodaghi1 and A Prieur1
1Pediatric Rheumatology, Hospital Necker Enfants Malades, Paris, France
2Ophtalmology, Hopital La Pitié, Paris, France
3Ophtalmology, Hopital Necker Enfants Malades, Paris, France

Pediatric Rheumatology 2008, 6(Suppl 1):P83

Background: Chronic Uveitis (CU) is a severe complication of JIA. We reviewed the clinical course of CU in our JIA patients.


Results: Seventy five children out of 715 children followed for JIA presented CU, 69 medical records were analysed. No CU was detected in systemic, RF positive and psoriatic JIA. Sixty CU were observed in 352 oligoarticular JIA subtype, 7 in 122 polyarticular and 2 in ERA JIA subtype. 70% of CU were bilateral. Seventy eight percent of CU were diagnosed at systematic examination. CU was anterior in 41 patients and a panuveitis was diagnosed in 18. Complications were observed in 42 patients (61%), and in 29 of them, complications were present at diagnosis. Synechia, hyperpression and band keratopathy were the most frequent complications. Marked visual loss (< 5/10) was present at first eye examination in 20 children (29%) (50% were bilateral cases). At last examination, visual loss was present in 14 children (20%), and 3 children (4%) were blind. Medical treatment consisted in local steroids, mydriatics, systemic corticosteroids, methotrexate and anti-TNF drugs. Twenty-one children underwent surgical treatment. At final examination, only 11 children had presented a favourable outcome. An unfavourable outcome, defined as the need of multiple surgical episodes, was observed in 21 patients. A chronic course with flares is still present in the other 37 patients.

Conclusion: CU is a severe complication of JIA. Eye examination is extremely important, particularly in oligo/polyarticular subtype with ANA and must be done systematically in all children as soon as JIA is suspected.

P84 Use of Adalimumab in young patients with chronic uveitis in whom infliximab loses its efficacy
TG Giani, GS Simonini, FF Fantini, RC Caputo, CDL de Libero, GC Colarusso and RC Cimaz
A. Meyer Children Hospital Department of Pediatrics, University of Florence, Florence, Italy

Pediatric Rheumatology 2008, 6(Suppl 1):P84

Background: Adalimumab has been shown to be efficacious in childhood uveitis.

Materials and methods: We have switched to Adalimumab treatment eight patients with chronic uveitis in whom, after 15–39 months of Infliximab infusions, recurrences of eye inflammations were increasing. Four were males, four females; in three cases uveitis was associated with JIA, in one with early-onset sarcoidosis, in one with Behçet disease, while three patients suffered from idiopathic uveitis. Adalimumab was administered subcutaneously at the dosage of 24 mg/sq. meter every 2 weeks. Up to now (April 2008) patients received from 18 to 24 injections each.

Results: At the onset of Adalimumab treatment in four patients uveitis was active. One of them rapidly improved already after the first injections, while another two progressively recovered over the subsequent injections; in the fourth, after an initial, partial remission, frequent flares were observed and Adalimumab was discontinued. In the four patients who were in remission at the onset of Adalimumab, one of them maintained a durable remission, one achieved a remission after 2 flares. One showed worsening activity, and an in another because of persistent inflammation requiring pulses of methylprednisolone, Adalimumab was discontinued. In 3 patients visual acuity has already improved during Adalimumab treatment, while in the remainder 5, either it deteriorated or remained stable.

Conclusion: Our data suggest that Adalimumab may to be effective in children with chronic uveitis even if they previously failed another anti-TNF agent. However, long term follow-up efficacy data still need to be established.

P85 Abatacept treatment improves health-related quality of life, pain, and sleep quality in juvenile idiopathic arthritis patients
N Ruperto1, DJ Lovell2, T Li1, P Quartier1, J Chavez1, C Huemer1, A Kivitz1, F Blanco1, I Foeldvari1, M Hofer1, L Sigal1, A Block3, A Covucci3, A Martini1 and EH Giannini1
1PRINTO, Genoa, Italy
2PRCSG, Cincinnati, OH, USA
3Bristol-Myers Squibb, Princeton, NJ, USA

Pediatric Rheumatology 2008, 6(Suppl 1):P85

Background and purpose: Health-related Quality of Life (HRQOL) in children with juvenile idiopathic arthritis (JIA) is significantly impaired due to pain, joint damage and inflammation. The purpose of this study was to examine the effect of abatacept treatment in JIA patients on HRQOL, pain and sleep quality.
Methods: 190 JIA patients were treated with abatacept for 4 months in an open-label lead-in period (Period A). ACR Pedi 30 responders (n = 123) were then randomized 1:1 to receive abatacept or placebo for up to 6 months in a double-blind withdrawal period (Period B). HRQOL was assessed by the Child Health Questionnaire (CHQ), sleep quality was measured by the Children’s Sleep Habits Questionnaire (CSHQ), and pain by a 0–100 mm VAS. Mean change from baseline in each period was calculated and compared between the treatment groups (in Period B), and the change over time was examined.

Results: At study entry patients had considerably lower HRQOL than the general population. After 4 months of abatacept treatment in Period A, substantial improvements were seen across all patient reported measures. Improvements in CHQ scores were statistically significant in 14 out of 15 health concepts, with the greatest increase in the physical domain. Pain and sleep problems were statistically significantly reduced. At the end of Period B, most abatacept patients maintained or continued these improvements, while placebo patients generally experienced declining HRQOL, increased pain and sleep problems.

Conclusion: Abatacept treatment significantly improved multiple aspects of HRQOL, pain, and sleep quality in JIA patients. Such improvements were prolonged with continued abatacept therapy.

P86
Reduction in missed school days and improvement in parent activity participation in children with juvenile idiopathic arthritis treated with abatacept
N Ruperto1, DJ Lovell2, T Li3, E Paz1, G Horneff1, HI Huppertz1, CJ Deslandre1, K Minden1, M Punaro1, AF Nunez1, L Sigal1, A Block3, A Covucci3, A Martini1 and EH Giannini2
1PRINTO, Genoa, Italy
2PRCSG, Cincinnati, OH, USA
3Bristol-Myers Squibb, Princeton, NJ, USA

Background and purpose: Chronic pain and physical disability from juvenile idiopathic arthritis (JIA) limits patient’s capacity to participate in usual daily activities, and often cause children to miss school and parents to miss work. The purpose of this study was to investigate the change in activity participation in both children with JIA and their parents, following abatacept treatment.

Methods: 190 JIA patients were treated with abatacept for 4 months in an open-label lead-in period (Period A). ACR Pedi 30 responders (n = 123) were then randomized 1:1 to receive abatacept or placebo for 6 months in a double-blind withdrawal period (Period B). Activity participation for the child and the parents were assessed, along with clinical and quality of life (QOL) parameters. Mean change from baseline in each period was analyzed, and the two treatment groups were compared.

Results: During Period A, there was a gradual reduction of missed activity days for both children and parents. In Period B, children randomized to continue abatacept reduced another 1.5 days/month of missed school, compared to an increase of 0.56 days/month from placebo. Parents of abatacept patients maintained their gain in usual activity from Period A, while parents of placebo patients had 1.1 days/month of missed activities. The improvements in activity were consistent with clinical responses and QOL improvements observed.

Conclusion: Abatacept treatment improved patient’s ability to participate in daily activities and parents get back to usual daily activities. This demonstrates real-life tangible benefits to JIA patients as a result of clinical and QOL improvements.

P87
Temporomandibular joint arthritis in patients with juvenile idiopathic arthritis: efficacy of intraarticular corticosteroid injection as measured by MRI and clinical examination
S Schroeder1, E Cannizzaro1, C Kellenberger2, T Peltoniäki1 and RK Saurenmann1
1Rheumatology, University Childrens Hospital, Zurich, Switzerland
2Diagnostic Imaging, University Childrens Hospital, Zurich, Switzerland
3Clinic for Orthodontics and Pediatric Dentistry, University of Zurich, Zurich, Switzerland

Pediatric Rheumatology 2008, 6(Suppl 1):P87

Background: Untreated temporomandibular joint (TMJ) arthritis in children with juvenile idiopathic arthritis (JIA) can lead to disturbed growth of the mandible. Because TMJ arthritis is often asymptomatic the efficacy of intraarticular steroid injections is difficult to assess clinically.

Materials and methods: JIA-patients with active TMJ arthritis on MRI were injected with 5 mg triamcinolone into affected joints. Clinical examination at baseline and after injection and control MRI was performed. A cohort of patients without TMJ inflammation on MRI served as control group for the clinical symptoms.

Results: 21 study patients and 17 control patients were examined. The baseline mean maximal mouth opening was significantly different with 41 mm in study patients compared to 46 mm in controls (p = 0.005). After a median time of 42 days the mean maximal mouth opening increased by 1.8 mm in the study group (p < 0.003) as compared to 0.5 mm in the controls (p = 0.15). Pain on chewing/yawning had resolved in all 5 patients and tenderness in 7/11 TMJs respectively. On follow up MRI 23/36 affected joints showed improvement and 6/36 complete resolution of inflammation.

Conclusion: In our JIA patients with MRI proven active TMJ arthritis intraarticular steroid injection led to resolution of clinical symptoms and significantly improved mouth opening in most patients. However, MRI examination showed only improvement but not complete resolution of inflammation in the majority of patients. Longer follow up is warranted to assess the significance of persistent MRI changes for the mandibular growth in our patients.

P88
Etanercept discontinuation in a cohort of juvenile idiopathic arthritis patients: etanercept inefficacy but not intolerance is associated with oral corticosteroid use
TR Southwood, CL Cummins, C Cotter and J Rahman
University of Birmingham, Birmingham, UK

Pediatric Rheumatology 2008, 6(Suppl 1):P88

The British Society for Paediatric and Adolescent Rheumatology (BSPAR) Biologics Register monitors JIA patients treated with
etanercept ± methotrexate. We report duration of etanercept use and reasons for discontinuation, defined as cessation due to disease control or treatment failure; not including precautionary or temporary drug discontinuation for transient adverse events. Kaplan-Meier survival analysis was conducted with remaining patients censored at five years follow-up.

Results: From 2004–8, 434 etanercept treated JIA patients were enrolled; 68% female, 15.7% systemic arthritis, mean age at starting etanercept 11 years (2–21 years). At initiation of etanercept, 173 (40%) were also being treated with oral corticosteroids (the “steroid+” group). In 846 patient years of follow up, 83/434 patients (19.1%) discontinued etanercept for recorded reasons, 46 of whom (55%) were in the steroid+ group (table 1). Discontinuations were due to treatment inefficacy rather than treatment intolerance in the steroid+ group (p = 0.01). Of the 5 discontinuations due to infection related adverse events, 4 were in the steroid+ group. Using 5 year Kaplan-Meier analysis, 55% of all etanercept treated patients (95% confidence intervals 44.4%–65.6%) had not experienced treatment failure. Discontinuation at 5 years was not associated with initial disease severity by physicians global assessment, systemic arthritis subtype, starting etanercept before age 10, disease onset before age 5, concurrent methotrexate use or chronic anterior uveitis.

P89

Observation of juvenile idiopathic arthritis in children with MEVF gene mutations in Armenia

Khloyan Gayane1,2, RK Saurenmann1, Amaryan Gayane1 and Karibian Alan1

1Arabkir Joint Medical Centre, Institute of Child and Adolescent Health, Yerevan, Armenia
2Centre of Medical Genetics and Primary Health Care, Yerevan, Armenia

Pediatric Rheumatology 2008, 6(Suppl 1):P89

Background: The prevalence of Familial Mediterranean fever (FMF) in Armenian people is very high. Acute recurrent or chronic arthritis are possible manifestations of FMF and differentiation from juvenile idiopathic arthritis (JIA) is important.

Aim: To study the correlation of MEVF mutations with disease susceptibility in patients with JIA.

Methods: Retrospective chart review of all patients with JIA for MEVF mutations and JIA characteristics.

Results: MEVF analysis was available for 44/69 patients, 7/8 with systemic onset(So) JIA and 37/61 with other types of JIA. MEVF mutations were found in 27/44 patients tested (61%). 3/7 patients (43%) with SoJIA had MEVF mutations, all heterozygous. Of the 24/37 patients (65%) with other forms of JIA had confirmed MEVF mutations and 12/24 had typical episodes of FMF. With colchicine in addition to standard JIA treatment FMF episodes resolved but they continue to have refractory arthritis. Of the 12 patients without typical FMF episodes 10 had only arthritis and 2 had rare episodes of thoracic pain in addition to the arthritis. In 9/12 patients (10 with arthritis only and 2 with thoracic pain) a heterozygous MEVF mutation was found, in 1 patient (8%) homozygous M694V and 2 (17%) had compound heterozygous M694V/M680I mutations.

Conclusion: In our Armenian JIA patients 61% had MEVF mutations, more than expected. In a population with a high prevalence of FMF MEVF mutations should be tested in children with JIA even in the absence of typical FMF symptoms as chronic arthritis may be the only symptom of FMF.

P90

Bone mineral density improvement after one year of treatment with etanercept in patients with juvenile idiopathic arthritis

G Susic1, R Stojanovic1, N Damjanov1, J Vojinovic2 and G Vijatov3

1Institute of rheumatology, Belgrade, Serbia
2Clinic of Pediatrics, University Clinical Center, Nis, Serbia
3Institute for Child and Youth Health Care, Novi Sad, Serbia

Pediatric Rheumatology 2008, 6(Suppl 1):P90

Background: Multiple risk factors are playing role in development of osteopenia in JIA. One of the most important is inflammatory nature of disease. Etanercept induces rapid and sustained suppression of JIA disease activity and could have protective effect on bone.

Aim of the study: To assess influence of etanercept on bone mineral density (BMD) in patients with JIA.

Patients and methods: In prospective study of 37 JIA pts (26 F, 11 M), mean age 16.3 yrs. with polyarticular course, we have assessed BMD and bone mineral content (BMC) by dual x-ray absorptiometry on the lumbar spine (L2–L4) before and one or two years (in 13 pts) after introduction of etanercept. Results of osteodensitometry assessment (mean value) are presented on table 1.

After the first year of treatment we have noticed significant improvement of all osteodensitometric values. Mean value difference for BMD, compare to baseline was 7.1% (p < 0.001) for Z score 17.76% (p = 0.002), for BMC 13.13% (p < 0.001) and for BMDvol 5% (p < 0.001). Bone mineral status continued to increase during the second years of treatment as well (13 pts) (p < 0.001).

Conclusion: Our results demonstrated efficacy of etanercept, as TNF blocker, in improving bone mineral status and precluding development of osteoporosis in children with JIA. This beneficial effect on bone was demonstrated on the end of second year of treatment.

Table 1 (abstract P90)

<table>
<thead>
<tr>
<th>variables</th>
<th>baseline</th>
<th>after 1st year</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMD (g/cm²)</td>
<td>0.909</td>
<td>0.965</td>
</tr>
<tr>
<td>Z (SD)</td>
<td>-1.2</td>
<td>-0.93</td>
</tr>
<tr>
<td>BMC (g/cm)</td>
<td>32.68</td>
<td>36.08</td>
</tr>
<tr>
<td>BMDvol (g/cm³)</td>
<td>0.314</td>
<td>0.329</td>
</tr>
</tbody>
</table>
P91
Spinal mobility: the pattern in a population of children between 5–16 years old, in Bogotá Colombia
P Guarnizo-Zuccardi, M Rodríguez and D Suarez
Clinica Infantil Colsubsidio, Bogota, Colombia
Pediatric Rheumatology 2008, 6(Suppl 1):P91

Background: Shobert test is a useful tool for evaluation of spinal mobility. Normative values of spinal mobility have not been established for Latin-American children.

Objective: To define the ranges of normal anterior spinal flexion in children between 5–16 years old in a Colombian population.

Methods: 502 were stratified by sex and age in Ciudadela Colsubsidio School in Bogotá, to evaluate anterior spinal flexion by shobert test. Measurements were repeated three times by child, mean was calculated for analysis. Children with spinal and chronic diseases were excluded. Means and standard deviations for shobert test were calculated for each group. ANOVA with sex and age as between-subject factors was used to examine mean differences across de spinal mobility measures.

Results: Shobert test mean was 6.3 cm and 6.5 cm for girls and boys respectively. No significant statistical differences were found between ages (5–16 y). Analysis by gender showed a significant statistical differences only in the seven years old group (p = 0.01).

Conclusion: Anterior spinal flexion mean by shobert test was similar across the twelve groups studied; the differences found in the 7 years old group is not considered to have a clinical significance. There’s no need of normality charts by age and sex for this population. Anterior spinal flexion mean was lower in this population than in other population studied.

References

P92
Temporomandibular joint involvement in children with juvenile idiopathic arthritis
E Cannizzaro1, S Schroeder1, I Bolt1, L Müller2, Ch Kellenberger3 and T Saurenmann1
1Rheumatology, University Children’s Hospital Zurich, Zurich, Switzerland
2Clinic for Orthodontics and Pediatric Dentistry, University of Zurich, Zurich, Switzerland
3Diagnostic Imaging, University Children’s Hospital Zurich, Zurich, Switzerland
Pediatric Rheumatology 2008, 6(Suppl 1):P92

Background: Temporomandibular joint (TMJ) arthritis can lead to severe mandibular growth disturbances in children with juvenile idiopathic arthritis (JIA). The study aim was to determine the rate of TMJ involvement in our JIA patients and find factors associated with TMJ arthritis.

Materials and methods: Retrospective chart review of all JIA patients. Clinical criteria of TMJ arthritis included: presence of mandibular asymmetry, retrognathia, reduced maximal mouth opening (< 40 mm), asymmetric mouth opening and/or tenderness of the TMJ. Radiologic criteria (orthopantogramm and/or MRI) were synovial membrane and/or bone contrast enhancement and/or destruction of the mandibular head.

Results: After a mean follow up time of 3.95 years 81/226 patients had developed TMJ arthritis. The rate differed among JIA subtypes (p = 0.0016) with 61% in extended oligoarticular, 50% in polyarticular RF negative, 40% in psoriatic, 36% in systemic, 33% in polyarticular RF positive, 30% in persistent oligoarticular, 16% in ERA and 11% in unclassified JIA. Risk factors included: female sex (p = 0.02), younger age at onset of JIA (p = 0.016), a higher mean number of active joints at each visit (p = 0.033) and involvement of joints of the upper extremity (p < 0.0001). Uveitis, ANA or RF positivity, ESR or CRP were not correlated with TMJ involvement. HLA B27 had a statistically significant inverse correlation with TMJ involvement (p = 0.011).

Conclusion: The rate of TMJ involvement was 36%. Girls, patients with polyarticular joint involvement, with younger age at onset and with involvement of upper extremity joints had a higher risk for TMJ arthritis. Presence of HLA B27 seemed to be protective.

P93
The use of Etanercept and Adalimumab in the management of JIA: a 5-year follow-up study
M Trachana1, P Pratsidou-Gertsi1, F Kanakoudi-Tsakalidou1, C Diaf1, G Pardalos1 and M Badouraki2
1Pediatric Immunology and Rheumatology Referral Center, First Department of Pediatrics, Aristotle University, Thessaloniki, Greece
2Department of Radiology, Ippokration General Hospital, Thessaloniki, Greece
Pediatric Rheumatology 2008, 6(Suppl 1):P93

Aim: To evaluate the 5-yr use of 2 anti-TNF preparations, Etanercept (ET) and Adalimumab (AD), in children with refractory to conventional treatment JIA.

Patients and methods: The safety and efficacy of ET and AD were assessed in 46 children aged 2–16 yrs. 32/46 received ET and 14 AD together with a DMARD (45/46), mainly methotrexate, and prednisone (22/46). All pts were assessed clinically, cardiologicaly, hematologicaly, biochemicaly and immunologically pre- and every 3–6 mo port-treatment. Efficacy was assessed by the application of ACRped criteria.

Results: Safety: Common respiratory tract infections were recorded in 28% of pts (10/34 under ET and 3/14 under AD). Serious infections were recorded in 4.7% (1 ET, 1 AD). No other serious adverse effects were recorded. Efficacy: ACRped 50–70. 1st yr: 88% of the ET and 68% of the AD group. 2nd yr: 81% of the ET and 66.7% of the AD group. 3rd yr: 83% of the ET and 100% of the AD group. During the 5-yr period, 11/46 pts (28%) switched from ET to AD or vice versa. Of all patients, 32.5% discontinued anti-TNF treatment due to remission and 52.2% had a satisfactory response (ACRped 50–70), while 8.7% had a poor response either to ET or AD.

Conclusion: Most of the patients with refractory to conventional treatment JIA respond satisfactorily to the long-term administration of anti-TNFs. The first 2 years are critical to predict a good and sustained response. Although serious
infections are rare, a systematic vigilance is warranted in order to avoid fatal outcomes.

P94
Quantitative assessment of synovitis in juvenile idiopathic arthritis using Dynamic Contrast-Enhanced Magnetic Resonance Imaging
C Malattia1, MB Damasio1, C Basso2, A Verri2, F Magnaguagno1, A Parodi1, S Viola1, A Ravelli1, P Tomà1 and A Martini1
1Istituto G. Gaslini, Genova, Italy
2DISI, Università di Genova, Genova, Italy

Objective: To evaluate the capability and reliability of Dynamic Contrast-Enhanced Magnetic Resonance Imaging (DCE-MRI) in the assessment of disease activity in juvenile idiopathic arthritis (JIA).

Methods: In 22 JIA patients 12 wrists and 10 hips were studied with DCE-MRI. A 3D FFE Dynamic sequence was acquired after contrast injection. Two readers delineated independently a region of interest (ROI) in the area of maximal synovial enhancement. Enhancement curves were obtained plotting pixel intensity against time from the ROIs. Maximum level of synovial enhancement (ME), maximum rate of enhancement (MV) and intensity against time from the ROIs. Maximum level of synovial enhancement. Enhancement curves were obtained plotting pixel intensity against time from the ROIs. Maximum level of synovial enhancement (ME), maximum rate of enhancement (MV) and rate of early enhancement (REE) were obtained from the curves. Correlations with clinical parameters of disease activity and with static MRI synovitis score were investigated.

Results: The inter-reader agreement assessed by intra-class correlation coefficient (ICC) for ME (ICC = 0.98), MV (ICC = 0.97) and REE (ICC = 0.84) was excellent. ME and MV, as well as clinical parameters of disease activity, were significantly higher in patients with wrist active arthritis than in those with hip disease (p < 0.0001) and p < 0.01 respectively. In patients with wrist arthritis REE was correlated with wrist swelling score (r = 0.72), ESR (r = 0.69), pain assessment scale (r = 0.63) and C-HAQ (r = 0.60). In patients with hip arthritis ME was correlated with the hip limitation of movement score (r = 0.69). Static MRI synovitis score was correlated with MV (r = 0.63) in patients with wrist arthritis and with ME (r = 0.68) in those with hip arthritis.

Conclusion: DCE-MRI represents a promising and reliable method for quantitative assessment of disease activity and with static MRI synovitis score were investigated.

P95
Knee disease in juvenile idiopathic arthritis (JIA): correlation between clinical and ultrasonographic findings
M McCarron1, M Wray1, L Pascoli1, C McAllister1 and M Rooney2
1Rheumatology, Musgrave Park Hospital, Belfast, UK
2Musculoskeletal Research Group, Queen’s University, Belfast, UK

Objective: To evaluate the capability and reliability of Dynamic Contrast-Enhanced Magnetic Resonance Imaging (DCE-MRI) in the assessment of disease activity in juvenile idiopathic arthritis (JIA).

Methods: We are undertaking a five year prospective study of children with newly diagnosed JIA who have knee involvement. Review is three monthly with clinical assessment and US of knee(s) at each visit. Knee swelling is graded 0–4. US scans were performed by an experienced rheumatologist MR using a Sonosite 180 Plus (L38 5–10 MHZ linear transducer) or Esaote MyLab25 scanner (LA523E 7.5–12 MHZ linear transducer). The scans have been scored independently by 2 observers unaware of the clinical findings (graded 0–3).

Results: 48 children have been recruited and to date, 25 have been followed for 2 years. To date 124 scans have been scored for effusions and synovial hypertrophy. There was good correlation between clinical and US scores r = 0.7. In 78 clinically normal knees, 50 had normal US scans, 21 had mild effusions and 7 had moderate effusions. Of the 18 patients with oligoarticular disease, synovial hypertrophy was more marked in the 9 patients who required repeat IA steroid injections.

Conclusion: There was good correlation between clinical and US findings. However 36% of clinically normal knees had evidence of effusion on ultrasound suggesting that ultrasound is indeed more accurate and may be of value in determining disease classification. Detection of disease activity by US, in particular synovial hypertrophy may prove a useful indicator for recurrent disease.

P96
Intra- and interobserver reliability of ultrasonographic cartilage thickness assessments in small and large joint in healthy children
AH Spannow1, E Stenboe1, MP Jensen2 and T Herlin1
1Dept Paediatrics Aarhus University Hospital Skejby, Aarhus, Denmark
2Dept. Rheumatology Aarhus University Hospital, Aarhus, Denmark

Objective: To evaluate the capability and reliability of Dynamic Contrast-Enhanced Magnetic Resonance Imaging (DCE-MRI) in the assessment of disease activity in juvenile idiopathic arthritis (JIA).

Methods: We are undertaking a five year prospective study of children with newly diagnosed JIA who have knee involvement. Review is three monthly with clinical assessment and US of knee(s) at each visit. Knee swelling is graded 0–4. US scans were performed by an experienced rheumatologist MR using a Sonosite 180 Plus (L38 5–10 MHZ linear transducer) or Esaote MyLab25 scanner (LA523E 7.5–12 MHZ linear transducer). The scans have been scored independently by 2 observers unaware of the clinical findings (graded 0–3).

Results: 48 children have been recruited and to date, 25 have been followed for 2 years. To date 124 scans have been scored for effusions and synovial hypertrophy. There was good correlation between clinical and US scores r = 0.7. In 78 clinically normal knees, 50 had normal US scans, 21 had mild effusions and 7 had moderate effusions. Of the 18 patients with oligoarticular disease, synovial hypertrophy was more marked in the 9 patients who required repeat IA steroid injections.

Conclusion: There was good correlation between clinical and US findings. However 36% of clinically normal knees had evidence of effusion on ultrasound suggesting that ultrasound is indeed more accurate and may be of value in determining disease classification. Detection of disease activity by US, in particular synovial hypertrophy may prove a useful indicator for recurrent disease.

P96
Intra- and interobserver reliability of ultrasonographic cartilage thickness assessments in small and large joint in healthy children
AH Spannow1, E Stenboe1, MP Jensen2 and T Herlin1
1Dept Paediatrics Aarhus University Hospital Skejby, Aarhus, Denmark
2Dept. Rheumatology Aarhus University Hospital, Aarhus, Denmark

Introduction: There is an increasing interest among paediatric rheumatologist for using ultrasonography (US) in the daily clinical examination of children with JIA. Loss of joint cartilage may be an early feature of destructive disease in JIA. However, US still needs validation before it can be used as a diagnostic bedside tool in a pediatric setting.

Purpose: This study aims to assess the inter- and intraobserver reliability of US measurements of cartilage thickness in the joints of healthy children.

Materials and methods: 740 joints of 74 healthy children (27 girls/47 boys), mean aged 11.3 years were examined with bilateral US in 5 preselected joints to assess the interobserver variability. In 17 of these children (6 girls/11 boys), mean aged 10.1 years, 170 joints was examined in an intraobserver substudy, with a 2 week interval between the first and second examination. All US measurements were obtained blinded.

Results: Knee 0.26 mm** diff. interobserver), Ankle −0.14 mm**, Wrist 0.09 mm**.

Conclusion: We found a good inter- and intraobserver agreement expressed in CV less than 10% in 3 out of 5 examined joints. The inter- and intraobserver variation seemed not to
Materials and methods:
15 ankle regions with clinical signs in injection and follow-up of ankle involvement with JIA, for diagnosis of inflammation, guidance of steroid usefulness of US and Doppler-US of the ankle region in children.

Results:
At start synovial hypertrophy was found in 24, and synovial hyperaemia was measured after 1 and 4 weeks. US demonstrated inflammation in 24 compartments: 12 talocrural-, 6 subtalar-, 1 talonavicular joint and 5 tendonsheaths, respectively. US-guided steroid injection was successfully performed and the effect on synovial hypertrophy, effusion respectively. US guided steroid injections in small (MCP, PIP, MTP) joints in children. Often the child is misleadingly found to be without any joint affection and conventional radiography, often used as first choice imaging, will be reported as normal.

In a five-year prospective follow-up study (US-MRI-Skejby protocol) we are investigating JIA joint pathologies expressed by US (synovitis, effusion, cartilage thickness, erosions) comparing them with MRI and conventional radiography findings in relation to JIA onset type, disease activity, duration and treatment.

We present two cases of early-onset JIA from this study.

Materials and methods:
Clinical examination, laboratory tests and US and MRI was obtained on the same examination day and X-ray within a 2 weeks period.

One girl (2 yrs) and one boy (2 1/2 yrs) with 2–6 months duration of symptoms before diagnosis. Both were ANA positive, CRP slightly elevated in case 1.

Results:
Synovitis in affected joints was detected by US and MRI but not by X-ray.

Conclusion:
US and MRI favours conventional radiography in detecting early inflammatory changes in smaller children with EO-JIA. Although detailed information is given by MRI, the use of MRI is limited to one anatomical region and the smaller children it cannot be performed without general anaesthesia. Thus, US seem most helpful in detecting early inflammatory changes in EO-JIA.

P99
Ultrasound guided joint fluid aspiration and corticosteroid injection in patients with juvenile idiopathic arthritis (JIA)
C Heuck, AH Spannow and T Herlin
Aarhus University Hospital Skejby, Aarhus, Denmark

Background:
Musculoskeletal ultrasound (US) is a rapidly evolving and powerful diagnostic modality, which is gaining popularity for the evaluation and management of joint damage and soft tissue diseases in children with JIA. Several studies have shown that clinical examination underestimates the presence of intra-articular fluid when compared to US. US guided aspiration allows direct observation of the joint effusion and needle placement and enables correct intra-articular corticosteroid injection avoiding the risk of steroid-induced subcutaneous atrophy. This contrasts X-ray guided techniques. In small joints such as MCP, PIP and MTP the effusion is mainly located proximal to the joint space.

Methods:
US standard scans were performed with B-mode using a linear 6–14 MHz transducer (Hitachi EUB-6500 CFM).

Results:
US guided steroid injections in small (MCP, PIP, MTP) and large (hip, knee, ankle, wrist, elbow) joints in JIA more than 50 patients were performed in the period December 2007 to
April 2008. In children with systemic JIA with massively swollen joints we found that US disclosed surprisingly modest fluid effusion compared to severe synovial hypertrophy. Corticosteroid induced atrophy were not noticed.

**Conclusion:** In our experience US improves correct needle placement in the joint space and US guided procedures seem to be superior to conventional injection and aspiration techniques. Implementation of US guided injections in routine pediatric rheumatology practice will conceivably allow improved treatment results and decrease the risk of iatrogenic complications.

**P100**

**The correlation between clinical and ultrasonographic findings of ankle disease in JIA**

JFT Burns1, SA Wright1, C McCallister1 and ME Rooney2

1Musgrave Park Hospital, Belfast, UK
2Queen’s University/MPH, Belfast, UK

**Background:** The ankle joint is frequently involved in juvenile idiopathic arthritis (JIA) but it is unclear whether this is predominantly due to synovitis, tenosynovitis or both. We therefore compared clinical and ultrasonographic findings in swollen ankle joints of children with JIA to better delineate the anatomical basis for swelling.

**Methods:** 34 patients with 49 clinically swollen ankles were included. (19 polyarticular JIA, 13 oligoarticular JIA, 1 systemic JIA and 1 psoriatic JIA). All cases had at least one clinically swollen ankle joint US scans were performed by an experienced rheumatologist using a Sonosite 180 Plus (L3B 5–10 MHz linear transducer) or Esaote MyLab 25 scanner (LAS523E 7.5–12 MHz linear transducer).

**Results:** 69% of ankles had tenosynovitis and 39% had tenosynovitis alone. Only 29% of swollen ankles had a tibiotalar effusion alone. 33% had both tenosynovitis and a tibiotalar effusion. 69% of ankles had tenosynovitis and 39% had tenosynovitis alone. Only 29% of swollen ankles had a tibiotalar effusion alone. 33% had both tenosynovitis and a tibiotalar effusion.

When results were analysed by JIA subtype we found 81% of swollen ankles had a tibiotalar effusion alone. 33% had both tenosynovitis and a tibiotalar effusion. 69% of ankles had tenosynovitis and 39% had tenosynovitis alone. Only 29% of swollen ankles had a tibiotalar effusion alone. 33% had both tenosynovitis and a tibiotalar effusion.

As a result of these findings we are performing a prospective study. Preliminary analysis of the first 15 ankles confirms the clinical overdiagnosis of tibiotalar synovitis and underdiagnosis of tendon involvement.

**Conclusion:** In JIA with ankle disease, 39% of cases the main ankle joint was not involved and tenosynovitis, sometimes in isolation, was the dominant finding. This has implications for therapeutic intervention and also for an improved classification of children with JIA especially with ankle involvement.

The results of the prospective study will be given in full.

**P101**

**A comparison of clinical vs ultrasound determined synovitis in juvenile idiopathic arthritis (JIA)**

S Magni Manzoni1, A Ravelli2, C Klersy1, C Visconti1, S Lanni1, E Borali1, V Muratore1, C Montecucco1 and O Epis1

1Dept. Pediatrics, Fondazione Policlinico IRCCS San Matteo, Pavia, Italy
2Pediatrica II, IRCCS G. Gaslini, Genova, Italy

**Purpose:** Studies in rheumatoid arthritis have shown higher prevalence of subclinical synovitis defined by US in respect to clinical examination. We investigated the relative sensitivity of clinical and sonographic assessment of synovitis in JIA.

**Methods:** In 34 patients, the clinician (SMM) assessed 52 joints and computed count of joints with swelling, pain/tenderness, restricted motion and active disease (AD). A global articular severity score (GASS) was obtained by grading symptoms in each joint (0–3 scale) and summing scores. Clinical assessments included physician’s and parent’s global ratings, functional ability and acute phase reactants. The sonographer (OE) scanned independently the same 52 joints for synovial hypertrophy (SI), synovial fluid (SF) and power Doppler (PD), each graded on a 0–3 scale. Agreement and correlations were assessed with Cohen’s kappa and Spearman’s correlation, respectively (>0.4 = moderate agreement/correlation).

**Results:** 1768 joints were assessed. Knees, wrists, proximal interphalangeal joints and ankles were the most frequently affected joints, either clinically and on US. Table 1 shows kappa values for clinical vs. US assessments:

<table>
<thead>
<tr>
<th>SI</th>
<th>SF</th>
<th>PD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swelling</td>
<td>0.41</td>
<td>0.45</td>
</tr>
<tr>
<td>Pain/tenderness</td>
<td>0.29</td>
<td>0.27</td>
</tr>
<tr>
<td>Restricted motion</td>
<td>0.29</td>
<td>0.21</td>
</tr>
</tbody>
</table>

Disagreement was greater for intertarsal and metatarsophalangeal joints. US scores were moderately correlated with AD and GASS and poorly correlated with other clinical measures.

**Conclusion:** Swelling was the only clinical feature for which there was agreement with US. US revealed greater sensitivity than clinical examination in detecting synovitis in foot joints. These findings have important implications for application of US in clinical trials and predictive studies.

**P102**

**Exploring the ceiling effect of the revised Childhood Health Assessment Questionnaire in a European patient sample**

W Groen1, J Van der Net1, M Nørgaard3, E Yakut2, K Berggren2, E Sandstedt2, J Scott5, S Maillard4 and L Dougan6

1University Children’s Hospital, Utrecht, Netherlands
2Hacettepe University, School of Physical Therapy and Rehabilitation, Ankara, Turkey
3Department of Physiotherapy, Århus University Hospital, Skejby, Århus, Denmark
4Institute of Child Health, Great Ormond Street Childrens Hospital, London, UK
5Birmingham Children’s Hospital NHS foundation trust, Birmingham, UK
6Royal Hospital for Sick Children, Glasgow, UK
7Astrid Lindgren Children’s Hospital, Karolinska University Hospital, Stockholm, Sweden
8Queen Silvia Children’s Hospital, Göteborg, Sweden

**Background:** The original version of the Childhood Health Assessment Questionnaire (CHAQ30orig) suffers from a ceiling effect and hence has reduced clinical validity [1]. The effect of
Table 1 (abstract P102) Median, ceiling effect, KS results, and interquartile range of five CHAQ scoring methods

<table>
<thead>
<tr>
<th>Scoring method</th>
<th>Median (range)</th>
<th>Ceiling effect (%)</th>
<th>KS-statistic</th>
<th>P-value</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cat I Chaq30orig</td>
<td>0.81 (0–2.13)</td>
<td>20.8*</td>
<td>0.87</td>
<td>0.43</td>
<td>1.38</td>
</tr>
<tr>
<td>Chaq30item</td>
<td>0.36 (0–1.04)</td>
<td>20.8*</td>
<td>0.87</td>
<td>0.50</td>
<td>0.43</td>
</tr>
<tr>
<td>Chaq38item</td>
<td>0.38 (0–1.26)</td>
<td>8.3</td>
<td>0.86</td>
<td>0.45</td>
<td>0.54</td>
</tr>
<tr>
<td>Cat II Chaq30item</td>
<td>–0.24 (–1.26–0.40)</td>
<td>0</td>
<td>0.84</td>
<td>0.49</td>
<td>0.48</td>
</tr>
<tr>
<td>Chaq38item</td>
<td>–0.34 (–1.26–0.42)</td>
<td>0</td>
<td>0.69</td>
<td>0.73</td>
<td>0.64</td>
</tr>
</tbody>
</table>

adding eight more demanding items and a new continuous response option (CATII) was tested.

Methods: Twenty-four children with JIA [2] were recruited from eight centres across Europe. Demographic, clinical, and CHAQ data were obtained. Five different score calculations were applied: the original method (CHAQ30orig), and the mean item scores for the 30 and 38-question versions with two categorical response options (Chaq30item CAT I and II and Chaq38item CAT I and II). Descriptive statistics were calculated and CHAQ-data were tested for normality. A ceiling effect was defined by 15% or more patients scoring the best possible score.

Results: (preliminary, based on 30% of total data).
A ceiling effect was observed in CHAQ30orig and CHAQ30item (20.8% for both). The median scores, KS-statistics, p-values, and interquartile range (IQR) are presented in Table 1.

Discussion: The CHAQ38 with CATII scoring showed best overall distribution characteristics: no ceiling effect, more normally distributed, and the second largest IQR. (In September 2008 final results are presented).

References

P103
Do parent’s global rating of well-being and disease activity of children with juvenile idiopathic arthritis yield different information?
N Ullmann 1, A Consolaro1, G Filocamo1, S Verazza1, S Dalpra1, C Ferrari1, R Caorsi1, S Viola1, C Visconti2, A Martini1 and A Ravelli1
1Istituto G. Gaslini, Genova, Italy
2I.R.C.S Policlinico S. Matteo, Pavia, Italy

Pediatric Rheumatology 2008, 6(Suppl 1):P103

Background: The parents of children with juvenile idiopathic arthritis (JIA) are traditionally asked to provide a global assessment of disease status by rating the child’s overall level of well-being (WB) on a 10-cm visual analogue scale (VAS). However, it has been advised that this measure does not provide a precise assessment of DA because it is largely affected by the presence of disease damage. For this reason, it has been suggested to substitute the VAS for WB with a VAS assessing specifically the level of DA.

Objective: To compare the construct validity of parent’s global assessment of WB (Par WB) and parent’s global assessment of DA (Par DA) in JIA.

Materials and methods: A parent of 403 JIA patients seen between 2007 and 2008 was asked to rate in 723 visits the level of child’s WB and DA on two separate VAS. Construct validity of the two scales was compared by assessing their Spearman’s correlation with other JIA outcome measures.

Results: Table 1 shows Spearman’s correlations.

Conclusion: Par WB and Par DA were highly correlated each other and their construct validity was very similar. These findings indicate that these two measures provide the same information and can, thus, be used interchangeably.

P104
Performance of different sets of criteria for clinical response evaluation in a non-selected cohort of juvenile idiopathic arthritis (JIA) patients
R Gutiérrez-Suárez1,2 and R Burgos-Vargas1
1Hospital General de México, México D.F., Mexico
2Hospital Shriners para niños. A.C., México D.F., Mexico

Pediatric Rheumatology 2008, 6(Suppl 1):P104

Objective: To compare the performance of 4 sets of criteria for clinical response evaluation in JIA patients.

Methods: An observational study of a non-selected cohort of JIA patients in the out-patient clinic was conducted. Four sets of criteria were compared: DAS, DAS28, CDAI and SDAI were evaluated and compared with the ACR-Ped-30 and the clinician judgment of response (CJR) (100 mm-VAS) as the gold standard to evaluate clinical response in JIA patients. Performance was assessed by the receiver operating characteristic (ROC) curve analysis and other statistics for diagnostic tests.

Results: 50 JIA patients (female/male ratio: 1.2:1; mean age at diagnosis: 6.4 ± 3.3 years; mean disease duration: 5.3 ± 2.7 years) were evaluated. The area under the ROC curve (AUC) was 0.842 (0.691–0.994); 0.68 (1.03–0.4075); 80.9; 87.5; 97.1; and 46.6; respectively for the CJR in comparison with the ACR-Ped-30 as gold standard; and of 0.752 (0.532–0.868); 2.00 (1.05–3.80); 80.0; 60.0; 82.3 ± 56.2; respectively for the DAS28; 0.752 (0.599–0.906); 2.89 (1.23–6.83); 77.1; 73.3; 87.1 57.8; respectively for the SDAI; and 0.705 (0.542–0.868); 2.23 (1.06–4.68); 74.2; 66.6 83.8; 52.6; respectively for the CDAI, when compared with the CJR. The
Performance of the four sets of criteria in comparison with the ACR-Ped-30 was poor.

**Conclusion:** In the daily clinical practice the DAS 28, SDAI can be used for the evaluation of clinical response in JIA patients.

**P105 Accuracy of preliminary remission criteria some JIA category**

F Fantini1, A Salmaso2, V Gerloni2, M Gattinara2, B Teruzzi2, I Pontikaki2, and A Lurati1
1Fornaroli Hospital Rheumatology Unit, Magenta, Italy
2Gaetano Pini Institute Chair of Rheumatology, Milan, Italy

Pediatric Rheumatology 2008, 6(Suppl 1):P105

To evaluate disease course in juvenile idiopathic arthritis (JIA) by applying newly developed preliminary definitions of remission, to assess probability of relapse of disease. Charts of patients with JIA followed since 1970 were reviewed. First episode of remission off medication status, as defined by Wallace et al., has been focused. The cohort included 761 patients (67.8% females, 32.2% males) with JIA. Mean disease onset age (± SD) was 6.25 ± 4.4 years (range 0.5–15.9). Disease mean duration to last visit was 10.02 ± 4.31 years. Follow up mean period was 7.6 ± 6.4 years (range 1.5–35 years). A total of 263 (34.56%) patients achieved remission according to criteria (persistent oligoarthritis 42.9%, extended oligoarthritis 13.1%, seronegative polyarthritis 22.4%, systemic arthritis 33.7%, enthesitis related arthritis (ERA) plus juvenile psoriatic arthritis (JPsA) 33.4%). No patients with seropositive polyarthritis achieved remission status (p < 0.001). In remitted patients the mean survival function (± SEM) before relapse calculated by life table survival curve was of 20.9 (± 1.3) months overall: 21.7 (± 0.46) in persistent oligoarthritis, 25.0 (± 6.6) in extended oligoarthritis, 26.7 (± 13.2) in seronegative polyarthritis and 17.6 (± 2.44) in ERA + JPsA. The log rank test did not show a significant difference between the JIA categories survival curves (p = 0.1). In our cohort about one-third of cases obtained a remission episode in 4 decades of observation. Finally, if a remission was achieved, the mean duration before a relapse was about 20 months.

**P106 Preliminary validation of the Juvenile Arthritis Multidimensional Assessment Report (JAMAR) in 403 clinic patients**

N Solari1, G Filocamo1, B Schiappapietra1, A Consolaro1, S Magni-Manzoni2, S Viola1, N Ruperto1, C Saad-Magalhaes1, D Tani1, S Serpico1, A Martini1 and A Ravelli1
1IRCCS G Gaslini, Genova, Italy
2IRCCS Policlinico S Matteo, Pavia, Italy

Pediatric Rheumatology 2008, 6(Suppl 1):P106

Objective: To provide preliminary evidence of validity of the JAMAR in a large sample of JIA patients.

**Methods:** The JAMAR includes: Juvenile Arthritis Functionality Scale (JAFS) (0 = normal; 30 = worst), Pediatric Rheumatology Quality of Life (PRQL) questionnaire (0 = best; 30 = worst); visual analogue scales (0 = best; 10 = worst) for parent/patient rating of well-being (WB), pain (P), disease activity (DA); parent/patient assessment of morning stiffness, disease status, satisfaction about disease outcome.

**Results:** The JAMAR was completed by 403 patients in 696 visits between March 2007 and February 2008. All completers reported that JAMAR was easy to understand and fill. Completion time was < 10 minutes. Results of quantitative JAMAR assessments are shown in the table 1 together with assessments made by attending physician.

**Conclusion:** The JAMAR proved to be feasible and to have good face and content validity. Parents and physicians revealed fair concordance in assessing overall disease activity. Around half and 2/3 of patients, respectively, were judged to be in remission or in satisfactory state by parents.

---

Table 1 (abstract P106) Percentage of parents reporting morning stiffness, remission, continued activity, flare, and satisfaction about outcome was 34.3, 47.9, 29.5, 22.6, and 72.1, respectively

<table>
<thead>
<tr>
<th>Parent WB</th>
<th>Parent DA</th>
<th>Parent P</th>
<th>JAFS</th>
<th>PRQL</th>
<th>MD global</th>
<th>No. swollen joints</th>
<th>No. tender joints</th>
<th>No. restricted joints</th>
<th>No. active joints</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>2.3</td>
<td>2.4</td>
<td>2.1</td>
<td>1.5</td>
<td>3.9</td>
<td>2.3</td>
<td>1.8</td>
<td>2.1</td>
<td>2.1</td>
</tr>
<tr>
<td>Median</td>
<td>1</td>
<td>1</td>
<td>0.5</td>
<td>3</td>
<td>0.5</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Minimum</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Maximum</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>26</td>
<td>23</td>
<td>10</td>
<td>35</td>
<td>49</td>
<td>46</td>
</tr>
</tbody>
</table>
Table 1 (abstract P107) Spearman’s correlations for PRQL and CHQ

<table>
<thead>
<tr>
<th></th>
<th>Parent global</th>
<th>Parent pain</th>
<th>Functional ability</th>
<th>MD global</th>
<th>Restricted joints</th>
<th>Active joints</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRQL</td>
<td>PhH 0.65</td>
<td>0.68</td>
<td>0.57**</td>
<td>0.39</td>
<td>0.35</td>
<td>0.34</td>
</tr>
<tr>
<td></td>
<td>PsH 0.38</td>
<td>0.40</td>
<td>0.30**</td>
<td>0.19</td>
<td>0.18</td>
<td>0.16</td>
</tr>
<tr>
<td>CHQ</td>
<td>PhS −0.61</td>
<td>−0.63</td>
<td>−0.51**</td>
<td>−0.45</td>
<td>−0.35</td>
<td>−0.43</td>
</tr>
<tr>
<td></td>
<td>PsS −0.28</td>
<td>−0.25</td>
<td>−0.26**</td>
<td>−0.13</td>
<td>−0.14</td>
<td>−0.18</td>
</tr>
</tbody>
</table>

*JAFS, **CHAQ.

Results: All completers reported that PRQL was easy to understand and fill. Completion time was < 5 minutes. Table 1 reports Spearman’s correlations for PRQL and CHQ.

Conclusion: The PRQL proved feasible and showed good face and content validity. Construct validity was comparable to that of an established pediatric HRQL measure (the CHQ).

P108

Does incorporation of aids/devices and help make a difference in the childhood health assessment questionnaire disability index? Analysis from the printo juvenile idiopathic arthritis database

Background: The ceiling effect and skewness of score distribution (i.e. tendency for scores to cluster at or towards the normal end of the scale) are potential limitations of outcome measures in JIA.

Objective: To characterize ceiling effect and score distribution of the main JIA outcome measures.

Methods: A total of 1818 visits made from 1989 to 2006 were examined. Percentage of patients with score = 0 and score distribution were assessed for physician and parent global assessments, CHAQ, joint counts, and ESR.

Results: Frequency of ceiling effect for each measure is shown in table 1. Physician global assessment revealed a tendency towards normal distribution, whereas all other measures were skewed towards the normal end of the scale. However, physician global assessment scores tended to cluster at the two ends of the scale (i.e. towards the 0 and 10 scores). In 69.2% of the visits CHAQ score was > 0.5%. In 19.9% of the visits 5 or more active joints were detected.

Conclusion: Ceiling effect was greater for ESP, CHAQ and tender and restricted joint counts. In only 1/5 of the visits made in a wide time frame JIA patients receiving routine care in a tertiary center met inclusion criteria (i.e. active joint count ≥ 5) for recent clinical trials of second-line or biologic agents.

Table 1 (abstract P109)

<table>
<thead>
<tr>
<th></th>
<th>Physician global</th>
<th>Parent global</th>
<th>Parent pain</th>
<th>CHAQ</th>
<th>No. swollen joints</th>
<th>No. tender joints</th>
<th>No. restricted joints</th>
<th>No. active joints</th>
<th>ESR*</th>
</tr>
</thead>
<tbody>
<tr>
<td>% score = 0</td>
<td>20.2</td>
<td>22.7</td>
<td>26.7</td>
<td>40.8</td>
<td>27.1</td>
<td>36.5</td>
<td>34.2</td>
<td>23.1</td>
<td>51.7</td>
</tr>
</tbody>
</table>

*% < 20 mm/h.
2Department of Pediatric Physiotherapy, Sophia Children’s Hospital, Erasmus University, Rotterdam, Zuid-Holland, Netherlands  
3Department of Physiotherapy (HO-Q), Leiden University Medical Centre, Leiden, Zuid-Holland, Netherlands  
4Department Physiotherapy, University Hospital Groningen, Groningen, Groningen, Netherlands  
5Department Paediatric Physiotherapy, University Medical Center Nijmegen St. Radboud, Nijmegen, Gelderland, Netherlands  

Pediatric Rheumatology 2008, 6(Suppl 1):P110  

Background: Adding 8 more demanding items to the original Childhood Health Assessment Questionnaire (CHAQ) lowers the ceiling effect of this questionnaire [1]. In this cross-sectional study the score distribution of two categorical response options of the revised CHAQ was explored.  

Materials and methods: Five Dutch tertiary centres for paediatric rheumatology recruited 63 JIA patients (48 female). Demographic, clinical and CHAQ data were obtained. We applied the domain scores of the original CHAQ (CHAQ30orig) and the plain mean scores of the revised CHAQ that made use of two categorical response options (Chaq30itemCat I/II and Chaq38itemCat I/II). Descriptive statistics were calculated and normal distribution was tested by the Kolmogorov-Smirnov test. A ceiling effect was defined by 15% or more patients scoring the highest possible score [2].  

Results: The JIA patients were 11.7 (6.8–16.8) years old and diagnosed as polyarthritis (30), systemic arthritis (13), persisted oligoarthritis (13) and extended oligoarthritis (7). The mean disease duration was 4.9 (1 month–14.1 year.) year. The CHAQ30orig and CHAQ30itemCat I showed a ceiling effect (both 20%)*. The median scores, KS-statistics, p-values, and interquartile range (IQR) are presented in table 1.  

Conclusion: For JIA patients at the mild end of disability, the continuum of Cat II response options, in which the JIA patients compared their physical ability among healthy peers, of the CHAQ38 provides a better sensitivity then the original score options.  

Acknowledgements  
We would like to thank J.H. Cappon, paediatric physiotherapist.  

References  

Table 1 (abstract P110) Ceiling effect, KS-test results and Interquartile range of original and revised CHAQ

<table>
<thead>
<tr>
<th>Questionnaire</th>
<th>Median score (range)</th>
<th>% at ceiling (0-score)</th>
<th>KS-statistic</th>
<th>P-value</th>
<th>IQR (P75–P25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cat I</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chaq30orig</td>
<td>0.50 (.00–2.50)</td>
<td>20%*</td>
<td>1.23</td>
<td>.10</td>
<td>.06</td>
</tr>
<tr>
<td>Chaq30item</td>
<td>0.19 (.00–1.55)</td>
<td>20%*</td>
<td>1.49</td>
<td>.02</td>
<td>.02</td>
</tr>
<tr>
<td>Chaq38item</td>
<td>0.26 (.00–1.70)</td>
<td>9.5</td>
<td>1.24</td>
<td>.09</td>
<td>.03</td>
</tr>
<tr>
<td>Cat II</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chaq30item</td>
<td>−0.17 (−1.45–40)</td>
<td>0</td>
<td>1.29</td>
<td>.07</td>
<td>.05</td>
</tr>
<tr>
<td>Chaq38item</td>
<td>−0.24 (−1.52–42)</td>
<td>0</td>
<td>1.04</td>
<td>.23</td>
<td>.25</td>
</tr>
</tbody>
</table>

P111  
Grading of joint indices for severity reflects better the burden of joint disease and its impact on child’s well-being in juvenile idiopathic arthritis (JIA)  
C Visconti1, A Rавelli2, C Klersy1, S Lanni1, S Caimmi1, E Borali1, V Muratore1 and S Magni-Manzoni1  
1Dep Pediatrics, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy  
2Pediatrica II, IRCCS G. Gaslini, Genova, Italy  

Pediatric Rheumatology 2008, 6(Suppl 1):P111  

Background and aim: The severity of joint disease in JIA can be quantified by counting the number of joints with swelling, tenderness/pain on motion, and restricted motion, and by calculating, through these parameters, the number of active joints (NAJ). Alternatively, a global articular severity score (GASS) can be obtained by grading symptoms in each joint and summing the scores obtained in all joints. Although the former method is currently preferred, it is unclear which method is more advantageous to capture the impact of joint disease on child’s health and well-being. We aimed to compare the ability of NAJ and GASS to capture the impact of joint disease on child’s health and well-being by assessing their correlation with physician’s, parent’s and patient’s subjective ratings and functional ability assessment.  

Methods: Thirty-four JIA patients underwent a standardized joint assessment and had both NAJ and GASS calculated. Correlation of NAJ and GASS with physician’s, parent’s and patient’s global rating, parent’s and patient’s pain rating, and functional ability assessment through the Juvenile Arthritis Functionality Scale (JAFS) was evaluated using Spearman’s correlation coefficient.  

Results: Table 1 shows Spearman’s correlations between global joint scores and other JIA outcome parameters.  

Conclusion: All correlations were greater for the GASS than for the NAJ, suggesting that the GASS reflects better the burden of joint disease and its impact on child’s well-being.  

Table 1 (abstract P111) Spearman’s correlations between global joint scores and other JIA outcome parameters

<table>
<thead>
<tr>
<th>MD global</th>
<th>Parent global</th>
<th>Patient global</th>
<th>Parent pain</th>
<th>Patient pain</th>
<th>JAFS parent</th>
<th>JAFS patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>NAJ</td>
<td>0.49</td>
<td>0.18</td>
<td>0.17</td>
<td>0.24</td>
<td>0.35</td>
<td>0.43</td>
</tr>
<tr>
<td>GASS</td>
<td>0.69</td>
<td>0.42</td>
<td>0.38</td>
<td>0.50</td>
<td>0.51</td>
<td>0.52</td>
</tr>
</tbody>
</table>
PI112
Comparison of the accuracy of different definitions of clinical remission (CR) and minimal disease activity (MDA) in juvenile idiopathic arthritis (JIA)
S Davi, A Consolaro, C Ferrari, S Federici, R Vitale, G Filocamo, A Loy, N Ruperto, A Martini and A Ravelli
IRCCS G. Gaslini, Genoa, Italy

Background: Since the introduction of biologic agents, expectations of medical treatment for chronic arthritides have increased markedly. It is now agreed upon that estimation of effectiveness of these drugs requires not only the assessment of relative improvement in signs and symptoms, but the evaluation of their ability to induce a state of CR or, at least, MDA. In recent years, several criteria for assessing CR and MDA in adult rheumatoid arthritis (RA) or JIA have been developed.

Objective: To apply existing definitions of CR or MDA in a large sample of visits made in JIA patients.

Methods: 851 visits made in 446 patients between 1992 and 2006 were assessed. CR was defined as achieving: 1) DAS28 score \(< 2.4; 2\) SDAI score \(\leq 3.3\); 3) CDAI score \(\leq 2.8\); 4) Clinical remission criteria for RA; 5) preliminary definition of CR for JIA. LDA was defined as achieving: 1) DAS28 score \(< 3.6\); 2) SDAI score \(\leq 11\); 3) CDAI score \(\leq 10\); 3) LDA criteria for RA; 4) LDA criteria for JIA.

Results: Table 1: shows the percentage of patients classified in state of CR or MDA by each criterion.

Conclusion: Definition of CR in JIA proved more restrictive than correspondent definitions for adult RA. The proportion of patients classified in MDA by JIA criteria and DAS28, CDAI and SDAI criteria was similar, whereas RA criteria for LDA led to classify relatively more patients in such state.

Table 1 (abstract PI112) The percentage of patients classified in state of CR or MDA by each criterion

<table>
<thead>
<tr>
<th>Variables</th>
<th>DAS28</th>
<th>SDAI</th>
<th>CDAI</th>
<th>RA criteria</th>
<th>JIA criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>19.3</td>
<td>19.2</td>
<td>18.7</td>
<td>13.0</td>
<td>10.8</td>
</tr>
<tr>
<td>MDA</td>
<td>25.7</td>
<td>23.4</td>
<td>22.7</td>
<td>38.3</td>
<td>21.9</td>
</tr>
</tbody>
</table>

PI113
Responsiveness of different sets of criteria for clinical response evaluation in a non-selected cohort of juvenile idiopathic arthritis (JIA) patients
R Gutiérrez-Suárez and R Burgos-Vargas
Hospital General de México, Mexico, Mexico

Objective: To evaluate the responsiveness of 4 sets of criteria for clinical response evaluation and the ACR-Ped-30 variables in a non-selected cohort of patients with JIA.

Methods: An observational study of a non-selected cohort of 50 JIA patients in the out-patient clinic was conducted. Four sets of criteria: DAS, DAS28, CDAI and SDAI and the variables of the ACR Ped-30 were evaluated at 26 and 54 weeks.

Table 1 (abstract PI113) Variables Effect size Standardized Mean Response RRC

<table>
<thead>
<tr>
<th>Variables</th>
<th>Effect size</th>
<th>Standardized Mean Response</th>
<th>RRC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physician's global assessment of disease activity</td>
<td>0.76</td>
<td>0.89</td>
<td>1.28</td>
</tr>
<tr>
<td>No. of active joints</td>
<td>0.22</td>
<td>0.17</td>
<td>0.48</td>
</tr>
<tr>
<td>No. of joints with limitation on motion</td>
<td>0.18</td>
<td>0.15</td>
<td>0.38</td>
</tr>
<tr>
<td>C-reactive protein</td>
<td>0.45</td>
<td>0.38</td>
<td>0.60</td>
</tr>
<tr>
<td>CHAQ disability index</td>
<td>0.35</td>
<td>0.30</td>
<td>0.42</td>
</tr>
<tr>
<td>Parent's assessment of child's well-being</td>
<td>0.78</td>
<td>0.65</td>
<td>1.53</td>
</tr>
<tr>
<td>Limited joint count Ritchie Articular Index</td>
<td>0.12</td>
<td>0.08</td>
<td>0.38</td>
</tr>
<tr>
<td>Swollen joint count (44)</td>
<td>0.28</td>
<td>0.20</td>
<td>0.80</td>
</tr>
<tr>
<td>Tender joint count (28)</td>
<td>0.27</td>
<td>0.20</td>
<td>0.86</td>
</tr>
<tr>
<td>Swollen joint count (28)</td>
<td>0.30</td>
<td>0.26</td>
<td>0.78</td>
</tr>
<tr>
<td>DAS</td>
<td>0.18</td>
<td>0.47</td>
<td>0.70</td>
</tr>
<tr>
<td>DAS28</td>
<td>0.57</td>
<td>0.44</td>
<td>1.12</td>
</tr>
<tr>
<td>SDAI</td>
<td>0.60</td>
<td>0.57</td>
<td>1.30</td>
</tr>
<tr>
<td>CDAI</td>
<td>0.58</td>
<td>0.48</td>
<td>1.20</td>
</tr>
</tbody>
</table>

Responsiveness was assessed with the effect size (ES), the standardized mean response (SMR) and the responsiveness-retrospective coefficients (RRC).

Results: See table 1.

Conclusion: The 4 sets of criteria for evaluation appear to be responsive outcome measures in a non-selected cohort of patients with JIA evaluated in the daily clinic.

PI114
Comparison of physician's, parent's and patient's global ratings made on linear or 21-circle visual analogue scales (VAS) in juvenile idiopathic arthritis (JIA)
S Dalprà, S Verazza, C Ferrari, A Parodi, S Davi, B Schiappapietra, A Consolaro, G Filocamo, S Viola, A Martini and A Ravelli
IRCCS G Gaslini, Genova, Italy

Background: Physician's and parent's global ratings of disease status in JIA are assessed using a 10-cm linear VAS anchored at two ends. However, such measure may lead to clustering of scores at ends of scale. Furthermore, a ruler is required to compute scores. Substitution of linear VAS with 21-circle VAS (each circle = 0.5 cm) has been proposed to increase feasibility and precision.

Objective: To compare construct validity of physician's and parent's ratings made on linear or 21-circle VAS.

Methods: In 723 visits (2007–2008), the physician rated disease activity and a parent rated child's well-being and pain on 21-circle VAS. A historical sample of 1429 visits (1988–2006) including same assessments made on linear VAS was used for comparison. Construct validity of VAS was compared by calculating Spearman's correlations with other JIA outcome measures.

Results: See table 1.

Conclusion: 21-circle VAS yielded better correlations for physician's global assessment, whereas correlations for parent's
Table 1 (abstract P114)

<table>
<thead>
<tr>
<th></th>
<th>Parent global</th>
<th>Parent pain</th>
<th>Functional scale</th>
<th>MD global</th>
<th>Active joints</th>
</tr>
</thead>
<tbody>
<tr>
<td>21-circle VAS</td>
<td>0.52</td>
<td>0.50</td>
<td>0.48*</td>
<td>--</td>
<td>0.85</td>
</tr>
<tr>
<td>Parent global</td>
<td>--</td>
<td>0.76</td>
<td>0.59*</td>
<td>0.52</td>
<td>0.44</td>
</tr>
<tr>
<td>10-cm VAS</td>
<td>0.57</td>
<td>0.57</td>
<td>0.43**</td>
<td>--</td>
<td>0.62</td>
</tr>
<tr>
<td>Parent global</td>
<td>--</td>
<td>0.81</td>
<td>0.57**</td>
<td>--</td>
<td>0.45</td>
</tr>
</tbody>
</table>

*JAFS; **CHAQ.

ratings were greater with linear VAS. This shows that overall construct validity of the two scales is comparable.

P115
Final validation of a new composite disease activity score for juvenile idiopathic arthritis: the Juvenile Arthritis Disease Activity Score (JADAS)
A Consolaro1, N Ruperto1, A Bazzo1, S Magni-Manzoni2, MA Pelagatti1, A Pistorio1, A Magnani1, C Malattia1, I D'Agostino1, G Filocamo1, A Martini1 and A Ravelli1
1IRCCS G. Gaslini, Genova, Italy
2IRCCS Policlinico San Matteo, Pavia, Italy

Objective: To complete validation of the Juvenile Arthritis Disease Activity Score.

Materials and methods: The JADAS is composed of the following measures: 1) physician’s global assessment (0–10); 2) parent’s global assessment (0–10); 3) active joint count (assessed in 71, 27 or 10 joints); 4) ESR (normalized to 0–10). It yields a score ranging from 0 to 40, 57 or 101, depending on whether the whole 71-joint count (JADAS-71) or the 27-joint (JADAS-27) or 10-joint (JADAS-10) reduced counts are used. The 3 versions of the JADAS were tested on juvenile idiopathic arthritis patients included in 2 trials on methotrexate (n = 595) and meloxicam (n = 225). Construct validity was assessed by calculating Spearman’s correlation between baseline-endpoint changes in JADAS, C-HAQ and 2 adult scores (DAS28, CDAI). Discriminative validity was assessed by examining the ability of JADAS to discriminate between different levels of ACR Pediatric response in the 2 trials.

Results: Table 1 shows Spearman’s correlations on changes in the 2 clinical trials.

Conclusion: Overall, the JADAS versions including the reduced joint counts (either 27 or 10) revealed better or, at least, similar validity as compared with the version including the 71 (i.e. complete) joint count. Use of JADAS versions with reduced joint counts is advised due to their greater feasibility.

P116
Impact of involvement of individual joint groups on subdimensions of functional ability scales in juvenile idiopathic arthritis
S Meiorini1, G Filocamo2, E Palmisani2, I Sala3, S Magni Manzoni2, S Lanni2, S Viola2, A Buoncompagni2, A Pistorio2, N Ruperto1, A Martin1 and A Ravelli1
1Hospital de Ninos Ricardo Gutierrez, Buenos Aires, Argentina
2IRCCS G Gaslini, Genova, Italy
3IRCCS Pol San Matteo, Pavia, Italy

Objective: To investigate the influence of disease in individual joint groups on subdimensions of functional ability questionnaires in children with juvenile idiopathic arthritis (JIA).

Methods: 206 patients who had the Childhood Health Assessment Questionnaire (C-HAQ) and the Juvenile Arthritis Functionality Scale (JAFS) completed simultaneously by a parent and received a detailed joint assessment were included. In each patient, joint involvement (defined as presence of swelling, pain on motion/tenderness and/or restricted motion) was classified in 3 topographic patterns: Pattern 1 (hip, knee, ankle, subtalar and foot joints); Pattern 2 (wrist and hand joints); Pattern 3 (elbow, shoulder, cervical spine and temporomandibular joints). Frequency of reported disability in each instrument subdimension was evaluated for each joint pattern, present either isolatedly or in mixed form.

Results: Among patients with Pattern 1, the JAFS revealed the greatest ability to capture and discriminate functional limitation, whereas impairment in the C-HAQ was more diluted across several subdimensions. Both C-HAQ and JAFS appeared to be less reliable in detecting functional impairment in the hand and wrist (Pattern 2) than in other body areas. Overall, the JAFS revealed a superior ability to discriminate the relative functional impact of impairment in individual joint groups among patients with mixed joint patterns.

Conclusion: In children with JIA, a functional measure focused to assess the function of individual joint groups (the JAFS) may detect with greater precision the functional impact of arthritis in specific body areas than does a standard questionnaire based on the assessment of activities of daily living (the C-HAQ).

P117
Development and initial validation of the parent acceptable symptom state in juvenile idiopathic arthritis (JIA)
G Filocamo1, B Schiappapietra1, S Magni Manzoni2, S Lanni2, N Solar1, S Viola1, A Pistorio1, N Ruperto1, D Tani1, A Martin1 and A Ravelli1
1IRCCS G Gaslini, Genova, Italy
2IRCCS Pol San Matteo, Pavia, Italy

Objective: The parent acceptable symptom state (PASS) constitutes the symptom threshold beyond which parents consider their child’s health status as satisfactory. The PASS represents an ambitious target for disease management.
and progression of JIA and there are no reliable predictors of outcome.

**Background:** Currently there is little research into initiation and progression of JIA and there are no reliable predictors of outcome in early disease, resulting in suboptimal treatment.

**Methods:** We are undertaking a five-year prospective study of children with newly diagnosed and untreated JIA. At least one knee was involved requiring intra-articular steroid injection. Detailed clinical, imaging, and laboratory parameters were measured at T0 and 3/12 for 2 years. At outset we obtained synovial biopsies. We report the outcome on those children for whom data is available for one year.

**Results:** At onset, of the first 32 children, 20 had oligoarticular (OJIA) disease. At one year, 2 had been reclassified as polyarticular (PJIA), 3 as extended oligo. Initially 9 had PJIA and, at 1 year, this increased to 11. At outset 2 had psoriatic, and 1 had enthesitis related arthritis.

At one year, all but 3 OJIA patients improved. Physician’s global evaluation (PGE) and ANA status predicted recurrent synovitis at the biopsied joint, (p < 0.01) and (p < 0.02) respectively. PGE predicted the frequency of injections at any joint (p < 0.01). At one year, all 11 with PJIA had improved clinical and laboratory parameters.

PJIA showed increased synovial pathology compared with OJIA (mean vessel score 6.9 vs. 2.6 (p < 0.05), mean B-cell score 1.7 vs. 1 (p < 0.05)).

**Conclusion:** In OJIA, PGE and ANA status predict recurrent synovitis. To date no correlation has been observed between histological findings and recurrent synovitis in OJIA. We will report on findings of our enlarged cohort who reach one year follow-up.

### Table 1 (abstract P117) The PASS threshold

<table>
<thead>
<tr>
<th>Parent global</th>
<th>Parent pain</th>
<th>JAFS</th>
<th>PRQL</th>
<th>MD global</th>
<th>Active joints</th>
<th>Limited joints</th>
</tr>
</thead>
<tbody>
<tr>
<td>75\textsuperscript{th} centile</td>
<td>2</td>
<td>1.5</td>
<td>1</td>
<td>4</td>
<td>1.5</td>
<td>1</td>
</tr>
</tbody>
</table>

Parent global (OR 4.6), PRQL (3.9), JAFS (4.0), MD global (2.6) and CRP (3.9) were the strongest contributors of PASS in logistic regression analysis (AUC: 0.92). Among patients judged in remission, flare or continued activity by the parent and physician, the percentage of those in PASS was 98, 46 and 49 (p < 0.0001), and 93, 57 and 27 (p < 0.0001), respectively.

**Objective:** To devise and validate the PASS in patients with JIA.

**Methods:** 369 parents completed a multidimensional questionnaire (the JAMAR), including Juvenile Arthritis Functionality Scale (JAFS) (score 0–30), Pediatric Rheumatology Quality of Life (PRQL) questionnaire (score 0–30) and traditional JIA outcome measures, and stated whether they considered their children’s status satisfactory or not. PASS thresholds were estimated based on parent opinion and targeting the 75\textsuperscript{th} percentile of cumulative distribution. Stepwise logistic regression was used to assess contributors to PASS. PASS was validated by analyzing proportions of patients who were judged by parent or physician in remission, flare or continued activity.

**Results:** 72.9% of parents reported their children being in PASS (table 1).

**Conclusion:** We devised the PASS for JIA. The PASS demonstrated good validity by discriminating strongly between patients in remission or active disease.

### P118

**Early untreated juvenile idiopathic arthritis: predictors of outcome**

L Pascoli\textsuperscript{1}, S Blelock\textsuperscript{1}, C Mc Allister\textsuperscript{2}, S Clarke\textsuperscript{1}, D Gibson\textsuperscript{1} and M Rooney\textsuperscript{1}

\textsuperscript{1}Queen’s University Belfast, Belfast, UK

\textsuperscript{2}Musgrave Park Hospital, Belfast, UK

**Pediatric Rheumatology 2008, 6(Suppl 1):P118**

**Background:** Currently there is little research into initiation and progression of JIA and there are no reliable predictors of outcome in early disease, resulting in suboptimal treatment.

**Methods:** We are undertaking a five-year prospective study of children with newly diagnosed and untreated JIA. At least one knee was involved requiring intra-articular steroid injection. Detailed clinical, imaging, and laboratory parameters were measured at T0 and 3/12 for 2 years. At outset we obtained synovial biopsies. We report the outcome on those children for whom data is available for one year.

**Results:** At onset, of the first 32 children, 20 had oligoarticular (OJIA) disease. At one year, 2 had been reclassified as polyarticular (PJIA), 3 as extended oligo. Initially 9 had PJIA and, at 1 year, this increased to 11. At outset 2 had psoriatic, and 1 had enthesitis related arthritis.

At one year, all but 3 OJIA patients improved. Physician’s global evaluation (PGE) and ANA status predicted recurrent synovitis at the biopsied joint, (p < 0.01) and (p < 0.02) respectively. PGE predicted the frequency of injections at any joint (p < 0.01). At one year, all 11 with PJIA had improved clinical and laboratory parameters.

PJIA showed increased synovial pathology compared with OJIA (mean vessel score 6.9 vs. 2.6 (p < 0.05), mean B-cell score 1.7 vs. 1 (p < 0.05)).

**Conclusion:** In OJIA, PGE and ANA status predict recurrent synovitis. To date no correlation has been observed between histological findings and recurrent synovitis in OJIA. We will report on findings of our enlarged cohort who reach one year follow-up.

### P119

**Investigating the use of a limited core outcome variable set for the classification of response following methotrexate treatment in juvenile idiopathic arthritis (JIA)**

SP Hirani\textsuperscript{3}, L Kassoumeri\textsuperscript{2}, A Etheridge\textsuperscript{2}, K Mulligan\textsuperscript{1}, Collaborators PRINTO\textsuperscript{3}, N Ruperto\textsuperscript{3}, P Woo\textsuperscript{4}, L Wedderburn\textsuperscript{2} and SP Newman\textsuperscript{1}

\textsuperscript{1}UCL Behavioural Medicine, London, UK

\textsuperscript{2}UCL Institute of Child Health, London, UK

\textsuperscript{3}Paediatric Rheumatology International Trials Organization, Genova, Italy

\textsuperscript{4}UCL Centre of Paediatric and Adolescent Rheumatology, London, UK

**Pediatric Rheumatology 2008, 6(Suppl 1):P119**

**Background:** The utility of the core outcome variable (COV) classification procedure as a method of gauging response to treatment in JIA is often jeopardised by missing data. To investigate how accurately cases are classified as responders or non-responders with a limited set of data, this study systematically examined how the exclusion of core variables influenced classification.

**Methods:** From a complete dataset of 410 JIA patients (provided by PRINTO), variables were systematically excluded and cases reclassified as responders or non-responders according to the criteria of improvement at 30%, 50% or 70%. Comparisons of the sensitivity, specificity were utilised to anticipate how the exclusion of core variables influenced classification.

**Results:** The systematic removal of one variable resulted in lowered accuracy of classification in the ranges of 86.5–91.8%, 81.7–93.9% and 79.5–88.6% at the 30%, 70% and 50% criteria levels. Exclusion of the CHAQ had the least impact, while exclusion of the number of active joints had the greatest impact on accuracy. As the percentage criteria became more stringent the overall accuracy reduced, however even at the 70% criteria levels. Exclusion of the CHAQ had the least impact, while exclusion of the number of active joints had the greatest impact on accuracy.

**Conclusion:** It is possible that a limited set of variables can lead to a relatively accurate indication of the response to treatment by JIA patients, but careful consideration of the precise variable(s) omitted is required.
P120

**Investigating which variables from the core outcome variables in juvenile idiopathic arthritis (JIA) are the best predictors of classification as a responder to treatment with methotrexate (MTX)**

SP Hirani1, L Kassoumeri2, K Mulligan1, Collaborators PRINTO1, N Ruperto2, P Woo3, LR Wedderburn4 and SP Newman5

1UCL Behavioural Medicine, London, UK
2UCL Institute of Child Health, London, UK
3Paediatric Rheumatology International Trials Organisation, Genova, Italy
4UCL Centre of Paediatric and Adolescent Rheumatology, London, UK

**Pediatric Rheumatology** 2008, **6(Suppl 1)**:P120

**Background:** Percentage change scores over six core outcome variables (COV) are utilised to classify response to treatment in JIA. This study aimed to determine the relative contribution of each of the COV towards the classification of improvement following treatment, at the ACR30, 50 and 70 levels.

**Methods:** Using a dataset of 410 JIA patients treated with MTX, (provided by PRINTO) 3 sets of logistic regression analyses were conducted, one at each classification level, to determine the likelihood of a classification of improvement. For each level a series of univariate logistic analyses were conducted to identify, from the six COV, individually significant (p < 0.05) predictors of improvement. These variables were entered into a stepwise multivariate logistic analysis to identify independent predictors of classification (p < 0.01) at each level.

**Results:** For all three classification criteria, each core variable change score was an individually significant predictor of improvement as classified using classical procedures. Within multivariate analyses, physician global rating was the ‘best’ indicator of improvement at all criteria levels. ESR did not contribute significantly above other variables in all the multi- variate analyses. The remaining variables all contributed significantly in the 30% and 50% models. The limited variable models showed relatively good classification of cases, 93.9, 89, and 87.3% at the 30%, 50% and 70% levels respectively.

**Conclusion:** Individually all the core variables are important indicators of improvement in JIA. However, when used in combination a limited set of variables can lead to a relatively accurate indication of response to treatment by JIA patients.

P121

**Associations between continuous measures of disease activity in adult RA and the pediatric ACR response measures: a secondary analysis of JIA data**

S Ringold2, Y Chon1 and NG Singer1

1University Hospitals/Case Medical Center and Rainbow Babies and Children’s Hospital, Cleveland, OH, USA
2Children’s Hospital & Regional Medical Center/University of Washington, Seattle, WA, USA
3Amgen, Inc, Thousand Oaks, CA, USA

**Pediatric Rheumatology** 2008, **6(Suppl 1)**:P121

**Objectives:** To measure correlations between the DAS, DAS28, Simplified Disease Activity Index [SDAI], and Clinical Disease Activity Index [CDAI] and ACR responses; to determine validity of these measures in polyarticular-course juvenile idiopathic arthritis (polyJIA).

**Methods:** Retrospective analysis of 2 etanercept trials. Disease activity was calculated at baseline, 3 mo, and 6 mo. Data were analyzed independent of treatment arm. Visits were classified by highest level of pediatric ACR response. EULAR response levels were based on DAS/DAS28 values. Correlation coefficients were calculated between the above measures. Areas under the receiver operating characteristic curve assessed discriminative characteristics of each continuous measure to the pediatric ACR response measures.

**Results:** Mean DAS, DAS28, CDAI, and SDAI were 3.7, 4.7, 30.8, and 36.4 respectively at baseline, corresponding to high disease activity levels for the DAS, CDAI and SDAI, and moderate for the DAS28. At 3 mo, mean values corresponded to low disease activity for the DAS/DAS28, and moderate for the CDAI/SDAI. At 6 mo, mean scores corresponded to low disease activity for the DAS/DAS28/CDAI, and moderate for the SDAI. Good EULAR response was seen at 3 and 6 mo. Correlation between the continuous outcome measures and the pediatric core set components was moderate to very good, with the closest correlation observed between the active joint count (kappa = 0.62–0.97).

**Conclusion:** Good correlation was seen between the DAS, DAS28, CDAI, and SDAI and the ACR pediatric measures of response, supporting value for prospective validation in polyJIA.

**Acknowledgements**

Statistical support by Immunex (a wholly owned subsidiary of Amgen) and Wyeth.

P122

**Abstract withdrawn**

Pediatric Rheumatology 2008, **6(Suppl 1)**:P122

P123

**The anti-inflammatory stage of monocytes after long-term stimulation with LPS is mediated by p38 MAP kinase dependent epigenetic silencing**

D Viemann1, P Koenen1, K Barczyk2, L Steinmueller2 and J Roth1

1University Hospital of Muenster, Institute of Immunology, Muenster, Germany
2University Hospital of Muenster, Department of Pediatrics, Muenster, Germany

**Pediatric Rheumatology** 2008, **6(Suppl 1)**:P123

Lipopolysaccharide (LPS) as major constituent of Gram-negative bacteria is known to elicit a rapid pro-inflammatory primary response in immune cells. Multiple findings indicate that monocytes next to its crucial function in the early stage of LPS signaling might additionally play an essential role in the resolution of systemic inflammatory responses. We therefore compared gene expression profiles of short-term and long-term LPS-stimulated monocytes. Surprisingly, we revealed an anti-inflammatory gene expression program after long-term LPS treatment. Blocking different signaling pathways revealed p38 MAP kinase to be significantly involved in the regulation of this anti-inflammatory program. Functional clustering analysis showed that chromatin remodeling genes are significantly overrepresented in the group of p38 MAP kinase-dependent genes. To test whether epigenetic modifications cause
transcriptional silencing in long-term LPS-treated monocytes and whether this process is p38 MAP kinase-dependent we performed chromatin-immunoprecipitations. We confirmed for pro-inflammatory genes an increased trimethylation of histone 3 (H3K4me3) and increased acetylation of histone 4 (AcH4) after 4 h LPS treatment indicating increased transcription whereas after 16 h of LPS treatment AcH4 decreased. Blocking p38 MAP kinase reversed the long-term LPS effect causing a strong increase of AcH4 and methylation of H3K9 both indicators of high transcriptional activity. Our results show that p38 MAP kinase contributes significantly to an anti-inflammatory gene expression program in monocytes after long-term LPS treatment. The application of p38 MAP kinase inhibitors currently proposed as novel anti-inflammatory agents might result in deleterious effects on innate immune-regulatory mechanisms.

P124
TGF-β signalling contributes to thymic epithelial cell damage and regeneration following myeloablative conditioning and stem-cell transplantation
MJ Hauri-Hohl and GA Hollander
Pediatric Immunology, Center for Biomedicine, Basel, Switzerland

Hematopoietic stem cell transplantation (HSCT) is considered a potentially curative therapy for a number of severe autoimmune diseases. The rationale consists of deleting auto-reactive T and/or B cell clones and re-constructing a functional immune system tolerant to auto-antigens. Re-emergence of T cell immunity following myeloablation largely depends on thymic de novo production of naïve T cells. The thymic stroma – mainly consisting of thymic epithelium (TE) – is responsible for the attraction of thymocyte precursor cells, support of developing T cells and appropriate positive and negative selection of a broad T cell receptor repertoire. Several reports including ours have demonstrated a negative impact of conditioning on TE numbers and function, which results in delayed T cell reconstitution. We have recently described the contribution of TGF-β signalling to thymic epithelial cell damage after irradiation, yet the underlying molecular mechanisms remain elusive.

In this report we analyse the involvement of TGF-β family members and downstream molecules in TE injury and regeneration following irradiation using different mouse models and in vitro assays. We demonstrate the detrimental effects of active TGF-β protein released by thymocytes early after irradiation on proliferation and phenotype of TE with a direct consequence on the dynamics of T cell reconstitution. The particular importance of TE in the process of efficient T cell development necessitates the development of strategies to protect the TE compartment and enhance its restoration in the context of pre-HSCT conditioning.

P125
Functional characterization of GM-CSF induced monocyte subsets
J Dabritz1, J Ehrchen2, H Wittkowski2, K Barczyk2, J Roth1 and D Foell1
1Department of Paediatrics, University of Muenster, Muenster, Germany
2Institute of Immunology, University of Muenster, Muenster, Germany
3Department of Dermatology, University of Muenster, Muenster, Germany

P126
IL-1 beta receptor antagonist efficacy in the treatment of idiopathic recurrent pericarditis
P Picco1, F Traverso1, G Brisca1, A Parodi1, A Loy1, M Gattorno1 and A Martini2
1IRCCS G. Gaslini, Genova, Italy
2IRCCS G. Gaslini and Universita di Genova, Genova, Italy

Objective: To assess the efficacy of IL-1 beta receptor antagonist (IL-1RA) in the treatment of steroid dependent idiopathic recurrent pericarditis (RP).

Methods: Three patients (1 male, 2 females, aged between 13 and 16) were enrolled. RP was defined by “pericardial” pain and ≥ 1 of the following signs: fever, pericardial friction rub, electrocardiographic changes, echocardiographic evidence of pericardial effusion, elevated acute phase reactants.

Patients showed recurrent flares of pericarditis with malaise, precordial pain, tachycardia, fever, sometimes fever. 2/3 developed a life-threatening cardiac tamponade needing pericardiotomy. None of them presented signs or symptoms consistent with a chronic rheumatic disease: antinuclear, anti-cosackie and
anti adenovirus antibodies were negative. Genetic analysis ruled out Familial Mediterranean Fever. Mean disease duration was 2 years and mean rate of recurrences was 4 yearly. Pericarditis seemed steroid dependent and poorly responsive to colchicine.

Results: IL-1RA administration was associated with a dramatic disappearance of symptoms and normalization of acute phase reactants. In all three patients IL-1RA was stopped after the achievement of a complete remission. In all cases, withdrawal was followed by a flare after a few weeks. The reinstitution of IL-1RA was associated with a new immediate response. All patients were maintained on IL-1RA treatment whilst steroids were tapered and stopped; at a mean follow-up of 4 months, none of them has experienced a disease relapse.

Conclusion: IL-1 RA may be effective in the treatment of idiopathic recurrent pericarditis; moreover, this preliminary finding seems to suggest that these patients could be affected by a new, not yet identified, genetic autoinflammatory disease.

P127

Diagnostic value of 18F-FDG-PET and PET-CT in children with fever of unknown origin or unexplained signs of inflammation

J Däbritz1, N Jasper1, H Wittkowski1, M Löffler2, M Weckesser2 and D Foell1

1University of Muenster, Dept. of General Paediatrics, Münster, Germany
2University of Muenster, Dept. of Nuclear Medicine, Münster, Germany

Pediatric Rheumatology 2008, 6(Suppl 1):P127

Background: Fever of unknown origin (FUO) and unexplained signs of inflammation are challenging medical problems and predominantly caused by infections, malignancies and noninfectious inflammatory diseases. The aim of this study was to assess the diagnostic value of fluorine-18 fluorodeoxyglucose positron emission tomography (18F-FDG-PET) and of its combination with computer tomography technology (PET-CT) in the diagnostic work-up in pediatric patients.

Methods: 47 FDG-PET and 23 PET-CT-scans of 63 patients (median age 7.2 years, 32 M, 31 F) were analyzed in this retrospective study. The diagnostic value of PET investigations in pediatric patients presenting with FUO (group 1, n = 41 scans) or unexplained signs of inflammation without fever (group 2, n = 29 scans) was analyzed.

Results: Of the total number of FDG-PET/PET-CT scans 32/57% were clinically helpful or diagnostic, respectively. In 54% (n = 38) of all scans the PET either was negative or findings could neither be confirmed nor excluded by extensive further diagnostic procedures. In scans with pathological findings (n = 32) further investigations confirmed the PET results in 81% (n = 26) of the cases. The accuracy of combined scans in these patients was 93%. A diagnosis in pediatric patients with FUO could be established in 32%, in patients with other signs of inflammation in 52%.

Conclusion: This is the first study demonstrating that FDG-PET and PET-CT may be a valuable imaging technique in the evaluation of children with FUO and unexplained signs of inflammation. Pathological findings help direct the diagnostic work-up in these patients. Because of its better accuracy, PET-CT is superior to 18F-FDG-PET.

P128

A retrospective clinical analysis of medical treatments used for symptomatic relief of Raynaud’s phenomenon in children at Royal Liverpool Children’s Hospital, UK

K Gargh and L McCann

Royal Liverpool Children’s Hospital, Liverpool, UK

Pediatric Rheumatology 2008, 6(Suppl 1):P128

Background: Literature on treatment of Raynaud’s phenomenon (RP) in the paediatric age group is scarce, and practice varies. We completed a retrospective analysis of patients with RP treated by paediatric rheumatologists at Royal Liverpool Children’s Hospital to assess clinical response to medical treatments including calcium channel blockers (nifedipine and amlodipine) and Glyceryl trinitrate (GTN) patches.

Methods: Clinic letters and case notes were reviewed. RP was graded as mild, moderate or severe according to frequency and severity of symptoms. Response to treatment was assessed by reduction in symptoms without significant adverse effects.

Results: A total of 45 patients were included in the study of which 42 (32 with primary and 10 with secondary Raynaud’s) had sufficient data available for analysis. 14 patients did not receive any medical intervention. 28 patients received one or more medical treatments sequentially over time. GTN patches were used in 18 patients of whom 9 (50%) demonstrated a good response. Three more patients await assessment. Six patients failed to improve, or had adverse effects. Nifedipine was used in 11 patients of whom 4 (36%) showed a good response. Amlodipine was used in 12 patients of whom 3 (25%) showed a good response.

Conclusion: No one treatment option is uniformly efficacious in patients with Raynaud’s. GTN patches seem to be effective without significant adverse effects. Amlodipine and nifedipine were useful in smaller percentages of patients. Clinical response was similar in patients with primary and secondary Raynaud’s. Responses according to severity of disease are discussed.

P129

Erdheim-Chester disease in children: clinical, radiologic, treatment characteristics of three cases

S Eyssette-Guerreau1, C Job-Deslandre2, M Taghian3, J Donadieu4, P Thierry3, J Haroche5, M Taylor1, I Koné-Paut1 and TA Tran1

1Department of Paediatrics, Pediatric Rheumatology, Bicêtre university hospital, Le Kremlin-Bicêtre, France
2Department of Rheumatology, Cochin university hospital, Paris, France
3Department of Paediatric, hospital of Vesoul, Vesoul, France
4Department of Pediatric Onco-hematology, Trousseau university hospital, Paris, France
5Department of Internal medicine, La Pitié-Salpêtrière university hospital, Paris, France

Pediatric Rheumatology 2008, 6(Suppl 1):P129

Background: Erdheim-Chester disease (ECD) is a rare non-Langerhans cell histiocytosis (NLH), characterized by bilateral metaphyseal sclerosis of long bones and visceral infiltration. The histopathological hallmark is a xanthogranulomatous infiltration
Pediatric Rheumatology 2008, 6(Suppl 1): P130

Etanercept efficacy in the treatment of chronic isolated inflammatory coxitis
A Parodi¹, P Picco¹, C Malattia¹, S Davi¹, S Dalprà¹, F Traverso¹, MC Ponti¹, A Buoncompagni¹, A Loy¹, S Viola¹ and A Martini²
¹Istituto G. Gaslini, Genova, Italy
²Istituto G. Gaslini and Università di Genova, Genova, Italy

Background: Chronic isolated inflammatory coxitis (CIIC) is characterized by exclusive involvement of coxo-femoral joints and an aggressive course leading to permanent structural damage, often requiring surgical treatment. Early commencement of disease-modifying or corticosteroid therapy has been suggested. To date, treatment with biological agents has not been reported. We describe the favourable response to etanercept in two girls with CIIC.

Patients: Patient 1 (15 years) and patient 2 (17 years) presented with a history of hip pain and limp lasting 3 and 5 years, respectively. Previous disease-modifying therapy was ineffective. Hip radiograph showed bilateral joint space narrowing in both patients and ankylosis of right hip in patient 2. ANA and HLA-B27 were negative in both cases. Active phase reactants were mildly increased in patient 2. Magnetic resonance imaging (MRI) was obtained immediately before and after treatment with etanercept.

Results: Treatment with etanercept was followed by a significant improvement of pain and limitation of motion in patient 1: MRI after 6 months showed considerable reduction of synovial effusion. Synovitis and bone marrow oedema of femoral head, previously visualized, were not detectable. Mild clinical improvement and normalization of inflammatory parameters were observed in patient 2: MRI after 12 months showed no progression of structural damage. MRI findings of disease activity were not detectable.

Conclusion: Etanercept treatment was effective in our patients. Clinical and radiological improvement was more evident in the patient with a shorter disease duration. Early treatment with anti-TNF agents should be considered in patients with CIIC to prevent severe structural damage.

P131

The outbreak of Rheumatic Fever in the city of Trieste
A De Cunto, P Salieri, I L’Erario, F Verzegnassi, N Giurici and L Lepore
IRCCS Burlo Garofolo, Trieste, Italy

Pediatric Rheumatology 2008, 6(Suppl 1): P131

The annual incidence of rheumatic fever (RF) in developed countries is 0.5–1/100,000 among subjects at risk. The decline in the incidence of RF observed in the past decades was mostly attributed to improvement of the living conditions and the availability of medical care and widespread use of antibiotics. However, focal outbreaks were reported in the past, probably due to resurgence of rheumatogenic strains.

We described the series of RF diagnosed in the city of Trieste between April 2007 and April 2008. 10 cases of acute RF were reported, 7 females and 3 males. The median age was 6.11 years (4.6–10 years). 7/10 of patients had a history of recent upper respiratory tract infection, 3/10 received oral amoxicillin. Migratory polyarthritis occurred in 50% of patients; carditis in 60% (in 2 of 10 valvular regurgitation was demonstrated by echocardiography without accompanying auscultatory evidence). Chorea occurred in 30% of patients. No patient presented erythema marginatum or subcutaneous nodules. All patients with chorea received corticosteroids with prompt resolution of symptoms except one who responded to valproate and IgIV.

The annual incidence of rheumatic fever in the past ten years in our region was 4–6/100,000 per year. We reported the RF outbreak that occurred in the last year in Trieste (43/100,000 population), the capital of the Friuli Venezia Giulia region. This resurgence was focal and not countrywide.

We observed a relatively low incidence of arthritis and high incidence of corea, probably due to a particular rheumatogenic strain that we were unable to identify so far.

P132

Treatment of the low bone mineral density with intravenous pamidronate in pediatric patients: review of a protocol of a single-day infusion twice a year
S Ricart, J Anton, M del Rio and J Ros
Hospital Sant Joan de Déu, university of Barcelona, Barcelona, Spain

Pediatric Rheumatology 2008, 6(Suppl 1): P132

Background: On the basis of effectiveness of bisphosphonates in adults, a simple protocol for the treatment of low bone mineral density in children was developed in 1995 in our centre.

Objectives: To review the effectiveness of a single-day infusion of pamidronate twice a year in children. Secondary, to describe its efficacy in relation to the etiology of osteoporosis.
Materials and methods: Retrospective review of patients treated with pamidronate from January 1995 to June 2006 in Sant Joan de Déu hospital (Spain). Patients: younger than 18 years that underwent treatment with the protocol for at least one year and with z-score < −2.5, fractures and z-score < −1 or documented bone pain with z-score < −1. They were classified into 4 groups: osteogenesis imperfecta, chronic treatment with steroids, disuse and other conditions. Interventions: single intravenous administration of pamidronate (30 mg in prepubescent patients and 60 mg in all other patients) every six months. Clinical, radiological data and bone mineral density were obtained basal and after each cycle. For each patient the ratio fractures/year during the treatment and the total increase in z-score (total ΔZ) after the treatment were calculated.

Results: 56 patients were included. Overall, fractures/year decreased from 1.75 basal to 0.46 during the treatment. Osteogenesis imperfecta group had better total ΔZ (1.25). Disuse group had clinical improvement although poor total ΔZ increase (0.12).

Conclusion: There is a clinical improvement in all patients. The OI group has the best gain in bone mineral mass. The protocol is safe, simple and well tolerated by patients and families.

P133
Treatment of osteogenesis imperfecta with intravenous pamidronate in pediatric patients: comparison between a single-day infusion twice a year protocol with other regimens described in the literature
S Ricart, J Anton, M del Rio and J Ros
Hospital Sant Joan de Deu, University of Barcelona, Barcelona, Spain

Pediatric Rheumatology 2008, 6(Suppl 1):P133

Background: In 1995 our institution developed a protocol to treat children with pamidronate. Several protocols have been published to treat osteogenesis imperfecta (OI) in the last decades. Objectives: to review the usefulness of our protocol in OI and to compare it with published protocols.

Materials and methods: Retrospective review of OI patients treated with pamidronate from 1995 to 2006 in our centre. Inclusion criteria: OI < 18 years with z-score < −2.5, fractures and z < −1 or documented bone pain with z < −1. Treatment:

Table 1 (abstract P133) Comparison between our protocol and the ones published by Glorieux and Arikoski

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>20</td>
<td>30</td>
<td>12</td>
</tr>
<tr>
<td>Dose (mg/Kg/year)</td>
<td>2.4(0.3)</td>
<td>6.8(1.1)</td>
<td>12</td>
</tr>
<tr>
<td>Periodicity of</td>
<td>6</td>
<td>3–4</td>
<td>3</td>
</tr>
<tr>
<td>infusions (m)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basal z-score</td>
<td>−4.3(2)</td>
<td>−5.3(1.2)</td>
<td>“</td>
</tr>
<tr>
<td>Final z-score</td>
<td>−3.38(2.4)</td>
<td>−3.4(1.5)</td>
<td>“</td>
</tr>
<tr>
<td>Years of treatment</td>
<td>3**</td>
<td>2.1(range 1.3–5)</td>
<td>1</td>
</tr>
<tr>
<td>Mean annual increase in: z-score</td>
<td>0.49(0.1)</td>
<td>0.95</td>
<td>“</td>
</tr>
<tr>
<td>BMD</td>
<td>21.1(5.1)</td>
<td>41.9(29)</td>
<td>63.5(37.3)</td>
</tr>
</tbody>
</table>

Mean(SD), m: months. “Data not available. ** For comparability with the other series only the results of the first 3 years are shown.

P134
Idiopathic hypereosinophilic syndrome (HES) in a 15 year-old girl
M Jelusic, L Tambic-Bukovac and I Malcic
Department of Paediatrics, Division of Paediatric Rheumatology, University Hospital Centre, Zagreb, Croatia

Pediatric Rheumatology 2008, 6(Suppl 1):P134

Case report: The hypereosinophilic syndrome (HES) is a group of diseases characterized by persistent and marked blood eosinophilia, with end-organ involvement and no recognized secondary cause. We present a 15 year-old girl who was admitted to our Department in January 2008 with a four-week history of headache, arthralgias, myalgias, sore throat and angioedema. Laboratory test revealed significant leucocytosis (76 × 10^9/L with 88% eosinophils), thrombocytosis (758 × 10^9/L), elevated ESR (82 mm/h) and IgE 348.3 (n.v. < 114 g/L), and hypergamaglobulinemia. Extensive allergologic, immunologic, infectious, and toxicological studies were negative. Bone marrow biopsy showed increased cellularity with increased granulopoiesis predominated by cells of the eosinophilic lineage, with a normal karyotype. Patient was negative for the FIP1LI-PDGFRα fusion kinase and BCR-ABL gene fusion by RT-PCR: Abdomen CT showed diffuse small intestine wall thickness, and cardiac echocardiogram showed thickness of the left ventricular wall and interventricular septum. The biopsy of myocardium and small intestine was planned, but in a mean time patient’s condition was worsened. She developed hypoproteinaemia (46 g/L), generalised oedema, and diarrhoea. A diagnosis of idiopathic HES was made and methylprednisolone was introduced in the therapy. She had rapid response to methylprednisolone (within 12 hours), with normalisation of the blood counts, protein level and regression of oedema. Methylprednisolone was slowly tapered, and at present, HES is in complete clinical and laboratory remission.

Conclusion: Although HES is extremely rare in childhood, it has to be considered, when a patient is presented with significant leucocytosis and eosinophilia.
P135
Inflammatory bowel disease in children
M Desgranges1, F M. Rüemmele1, A Duquesnes2, JL Ginie3, O Goulet1, P Quartier1 and B Bader-Meunier1
1Hotel Necker, Paris, France
2Hospices civils de Lyon, Lyon, France
3Centre hospitalo-universitaire d’Angers, Angers, France
Pediatric Rheumatology 2008, 6(Suppl 1):P135
Purpose: To describe the clinical presentation of inflammatory arthritis associated with inflammatory bowel disease (IBD) in children.
Methods: Retrospective study conducted in 3 French pediatric centres. Children presenting with IBD associated with inflammatory arthritis were included.
Results: Nine children aged from 2.8 to 14.9 years presented with a Crohn’s disease associated with arthritis. Rheumatic disease occurred 25 to 41 months before the diagnosis of IBD (3 children), 8 to 62 months after the diagnosis of IBD (4 children) or at the same time of IBD (2 children). In the first three children, polyarticular form of juvenile idiopathic arthritis and Still’s disease were initially diagnosed. IBD was diagnosed 2 to 7 months after the initiation of etanercept (2 children) and anakinra (1 child). Arthritis developed in children who received corticosteroids, infliximab, methotrexate and/or azathioprine because of IBD. Patients presented with peripheral arthritis, involving knees (7 children), ankles (5 children), and rarely hips, fingers, elbows and shoulders. 12/18 relapse of arthritis occurred at the same time as relapses of IBD. Abdominal manifestations included diarrhea, anal abscess, abdominal pain, vomiting, and loss of weight. Mean C reactive protein value and erythrocyte sedimentation rate were 102 mg/L and 58 mm at onset of the disease respectively.
Discussion: IBD may be diagnosed several years after the occurrence of arthritis and must be searched for in children presenting with arthritis and abdominal involvement and/or weight loss. IBD may develop in children who receive etanercept while infliximab does not prevent the occurrence of inflammatory arthritis.

P136
Myobacterial arthritis as a complication of a Bacille Calmette-Guérin (BCG) vaccination in an immunocompetent child
B Déralvi1, T Verebély1, L Kovács1, J Feinberg2 and Gy Póder1
11st Dept. of Pediatrics Semmelweis University, Budapest, Hungary
2Human Genetics of Infectious Diseases, INSERM U550, Université Paris Descartes, Necker Medical School, Paris, France
Pediatric Rheumatology 2008, 6(Suppl 1):P136
BCG vaccine (attenuated strain of virulent Mycobacterium bovis) is worldwide administered in the first weeks of life. Systemic BCG infection or osteomyelitis are rare infrequent complications especially in immunocompromised individuals. We report a case of an immunocompetent infant with BCG arthritis.

A 17 month old boy presented with monoarthritis involving his knee, which started 7 month earlier, responding to NSAID therapy, respectively. On physical examination the only finding was the painful effusion and functional limitation of the right knee, with hyperaemic skin reaction above it. His BCG scar was normal. Laboratory evaluation showed mildly elevated CRP (21 mg/l) and C3. RF, ANA, ENA and serological tests for infections were unrevealing. X-ray showed bony overgrowth of the distal femoral epiphysis without osteomyelitis. Ultrasound and MRI of the knee showed intra- and extraarticular effusion. Aspirates were turbid with 95% of polymorphs and were sterile with culture, no presence of acid-fast bacilli were detected. Further culture identified BCG vaccine strain of M. bovis. Twelve weeks of isoniazid therapy was ineffective, surgical bursectomy gave a complete healing. Histological examination revealed granulomatous inflammation with ceasing necrosis. Hypererg PPD test, normal T-cell functions, NBT-test and analysis of the IFNγ/IL-12 pathway ruled out primary immunodeficiency, HIV-test was negative as well.
BCG arthritis (chronic, painful, affecting the bursa) is a rare complication of the vaccine after a long latent period. Detecting BCG mycobacterium with PCR-reaction from the aspirat could shorten the diagnostic time. Primary immunodeficiencies associated with an increased susceptibility to mycobacterial infections should be ruled out.

P137
Chronic granulomatous disease in an infant with sweet syndrome
S Hanedan1, B Sahin1, N Akty Ayaz2 and H Aldemir1
1Bakirkoy Maternity and Childrens’ Education and Research Hospital, Istanbul, Turkey
2Hacettepe University Medical Faculty, Ankara, Turkey
Pediatric Rheumatology 2008, 6(Suppl 1):P137
Sweet syndrome is a rare and recurrent febrile neutrophilic dermatosis that is characterized by pyrexia, leukocytosis, painful erythematous plaques of skin and neutrophile infiltration of the dermis. An 1.5 – month old boy presented with the complaints of fever and rash. He was pale and had widespread lymphadenopathy. He had oral candidiasis and eruption characterized by macules and plaques on an erythematous basis. He was anemic and tromboctopenic. His ESR and CRP levels were high. Antibiotherapy was started with the possible diagnosis of sepsis. But there was no growth in his cultures. Viral serology was also negative. After a course of antibiotics he was still febrile and his skin lesions did not diminish. Skin biopsy was performed and the histopathological examination confirmed neutrophilic infiltration of the dermis. According to the diagnostic criteria developed by von den Diesch, the diagnosis of Sweet syndrome was made. He was evaluated for a possible accompanying immunodeficiency and a diagnosis of chronic granulomatous disease was confirmed with NBT test. He was evaluated for the presence of malignancies and collagen vascular diseases, but none was present. His clinical and laboratory findings improved after systemic steroid treatment. Here, a rare syndrome accompanied by a concurrent rare immunodeficiency is presented. In the literature there was 2 cases reported with these associations. But still any relationship between them remains to be described.
**P138**

**Assessment of children presenting with rheumatic complaints to a tertiary center in Turkey: differences in an Eastern Mediterranean population**

O Bircan Cakaytar, A Duzova, O Teksam, N Akty Ayaz, O Derman, A Bakkalaglu, G Kale and S Ozen

Hacettepe University, School of Medicine, Ankara, Turkey

**Pediatric Rheumatology 2008, 6(Suppl 1):P138**

Aim: To evaluate the profile of rheumatic complaints in children in Turkey. The data of the first half of a 6-month prospective study is presented.

Methods: Demographic features, medical history, symptoms and signs of children with rheumatic complaints were analysed prospectively in a tertiary health center in central Anatolia. A detailed rheumatologic examination was done. Complete blood counts, ESR, CRP measurement were performed in all patients; other studies were done if necessary.

Results: From 01\(^{st}\) December 2007 to 29\(^{th}\) February 2008, a total of 241 children (M/F: 124/117; mean age 8.0 ± 4.0 years) were enrolled. Knee, ankle, hip and wrist were the most frequently involved joints. 61.8% had rheumatic diseases, and 38.2% had non-rheumatic diseases. The common causes constituted of familial Mediterranean fever (12.0%), other periodic fever syndromes (2.1%), HSP (8.7%) and other vasculitides (3.7%), JIA (10.0%), toxic syndovitis (6.6%), rheumatic complaints during the course of an infectious disease (7.9%), growth pain (12.9%), orthopedic problems (18.7%); acute rheumatic fever (1.7%), malignancy (1.7%), SLE (1.2%), dermatomyositis (0.4%), overlap syndrome (0.4%) and fibromyalgia (0.8%) were rare.

Conclusion: This is the first study assessing the profile of rheumatic complaints in this part of the world. Our results have showed that auto-inflammatory diseases are strikingly high. Vasculitides and HSP are higher, whereas fibromyalgia is very rare compared to Western Europe. The frequency of ARF has decreased.

**P139**

**A rare case of sarcoid osteitis in a child with response to methotrexate**

C Goel, S Balan, H Venning, V Goel, N Camina, L Hutchinson and S Rangaraj

Queen’s Medical Centre, Nottingham University Hospitals, Nottingham, UK

**Pediatric Rheumatology 2008, 6(Suppl 1):P139**

Sarcoidosis is a disease of unknown origin characterised by noncaseating granuloma and can involve any tissue or organ. Osseous involvement in sarcoidosis is rare in children and long tubular bone involvement is even rarer. We present a case histologically proven as sarcoid osteitis of radius and humerus that had a dramatic response to methotrexate.

A 9 year old Jamaican boy with known sarcoidosis, diagnosed in Kingston by cervical lymph node biopsy initially presented to us with high grade pyrexia, peripheral lymphadenopathy and painful shiny swelling in both shin. Tentative diagnosis made was sarcoid related osteitis. X-ray of legs (Figure 1) showed periosteal reaction in leg bones. He was treated with subcutaneous methotrexate.

After 3 years of drug-induced remission, methotrexate was stopped. Eight months after stopping methotrexate he presented with painful swelling of left arm and forearm. Radiograph showed circumferential lesion with periosteal reaction and MRI scan confirmed surrounding oedema suggestive of acute lesion. Sarcoid osteitis was confirmed on biopsy by the presence of characteristic non caseating granuloma with giant cells. He was restarted on methotrexate upon which the lesions resolved in a few weeks.

Authors conclude that long bone involvement in a child with sarcoidosis is rare but we should have low threshold for biopsy in known case of sarcoidosis presenting with radiological feature of osteitis to confirm the diagnosis and for treatment. In our case there was excellent response to methotrexate.

Reference


**P140**

**Brucellosis – forgotten but not gone**

RP Khubchandani, Č Khemani, V Vishwanathan and PR Chickermame

Jaslok Hospital, Mumbai, India

**Pediatric Rheumatology 2008, 6(Suppl 1):P140**

Brucellosis, a zoonotic infection, is transmitted to children primarily by consumption of unpasteurized milk products. It can present with symptom complexes that mimic common chronic arthritis/connective tissue disorders, notably Still’s disease. We describe three children (Table 1) suffering from brucellosis, seen in the last year in our rheumatology services. These cases reemphasize the need for pattern recognition in rheumatologic disease. All three were referred by primary care physicians with a working diagnosis of systemic onset JIA/autoimmune disorder. However the lack of a “perfect fit” for such diagnoses,(pattern of fever, absence of rash/serositis, normal white cell/platelet counts) led us to explore a history of travel/residence in endemic areas and ingestion of unpasteurized milk. A family history of similarly afflicted members in one case was also relevant.

Serology is helpful but false positives may occur in hypergammaglobulinemic states. Blood cultures take weeks and the organism is a fastidious one. All three children responded well to a combination of streptomycin (2 weeks) and doxycycline (6 weeks).
Hypokalemic paralysis revealing Sjögren’s syndrome (case report)

L Minxová, S Škalová and R Slezák
Paediatric and Stomatologic Department of University Hospital, Hradec Králové, Czech Republic
Pediatric Rheumatology 2008, 6(Suppl 1):P141

Case report: A 16-year old girl presented with rapid onset of progressing muscular weakness, dysphagia, dysphonia and significant wasting. She lost 13 kg during the last year. On examination she was dystrophic (BMI 15.7) and had clinical signs of severe myopathy. Laboratory findings confirmed myopathy (CPK 106,4 ukat/L, ALT 0,96 ukat/L, AST 2,86 ukat/L, myoglobin 1582 ug/L), inflammatory markers were elevated (ESR 60/92, CRP 37 mg/L). There was marked hypokalemia (S-K 1,8 mmol/l) suggesting hypokalemic paralysis. Diagnosis of distal renal tubular acidosis (dRTA) was based on confirmation of hyperchloremic metabolic acidosis (S-CI 120 mmol/l, pH 7,31, BE-10) with normal serum anion gap, severe hypokalemia, high urinary pH (pH 7,5) and positive urinary anion gap. Other signs of renal tubular impairment were obvious (high urinary beta-2-microglobulin 213 mg/l, glomerulo-tubular proteinuria 1,01 g/24 h).

Positive autoimmune tests (high positivity of rheumatoid factor, IgG, IgA, IgM, positive ANA/IF, ENA SS-A/Ro, SS-B/La, elevation of circulating immunocomplexes and IgG) and mildly reduced values of sialometric measurements revealed primary Sjögren’s syndrome (SS) as the underlying cause of dRTA. The renal biopsy confirmed chronic tubulo-interstitial nephritis compatible with this diagnosis. Full recovery of muscle weakness and laboratory findings of hypokalemia and acidosis followed potassium and alkali replacement. Corticosteroids were administered with subsequent addition of cyclosporine A because of disease activity. The girl is in longterm remission.

Conclusion: We report the patient with severe hypokalemia and subsequent hypokalemic paralysis. The cause of hypokalemia was dRTA as the manifestation of renal impairment in primary Sjögren’s syndrome.

P142
Pyomyositis: a difficult diagnosis of an emerging disease in Italian immunocompetent children
PS Buonuomo1, A De Cunto2, L Lancell1, C Bracaglia1, P Salierno2, S Colafati2, L Lepore2, E Cortis1 and AG Ugazio1
1Department of Pediatrics, Pediatric Rheumatology, Ospedale Pediatrico “Bambino Gesù” IRCCS, Rome, Italy
2Clinica Pediatrica di Trieste, IRCCS Burlo Garofolo, Trieste, Italy
3Department of Pediatrics, Pediatric Infectious Disease, Ospedale Pediatrico “Bambino Gesù” IRCCS, Rome, Italy
4Department of Radiology, Ospedale Pediatrico “Bambino Gesù” IRCCS, Rome, Italy
Pediatric Rheumatology 2008, 6(Suppl 1):P142

Seven male and 1 female child with primary pyomyositis (mean age 11.4 years, range 3–1), were diagnosed in 2 Italian Pediatric Hospitals since 2005. The most frequently reported symptoms were fever, increasing hip pain with functional impairment, and general malaise for several days prior to admission. None had an underlying disease or a compromised immune system. Laboratory studies showed an elevated C-reactive protein and erythrocyte sedimentation rate while the CPK level was always within normal range.

X Rays and ultrasonography of the region involved were unremarkable in all patients, while MRI was diagnostic. Primary pyomyositis (PM) is a subacute, deep bacterial infection of the large skeletal muscles (often gluteal), generally related to Staphylococcus aureus infection (50–90%), Mycobacterium tuberculosis, Streptococcus pyogenes or anaerobic bacteria. It is frequent in tropical areas, while very few cases have been reported in Europe and the U.S where it is usually associated with immune deficiency (HIV, diabetes, tumors, liver or renal disease, or organ transplantation). Neglected cases may result in overwhelming sepsis, which might prove fatal, or in the formation of abscesses, requiring surgery. Because of the lack of specificity of laboratory testing, high clinical suspicion and early radiological evaluation are the key to diagnosis. MRI is the most effective and non invasive instrument in helping to diagnose and define the anatomic extent of the infection and differentiate between the early stage of diffused muscle inflammation and the subsequent abscess formation.

We believe MRI should be performed as soon as this condition is suspected.

P143
TNF-alfa blockers- promising therapy for chronic uveitis in very young children
T Tauber, G Dolinski and Y Morad
Assaf Harofe Medical Center, Zrifin, Israel
Pediatric Rheumatology 2008, 6(Suppl 1):P143

The term uveitis is used clinically to describe a heterogeneous group of diseases, characterized by inflammation of intraocular structures. Although frequently associated with systemic inflammatory or
autoimmune diseases such as Behcet’ disease, JIA, JAS, Sarcoidosis, a
significant number are labeled “idiopathic”.

TNF-alpha blockers which are an effective treatment for
systemic diseases associated with uveitis, were found effective in
uveitis in animal studies and later in clinical trials.

Three types of TNF-alpha blockers are currently being used:
Etanercept, Infliximab and Adalimumab. For Adalimumab no
sufficient data exist regarding the use in pediatric age however
recent studies show clear preference for Infliximab over
Etanercept for childhood uveitis.

We present four children (age 4, 4.5, 6, 12) diagnosed with
chronic childhood uveitis at a very young age which were
successfully treated with Infliximab in the pediatric rheumatology
clinic at our institution. All of them were initially treated
conventionally, and switched to Anti-TNFα because of ineffec-
tiveness of conventional treatment or severe side effects.

Regardless of the small cohort we found Infliximab efficient and
safe to use in chronic childhood uveitis at a young age.

**P144**

*Use of anti-TNF Etanercept in paediatric patients with autoimmune disease and ocular
involvement: the Parma experience*

M Rossi, S Gonzales, J Orsoni, L Zavota, A De Fanti and GC Izzi
University Hospital, Parma, Italy

**P144**

*Objective:* Previous studies showed that treatment with anti-
TNF Etanercept in patients with autoimmune disease such as
juvenile rheumatoid arthritis (JRA) or Behcet’ Disease provides
clinical improvement and efficacy. We evaluated the effective-
ness of anti-TNF therapy on ocular involvement and its toxicity.

**Methods:** 6 Patients with autoimmune disease, followed in our
Centre, have been evaluated since January 2007 until May 2008;
4 of them were treated with Etanercept since the beginning of
the study, 1 for 5 months and 1 for 3 months. In all patients Etanercept was added to a polipharmacological immunomodu-
lating therapy scheme, including Cyclosporine, Methotrexate
and steroids. Safety was assessed by monitoring rates of serious
adverse events (SAEs), effects on hepatic and renal function and
serious infections rates. Efficacy on ocular involvement was
assessed by monitoring and measuring inflammatory relapses.

**Results:** All patients studied received complete efficacy
assessments. During the study period we observed neither
SAEs nor serious infectious diseases. All patients enrolled in the
study didn’t show any effect on hepatic and renal function due to
Etanercept’s use. Concerning the effectiveness of Etanercept on
ocular involvement, we observed only 1 inflammatory relapse in
1 patient, at the beginning of anti-TNF treatment.

**Conclusion:** In our study Etanercept shows an acceptable
safety profile on hepatic and renal function and on the risk of
serious infections in children with ocular involvement in
autoimmune diseases; moreover, it provides significant improve-
ment in disease’s ocular manifestations.

**P145**

*Effectiveness of the treatment with intravenous pamidronate in children with rheumatic diseases*

A Marco, I Calvo and B Lopez
Hospital Infantil la Fe, Valencia, Spain

**P145**

**Introduction:** In patients with systemic diseases bone mineral
density is diminished due to the underlying disease, the
secondary loss of bone mass, the diminution of mobility and
the treatment with steroids. Bisphosphonates inhibit bone
resorption: they produce reduction of the apoptosis in
osteonblasts and induce apoptosis in osteoclasts [1, 2].

**Objective:** To value the effectiveness of the treatment with
intravenous pamidronate in children with secondary osteopor-
osis or osteopenia to rheumatic diseases.

**Materials and methods:** Retrospective analytical study:22 children, ages between the 4 and 17 years and clinical
diagnosis of osteopenia, osteoporosis, calcinosis secondary to
rheumatic diseases (Juvenile Idiopathic Arthritis, Systemic Lupus
Erythematosus, Juvenile Dermatomiositis, Overlap Syndrome,
Panarteritis Nodosa, Familiar Mediterraneaenean Fever). Criteria of
inclusion: the patients had to fulfill the criteria of osteopenia and
osteoporosis defined according to z-score or bone mineral
density; and the diagnostic criteria of the referred diseases.

Information about the underlying disease, the treatment
received and steroids’ dose and duration was collected. The
administration of intravenous pamidronate was made according
to the protocol established by Glorieux et al.

**Results:** All the patients treated with intravenous pamidronate
presented a significant increase in bone mineral density, clinical
improvement, decrease of the number of fractures, reduction in
bone pain and improvement of the quality of life. In all the
patients with calcinosis a reduction was observed and in one
patient it even disappeared.

**References**

1. Noguera A, Ros JB, Pavia C, Alcover E, Valls C, Villaronga M
and González E: Bisphosphonates, a new treatment for
glucocorticoid-induced osteoporosis in children. J Pediatr
Endocrinol Metab 2003, 16:529–536.

2. Shaw NJ and Bishop NJ: Bisphosphonate treatment of

**P146**

*Autoimmune response following influenza vaccination*

N Toplak1, T Kveder2, A Trampus-Bakija3 and T Avčin1
1Department of Allergology, Rheumatology and Clinical
immunology, University Children’s Hospital, University
Medical Centre, Ljubljana, Slovenia
2Department of Rheumatology, Laboratory for Immunology,
University Medical Centre, Ljubljana, Slovenia
33 Unit of Special Laboratory Diagnostics, University Children’s
Hospital, University Medical Centre, Ljubljana, Slovenia

**P146**

The aim of this study was to assess autoimmune response
following annual influenza vaccination in apparently healthy
adults, staff at a children’s hospital.

92 healthy adult subjects were tested for autoantibodies including
antinuclear antibodies (ANA), anti-extractable nuclear antigen
antibodies (anti-ENA), antiphospholipid antibodies (aPL), namely
anticardiolipin antibodies (aCL), anti-beta2-glycoprotein 1 antibo-
dies (aβ2-GPI) and lupus anticoagulant (LA). Blood samples were
taken from each participant before annual influenza vaccination,
one month and six months after vaccination.
Before influenza vaccination 26% of participants were positive for ANA, 1% for anti-ENA, 16% for aCL, 7% for a|2-GPI and 2% for LA. One month after influenza vaccination 76% of participants showed no change in autoantibodies titres. Six months after influenza vaccination 74% of participants showed no change in autoantibodies titres. Overall, there was no statistically significant difference in the percentage of positive ANA, aCL, a|2-GPI and LA before and 6 months after the vaccination. Five participants developed avascular bone defects 6 months after the vaccination and one who was initially low positive for ANA became highly positive (1:320). Eleven patients had only transiently increased autoantibodies. Persistently positive or progressively increased levels of autoantibodies during 6 months’ follow up were observed in 6 persons (7%).

Our study showed a high percentage of positive autoantibody testing among healthy adult staff at a children’s hospital. There was no statistically significant difference in the percentage of positive autoantibodies before and after influenza vaccination. However, our study clearly demonstrated induction of autoantibodies production in selected subjects.

P147
Mesenchymal stem cell transplantation in children – a two year follow-up
N Tzaribachev1, M Vaegler1, A Schaefer2, M Rudert3, P Reize4 and I Mueller1
1University Children’s Hospital, Tuebingen, Germany
2University Hospital, Dept. of Radiology, Tuebingen, Germany
3University Hospital, Dept. for Orthopaedics, Munich, Germany
4Hospital for Orthopaedics, Stuttgart, Afghanistan

Background: Children with haematological or autoimmune diseases (e.g. lupus erythematosus) are prone to acquire avascular osteonecrosis (AVN) following treatment with high dose steroids. More than 35% of those with advanced AVN stages (Marcus/Enneking II and III) fail to respond solely to core decompression.

Multipotent mesenchymal stromal cells (MSC) are capable of transforming into various mesenchymal tissues, e.g. bone. A combination therapy might be of benefit for those children.

Objective: We aim to show that the regeneration process of osseous structures is possible by local MSC application for steroid induced AVN in a child.

Patients and methods: One female patient with leukaemia and steroid induced AVN of the right knee (Marcus Enneking stage II-III) was treated with core decompression and local application of autologous MSC. The healing process was followed by MRI and CT-scan over a two year period.

Results: No early or late adverse events occurred. Two weeks after the procedure our patient was pain-free. Follow-up MRIs on day +72 and +210 showed a slow regress of the initial bone marrow edema and a continuing regeneration of the osseous defect. The CT-scan 24 months later documented the re-osification of the initial lesion.

Conclusion: Local MSC-application might be a promising treatment option for advanced steroid induced AVN in children with haematological or autoimmune diseases. Results of a prospective study are under preparation.

References
The author wishes to thank all who responded the survey.

Acknowledgements

Main differences were found. Support programmes should be focused on the areas where significant differences in the following areas: Number of paediatric rheumatologists per capita, number of centres, accessibility of treatments, research activities and relative average income of paediatric rheumatologists.

Conclusion: The results of this survey can help to define future strategies to improve paediatric rheumatology services in two ways. European standard of care should be developed to stimulate the governments of “underperforming countries” and build equal European standard of care it is necessary to study and understand these differences.

Materials and methods: During April 2008 international paediatric rheumatology community was invited to complete the survey using http://www.surveymonkey.com web based instrument. The invitation letters were sent by e-mail to all PReS members and PRINTO members from European countries. Survey consisted of 36 questions structured in 6 domains: About you About the country you currently work in About your centre About your research and international co-operation About your routine About your wishes.

Results: 133 responses were collected before May 22nd 2008 from 33 countries, among them 12 from 8 non-European countries. The responses were stratified according the gross income per capita http://web.worldbank.org and 2 groups of countries were created. Comparison of these two groups showed significant differences in the following areas: Number of paediatric rheumatologists per capita, number of centres, accessibility of treatments, research activities and international co-operation, language skills and relative average income of paediatric rheumatologists.

Conclusion: The results of this survey can help to define future strategies to improve paediatric rheumatology services in two ways. European standard of care should be developed to stimulate the governments of “underperforming countries” and support programmes should be focused on the areas where main differences were found.

Acknowledgements

The author wishes to thank all who responded the survey.

P150
UK paediatric rheumatology and its clinical trials network

MW Beresford, EM Baildam, PA Brogan, HE Foster, AV Ramanan, ME Rooney, JJ Shah, W Thompson, LR Wedderburn and PW Woo

Royal Liverpool Children’s Trust, Liverpool, UK

Institute of Child Health, London, UK

Newcastle Hospitals NHS Trust, Newcastle, UK

Bristol Royal Hospital for Children & Royal National Hospital for Rheumatic Diseases, Bristol, UK

Queen’s University Belfast, Belfast, UK

University College London, London, UK

University of Manchester, Manchester, UK

Pediatric Rheumatology 2008, 6(Suppl 1):P150

Background: There is striking paucity of a rigorous evidence-base for the treatment of paediatric musculoskeletal diseases. The Medicines for Children Research Network (MCRN) improves coordination and quality of clinical trials and related studies across the UK. It has joined in partnership with the Arthritis Research Campaign (arc), the major UK charitable funder of musculoskeletal research, to form the MCRN/arc Paediatric Rheumatology CSG.

Methods: The MCRN has extensive expertise in supporting non-commercial, pharmaceutical-sponsored and investigator-led studies. The CSG is a multi-disciplinary group comprising clinicians, academics, basic scientist, pharmacy, and clinical trials unit support. Through consultation with stakeholders, its remit includes: developing a comprehensive portfolio for clinical trials/related studies covering the spectrum of paediatric rheumatology; ensuring consumer involvement; upholding Good Clinical Practice.

Results: The CSG has developed topic-specific groups (TSGs) outlined in Table 1. Key “themes” across TSGs include: acceptability of intervention; quality of life; health economics; cardiovascular risk; skeletal health; rare diseases; orphan drugs; international collaboration. Key “tools” include: characterised phenotype cohort studies; biomarkers; genotype/phenotype/proteomics; pharmacogenomics; pharmacokinetic studies; mechanism of disease; Phase II and III studies. Strategic development of protocols is underway. Regionally based networks assist with feasibility, site selection, financial, ethical and governance arrangements, staff recruitment, training, participant recruitment and trial monitoring. Table 2 illustrates studies already MCRN adopted and supported in this way.

Conclusion: An integrated national research network provides an excellent infrastructure to collaborate closely with international trial networks (e.g. CARRA, PRINTO) while fostering a unique contribution to the transformation of clinical care of children.

<table>
<thead>
<tr>
<th>Topic Specific Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Auto Inflammatory Diseases</td>
</tr>
<tr>
<td>Bone Health</td>
</tr>
<tr>
<td>Juvenile Dermatomyositis</td>
</tr>
<tr>
<td>Juvenile idiopathic arthritis (JIA)</td>
</tr>
<tr>
<td>Juvenile-onset SLE</td>
</tr>
<tr>
<td>Rare disorders (Initial focus on Scleroderma)</td>
</tr>
<tr>
<td>Uveitis in JIA</td>
</tr>
<tr>
<td>Vasculitis</td>
</tr>
<tr>
<td>Formulations &amp; Pharmacy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2 (abstract P150) Studies recently adopted by MCRN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acronym</td>
</tr>
<tr>
<td>---------</td>
</tr>
<tr>
<td>POPS Study</td>
</tr>
<tr>
<td>UK JSE Cohort Study and Repository</td>
</tr>
<tr>
<td>MYCYC</td>
</tr>
<tr>
<td>SPARKS CHARMS</td>
</tr>
</tbody>
</table>
**P151**

**Successful treatment of relapsing Pigmented Villonodular Synovitis (PVNS) of the knee with radiosynoviorthesis**

C Costantini, GF Dalla Pozza, G Bertoni, G Martini and F Zulian

1 Paediatric Unit, Treviso, Italy
2 Nuclear Medicine Dept., Treviso, Italy
3 Orthopaedic Dept., Treviso, Italy
4 Department of Paediatrics, Padova, Italy

Pediatric Rheumatology 2008, 6(Suppl 1):P151

PVNS is a rare disorder characterised by benign proliferation of synovial tissue. The treatment is surgical but relapse rate is high (8% to 46%). We report a 13 years old girl with PVNS of the left knee diagnosed in February 2003. Three months after diagnosis she underwent surgical synovectomy. Two years later severe swelling of left knee with pain and limitation of movement developed and MRI confirmed the relapse of PVNS. She was treated with 3 intraarticular injections of etanercept two months apart with mild reduction of fluid but not of synovial hypertrophy. In November 2006 radiosynoviorthesis with one intraarticular injection of $^{186}$Re was performed. No side effects were reported and patient presented an important reduction of pain and improvement of range of motion. Six months after the procedure MRI showed marked decrease of fluid accumulation, and a mild improvement of range of motion. Six months after the procedure and patient presented an important reduction of pain and limitation of movement. In our case radiosynoviorthesis has been showed as a safe and effective treatment in relapsing PVNS, which can be considered both as alternative to surgical synovectomy and complementary to it in order to obtain a more persistent remission of the disease. The collaboration between paediatric rheumatologist, nuclear physician and orthopaedic surgeon is fundamental in establishing the timing of the procedure as well as type and dose of radioisotope to be used according to the age of the patient and the PVNS extension.

**P152**

**pGALS performs well in the hands of a medical student**

AL Rowan, S Jandial, A Myers, B Bateman, M Friswell and HE Foster

1 Newcastle University, Newcastle upon Tyne, UK
2 Newcastle Hospitals NHS Trust, Newcastle upon Tyne, UK
3 Northumbria Healthcare NHS trust, Northumberland, UK

Pediatric Rheumatology 2008, 6(Suppl 1):P152

**Background:** pGALS (paediatric Gait, Arms, Legs and Spine) is a paediatric musculoskeletal (pMSK) screening examination validated for use in school-aged children [1], aimed at medical students. It is envisaged that pGALS will improve clinical skills and facilitate access to specialist care. Our aim was to assess the validity of pGALS in student hands and compare it to assessment by a consultant paediatric rheumatologist.

**Methods:** The student (AR) received standard undergraduate pMSK teaching. pGALS was performed on children attending paediatric rheumatology clinics, with the student blinded to diagnosis and background information. Findings were recorded as “abnormal” or “normal” and compared to a same day examination by a consultant (HF/MF).

**Results:** The study included 59 children, median age 12 (range 4–17 yrs). 45 (76%) had juvenile idiopathic arthritis. Overall, sensitivity for whether a child was deemed “normal” or “abnormal” was 95%, with specificity 88%. Student pGALS had good sensitivity (60–100%) and specificity (89–100%) at all joints, except for TMJ (sensitivity 0%, specificity 98%). Missed abnormalities were mostly loss of range-of-motion at the foot, ankle and TMJ; however in these children, abnormalities elsewhere were detected. Student median time was 4.25 min (range 2.25–8.5), compared to consultant median of 2 min (range 2–8) [p = 0.001]. Pain score median was 0 (range 0–8).

**Conclusion:** pGALS is quick, acceptable and performs well in determining if the child has a normal MSK examination or not when used by a student. However, interpretation of abnormal versus normal, especially at the foot, ankle and TMJ, need to be addressed in clinical teaching.

**Reference**


**P153**

**Development of a web-based register for the Dutch national study on biologicals in juvenile idiopathic arthritis:**

FHM Prince, IS Ferket, SS Kamphuis, W Armbrust, RT ten Cate, EPAH Hoppenreijis, Y Koopman-Keemink, MAJ van Rossum, M van Santen-Hoeufft, M Twilt and LWA van Suijlekom-Smit

1 Erasmus MC Sophia Children’s Hospital, Rotterdam, Netherlands
2 UMCG Beatrix Children’s Hospital, Groningen, Netherlands
3 Leiden University Medical Centre, Leiden, Netherlands
4 Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands
5 Hagaziekenhuis Juliana Children’s Hospital, Den Haag, Netherlands
6 AMC Emma Children’s Hospital, Amsterdam, Netherlands
7 Academic Hospital Maastricht, Maastricht, Netherlands

Pediatric Rheumatology 2008, 6(Suppl 1):P153

**Objectives:** Most clinical studies use paper case record forms (CRFs) to collect data. In the Dutch multicentre observational study on biologicals we encountered several disadvantages of using the paper CRFs. These are delay in data collection, lack of overview in collected data, and difficulties in obtaining up-to-date interim reports. Therefore we wanted to create a more effective method of data collection compared to CRFs on paper in a multicentre study.

**Methods:** We designed a web-based register with the intention to make it easy to use for participating physicians and at the same time accurate and up-to-date. Security demands were taken into account to secure the safety of the patient data.

**Results:** The web-based register was tested with data from 161 juvenile idiopathic arthritis patients from nine different centres. Internal validity was obtained and user-friendliness guaranteed. To secure the completeness of the data automatically generated email alerts were implemented into the web-based register. More transparency of data was achieved by including the option to automatically generate interim reports of data in the web-based register. The safety was tested and approved.
**P154**

**Current educational status of pediatric rheumatology in Europe: the survey results**

E Demirkaya, S Ozen, T Saurenmann and W Kuis

1Hacettepe University, School of Medicine, Ankara, Turkey
2Zurich University Children's Hospital, Zurich, Switzerland
3Department of Pediatric Immunology and Rheumatology, Utrecht, Netherlands

**Pediatric Rheumatology 2008, 6(Suppl 1):P154**

**Aim:** To understand the status of education and problems the pediatric rheumatology practice in Europe, through a survey.

**Methods:** A 26-item questionnaire was conducted during the 14th Congress of the Pediatric Rheumatology European Society in Istanbul, 2007. Physicians who were practicing or studying within the field of pediatric rheumatology for at least one year were included in the survey.

**Results:** One hundred twenty eight physicians, 79 pediatric rheumatologists (five pediatric immunologists, 10 pediatric nephrologists), 34 pediatric rheumatology fellows and 15 adult rheumatologists completed the survey. The physicians were from: Europe 95 (81.9%), South America 12 (10.4%), Middle East 5 (4.3%), Asia 2 (1.7%), Africa 2 (1.7%). The duration of training for pediatric rheumatology ranged between 1–5 years (mean: 3.12 ± 1.11). Sixty physicians (47.2%) evaluated their education as unsatisfactory and among those, 48 physicians (50.5%) were from Europe. Subjects reported that they were capable of doing: intraarticular injections (83.3%); soft tissue injections (47.6%); evaluation of radiographs (67.5%); whereas competence in the evaluation of computed tomography/magnetic resonance imaging (30.5%); and musculoskeletal sonography (16.7%) were much less. Pediatric rheumatology has established a significant position in pediatrics. However, being a relatively new field in the realm of pediatrics, pediatric rheumatology education at the European level needs to be further discussed, revised and uniformed.

**Conclusion:** By digitalizing the CRF we achieved our aim to provide easy, rapid and safe access to the database and contributed to a new way of data collection. Although the web-based register was designed for the current multicentre observational study, this type of instrument can also be applied to other types of studies. We expect that especially collaborative study groups will find it an efficient tool to collect data.

**P155**

**A review of symptoms associated with Benign Joint Hypermobility Syndrome in children**

H Mato, T Berde, N Hasson, R Grahame and S Maillard

Great Ormond Street Hospital, London, UK

**Pediatric Rheumatology 2008, 6(Suppl 1):P155**

**Background:** Many symptoms related to Benign Joint Hypermobility Syndrome (BJHS) have been poorly recognised and treatment for this condition has been very varied. The unit at Great Ormond Street Hospital has a specific hypermobility service and have developed an assessment form to capture the symptoms of BJHS.

**Materials and methods:** A retrospective review of the assessments of the children who attended the hypermobility clinic over an 8 month period was completed.

**Results:** The data was collected from 54 children, of whom 82% were Caucasian and 66% Female. 48% had a family history of BJHS. Marfanoid habitus was complete in 30%. Scoliosis was present in 19%. Pain was a significant feature (88%) with neck pain (32%), back pain (44%), shoulder pain (26%), wrist pain (32%), hip pain (38%), knee pain (61%), foot pain (64%), headaches 40% and abdominal pain (35%). Fatigue was present in 82%. 98% had flat feet, 75% bruised easily and 43% had Chondromalacia patellae. Only 35% attended full time school and only 6% completed in all PE activities. The mean CHAQ score was 0.75. Patients presented with a very specific pattern of muscle weakness of hip abductors and extensors, inner range quads (into hypermobile range) and plantar flexors. Previous treatment included pain relief (85%), stretches (12%), exercises (33%), weights (6%), hydrotherapy (4%), podiatry (42%), insoles (35%) and OT (13%).

**Conclusion:** BJHS is a complex condition with many associated symptoms which require specific management in order to prevent loss of physical function and poor school attendance.

**P156**

**The differential diagnosis of children with joint hypermobility: a review of the literature**

LJ Tofts, EJ Elliott, C Munns, V Pacey and DO Sillence

The Children's Hospital at Westmead, Sydney, Australia

**Pediatric Rheumatology 2008, 6(Suppl 1):P156**

**Background:** To critically review publications relating to the diagnosis of joint hypermobility and instability and discuss an evidence-based approach to children presenting with joint hypermobility.

**Methods:** Papers with an emphasis on the diagnosis of joint hypermobility including Heritable Disorders of Connective Tissue (HDCT) in which joint hypermobility is a prominent feature were identified.

**Results:** 3330 papers were identified, 1534 of which pertain to instability of a particular joint. 1666 papers related to the diagnosis of Ehlers Danlos syndromes and a further 330 to joint hypermobility.

**Conclusion:** There are inconsistencies in the literature on joint hypermobility and how it relates to and overlaps with the milder forms of HDCT. There is no clear and reliable method of differentiating between “Joint Hypermobility Syndrome”, familial articular hypermobility and Ehlers-Danlos syndrome (hypermobility type). These three disorders may, in fact be the same. We have described our approach to a child presenting with joint hypermobility and the expert opinion and published evidence from which this has developed.

We conclude that there is value in both clearly identifying the underlying genetic cause of an individual child's joint hypermobility as well as identifying those hypermobile children who have symptoms such as pain and fatigue and would benefit from multidisciplinary rehabilitation management. We recommend that the term “Joint Hypermobility Syndrome” should be reserved to describe symptom(s) which are complications of joint hypermobility. We use this term in children who have symptomatic joint hypermobility irrespective of the underlying HDCT.
P157
Visual test for detection of pathological glycosaminoglycans excretion in mucopolysaccharidoses. A diagnostic tool in paediatric rheumatology
MJ Rua, L Rodriguez, F Andrade, JA Prieto, M Montejo, P Sanjurjo and L Aldamiz-echevarria
Department of Paediatrics Cruces Hospital, Baracaldo-Bilbao, Spain
Pediatric Rheumatology 2008, 6(Suppl 1):P157

Introduction: Mucopolysaccharidoses (MPS) are lysosomal storage disorders characterized by a deficiency/absence of a enzyme involved in the degradation of glycosaminoglycans (GAG). The diagnosis is frequently delayed as the quantification of GAG in urine is not routinely performed. We developed a qualitative method to detect high GAG levels in urine to provide an early diagnosis even in low suspicion cases of MPS in children.

Methods: Glycosaminoglycans react with 1,9-dimethylmethylen blue (DMB) in acidic medium yielding a pink colour. Optimum DMB concentration discriminates between pathological and normal excretion. Test: 50 μL of urine with 2 ml of DMB solution. The final colour is compared against a scale.

Results: A pink colour is developed when the sample contains more than 200 mg/L of GAG. The selected concentration gave a high GAG excretion. In some patients under enzymatic treatment, Hurler, Hunter and Morquio and Sly diseases whose GAG excretion is low and in positive response in all untreated patients. Negative or dubious more than 200 mg/L of GAG. The selected concentration gave a positive response in all untreated patients. Negative or dubious cases were essayed.

Conclusion and proposal: GAG testing has proved to be a useful diagnostic tool for MPS with high GAG excretion. This test provides an aid to rheumatologist in detecting patients with alerting musculoskeletal symptoms like joint stiffness, flexion contractures without evident inflammation, carpal tunnel syndrome or multiple trigger finger in cases of MPS-I. We suggest using GAG testing in the screening of such dubious cases.

P158
Development of a disease severity scoring system for patients with Pompe disease
E Giannini¹, K Berger², A van der Ploeg³, L Case⁴, C Dandrea⁵, P Kishnani⁶ and D Marsden⁷
¹Cincinnati Children’s Hospital, Cincinnati, OH, USA ²NYU School of Medicine, New York, NY, USA ³Sophia Children’s Hospital, Rotterdam, Netherlands ⁴Duke University Medical Center, Durham, NC, USA ⁵Genzyme Corporation, Cambridge, MA, USA
Pediatric Rheumatology 2008, 6(Suppl 1):P158

Introduction: A Disease Severity Scoring System (DS3) measures disease burden in patients. It consists of critical health domains, each described by relevant clinical assessment(s) quantified via reliable, valid and feasible methods. DS3s are particularly useful in rare, heterogeneous diseases in which evaluating severity and prognosis is difficult. Properly configured, a DS3 provides inter- and intra-patient comparisons through time across critical organ systems. A DS3 is being developed for Pompe disease, a rare, autosomal recessive, and heterogeneous, neuromuscular disorder.

Description: Experts were assembled to identify critical Pompe disease health domains. A broader “Delphi” physician group helped capture standard medical practice(s) for severity measurement within each critical domain: Cardiac, Respiratory, Proximal Muscle, Physician Reported Outcomes and Patient Reported.

Outcomes: Within each domain, 1–2 clinical assessments were identified. To test this preliminary model, 9 cases from the Pompe Registry representing a severity spectrum were scored.

Results: Results were compared to results from a blinded small expert group assessment of the cases using a scale similar to the Clinical Global Impression (CGI) Severity scale, yielding a 0.93 coefficient of correlation, indicating preliminary DS3 consistency with expert opinion, suggesting preliminary DS3 validity, reliability and relevance. Validity and reliability testing are being completed with standardized methods.

Conclusion: Preliminary results indicate the Pompe DS3 model will help standardize disease terminology and highlight key clinical assessments to quantify disease severity. This tool can become a universal disease “staging” system that permits more exact prediction of important disease outcomes and identify the need for specific medical interventions.

P159
The Pompe Registry: tracking Pompe disease symptoms in a broad patient population
B Byrne¹, PS Kishnani², L Case³, L Merlini⁴, W Müller-Felber⁴, A Van der Ploeg⁵, D Marsden⁶ and S Prasad⁷
¹Congenital Heart Center University of Florida, College of Medicine, Gainesville, FL, USA ²Duke University Medical Center, Durham, NC, USA ³Department of Medical Genetics, University of Ferrara, Ferrara, Italy ⁴Department of Neurology, University of Munich, Munich, Germany ⁵Erasmus Medical Center, Sophia, Rotterdam, Netherlands ⁶Genzyme Corporation, Cambridge, MA, USA
Pediatric Rheumatology 2008, 6(Suppl 1):P159

Introduction: Pompe disease is a rare, progressive, often fatal metabolic myopathy, which manifests as a clinical spectrum that varies with respect to age at onset, rate of disease progression, and extent of organ involvement. The underlying pathology is deficiency of acid alpha-glucosidase (GAA). To gain a better understanding of Pompe disease, a global, voluntary, observational Registry was developed to collect anonymous, longitudinal data.

Preliminary data overview: As of March 2008, 494 patients from 23 countries were enrolled; the majority (72%) Caucasian. Europe and North America enroll 87% of patients. Median age of infants at symptom onset was 2.0 months (n = 94) and at diagnosis was 4.0 months (n = 93). Median age of adults at symptom onset was 27.7 years (n = 293) and at diagnosis was 35.3 years (n = 289). Symptoms most frequently reported by
patients ≥ 18 years old (n = 321) include: muscle weakness (lower extremities (80%), upper extremities (69%), trunk (53%)); shortness of breath after exercise (61%) and at rest (31%); dependence on respiratory support (38%); sleep disturbance/apnea (35%); orthopnea (32%); and scapular winging (31%). Approximately half of patients genotyped expressed the IVS1-13T>G mutation.

Summary: These results show significant delay from symptom onset to diagnosis in adult patients, highlighting the need for greater disease awareness. Registry data on prevalence and age at onset of symptoms may allow earlier patient identification, enabling intervention before irreversible muscle damage occurs. Analysis of registry data over time may increase understanding of the evolution of, and interaction between, impairments and function under varying conditions and interventions, allowing improved clinical management.

P160 Psychological impairment in adolescents with JIA: should we continue the search for evidence?
CE Fuchs, G Sinnema, SM van Geelen, HJM Hermans and W Kuis
Wilhelmina Children’s Hospital, University Medical Center Utrecht, Utrecht, Netherlands

Background: Previous studies suggest that adolescents with JIA cope relatively well with the consequences of their painful and potentially incapacitating illness, and that, with regard to their psychosocial functioning, there seem to be few differences between them and healthy teenagers. The discrepancy between these findings and clinical experience gave us reason to search for a more subtle care and research method directly related to the adolescent patients’ own experience. In this study, it is assumed that a person consists of different self-positions, ordered into a flexible and varied hierarchy that can alter over time, and in accordance to the demands of diverse contexts. Chronic illness could possibly lead to a more one-sided organization of a person’s experience.

Methods: To study this hypothesis, 24 healthy teenagers, 36 adolescents with juvenile idiopathic arthritis (JIA) and 42 adolescents with chronic fatigue syndrome (CFS) completed the Personal Position Repertoire – a method designed to analyze the organization of an individual’s personal positioning.

Results: The main findings of this study show that adolescents with JIA position themselves very similar to healthy teenagers. Their focus seems to be to present themselves as strong and healthy, perhaps at the cost of suppressing, or neglecting, their vulnerable and unwell sides. In notable contrast to this, adolescents with CFS position themselves as significantly less healthy and strong and potentially incapacitating illness, and that, with regard to the illness and provide them with tools for a better adjustment and adaptation to their JIA.

Conclusion: This form of educational programme seems suitable for adolescents with JIA providing them with information about the illness and its management. It also offers an opportunity to meet with peers and discuss the illness, its impact on their lives and related social and psychological issues in a group context.

Reference

P162 Exercise limitation in juvenile onset Mixed Connective Tissue Disease (MCTD)
JJ van der Net, A van Royen-Kerkhof, T Takken and B Wissink
Wilhelmina Children’s Hospital of the University Medical Center Utrecht, Utrecht, Netherlands

Background: An educational programme developed for adolescents with JIA has been implemented three times at Astrid Lindgrens Children’s Hospital in Stockholm, most recently in the fall of 2007. The aim is to increase understanding of the illness and provide them with tools for a better adjustment and adaptation to their JIA.

Methods: The programme consists of seven sessions. Each session has a different topic e.g. exercise and ergonomics, pain, medical treatment, relationships etc. Seven adolescent’s ages 14–16 years completed the programme during 2007. A self reported questionnaire MEPS (Medical, Exercise, Pain and Social Support) was used for evaluation. The MEPS has been developed for evaluation of educational programs for adolescents with JIA and their parents. It has been established in research to possess satisfactory reliability and validity.

Results: The results from MEPS showed that in the medical area four of nine items improved e.g. knowledge about symptoms of inflammation. In the social support area three of four items improved or scored high from the beginning e.g. appreciation of meeting peers with JIA. In the pain area two of six items improved e.g. confidence in self-efficacy to manage pain.

Conclusion: This form of educational programme seems suitable for adolescents with JIA providing them with information about the illness and its management. It also offers an opportunity to meet with peers and discuss both the illness, its impact on their lives and related social and psychological issues in a group context.

Reference

P161 Evaluation of education for adolescents with JIA with MEPS (Medical, Exercise, Pain and Social Support)
K Berggren, S Röstlund and E Gärneus
Astrid Lindgrens Children Hospital, Stockholm, Sweden

Background: An educational programme developed for adolescents with JIA has been implemented three times at Astrid Lindgrens Children’s Hospital in Stockholm, most recently in the fall of 2007. The aim is to increase understanding of the illness and provide them with tools for a better adjustment and adaptation to their JIA.

Methods: The programme consists of seven sessions. Each session has a different topic e.g. exercise and ergonomics, pain, medical treatment, relationships etc. Seven adolescent’s ages 14–16 years completed the programme during 2007. A self reported questionnaire MEPS (Medical, Exercise, Pain and Social Support) was used for evaluation. The MEPS has been developed for evaluation of educational programs for adolescents with JIA and their parents. It has been established in research to possess satisfactory reliability and validity.

Results: The results from MEPS showed that in the medical area four of nine items improved e.g. knowledge about symptoms of inflammation. In the social support area three of four items improved or scored high from the beginning e.g. appreciation of meeting peers with JIA. In the pain area two of six items improved e.g. confidence in self-efficacy to manage pain.

Conclusion: This form of educational programme seems suitable for adolescents with JIA providing them with information about the illness and its management. It also offers an opportunity to meet with peers and discuss both the illness, its impact on their lives and related social and psychological issues in a group context.

Reference

P162 Exercise limitation in juvenile onset Mixed Connective Tissue Disease (MCTD)
JJ van der Net, A van Royen-Kerkhof, T Takken and B Wissink
Wilhelmina Children’s Hospital of the University Medical Center Utrecht, Utrecht, Netherlands

Objective: To study the impact of musculoskeletal and cardiorespiratory impairment on the exercise capacity in children with mixed connective tissue disease (MCTD).

Methods: Twelve children diagnosed with MCTD (age 11–19) were studied in this retrospective chart review. Maximal exercise testing was used to determine the peak oxygen uptake (VO2peak) of the patients and a hand-held dynamometer was used to measure muscle strength. Cardiopulmonary function tests were used to measure obstructive or restrictive pulmonary impairment or cardiac failure.
Results: VO$_{2\text{peak}}$ was significantly lower in patients with MCTD compared to the VO$_{2\text{peak}}$ of healthy subjects (z-score $-1.9$, $p = 0.008$). The strength of the proximal muscles (hip flexors, shoulder abductors, knee extensors) of the patients was significantly lower than the controls, whereas the strength of the distal muscles (dorsal flexors of the foot and grip strength) was rather similar. No clinical relevant cardiopulmonary impairment was observed.

Conclusion: The exercise capacity, as well as proximal muscle strength is impaired in children with MCTD and differs significantly from healthy subjects. Since pulmonary problems were non dominant in this patient group, the decreased exercise capacity seems to be due to impairment of the musculoskeletal system.

P163
Long term follow up of children with rheumatological conditions who participated in a two week rehabilitation programme
H Mato, S Sian, A Charmartin, C Pilkington and S Maillard
Great Ormond Street Hospital, London, UK

Background: Physiotherapy is an important intervention in the management of children with rheumatological disease. At Great Ormond Street Hospital an intensive rehabilitation programme is provided. This small study assesses the long term effectiveness of this programme.

Materials and methods: A retrospective review of the notes was completed looking at the assessments completed in outpatient follow up appointments of the children who had attended the intensive rehabilitation programme.

Results: 32 children were included in the review with the diagnoses of Benign Joint Hypermobility Syndrome (BJHS), juvenile idiopathic arthritis (JIA), Juvenile Dermatomyositis (JDM) and Chronic Pain Syndrome (CPS). The mean follow up was 6 months of which 80% had maintained or increased their muscle strength since discharge. There was 100% school attendance and return to sport and 25% were doing as much sport as their peers. Pain and fatigue had also improved in 95% and 15% were discharged from care and further 75% were planned to be reviewed between 6–12 months.

Conclusion: A 2 week intensive rehabilitation programme is effective therapy in many children with Rheumatological diseases and the improvements gained during this treatment are maintained up to 6 months following discharge. This appears to be effective treatment both in the short term and long term in regaining fitness and strength and in reducing symptoms of pain and fatigue.

P164
An in-depth analysis of young people’s experience of their juvenile idiopathic arthritis (JIA) once receiving Etanercept
P Livermore*, P Woo and LR Wedderburn
1Great Ormond Street Children’s Hospital, London, UK
2Institute of Child Health, UCL, London, UK

Background: At our institution a biologics clinic has been established to see specifically those children with JIA on anti-TNF treatment. It was through regular contact with these patients that it became apparent that some of these patients have difficult thoughts and concerns about biological therapies that are not being acknowledged fully. Little is published about the psychological responses of young people with JIA to success or failure of treatment and how they influence attitudes to future treatments.

Methods: An Interpretive Hermenutic Phenomenological approach was used to allow in-depth examinations of the young people’s personal accounts of their lived experiences. Data was obtained from 6 individuals (aged 10–14 yrs) with JIA, receiving anti-TNF therapy during a routine clinic appointment using audio-taped unstructured interviews aided by spider diagrams. The interviews were carried out with informed consent, after ethical approval was given. The data were analysed using Colazzi’s method.

Results: Overall response as either positive or negative, hinged on perceived success of their biologic therapy and interestingly on their relationships with school friends.

Conclusion: This study will assist in providing these patients with a better package of care, by providing the clinician with a deeper insight into how young people view their biologic treatments. As one individual said “Enbrel is useless cus it doesn’t work for me. I don’t get a say in anything. They pretend you do, but you still have to take the things. It’s my body, but when I say I don’t want it, they say I have to have it.”

P165
A qualitative investigation into the variables which affect the physiotherapy group treatment sessions in the rheumatology unit
S Sian, H Mato, L Pearce and S Maillard
Great Ormond Street Hospital, London, UK

Background: Intensive physiotherapy rehabilitation is reported to improve the physical outcomes of children with rheumatological conditions. These treatments are provided as group therapies and different communication techniques are vital in assuring the effectiveness of the group.

Materials and methods: Observational analysis was conducted within daily group treatments over a 4 week period. Frequency of verbal and non-verbal communications between physiotherapists and patients were recorded for two stages; the introductory rehabilitation session and the consecutive sessions. Semi-structured interviews were undertaken with the therapists to determine their views of important communication strategies.

Results: A number of themes emerged as significant factors in influencing the children in the groups. These included touch, facial expressions, emotional distraction (such as humour), thought distraction (such as no mention of pain) and group distraction (talking with the other children). Respect for the therapists was common as well as response to change of voice, tone and volume and eye contact. These factors influenced behaviour including adherence, confidence, responsibility, reluctance and compliance. Patient engagement, empowerment and peer encouragement were also important factors. The therapists were aware that distraction techniques, facial expressions and tone of voice were important in order to ensure the group was cohesive and effective.

Conclusion: Group treatments are an effective way of providing physiotherapy and offer many unique benefits that one to one therapy cannot offer. They should be considered when developing a physiotherapy service for rheumatology.
Development of a multidisciplinary consultation in pediatric rheumatology in Switzerland with a link to daily life of the patient
B Fonjallaz1, A Utiger1, G Aubel1, E Roux2 and MF Hofer1
1Pediatric Rheumatology of Suisse Romande, Lausanne and Geneva, Switzerland
2Geneva League against Rheumatism, Geneva, Switzerland

Pediatric Rheumatology 2008, 6(Suppl 1):P166

Background: Pediatric patients consulting a rheumatologist are suffering from chronic diseases leading to a decreased quality of life associated with fears and many daily life problems.

Aim: We developed a multidisciplinary approach to help the patients and their parents in their daily life with the disease and try to improve their quality of life.

Methods: We established a multidisciplinary network in the French part of Switzerland, within and outside the hospital, with pediatric rheumatologists, nurses, physical therapists and occupational therapists. The patients are seen by the different members of the team according to their needs, and after consent of the physician, patient and parents. The nurses are providing a link between the consultation and the daily life of the child (family, home, school). With the different members of the team, we evaluated the needs of the patients and the goals of the network.

Results: We identified different items for patients' needs: support, help, information, prevention, teaching for the patient and the family; and for the goals of the network: best integration of the child (school, daily activities), autonomy of the patient and his family, improve the quality of life, create a link between the different professionals to improve the outcome of the therapies.

Conclusion: By establishing a multidisciplinary approach of care for the children with rheumatic diseases, we identified the items, which are to our opinion the most pertinent in order to improve the quality of the care to these patients.

Are parents’ views about their child’s treatment for juvenile idiopathic arthritis (JIA) related to evaluations of their child’s quality of life (QoL)? – SPARKS CHARM study
K Mulligan1, A Etheridge2, L Kassoumeri3, P Woo2, LR Wedderburn7 and S Newman1
1Centre for Behavioural & Social Sciences in Medicine, University College London, London, UK
2Rheumatology Unit, Institute of Child Health, UCL, London, UK

Pediatric Rheumatology 2008, 6(Suppl 1):P167

Background: Children with JIA experience impaired QoL. Although treatment with methotrexate (MTX) has been found to improve QoL, some children experience difficulties in taking it. This study examined the influence of parents’ attitudes to MTX and treatments in general on assessment of their child’s QoL.

Methods: Mothers or fathers of 143 children aged ≥ 5 with JIA, completed questionnaires about general beliefs regarding treatment (Treatment Representations Inventory, subscales – treatment value, concerns, cure and decision satisfaction) and specific beliefs regarding benefits and difficulties in taking MTX. Core outcome variables (COV), except ESR, were used to provide information on disease severity. Data were analysed by correlations followed by multiple linear regression with QoL, assessed by the Child Health Questionnaire (CHQ), as the dependent variable.

Results: Scores on the CHQ indicated greater impairment on physical (40.2,s.d.14.6) than psychosocial (47.6,s.d.12.2) QoL. Physical QoL was related to all COV (correlations 0.283 to −0.708), parents’ views about the benefits of MTX (r = 0.303, p < 0.001), difficulties taking MTX (r = −0.334, p < 0.001), treatment concerns (r = −0.459, r < 0.001) and beliefs in treatment cure (r = 0.328, p < 0.001). Psychosocial QoL was related to 2 of the COV (CHAQ r = −0.427, p < 0.001 and parent global assessment, r = −0.429, r < 0.001) plus difficulties taking MTX (r = −0.217, p < 0.01) and treatment concerns (r = −0.426, r < 0.001). Multivariate analysis indicated that general concerns about treatment made a unique contribution to the explanation of both physical and psychosocial QoL, after controlling for disease severity.

Conclusion: Parents’ concerns about treatment of JIA are important in understanding variability in both physical and psychosocial QoL of their children.

Joint hypermobility in the Iranian school students
V Ziaee1 and MH Moradinejad2
1Sports Medicine Research Center, Tehran University of Medical Center, Tehran, Iran
2Children’s Medical Center, Tehran University of Medical Center, Tehran, Iran

Pediatric Rheumatology 2008, 6(Suppl 1):P168

Background: The term benign hypermobility syndrome is applied to those children with musculoskeletal pain associated with generalized hypermobility of the joints without any associated congenital syndrome or abnormality of connective tissue, such as Marfan’s or Ehlers-Danlos syndrome. The aim of this study was to determine the prevalence of joint hypermobility among school students and to define the characteristics of patients with joint hypermobility.

Methods: This study was conducted between January 1994 and July 2004 among school students in Tehran. The clinical features were often associated with intermittent nocturnal pains, and are characterized by the occurrence of musculoskeletal symptoms in the absence of demonstrable systemic rheumatologic disease. The degree of joint was scored by modified criteria of Carter and Wilkinson.

Results: Two hundred fifty two students (132 females and 120 males) with a mean age of 8.7 years (range 6–16) were examined. Joint hypermobility was observed in 30 (11.8%) of the students. There were 12 male (40%) and 18 female (60%) hypermobile subjects. Our results show that phenotype has no relation with joint mobility.

Conclusion: Although hypermobility does not seem to be very problematic in young people, as in our focus group, we believe that it is important for physicians to recognize this problem to ensure correct diagnosis and treatment, since it may lead to mimic rheumatic diseases in the future.

References

P169
Pain experience in children with juvenile idiopathic arthritis on TNFα-inhibitors
JH Jeppesen1, T Herlin2 and M Thastum1
1Department of Psychology, University of Aarhus, Aarhus, Denmark
2Aarhus University Hospital, Skejby, Aarhus, Denmark

Background: The use of TNFα-inhibitors has proven its efficacy in children with severe juvenile idiopathic arthritis (JIA) unresponsive to standard therapy. Pain reduction or elimination could therefore be expected. However, multiple factors besides disease activity contribute to the pain experience in children with JIA.

The aim of this study was to examine pain experience in children treated with TNFα-inhibitors, and whether it was associated with pain-specific beliefs and pain-coping strategies.

Materials and methods: Children with JIA treated with TNFα-inhibitors (n = 42, mean age 13.4 ± 2.4 years, 69.0% girls) completed the Pain Coping Questionnaire, a revised version of the Survey of Pain Attitudes, and a 2-week pain diary (range 0–5).

A composite arthritis activity score was calculated (range 0–9).

Results: The mean arthritis activity score was 0.9 ± 1.7 (range 0–9) and the mean average score of pain was 1.0 ± 1.2 (range 0–4.7). Thirteen children (31.0%) reported pain every day (average pain score = 2.3). The arthritis activity and the pain experience didn’t correlate significantly (r = 0.203, p = 0.221).

Significant correlations were obtained between the pain experience and the pain-coping subscale of catastrophizing, the pain belief subscales of disability, harm, emotion, and solicitude.

Conclusion: The results indicated that pain was still a considerable problem in our sample, even though many of the children were in remission with biological agents. No association was found between the arthritis activity and the pain experience.

Health beliefs and use of the pain-coping strategy catastrophizing were significantly associated with the pain experience in children with JIA treated with TNFα-inhibitors.

P170
Complex regional pain syndrome with dystonia in childhood
SM Maillard, R Howard and N Hasson
Great Ormond Street Hospital, London, UK

Background: We present 6 children with Complex regional pain syndrome (CRPS) in whom dystonia, including abnormal posture and involuntary movement was a prominent feature. CRPS is known to occur in childhood usually involving severe limb pain, colour and temperature change, with associated loss of function. Dystonia associated with CRPS has never been described in children, although a few cases in adults have been reported. Here we review the presentation, diagnostic implications, management and prognosis.

Materials and methods: A retrospective case note review.

Results: Six children (5 F, 1 M; age range 11–18 years) with CRPS were identified as having dystonia. The initial presenting limb was the foot in all cases, although all 4 limbs were included in 1 instance. The degree of dystonia varied from mild shaking at rest to extreme and violent movement of the whole limb increasing with touch. Although the other features of CRPS were also present, including mechanical and thermal allodynia and temperature changes, the presence of dystonia led to diagnostic confusion. Management of these cases was also difficult and protracted but in the majority some improvement was obtained using multidisciplinary management. Physiotherapy was the most successful intervention.

Conclusion: Dystonia has not previously been recognised as a feature of CRPS in children and may confound diagnosis. Children with CRPS can develop abnormal movement and this is often linked to a more severe and complex presentation requiring a very intensive rehabilitation approach.

P171
A review of the management of Complex Regional Pain Syndrome; an experience of an inpatient rehabilitation unit
H Mato, S Sian, N Hasson and S Maillard
Great Ormond Street Hospital, London, UK

Background: Complex Regional Pain Syndrome (CRPS) is a rare pain condition that causes severe pain in one or more limbs and results in severe loss of function. The management of this condition is difficult and requires a very intensive approach. In-patient rehabilitation is able to provide the intensity of physiotherapy that is required to effectively manage this condition.

Materials and methods: A retrospective case note review was performed for 23 patients with a diagnosis of CRPS. All children were seen at Great Ormond Street Hospital, which has an ambulatory rehabilitation unit able to provide an intensive programme including twice daily physiotherapy, advice on pacing and pain management over a 2–3 week period. The main philosophy of the programme is that function is regained before pain is reduced.

Results: See table 1. The mean age was 10.38 years and 72% female. Presentation included symptoms of cold, mottled skin (30%) skin allodynia (56%) and loss of function (82%) predominantly in a lower limb (95%). 65% were using walking aids. 80% were hypermobile and 100% had a significant loss of muscle strength in specific lower limb muscle groups, including hip abductors, hip extensors, inner range quadriceps and plantar flexors. The therapy included active muscle retraining to regain normal movement, function and muscle strength in 100%, only 40% also had a skin desensitisation programme. All children improved in symptoms and function including school attendance.

Conclusion: An intensive rehabilitation approach to the management of children with CRPS is very effective in reducing pain and restoring function.
Acute lymphocytic leukemia (ALL) may initially present with musculoskeletal symptoms such as pain or swelling, even before appearance of blasts in the peripheral blood. Fifteen to 30% of all ALL patients have musculoskeletal complaints at disease onset. Such presentation may lead to misdiagnosis of the patients causing a delay in proper management. Here, we present 5 patients who were referred to Pediatric Rheumatology Department for the evaluation of arthritis and were finally diagnosed as ALL (table 1).

The peripheral blood changes were absent or subtle in these patients. Some clinical, laboratory, and radiological clues helped to establish the diagnosis of ALL. We aimed to discuss the usefulness of history, physical findings, and simple laboratory and radiographic tests in decision-making.

### Table 1 (abstract P172) Five patients who were referred to Pediatric Rheumatology Department for the evaluation of arthritis and were finally diagnosed as ALL

<table>
<thead>
<tr>
<th>Patient</th>
<th>Presentation</th>
<th>Provisional diagnosis</th>
<th>Final diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 y, ♂</td>
<td>Migratory arthritis, fatigue</td>
<td>Acute rheumatic fever</td>
<td>ALL</td>
</tr>
<tr>
<td>3 y, ♂</td>
<td>Fever, arthritis of the left hip</td>
<td>Septic arthritis</td>
<td>ALL</td>
</tr>
<tr>
<td>2 y, ♀</td>
<td>Arthritis of the right hip</td>
<td>Transient synovitis</td>
<td>ALL</td>
</tr>
<tr>
<td>3 y, ♂</td>
<td>Pain in legs, inability to walk</td>
<td>JIA</td>
<td>ALL</td>
</tr>
<tr>
<td>6 y, ♀</td>
<td>Arthritis of the left elbow, fatigue</td>
<td>Postviral arthritis</td>
<td>ALL</td>
</tr>
</tbody>
</table>

**P173**

**Chronic musculoskeletal pain syndrome in children: Preliminary validation of physiotherapy assessment methods**

K Mikešová, Y Šulcová, M Vránová, J Tuková, P Šcerbanovská, D Nemcová and P Doležalová

*1st Medical School, Charles University in Prague and General University Hospital, Prague, Czech Republic*

**Pediatric Rheumatology 2008, 6(Suppl 1):P173**

**Introduction, aim:** Chronic musculoskeletal pain syndrome (CPS) is difficult to diagnose and treat, but also to assess efficacy of its therapies. Psychology and physiotherapy methods have been variably applied. We aimed to develop a novel battery of physiotherapy tests to combine them with existing psychology methods in order to obtain a complex CPS assessment tool.

**Patients and methods:** Following groups were examined: Patients with the new diagnosis of CPS (n = 16), patients with active JIA (n = 17) and 25 age and sex matched healthy children (median age 15, range 11–18 years). In each individual a trained physiotherapist assessed: hypermobile joints (Beighton score), painful points (MPPS), stability (balance test), walking (plain, stairs), limitation of joint movement, presence of skin changes (colour, temperature, sweating), superficial and deep skin perception, hand function.

**Results:** While hypermobile scores did not differ between the groups, fibromyalgia score was significantly higher in CPS patients than in healthy children (p = 0.02), but not in JIA patients (p = 0.08). Balance test differed significantly between both disease groups (CPS, JIA) and healthy children (p = 0.004, 0.04, resp.) as did presence of walking difficulties (p = 0.0001, 0.0002) and joint limitation. Presence of skin colour changes and hand function limitation distinguished CPS from healthy children (p = 0.02).

**Conclusion:** Combination of painful point survey, balance and walking, skin colour change and hand function limitation tests appear to be useful methods to assess physical aspects of pain syndromes. Ability of the proposed tool to reflect significant clinical change is currently explored in a longitudinal follow-up study.

**Acknowledgements**

Supported by IGAMZCR NR-8808-3.

**P174**

**Effect of Botulinum Toxin type-A (Botox®) on neck pain and craniofacial headaches caused by trapezius spasm in a child with generalised joint hypermobility resulting from Noonan’s Syndrome**

L J Tofts, S Hayden and M C Waugh

*The Children's Hospital at Westmead, Sydney, Australia*

**Pediatric Rheumatology 2008, 6(Suppl 1):P174**

**Background:** A twelve year old female with generalised joint hypermobility (Beighton 8/9) from Noonan’s syndrome presented with chronic neck pain which caused frequent headaches. Touching the trapezius reproduced the pain and range of movement at the cervical spine was decreased. She had been managed unsuccessfully with manual techniques, mobilisation, stretches and TENS over the prior twelve months. Poor sleep due to pain caused fatigue and decreased participation in school and physical activity.

**Materials and methods:** N of 1 trial design to investigate the efficacy of Botox® to reduce muscle spasm.
Baseline measures of weekly average pain (VAS), maximum pain (VAS), episodes of neck pain, episodes of headache and doses of paracetamol (acetaminophen) were obtained over 5 weeks. The intervention consisted of injecting 25 units of Botox® into each trapezius (total 50 units) over multiple sites. Outcome measures were recorded for seven weeks following treatment. Data was analysed using the c-statistic method in Excel®.

**Results:** At six weeks average pain score decreased from a median of 48.5 to 20.0 (c-statistic p = 0.012). Maximum pain decreased from a median of 72.0 to 40.0 (c-statistic p = 0.009). Episodes of neck pain per week reduced from a median of 4 to 2 (c-statistic p = 0.009). No significant change was seen in the number of episodes of headaches per week, which reduced from 2 to 1 (p = 0.057). Analgesic requirement reduced from 4 paracetamol per week to 2 (c-statistic p = 0.012).

**Conclusion:** Botulinum toxin injections were an effective treatment.

**P175**

**Depression, anxiety and pain in juvenile idiopathic arthritis**

D Erdogdu, O Kasapcopur, G Cimen, N Arisoy and L Kayaalp
Istanbul University, Cerrahpasa Medical Faculty, Istanbul, Turkey

**Background:** This study investigated children with juvenile idiopathic arthritis in terms of depression, anxiety, behavioral problems, self esteem, analyzed the associations of these psychological features between subtype and pain intensity.

**Materials and methods:** The sample was 45 children with JIA (oligoarticular JIA; 19, polyarticular JIA; 26), aged 6 to 12 years. Pain was measured by the VAS. Children and parents were administered the Child Behavior Checklist, Kovacs Depression Inventory, State-Trait Anxiety Inventory, Piers-Harris Self Esteem Scala. The psychiatric diagnoses were made according to DSM-IV criteria.

**Results:** There was no statistically significant difference in between the disease subtype groups and between the pain groups as to the sociodemographic features. The frequency of depression and anxiety diagnosis which were made according to the DSM-IV criteria was 31% and 17.7% in 45 JIA patients. For the 45 patients the average CDI score was 7.60 and the average Trait Anxiety Inventory score was 34.31. For the 42 patients which were allocated into pain groups, the average CDI score was 7.67 and the average Trait Anxiety Inventory score was 34.10. There was no statistically significant difference between the groups as to the depression and anxiety scale scores. Pain was not correlated with depression and anxiety scores.

**Conclusion:** Clinical diagnosis of depression or anxiety is identified at high rates in children with JIA but depression and anxiety scale scores were identified as close to the average normal scores and are not found associated with pain intensity. Subtype is also not found associated with these scale scores in JIA.

**P176**

**Familial Mediterranean Fever (FMF) and renal disease: first report on 29 Sicilian patients**

A Vitale, F La Torre, G Conti, C Fede, R Chimenz and G Calcagno
Department of Pediatrics, Pediatric Rheumatology, Messina, Italy

**Background:** Familial Mediterranean Fever (FMF) is characterized by recurrent attacks of fever and serositis. Amyloidosis is its most crucial complication. Methods: Between 2002 and 2007, 29 patients (11 girls, 18 boys) median age 316 months in whom FMF was diagnosed and with a follow-up period of at least six months were included in the study. The mean age of the patients at the time of the onset was 110 +/- 106 months. Genetic mutations more frequently detected were M680I (12/29) and M694V (8/29). Age of starting colchicine was 267 +/- 180 months. The patients were followed at 6 month intervals; at each visit, daily urinary protein excrections were calculated.

**Results:** 5 patients showed a proteinuric stage without fever attacks, but two of them were non compliant with the treatment. There were no significant differences (age at onset, initial dose of colchicine and serum amyloid A levels) in the two groups. The FMF patients with elevated proteinuria showed a short time between the age of onset and the starting of colchicine than ones with normal proteinuria. Two patients with pathological proteinuria did not have MEFV gene mutations. After the increase of colchicine, there was the complete resolution of proteinuria in all patients.

**Conclusion:** Colchicine is an effective medication in the prevention and treatment of amyloidosis; in contrast to other reported studies, there was no correlation between amyloidosis and M694V homozygosity in this cohort. Ten patients of our population who received a delayed diagnosis (median age of diagnosis 40 years) don’t show renal damage.

**P177**

**Attacks of severe dysmenorrhea as the sole manifestation of Familial Mediterranean Fever (FMF)**

A Vitale¹, F La Torre¹, C Caruso², C Fede¹ and G Calcagno¹
¹Department of Pediatrics, Pediatric Rheumatology, Messina, Italy
²Department of Gynecological, Obstetrical Sciences and Reproductive Medicine, Messina, Italy

**Background:** Familial Mediterranean Fever (FMF) is an autosomal recessive disease (MEVF gene) characterized by recurrent fever and inflammatory serositis. Although majority of patients have random pattern of attacks, some reports described precipitating factors. A literature review indicated that FMF attacks occurring only during menstruation are rarely seen. We report the cases of three patients with severe dysmenorrhoic pain as unusual clinical presentation of FMF. They were 3 females with a mean age at onset of 12 years. They never had typical attacks of fever and abdominal or chest pain, but they suffered from regular and severe dysmenorrhoic pain. Leukocytosis and C-reactive protein (CRP) elevation were noted during these attacks in all patients. Unlike dysmenorrhoea, none of these patients’ attacks responded to non-steroidal anti-inflammatory drugs. The diagnosis of FMF was based on typical clinical and laboratory features. On investigation of MEFV, M694V was the most frequent mutation.

All patients responded well to colchicine, and amyloidosis was not documented in any patients.
In conclusion, we suggest that gynecologists must be aware of FMF in the differential diagnosis of dysmenorrhea or endometriosis especially in the people of Mediterranean origin [1].

**Reference**


**P178**

**Prospective validation of the diagnostic score for molecular analysis of hereditary autoinflammatory syndromes in Italian children with periodic fever**

S Federici1,2, F Caroli1, MP Sormani3, A Meini4, R Caorsi1, G Martini5, G Simonini6, R Consolini7, S Plebani4, M Baldi7, I Ceccherini6, A Martini1 and M Gattorno1

1O U Pediatrica II Istituto G. Gaslini and Dipartimento di Pediatria, University of Genoa, Genoa, Italy
2Unità di Genetica Molecolare, Istituto G. Gaslini, Genoa, Italy
3Unità di Biostatistica, DISSAL, University of Genoa, Genoa, Italy
4Dipartimento di Pediatria, Unità di Immunologia e Reumatologia Pediatrica, Spedali Civili e University of Brescia, Brescia, Italy
5Dipartimento A.I. di Pediatria, University of Padua, Padova, Italy
6O U Reumatologia Pediatrica, Ospedale Meyer, Firenze, Italy
7Department of Pediatrics and Reproductive Medicine, University of Pisa, Pisa, Italy
8Dipartimento di Genetica Umana, Ospedale Galliera, Genoa, Italy

Pediatric Rheumatology 2008, 6(Suppl 1):P178

**Objective:** Aim of the study was to verify in a prospective study the sensitivity and specificity of a recently elaborated diagnostic score for the prediction of the presence of mutations of genes associated with periodic fever [1].

**Patients and methods:** Detailed clinical information of 100 Italian patients with a clinical history of periodic fever was collected since June 2007. For each patient the Diagnostic score (www.printo.it/periodicfever was calculated. According to previous experiences a cut-off > 1.32 was chosen to define those patients at high risk to carry relevant mutations. All patients were screened for mutations of MVK, TNFRSF1A and MEFV genes.

**Results:** Ten patients displayed relevant (homozygous or compound heterozygous) mutations for MVK and MEFV genes. No structural mutations of TNFRSF1A gene were found. 10 patients displayed low-penetrance mutations of the TNFRSF1A gene (R92Q) or a single mutation of the MEFV gene. 80 patients were negative to all the three genes. The Diagnostic score revealed high sensitivity (90%) and specificity (65%) in discriminating positive and negative patients. The regression tree analysis [1] was able to provide the correct identification of the affected gene in 7 out of the 9 positive identified by the diagnostic score.

**Conclusion:** This study confirm the validity of the Diagnostic score as a useful tool for the identification of children at higher risk to carry relevant mutations of genes associated with periodic fever.

**Reference**


**P179**

**Differences in the severity of the phenotype of children and adolescents with Familial Mediterranean Fever residing in Turkey and Germany**

N Akhay Azay2,3, S Özen1, E Lainka1, E Taskiran1, A Duzova1, N Besbas1, A Bakaloogl1 and T Kallinich1

1Hacettepe University Medical Faculty, Ankara, Turkey
2University of Duisburg, Essen, Germany
3Charité University Hospital, Berlin, Germany

Pediatric Rheumatology 2008, 6(Suppl 1):P179

Familial Mediterranean Fever (FMF) is worldwide the most common autoinflammatory disease. It has been long known that environmental factors affect the phenotype.

To substantiate this hypothesis we compared the disease-severity in Turkish FMF patients living in Turkey and Germany, based on a modified score for children. A total of 53 Turkish children living in Turkey were compared to 45 Turkish children born and raised in Germany. Mean age among the group from Turkey and Germany was 42.2 (range 2–120 months) and 44.29 (range 3–178 months) months, respectively. M694V was the leading mutation in both groups. The score developed by Livneh et al was modified by the integration of the recommended age-related doses, previously published by us. Additionally, disease severity was determined by the use of the scoring system developed by Pras et al. There was no correlation between the disease severity defined by the different scoring systems and the acute phase reactants.

According to the modified Livneh score, 78.2% of patients from the group living in Turkey had a severe course compared to 34.1% from the group living in Germany. Pras scores were also higher in the patients born and raised in Turkey (34.5%) compared to patients living in Germany (15.4%). The difference between the two groups for both scoring systems were statistically significant (p < 0.05 for both).

We suggest that environmental factors may affect the severity of FMF even if they were coming from the same ancestors.

**P180**

**Familial Mediterranean Fever (FMF) before the age of one year**

F Delion, I Touitou and I Kone-Paut

Hôpital de Bicêtre, Paris, France

Pediatric Rheumatology 2008, 6(Suppl 1):P180

**Background:** Familial Mediterranean Fever is an autosomic recessive autoinflammatory disease reaching populations of Mediterranean countries. It is mainly a paediatric affection, with a usual presentation at the age of 4 years. However, some cases may start within the first year of life. Only few is known, on their presentation, course and outcome.
Objectives: To identify FMF symptoms in patients before the age of one year. To compare these patients to those with later onset of FMF (after the age of one year).

Population and methods: Retrospective chart review of genetically confirmed FMF patients, comparing clinical symptoms, ethnic origin, response to colchicine and MEFV gene mutations, in the two age groups of patients.

Results: We identified 446 patients divided as such: 37 in the early-onset group (A) and 409 in the other group (B). A statistically significant difference was noted between the 2 groups (A vs B) for the ethnic origin (Sefaradic Jews p < 0.001), male preponderance (p < 0.015), number of crises/month (p < 0.015), response to colchicine treatment, and type of mutations in codon 694 and 680 (for M694V, p < 0.04).

Conclusion: This study shows a 10% prevalence rate of FMF before the age of 1 year, and highlights the difficulty to make early diagnosis. The early appearance of the first symptoms may be predictive of disease severity, as these patients have more severe phenotype and carry mutations known as the most severe.

P181

Evidences for the need of new Diagnostic Criteria for PFAPA syndrome

R Caorsi¹, A Meini², MP Sormani³, M Cattalini², MA Pelagatti¹, F Zulian⁴, E Cortis⁵, G Calcagno⁶, A Tommasini⁷, F Traverso¹, S Federici¹, J Frenkel⁸, S Plebani⁹, A Martin⁰ and M Gattorno¹

¹UO Pediatría II, G. Gaslini Institute and Department of Pediatrics, University of Genoa, Genova, Italy
²Dipartimento di Pediatria, Unità di Immunologia e Reumatologia Pediatrica, Spedali Civili and University of Brescia, Brescia, Italy
³Unità di Biostatistica, DISSAL, Università degli Studi di Genova, Genova, Italy
⁴Dipartimento A.I. di Pediatria, University of Padua, Padova, Italy
⁵Ospedale Pediatrico Bambino Gesù, Roma, Roma, Italy
⁶Unità di Pediatria, Policlinico “G. Martino”, Messina, Italy
⁷IRCCS Burlo Garofalo, Dipartimento di Pediatria, University of Trieste, Trieste, Italy
⁸Department of General Pediatrics, Wilhelmina Children’s Hospital, University Medical Center Utrecht, Utrecht, Netherlands

Pediatric Rheumatology 2008, 6(Suppl 1):P181

Objective: The clinical manifestations of PFAPA syndrome largely overlap with those of monogenic Autoinflammatory diseases: Familial Mediterranean Fever (FMF), tumor necrosis factor (TNF) receptor-associated periodic syndrome (TRAPS) and Mevalonate kinase deficiency (MKD). Aim of this study is to evaluate the specificity of the available diagnostic criteria for PFAPA.

Patients and methods: 307 consecutive patients with a clinical history of periodic fever were screened for mutations of MKV, TNFRSF1A and MEFV genes and detailed clinical information was collected. PFAPA diagnostic criteria were applied in all these patients. The clinical parameters associated with an high risk to be affected by an Autoinflammatory disease were identified on the basis of a univariate and multivariate analysis in both genetically positive and negative patients complying PFAPA criteria.

Results: 133 out of 307 patients satisfying PFAPA criteria. 33 carried relevant mutations on the screened genes (27 MKD, 3 TRAPS, 3 FMF), 28 were heterozygous for MEFV mutations, 7 carried R92Q mutation of TNFRSF1A gene, showing the low specificity of current criteria. Rash (OR = 2.975, p = 0.009), abdominal pain (OR = 3.261, p = 0.005) and vomiting (OR = 2.445, p = 0.3) were the variables most correlated to the positivity at the genetic test.

Conclusion: Current PFAPA criteria display a low specificity. According to this study, the presence of gastrointestinal manifestations and skin rash in patients fulfilling the current PFAPA criteria should orientate towards the exclusion of monogenic periodic fevers by molecular analysis. Consistent modifications of ongoing clinical criteria are proposed.

P182

International PFAPA syndrome registry: cohort of 214 patients

MF Hofer¹, P Pilet², S Berg³, R Brik⁴, P Dolezalova⁵, I Kone-Paut⁶, J Anton⁷, J Touitou⁸, B Bader-Meunier⁹, D Kaiser¹⁰, D Rigante¹¹, A Duquesne¹², C Wouters¹³ and M Gattorno¹⁴

¹Pediatric Rheumatology of Suisse Romande, Lausanne – Geneva, Switzerland
²Pediatric Rheumatology, Bordeaux, France
³Pediatric Rheumatology, Gothenburg, Sweden
⁴Pediatric Rheumatology, Haifa, Israel
⁵Pediatric Rheumatology, Prag, Czech Republic
⁶Pediatric Rheumatology, Kremlin-Bicêtre, France
⁷Pediatric Rheumatology, Barcelona, Spain
⁸Unit of auto-inflammatory diseases, Montpellier, France
⁹Pediatric Rheumatology, Paris, France
¹⁰Pediatric Rheumatology, Lucerne, Switzerland
¹¹Pediatric Rheumatology, Rome, Italy
¹²Pediatric Rheumatology, Lyon, France
¹³Pediatric Rheumatology, Leuven, Belgium
¹⁴Pediatric Rheumatology, Genoa, Italy

Pediatric Rheumatology 2008, 6(Suppl 1):P182

Background: PFAPA syndrome is a periodic fever syndrome with diagnostic criteria including unspecific symptoms and exclusion of other fever syndromes.

Aim and methods: To investigate the clinical spectre, clinical course and long-term follow-up of PFAPA, we established a web-based multicentric registry as an international collaboration within the working party “periodic fevers” of PrEoS. Patients with PFAPA were included according to previously published criteria.

Results: We included 214 patients from 14 centres: 122 males, 92 females, median age at onset 1.9 year. The main clinical manifestations were present in a majority of the patients: pharyngitis (94%), cervical adenitis (83%), aphpous stomatitis (59%); 48% of the patients presented all 3 clinical features. 170 patients presented additional symptoms (gastrointestinal symptoms 131, arthralgias and/or myalgias 86, arthritis 4, skin rash 36, neurological symptoms 8). In 79 patients a genetic testing was done for periodic fever syndromes (FMF 49, TRAPS 52, HIDS 46, CAPS 7) and was negative, except for 8 cases (polymorphisms: 3, carrier for MEFV mutation: 5) without known clinical significance. Improvement or remission was observed in 99/105 patients with steroids, in 28/35 patients with tonsillectomy and in 5/15 patients with cimetidine.
Discussion: We describe the largest cohort of PFAPA patients presented so far. We confirm that PFAPA syndrome may present with varied clinical manifestations and that the diagnostic criteria lack of precision. Based on detailed analysis of this cohort, a new definition of PFAPA with better-defined criteria should be discussed in an international consensus conference.

P183
Periodic Fever accompanied by Aphthous stomatitis, Pharyngitis, and cervical Adenitis syndrome (PFAPA syndrome) in adults
S Padeh, N Stoffman and Y Berkun
Edmond and Lily Safra Children’s Hospital, Sheba Medical Center, Tel Hashomer, Israel

Background: The syndrome of periodic fever characterized by abrupt onset of fever, malaise, aphthous stomatitis, tonsillitis, pharyngitis and cervical adenopathy (PFAPA syndrome) has been described only in pediatric patients. It usually begins before the age of 5 and in most cases resolves spontaneously before the age of 10 years. The aim of this report is to describe a series of adults with PFAPA syndrome.

Methods: A 6 years retrospective descriptive study included all newly diagnosed incident adult cases aged 18 years and over referred to our center with symptomatology suggestive of PFAPA syndrome. Patients’ medical records were reviewed for past history of the disease, demographic characteristics, symptoms and signs, course of the disease, laboratory findings and outcome following corticosteroid therapy. The comparison group included our pediatric cohort children (N = 320, age between 0.5 to 18 years) followed-up since 14 years (1994).

Results: Fifteen adult patients were diagnosed with PFAPA syndrome. Episodes of fever occurred at 4.6 ± 1.3-week intervals, beginning at the age of 20.9 ± 7.5 years. All patients had monthly attacks at the peak of the disease, with attacks recurring between 4–8 weeks intervals over the years. Between episodes, all patients were apparently healthy, without any accompanying diseases. Attacks were aborted by a single 60 mg of oral prednisone in all patients.

Conclusion: This study reports the presence of PFAPA syndrome in adult patients. Although rare, an increased awareness by both patients and family physicians of the clinical syndrome has resulted in more frequent diagnosis in adult patients.

P184
Characteristics of a PFAPA cohort in a single European centre
P Scerbanovska and P Dolezalova
Department of Pediatrics and Adolescent Medicine, Charles University, 1st Medical School, Prague, Czech Republic

Background: PFAPA is characterized by periodic fever, aphthous stomatitis, pharyngitis and cervical adenitis. Children are healthy between fever attacks. First manifestation is usually before 5 years of age. The ethiopathogenesis is unknown. There are few diagnostic criteria which help to make the clinical diagnosis. Laboratory parameters are non – specific.

Methods: Retrospective case analysis.

Results: Over the years 2004–2007 17 boys and 15 girls were diagnosed with PFAPA out of 87 patients referred to the fever clinic (36.8%). Median age at onset was 24 months (4–56), interval between attacks 4 weeks (2–12) and fever duration 3.5 days (1.5–7). Fever was generally above 39˚C, associated with pharyngitis in 23 cases (71.9%), cervical adenitis in 24 (75%) and aphthous stomatitis in 11 (34.4%). Other symptoms: abdominal pain, arthralgia (each in 7 cases), vomiting and headache (each in 4 cases). All children had elevated inflammatory parameters during attack (median: CRP 64.5 g/l, ESR 32/h) with subsequent normalization. The single prednisone dose of 1 mg/kg administered at the onset of an episode helped to reduce symptoms in 16/18 children. In 2 cases tonsillectomy led to the resolution of symptoms. After the median follow-up of 8.7 months (3.1–35.5) 4/32 patients (12.5%) have been in the full remission.

Conclusion: PFAPA appears to be a relatively common cause of recurrent fever in early childhood. The diagnosis was made after clinical exclusion of hereditary fevers and other systemic diseases or immune deficiencies. Our current diagnostic algorithm, therapy and follow-up scheme need further prospective evaluation.

P185
PFAPA syndrome: is it a family history?
M Cochard1, JClet2, L Lé1, P Pillet2, T Guéron1, X Onrubia3 and M Hofer1
1Pediatric Rheumatology, Pediatric Departments, CHU Lausanne and Geneva, Switzerland
2Pediatric Rheumatology, Pellegrin-enfants Hospital, CHU Bordeaux, France
3Pediatricians, Châtel-St-Denis, Switzerland

Background: PFAPA syndrome is a recurrent febrile disease characterized by periodic fever, aphthous stomatitis, pharyngitis and cervical adenitis. Since first description no clear etiology has been found, no genetic origin was underlined and no familial tendency was reported until now. To better understand this disease, we created a web-based international registry (8 countries and 14 centers).

Aim: To investigate the familial tendency to present PFAPA or another rheumatologic disease.

Patients and methods: In 2 of the participating centers (Lausanne-Geneva, Switzerland; Bordeaux, France), we questioned all parents during a phone call interview to complete the family history. We used the same questionnaire for a control group from a general pediatric consultation. We asked for positive family history of recurrent fevers, PFAPA and rheumatologic diseases. Patients and controls are matched for age and sex.

Results: We recruited 84 patients with PFAPA and 47 control children. Family history for recurrent fever was positive in 37/84 (44%, p = 0.00), always negative in the control group. 9/84 (10%, p = 0.02) PFAPA patients had a family member with PFAPA, none in the control group. The family history for rheumatologic diseases (arthritis, polyarthritis) 14/84 (17%, p = 0.0122) is also more frequently positive in the PFAPA group than in the control 1/47 (2%).

Conclusion: These data show that history of recurrent fever and PFAPA is found more often in patients with PFAPA than in
the general pediatric population. They suggest a familial susceptibility and a potential genetic origin for the PFAPA syndrome. This opens a wider spectrum for future research.

**P186**

**Efficacy of tonsillectomy in a family with a PFAPA-like phenotype**

MG Alpigiani1, M Haupt1, A Calcagno1, M Gattorno2, I Ceccherini3 and B Tambron1

1 Institute G. Gaslini, Department of Pediatrics, University of Genova, Genova, Liguria, Italy
2 Institute G. Gaslini, Second Division of Pediatrics, University of Genova, Genova, Liguria, Italy
3 Institute G. Gaslini, Laboratory of Molecular Genetics, University of Genova, Genova, Liguria, Italy

Pediatric Rheumatology 2008, 6(Suppl 1):P186

**Background:** PFAPA syndrome is one possible cause of periodic fever in childhood. The etiopathogenesis is unknown. The diagnosis is clinical and differential to exclude other similar diseases. Laboratory findings show only non-specific acute inflammatory response. The disease usually appears in early childhood. The most effective therapy is one-two low doses of oral corticosteroid, which however doesn’t prevent recurrences. Effectiveness of tonsillectomy is still debated. Family history of the disorder is usually negative and it’s unclear whether there is a genetic defect.

**Case report:** Female, age 2.5 years, clinical manifestations and family history suggestive of PFAPA syndrome. The girl had a history of high fever with pharyngitis and cervical lymphoadenitis, almost every 15 days from the age of 6 months. Fever disappeared after steroid therapy (betamethasone). During the febrile episodes, acute phase reactants were increased. Between the episodes, the girl was well with a normal growth. The main infectious diseases and the most common causes of monogenic fevers were excluded. The patient’s family tree shows that almost all the members of her mother’s family had a similar clinical history in childhood, and in all the cases clinical manifestations disappeared after adenotonsillectomy. Our patient was treated with adenotonsillectomy in October’07 and, to date, she no longer had fever or other PFAPA symptoms.

**Conclusion:** Although the mechanisms underlying this syndrome are unknown, tonsillectomy can be offered as an effective intervention for PFAPA syndrome. Even though PFAPA syndrome has no documented genetic basis, this family history is very interesting and should be further studied.

**P187**

**Height and weight development following cyclical intravenous pamidronate in children and adolescents with chronic recurrent multifocal osteomyelitis (CRMO)**

PM Miettunen, A Nettel-Aguirre and JD Kellner

University of Calgary, Calgary, Alberta, Canada

Pediatric Rheumatology 2008, 6(Suppl 1):P187

**Objectives:** Treatment with cyclical intravenous pamidronate (IVP) improves clinical course in children with chronic recurrent multifocal osteomyelitis (CRMO), but theoretically might affect longitudinal growth. In this study we analyzed growth during IVP treatment in ten CRMO patients.

**Methods:** 10 patients (5 M, 5 F) were enrolled, with mean (range) age 11.4 (4.5–16.3) years at IVP treatment. All patients received a 3-day infusion of IVP (0.5 mg/kg/day for the first dose; 1 mg/kg/day subsequently), followed by 1-day infusion monthly or 3-day infusion every 3 months until resolution of MRI documented bone inflammation. Weight and height were measured prior to first IVP, at 1-year, and at final follow-up, and results were transformed into age- and gender-matched z-scores. Hotelling’s test on the bivariate height and weight differences between 2 time points was performed.

**Results:** Patients received a mean (range) 6.23 (2.5–11.5) mg/kg/year of IVP to achieve resolution of MRI documented inflammation. Follow-up was a mean (range) 27.4 (16–46) months. At baseline, 4/10 children had low baseline height z-scores (z < −1.0), compared to 1/10 at final follow-up. At one year, height and weight z-scores jointly had increased significantly (p = 0.014). Univariate point estimates and 95% confidence intervals (95% CI) for average differences post-pre were height = 0.192, (95% CI 0.16, 0.54), and weight = 0.574, (95% CI 0.10, 1.04).

**Conclusion:** At 1-year following first pamidronate treatment, age-and gender-specific height and weight z-scores remained similar or increased, suggesting that 1. Pamidronate in pediatric CRMO does not have a detrimental effect on longitudinal growth. “Catch-up growth” can occur in this selected population.

**P188**

**Chronic recurrent multifocal osteomyelitis: 17 case reports and literature review**

A Insalaco, E Bozzola, A Campana, G Pagnotta, RM Tonioi, GC Ciofetta, D Barbuti and E Cortis

Ospedale Pediatrico Bambino Gesù. Pediatric Rheumatology, Roma, Italy

Pediatric Rheumatology 2008, 6(Suppl 1):P188

**Objective:** To analyse the clinical presentation of chronic recurrent multifocal osteomyelitis (CRMO) and to review diagnostic criteria.

**Study design:** We reviewed the medical charts of 17 patients with CRMO and we compared with 107 cases reported in literature.

**Results:** CRMO primarily affects girls with a mean age at onset of 8.5 years and a mean time to diagnosis of 8.5 months. Most patients were diagnosed in less than 1 month, but 2 cases presented a delay due to atypical presentation. At onset, 14 patients had inflammatory pain and 6 local swelling and fever. The lower limbs were predominantly affected, followed by the axial skeleton, the upper limbs and lastly by the mandible. Laboratory parameters provided non-specific information on CRMO. Radiographic studies were needed to exclude other pathologies. The diagnosis should be reached by isotope bone scanning or by magnetic resonance imaging. In doubt case bone biopsy was request to confirm the diagnosis.

**Conclusion:** We propose the following criteria for CRMO diagnosis: 1) acute or insidious onset of multifocal bone pain accompanied by fever and/or swelling 2) bone scans evidence of multifocal bone lesions 3) evidence of chronic bone inflammation with exclusion of other diseases at biopsy, in doubt cases.

**References**

Pediatric Rheumatology 2008, 6(Suppl 1) P190

When is CRMO NOT CRMO?
A McMahon and C Pilkington
Great Ormond Street Hospital, London, UK

Pediatric Rheumatology 2008, 6(Suppl 1):P190

A 3 year old girl presented with a limp and a hot, swollen ankle. X-Ray showed active osteomyelitis. ESR > 60 mm/hr, Hb 11.3 g/dl, WCC 7.9 × 10^9/L, Platelets 808 × 10^9/L. Intravenous antibiotics were commenced. One week later, the left ankle became swollen, X-Ray showed osteomyelitis. Bone scan showed several areas of increased uptake, right femoral neck, both knees, both ankles, and scapula. A presumptive diagnosis of chronic recurrent multifocal osteomyelitis was made. Management was with intravenous followed by oral antibiotics. Upon rheumatology review 4 months later, she had clinically improved, non-steroidal anti-inflammatory agents were advised, it was felt a bone biopsy was not indicated. 2 months later, she had developed episodic lower back pain, both day and night. She did not like walking and had lost weight. She was pale and had developed a kyphosis in L2–3 region with a scoliosis. Spinal X-Ray revealed multiple crush fractures with marked osteopenia. Repeat bloods showed Hb 7.0 g/dl, WCC 17 × 10^9/L and platelet count of 200 × 10^9/L. Blood film demonstrated multiple lymphoblasts. Bone marrow examination revealed common acute lymphoblastic leukaemia.

At presentation, chronic recurrent multifocal osteomyelitis may mimic acute osteomyelitis; however, definitive diagnosis is with a bone biopsy. Bone scans can be useful to identify additional foci of involvement that can be present concurrently or sequentially. One case report of CRMO following ALL has been documented [1]. This case illustrates a rare presentation of CRMO clinical symptomatology and radiological findings with an underlying diagnosis of ALL.

Reference

P191

A case of chronic recurrent multifocal osteomyelitis successfully treated with etanercept
N Akty Ayaz, T Topaloglu, F Ozaltin, MÇağlar Tuncali and A Bakkaloglu
Hacettepe University Medical Faculty, Ankara, Turkey

Pediatric Rheumatology 2008, 6(Suppl 1):P191

Chronic recurrent multifocal osteomyelitis (CRMO) is a disease of unknown origin characterised by multifocal recurrent bone lesions without any microbial agent detected from the lesion. A 9-year-old girl presented with the complaint of leg and arm pain. From her previous history it was learned that she had had back pain 2 years ago and at another medical center she had been evaluated with vertebral magnetic resonance imaging, vertebral tuberculosis had been suspected there and she had been given antituberculous treatment and non-specific antibiotic treatment. During follow up, she had had new lesions in the sternum and radius. She was re-evaluated in our clinic and bone scintigraphy was performed with the possible diagnosis of CRMO. On scintigraphy she had increased uptake of radioactive material at the level of T12 vertebra and corpus sterni. Her previous biopsy specimens were found to be non-specific chronic osteomyelitis. She had a very high sedimentation rate and elevated CRP levels. During follow up with nonsteroid anti-inflammatory agents she developed a severe achilles tendonitis. She had a positive HLA B27 test. Due to the progression of her disease both clinically and laboratory values she was started etanercept treatment. After a follow up period of 6 months she was clinically silent and her control bone scintigraphy was obviously better than her first scintigraphy.
From the previous studies it is known that there is intense expression and production of TNF-α in bone lesions. We conclude that especially in refractory CRMO cases etanercept may be an effective treatment option.

**P192**

The diagnostic role of hyperferritinemia in a tertiary care pediatric rheumatology setting

I Sala, L Trail, B Lattanzi, N Solari, E Palmisani, A Parodi, C Malattia, A Buoncompagni, A Loy, A Martini and A Ravelli

IRCSS G. Gaslini, Genova, Italy

Pediatric Rheumatology 2008, 6(Suppl 1):P192

**Background:** Serum ferritin is a laboratory marker that reflects the level of macrophage activation in systemic inflammatory illnesses. Sharply increased levels of ferritin are usually found in the acute phase of macrophage activation syndrome (MAS).

**Objectives:** 1) To investigate the prevalence of hyperferritinemia (ferritin > 500 μg/dl) in patients with systemic inflammatory conditions who had this laboratory test requested in the context of the diagnostic workup. 2) To determine the prevalence of specific diagnoses among patients with hyperferritinemia.

**Results:** More than 4000 determinations of ferritin requested by the study unit were performed between January 2004 and December 2007 by the central laboratory of the study hospital. Hyperferritinemia was found in 408 determinations in 87 patients. The most common specific diagnoses in patients with hyperferritinemia were the following: systemic juvenile idiopathic arthritis (sJIA) (48.3%), systemic lupus erythematosus (SLE) (5.7%), protein intolerance with lysinuria (4.6%), virus-associated haemophagocytic syndrome (3.4%), hematologic disorders (3.4%), juvenile dermatomyositis (2.3%), polyarticular JIA (2.3%), systemic vasculitis (2.3%), autoinflammatory syndrome (2.3%). Twelve patients (13.8%) had a nonspecific systemic inflammatory syndrome. Twenty-seven (31%) of the 87 patients with hyperferritinemia developed features consistent with MAS.

**Conclusion:** The most frequent specific diagnoses in patients with hyperferritinemia were sJIA and SLE. However, hyperferritinemia was seen in a number of children with systemic inflammatory syndromes, which were mainly characterized clinically by persistent fever, but did not fit any specific diagnostic categories and remained of undetermined etiology. Around one third of the patients with hyperferritinemia developed features consistent with MAS.

**P193**

Fever without apparent sources in children: a nation-wide study in Japan

K Kasai1, M Mori2, R Hara3, T Miyamae2, T Imagawa2 and S Yokota2

1Department of Infectious Diseases and Rheumatology, Hyogo Prefectural Kobe Children’s Hospital, Hyogo, Japan
2Department of Pediatrics, Yokohama City University, Yokohama, Japan

Pediatric Rheumatology 2008, 6(Suppl 1):P193

**Background:** This study is addressed to implement a clinical decision support system for diagnostic management of children with fever without apparent sources.

**Patients and methods:** A questioner was sent to 2,843 hospitals to ask about patients with prolonged and/or recurrent fever without apparent sources in recent 5 years. The definition was as follows: 1) children with fever > 38°C for more than 2 weeks and with uncertain diagnosis in 1 week of evaluation during hospitalization, and 2) children with periodic fever.

**Results:** Among 960 cases fulfilled the definition. 828 (86%) were diagnosed as having diseases of known causes. 190 (23%) were infectious diseases (acute focal bacterial nephritis 31, cat-scratch disease 23, urinary tract infection 20, osteomyelitis 9 and tuberculosis 8), 447 (54%) were rheumatic diseases (JIA 221, vasculitis syndrome 39, inflammatory bowel diseases 34, SLE 25, and MCTD 12). 67 (8%) were leukemia/malignancy (acute lymphatic leukemia 38, malignant lymphoma 9, neuroblastoma 4, Castleman disease 3). Autoinflammatory syndrome was diagnosed in 89 cases (PFAPA 45, FMF 17, CINCA 9, HIDS 9, and others). Other diseases included subacute necrotizing lymphadenitis, hemophagocytic syndrome, drug-induced fever, and ADEM.

**Conclusion:** Rare infectious diseases such as cat-scratch disease and tuberculosis were reminded in addition to routine investigation of infection. Along with these work-ups, malignancies and rheumatic diseases should be investigated. To have final diagnosis of auto-inflammatory syndrome, clinical characteristics such as fever pattern, skin rash, arthritis, and genetic analysis are needed. We established an algorithm as a clinical decision support system for diagnosis.

**P194**

Prevalence of monogenic autoinflammatory diseases among Pediatric Rheumatology centers: the Eurofever PReS/PRINTO survey

M Gattorno1, J Frenkel2, S Ozen3, F De Benedetti4, I Koné-Paut5, N Neven6, H Girschick7, H Özdogan8, C Wouters9, P Woo10, M Hofer11, P Dolezalova12, N Toplak13, V Richard14, A Martini1 and N Ruperto1

1UO Pediatria II, Istituto Gaslini and Dipartimento di Pediatria, Università di Genova, Genova, Italy
2University Medical Center, Utrecht, Utrecht, Italy
3Hacettepe University Faculty of Medicine, Ankara, Turkey
4Bambino Gesù Pediatric Hospital, Roma, Italy
5Centre Hospitalo-Universitaire de Bicêtre, Le Kremlin Bicêtre, France
6Hôpital Necker-Enfants Malades, Paris, France
7University of Würzburg, Würzburg, Germany
8University of Istanbul, Çerrahpaşa Medical Faculty, Istanbul, Turkey
9Universitair Ziekenhuis Leuven, Leuven, Belgium
10University College London, London, UK
11Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland
12Department of Paediatrics, Charles University, Prague, Czech Republic
13Department of Rheumatology University Children’s Hospital, Ljubljana, Slovenia
14Faculty Children’s Hospital 1st Department for Children and Adolescents, Kosice, Slovakia

Pediatric Rheumatology 2008, 6(Suppl 1):P194

**Background:** Due to the rarity of Autoinflammatory diseases, affected patients are usually seen in a number of different
centers. Aim of the study was to analyze the prevalence of the autoimmune inflammatory diseases followed by Centers of Pediatric Rheumatology.

Methods: A secured web-based questionnaire on the number patients with genetically defined or clinical suspected Autoinflammatory disorders among the centers of Pediatric Rheumatology members of the Pediatric Rheumatology Trial International Organization (PRINTO, http://www.printo.it) was performed.

Results: 126 Centers from 38 Countries (94 in Europe, 13 South America, 12 Asia, 5 Australia, 2 Africa) relayed to the survey. Among the patients with a genetic proven disease 73 were affected by TRAPS, 118 by HyperIgD syndrome, 153 by cryopyrinopathies, 71 by PAPA syndrome, 66 patients by Blau’s syndrome. A genetically proven FMF was reported in 2484 patients (1947 from countries of the Middle east and north Africa, 537 from other countries). A number of patients with a clinical suspected Autoinflammatory were also reported: 68 with suspected TRAPS, 84 HyperIgD, 57 cryopyrinopathies, 50 PAPA, 60 Blau’s syndrome. The ratio between genetically proven vs suspected disease was 1:97 in Western European countries and 0.6 in Countries where the molecular analysis is not available.

Conclusion: A relevant number of patients with genetically defined or clinical suspected Autoinflammatory diseases are followed by different Centers of Pediatric Rheumatology worldwide. A network of registries for the proper collection of data coming from these patients and an improvement of the possibilities for the molecular diagnosis in non-Western European Countries are recommended.

P195
Mevalonate kinase deficiency (MKD): long-term follow-up of clinical and biological features in 40 patients
B Florkin1, L Cuisseau2, C Acquaviya-Bourdain3, D Rabier4, B Neven5, P Quartier6 and AM Prieur1

1Necker Enfants Malades Hospital, Immuno-hematology Unit, Paris, France
2Cochin Hospital Molecular Genetics, Paris, France
3Debrousse Hospital, Lyon, France
4Necker Enfants Malades Hospital, Biochemistry Department, Paris, France

Pediatric Rheumatology 2008, 6(Suppl 1):P195

MKD causes hyper-IgD syndrome and mevalonic aciduria. Disease severity and clinical phenotype has not yet been linked to specific mutations. In this study, we intended to review disease severity and clinical phenotype has not yet been linked to specific mutations. In this study, we intended to review Disease severity and clinical phenotype has not yet been linked to specific mutations. In this study, we intended to review Disease severity and clinical phenotype has not yet been linked to specific mutations.

Methods:

A retrospective chart review of patients referred to us with FMF symptoms. Systematic genetic screening of exon 2 and 10 was performed in MEFV gene. A subset of patients was also investigated for other hereditary recurrent fevers.

Results:

We analysed 94 patients (sex-ratio:1). 42% were Jews and 17% were Arabs. Familial history of FMF was found in 23%, MICI in 10%, amyloidosis in 3% and Behçet in 3%. Median age of onset was 2 y. Fever was >39°C in 80%, duration and frequency of an attack varied (<24 h: 8%, 1–3 d: 56%, >3 d: 36%; >2/m: 15%, I–2 m: 48% <1 m: 37% respectively). Peritonitis occurred in 97%, pleuritis in 25%, arthralgia in 53%; arthritis in 4 cases; skin rashes in 20%, aphthosis in 15% and lymphadenopathy in 9%. MEFV mutation were: M694V (60%), M694I (7%). The R92Q mutation was retrieved in 3/21 patients tested and the V377I MKD mutation in 1/6. Colchicine treatment was required in 82% of them and was effective in >90% of them. Associated diseases in these patients were PFAPA (4), Ankylosing spondylitis (5), Crohn’s disease (1) and Castleman disease (1).

Discussion:
The clinical picture of MEFV heterozygotes resembles that of homozygote patients. This study displays a wide variety of associated diseases. Complete screening of both MEFV and other auto-inflammatory gene mutation may increase our understanding of disease expression.

P197
Anakinra for secondary amyloidosis in an adolescent with FMF and Behçet Disease
Y Bilginer, N Aktay Ayvaz and S Ozen
Hacettepe University School of Medicine Pediatric Nephrology and Rheumatology Unit, Ankara, Turkey

Pediatric Rheumatology 2008, 6(Suppl 1):P197

Familial Mediterranean Fever (FMF) is associated with mutation in the gene coding for pyrin which lead to accentuated innate immune responses involving the IL1 and probably Th1 pathways. We present a teenager who had FMF and Behçet disease and developed secondary amyloidosis. We hypothesized that...
anti-IL1 treatment would be beneficial for both controlling the disease activity and maintaining renal function. A 17 year old girl with FMF (M694V/M694V) and Behcet disease unresponsive to colchicine (2 mg/day), methotrexate and indomethacine therapy developed proteinuria during her therapy of eight years. She has arthritis, fever and erythema nodosum as well as aphthous lesions twice a month. She suffered a poor quality of life and often unable to attend school. Acute phase reactants, ESR 89 mm/hour, CRP 6.4 mg/dl were high independent of her attacks. 10 months ago she developed proteinuria of 300 mg/dl proteinuria with dipstick and 1.8 gr/day proteinuria was found. Her renal function tests were normal. The renal biopsy confirmed the diagnosis of secondary amyloidosis. Anakinra was started at 1 mg/kg/day subcutaneously without stopping colchicine treatment with a special permission from the Ministry of Health. Isoniazid was also started because of the marked tuberculin reaction. In the following 6 months the patient was free of clinical symptoms. Acute phase reactants decreased. The level of proteinuria did not increase and renal functions remain stable.

We suggest that secondary amyloidosis due to autoinflammatory diseases is a new indication for the use of anti-IL1 treatment.

**P198**

**Differentiation of post streptococcal reactive arthritis from acute rheumatic fever**

J Barash^1,2^, E Mashhouch^1^, P Navon-Elkan^2^, Y Berkun^3^, L Harel^4^, T Tauber^5^, S Padeh^5^, P Hashkes^6^ and Y Uziel^7^  

^1^ Kaplan Medical Center, Rehovot, Israel  
^2^ Shaarei Zedek Medical Center, Jerusalem, Israel  
^3^ Sheba Medical Center, Tel Hashomer, Israel  
^4^ Schneider Children’s Hospital, Petah Tikva, Israel  
^5^ Asaf Harofeh Medical Center, Zrifin, Israel  
^6^ Cleveland Clinic, Cleveland, USA  
^7^ Meir Medical Center, Kfar Saba, Israel

**Objective:** We performed a retrospective study comparing clinical and laboratory aspects of patients with acute rheumatic fever (ARF) and post streptococcal reactive arthritis (PSRA), in order to answer the question whether these are two separate entities or varying clinical manifestations of the same disease.

**Study design:** We located through the Israeli internet based paediatric rheumatology registry 68 patients with ARF and 159 patients with PSRA, treated by 8 paediatric rheumatologists. The medical records of these patients were reviewed for demographic, clinical and laboratory variables and the data compared and analyzed by univariate, multivariate and discriminant analysis.

**Results:** Four variables were found to differ significantly between ARF and PSRA and serve also as predictors: sedimentation rate, C-reactive protein, duration of joint symptoms after starting anti-inflammatory treatment and relapse of joint symptoms after cessation of treatment. A discriminative equation was calculated which enabled us to correctly classify more than 80% of the patients.

**Conclusion:** Based on simple clinical and laboratory variable we were usually able to differentiate ARF from PSRA. It appears that they are different entities, although both are associated with streptococcal infection and involve the joints.

**P199**

**Hiper IgD syndrome (HIDS): clinical and genetic features in five patients**

A Marco^1^, I Calvo^1^, B Lopez^2^, JI Arostegui^2^ and J Yagüe^2^  

^1^ Hospital Infantil la Fe, Valencia, Spain  
^2^ Hospital Clinic, Barcelona, Spain

**Introduction:** The Hiper-IgD Syndrome (HIDS) is an autoinflammatory disease characterized by recurrent febrile episodes each 4–8 weeks accompanied by an intense inflammatory reaction, lymphadenopathy, abdominal pain, diarrhea, arthralgias, hepatosplenomegaly and cutaneous signs [1]. Mutations in the gene that codifies the enzyme mevalonate kinase (MVK), located in the chromosome 12q24, have been demonstrated to be the cause of this syndrome [2].

**Objective:** We describe the clinical and genetic findings of three families (five patients) with diagnosis of HIDS and confirmed mutational analysis.

**Methods:** We present a retrospective analysis of the patients and its genealogical tree. The mutational analysis was made by the service of Immunology of the Hospital Clinic of Barcelona.

**Results:** Clinically the five patients presented the typical symptomatology with recurrent febrile episodes, intense abdominal pain (a case required several exploratory laparotomies), cervical lymphadenopathy, diarrhea and hepatosplenomegaly. One of the patients presented a chilotorax that resolved after discarding amiloidosis and initiating treatment. In all cases mutations I268T or V377I were detected. In two of the families, the parents demonstrated to be heterozygote carriers of one of the two found mutations. All the patients have required steroids to high doses, nevertheless, three of the cases have developed steroid dependency with necessity of biological treatment with Anakinra, a recombinant, nonglycosylated synthetic form of the human interleukin-1 receptor antagonist (IL-1Ra), that in last publications has demonstrated to be the election treatment since the Hiper IgD Syndrome is part of the autoinflammatory diseases in whose common pathogenic mechanism the IL-1 takes part.

**References**

2. Haas D and Hoffmann GF: Mevalonate kinase deficiencies: from mevalonic aciduria to hyperimmunglobulinemia D syndrome. Orphanet J Rare Dis 2006, 1:13
complication to systemic onset juvenile idiopathic arthritis (SoJIA) with significant morbidity and mortality. We present a 12 year old boy admitted to hospital with a 2 week history of fever, malaise, muscle tenderness, and skin rash. Initially an infection was suspected based on symptoms and an exceptional high CRP (3717 nmol/l), however despite antibiotics and a rapidly decreasing CRP the clinical status deteriorated. The patient became somnolent and rigid in all four extremities having weak deep tendons reflexes. Laboratory studies showed an elevated CRP (2158 nmol/l), relative pancytopenia, coagulopathy, high serum ferritin (1254 µmol/l), and increasing liver transaminases. MRI of the cerebrum showed progressive lesional changes on T2-weighted FLAIR sequence in the cortex and basal ganglia. Bone marrow examination was normal, and did not show hemophagocytosis.

MAS based on SoJIA was suspected and treatment with cyclosporine A (4 mg/kg/day) and high dose methylprednisolone (12 mg/kg/day for 3 days) was initiated. The patient did not respond to initial treatment. Anti-TNF-α monoclonal antibody Infliximab (5 mg/kg) was added to the treatment and repeated after 2 and 6 weeks. The patient rapidly improved clinically and biochemically and went into full recovery after four months. MAS complicated with severe CNS involvement is associated with an extremely high mortality rate. Our case supports the addition of infliximab when standard treatment fails.

P201
Dutch type periodic fever in a Turkish infant also having MEFV mutation
B Makay, F Demirciooglu, M Duman and E Unsal
Dokuz Eylul University Hospital, Izmir, Turkey

Reference

P202
A strange fever in two brothers
F La Torre, A Vitale and G Calcagno
Universities, Messina/Sicily, Italy

Reference

P203
Chronic granulomatous disease (CGD) presenting as quotidian fever
K Moenkemoeller1, R Cremer1, J Roesler2, A Schulz3, M Weiss1 and C Schuetz2
1Kinderkrankenhaus, Kliniken der Stadt Koeln gGmbH, Koeln, Germany
2Klinik und Poliklinik für Kinder- und Jugendmedizin, Universitätsklinikum Carl Gustav Carus, Dresden, Germany
3Klinik für Kinder- und Jugendmedizin, Universitätsklinikum Ulm, Ulm, Germany

Reference
I. Pediatric Rheumatology 2008, 6(Suppl 1):P203

Page 84 of 110
making. We identified CGD in a five year old Turkish boy with systemic inflammation mimicking systemic onset JIA (SOJIA).

**Clinical case:** The patient presented with 7 days of spiking fever not responding to oral antibiotics, arthralgias and a maculopapular rash. Laboratory results showed leukocytosis, thrombocytosis, CrP of 240 mg/l, ESR 100 mm. The symptoms persisted under intravenous antibiotic treatment. Focus work-up gave no evidence of an infectious origin, malignancy, IBD, vasculitis, connective tissue disease or periodic fever syndrome.

Due to suspicion of incomplete SOJIA a steroid pulse was given. Disease activity responded promptly, consequently methotrexate was added.

After steroid reduction fever and arthralgias recurred and inflammation increased. Physical and radiological examinations and echocardiography were normal. Another steroid pulse was successful and Ciclosporine was added. Again systemic inflammation appeared with decreasing steroids. Thorax x-ray showed interstitial infiltrates. CT identified a ground-glass pattern, a circular pleural lesion and a small hypodense hepatic lesion. Those two abscesses led us to perform granulocyte function testing: Dihydorhodamine-testing showed absent NADPH-oxidase activity. Aspergillus fumigatus was cultivated following pulmonary lavage.

The child responded well to antibiotic and anti-fungal treatment. Stem cell transplantation is being discussed as a curative treatment.

**Conclusion:** SOJIA as one cause of systemic inflammation is an exclusion disorder. The incidental finding of abscesses in our case led to CGD. This emphasizes the need for repeated diagnostic approaches in patients with unexplained fever attacks.

**P204**

Periodic fever syndrome with aphthous stomatitis, pharyngitis and cervical adenopathy treated with ketotifen – a case report

N Toplak, V Glavnik, M Kuhar and T Avcin
Department of Allergology, Rheumatology and Clinical Immunology, University Children’s Hospital, University Medical Centre, Ljubljana, Slovenia

*Pediatric Rheumatology* 2008, 6(Suppl 1):P204

**Background:** The pathogenesis of PFAPA syndrome is unknown. According to Stojanov et al. cytokine profile in PFAPA syndrome suggests Th1 mediated inflammatory process resulting in continuous inflammation and reduced Th2 anti-inflammatory response. Interferon γ might be responsible for suppressing the production of IL-4 and IL-10. Hung et al. showed suppressive effects of ketotifen on the expression of Th1 and Th2 related chemokines of human monocytes.

**Case report:** We report a case of a four year old girl with PFAPA syndrome. Attacks of fever started in the first year of life and recur every 2–4 weeks. The genetic testing for FMF, HIDS and TRAPS was negative. No immunodeficiency or autoimmune disease was proven. She responded well to oral corticosteroid treatment but intervals between attacks became shorter. Given the recent finding of possible suppressive effect of ketotifen on Th1 and Th2- related chemokines of monocytes and favourable safety profile of this medication, the patient was prescribed ketotifen 1 mg twice per day for 8 months. During this period we observed significant prolongation of interval between fever attacks. She had only 3 attacks in 8 months. During the period of treatment with ketotifen she was without febrile attacks for 3 months, the longest period ever. After cessation of therapy with ketotifen attacks recur with previous frequency.

**Conclusion:** Our case report suggests possible beneficial effect of ketotifen on the frequency of fever attacks in patients with PFAPA syndrome. Ketotifen may be considered as an alternative medication in patients with PFAPA syndrome and recurrent fever attacks.

**P205**

The association of Familial Mediterranean Fever and cryptogenic cirrhosis

E Baskin, F Ozcay, US Bayrakci, F Ozbay Hosnut and KS Gülleroglu
Baskent University, Ankara, Turkey

*Pediatric Rheumatology* 2008, 6(Suppl 1):P205

Familial Meditarranean Fever (FMF) is an ethnically related genetic disease, characterized by spontaneously resolving episodes of fever and pain. Amyloidosis of the amyloid A type is the most important manifestation of FMF, affecting many organs, including the kidneys, adrenal glands, intestines, spleen, thyroid, heart, lungs and liver. There is an increasing concern about the association of non-amyloid chronic liver disease and FMF.

We present a 9 year-old male patient from consangous parents who had episodes of recurrent diarrhea, fever, vomiting and abdominal pain since 6 month-old. He was found to have hepatosplenomegaly on his physical examination. Liver biopsy revealed the diagnosis of cryptogenic cirrhosis without any deposition of amyloid. He was also found to have homozygous M694V gene mutation and colchicine was started while he was 7 year-old.

The relation of cryptogenic cirrhosis and FMF is still obscure. Non-amyloid liver disease could be found in patients with FMF as a coincidental finding or as an association and patients with cryptogenic cirrhosis should be investigated for the presence of FMF.

**P206**

Quality of life of school-age children with Familial Mediterranean fever: a preliminary study

B Makay, E Unsal and N Arslan
Dokuz Eylul University Hospital, Izmir, Turkey

*Pediatric Rheumatology* 2008, 6(Suppl 1):P206

**Background:** Familial Mediterranean fever is a chronic health condition characterized by periodic fever, abdominal and chest pain, arthritis, and rash. The impact of disease and treatment on quality of life (QOL) of patients had been investigated in adults. However, there is no data about the QOL of pediatric FMF patients.

**Objective:** The aim of this study was to assess the quality of life of school-age children with FMF.

**Methods:** Thirty patients were evaluated using age-appropriate versions of “Pediatric Quality of Life™ Generic Core Scale”. The PedsQL™ assesses: 1. Physical Functioning (8 items), 2. Emotional Functioning (5 items), 3. Social Functioning (5 items), and 4. School Functioning (5 items). The patients were divided into 2 age groups: “8–12 years” (n = 14) and “13–18 years” (n = 16). The control group consisted of 81 healthy children. SPSS version 11.0 was used for statistical analysis.

**Results:** The total PedsQL score of all FMF patients was significantly lower than that of the controls: 75 ± 16 vs
Pediatric Rheumatology 2008, 6(Suppl 1)

http://www.ped-rheum.com/supplements/6/S1

84 ± 10 (p = 0.001). The patients aged between 8–12 years had significantly lower PedsQL score than controls: 71.5 ± 19 vs 86 ± 8.5 (p < 0.000). However, no statistical significance was found between the total scores of patients aged between 13–18 years and age-matched healthy controls: 78 ± 13 vs 82 ± 11 (p = 0.22).

Conclusion: This preliminary study suggested that FMF may impair the quality of life, particularly in younger children. Further studies with larger group of patients are needed to evaluate the factors affecting the quality of life in patients with FMF.

P207
Profile of cytokines, growth factors and chemokines during attacks of FMF
Y Bilginer1, P Roux-Lombard2, Michel Dayer J2, A Bakkaloglu1 and S Ozen1
1Hacettepe University School of Medicine Pediatric Nephrology and Rheumatology Unit, Ankara, Turkey
2Hopital Universitaires de Geneve, Geneva, Switzerland

Pediatric Rheumatology 2008, 6(Suppl 1):P207

Attacks of Familial Mediterranean fever (FMF) represent one of the most devastating states of inflammation. FMF is an autoinflammatory disease caused by mutations in the gene coding for pyrin. We aimed to assess the characteristics of inflammation in FMF patients during an acute attack by evaluating some growth factors, chemokines and cytokines. Six patients (median 11 years (7–16)) were sampled 12–36 hour after the onset of a typical FMF attack. All had elevated acute phase reactants. All six had homozygote mutations in the MEFV gene. Various cytokines, chemokines, growth factors and CD40 ligand were measured by a commercially available multiplex beads immunoassay based on Luminox platform. IL1Ra (median 1047 pg/ml), TNF alpha (median 3.05 pg/ml) and IL6 (median 19.14 pg/ml) levels were elevated whereas IL2, IL10, IL12, IL17 and IL13 were not detectable in any of the samples. EGF, VEGF and HGF were markedly elevated as well. Among the chemokines, MIP1b, CCL11, CXCL11 and CXCL5 were all detectable at a varying range. CD40 L was also markedly elevated.

IL1Ra is induced by inflammatory stimuli with IL1 and reflects the IL1-dependent inflammatory response. Chemokines were elevated reflecting the neutrophil inflammation and recruiting in this disease. The growth factors were thought to be elevated as an inflammatory response phenomena. The CD40L induction may be serving as a link between the innate immune response and adaptive on during the attacks of FMF.

The protein fingerprint of FMF will shed light on the pathogenesis of the disease and help us guide disease activity and severity.

P209
The phagocyte specific protein S100A12 as a novel biomarker in Muckle-Wells Syndrome before and during therapy with Anakinra and Canakinumab (ACZ885)
H Wittkowski1, JB Kuemmerle-Deschner2, K Gramlich2, N Tzaribachev2, SD Felix3, T Jung3, J Roth1, C Rordorf2 and D Foell1
1University Hospital Muenster, Department of Pediatrics, Muenster, Germany
2University Childrens Hospital Tuebingen, Pediatric Rheumatology, Germany
3Novartis Pharma AG, Basel, Switzerland

Pediatric Rheumatology 2008, 6(Suppl 1):P209

Background: The pro-inflammatory Damage Associated Molecular Pattern (DAMP) molecules Myeloid-Related Protein (MRP)-8/14 have been recently identified as ligands and activators of TLR-4. Familial Mediterranean Fever (FMF) is an auto-inflammatory syndrome associated with activation of phagocytic cells and oversecretion of the proinflammatory cytokine IL-1β. Our aim was to evaluate MRP8/14 serum levels in FMF patients during high inflammatory episodes and during successful therapy.

Patients and methods: 70 genetically proven FMF patients were followed up longitudinally over a period of 18 months. Serum concentration of MRP-8/14 determined by ELISA and additionally ESR, CRP and SAA as classical inflammation markers were analysed before starting of therapy and during colchicine treatment. As control groups we measured 17 Neonatal-Onset Multisystem Inflammatory Disease (NOMID), and 18 Muckle Wells Syndrome (MWS) patients.

Results: The mean serum levels of MRP8/14 in inflammatory episodes in FMF (343,210 ± 202,210 ng/ml; n = 17) were significantly higher than in NOMID (2,830 ± 580 ng/ml; p < 0.001), or in MWS (3,205 ± 585 ng/ml; p < 0.001). FMF patients treated with colchicine and not exhibiting any attacks during the study period (5,480 ± 1,900 ng/ml; n = 28) had significantly lower MRP8/14 levels than patients treated with colchicine exhibiting complains typical for FMF (34,700 ± 14,580 ng/ml; p < 0.001; n = 20), and also than Homozygous patients never experiencing any clinical signs without colchicine treatment (22,310 ± 10,110 ng/ml; p < 0.05 n = 5).

Conclusion: MRP8/14 as a marker of phagocyte activation is highly oversecreted in patients with FMF. Measurement of MRP8/14-levels in FMF might be a valuable tool to reflect disease activity, response to anti-inflammatory therapy, and even subclinical inflammatory activity.
active disease were included in this study. After Anakinra treatment therapy was switched to Canakinumab (ACZ885). Muckle-Wells-Syndrome Disease-Activity-Score (MWSDAS), SAA, CRP, ESR and S100A12 values were recorded one day before (baseline) and during treatment with Anakinra (day 30–120) and Canakinumab (day 8).

Results: MWSDAS, and all inflammation markers fell significantly from baseline to follow-up in both treatment groups. S100A12 was significantly lower with Canakinumab than with Anakinra therapy (87 ± 64 ng/ml vs. 145 ± 58; p < 0.05). With Canakinumab, 88% of values were within normal limits within one week of treatment (<120 ng/ml) whereas only 50% of values reached normal range with Anakinra. Correlation between S100A12 and MWSDAS as well as ESR, CRP and SAA was significant (p < 0.05).

Conclusion: S100A12 is a sensitive marker of inflammation in patients with MWS and may be a valuable parameter to monitor subclinical inflammation. Data indicates that treatment with canakinumab, in contrast to anakinra, normalized S100A12 levels in the majority of patients.

P210
Clinical phenotype and CARD15 gene mutation with Blau Syndrome in Chinese children and their parents
C Li, X He, J Zhang, T Han and W Kuang
Beijing Children’s Hospital, Beijing, PR China

Pediatric Rheumatology 2008, 6(Suppl 1):P210

Background: Blau Syndrome characterized by granulomatous polyarthritis, uveitis and rash with a typical onset before 5 years. We summarized the article to find the clinical features of our patients and analyze CARD15 gene mutation of the patients and their parents.

Materials and methods: Studied on clinic and basis aspect of cases of Blau Syndrome in Beijing Children’s Hospital from the year of 2006 to 2007.

Results: 8 patients were diagnosed. The onset age was from 1 month to 5 years. Three of them were misdiagnosed as JIA and Takayasu’s arteritis respectively. One case had family history. All patients had typical rash, joint problem, bilateral panuveitis. Two had hearing lose, four had Takayasu’s arteritis with hypertension, and two of them had renal artery stenosis with severe hypertension and aortitis. Histologically, there was synovial and dermis proliferation with non-caseating giant cell granulomas in all of the patients. We analyzed 6 patients and their parents’ NOD2/CARD15 gene. We have found six mutations in them. R334W and R334Q were reported previously abroad, E383D, R471C and R587C are new mutations. In the treatment, all of them received NSAIDS, steroid treatment, one of them also with TNF blockers. All of them were efficiency.

Conclusion: Blau syndrome is a rare auto-inflammatory disease. We diagnosed 8 patients in Chinese Children. That indicate Blau syndrome also can involve Chinese population. They had CARD15 gene mutation and some of the mutations are special changes in Chinese population.

P211
Infantile Onset Panniculitis with Uveitis and Systemic Granulomatosis: immunohistochemical findings
CH Wouters¹, P Quartier², B Bader Meunier², D Stichweh³, M Punaro³, T Martin⁴, T Roskams¹ and CD Rose⁵
¹University Hospital Gasthuisberg, Leuven, Belgium
²Hôpital Necker-Enfants Malades, Paris, France
³Texas Scottish Rite Hospital, Texas, USA
⁴Casey Eye Institute, Portland, USA
⁵duPont Children Hospital, Delaware, USA

Pediatric Rheumatology 2008, 6(Suppl 1):P211

Infantile-Onset Panniculitis with Systemic Granulomatosis is a recently described clinicopathologic entity, considered part of the spectrum of pediatric granulomatous inflammatory diseases. Through the International Registry of Pediatric Granulomatous Arthritis (PGA), we now identified 5 children with this disorder, all manifesting from very young age panniculitis, fever, hepatosplenomegaly, arthritis, uveitis and acute phase response. Underlying infections, immune deficiency and autoimmune disease, were excluded. No CARD15 or CIAS1 mutations were found. Histologically, the subcutaneous nodules showed a non-vasculitic non-cytophagic lobular panniculitis. Giant and epitheloid cell granulomas were found in liver (pt 1, 5), synovium (pt 2), lymph node (pt 3, 5), colon (pt 3), subcutaneous fat (pt 3), dermis and lung (pt 4).

Immunohistochemical study of the granulomas revealed the presence of abundant CD68+ macrophages, numerous CD4+ T lymphocytes and few CD8+ cells. TNF stainings were only weakly positive, conversely abundant IL-6 staining was apparent, especially in the corona of lymphocytes. Despite steroid and cyclosporin treatment, the course was progressive in patient 1 with severe lung involvement and death from respiratory insufficiency at age 14. In patients 2, 3, 4 and 5, therapy with anti-TNF MoAbs allowed better disease control. Infantile onset Panniculitis with Systemic Granulomatosis may be a potentially fatal granulomatous disease in children. Through the International Registry of Pediatric Granulomatous Arthritis (PGA), we now identified 5 children with this disorder, all manifesting from very young age panniculitis, fever, hepatosplenomegaly, arthritis, uveitis and acute phase response. Underlying infections, immune deficiency and autoimmune disease, were excluded. No CARD15 or CIAS1 mutations were found. Histologically, the subcutaneous nodules showed a non-vasculitic non-cytophagic lobular panniculitis. Giant and epitheloid cell granulomas were found in liver (pt 1, 5), synovium (pt 2), lymph node (pt 3, 5), colon (pt 3), subcutaneous fat (pt 3), dermis and lung (pt 4).

Immunohistochemical study of the granulomas revealed the presence of abundant CD68+ macrophages, numerous CD4+ T lymphocytes and few CD8+ cells. TNF stainings were only weakly positive, conversely abundant IL-6 staining was apparent, especially in the corona of lymphocytes. Despite steroid and cyclosporin treatment, the course was progressive in patient 1 with severe lung involvement and death from respiratory insufficiency at age 14. In patients 2, 3, 4 and 5, therapy with anti-TNF MoAbs allowed better disease control. Infantile-onset Panniculitis with Systemic Granulomatosis may be a potentially fatal granulomatous disease in children. Although the response to anti-TNF MoAbs in four of our patients is of note, the paucity of TNF with overwhelming presence of IL-6 in situ in granulomas suggest the implication of alternative immune-inflammatory pathways. The role of the Th17 pathway is currently under investigation.

P212
Different pattern of synthesis and secretion of IL-1β in patients with CIAS-1 and TNFRSF1A mutations responding to IL-1 blockade
D Lasiglie¹, S Carta², S Tassi², F Ferlito¹, A Piccini², A Martini¹, A Rubartelli² and M Gattorno¹
¹12th Division of Pediatrics, “G. Gaslini” Institute and Department of Pediatrics University of Genoa, Genoa, Italy
²Laboratory of Experimental Oncology E/Cell Biology, Istituto Nazionale per la Ricerca sul Cancro, Genoa, Italy

Pediatric Rheumatology 2008, 6(Suppl 1):P212

Aim: To compare the in vitro secretion of IL-1β in patients carrying CIAS-1 mutations and TRAPS patients, in an effort to
understand the mechanism modulating IL-1β secretion in the different pathologies responding to anti-IL-1 treatment. **Methods:** Monocytes from 6 CINCA and 4 TRAPS patients selected for treatment with Anakinra were activated with 1 μg/ml of LPS for 3 hours, at baseline and after 7 days from the beginning of the treatment. For comparison, monocytes from 24 healthy donors were also studied. Intracellular pro-IL-1β and secreted IL-1β were analysed by Western blotting and ELISA before and after a short exposure (15 min) to exogenous ATP that accelerates IL-1β secretion. **Results:** In healthy subjects LPS-induced IL-1β secretion was variable but consistently = 5 ng/ml and it was markedly increased by exposure to exogenous ATP (up to 20 ng/ml). Monocytes from CINCA patients secreted abnormally elevated amounts of IL-1β after LPS stimulation (up to 40 ng/ml) that were not increased by ATP. Conversely, monocytes from TRAPS patients did not secrete more IL-1β than healthy controls in response to LPS, but similarly to CINCA patients presented a low response to ATP. **Conclusion:** Despite a similar clinical response to anti-IL1 treatment, the pattern of IL-1β secretion of monocytes from Anakinra-responder TRAPS patients significantly differ from that observed in patients CIAS-1 mutations. This study suggests a different hierarchy in the pathogenic mechanisms leading to the inflammatory response in different diseases responsive to anti-IL-1 treatment.

**P213**

**Myeloid cells which secrete S100 proteins in juvenile dermatomyositis may contribute to disease activity**

H Varsani, H Wittkowski, J Roth, J Holton and LR Wedderburn
Institute of Child Health, London, UK

**Pediatric Rheumatology** 2008, 6(Suppl 1):P213

**Background:** Juvenile dermatomyositis (JDM) is thought to involve an autoimmune myositis, yet the elements of the immune response which damage muscle tissue in JDM remain unclear. Muscle tissue from early JDM shows infiltration by predominantly macrophage/myeloid cells. Traditional histopathology would suggest that these cells have a scavenger or ‘repair’ function; our data suggest otherwise. We have analysed production of the highly proinflammatory S100 proteins MRP8/14 in JDM patients.

**Methods:** 40 children with JDM (32 female) were recruited through the UK JDM Registry and Repository. Muscle biopsy tissue (n = 33) serum (n = 39) and clinical data (physicians global assessment, CMAS, CK) were analysed. Serum MRP8/14 was measured by ELISA in JDM and 50 healthy age-matched children. Muscle biopsies were analysed by 2-colour immunofluorescence, stained with antibodies to human CD68, CD14, CD163, CD15, DC-LAMP, MRP14 and the heterodimer MRP8/14.

**Results:** MRP8/14 were significantly raised in serum from children with JDM (2428 ± 1717 ng/ml) compared to age matched controls (340 ± 40 ng/ml). Serum MRP8/14 levels correlated with CMAS (r = 0.525) PGA (r = 0.498) and CK (r = 0.688). Muscle biopsy analysis frequently showed early diffuse infiltrate of MRP14+ cells. Lineage analysis of infiltrating MRP14+ cells showed that the majority were CD68+ (76.6%) with a minority of MRP14+ cells being CD14+ (21.9%), CD163 (20.2%) or CD15+ (19.6%). Infiltrating DCs did not express MRP proteins.

**Conclusion:** MRP8/14 levels in serum of patients with JDM correlate with disease activity, and a subpopulation of pro-inflammatory macrophages in muscle tissue may be a source of these highly inflammatory proteins.

**P214**

**Differences in therapeutic approach to juvenile dermatomyositis between Europe and Latin America**

LT Trail1, C Ferrari1, R Cuttica2, MM Katsicas3, R Russo3, M Bandeira4, V Ferriani2, S Oliveira5, C Saad-Magalhaes2, CA Silva6, V Bacau, R Burgos-Vargas10, E Solis-Vallejo11, S Maillard12, C Piklington12, R Barcellona1, M Beltramelli11, L Breda1, C Bruno1, R Cimaz1, E Cortis1, R Gallizzi1, F Garofalo1, A Meini1, R Podda1, A Stabile1, A Martini1 and A Ravelli1

1Italian Pediatric Rheumatology Study Group, Italy, Italy
2Hospital General de Ninos Pedro de Elizalde, Buenos Aires, Argentina
3Hospital Garrahan, Buenos Aires, Argentina
4Hospital Pequeno Principe, Curitiba, Brazil
5Hospital da Universidade, Ribeirao Preto, Brazil
6Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil
7Hospital das Clinicas UNESP, Botucatu, Brazil
8Hospital Das Clinicas, Sao Paulo, Brazil
9CMN Siglo XXI, Mexico City, Mexico
10Hospital General de Mexico, Mexico City, Mexico
11CMN La Raza, Mexico City, Mexico
12Great Ormond Street Hospital, London, UK

**Objective:** To investigate the differences in the therapeutic approach to juvenile dermatomyositis (JDM) between pediatric rheumatology centers in Europe (EU) and Latin America (LA).

**Methods:** 490 patients with JDM and disease duration > 2 years seen in 27 centers in EU (Italy, UK) and LA (Argentina, Brazil, Mexico) after 1980 were enrolled in a multinational, multicenter study aimed to investigate the long-term disease outcome. Median follow-up duration was 7.7 years (range

| Table 1 (abstract P214) Frequency of drugs administered to JDM patients in EU and LA centers |
|---------------------------------|---------------|--------------|-------------|----------|----------|--------|-------------|--------|
| Oral/iv steroids | Pulse iv steroids | MTX | CyA | Iv Ig | AM | AZA | Oral CPM | Pulse iv CPM |
| EU (N = 246) | 97.6 | 50 | 50.8 | 35 | 17.1 | 26 | 13.4 | 5.3 | 8.5 |
| LA (N = 236) | 99.6 | 33.2 | 61.4 | 15.7 | 17.4 | 39 | 5.9 | 2.1 | 4.2 |

MTX: methotrexate; CyA: cyclosporine A; AM: antimalarials; AZA: azathioprine; CPM: cyclophosphamide.
2–25.2 years). Gender ratio, onset age, and follow-up duration were comparable between EU and LA patients. At study visit, EU patients had a greater frequency of active disease, as measured with MDAA (51.1% vs. 35.2%) and DAS (64.8% vs. 54%), whereas LA patients had a greater frequency of muscle weakness, as measured with the CMAS (62.9% vs. 44.3%), and muscle damage, as measured with the MDI (41% vs. 30.1%).

Results: Table 1 shows the frequency of drugs administered to JDM patients in EU and LA centers.

Conclusion: Use of pulse iv steroids, CyA, AZA and CPM was more common in EU centers, whereas LA centers used more frequently MTX and AM. EU and LA centers administered iv Ig with equal frequency.

P215
Treatment of refractory juvenile dermatomyositis with tacrolimus
J Hassan, JJ van der Net and A van Royen-Kerkhof
Wilhelmina Children’s Hospital, University Medical Center Utrecht, Utrecht, Netherlands

Background: Corticosteroid and second line agents such as methotrexate have dramatically improved the outcome for patients with Juvenile Dermatomyositis (JDM). Nevertheless, some patients suffer persisting disease activity despite these treatments. Tacrolimus, an inhibitor of T-cell activation and proliferation, is one of the new therapeutic options for JDM. However, little is known about its efficacy in this patient group. We report the clinical course of three patients with refractory JDM who were treated with tacrolimus.

Patients: Three corticosteroid dependent children with extensive skin disease and severe muscle weakness were started on oral tacrolimus treatment and followed-up for 7–9 months. Patient 1: 11 year old boy, age of onset 6.1 years. Patient 2: 7 year old girl, age of onset 5.8 years. Patient 3: 9 year old girl, age of onset 4.4 years.

Results: All three patients showed impressive improvement of mainly the cutaneous lesions, and overall disease activity decreased along with the muscle enzyme levels (Figure 1), while corticosteroids could be tapered. All children became more physically active. None of the patients showed recovery of muscle strength, probably due to irreversible muscle damage related to the long-standing myositis.

Conclusion: Tacrolimus is an effective and safe second line agent in the treatment of chronic refractory JDM and improves the skin involvement substantially.

P216
Abstract withdrawn
Pediatric Rheumatology 2008, 6(Suppl 1):P216

P217
Gastroparesis associated with Juvenile Dermatomyositis
N Martin1, J Davidson1, H Harris2 and P Gillett1
1Royal Hospital for Sick Children, Edinburgh, UK
2Victoria Hospital, Kirkcaldy, UK

Background: Gastrointestinal involvement is well recognised in juvenile dermatomyositis (JDM) Dysphagia due to pharyngeal and upper oesophageal dysmotility occurs in 33% of UK patients [1]. Gastrointestinal vasculitis with ulceration and intestinal perforation is also described. There is only one previous report highlighting gastric dysmotility associated with juvenile dermatomyositis [2].

Cases: We present two cases where gastroparesis was associated with JDM and improved with immunosuppression. Clinical features and investigations are summarised in Table 1.

Conclusion: Gastric dysmotility may complicate JDM. In both these cases it presented with intractable vomiting and otherwise normal gastrointestinal investigations. Neither had evidence of otherwise active JDM at the time of onset of their vomiting but both responded to immunosuppression.

References

P218
What is the mortality of Juvenile Dermatomyositis (JDM) in the modern treatment era
S Smith, A Juggins, S Evans and C Pilkington
Institute of Child Health UCL, London, UK

Background: Despite modern treatment approaches Juvenile Dermatomyositis (JDM) remains a serious and potentially life
threatening disease. There are few studies which have documented mortality among large series of cases of JDM treated with modern therapeutic approaches. The Juvenile Dermatomyositis National Registry and Repository, UK and Ireland (JDRR) was established in 2000 to facilitate research and improve knowledge about JDM.

Methods: Children were recruited through the JDRR cohort study. Mortality attributed to JDM or its complications was recorded. A survey of contributors in The Juvenile Dermatomyositis Research Group was also conducted to establish mortality in JDM cases that had not been recruited to the JDRR study.

Results: 245 children (166 females) with myositis have been recruited to the JDRR. Of these, 208 have a diagnosis of JDM or JDM with overlap features (148 females). The total years of JDM disease documented is 1353 patient years. There have been 2 recorded deaths, a rate of 0.96% or 0.15 per 100 patient years of disease. However physicians in contributing centres were aware of 1 death attributable to JDM in cases that could not be recruited to the study before death.

Conclusion: Mortality due to rare diseases can be difficult to estimate accurately. Within the UK and Ireland JDRR study, mortality due to JDM since 2000 has been 0.96%. However this may underestimate deaths as the JDRR does not necessarily recruit all cases of JDM within the UK. JDM remains a serious and life threatening disease of children despite modern therapies and specialist care.

Acknowledgements
On behalf of the JDRG.

P219
Respiratory involvement in juvenile dermatomyositis

M Fabi1, M Le Bourgeois2, C Bodemer3, V Beguin2, AM Prieur4, P Quartier4 and J de Blic5

1Pediatric Unit, Ospedale S.Osola-Malpighi, Bologna, Italy
2Service de Pneumologie et Allergologie Pédiatriques, Hôpital Necker- Enfants Malades, Paris, France
3Service de Dermatologie Pédiatrique, Hôpital Necker- Enfants Malades, Paris, France
4Service de Rheumatologie Pédiatriques, Hôpital Necker- Enfants Malades, Paris, France

Pediatric Rheumatology 2008, 6(Suppl 1):P219

Background: Juvenile dermatomyositis (JDM) is a rare chronic idiopathic inflammatory disorder primarily affecting the striated muscle and the skin. Pulmonary involvement is a common complication and cause of morbidity and mortality, but few data are available concerning pulmonary function impairment in childhood. The aim of this prospective study was to assess pulmonary function impairment in JDM.

Materials and methods: 16 patients (9 girls) with diagnosis of JDM (age 3–16.2 yrs) performed pulmonary function tests (PFT). 14 were receiving treatment; all had muscular testing. The most frequent respiratory pattern is restrictive syndrome secondary to respiratory muscular deficit and evidenced by a reduction of lung volumes with normal DLCO and chest x-ray. We couldn’t detect any risk factor predicting a major lung involvement, but

Table 1 (abstract P217) Clinical features and investigations

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Case 1</th>
<th>Case 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Juvenile dermatomyositis with overlap features</td>
<td></td>
<td>Juvenile dermatomyositis</td>
</tr>
<tr>
<td>Age at onset of gastric dysmotility symptoms</td>
<td>Seventeen</td>
<td>Thirteen</td>
</tr>
<tr>
<td>Age at diagnosis of connective tissue disorder</td>
<td>Eleven</td>
<td>Sixteen</td>
</tr>
<tr>
<td>Rash, proximal weakness, raised muscle enzymes (CK 6926 units/l, ALT 126 units/l)</td>
<td></td>
<td>Rash, muscle pain, raised muscle enzymes (ALT 143 units/l LDH 1097 units); abnormal muscle MRI</td>
</tr>
<tr>
<td>Other clinical features</td>
<td>Sialadenitis</td>
<td>Polyarthritis</td>
</tr>
<tr>
<td>Pulmonary fibrosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal features</td>
<td>Vomiting</td>
<td>Recurrent vomiting and abdominal pain</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight loss</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Required NJ feeding</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ANA 1/640</td>
<td></td>
<td>ANA 1/640</td>
</tr>
<tr>
<td>RF, Anti Ro, La, Sm, RNP positive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastric emptying study grossly delayed</td>
<td></td>
<td>Normal endoscopy</td>
</tr>
<tr>
<td>H. Pylori negative</td>
<td></td>
<td>H. Pylori negative</td>
</tr>
<tr>
<td>Barium normal</td>
<td></td>
<td>Methotrexate</td>
</tr>
<tr>
<td>Normal endoscopy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coeliac screen negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td>Prednisolone</td>
<td></td>
</tr>
<tr>
<td>Mycophenolate Mofetil, Intravenous immunoglobulin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Response to treatment</td>
<td>Normal gastric emptying study</td>
<td>Reduced frequency and severity of symptoms</td>
</tr>
</tbody>
</table>
the longer is the follow-up, the more frequent a functional impairment is present.

**P220**

**Treatment of calcinosis with biphosphonates in juvenile dermatomyositis**

Y Bilginer1, R Topaloglu1 and N Gonc2

1Hacettepe University School of Medicine, Pediatric Nephrology and Rheumatology, Ankara, Turkey
2Hacettepe University School of Medicine, Pediatric Endocrinology, Ankara, Turkey

*Pediatric Rheumatology* 2008, 6(Suppl 1):P220

Juvenile dermatomyositis (JDM) is a multisystem disease that is characterized by nonsuppurative inflammation of striated muscle and skin. Dystrophic calcification occurs in up to 40% of children. We present our treatment approach in four JDM patients with calcinosis. Four female patients (median age 8.5 years, range 6–14) had been diagnosed as JDM in our center. Two of them presented with severe disease and calcifications in the the other two, despite successful treatment of myopathy with steroids, methotrexate and cyclosporin, calcinosis had developed within 10 months (ranging 4–16 months) of initial diagnosis. Two of the patients who had generalized calcinosis and severe osteoporosis were given iv pamidronate and the other two were treated with oral alendronate in addition to oral diltiazem, calcium and vitamin D supplementation. After 7 months of treatment (ranging 5–14 months) clinical and radiological examination revealed dramatic regression of the calcinosis. Bone mass improved as determined by bone absorptiometry. Biphosphonates oral or iv according to the severity of the disease could be a useful therapy in patients with JDM and calcinosis in addition to aggressive therapy of inflammation.

**P221**

**Successful autologous stem cell transplantation (ASCT) in a patient with juvenile dermatomyositis**

U Holzer, N Tzaribachev, J Kuenmerle-Deschner, C Well, P Lang, R Handgretinger and I Mueller

Children’s Hospital, Tuebingen, Germany

*Pediatric Rheumatology* 2008, 6(Suppl 1):P221

Juvenile dermatomyositis (JDM) is a chronic inflammatory disorder, which primarily affects muscle and skin. Patients usually present with progressive muscle weakness accompanied by an erythematous rash over the joints and across the face. Articular, cardiac, pulmonary, and gastrointestinal manifestations may occur resulting in severe morbidity. We report a 16 year old patient, who was diagnosed with JDM four years ago with severe muscle weakness and skin involvement. Despite therapy including methotrexate, steroids, immunoglobulins, cyclosporine A and rituximab a sustained remission could not be achieved. The patient developed progressive contractures due to persistent inflammatory reactions. Due to treatment-refractory disease immunoablation followed by an autologous stem cell transplantation (ASCT) was performed. The stem cells were mobilized by application of 2 g/m² cyclophosphamide. After immunoablation using ATG (thymoglobuline10) 10 mg/kg, cyclophosphamide 120 mg/kg and fludarabine 150 mg/m², CD3/CD19-depleted CD34 + stem cells (7.5 x 10⁶/kg) including 2.9 x 10⁷/kg T-cells were transferred. The haematological reconstitution with leucocytes >1000/ml and granulocytes >500/μl was achieved on day +7 and day +8, respectively. Substitution of erythrocytes or platelets was not necessary. No severe infections or organ toxicity (WHO) were observed. During the 9 months after this therapy a marked improvement of the patient was observed clinically and in the MRI. The Childhood Myositis Assessment Scale (CMAS) changed from 6 to 43, the Karnofsky index increased from 50% to 90% post ASCT. Taken together we could demonstrate for the first time that an ASCT is a therapeutic option with low toxicity for patients with severe, therapy-refractory JDM.

**P222**

**Methotrexate in management of dermatomyositis in a child with insulin-dependant diabetes with chronic hepatitis**

RP Khubchandan, RP Hasija and C Khemani

Jaslok Hospital, Mumbai, India

*Pediatric Rheumatology* 2008, 6(Suppl 1):P222

We present our experience with a four-year (2004–2008) follow-up of a child with multiple autoimmune syndromes. SB, now 13 years old, was symptomatic since 2.5 years with relapsing hepatitis, eventually diagnosed at age 6 years, as chronic lobular hepatitis (ANA positive, AntiLKM/Antimicrosomal/AntiSmoothMuscle Antibodies negative). At 4 years, she was detected to have Type I Diabetes Mellitus (Islet Cell Antibodies positive) and she presented to us at 9 years, with Dermatomyositis (Gottrons papules, CPK 12,310 units, CMAS 2/52). She was started on steroids and azathioprine. Her insulin requirements increased from 20 units/day to 120–140 units/day and she needed a dose of 0.5 mg/kg/day of prednisolone to keep a near normal CMAS and muscle enzymes within normal limits. In October 2007, azathioprine was substituted by subcutaneous methotrexate (10 mg/m²). This led to reduction of daily prednisolone to 0.1 mg/kg/day, improved glycemic control, halving the insulin requirements, improved growth, with no worsening of liver function. She was started on Growth Hormone in 2008 for short stature and this has not altered her glycemic control till the time of reporting. She has hyperlipidemia controlled with diet and statins but has not developed candidiasis or other endocrinopathies during follow up. In conclusion, despite her previous auto-immune liver disease, methotrexate has proven thus far to be a safe and effective steroid sparer in the management of her dermatomyositis.

**P223**

**Efficacy of thalidomide for a girl with inflammatory calcinosis, a severe complication of juvenile dermatomyositis**

T Miyamae, M Kikuchi, K Kasai, R Hara, U Kaneko, T Shinoki, T Imagawa, M Mori and S Yokota

Department of Pediatrics, Yokohama City University, Yokohama, Japan

*Pediatric Rheumatology* 2008, 6(Suppl 1):P223

**Background:** Juvenile dermatomyositis (JDM) is a systemic connective tissue disease characterized by typical skin rash and
chronic muscle inflammation of unknown etiology. Calcinosis is one of the severe complications of JDM. It occurs in up to 30% of patients and results in major disability.

**Case report:** A girl, 14 years of age, was diagnosed as having JDM when she was 4 years old after a few months of increasing lethargy, muscle pain, muscle weakness, and rash. Calcinosis was recognized 18 months after disease onset. During 3 months, clinical manifestations and abnormal laboratory findings were effectively treated with prednisolone. However, generalized calcinosis rapidly progressed with high fever, multiple skin/subcutaneous inflammatory lesions, and increased level of CRP. Methylprednisolone pulses, cyclophosphamide, cyclosporine, azathioprine, and magnesium hydroxide/aluminum hydroxide were applied but failed. Examination of subcutaneous calcium milk revealed remarkably elevated levels of IL-6, TNF-α, and IL-1β. Being encouraged by partial effectiveness with etanercept, thalidomide was started when she was 12 years old. Clinical manifestations were subsided, and inflammatory markers showed remarkable improvement. However, recent examination by whole body PET-CT over 15 months thalidomide treatment still demonstrated hot spots around subcutaneous calcified lesion.

**Conclusion:** It suggested that thalidomide for calcium milk around the generalized calcinosis in a JDM patient could be effective to improve inflammatory manifestations and patient’s QOL. We speculated that subcutaneous pooling of calcium milk may be the cause of inflammation and subsequent calcinosis in JDM, and TNF blockade by thalidomide will be beneficial for inhibiting systemic spreading of inflammation.

**P224**

**Characteristics of juvenile onset systemic sclerosis patients in an adult single centre cohort. Does this patient population present a survival bias?**

I Foeldvari¹, S Nihtanova², A Wierk¹ and CP Denton²

¹Hamburger Zentrum für Kinder- und Jugendrheumatologie, Hamburg, Germany
²Centre for Rheumatology, Royal Free Hospital, London, London, UK

Pediatric Rheumatology 2008, 6(Suppl 1):P224

Juvenile systemic sclerosis (jSSc) is a rare autoimmune disease in childhood. Currently data regarding long-term outcome of jSSc is scarce. We evaluated a large single centre cohort to learn more about the characteristics of jSSc patients in an adult cohort. From more than 1800 cases of SSC, 46 adults with jSSc were identified. The median age of onset was 13.06 years (range 5 to 16). 35 (76%) were female. Median age at last visit was 32.67 years (range 16 to 71). The median disease duration was 21.15 years (range 3 to 58). 39% of the patients had a diffuse and 61% a limited subtype of SSC. 20 (43.5%) of the 46 patients showed overlap features of other connective tissue diseases. Three (6.5%) patients had anticientromere antibodies. 12 (26%) patients were anti-Scl 70 positive. The most common organ involvements were oesophageal in 33 patients (72%), pulmonary fibrosis in 22 patients (47%), bowel involvement in 9 patients (20%) and pulmonary hypertension in 7 patients (15%). Interestingly 7 patients (15%) did not have any major organ involvement beside skin and vascular involvement. The survival of the 46 patients after 15, 20 and 25 years was 97%, 93% and 83%. The mean disease duration of these patients was 28.86 years (range 17 to 47).

This patient population has similar organ involvement and disease subtype characteristics as expected from an adult SSc cohort. It is likely the study cohort of patients reflect a survival bias. The antinuclear antibody pattern contrasts markedly with adult SSc.

**P225**

**Abstract withdrawn**

Pediatric Rheumatology 2008, 6(Suppl 1):P225

**P226**

The prospective juvenile systemic sclerosis inceptions cohort – http://www.juvenile-scleroderma.com

I Foeldvari¹, J Anton², J Chaitow³, E Baildam⁴, G Higgins⁵, T Lehman¹, C Len¹, S Maillard⁶, A Reif⁷, R Russo⁸ and F Zulian¹

¹Hamburger Zentrum für Kinder- und Jugendrheumatologie, Hamburg, Germany
²Pediatric Rheumatology, University Children’s Hospital, Barcelona, Spain
³Pediatric Rheumatology, University Children’s Hospital, Sydney, Australia
⁴Pediatric Rheumatology, University Children’s Hospital, Liverpool, UK
⁵Pediatric Rheumatology, University Children’s Hospital, Columbus, USA
⁶Pediatric Rheumatology, University Children’s Hospital, New York, USA
⁷Pediatric Rheumatology, University Children’s Hospital, Sao Paolo, Brazil
⁸Pediatric Rheumatology, GOS, London, UK
⁹Pediatric Rheumatology, University Children’s Hospital, Los Angeles, USA
¹⁰Pediatric Rheumatology, University Children’s Hospital, Buenos Aires, Argentina
¹¹Pediatric Rheumatology, University Children’s Hospital, Padua, Italy

Pediatric Rheumatology 2008, 6(Suppl 1):P226

**Introduction:** Juvenile systemic sclerosis (jSSc) is a rare disease. We developed a prospective assessment protocol for disease involvement manifestations and progression of jSSc.

**Objectives:** To learn about the evolution of organ involvement, the reliability of proposed assessment tools to measure change in organ involvement, and the outcome of patients in an early jSSc cohort.

**Methods:** Early jSSc patients, enrolled within 18 months after the first non-Raynaud symptom of the disease, will be followed over 36 months using a standardized assessment protocol. No specific therapy will be suggested. An Internet platform was created to make the project accessible: http://www.juvenile-scleroderma.com. Interested colleagues can request the protocol, assessment tools, and a model consent form to apply for local IRB approval. After they receive local IRB approval, they will receive an access code to the internal side of the homepage, where the detailed protocol of the project and the assessment sheets for the visits in PDF format are available. Data entry of the patients is de-identified. The data will be summarized every 6 to 12 months and presented at rheumatology meetings. The principal investigator of each center

**Page 92 of 110**

(page number not for citation purposes)
will be listed as co-author according to the number of enrolled patients. Every 12 months the assessment tools will be evaluated, with the help of a biostatistician, according the OMERACT criteria. **Conclusion:** This project will represent the first prospectively followed cohort of JSSc patients, and will enable us to learn about evolution disease and about the reliability of the proposed assessment tools.

**P227**

**Extracranial linear localized scleroderma associated with longstanding epileptic encephalopathy unresponsive to methotrexate and prednisone**

D Rigante¹, D Battaglia², I Contaldo², I La Torraca¹, L Avallone¹, A Compagnone¹, G Bersani¹ and A Stabile¹  
¹Dept. of Pediatric Sciences, UCSC, Rome, Italy  
²Div. of Infantile Neuropsychiatry, UCSC, Rome, Italy

*Pediatric Rheumatology* 2008, 6(Suppl 1):P227

We report a boy, who achieved developmental milestones without delay, presenting complex partial seizures (left-deviation of the head, staring gaze, oral automatism and tonic-clonic generalization) at 7 years: his blood/cerebrospinal fluid tests were all within normal limits, enclosed those for inborn errors of metabolism. Progressive signs of psycho-motor regression were simultaneously observed by caregivers in combination with a band of linear ivory-coloured indurated lesion on the dorsal region of the right foot, which was diagnosed as linear localized scleroderma (LS). Immunological tests performed at 8 years revealed only low-titre positivity of anti-nuclear antibodies. Various brain CT and MRI scans resulted negative. In the following years tonic-clonic seizures were observed with daily recurrence in spite of different antiepileptic drugs. At 16 years we evaluated this patient for the first time: asymmetrical tonic fits had multiple daily frequency and therapy consisted of clobazam/methsuximide; EEG revealed disrupted electrical cerebral activity; brain MRI was normal; the skin lesion was extended to the whole right inferior limb. Methotrexate (MTX) and prednisone (0.5 mg/kg/day). Semeiological features of seizures remained and no control upon their frequency could be reached, whilst LS remained stable.

The exact nature of multi-resistant epilepsy associated with extracranial linear LS remains a matter of debate and the immunologic process leading to the pathologic collagen deposition might be dissociated from the specific neurological disturbance.

**P228**

**Borrelia burgdorferi antibodies in childhood scleroderma**

E Musiej-Nowakowska¹, L Rutkowska-Sak¹, M Wierzbowska¹, M Kwiatkowska¹ and J Zabek²  
¹Pediatric Clinic, Institute of Rheumatology, Warsaw, Poland  
²Department of Microbiology and Serology, Institute of Rheumatology, Warsaw, Poland

*Pediatric Rheumatology* 2008, 6(Suppl 1):P228

**Background and aim:** A possible aetiological connection between skin sclerosis and infection with Borrelia burgdorferi (Bb) has been discussed. Studies investigating the link between Bb and morphea have produced conflicting results. In several series, all patients with morphea tested have been seronegative. Other studies have found specific antibodies to Bb in between 6% and 54% of patients with morphea. To establish the frequency of ANA and specific antibodies to Bb in children with scleroderma.

**Materials:** 44 children with scleroderma (4-SS, 40-LS) were tested. Clinical forms of LS: linear-10, morphea-8, morphea generalisata-4, profunda-6, pansclerotic-2, en coup de sabre (CSLS)-1, linear + morphea-7, CSLS + morphea-2. The patients sera were tested for ANA and Borrelia-specific IgG and IgM (recom – Blot BorreliaigG and IgM Microgen).

**Results:** ANA were detected in 3 of 4 patients with SS (75.0%) and 16 of 40 (40.0%) with LS. In 9 of 40 patients with LS (22.5%) were found antibodies to Bb with any correlation to the type of LS or its activity as well as to the presence of ANA. 5 children (12.5%) had positive IgM, another 2 (5.0%) – positive IgG and 2 children (5.0%) – both IgM and IgG. None of the patients had documented clinical evidence of previous infection with B. burgdorferi. All 4 patients with SS tested for the antibodies to Bb have been negative.

**Conclusion:** The role of the antibodies to Borrelia burgdorferi in the localized scleroderma is still unclear. Our results do not suggest a possible aetiological connection between Borrelia burgdorferi infection and systemic scleroderma.

**P229**

**Mycophenolate Mofetil in severe or methotrexate refractory localized scleroderma**

G Martini¹, F Falcini², H Girschick³, D Goldsmidt⁴ and F Zulian⁵  
¹Department of Paediatrics, Padova, Italy  
²Internal Medicine, Transition Unit, Florence, Italy  
³Immunology and Rheumatology, Univ. Kinderklinik, Wuerzburg, Germany  
⁴St. Christopher’s Hospital for Children, Drexel, USA  
⁵Department of Paediatrics, Padova, Italy

*Pediatric Rheumatology* 2008, 6(Suppl 1):P229

Juvenile Localized Scleroderma (JLS), is characterised by presence of areas of skin thickening, which is relatively benign, but if deeper tissues such as muscle and bone are involved severe deformities may develop. Mycophenolate Mofetil (MMF) is increasingly utilised both for treatment of systemic sclerosis and immune-mediated skin diseases such as psoriasis, graft-versus-host and lichen planus. Our aim was to evaluate efficacy and safety of MMF in the treatment of JLS. Seven patients entered the study (3 M, 4 F). The JLS clinical subtypes were Pansclerotic morphea (2 pts), Generalized Morphea (1), En coup de Sabre (ECDS) (1), Mixed (ECDS/Linear) (3). The age at onset of the disease was 7.5 yrs (range 3–16.9) and the disease duration at diagnosis was 1.9 years (range 3 months–4 years). Previous treatments before starting MMF were oral steroids in 6 pts, IV steroids in 5, MTX in 5, while the patient with ECDS received no treatment. MMF was started because of steroids side effects in one patient and MTX resistance in 5. In ECDS MMF was chosen because of concomitant cerebral vasculitis. All treated patients presented clinical improvement which allowed withdrawal of steroids. Over the follow-up of 27 months (range 6–36 months) only mild abdominal discomfort in one patient.
was reported. In conclusion MMF seems to be effective in severe or MTX-refractory JLS and is generally well tolerated. Further controlled studies are necessary to confirm these data.

P230
Efficacy and safety of methotrexate treatment of juvenile localized scleroderma
MK Osminina, NA Geppe, GV Tougarinova, GM Rabieva and YO Kostina
Moscow medical Sechenov Academy, Moscow, Russian Federation
Pediatric Rheumatology 2008, 6(Suppl 1):P230
Our goal is to study the efficacy and safety of MTX in juvenile localized scleroderma (JLS).

Retrospective study of 59 children with JLS from 3 to 17 y (M = 10.3) treated with MTX was performed. Group 1 (n = 18) – received prednisone 0.5 mg/kg for 6 weeks, tapered to 0.1 mg/kg for 12 months + MTX 10 mg/body weekly for 13.7 mo. Group 2 (n = 41) – MTX the same doses and duration. The efficacy was measured in 6 & 12 months using skin score, activity and sclerosis indexes (IA, IS) (1–3 points) of skin damage, the safety by clinical & laboratory methods. Group 1 patients had spread linear skin involvement (hemitype), with skin score significantly higher (p < 0.01) than in group 2, where children had mostly local linear skin damage. Previously 9 pts from Group 1, 31 pts from Group 2 received penicillamine (PA) with no effect.

MTX therapy was effective in 73% of children unsuccessfully treated with PA & in 98% of patients received MTX as the first medication. Effect of therapy was significantly better in pts with disease duration less than 6 mo. In Group 1 significant improvement (p < 0.01) in skin score, IA, IS had been already achieved in 6 months of treatment, in Group 2 only in 12 mo. MTX was effective in children with linear skin, periarticular contractures. Nausea was the main adverse effect, in 17% of pts, with no correlation with genetic polymorphisms of methylenetetrahydrofolate reductase.

MTX is effective and safe in linear JLS.

Reference

P231
Long term follow-up of children with juvenile systemic sclerosis, mixed connective tissue disease and pulmonary disease
C Dracou1, G Syridou1, S Drakonaki1 and G Grigoriadou2
1Paediatric Rheumatology Outpatients’ Clinic, 2nd Dept. of Paediatrics, NHS
2Dept. of Paediatric Cardiology, “P. & A. Kyriakou” Children’s Hospital, Athens, Greece
Pediatric Rheumatology 2008, 6(Suppl 1):P231
Background: Pulmonary disease may be developed in children with juvenile systemic sclerosis (J-SSc) [1] and mixed connective tissue disease. Limited information is available concerning juvenile mixed connective tissue disease (J-MCTD).

Materials and methods: To evaluate the prognostic value of pulmonary disease in children with J-SSc and J-MCTD we reviewed the children’s records with a diagnosis of J-SSc and J-MCTD since 1989 and a minimum follow-up of 5 years.

Results: Six (5 female, 1 male) children with J-SSc or J-MCTD were studied. The age at the disease onset ranged from 2–13 yrs. The follow-up duration was 6–18 yrs (mean 10 yrs). Four children had J-SSc and two had J-MCTD. Three children developed interstitial lung involvement proven by HRCT or chest x-ray. Pulmonary arterial hypertension (PAH) occurred in three children, two with J-SSc and one with J-MCTD. One of the two children with J-SSc, x-ray findings of lung involvement and PAH died. In this child the involvement of the respiratory system occurred within the first year of the disease. In the two other children with J-SSc or J-MCTD, interstitial lung involvement and PAH subsided after a course of aggressive therapy with corticosteroid, cyclophosphamide and bosentan. Bone marrow transplantation was performed in one child with J-SSc and PAH.

Conclusion: Severe pulmonary disease may implicate the clinical course of J-SSc and J-MCTD. Pulmonary arterial hypertension indicates very poor prognosis. HRCT may identify those children with interstitial lung involvement who are candidates for aggressive therapy.

Reference

P232
The addition of granulocyte macrophage colony stimulating factor (GM-CSF) to juvenile systemic lupus erythematosus serum can reduce abnormal neutrophil apoptosis
AJ Midgley1, Z McLaren1, RJ Moores2, SW Edwards3 and MW Beresford1
1Institute of Child Health, University of Liverpool, Liverpool, UK
2Infection and Immunity, University of Liverpool, Liverpool, UK
3School of Biological Sciences, Liverpool, UK
Pediatric Rheumatology 2008, 6(Suppl 1):P232
Background: Juvenile-onset Systemic Lupus Erythematosus (JLE) differs from adult-onset SLE yet few studies explore its immunopathology. We have previously demonstrated that serum from JLE patients induces increased apoptosis in neutrophils from both healthy controls and JLE patients, when compared to control serum. Quantification of cytokines that inhibit apoptosis were found to be decreased in JLE serum compared to control serum. Here we aim to investigate whether the addition of these cytokines could abrogate the increased neutrophil apoptosis associated with incubation in JLE serum.

Materials and methods: Children (diagnosed < 17 years) with JLE and non-inflammatory conditions (control) were included in this study. Following written informed consent, heparinised whole blood and serum was collected. Neutrophils were isolated from healthy controls and incubated alone or with 10% JLE or control serum. Neutrophils were also incubated with JLE serum with the addition of either 20 pg/ml GM-CSF, 40 pg/ml TNF-alpha or 20 pg/ml IL-6. Apoptosis (mean ± SEM) was measured by flow cytometry after two hours.

Results: Neutrophils incubated with JLE serum plus TNF-alpha (15.3 ± 3.26%) or JLE serum plus IL-6 (14.5 ± 3.9%) had similar
apoptosis to those neutrophils incubated with JSLE serum alone (14.2 ± 3.21%). However those cells incubated with JSLE serum plus GM-CSF (7.5 ± 1.36%) had decreased apoptosis compared to JSLE serum alone.

Conclusion: Apoptosis of neutrophils induced by incubation with JSLE serum can be reduced with the addition of GM-CSF.

P233
Pediatric lupus nephritis: impact of ethnicity on histological subtype and initial presentation
R Jurencak, PN Tyrrell, SM Benseler, LT Hiraki and ED Silverman
The Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada
Pediatric Rheumatology 2008, 6(Suppl 1):P233

Objective: 1) To determine the association between ethnicity and lupus nephritis (LN) subtype, 2) To compare clinical and laboratory characteristics of LN subtypes.

Methods: A single-center cohort study of all consecutive patients <18 years of age with biopsy proven LN diagnosed in 1980–2006 was performed. Self-designated ethnicity, clinical and laboratory features including renal function, urinalysis and overall activity (SLEDAI) were recorded. Associations of ethnicities, LN subtypes, clinical and laboratory variables were tested using chi-squared analysis, t-test and ANOVA; Bonferroni and Tukey correction were used for all multiple comparisons.

Results: 150 LN patients were included in the study; 81% females, mean age 12.9 years (SD = 3.1). 44 children were Caucasian, 45 Asian, 22 South Asian, 30 Black and 9 of other ethnic origin. Diffuse proliferative LN (DPGN) was seen in 38%, focal proliferative LN (FPGN) in 31%, membranous LN in 17% and mesangial LN in 14%. All ethnic groups had similar proportions of all LN subtypes. Disease activity (SLEDAI) at the time of LN diagnosis was highest in patients with DPGN. Nephrotic range proteinuria was significantly more common in DPGN than in FPGN or mesangial LN, but not membranous LN. Patients with DPGN presented significantly more frequently in renal failure as compared to mesangial or membranous LN, but not FPGN.

Conclusion: Ethnicity does not influence the LN subtype. Renal failure is present in 1/3 of patients with DPGN and FPGN at diagnosis. Of all LN subtypes, DPGN at presentation was associated with the highest disease activity, nephrotic range proteinuria and renal failure.

P234
Mycophenolate Mofetil (MMF) for the treatment of juvenile onset systemic lupus erythematosus
FF Falconi1, CS Capannini1, MG Martini1, LTF La Torre3, VA Vitale3, NF Nacci1, MCM Matucci Cerinic1, CR Cimaz4 and ZF Zulian2
1Department of Biomedicine, Division of Rheumatology, Transition Unit, University of Florence, Florence, Italy
2Department of Paediatrics, Rheumatology Unit, University of Padua, Padua, Italy
3Department of Paediatrics, Rheumatology Unit, University of Messina, Messina, Italy
4A. Meyer Children’s Hospital, Rheumatology Unit, University of Florence, Florence, Italy
Pediatric Rheumatology 2008, 6(Suppl 1):P234

Aim: To evaluate the efficacy and safety of MMF in juvenile SLE in a multicenter study.

Methods: Medical charts of 26 pts, 25 F, 1 M, mean age at SLE diagnosis 12.7 yrs (range 5–18), mean age at MMF starting 15.9 yrs (range 7.5–26.8), followed in Florence, Padua, and Messina, Italy, treated with MMF from 2004 to 2007, were retrospectively analyzed. Clinical and laboratory evaluation included: blood count, ESR, CRP, ANA, anti-dsDNA, LFT, coagulation, C4, renal function, Coombs’ test, aCL, anti(2)GPI and LAC at baseline and every 6 months. Disease activity was monitored by the SLEDAI score. Treatment duration was 24 ± 14.8 months (range 2–52). MMF (1.5–2 g/day) was started due to steroid toxicity (n = 9 pts), CyA toxicity (n = 5), disease activity (n = 8) or nephropathy progression despite previous immunosuppression (n = 4). 9/26 pts, before MMF had renal disease (7 WHO Class IIb, 1 Class III, 1 Class IV). In 5/9 MMF was the first treatment, while 4/9 had received immunosuppressants.

Results: MMF was effective in reducing disease activity, steroid sparing in 14/26 (54%), stabilizing the disease in 8 (31%) and ineffective in 4 (15%). In 9/13 (69%) without renal involvement a good response was registered. Among pts with renal involvement, MMF was effective in 5/13 (38%), partially effective in 4 (31%) and ineffective in 4 (31%). 2 pts stopped MMF for diarrhoea and abdominal pain.

Conclusion: MMF seems to be effective and safe in juvenile SLE, especially in patients without renal involvement. SLEDAI scores were significantly reduced at 6 and 12 months; p < 0.05.
mainly consisted in NSAIDs (7/10), steroids (8/10), and methotrexate (6/10) and more rarely hydroxychloroquine (2/10), colchicine (1/10), dapsone (3/10), salazopyrine (2/10), azathioprine (1/10).

Pt 1 died of aortic insufficiency and others presented recurrent flares with chronic destroying chondritis.

Conclusion: Pediatric RP shares the main clinical features of its adult counterpart, even if secondary forms seem to be less frequent. Laboratory findings are nonspecific, and biopsies may be unnecessary. Evolution is marked by chronic destroying chondritis and could lead to fatal lesions despite immunosuppressive treatment.

Table 1 (abstract P236) Comparison of percentage frequency of the main clinical and laboratory features of MAS in patient groups. (NA: not available)

<table>
<thead>
<tr>
<th>Feature</th>
<th>MAS BM+</th>
<th>MAS BM−</th>
<th>SLE-GI</th>
<th>SLE-MS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>95.0</td>
<td>83.3</td>
<td>21.2</td>
<td>64.2</td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>47.4</td>
<td>55.6</td>
<td>12.1</td>
<td>10.4</td>
</tr>
<tr>
<td>CNS dysfunction</td>
<td>37.5</td>
<td>28.6</td>
<td>3.0</td>
<td>8.5</td>
</tr>
<tr>
<td>Haemorrhages</td>
<td>40.0</td>
<td>33.3</td>
<td>9.1</td>
<td>NA</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>90.0</td>
<td>44.4</td>
<td>63.6</td>
<td>NA</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>90.0</td>
<td>61.1</td>
<td>18.2</td>
<td>NA</td>
</tr>
<tr>
<td>Hypertransaminasemia</td>
<td>80.0</td>
<td>93.8</td>
<td>30.3</td>
<td>NA</td>
</tr>
<tr>
<td>Hypertriglyceridemia</td>
<td>75.0</td>
<td>88.2</td>
<td>20.0</td>
<td>NA</td>
</tr>
<tr>
<td>Hypofibrinogenemia</td>
<td>37.5</td>
<td>42.9</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Hyperferiitinemia</td>
<td>92.9</td>
<td>94.4</td>
<td>0</td>
<td>NA</td>
</tr>
</tbody>
</table>

P237 Effective use of rituximab in combination with low dose cyclophosphamide in childhood onset systemic lupus erythematosus (SLE) with relapsing class IV nephritis

PM Miettunen, LA Hamiwka, AW Wade, JP Midgley and S Grisaru
University of Calgary, Calgary, Alberta, Canada

Objectives: We evaluated effectiveness of rituximab, an anti-CD20 monoclonal antibody, in combination with low dose cyclophosphamide and intravenous (IV) methylprednisolone in three pediatric SLE patients with relapsing class IV nephritis.

Methods: Patients 1 and 2: Identical twin females with SLE, complicated by biopsy proven class IV nephritis at age 6-years and treated with NIH cyclophosphamide protocol (NIHCP), had biopsy documented Class IV renal flare at age 10-years; unresponsive to mycophenolate mofetil (MMF) and corticosteroids.

Patient 3: A 12-year old female with SLE, complicated by biopsy documented Class IV nephritis and treated with NIHCP, had 2 further renal flares, which responded to a cumulative dose of 36 grams of cyclophosphamide. At age 16, she had another biopsy documented Class IV renal flare, despite maintenance with MMF.

All patients received pulse therapy with: IV cyclophosphamide 0.5 g/m² with IV methylprednisolone (IVMP) 250 mg on days 1 and 23; IV rituximab 375 mg/m² on days 2, 9, 16 and 23.
Results: All 3 patients had a dramatic improvement in urine protein-creatinine ratios, and normalization of blood pressure. Despite low-dose daily corticosteroids, all patients had an increase in generalized SLE activity by 4 weeks following rituximab therapy, which responded to re-introduction of MMF. No side effects apart from expected decrease in B-cell counts were noted.

Conclusion: Rituximab in combination with low dose cyclophosphamide and IVMP was effective in controlling recurrent class IV nephritis in 3 pediatric SLE patients. Re-introduction of mycophenolate mofetil was required within 4 weeks following rituximab therapy to maintain disease remission.

P238 Atypical onset as predictor of poor outcome in Pediatric Systemic Lupus Erythematosus (pSLE)

A Taddio¹, E Rossetto¹, L Leopre¹, AC Brescia², C Bracaglia¹, S Caminiti³, E Cortis³, D Rigante⁴, A Stabile³, M Monticelli¹, L Ronfani¹ and CD Rosé²

¹Institute for Maternal and Child Health – IRCCS Burlo Garofolo, Trieste, Italy
²Division of Rheumatology A.I. duPont Hospital for Children, Department of Pediatrics, Thomas Jefferson University, Wilmington/DE, USA
³Division of Rheumatology, Department of Pediatric Medicine, IRCCS Ospedale Pediatrico Bambino Gesù, Rome, Italy
⁴Department of Pediatric Sciences, Università Cattolica Sacro Cuore, Rome, Italy

Pediatric Rheumatology 2008, 6(Suppl 1):P238

Purpose: Pediatric Systemic Lupus Erythematosus (pSLE) is a multisystem, inflammatory, autoimmune disease. This study is based on the observation that there are limited data on the prognostic factors of children affected by SLE and weak data correlating the course of the disease with its onset. The primary aim of this study is to assess if atypical onset influence the severity of organ damage in pSLE.

Methods: This is a multicenter IRB-approved chart review. We enrolled all patients affected by pSLE. Medical records were reviewed focusing on clinical features at onset, intended as date of diagnosis and the following 15 days. As atypical onset we meant organ involvement present at onset of pediatric SLE described in literature http://www.pubmed.com/index, but not included in ACR criteria. The primary outcome was established to be the presence of at least 1 score of System Lupus International Collaborating Clinics/American College of Rheumatology Damage Index for Systemic Lupus Erythematosus (SLICC/ACR). Data on 100 patients were analyzed with multivariate analysis.

Results: Our population consisted in: 68 Caucasians, 24 Afro-Americans, 5 Latin-Americans and 2 Asians. There were 79 females and 21 males. They were followed up for an average of 5.3 years. 24% of patients presented atypical clinical features at onset. At multivariate analysis a significant association with outcome variables was showed for the presence at onset of atypical manifestations (p = 0.004) and renal involvement (p = 0.027).

Conclusion: Our data suggest that the presence of renal involvement and atypical manifestations at onset influence the prognosis of patients affected from pSLE.

P239 Clinical characteristics of cutaneous vasculitis secondary to systemic lupus erythematosus

Ye Zhizho, Li Bo, Li Jianso, Guo Fenlia, Wang Xun and Yin Zhihu

Xiangmihu Branch of Shenzhen Fourth People’s Hospital, Shenzhen City, China

Pediatric Rheumatology 2008, 6(Suppl 1):P239

Background: Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by a wide spectrum of clinical and immunological manifestations. Cutaneous vasculitis (CV) is very common in SLE. The present study was to elucidate the clinical features of CV secondary to SLE.

Materials and methods: All of the included 278 patients (256 female, 22 male) fulfilled 4 or more of the revised 1997 ACR Criteria for the classification of SLE. Clinical and laboratory data were obtained when patients were included in our study.

Results: CV secondary to SLE was found in 103 (37%) among the 278 patients, 84 (82%) was female and 19 (18%) was male. The commonest presentation was acroerythema. The site most commonly affected was fingertips and palms. The other sites often affected were the lower limbs, upper limbs, trunk and face in order of frequency. The duration of the skin lesions ranged from less than a week to several months. Patients with secondary CV presented a lower female/male ratio and a higher mean SLEDAI score and also had a higher frequency of Raynaud phenomenon and blood system involvement and hypergammaglobulinemia and anticardiolipin antibodies (aCL) (p < 0.05).

Conclusion: The presentation of CV secondary to SLE was heterogeneous and the secondary CV in SLE was associated with a lower female/male ratio, a higher mean SLEDAI score, a higher frequency of Raynaud phenomenon and blood system involvement and hypergammaglobulinemia and aCL.

P240 Frequency and significance of anticardiolipin antibodies in Chinese patients with primary Sjögren’s syndrome

Li Bo, Ye Zhizho, Hu Qixia, Guo Fenlia and Zhuang Junhan

Xiangmihu Branch of Shenzhen Fourth People’s Hospital, Shenzhen, Guangdong, PR China

Pediatric Rheumatology 2008, 6(Suppl 1):P240

Background: Although aCL antibodies are often found in serum samples from patients with primary Sjögren’s syndrome (pSS), their clinical significance remains unclear. The aims of this study were to investigate the prevalence of aCL antibodies and their correlation with the main typical clinical and serological manifestations in Chinese patients with pSS.

Materials and methods: Patients were consecutively recruited among the patients with pSS seen in our rheumatic department between March 2001 and October 2007. All the included patients met the revised European Community Criteria for pSS. All patients fulfilling the clinical criteria for rheumatoid arthritis (RA), SLE, polymyositis, systemic sclerosis or other diffuse connective tissue diseases were excluded from pSS
group. Any patients with sarcoidosis, graft-versus-host disease, acquired immune deficiency syndrome or preexisting lymphoma were also excluded.

Results: ACL antibodies were found in 26 (28%) patients; IgG-aCL in 14 patients, IgM-aCL in 9 patients and IgA-aCL in 3 patients. Cutaneous vasculitis and concurrent autoimmune disease (thyroidal disease, primary biliary cirrhosis) were more frequent in the aCL-positive group than in the aCL-negative group (p < 0.05). Patients with positive aCL presented a higher prevalence of positive ANA and hypergammaglobulinemia (p < 0.05).

Conclusion: The prevalence of aCL antibodies in our patients with pSS was 28% and are mainly IgG-aCL and IgM-aCL. ACL antibodies may play a pathogenic role in patients with pSS. Detection of aCL antibodies in patients with pSS may indicate doctor to find if concurrent autoimmune diseases (thyroidal disease, primary biliary cirrhosis) exist.

P241
Macroscopic activation syndrome: an under-recognised complication in juvenile systemic lupus erythematosus
C Sundaramoorthy, A Chieng and P Riley
Booth Hall Children’s Hospital, Manchester, UK

Pediatric Rheumatology 2008, 6(Suppl 1):P241

Macroscopic activation syndrome (MAS) is a life-threatening complication in juvenile systemic lupus erythematosus (JSLE). We report three cases of MAS in Juvenile SLE which occurred over the last 6 months. Interestingly, in all the 3 cases, MAS occurred acutely at the time of first presentation of lupus. All of them had fever at presentation. Two of them had lymphadenopathy and splenomegaly and one had hepatomegaly. All three of them had renal, one had heart and lung and another had central nervous system involvement. Table 1 summarises the laboratory findings.

Interestingly, the ferritin levels were <2000 in two of the three cases. In all the three cases, JSLE/MAS was suspected early and serology and bone marrow were done within 48 hours of referral to the rheumatologist. All three of them resolved with intravenous Methylprednisolone. Diagnosis of MAS can be difficult because some of its clinical features overlap those of lupus itself. High index of suspicion will help in early diagnosis and prompt initiation of treatment which are important for a better outcome.

<table>
<thead>
<tr>
<th>Table 1 (abstract P241) Laboratory findings</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Findings</strong></td>
</tr>
<tr>
<td>Pancytopenica</td>
</tr>
<tr>
<td>Alanine aminotransferase</td>
</tr>
<tr>
<td>Lactic dehydrogenase</td>
</tr>
<tr>
<td>Triglycerides</td>
</tr>
<tr>
<td>Ferritin</td>
</tr>
<tr>
<td>Bone marrow haemophagocytosis</td>
</tr>
<tr>
<td>Antinuclear antibodies</td>
</tr>
<tr>
<td>Anti-DNA antibodies</td>
</tr>
<tr>
<td>C3</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate</td>
</tr>
<tr>
<td>C-reactive protein</td>
</tr>
</tbody>
</table>

P242
Musculoskeletal sonography in juvenile systemic lupus erythematosus
E Demirikaya1, L Ozçakar1, S Haghari1, N Aktay Ayaz1, T Türker2, F Özaltın1, A Bakkaloglu1 and S Ozen1
1Hacettepe University, School of Medicine, Ankara, Turkey
2Gulhane Military Medical Academy, Ankara, Turkey

Pediatric Rheumatology 2008, 6(Suppl 1):P242

Objective: Musculoskeletal involvement of juvenile systemic lupus erythematosus (JSLE) is basically an arthralgia and/or arthritis attacking typically the small joints of the hands, wrists and knees. We aimed to demonstrate the role of sonography in depicting periarticular changes in JSLE and to find out whether certain tendons of JSLE patients were different from those of healthy controls.

Methods: Thirty JSLE patients (27 female, 3 male) were recruited for this study. For comparison of the sonographic data, 32 healthy volunteers were included as a control group. Sonographic evaluations were performed by a physiatrist experienced in musculoskeletal sonography.

Results: Knee effusion was observed more frequently in the JSLE group in comparison with the control subjects (p = 0.00). When tendon thickness measurements were compared between the groups, flexor and extensor tendons of the third digit (at MCP joint level) of JSLE patients were found to be thinner (p values being 0.04 and 0.03, respectively). Tendon thickness values did not correlate with disease duration and SLE disease activity index scores (p values > 0.05).

Conclusion: The main findings of our study were relevant with i) increased involvement of the following sites in JSLE: knee, ankle, hand extensor tendons, wrist, elbow, hand flexor tendons (in decreasing order of frequencies) and ii) decreased extensor/flexor tendon thicknesses in the hands of JSLE patients. Physicians should be aware of the potentially disabling scenario of tendon pathologies. Defining the extent of joint and tendon pathologies in Pediatric SLE may guide us in the management of the disease.

P243
Retrospective study of juvenile systemic lupus erythematosus (JSLE) over the last 20 years: single center experience
L Tambic Bukovac, M Jelusic, D Batinic, M Vidovic, D Milosevic, K Vrljicak and Lj Nizic
Department of Paediatrics, University Hospital Centre, Zagreb University School of Medicine, Zagreb, Croatia

Pediatric Rheumatology 2008, 6(Suppl 1):P243

Introduction: Children represent approximately 15–20% of all systemic lupus erythematosus (SLE) patients, and they usually have a more severe disease at onset, higher rates of organ involvement, and a more aggressive clinical course than adults.


Results: There were 62 children, 52 girls and 10 boys, with the mean age at disease onset (± SD) 12.9 ± 2.4 years. Fifty-eight patients were followed for a mean period of 6.9 ± 5.3 yrs. The commonest presenting clinical features were constitutional (fever, fatigue) (68%), arthralgias (56%), renal involvement
(53%) and malar rash (29%). Renal biopsy revealed class IV lupus nephritis (LN) in 15 (45.5%), class III LN in 9 (27.3%), class II LN in 5 (15.1%) and class V LN in 4 (12.1%) cases. The patients presented significantly altered laboratory parameters including deficiency of complement C3 (93%) and C4 (95%), high ESR (95%), cytopenia (73%) and positive anti-dsDNA (100%). Only two patients had severe opportunistic infections: CNS nocardiosis and multifocal staphylococcal osteomyelitis, both with good outcome. Due to clinical presentation and laboratory data most patients were treated with oral corticosteroids, followed by cyclophosphamide, pulse steroid, hydroxychloroquine and azathioprine. During the study period two patients died, one because catastrophic antiphospholipid syndrome, other because of terminal renal failure.

Conclusion: There is no significant difference in clinical, immunopathological features and therapy regimens in our patients compared to those in most paediatric SLE studies.

P244
Efficacy of plasmapheresis in a case of severe pulmonary hemorrhage in pediatric Systemic Lupus Erythematosus
F Verzegnassi, A Saccari, A De Cunto, P Salierno, F Marchetti and L Lepore
IRCSS, Trieste, Italy

Pediatric Rheumatology 2008, 6(Suppl 1):P244

We report the case of a 13 year old girl with SLE initially treated with hydroxychloroquine for a mainly mucocutaneous involvement. Four months from onset, she presented renal involvement and an acute hemoptysis and she was admitted to our pediatric department. She also presented fever and abnormal laboratory findings (high serum creatinine level, severe proteinuria, Hb of 6.4 g/dl, high titre specific autoantibodies, low C3 and C4 levels). Kidney biopsy underlined stage 4a lupic nephropathy; chest X-ray and CT scan showed diffused alveolar involvement, as for pulmonary hemorrhage. Cerebral SPECT showed abnormalities consistent with neurolupus. The patient underwent blood transfusion, and was treated with high doses of metilprednisolone plus cyclophosphamide. Due to refractory anemia and worsening of respiratory symptoms (dispnoea with low peripheral oxygen saturation), she was additionally treated with 3 courses of Rituximab, and two further blood transfusions, with clinical stabilization but no major amelioration. After one week, severe clinical worsening with important dispnoea, cutaneous pallor, poor general condition, low peripheral oxygen saturation (78%) was present: Hb level was 4 g/dl, chest X-ray showed worsened alveolar involvement. The patient was treated with 3 courses of plasmapheresis and two blood transfusions, with immediate response of the respiratory symptoms, recovery from anemia and marked improvement of the chest X-ray.

Pulmonary hemorrhage is a severe complication in SLE associated with high mortality. It is described in 5–6% of patients, presenting with anemia, hemoptysis, respiratory symptoms and characteristic changes in chest imaging. We suggest plasmapheresis as an effective treatment to be considered promptly when suspecting this life-threatening complication.

P245
Neuromyelitis optica associated with systemic autoimmune diseases in children
RA Russo, S Tenembaum, H Arroyo and MM Katsicas
Hospital de Pediatria Garrahan, Buenos Aires, Argentina

Pediatric Rheumatology 2008, 6(Suppl 1):P245

Case reports: Neuromyelitis optica (NMO, Devic’s disease) is a severe autoimmune disorder predominantly involving optic nerves and spinal cord [1]. Usually isolated, it has been associated with systemic autoimmune diseases in adult patients [2]. We report 2 children with a systemic autoimmune disease who developed NMO. Patients were female; NMO symptoms started at age 8 and 12 years. Patient 1 had a diagnosis of Systemic Lupus Erythematosus (SLE) (fever, cytopenias, mesangial glomerulonephritis, positive ANA, anti-DNA, anti- Sm). She developed vomiting, tremor, hyperreflexia, paresthesia, neurogenic bladder and progressive vision loss 2 years after SLE onset. Neuroradiological investigations disclosed longitudinally extensive transverse myelitis and bilateral optic nerve involvement. Patient 2 had recurrent parotitis for 1 year before she developed vision loss, papillitis, dysphonia and paresthesia. She exhibited positive ANA, anti-Ro and anti-La, and objective eye dryness. MRI evidenced lesions in brainstem and spinal cord, and evoked potentials revealed optic nerve involvement. A diagnosis of Sjögren’s Syndrome (SS) associated with NMO was made. NMO-IgG was detected in both patients’ sera. Intravenous and p.o. high dose steroids, a 6-month course of monthly I.V. cyclophosphamide (up to 1 g/m²/dose), followed by azathioprine (2–3 mg/Kg/day) as maintenance therapy, were used in both (plasmapheresis in one). Visual, motor and sensitive symptoms dramatically improved. Mild relapses occurred in both children; they were successfully treated with steroids. Patients are currently well, with improved vision and residual lesions in MRI.

Conclusion: NMO can occur in the setting SLE or SS in children. Intensive immunosuppressive therapy may induce remission and prevent visual loss.

References

P246
Metabolic disease with autoimmune phenomena: 2 cases of SLE-like disease in young children diagnosed with lisyuric protein intolerance
C Sengler¹, J Gellermann², J Hennermann² and R Keitzer¹
¹Charité – Universitätsmedizin Berlin, Department of Pediatric Pneumology and Immunology, Berlin, Germany
²Charité – Universitätsmedizin Berlin, Department of Pediatric Nephrology, Berlin, Germany

Pediatric Rheumatology 2008, 6(Suppl 1):P246

The second son of consanguineous parents was repeatedly evaluated for failure to thrive, intermittent vomiting, diarrhea,
lesions in the right ear showed areas of necrosis and crusting involving his face, right external ear, scalp, nose and soles. The several non tender erythematous, polymorphous skin lesions presented with recurrence of skin lesions. Examination revealed his left ear. This was initially diagnosed as cellulitis and treated presented to the ENT department with a skin lesions involving Cutaneous lupus is rare in childhood. A 5-yr old Asian boy 6 years he developed a hemolytic u remic syndrome-like disease. hemophagocytosis, but no signs of malignancy. At the age of 6 months between JSLE/splenectomy 1 38 10 Specific diets had no effect. Bone marrow aspiration showed failure to thrive, muscle hypotonia, vomiting, protein avoidance and hepatomegaly. Immunologic abnormalities with positive autoantibodies, vasculitis, arthritis and glomerulonephritis have also been described. The underlying cause is a defective amino acid transport mechanism, leading to a lack of cationic amino acids in the serum and consecutive perturbation of the urea cycle. In the second case this diagnosis could even be confirmed by sequencing the SLC7A7 gene, revealing a new homozygous mutation (Cys427Arg).

P247
A 5 year old boy with Cutaneous Lupus
A Moorthy, A Sridhar, A Kinder and P Houtman
Children’s Hospital, University Hospitals of Leicester NHS trust, Leicester, UK

Pediatric Rheumatology 2008, 6(Suppl 1):P247

Cutaneous lupus is rare in childhood. A 5-yr old Asian boy presented to the ENT department with a skin lesions involving his left ear. This was initially diagnosed as cellulitis and treated with intravenous antibiotics with no significant improvement. He presented with recurrence of skin lesions. Examination revealed several non tender erythematous, polymorphous skin lesions involving his face, right external ear, scalp, nose and soles. The lesions in the right ear showed areas of necrosis and crusting without discharge. Multiple annular erythematous palpable lesions were present over postero lateral aspects of both soles. The trunk, limbs, genitalia and oral mucosa were spared. Systemic examination was unremarkable. He was growing along his previous weight and height centiles.

His immunological profile showed grossly elevated IgG levels with normal complement level. The autoimmune screen showed positive for ANA, anti-Ro and anti-La and negative ANCA. Histopathology of the skin lesion revealed marked perivascular lymphocytic infiltrates, red blood cell extravasations and arteriole wall inflammation in the dermis without fibrinoid necrosis. His immunological profile and histopathology confirmed the diagnosis of cutaneous lupus.

The skin lesions were treated with topical and oral steroids and subsequently with Hydroxychloroquine. The skin lesions rapidly resolved with the introduction of Hydroxychloroquine therapy. He has been followed up regularly in our Paediatric Rheumatology department and he remains clinically stable with no systemic features of Lupus.

Literature review reveals that Cutaneous Lupus is an uncommon clinical condition in this age group. Sub-acute presentation is uncommon and the response to Hydroxy Chloroquine is well documented. This boy never had any systemic symptoms. There was no history of Lupus in his mother. The initial presentation and the delay in diagnosis highlights the need for clinicians managing paediatric patients to be aware of this uncommon clinical condition.

References

P248
Splenectomy for refractory thrombocytopenia in juvenile systemic lupus erythematosus
LMA Campos, Fj Fiorot and CAA Silva
Instituto da Criança – Clinical Hospital, University of São Paulo, São Paulo/SP, Brazil

Pediatric Rheumatology 2008, 6(Suppl 1):P248

Background: The prevalence of autoimmune thrombocytopenia in juvenile systemic lupus erythematosus (JSLE) ranges

<table>
<thead>
<tr>
<th>Patient</th>
<th>SSR</th>
<th>ACS</th>
<th>MJS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>16</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Months between JSLE/splenectomy</td>
<td>1</td>
<td>38</td>
<td>10</td>
</tr>
<tr>
<td>Previous treatment</td>
<td>Pd, MP, CYC</td>
<td>Pd, MP, HCQ, IVG, AZA, C, RTX</td>
<td>Pd, MP, HCQ, IVG, AZA, C, MMF, RTX</td>
</tr>
<tr>
<td>Platelet count</td>
<td>3,000/mL</td>
<td>7,000/mL</td>
<td>10,000/mL</td>
</tr>
<tr>
<td>Splenectomy</td>
<td>Held</td>
<td>Held</td>
<td>Indicated (cancelled due to bone marrow hypoplasia-toxicity?)</td>
</tr>
<tr>
<td>Platelet count (time after surgery)</td>
<td>107,000/mL (2 w)</td>
<td>140,000/mL (1 d)</td>
<td>-</td>
</tr>
<tr>
<td>469,000/mL (2 m)</td>
<td>396,000/mL (3 d)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Recurrences</td>
<td>none</td>
<td>1 month after</td>
<td>-</td>
</tr>
</tbody>
</table>

Pd = prednisone; MP = Methylprednisolone pulse; CYC = Cyclophosphamide; HCQ = Hydroxychloroquine; IVG = Gammaglobulin; AZA = Azathioprine; C = Cyclosporine; MMF = mycophenolate mofetil; RTX = Rituximab.
from 7–52% (mean 14.5%) but profound rates (<50,000/mL) are uncommon. Although the exact mechanism is unknown, the spleen has been implicated either as the source of antiplatelet antibodies or the site of sensitized platelets destruction. Splenectomy is rarely indicated due to the increased risk of severe infections and controversial effectiveness.

**Materials and methods:** From 1983 to 2007, 5079 patients were followed at the Pediatric Rheumatology Unit and JSLE occurred in 228 (4.5%). We report three female JSLE patients with refractory thrombocytopenia to whom splenectomy was indicated.

**Results:** Data are described in table 1. Thrombocytopenia preceded JSLE diagnosis in a mean of 30 months. All patients had initial normal bone marrow and positive antiphospholipid antibodies.

**Conclusion:** Splenectomy should be considered for the treatment of thrombocytopenia refractory cases. Results are variable. Bone marrow hypoplasia should be excluded.

**P249**
**Rituximab for treatment of severe lupus nephritis**
E Baskin, US Bayrakci, S Ozen, Y Bilginer, KS Gulleroglu and H Ozdemir
1Baskent University Department of Pediatric rheumatology and nephrology, Ankara, Turkey
2Hacettepe University Department of Pediatric rheumatology and nephrology, Ankara, Turkey

**Pediatric Rheumatology 2008, 6(Suppl 1):P249**

**Background:** Systemic lupus erythematosus (SLE) is a challenging disease to diagnose and manage. Treatment of lupus nephritis in resistant cases is still a matter of debate.

**Aim:** To investigate the effectiveness of rituximab (Rx) in treatment resistant cases of lupus nephritis.

**Materials and methods:** Five female patients with a median age of 14 years (range: 12–16 years) with class IV (3/5) and class II (2/5) lupus nephritis were treated with rituximab, steroids and plasmapheresis. Rituximab was given with a dose of 500 mg/m² two times a week for 4 weeks in both patients while only one patient had a dose of 77 mg/m²/hour. Autoantibodies along with clinical findings fulfilled the criteria for both AIH and SLE. Arthritis and proteinuria with hematological findings attributable to SLE improved with high dose treatment with corticosteroids and azathioprine; however, remission of the liver disease could not be achieved. In conclusion, this case suggested that AIH and SLE might be indistinguishable from each other.

**P250**
**Autoimmune hepatitis or systemic lupus erythematosus? A diagnostic dilemma**
B Makay, S Demirpence, N Arslan, E Ozer and E Unsal
Dokuz Eylul University Hospital, Izmir, Turkey

**Pediatric Rheumatology 2008, 6(Suppl 1):P250**

Autoimmune hepatitis (AIH) is a chronic inflammatory liver disease of unknown etiology associated with circulating autoantibodies and hypergammaglobulinemia. Patients with AIH occasionally suffer from other autoimmune diseases. Similarly, systemic lupus erythematosus (SLE) is an autoimmune disorder affecting multiple organs and coexisting with other autoimmune diseases. Although the liver is not a major target for damage in SLE, clinical and biochemical evidence of liver abnormalities are common. However, the difference between the hepatic involvement of SLE and autoimmune hepatitis has not been clearly defined due to similarities in clinical and biochemical features.

We report a 16-year-old girl with an overlap syndrome involving AIH and SLE. She presented with failure to thrive, jaundice, non-erosive arthritis, and oral afous lesions accompanied by hyperbilirubinemia, elevated ALT, leukopenia, hypocomplementemia, and direct Coombs positivity. Serologic tests showed that she was positive for ANA and anti-Ro antibody as well as anti-gludin IgG and anti-endomisium IgA. Liver biopsy showed portal and periportal hepatitis with lymphocytic infiltration and piecemeal necrosis. International autoimmune hepatitis score demonstrated definite AIH. She had proteinuria at the follow-up (77 mg/m²/hour). Autoantibodies along with clinical findings fulfilled the criteria for both AIH and SLE. Arthritis and proteinuria with hematological findings attributable to SLE improved with high dose treatment with corticosteroids and azathioprine; however, remission of the liver disease could not be achieved. In conclusion, this case suggested that AIH and SLE might be indistinguishable from each other.

**P251**
**Use of Rituximab in child with SLE and myocardial involvement**
S Balan, C Goel, S Rangaraj, H Venning, N Camina and L Hutchinson
Nottingham University Hospitals, Nottingham, UK

**Pediatric Rheumatology 2008, 6(Suppl 1):P251**

A twelve year old girl of Pakistani origin first presented at the age of nine with weakness, lethargy, fever, and was diagnosed as SLE with progressive multisystem involvement with LV dysfunction, vasculitic skin lesions, hepatitis, hemiplegia and nephritis. She was treated initially with Cyclophosphamide and intravenous steroids, and thereafter maintained on Methotrexate. She was also treated with Azathioprine and Mycophenolate mofetil as single agents for some time as she became non compliant with Methotrexate.

Three years into diagnosis she had symptoms of increasing tiredness, breathlessness and tachycardia. An echocardiogram confirmed ventricular dilatation suggesting myocardial involvement. She was recommenced on Cyclophosphamide with Methyprednisolone, and was also commenced on Frusemide and Enalapril which initiated control of her cardiac function. Her ejection fraction improved from 30% to 52%. Subsequently, after 6 months of Cyclophosphamide, Rituximab was tried as sole agent which is currently holding her lupus and myocardial changes in control for over 20 months. She has had 3 cycles of Rituximab, each given at 1 gram/kg, divided in two doses two weeks apart. Her latest ejection fraction is 45%.

There is very limited published evidence for Rituximab for cardiac involvement of SLE in children. Thus we would recommend that Rituximab be considered in this rare but potentially debilitating presentation of SLE for control as well as to limit the use of large doses of cytotoxic medications.
P252
The clinical course and long-term outcome of juvenile systemic lupus erythematosus
M Wierzbowska, P Gietka, L Rutkowska-Sak and E Musiej-Nowakowska
Institute of Rheumatology, Warsaw, Poland

Pediatric Rheumatology 2008, 6(Suppl 1):P252

The aim of the study was to examine the evolution of the clinical features, clinical course of juvenile systemic lupus erythematosus (jSLE) and to estimate most frequent long-term outcome of the disease according to SLICC/ACR Damage Index for SLE in a group of children whose disease began after 1985 and has been hospitalized in Institute of Rheumatology in Warsaw since 1985 till 2005. The study involved an analysis of medical records of 138 patients (119 girls, 19 boys; mean age at the onset of SLE 7.9 ± 0.2). They have been observed for the mean period of 12.5 ± 0.39. The statistical analysis proved that the occurrence of clinical and immunological features as well as the primary jSLE activity has been changing during the last twenty years. The number of clinical jSLE manifestations has also decreased and the mortality rate has fallen. The most frequent cause of death is nowadays generalized infections. Lower SLE Disease Activity Index (SLEDAI) scores are being observed on the beginning of jSLE. There is statistically significant less renal involvements and seizures at the onset of jSLE. Observed growth in frequency of psychosis, ds-DNA antibody presence, hair loss and haemolytic anemia was statistically significant. Most frequent long-term outcomes of the disease are: nephropathy, central nervous system involvement, vasculopathy and skin changes.

P253
A case with SLE and Pseudohypoparathyreoidism
B Varbanova and V Yotova
Medical University of Varna, Varna, Varna Bulgaria

Pediatric Rheumatology 2008, 6(Suppl 1):P253

SLE is often associated with endocrine disorders. We present a 19-year-old male patient with family history of diabetes type II, admitted for the dominating complaints of fever, arthralgia and arthritis, rash, weight loss and fatigue. Physical examination and investigations showed signs of vasculitis, hair loss, anemia, leucopenia, episcleritis, oral lesions, arthritis, nephritis, positive LE-phenomenon and high titres of ANA and anti-dsDNA antibodies. Those signs and criteria proved a diagnosis of SLE. Another set of clinical features was revealed, including obesity, round face, hypertrichosis, saddle-back nose, divergent strabismus, short and broad fingers, dental enamel damage, catarrhaca, fibrous osteitis, positive Chvostek I, II and Weis symptoms. Seizures, growth and mental retardation were reported dating back from his early childhood. Laboratory findings of hypocalcaemia and hyperphosphoremia supported the diagnosis of Pseudohypoparathyroidism-Albright’s hereditary osteodystrophy (AHO). This case is reported for its rarity – a male patient with SLE and an inherited endocrinopathy. The association of AHO due to a genetically determined insufficiency of G_{sA} -cAMP-system with a disease, such as SLE, where an enhancement of Th2- mediated immune response is established, is intriguing and rises questions and speculations.

P254
Use of mycophenolate mofetil (MMF) in lupus nephritis (LN) in children
R Indaco¹, M Alessio¹, MR Caropreso², G Malgieri² and C Pecoraro²
¹Rheumatology Unit, Department of Pediatrics, Federico II University, Naples, Italy
²Nephrology Unit, Department of Pediatrics, Santobono-Pausillipon Hospital, Naples, Italy

Pediatric Rheumatology 2008, 6(Suppl 1):P254

Systemic lupus erythematosus (SLE) is a multisystemic autoimmune disease; 86% of children with SLE have renal involvement, that ranges from asymptomatic urinary findings to nephritic syndrome and renal failure. Cyclophosphamide (CYC) and corticosteroids (CCS) has been the standard of care for many years, despite their failure or potential toxicities. Studies have showed good results with MMF in LN. We evaluated, in an observational study, the efficacy of MMF as induction and maintenance therapy in LN in children. Eighteen patients (15 female and 3 male, median age 12.2 ys) were evaluated with biopsy-proven LN, 13/18 received CYC or CCS as induction and then MMF, 5/18 received MMF plus CCS as from start. The following parameters were recorded at baseline and follow-up: serum creatinine, urinary protein excretion in 24 hours, full blood count, complement components (C3–C4), ANA positivity, ENA profile, SLEDAI score and histologic indices of activity and chronicity by Austin and coll. The median treatment time with MMF was 3 years. Our patients showed return in the range of normality of serum creatinine (p < 0.01), urinary protein excretion in 24 hours (p < 0.01), full blood count, complement components (C3–C4) (p < 0.01), ANA positivity (p < 0.01), ENA profile (p < 0.01), SLEDAI score (p < 0.01) and histologic indices of activity and chronicity (p < 0.01). In all patients CCS was suspended in 2 months. We had only 2 patients with adverse effects (1 diarrhoea, 1 viral infection). MMF as induction and maintenance therapy can be efficacious and safe in treatment of LN in children.

References

P255
Safety of rituximab in children with auto-immune diseases
B Bader-Meunier, P Quartier and C Wouters
Hospital Necker, Paris, France

Pediatric Rheumatology 2008, 6(Suppl 1):P255

Purpose: Assessment of safety of rituximab in children with auto-immune diseases (AID) in published reports.

**Results:** We identified 169 children treated for refractory AID: autoimmune cytopenia (s) (104 patients), systemic lupus erythematosus (SLE) (52 patients), miscellaneous (13 patients). The mean follow-up period was 6 to 36 months. Patients received 2 to 4 rituximab infusions (350–750 mg/m²) associated with immunosuppressive drugs in 49/52 SLE patients. Replacement intravenous immunoglobulins therapy was given to 68/169 patients. Moderate side effects were observed in 50/169 patients: infusion-related reactions, infections, transient neutropenia > 0.5 × 10⁹/L and serum sickness disease. Severe side effects were observed after rituximab infusion in 11/169 (6.6%) patients: severe infusion related hypotension (4 patients), neutropenia < 0.2 × 10⁹/L (3 patients), (2 SLE patients), cerebral vasculitis (1 SLE patient). Two SLE patients who have received cyclophosphamide died from cerebral histoplasmiosis and Staphylococcus aureus endocarditis, and one boy who underwent autologous bone marrow transplantation for severe thrombocytopenic purpura developed severe enteroviral meningencephalitis; Ig G level was low at time of infection in 3/4 patients and not available in the fifth.

**Conclusion:** Severe adverse events were recorded in 6.6% of the rituximab-treated children. Patients who have received previous, concurrent and/or subsequent immunosuppressive drugs may experience severe infections, and must be closely monitored. A cohort study of children treated for auto-immune diseases with rituximab has been initiated in France since March 2008 to better assess the tolerance of this therapy.

**P256**

**Macrophage migration inhibitory factor gene polymorphisms in an Italian cohort of patients with Kawasaki disease**

G Simonini, E Corinaldesi, F Falcini, C Massai, M De Martino and R Cimaz

*A Meyer Children’s Hospital, Florence, Italy*

*Pediatric Rheumatology 2008, 6(Suppl 1):*P256

**Background:** MIF (macrophage migration inhibitory factor) is a proinflammatory cytokine regulator of host inflammatory and immune responses, and is expressed by many different cells types. Serum levels of MIF have been found to be increased in several inflammatory diseases, Kawasaki disease (KD) included.

**Objective:** To evaluate possible differences in MIF polymorphisms between patients with KD and healthy subjects, and between KD patients with and without coronary alterations. Methods. We screened for the MIF gene polymorphisms −173*A* allele in 69 patients discharged from our hospital with a diagnosis of Kawasaki disease and 60 healthy controls.

**Results:** The average age at disease onset was 29 months (range, 3–135 months). There were 43 females (33.3%) and 26 (20.2%) males. Eight children (12%) were non-responders to the first IVIG infusion. Nine children (13%) had coronary alterations (ectasia or aneurysms). Statistical analysis for MIF alterations (ectasia or aneurysms). Statistical analysis for MIF polymorphism and risk of CAA in KD.

Moreover, non-responders to a single IVIG infusion carried the MIF −173*C* allele more frequently than responders (6/8 = 75% vs 17/61 = 28%, p < 0.014).

**Conclusion:** Our study suggest a potential relationship between a MIF polymorphism and risk of CAA in KD.

**P257**

**Subclinical atherosclerosis and Kawasaki Disease (KD): results from an e-tracking study of arterial stiffness in a Sicilian population**

A Vitale1, F La Torre1, G Calcagno1, MS Russo2, S Careri3, FL De Luca2, MT Naso onofrio1, G Oreto2, A La Mazza2, C Fede1 and MP Calabro2

1Department of Pediatrics, Pediatric Rheumatology, Messina, Italy
2Department of Pediatrics, Pediatric Cardiology, Messina, Italy
3Department of Cardiology, Messina, Italy

*Pediatric Rheumatology 2008, 6(Suppl 1):*P257

**Background:** 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:** Twenty 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 carotid 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.

**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.

**Reference**


**P258**

**Kawasaki disease in Sicily: a 7 year survey**

A Vitale1, F La Torre1, R Barcellona2, A Lizzio2, C Fede1, S Costa1, S Russo2 and F Falcini1

1Department of Pediatrics, Pediatric Rheumatology, Messina, Italy
2Department of Pediatrics, Catania, Italy
3Department of Pediatrics, Sciacca, Italy
4Department of Biomedicine, Division of Rheumatology, Transition Unit, Florence, Italy

*Pediatric Rheumatology 2008, 6(Suppl 1):*P258

**Background:** Kawasaki disease (KD) is an acute self-limiting disease with long-term complications such as coronary artery aneurysms and anomalies (resulting in coronary artery disease). The disease is very rare in Sicily. The aim of this study was to assess the epidemiological characteristics of Kawasaki disease in Sicily.

**Methods:** We screened for the MIF gene polymorphisms −173*A* allele in 69 patients discharged from our hospital with a diagnosis of Kawasaki disease and 60 healthy controls.

**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.

**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.
P258

FOXP3 gene 543 SNP does not differ, FOXP3 mRNA expression vs not lower than in controls. IL-17 levels were 8-fold higher in KS

Materials and methods: The single nucleotide polymorphism (SNP) at position 543 of exon 5 of FOXP3 was investigated in European females (4.3%). FOXP3 mRNA expression was in heterozygosis (C > T), as actually reported in healthy controls. Results: 98 Caucasian children (55 M, 43 F, mean age at onset 36 mths), were diagnosed; 88/98 fulfilled the criteria while 10/98 had the incomplete form. The M: F ratio was 1.3: 1. 85% were children aged 36–40 months and 15% infants. Most cases occurred in August. The typical fever was present in 100%, conjunctivitis and exanthema in 98%, mucositis and extremity changes in 89%, and cervical lymphadenopathy in 79% of patients. 87/98 pts had received timely IVIG; 4 patients required a second infusion. Cardiac abnormalities developed in 10 pts (6 ectasia and 4 aneurysms) all in the group with delayed therapy; 3/4 were giant aneurysms, all in infants. Three patients in addition to CAA displayed peripheral artery involvement. At 4-yr follow-up all CAA normalized except for 3 giant CAA that regressed to dilatations.

Conclusion: The incidence rate of KD in Sicily, sex distribution and cardiac abnormalities are comparable to European reports. The seasonal distribution is different with a peak in summer.

P259

FOXP3 Polymorphism and gene expression in Italian patients with Kawasaki Syndrome

G Simonini, B Olivito, F Fant, T Giani, E Corinaldesi, M de Martino and R Cimaz

Rheumatology Unit-Dept. of Pediatrics, University of Florence, Firenze, Italy

Background: The transcription factor FOXP3 is a key regulator of immune homeostasis of natural regulatory T lymphocytes (Treg). Aim of our study was to investigate the link between the FOXP3 gene expression and polymorphism, and Kawasaki Syndrome (KS).

Materials and methods: The single nucleotide polymorphism (SNP) at position 543 of exon 5 of FOXP3 was investigated in 58 caucasian children patients with KS (F:30, M:28), recruited at our Paediatric Rheumatology Unit. In 6 patients we could evaluate the percentage of circulating CD4+ T cells co-expressing CD25 and FOXP3 by flow cytometry, mRNA transcripts of FOXP3 in PBMCs by Real Time PCR (with Rnase P as internal control gene), and the levels of IL-17 in PBMCs supernatants (5 x 10^6 cells) by a quantitative immunoassay Kit.

Results: In KS subject, 2 females (3.4%) showed the 543 SNP in heterozygosis (C > T), as actually reported in healthy European females (4.3%). FOXP3 mRNA expression was significantly lower (3-fold) than in healthy controls, while FOXP3 protein expression determined by flow cytometry was not lower than in controls. IL-17 levels were B-fold higher in KS than in controls (mean 340 vs 40 pg/mL).

Conclusion: Compared to healthy controls, in our patients, FOXP3 gene 543 SNP does not differ, FOXP3 mRNA expression was lower, without a correspondent lower protein expression, and IL-17 levels were much higher in patients. Due to the small number of patients, these results warrant further studies to evaluate FOXP3 expression in relationship with IL-17 in KS.

P260

Incidence and classification of childhood vasculitides in Denmark 1976–1998 according to the consensus criteria for the classification of childhood vasculitides

RAR Raja, LLS Soerensen, TH Herlin and SMN Nielsen

Pediatric clinic, JMC, Rigshospitalet, Copenhagen and Department of Pediatrics, Aarhus University Hospital Skejby, Aarhus, Copenhagen and Aarhus, Denmark

Background: In 2006 Ozen et al proposed new diagnostic criteria for the classification of childhood vasculitides. The aim of this retrospective study was to describe the incidence of Wegener’s Granulomatosis (WG), Polyarteritis Nodosa (PAN) and Takayasu Arteritis (TA) in Denmark during the period of 1976–1998. Furthermore, we wanted to classify them according to the Chapel Hill Classification Criteria as well as to the new consensus criteria and to compare if this altered the incidence of the different vasculitides.

Methods: In the Danish National Patient Register (DNPR) we searched for the following diagnosis in children aged 0–16 years:

- Wegener’s Granulomatosis;
- Polyarteritis Nodosa;
- Takayasu Arteritis;
- Unclassified primary systemic vasculitides.

After compiling the results from this search we contacted the pediatric centres where the patients had originally been admitted, in order to retrieve the relevant charts.

Results: The total number of patients found in the DNPR with possible vasculitides was 79. 48 patients from 11 Danish pediatric departments were included. 35 of these could not be classified as primary vasculitides. 13 patients were classified as follows: WG 11 and PAN 2. None of the patients changed diagnosis due to re-classification.

Conclusion: In this retrospective investigation and for these 3 diseases the diagnosis was equal for all patients with respect to the two sets of classification criteria. A prospective study of classification for all types of childhood vasculitides is ongoing in the regime of PRINTO.

P261

Serum and urine nitric oxide levels in children with Henoch-Schonlein Purpura during activity and remission – a study from North India

V Mahajan, S Singh, M Khullar and R Walker Minz

Post Graduate Institute of Medical Education and Research, Chandigarh, India

Background: A prospective study of classification for all types of childhood vasculitides is ongoing in the regime of PRINTO.

Methods: The study group consisted of 14 children with biopsy proven HSP. We measured serum and urine RNI and was lower, without a correspondent lower protein expression, and IL-17 levels were much higher in patients. Due to the small number of patients, these results warrant further studies to evaluate FOXP3 expression in relationship with IL-17 in KS.

P260

Incidence and classification of childhood vasculitides in Denmark 1976–1998 according to the consensus criteria for the classification of childhood vasculitides

RAR Raja, LLS Soerensen, TH Herlin and SMN Nielsen

Pediatric clinic, JMC, Rigshospitalet, Copenhagen and Department of Pediatrics, Aarhus University Hospital Skejby, Aarhus, Copenhagen and Aarhus, Denmark

Background: In 2006 Ozen et al proposed new diagnostic criteria for the classification of childhood vasculitides. The aim of this retrospective study was to describe the incidence of Wegener’s Granulomatosis (WG), Polyarteritis Nodosa (PAN) and Takayasu Arteritis (TA) in Denmark during the period of 1976–1998. Furthermore, we wanted to classify them according to the Chapel Hill Classification Criteria as well as to the new consensus criteria and to compare if this altered the incidence of the different vasculitides.

Methods: In the Danish National Patient Register (DNPR) we searched for the following diagnosis in children aged 0–16 years:

- Wegener’s Granulomatosis;
- Polyarteritis Nodosa;
- Takayasu Arteritis;
- Unclassified primary systemic vasculitides.

After compiling the results from this search we contacted the pediatric centres where the patients had originally been admitted, in order to retrieve the relevant charts.

Results: The total number of patients found in the DNPR with possible vasculitides was 79. 48 patients from 11 Danish pediatric departments were included. 35 of these could not be classified as primary vasculitides. 13 patients were classified as follows: WG 11 and PAN 2. None of the patients changed diagnosis due to re-classification.

Conclusion: In this retrospective investigation and for these 3 diseases the diagnosis was equal for all patients with respect to the two sets of classification criteria. A prospective study of classification for all types of childhood vasculitides is ongoing in the regime of PRINTO.

P261

Serum and urine nitric oxide levels in children with Henoch-Schonlein Purpura during activity and remission – a study from North India

V Mahajan, S Singh, M Khullar and R Walker Minz

Post Graduate Institute of Medical Education and Research, Chandigarh, India

Background: A prospective study of classification for all types of childhood vasculitides is ongoing in the regime of PRINTO.

Methods: The study group consisted of 14 children with biopsy proven HSP. We measured serum and urine RNI and
citrulline levels by spectrophotometry in the active phase and after remission.

**Results:** Serum RNI levels were $303.95 \pm 221.44$ nmol/ml in children with active HSP and $72.57 \pm 26.56$ nmol/ml during remission, the differences being statistically significant ($p = 0.002$). Mean urine RNI levels in children with active HSP were significantly higher than that seen during remission ($3.25 \pm 1.80$ vs. $1.68 \pm 0.65$ nmol/ml; $p = 0.003$). Similarly, serum citrulline levels during disease activity were $790.65 \pm 707.87$ nmol/ml as compared to $281.49 \pm 307.29$ nmol/ml at the time of remission, the differences being statistically significant ($p = 0.002$). Mean urine citrulline levels in children with active disease was $1969.94 \pm 1655.42$ nmol/ml as compared to $1099.34 \pm 955.82$ nmol/ml in children with remission, ($p = 0.007$).

**Conclusion:** Serum and urine RNI and citrulline levels were significantly higher during the active phase of HSP. These findings suggest that nitric oxide may perhaps have a role in the pathogenesis of HSP. Further, these laboratory parameters could be of value in monitoring disease activity.

**P262**

**Behcet Disease: treatment of vascular involvement in children**

Y Bilginer, N Bèsbas, N Aktay Ayvaz, A Bakkaloglu and S Ozen
Hacettepe University School of Medicine Pediatric Nephrology and Rheumatology Unit, Ankara, Turkey

**Pediatric Rheumatology** 2008, 6(Suppl 1):P262

Behcet disease is the only primary vasculitis that affects both arteries and veins of any size. We present our treatment strategy in Behcet disease with vascular involvement in seven childhood patients. All seven patients met the international criteria for the disease before the age of 16. Only one was a girl. The vascular involvement was as follows: Two patients had superficial vein thrombosis, two patients had atrial or ventricular thrombosis, two had sinus vein thrombosis and one had arterial involvement with pulmonary aneurysms.

The disease was diagnosed 4 months (range 3–24 months) before the vascular involvement in 4 patients and concomitant with diagnosis in 3 patients. All received colchicine, steroids and anticoagulant therapy. The ones with thrombosis in the venous system received additional azathioprine whereas those with pulmonary arterial or cardiac involvement initially received cyclophosphamide for 150–180 mg/kg total dose (IV or oral) and then were switched to azathioprine for a further 6 months. These patients have been followed up for period of 12 months (ranging 4–30 months) and so far are free of vascular relapses. One has developed a severe uveitis necessitating further therapy. In conclusion features of vascular involvement should be carefully sought for in patients with Behcet disease. Effective management is required for this feature of the disease that has a high morbidity.

**P263**

**Behcet Disease (BD) in two siblings affected with Familial Mediterranean Fever (FMF)**

G Calcagno, A Vitale, F La Torre, N Decembrino, C Fede and F Falci

1Department of Pediatrics, Pediatric Rheumatology, Messina, Italy

**Pediatric Rheumatology** 2008, 6(Suppl 1):P263

**Background:** FMF is a genetic autoinflammatory disease, characterized by attacks of fever and painful serositis. Behcet’s disease (BD) is an inflammatory disorder associated with vasculitis. Clinical manifestations of both diseases can mimic each other and the coexistence of both diseases in the same patient has been reported.

**Objective:** We observed 2 siblings (11 and 10 year-old) of Egyptian ancestry, with a single MEFV gene mutation and clinical symptoms of FMF and BD.

Their medical history of recurrent fever attacks started at the age of 14 and 6 months respectively. Fever was accompanied by cervical adenopathy, severe exudative pharyngitis, oral aphthosis, abdominal pain and diarrhoea, sometimes with bloody stools. At the age of 10 and 9 years, screening for autoinflammatory disorders was performed revealing a single mutated MEFV gene (E148Q). Since they fulfilled Tel Hashomer criteria, colchicine was started. Despite colchicines, both still presented shorter fever attacks, recurrent abdominal pain with diarrhoea, oral and genital aphthosis, mialgia and asthenia. Blood tests and abdominal ultrasound were normal. An ophthalmic evaluation showed panuveitis in both.

Recurrence of oral and genital ulcers, abdominal pain and uveitis strongly suggested the diagnosis of BD even though HLA B51 was not detected.

**Conclusion:** Diagnosis of FMF and BD is clinical. Our patients fulfilled Tel Hashomer criteria for FMF and international diagnostic criteria of BD. The increase of colchicine induced a sustained clinical improvement. Physicians have to be aware of the possible association of both conditions.

**Reference**


**P264**

**Behçet Syndrome and Hypogonadotropic Hypogonadism: case report**

G Calcagno, A Vitale, F La Torre, S Carcione, M Valenzise, C Fede and T Arrigo

1Department of Pediatrics, Pediatric Rheumatology, Messina, Italy
2Department of Pediatrics, Pediatric Endocrinology, Messina, Italy

**Pediatric Rheumatology** 2008, 6(Suppl 1):P264

**Background:** Behçet Disease (BD) is a sistemic chronic vasculitis.

**Clinical case:** A sixteen year old boy presented, three years before, gastrointestinal (abdominal pain, vomiting, diarrhea) and neurologic symptoms (headache, diplopia, ataxia, VI nerve paralysis), with fever, oral and genital aphthosis. Laboratory tests showed increased ESR, CRP). He carried B51HLA. Physical examination showed svere obesity, pseudomicropenis, rare pubic hair, pubertal stage G2P2. Thus BD was diagnosed. Treatment with corticosteroids and antiplatelet agents was started.

After 2 months, azathioprine and infliximab were added; but biological agent was stopped, because of adverse reactions; thus thalidomide was started. After the diagnosis, the patient presented a progressive weight increase (BMI 39) and a delayed
Wegener’s Granulomatosis: paediatric presentation with ischaemia of the feet and novel use of hyperbaric oxygen
T Chaudry, A McMahon and C Pilkington
Great Ormond Street Hospital, London, UK
Pediatric Rheumatology 2008, 6(Suppl 1):P265

Wegener’s Granulomatosis is a rare, chronic, multisystemic vasculitis, of unknown aetiology, affecting mainly the upper and lower respiratory tracts together with glomerulonephritis. However, the disease may involve any other organ. We report a 14-year-old previously healthy girl, who presented with severe ischaemic changes to both feet. 4 weeks prior to presentation she had an episode of epistaxis and conjunctivitis. She developed a blister on the distal dorsal aspect of her right foot, with bluish discoloration and pain. Within one week both feet had become ischaemic and swollen. The diagnosis of Wegener’s was made on the basis of skin histology (leucocytoclastic vasculitis), strongly positive PR3 ANCA, focal segmental glomerulonephritis on kidney biopsy and a nodule on chest CT, with associated raised inflammatory markers.

She was treated with intravenous antibiotics, high dose steroids, and daily iloprost infusions for 6 weeks, daily heparin, intravenous immunoglobulin, plasmapheresis, cyclophosphamide, rituximab and 30 sessions of hyperbaric oxygen. There was no further progression of the ischaemia of her feet and she now has islands of healthy tissue and granulation visible in previously ischaemic areas. Currently, she has preservation of anti-hypophysis antibodies, which are normal. Although no cases of BD and hypogonadotropic hypogonadism have been described, we report this case for the numerous patogenetic hypotheses that it could generate.

Reference

P267
Efficacy and safety of thalidomide in two sisters with severe refractory polyarteritis nodosa (PAN)
A Vitali1, F La Torre1, G Calcagno1, C Fede1, A Falcone1, V Ferrau1 and F Falcini2
1Department of Pediatrics, Pediatric Rheumatology, Messina, Italy
2Department of iomedicine, Division of Rheumatology, Transition Unit, Florence, Italy
Pediatric Rheumatology 2008, 6(Suppl 1):P267

Background: Polyarteritis nodosa (PAN) is a necrotizing vasculitis seldom reported on childhood, with a severe prognosis.

Patients: We report two sisters (16 and 8 years old) with PAN refractory to different drugs who had a persistent improvement over 5-years of thalidomide. In the older, the presenting symptoms were fever and migrant arthralgies. At onset, she was 6 year old. Laboratory work-up showed increased ESR, CRP, PTL count, and anemia. Over time
she developed ischemic colitis and a transient cerebral ischemic attack. Cerebral Angio MRI revealed multiple periventricular hyperintensities prompting the diagnosis of PAN. Steroids, cyclophosphamide, methotrexate, and azathioprine were unsuccessful, and the disease was complicated by neuropathy and ischemic lesions of several digits. Thalidomide was started in December 2003; since then, the disease is stable and laboratory work up normal. First clinical features of the younger sister occurred at three years of age. She had an acute stroke. Following hypertension, renal disease and neuropathy, PAN was diagnosed. Steroids, azathioprine and cyclophosphamide were given with scarce benefit. After another ischemic cerebrovascular event, thalidomide was effective in controlling the disease activity. No side effects have been observed.

Conclusion: Both our patients refractory to steroids and immunosuppressants had a significant improvement when thalidomide was introduced. No flares have been observed during a 5-year follow-up. Although the exact mechanism of action is not fully understood, thalidomide mainly prescribed in connective diseases, could be considered an alternative therapy in severe PAN.

Reference

P268 Rituximab is a therapeutic option for juvenile microscopic polyangitis
J Brunner1, M Freund2, M Prelog1, E Binder1, M Sailer-Höck1, T Jungraithmayr1, G Mayer3 and LB Zimmerhackl1
1Department of Pediatrics, Innsbruck Medical University, Innsbruck, Austria
2Department of Radiology, Innsbruck Medical University, Innsbruck, Austria
3Department of Nephrology, Innsbruck Medical University, Innsbruck, Austria

Pediatric Rheumatology 2008, 6(Suppl 1):P268

Introduction: Microscopic polyangitis is characterized by anti-neutrophil cytoplasmic antibodies (ANCA) and small vessel vasculitides. The diseases usually respond to cyclophosphamide (Cyc) but some patients are therapy resistant. Rituximab (RIT) is a chimeric antibody to CD20 causing lysis of B-lymphocytes and used for treatment of lymphomas. RIT has also been successfully used in patients with rheumatoid arthritis (RA), idiopathic thromobocytopenic purpura, autoimmune haemolytic anaemia, cold agglutinin disease, systemic lupus erythematosus and vasculitides.

Case report: A 16-year old female patient with hemoptysis, nephritis, dermatitis was diagnosed as a myeloperoxidase-ANCA positive microscopic polyangitis. The patient was resistant to conventional therapy or had relapsed repeatedly after cessation of cyclophosphamide (Cyc). The patient was treated with intravenous infusions of rituximab (RIT).

Conclusion: RIT seems promising and safe in pediatric microscopic polyangitis. Controlled studies should be conducted.

P269 Isolated eye-lid ptosis as initial manifestation of pediatric Behçet’s Disease (BD)
M Alessio, R Indaco, R Carломagno and A Romano
Department of Pediatrics Federico II University, Naples, Italy

Pediatric Rheumatology 2008, 6(Suppl 1):P269

BD is a chronic, multisystem inflammatory disorder. Neuro-Behçet’s disease could be the first sign of the disease, but is infrequently described in childhood [1]. Isolated cranial nerve involvement has been reported [2], but to the best of our knowledge this is the first report of isolated eye-lid ptosis, without reduction of ocular motility, at onset of pediatric BD.

PD is an 11-year-old girl first admitted in our hospital with bilateral eye-lid ptosis and headache. She was in good health until one month before the admission; she presented ptosis of eye-lids which was more evident on the left side, without other pathological findings. The normality of the EEG, cranial and midollar MRI, angio MRI, prostigmine test and laboratory tests excluded brain tumors, demyelinating diseases and miastenia gravis. She improved without therapy. After 4 months she experienced folliculitis of the trunk and wrist arthritis. After 8 months she suffered from oral and vaginal aphthosis. BD was diagnosed on the basis of these clinical signs according to the International Criteria. EEG, cerebral SPECT and an ocular examination were performed with normal results; HLA was B51 positive and this is an indicator of BD. Prednison therapy was started (1 mg/Kg/day) and symptoms greatly improved within 6 months.

We can hypothesize that a bilateral occlusion of little blood vessels, caused by an inflammatory process provokes a temporary dysfunction of neurons that control each of the eyelid elevator muscles.

In conclusion BD is an important differential diagnosis for the partial oculomotor palsy as present case.

References

P270 Polyarteritis Nodosa (PAN) in childhood: a report of two siblings with intractable disease controlled by mycophenolate mofetil (MMF)
FF Falcini1, CS Capannini1, NF Naçi1, IR Indaco2, BA Battagliese2, CR Carломagno2 and AM Alessio2
1Department of BioMedicine, Division of Rheumatology, Transition Unit, University of Florence, Florence, Italy
2Department of Paediatrics, Rheumatology Unit, Policlinico Federico II, Naples, Italy

Pediatric Rheumatology 2008, 6(Suppl 1):P270

Background: PAN is a systemic vasculitis with multisystem involvement rarely observed in childhood. We report two siblings (1 boy, 1 girl) with aggressive PAN who had a persistent sustained improvement with MMF.

Patients: The boy developed at 8 yrs musculoskeletal pain and painful nodules on the legs, than vertigo, tinnitus, and diploria, neuosensory ipoacusia, left central facial palsy and hypertension. Angio MRI revealed ischemic alterations on Willi’s circle and prompted to diagnose PAN. Despite aggressive therapy the boy developed ischemic lesions of 3 digits of hands and Iloprost...
was introduced; over a short time multiple ulcerative deep cutaneous lesions appeared on the legs. Due to persistent active disease, MMF (2 g/day) was started and up to now the clinical symptoms are stable and laboratory work up normalised.

The girl, at 30 months had neurological manifestations (head and eye rotation with no consciousness, optical bilateral neuritis); over time similar episodes recurred and periodic ataxia was diagnosed. Cerebral MRI showed areas of hyperintensity on the thalamus. At 7 yrs maculopapular rash on the face and upper extremities, arthralgia/mialgia and hypertension were complained. Skin biopsy confirmed necrotizing vasculitis of medium sized vessels and PAN was diagnosed. Deep cutaneous ulcers appeared on the legs. After a severe ischemic attack, confirmed by MRI lesions at the pons area, MMF was started. Since then the girl is stable.

**Conclusion:** MMF used in the treatment of SLE and primary vasculitis in children, should be considered as either alternative or adjunctive therapy in intractable severe persistent active PAN.

**P271**

**Hemorrhagic bullous henoch schonlein purpura: a diagnostic challenge for paediatricians**

TS Trapani1, MP Mariotti2, RM Resti1, DMM de Martino1 and FF Falcini1

1Department of Paediatrics, University of Florence, Anna Meyer Children’s Hospital, Florence, Italy

2Division of Paediatrics, Hospital of Pistoia, Pistoia, Italy

**Pediatric Rheumatology 2008, 6(Suppl 1):P271**

**Background:** Hemorragic bullous lesions have been noticed in 16%–60% of adults and in 2% of children with HSP. This unusual cutaneous manifestation may cause diagnostic challenge. We report two new paediatric cases.

**Patients:** A 9-year-old girl and 11-year-old boy were admitted to our hospital with abdominal pain, arthralgia, ecchymoses and petechiae at legs, arms and buttocks. Shortly, large, tense hemorrhagic bullae and vesicles (2 to 30 mm) developed over the purpuric rash, while petechiae spread over face and neck. Both patients were prostrate and drowsy with a diffuse oedema of periorbital region, hands and feet. Laboratory tests showed increased CRP 5.2 mg/dl, WBC 23 × 10⁹/L and PTL 623 × 10⁹/L. Serological investigation for viruses (Epstein Barr Virus, Cytomegalovirus, and Hepatitis-C Virus) and bacteria were negative. ANA, pANCA, cANCA absent. Urinalysis showed proteinuria (1 g/24 h) and hematuria (1074 red blood cells/field) in the girl. Cardiologic evaluation, lung X-ray, and abdominal ultrasound were unremarkable. Due to an aggressive infection of the cutaneous lesions, imipenem and teicoplanine were introduced. Three pulses of methylprednisolone were given to the girl, and then oral prednisone (2 mg/kg/daily) to control renal disease. Bullae faded within the next two weeks and necrotic lesions healed leaving a mild pigmentation and scars.

**Conclusion:** In childhood HSP the occurrence of hemorrhagic bullae may be a diagnostic challenge at onset in absence of other typical symptoms as many paediatric diseases including toxic epidermal necrosis, erythema multiform, pemphigus, bullous impetigo, dermatitis herpetiformis and staphylococcal scalded skin syndrome may present with bullous cutaneous lesions.

**P272**

**Case of vasculitis and sarcoidosis in a child with cystic fibrosis**

EM Baildam, G Olupitan and C Pain

Royal Liverpool Children’s Hospital, Mersey, UK

**Pediatric Rheumatology 2008, 6(Suppl 1):P272**

The occurrence of cystic fibrosis (CF) and sarcoidosis is not previously reported in childhood. Hypergammaglobinaemia and immune complex deposition may contribute to granulomatous formation in sarcoidosis.

Following diagnosis of cystic fibrosis at 3 months old and despite standard CF management of daily nebulized colomycin, cefaclor, intravenous colistin and tobramycin this female patient became colonized with pseudomonas and by mid childhood had impaired pulmonary function with FEV1 67%, FVC 81% predicted. At 11 yrs, she developed episodes of rash, joint swelling and pyrexia.

Skin biopsy: florid vasculitis affecting small and medium sized vessels. Colchicine 500 mg tds initially helped but aged 12 yrs, her renal function fell acutely with serum creatinine 197, urea 19.3, ACR of 20, and calcium 4.3. 1,25 OH Vitamin D levels high at 120 mmol/l and angiotensin converting enzyme (ACE) raised at 137 mmol/l.

Renal biopsy: extensive interstitial nephritis with multiple foci of non-caseating granulomata and multinucleated giant cells.

Renal angiography: small vessel vasculitis without microaneurysms.

She had episodes of red, sore eyes.

Conjunctival biopsy: non-necrotising epithelial granuloma.

Sarcoidosis was diagnosed.

A high resolution CT scan of the chest showed CF changes only.

The hypercalcaemia and ACE responded rapidly to methylprednisolone. Her lung and renal function improved on maintenance azathioprine and prednisolone. By 6 months she was unable to wean steroids adequately without flaring.

A report of mycophenolate use in a post-transplant adult cystic fibrosis patient encouraged us to try mycophenolate instead and she now remains in remission with improvement of her cystic fibrosis lung disease as well.

**P273**

**Takayasu’s arteritis in childhood**

J Brunner

Department of Pediatrics, Innsbruck Medical University, Innsbruck, Austria

**Pediatric Rheumatology 2008, 6(Suppl 1):P273**

Takayasu’s arteritis is the most frequently acquired, chronic, devastating, potential life threatening, granulomatous inflammation of arteries with a large diameter. This large vessel vasculitis is commonly involving the aorta and its main branches. Vessel wall inflammation leads to wall thickening, fibrosis and thrombus formation. Affected vessels may present with stenotic and/or aneurysmatic formation. Symptoms may reflect end organ ischemia. Making a diagnosis of vessel inflammation by biopsy of an involved vessel is impractical and unethical. Therefore vessel inflammation is diagnosed by clinical presentation, imaging techniques and laboratory investigations. TA occurs at any age with a predominance in adolescence and young adulthood. Larger series about TA in adults are available. The studies about TA in childhood are rare. Symptoms be either typical as...
hypertension and pulslessness, but a more unspecific presentation may also indicate TA. Therefore, the diagnosis of TA is always a challenge to clinicians, particularly some of more typical diseases in childhood can mimic TA.

**P274**

**Periphereh arterial aneurysms and monocytois in intravenous immunoglobulin treatment resistant Kawasaki disease**

E Baskin, US Bayrakci, Konuksever Di, S Turkay, B Varan, H Ercoban and Z Avci

1. Baskent University, Ankara, Turkey 2. Fatih University, Ankara, Turkey

Kawasaki disease (KD) is an acute febrile illness caused by vasculitis, occurring in early childhood, and activation of monocytes/macrophages plays a central role during acute KD. We described a 4 month-old boy diagnosed as KD with involvement of peripheral arteries as well as coronary arteries. He had diagnosed as KD in a local hospital because of fever lasting for 25 days, conjunctivitis, membranous desquamation from fingertips and rash. Patient was referred to our center because of resistant fever to IVIG treatment. Echocardiographic examination revealed right and left coronary artery aneurysms and leucocytosis (41000 mm3) with predominant monocytois (25%) was observed on peripheral blood smear. Examination of bone marrow aspirate was normal while CD4/CD8 and CD4, CD14 and CD16 levels after treatment with steroids.

**P275**

**Henoch-Schönlein Purpura – an unusual presentation (clinical case)**

S Pimenta, T Videira, I Cunha, A Caldas-Afonso and I Brito

1. Department of Rheumatology, Pediatric Rheumatology Unit, Hospital S. João, Porto, Portugal 2. Department of Rheumatology, Hospital Infante D. Pedro, Aveiro, Portugal 3. Department of Pediatrics, Faculty of Medicine of Porto, Hospital S. João, Porto, Portugal 4. Department of Rheumatology, Pediatric Rheumatology Unit, Faculty of Medicine of Porto, Hospital S. João, Porto, Portugal

Henoch-Schönlein Purpura (HSP) is the most frequent children’s vasculitis, predominant in male gender and more often between the ages of 2 and 14 years. The etiology is still unknown but generally it has a good outcome. The first event is typically a lower limb palpurpura, with involvement of the gut or kidney. The renal disease usually appears in the first month, progressing to renal insufficiency in about 5% to 20%.

The authors present a case of a male toddler, that soon after birth, began with intermittent episodes of diffuse erythematous-maculopapular rash on the face, trunk and upper limbs. These cutaneous manifestation where associated with transitory hematologic alterations and elevation of serologic IgA, which resolved after a short period of corticoids. Skin biopsy revealed vasculitis. Ten years later, the child complained about unspecific polyarthralgia and was referred to Pediatric Rheumatology. He was normotense, without signs of arthritis, but with diffuse erythematous-maculopapular rash on the face, trunk and upper limbs and macroscopic hematuria. Kidney biopsy revealed IgA nephritis and the diagnosis of HSP could be made. The treatment began using corticoid and ACE inhibitors, because of persistent microalbuminuria. He maintains the renal function stabilized, but complains of recidivant cutaneous lesions that require higher doses of corticoid. This clinical case relevance resides in the fact that these recidivant cutaneous lesions are found in atypical regions and that kidney involvement begun at a rather late period, when generally is revealed in the first months of the disease onset.
were defined as mononuclear cells triple positive for CD34/CD133/CD144 and CD34/CD133/VEGFR2.

**Results:** Median CEC count in progressive cPACNS was significantly raised to 480/ml (176–1152) compared to 36/ml (0–168) in non-progressive disease (p = 0.0007), 32/ml (0–152) in child control (p = 0.0050) and 24/ml (16–141) in patients with non inflammatory cerebrovascular pathology (p = 0.0016). CD34 + CD133 + CD144+ cells were significantly raised in patients with progressive disease compared to child controls (p = 0.005) and patients with non progressive disease (p = 0.03). There was a similar but non significant trend for EPCs expressing CD34/CD133/VEGFR2.

**Conclusion:** CECs can be used to track vascular injury due to cPACNS and differentiate progressive versus non-progressive cerebral vasculitis. We also demonstrated an increase in EPCs in progressive cPACNS, perhaps indicative of a compensatory reparative vasculogenic response.

**Reference**