

Poster presentations

P001 ASSOCIATION OF CHRONIC OLIGOARTHRITIS WITH HLA CLASS II ALLELES: DRB1, DQB1 AND DQA1 IN BULGARIAN CHILDREN

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HLA class II alleles (DRB1, DQB1 and DQA1) were investigated in 20 Bulgarian children (12 girls and 8 boys) with Juvenile chronic idiopathic oligoarthritis. Our patients are in age from 1.5 to 12 years (mean age 5.2 years). All they have minimal or moderate inflammatory activity based on clinical symptoms, ESR, CRP, RF-negative. Eight of the patients (all girls) have chronic anterior uveitis and positive ANA. In evolution of 1.5 to 2 years the patients remained in oligoarthritic type of JIA.

The control group included 130 unrelated healthy individuals from the Bulgarian population without family history of autoimmune disease.

Genomic DNA from JIA children and the controls was extracted from their venous blood using the standard salting-out method. HLA-DRB1, DQB1 and DQA1 genotyping was performed by PCR-SSP method. 13 HLA-DRB1, 6 DQB1 and 10 DQA1 allele groups were found in the patients and controls. Statistically significant predisposing association was established for DRB1*08 (OR=4.02, $p < 0.05$), DQB1*04 (OR=3.50, $p < 0.05$) and DQA1*0401 (OR=4.02, $p < 0.05$). Although no difference in allele association was observed in children with and without eye involvement, in these with chronic anterior uveitis the frequency of alleles mentioned was higher. These alleles show strong linkage disequilibrium and the same association has been found in all clinical types of JIA within the 12th IHWCS.

Conclusion: Our data confirm predisposing JCA associations found in other Caucasian populations. Since the same HLA class II association was found in children with and without eye uveitis, patients without eye involvement are not safeguarded against development of uveitis.

P002 DECREASE IN CELLULARITY AND CYTOKINE EXPRESSION BY AUTOLOGOUS STEM CELL TRANSPLANTATION (ASCT) IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA)

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Objective: ASCT has been used as an experimental treatment in refractory JIA. The aim of this study was to analyze the effects of ASCT at the site of inflammation. Therefore, we examined the changes in the cellular infiltrate and the expression of pro-inflammatory cytokines in the synovium in relation to clinical effects of ASCT.

Methods: JIA patients were treated with T-cell depleted ASCT after a conditioning regimen consisting of antithymocyte globuline, cyclophosphamide and total body irradiation. Synovial biopsies were obtained by needle arthroscopy in two JIA patients aged 14 and 5 years (one systemic and one polyarticular) before and six months after ASCT. Immunohistochemical analysis was performed using monoclonal antibodies to detect CD3+ T-cells, CD4+ T-cells, CD8+ T-cells, CD38+ plasma cells, CD55+ fibroblast-like synoviocytes, and CD68+ macrophages, as well as the expression of pro-inflammatory cytokines IL-1 β , IL-6, and TNF- α . Stained sections were examined by semiquantitative analysis (0-4). Double immunofluorescence was performed to determine CD3+/CD45RO+ and CD8+CD45RO+ cells. Results before and after ASCT were compared in relation to clinical outcome.

Results: ASCT was well tolerated in both patients. Aplastic periods lasted for 18 days. Lymphocytopenia (CD3 <500/ul) lasted for 30 days. Follow-up showed a marked decrease in arthritis severity as expressed in core set criteria for JIA after 3 and after 6 months. Clinical improvement was associated with a decrease in most semiquantitative scores for synovial inflammation and cytokine

expression: CD3: before 1.5 ± 0.5 vs after 1.0 ± 0.0 ; CD4: 1.5 ± 0.5 vs 0.5 ± 0.5 ; CD8: 1.5 ± 0.5 vs 0.5 ± 0.5 ; CD38: 0.5 ± 0.5 vs 0.5 ± 0.5 ; CD68 in the intimal lining layer: 2.5 ± 0.5 vs 0.5 ± 0.5 ; CD55: 1.0 ± 0.0 vs 1.5 ± 0.5 ; TNF- α : 3.0 ± 0.0 vs 1.0 ± 0.0 ; IL-1 β : 2.0 ± 1.0 vs 1.0 ± 0.0 ; and IL-6: 1.5 ± 0.5 vs 0.5 ± 0.5 . The percentages CD45RO+ memory T-cells in patient 1 were also reduced after therapy. Semiquantitative scores for CD55+FLS and CD38 + plasma cells were not decreased after therapy.

Conclusion: Clinical improvement after ASCT in JIA patients is associated with reduced synovial inflammation and a decrease in pro-inflammatory cytokine expression.

P003 EFFECTS OF DEXAMETHASONE ON DIFFERENTIATION AND MATRIX MINERALIZATION IN CULTURED GROWTH PLATE CHONDROCYTES

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Introduction: Long-term treatment with glucocorticoid leads to growth retardation. In vitro data suggest direct effects of glucocorticoids on growth plate chondrocytes. Since growth is the result of cell proliferation and differentiation, the aim of the present study was to investigate the effects of dexamethason on these pathways crucial for normal growth plate function.

Methods: Isolated chondrocytes from rat tibial growth plates were cultured as monolayer and three-dimensional cell-pellets. Cultures were treated with dexamethason (10^{-7} M) for 21 days. Cell proliferation was measured by pellet-weight and DNA-content. As marker for cell differentiation Collagen I, II, X and osteocalcin were analysed via RT-PCR. The extent of mineralization was analysed by van-Kossa staining.

Results: Dexamethason inhibited significantly the cell proliferation measured by an DNA content. Total protein amount was slightly reduced under dexamethason. However, protein normalized for DNA, was increased three fold in dexamethason treated cells ($7.6 \mu\text{g}$ vs. $22.7 \mu\text{g}$ /ng DNA). The expression of Collagen I, II and X measured as Col/ β -actin ratio were reduced about 63, 44, 42% respectively. No influence on osteocalcin expression was detectable. Mineralization was dramatically reduced after 21 days of Dexamethason.

Discussion: Dexamethason inhibited cell proliferation and cell differentiation of cultured growth plate chondrocytes. The question whether the increased amount of protein per cell could be explained by increased synthesis or reduced decomposition needs further investigations.

P004 SYNOVIAL MEMBRANE EXPRESSION OF MATRIX METALLO-PROTEINASES AND THEIR TISSUE INHIBITOR (TIMP-1) IN JIA

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Matrix metalloproteinases (MMPs) are a large family of proteolytic enzymes involved in the remodelling of extracellular matrix in many physiological and pathological conditions. TIMP-1 is the major natural inhibitor of MMPs. Aim of the study was to investigate the synovial membrane (SM) expression of MMP-1, MMP-3, MMP-13 and TIMP-1 in JIA.

Patients and Methods: SM obtained at synovectomy or arthroplasty from 9 JIA patients were studied. SM from an adult RA patient and from a 13-year old girl who underwent post-traumatic meniscectomy were also studied. Immunohistochemical study was performed according to standard technique. The following monoclonal antibodies were used: anti-CD68 (Dako, Denmark), anti- MMP-1, -MMP-3, -MMP-13, -TIMP-1 (Chemicon International, Canada). Slides were evaluated by 2 expert pathologists unaware of diagnosis according to the number of positive cells/high power field (hpf/40x).

Results: n JIA patients and RA control, MMP-1 and MMP-3 displayed a prevalent localization at the level of the lining layers with a high correlation (Spearman's rank test) with macrophagic infiltration

($r = 0.95$, $p < 0.001$; $r = 0.83$, $p = 0.003$). MMP-13 was expressed in 8/9 JIA patients and localized almost exclusively to the sublining areas. TIMP-1 tissue distribution was similar to that observed for MMP-1 and -3, even if with a lower intensity of staining.

Conclusion: In JIA overexpression MMP-1 and MMP-3 is clearly related with the degree of synovial inflammation. Inadequate expression of their tissue inhibitors may represent a crucial event for the development and perpetuation of tissue damage.

P005 MOLECULAR MECHANISMS THAT SHAPE THE KAPPA GENE REPERTOIRE OF CD19⁺ SLE B CELLS

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The human kappa chain repertoires from genomic V_kJ_k rearrangements of individual peripheral CD19⁺ B cells of two patients with systemic lupus erythematosus were analyzed by single cell PCR technique. 226 productive (pr) and 189 nonproductive (npr) V_kJ_k rearrangements were sequenced and compared to the adult IgM⁺ peripheral B cell V_kJ_k repertoire in addition to a previously reported peripheral B cell V_kJ_k repertoire of one SLE patient and to the human cord blood V_kJ_k repertoire. All six V_k families were present, but the distribution was nonrandom. In npr V_k1, V_k2 and V_k6 families were less frequent than expected, V_k3 were as frequent, and V_k4 and V_k5 were more frequent. Of interest, the npr SLE V_k repertoire did not differ significantly from the npr cord blood V_kJ_k repertoire. In comparison to the previously reported npr SLE V_k repertoire V_k2 rearrangements were significantly less frequent. Compared to the normal adult npr V_k repertoire V_k1 were as frequent, V_k2 and V_k3 families were less frequent, and V_k4 and V_k5 were more frequent. Furthermore, the V_k1 and 5 families were negatively selected contributing 30.5% and 7.1% in pr, respectively. In contrast, the V_k3 family was positively selected, contributing 37.6% in pr because of positive selection of L2, and A27. B3 (V_k4) and B2 (V_k5) were overrepresented in npr and not selected in pr, whereas O18/O8 was present as expected in npr and further negatively selected. J_k usage was nonrandom and resembling the neonatal repertoire. CDR3 average length was 27.1 bps in npr and 27.8 bps pr. Compared to adults, junctional diversity was as diverse due to comparable TdT and exonuclease activity at the V_kJ_k joint.

The usage of V_k genes within two SLE patients is biased by intrinsic molecular processes and selection after light chain expression, and is resembling in part the neonatal V_kJ_k repertoire.

P006 MANNANOSE BINDING LECTIN (MBL) POLYMORPHISMS INFLUENCE SUSCEPTIBILITY TO SYSTEMIC ONSET JIA (SYS-JIA) IN AN AGE DEPENDENT MANNER

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Background: Children with SYS-JIA are acutely unwell and often present with a high fever and evanescent rash, features that are highly suggestive of an infectious trigger.

Mannose binding lectin (MBL) is a serum protein important in innate immune defence. Serum levels of MBL are influenced by polymorphisms within the gene. This study aimed to establish whether any association exists between MBL polymorphisms and SYS-JIA.

Methods: 121 children with SYS-JIA from the UK National Repository for JIA and 156 UK Caucasian controls were typed for the two structural polymorphisms found in Caucasians (codon 52 and 54) using PCR-SSP based techniques.

Results: Comparison of allele frequencies between SYS-JIA patients as a whole and controls revealed no significant differences. However, age specific effects were observed. Children with a disease onset of <2 years had a higher frequency of codon 54 mutant alleles than those with a disease onset ≥ 2 (20.8% vs 9.3%, $p=0.03$). Whereas, children with a disease onset of ≥ 5 years of age had a higher frequency of codon 52 mutant alleles than those with a disease onset <5 (11.2% vs 3.9%, $p=0.03$).

Conclusions: MBL deficiency due to codon 54 mutation causes an increased susceptibility to SYS-JIA in children under the age of 2

years at disease onset. In contrast, in children with a disease onset before the age of 5 years an increased frequency of codon 52 mutant alleles is detected. These findings imply that, dependent on the age of onset of disease, different infectious triggers are important in susceptibility to SYS-JIA.

P007 INTRAARTICULAR ALTERATION OF TRYPTOPHAN METABOLISM IN JUVENILE IDIOPATHIC ARTHRITIS

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Object: The metabolism of L-tryptophan (L-Trp) plays an essential role in maintaining T cell proliferation. It is regulated by the tryptophan-catabolizing enzyme indoleamine 2,3-dioxygenase (IDO). Under certain conditions expression of IDO has been shown to correlate with the concentration of interferon γ (INF γ) and iNOS.

Material and methods: Samples derived from peripheral blood (PBMC: JIA patients n=30, controls n=9) and joint punctures (IAMC: JIA patients n=24). IDO, INF γ and iNOS were analysed using the Taq-Man technology. L-Trp was measured in cell lysates and plasma/supernatants using HPLC. Subsets of leukocytes (CD4, CD14) were separated with magnetic beads.

Results: Intraarticular IDO concentration was significantly higher than in PBMC. Concentrations of IDO and INF γ showed good correlation only in IAMC. No significant differences were observed analysing iNOS and INF γ . L-Trp was found in equal concentration in blood plasma and joint fluid. However, there were significant concentrations of L-Trp analysing intraarticular monocytes as well as lymphocytes.

Discussion: Our data support a regulatory function of INF γ on IDO expression in IAMC but not in PBMC. In sharp contrast to in vitro systems, we found an inverse correlation of IDO and L-Trp. We found IDO expression not to be limited to monocytes but also to be present in lymphocytes.

Conclusion: Despite increased intraarticular IDO expression, we detected relevant levels of intraarticular L-Trp. This would enable intraarticular T cells to escape from "immunosuppression by tryptophan starvation" which has been shown to be a relevant mechanism of T cell regulation in other models.

P009 MEASUREMENT OF BONE PARAMETERS IN COLLAGEN INDUCED ARTHRITIS BY QUANTITATIVE COMPUTED TOMOGRAPHY

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Objective: The abnormalities of bone in inflammatory arthritis - including the mechanisms or agents responsible - are still incompletely understood. In the present study, measurements by peripheral quantitative computed tomography (pQCT) were done in mice suffering from collagen induced arthritis (CIA) to establish a model for detailed studies on bone in inflammatory arthritis.

Material and Methods: Arthritis was induced in adult male DBA/1J mice by injection of bovine collagen II. An arthritis score was determined every week. A specialized pQCT device with high resolutions (Stratec Medizintechnik, Germany) was used to measure cortical density, trabecular density, cortical area and cortical thickness on the left proximal tibia.

Results: In control animals there was a slight increase of weight. Cortical density remained constant whereas there was an increase in cortical thickness and area. Trabecular density remained constant. In mice suffering from arthritis trabecular density decreased. Cortical density remained constant as well as cortical area.

Conclusions: Measurement of various bone parameters and therefore a detailed analysis of changes is possible in CIA mice. Mice suffering from arthritis show a decrease in trabecular density and a relative decrease in cortical area relative to control animals whereas cortical density remains constant. This model provides the basis for further standardized studies examining bone changes in inflammatory arthritis with or without treatment.

P011 IDENTIFICATION OF JOINT INFLAMMATION SPECIFIC T CELL RESPONSES IN JUVENILE IDIOPATHIC ARTHRITIS: POTENTIAL TARGETS FOR IMMUNOTHERAPY

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Objective: Juvenile Idiopathic Arthritis (JIA) is an auto-immune disease in which autoreactive T-cells play a central role in joint inflammation and destruction. The goal of our present study was to identify T cell responses in JIA against joint inflammation specific antigens.

Methods: The putative self-epitopes were selected by a computer search strategy designed for the rat model of Adjuvant Arthritis (AA), based on crossrecognition of the arthritogenic T cell clone A2b of mycobacterial HSP65 178-186 peptide and cartilage-associated components, suggesting molecular mimicry between a mycobacterial and a cartilage-derived epitope. A selection of human analogues of the recognized peptides in AA was made, and tested for T cell recognition in JIA patients by measuring proliferative activity of peripheral blood mononuclear cells.

Results: 4 out of 11 of the selected self-peptides were recognized by at least 20-40 % of JIA patients. Among these are peptides from the matrix metalloproteinase family (MMP) and peptides from the aggrecan/versican proteoglycan family. MMP-molecules are known to be involved in rheumatoid arthritis joint destruction, whereas the aggrecan protein plays a role in repair processes of cartilage.

This suggests that we have found T-cells, capable of reactivity to self antigens based on molecular mimicry with mycobacterial antigens.

Conclusion: With the identification of T cell epitopes inducing proliferative responses in JIA patients we have found potential targets for immunotherapy. Further analysis will show whether the found reactivity has to do with disease induction/maintenance or disease regulation/suppression.

P014 REMITTING OLIGOARTICULAR JIA: AN ACTIVE ROLE OF CD4CD25 REGULATORY T CELLS?

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Recently it became clear that, also in human, specialized regulatory T-cells expressing a CD4+CD25+CD45RO phenotype exist as part of the normal immune repertoire. These cells are dependent on signaling through CTLA4 and seem to have an important role in controlling autoimmunity. We hypothesized whether differences in CD4CD25 regulatory cells between oligoarticular and polyarticular JIA patients add to the differences in clinical course and determined number, phenotype and intracellular cytokine production of CD4CD25 regulatory T-cells in both groups. During remission of disease the number of CD4CD25 cells in peripheral blood of oligoarticular patients is comparable to the number in polyarticular patients. More than 98% of the CD4CD25 cells in blood are CD69-CD40L-, indicating that CD25 acts not merely as an activation marker. During disease activation in both oligoarticular and polyarticular patients the number of CD4CD25CD69-CD40L- cells increases. However, CTLA4 becomes up regulated on CD4CD25+ cells in oligoarticular, but not in polyarticular patients. In synovial fluid of 4 OA-JIA patients the number of CD4CD25+ cells is much higher than in peripheral blood, half of them also expressing CD69. Still, CTLA4 expression on all CD4CD25+ cells in SF is an 8-fold higher compared to CD4CD25+ cells in peripheral blood. We have indications that in oligoarticular JIA patients these cells are capable of producing IL10. Conclusion: In oligoarticular JIA patients CD4CD25 regulatory cells seem to play an important role in controlling disease by up regulation of CTLA4 and local production of IL10. Polyarticular patients were lacking this up regulation of CTLA4.

P015 INCREASED LEVELS OF SOLUBLE ADHESION MOLECULES IN RHEUMATIC FEVER

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Acute Rheumatic Fever results from abnormal immune response after Group A streptococcal pharyngitis but its pathogenesis is not completely elucidated. The participation of adhesion molecules was investigated in different stages of the disease by analyzing the levels of soluble forms of ICAM and ELAM. Serum levels sICAM and sELAM were measured with commercial ELISA kits in 9 children with rheumatic heart disease during the first month of symptoms (RHD-a), in 6 children with rheumatic heart disease in whom the carditis had started more than one month before (RHD-b), and in 20 normal controls (NC). sICAM levels in RHD-a were higher compared to RHD-b or normal controls (RHD-a = 378.11 ± 204.31 ng/ml, RHD-b = 238.79 ± 112.17 ng/ml, NC = 250.26 ± 72.51 ng/dl), although some patients in the group RHD-b presented high levels of sICAM. Serum levels of sELAM did not show significant differences when we compared RHD-a, RHD-b and NC (RHD-a = 50.92 ± 28.28 ng/ml, RHD-b = 47.79 ± 19.94 ng/ml, NC = 48.73 ± 19.70 ng/ml). These findings suggest that increased expression of some adhesion molecules in rheumatic heart disease could be involved in the immunopathogenesis of heart tissue damage. Since increased levels of sICAM were observed in some patients after many months of the acute carditis, it is possible that subclinical inflammatory activity is still present and may explain the progression of cardiac lesions observed in some patients. Although soluble adhesion molecules measurement lack specificity, longitudinal studies may establish their clinical usefulness for monitoring the prognosis in these patients. Furthermore, in the future, modulation of these molecules can play an important role in the treatment of rheumatic fever.

P016 EPITHELIAL EXPRESSION OF MRP8 AND MRP14, MODULATORS OF LEUKOCYTE ADHESION, DURING THE INITIAL PHASE OF SYSTEMIC ONSET JUVENILE RHEUMATOID ARTHRITIS

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Systemic onset juvenile rheumatoid arthritis (SOJRA) is an inflammatory disease which involves multiple organs such as liver, spleen, joints, lung, heart and skin. As for any other systemic autoimmune disease the pathophysiological mechanisms are not well understood, but it is widely accepted that activation of the innate immune system plays an important role in the pathophysiology of this disease. MRP8 (S100A8) and MRP14 (S100A9) are two calcium binding proteins which are expressed by neutrophils and monocytes during inflammatory processes whereas they cannot be found in lymphocytes or resting tissue macrophages. Complexes of both proteins are relevant during activation of phagocytes via modulation of cytoskeletal-membrane interactions. Analysing skin biopsies of SOJRA- patients during the early phase of disease we found that, beside activation of vascular endothelium and infiltration of leukocytes, epithelial activation is an initial phenomenon in this disease as shown by expression of MRP8 and MRP14 by keratinocytes. Infiltrating leukocytes also express these two proteins at high levels. Serum concentrations of both proteins reflect disease activity of SOJRA and decrease dramatically in patients undergoing autologous bone marrow transplantation. Since MRP8/ MRP14 are secreted by leukocytes and keratinocytes and have been shown to promote leukocyte adhesion to endothelial cells our data point to a novel pathomechanism in a systemic autoimmune disease in which epithelial cells play an active role.

P017 IL-15 EXPRESSION IN JUVENILE RHEUMATOID ARTHRITIS AND IN SCID MOUSE - HUMAN JRA SYNOVIUM MODEL

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Objectives: This study sought to (1) to assess expression of IL-15 in synovium derived from patients with different clinical forms of JRA, and (2) to evaluate a SCID model of JRA as an approach to study the mechanisms of IL-15 involvement in JRA pathophysiology.

Methods: Thirty three synovial tissue samples from patients with JRA, 7 from patients with RA, and 13 samples from patients with non-autoimmune arthropathies, were analyzed for the expression of IL-15 utilizing the dual approach of RNase Protection Assay and immunohistochemical analysis. The expression of IL-15 was also assessed in JRA synovial tissue fragments that had been implanted into SCID mice.

Results: The overall levels of IL-15 mRNA in the entire group of JRA patients were significantly higher than in the control group (mean \pm SD: 0.393 ± 0.244 vs 0.212 ± 0.085 of GAPDH expression, $p < 0.001$). When JRA patients were stratified based on the type of disease onset, higher values for IL-15 mRNA were noted in early-onset pauciarticular and polyarticular onset forms of the disease, while systemic onset disease was associated with lower levels of expression. Furthermore, the presence of IL-15 protein was confirmed by positive immunohistochemical staining in 4 of 5 synovial tissue samples. IL-15 continued to be expressed in JRA synovial tissue fragments implanted into SCID mice in parallel with other characteristics of synovial inflammation.

Conclusions: JRA synovium is characterized by increased levels of IL-15 expression. Effects of blocking IL-15 in *SCID mouse - human JRA synovium* chimeras, are being investigated.

P018 CAPSULAR DISTANCE IN THE HIP OF THE CHILD - NORMAL VALUES WITH US AND MRI

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Introduction: In a patient with juvenile idiopathic arthritis (JIA) and clinical signs of hip synovitis confirmed by ultrasonography (US), magnetic resonance imaging (MRI) revealed synovial proliferation and effusion mainly located posteriorly. This finding suggested that examination of the hip joint with US imaging of only the anterior aspect of the joint may not be sufficient when joint inflammation is suspected. Study I: Our aim was to establish the normal values for the anterior (ACD) and posterior (PCD) "capsular distances" by means of US and MRI. Study II: To evaluate any possible correlation between age, length, weight and ACD.

Patients and methods: Study I comprised 14 healthy children (9 girls and 5 boys; 28 hips) without any history of hip joint disease. One subject in each year span between 5-18 years were included. US was performed ventrally in a plane along the axis of the neck of femur with a 7.5 MHz linear transducer. The children were examined in both hips in three different positions; i.) supine with the hips in extension and spontaneous outward rotation of 10-15°, ii.) supine with the hips internally rotated 45° iii.) in a prone position with the heels separated and the hips in inward rotation of 45°. US was performed from the dorsal aspect in the same plane as described above. The ACD and PCD were measured by three independent examiners at the same occasion and ACD in the spontaneous external rotation was measured twice. MRI was performed with the children supine with the hips in extension and spontaneous external rotation of 10-15°, and then with the hips internally rotated 45°. ACD and PCD were measured. Study II comprised 28 healthy children (8 girls and 20 boys; 56 hips), two subjects in each year span between 3-16 years. US was performed with a 10-5 MHz linear transducer, by the same experienced examiner, ventrally in the same plane as in the previous study and in the positions described in i.) and ii.). Both hips were examined and each measurement repeated twice. Weight and length were recorded by an experienced children's nurse.

Conclusions: The PCD can be identified and measured by US with the hip in inward rotation. There was a good correlation between US- and MRI-measurements of the ACD and PCD. The mean ACD measured by US increased significantly ($p = 0.0001$) in inward rotation of the hip. No correlation of ACD with age, length or weight was found.

P023 TNF ALPHA PROMOTOR GENE POLYMORPHISMS IN JIA (JUVENILE IDIOPATHIC ARTHRITIS)

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Objective: To study the incidence of the four polymorphisms of the TNF alpha promoter gene: -308, -238, -376, -163, described so far, in systemic onset and oligoarticular JIA patients, the two ends of the spectrum of the inflammatory disease.

Patients and Methods: DNA was obtained using standard procedures from PBMC of 29 oligoarticular JIA patients, 26 systemics and

68 controls. MHC class I and class II alleles (A,B and DR) were determined using low resolution PCR technique. Screening for the presence of any mutation was performed using polymerase chain reaction-denaturing gradient gel electrophoresis (PCR-DGGE), followed, if positive, by restriction fragment length polymorphism analysis (RFLP). Statistical study was performed using the SPSSv9.0 statistical package.

Results: Our patients resembled other JIA populations regarding MHC class II associations with the oligoarticular subgroup. None of the four studied polymorphisms showed to be present more often in JIA patients than in controls. However, -308 polymorphism was strongly associated with B8 and DR3 ($p < 0.001$) and with the extended haplotype A1B8DR3 ($p = 0.003$). On the other hand, -376 and -238 polymorphisms presented always together but in one patient and were associated with the presence of B18 ($p < 0.001$). B35 seemed to be "protective" ($p = 0.012$).

Conclusions: The four TNF alpha promoter gene polymorphisms studied did not show any differences between patients and controls. The association of the -308 polymorphism with the extended haplotype A1B8DR3 was confirmed. An association between B18 and the -376_-238 tandem polymorphism is described. The results of the present study suggest that other factors different to the upregulation of the TNFalpha promoter gene have to play an important role in the overproduction of TNFalpha in some JIA patients.

P024 ASSOCIATION OF AN INTERFERON GAMMA RECEPTOR 1 (IFN γ R1) SNP WITH SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS (SJIA)

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In chronic inflammation there is a persistent imbalance of pro- and anti-inflammatory cytokines. The combined effect of mutations (in a number of genes involved in these pathways) may influence the reaction of the adaptive immune response to environmental agents and result in disease. The IFN γ R1 gene contains a mutation hotspot that confers dominant susceptibility to mycobacterial infection. A T to C polymorphism in intron 2 was shown an association with IgE levels in controls. Since T cells are polarised in JIA to Th1 or Th2 subtypes, we tested for association between sJIA and the AP1 polymorphism. A case control study was performed. Genotypes (TT, CT or CC) were obtained by RFLP and sequence specific oligonucleotide probing.

A significant difference in frequency of the genotypes was found between sJIA patients ($n = 75$) and controls ($n = 243$) ($p < 0.0001$). We found that there was an over representation of the CC genotype in sJIA patients. The association of the C allele with sJIA suggests that AP1 could be a functionally polymorphism, or in linkage disequilibrium with another functionally significant polymorphism elsewhere.

P025 HLA-DRB1-DQB1 ALLELES IN CHILDREN WITH RHEUMATIC HEART DISEASE IN LATVIA

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In Latvia since 1991 rheumatic fever cases tend to grove, reaching incidence 7,5/100 000 in 1998 and 2,1/100 000 in 2000.

The aim of this study was to investigate the association among different groups of the rheumatic heart disease (RHD) with HLA class II DRB1 and DQB1 alleles and/or haplotypes.

Materials and methods: The HLA-DRB1 and DQB1 typing has been carried out with the PCR - SSO method. Children with rheumatic heart disease ($n = 60$) and a healthy control group ($n = 60$) were analysed for HLA class II.

Results: Our data show that RHD was characterised by a distinct distribution of HLA class II alleles with increase of DRB1*07 OR=2,31, $p < 0,05$; HLA-DQB1*0401/0402 (OR= 6,26, $p < 0,05$) are positively associated with rheumatic heart disease (RHD). The trend toward protective association with the HLA-DRB1*06 (13) (OR=0,13, $p < 0,0007$); HLA-DQB1*0501 (OR=0,12, $p < 0,002$) was observed.

Conclusion: For 67,2% of patients treated from Rheumatic fever rheumatic hart disease have been diagnosed.

Our preliminary data show that HLA-DRB1 and HLA-DQB1 alleles/haplotype are associated with risk or protection from RHD.

P026 THE ROLE OF RANK AND RANKL IN THE PATHOGENESIS OF JUVENILE IDIOPATHIC ARTHRITIS

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Background: Bone remodelling and loss are regulated in part by a balance between RANK (receptor activator of NF- κ B), its ligand RANKL, and the soluble receptor OPG. RANKL is expressed on activated T cells and osteoblasts, and interacts with RANK on dendritic cells or osteoclasts, leading to osteoclast activation and bone resorption. T cells in the JIA synovium are activated and have a Th1 phenotype. Also, JIA is frequently associated with osteoporosis and/or bone erosions.

Objective: To investigate expression of RANK and RANKL in the JIA synovium.

Methods: Paired samples of PBMC and synovial fluid mononuclear cells (SFMC) from children with oligoarticular and polyarticular JIA, and control PBMC, were studied using RT-PCR and flow cytometry. We analysed expression of RANK and RANKL in T and non-T cell populations.

Results: RT-PCR on samples from 7 children with JIA showed that RANKL was expressed at higher levels in synovial T cells than either non-T cells or paired peripheral blood T cells, and that RANK was strongly expressed in both compartments. PBMC from controls showed no RANKL expression and only low levels of RANK mRNA. FACS analysis showed a large population of SFMC expressing RANK, which co-localised with markers characteristic of a dendritic cell phenotype (CD98, CD86, CD11c and HLA-DR). We detected no DC-SIGN expression until after culture in GMSCF and IL-4.

Conclusions: We suggest that RANK/RANKL interactions between activated T cells and osteoclasts may play a significant role in bone destruction in JIA.

P027 CRH GENE PROMOTER PLOYMORPHISM AND JIA

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Background: CRH (corticotrophin releasing hormone) is key hormone in the regulation of HPA (hypothalamo-pituitary-adrenal) axis and has an immunomodulatory role. Animal studies have shown that a defective cortisol response can lead to chronic arthritis. Studies in adult RA patients have shown an association with CRH gene polymorphisms. 4 polymorphisms are known of which 3 are in absolute linkage disequilibrium. The *BsmA1* promoter polymorphism alters the consensus sequence for transcription factor GH-CSE2 and hence is thought to have a functional role.

Objective: To establish whether there is an association between the *BsmA1* CRH promoter polymorphism and JIA.

Methods: 464 children with JIA and 263 Caucasian controls were typed for the promoter polymorphism using PCR-RFLP techniques. Genotype frequencies were compared between all patients and controls and between the different JIA subgroups using the χ^2 test. The controls were also typed for the *Afl111* polymorphism to determine if they are in LD with *BsmA1*.

Results: There was no difference in the genotype frequencies between all patients and controls ($p=0.981$) or between any of the JIA subgroups ($p=0.498$). Also, genotype frequencies were not significantly different when patients were subdivided by antinuclear antibody status or sex. The *Afl111* polymorphism was shown to be in complete linkage disequilibrium with the *BsmA1* polymorphism as observed in previous reports in the literature.

Conclusions: JIA is not associated with a *BsmA1* CRH gene promoter polymorphism.

P028 X-CHROMOSOME INACTIVATION ANALYSIS IN A FEMALE CARRIER OF IMMUNE DYSREGULATION, POLYENDOCRINOPATHY, ENTEROPATHY, X-LINKED SYNDROME (IPEX)

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IPEX is a severe disorder characterized by immune dysregulation, polyendocrinopathy, enteropathy and X-linked inheritance. The genetic alteration underlying the disease has recently been identified by positional cloning in FOXP3 gene, which codes a transcription regulator whose function is not yet known. An altered thymic

environment seems to be required for the generation of autoreactive cells, as shown by the animal model of the "scurfy" mouse. Female carriers in families of IPEX children are completely healthy. Whether this is due to a normal maturation of "scurfy" T cells in a chimeric thymus or to a selection disadvantage of these cells is not known. X-chromosome inactivation analysis in peripheral blood T lymphocytes may help to address this question. We evaluated X chromosome inactivation in freshly isolated mononuclear cells (B, CD4, CD8, monocytes) and in IL-2 cultured CD4 and CD8 T cells.

Methods: A peripheral blood sample was obtained from the mother of a child affected by IPEX. The woman carries the same mutation of the *Foxp3* gene described on her son, and is completely healthy. B cells (CD19), activated T cells (CD25), CD8 and CD4 T cells were obtained with MoAbs coated magnetic beads. Monocyte were obtained by adhesion to plastic tissue culture plates. T cell were also obtained by T cell negative isolation kit and cultured in RPMI medium with 10% FCS and IL-2. The cells were harvested on the day 14 and sorted in CD4+ and CD4 negative (CD8) using anti-CD4 coated magnetic beads (Dynal, Oslo, Norway). X inactivation study was performed by digesting and amplifying the exon 1 of the *Humara* locus, as described by Notarangelo et al (Life Sci 1997).

Results: We studied X chromosome inactivation in different cells of the mother of a child affected by IPEX. The X-chromosome analysis showed a random pattern of inactivation in all the cell lines tested. Discussion: The present study showed that the percentage of T cell expressing the mutated *Foxp3* allele in the peripheral blood of *Foxp3* mutation carriers is similar to the one of T cell expressing the normal allele. Although the test is not quantitative, these results seem to indicate that *Foxp3* mutation doesn't affect the chance of the single cell to survive or to undergo activation in peripheral blood compartment. These data may suggest that in female carriers normal T cells are able to control "scurfy" T cell or that "scurfy" T cell develop normally in chimerical thymus. The former hypothesis seems not likely as random X-inactivation also in activated T cells. These findings may help to interpret some clinical aspects of the disease.

In our case, now 7 yrs old, we observed a less aggressive course of the disease after the first years of life. Although this may be due to the immunosuppressive therapy he underwent, it is possible that autoreactive T cell generation diminish as thymus activity lowers. This hypothesis might explain a recent case report of a 3 yrs old child affected by IPEX died 2 years after BMT when host T cells raised to 30% (Casanova JL, NenglJMed 2001).

P029 RELATIVE HYPER-ACTH SECRETION IN CHILDREN WITH OLIGOARTICULAR ONSET IDIOPATHIC ARTHRITIS

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Although impaired cortisol response has been demonstrated in adult patients with active rheumatic disorders, few data are available about this topic in childhood.

We have investigated ACTH and cortisol plasma concentrations in a series of 13 patients (10 female, 3 male) with oligoarticular onset idiopathic juvenile arthritis (oJIA) in inactive phase of their disease according to Pavia core-set criteria. No patient was on steroid treatment or steroid intra-articular injection has not been performed since at least 6 months. The patients were prepubertal, without clinical signs of endocrine disease. Out of them 11 patients were ANA positive. We have ruled out patients with non chronic post-infectious arthritis. ACTH and cortisol (CRI) were evaluated at 8 a.m. and at noon. The endocrinological assay was performed using radioimmuno-logic tests. The data were matched with those obtained from a series of 11 healthy prepubertal children of control (C). The results are summarised in the table.

Our experience seems to suggest the existence of an impaired cortisol production also in inactive oJIA patients. In our cohort an increased ACTH secretion was necessary to maintain a normal adrenal function, thus suggesting the possibility of a partial resistance to ACTH in oJIA patients, irrespective to the disease activity, as already demonstrated in adult patients with rheumatoid arthritis.

Table 1

Hour	ACTH OIA	ACTH C	p	CRI OIA	CRI C	p
8.00	35.6 ± 4.4	23.8 ± 6.1	<0.001	15 ± 7.5	12.4 ± 2.5	NS
Noon	23.8 ± 9.1	15.4 ± 5.0	0.037	8.8 ± 3.4	8.3 ± 1.6	NS

P030 CLASSIFICATION OF 154 BRAZILIAN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA) USING THREE DIFFERENT CRITERIA

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In order to evaluate 3 different classification criteria for JIA, we studied 154 Brazilian children with chronic idiopathic arthritis followed at our Unit between 09/2000 and 02/2001. ACR (1976), EULAR (1977), ILAR (1997), ESSG for spondyloarthropathy and Vancouver criteria for juvenile psoriatic arthritis (JPsA) were applied. ACR and EULAR criteria excluded 17 and 19 patients respectively whereas the ILAR criteria excluded only 2 due to juvenile ankylosing spondylitis (JAS). In addition, 13 poly RF- children were re-classified by ILAR criteria in other categories such as JPsA, extended oligo and enthesitis related arthritis (ERA). We conclude that ILAR criteria is more enclosing and allows a more homogeneous classification of JIA despite its limitations reflected by the high percentage of children classified as "others", which could be solved at least in part by prospective studies involving genetic background of JIA.

Table 2 Classification of 154 JIA patients

ACR (N=137)		EULAR (N=125)		ILAR (N=152)	
Subtype	N (%)	Subtype	N (%)	Subtype	N (%)
Systemic	18 (13)	Systemic	18 (14)	Systemic	18 (12)
Pauci	47	Oligo	47 (38)	Oligo	37 (24)
ANA +	22 (16)	Poly RF -	55 (44)	Persistent	27 (73)
ANA -	18 (13)	JAS	2 (2)	Extended	10 (27)
Poly RF +	24 (18)	JPsA	3 (3)	Poly RF +	24 (16)
Poly RF -	55 (40)	JSA	0	Poly RF -	42 (28)
		JEA	0	ERA	13 (9)
				JPsA	5 (3)
				Others	13 (9)

JSA - juvenile spondyloarthropathy, JEA - juvenile enteroarthropathy.

P031 PATTERNS OF JOINT INVOLVEMENT AT ONSET DIFFERENTIATE OLIGOARTICULAR JUVENILE PSORIATIC ARTHRITIS FROM PAUCIARTICULAR JRA

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Objective: To compare the patterns of joint involvement of oligoarticular onset juvenile psoriatic arthritis (Oligo-JPsA) and pauciarticular onset juvenile rheumatoid arthritis (Pauci-JRA) patients in order to estimate the predictive performance of specific patterns for the diagnosis of Oligo-JPsA.

Methods: Twenty-three children who fulfilled the diagnostic criteria for JPsA (Vancouver Criteria) and who had fewer than 5 joints involved in the first 6 months of disease (Oligo-JPsA), and 64 children with Pauci-JRA (ACR criteria) were enrolled. Patients were also classified with respect to the ILAR criteria for juvenile idiopathic arthritis (JIA). Patterns of joint involvement at onset of disease and their ability to differentiate between Oligo-JPsA and Pauci-JRA/Oligo-JIA were evaluated.

Results: Small joint disease (defined as involvement of any of the MTP, PIP or DIP joints of the foot, or MCP, PIP or DIP joints of the hand) was significantly more frequent in Oligo-JPsA than in Pauci-JRA at disease onset. The odds of Oligo-JPsA patients having small joint disease or wrist disease within 6 months of disease onset were much higher than those with Pauci-JRA or Oligo-JIA ($p < 0.05$ or 0.001).

Conclusion: Small joint disease and wrist disease are suggestive of Oligo-JPsA. The use of a criterion consisting of small joint disease, and/or wrist disease and/or dactylitis instead of dactylitis alone may increase the ability to differentiate Oligo-JPsA from Pauci-JRA or Oligo-JIA.

P032 EVALUATION OF ILAR CLASSIFICATION CRITERIA FOR JUVENILE IDIOPATHIC ARTHRITIS IN TURKISH CHILDREN

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The aim of this study is to evaluate the ILAR classification criteria in Turkish children with chronic rheumatic diseases.

This study was conducted on 184 children with chronic rheumatic disease. The diagnosis of juvenile rheumatoid arthritis (JRA), juvenile spondyloarthropathies (JSpA) and juvenile psoriatic arthritis (JPsA) was put according to ACR, ESSG and Vancouver classification criteria, respectively. All cases were reevaluated according to ILAR classification criteria retrospectively. Fifty-one of the children in the study group had systemic onset JRA, 45 (24.4 %) had oligoarticular, 41 (22.2 %) had polyarticular JRA, 36 (19.5 %) had undifferentiated JSpA and 11 (5.9 %) had JPsA.

179 (97.2 %) out of 184 children were reclassified according to ILAR criteria. Fifty-one children with systemic JRA were reclassified as systemic arthritis. Thirty-two of 45 children with oligoarticular JRA were diagnosed as oligoarthritis, 9 were diagnosed as extended oligoarthritis and one patient diagnosed as enthesitis related arthritis (ERA). Three of the children could not be classified due to the presence of psoriasis in family history. Thirty-four of 41 children with polyarticular JRA were reclassified as polyarthritis and 6 of them as seropositive polyarthritis. One patient could not be classified as he meets the criteria of this and ERA group. Thirty-five of 36 children with JSpA met the ERA criteria. The remaining one case met the criteria of seropositive polyarthritis and he was included in the other's group.

In conclusion, ILAR classification criteria is also applicable for Turkish children with JIA. It is more practical as it covers both early stages of JSpA and JPsA. We believe that ILAR classification criteria would be more applicable with minor changes.

P034 RECLASSIFYING JCA PATIENTS FROM A FORMER DATABASE

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Introduction: Different classification criteria have been used for JRA (ARA/ACR) and JCA (EULAR). Recently criteria for JIA were proposed by ILAR. Follow-up data from former studies with JRA or JCA patients are more meaningful if reclassification is possible.

Questions are: is this possible and what are the difficulties?

Patients and methods: The Dutch sulfasalazine trial database containing the following data: onset- and course type of JCA, family history of psoriasis or HLA-associated disease, age at onset, gender, HLA-B27, rheumatoid factor (Rf) and other disease symptoms of 37 pauci- and 31 polyarticular JCA patients.

Results: The polyarticular patients were reclassified as Rf negative (20), Rf positive (8) and 3 as enthesitis related arthritis (2 boys > 8 years and HLA-B27+, 1 girl HLA-B27+ and family history of Bechterew). The pauciarticular patients were reclassified as follows: persistent oligoarthritis (18), extended oligoarthritis (8), polyarticular Rf positive (1) (polyarticular course; Rf+), psoriatic arthritis (1) (nail psoriasis), enthesitis related arthritis (5) (4 boys > 8 years and HLA-B27+ or anterior uveitis, 3 also sacroiliac joint pain (s.i.-pain); 1 girl with family history of acute anterior uveitis and s.i.-pain). Patients with a family history of psoriasis (3) and HLA-associated disease (1) had to be excluded and were difficult to reclassify not fulfilling the criteria for any specific category; so remaining as 'other arthritis'.

Conclusion: Reliable reclassification is possible if the database contains sufficient information, especially proper recording of other disease symptoms as psoriasis, dactylitis, nail abnormalities, enthesitis, s.i.-pain, acute anterior uveitis and family history.

P035 RECLASSIFICATION OF THE JUVENILE IDIOPATHIC ARTHRITIS PATIENTS ACCORDING TO THE ILAR CRITERIA

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Juvenile idiopathic arthritis (JIA) is a heterogeneous group of chronic arthritides of childhood, previously termed as juvenile chronic arthritis (JCA). The aim of the study: to reclassify the patients with previous diagnosis of JCA and validate the Durban criteria. Patients and method: The retrospective analysis of the history of 148 in-patients with diagnosis of JCA, hospitalized in the period July 1995 - May 2001, was performed. Average age was 12yrs (2-20), f 108 pts, m 40 pts.

Results of the classification are presented on the table.

Table 3

	EULAR classif. (%)	ILAR criteria						ERA	other
		syst.	poly RF-	poly RF+	oligo	ext. oligo	ERA		
Syst.	17 (11,49)	17							
Poly	49 (33,10)		31	13					5
Oligo	82 (55,41)				42	18	11	11	
All	148	17	31	13	42	18	11	16	
%	100	10,49	20,95	8,78	28,38	12,16	7,43	10,81	

Sixteen patients (10.81%) did not fulfill ILAR criteria and were designated as unclassified. Among these pts 31,25% had oligoarthritis with RF in sera, 25% pts had oligoarthritis and family history of psoriasis at the first degree relative.

Conclusion: Our results correspond to the previously published data, that above 90% children with chronic arthritides could be clearly classified according to new classification criteria. ILAR criteria seems as the attempt to understand better the outcome of these disorders.

P036 ESTIMATION OF ANTICARDIOLIPIN (ACL), ANTI- β_2 GLYCOPROTEIN I (ANTI- β_2 GPI) ANTIBODIES AND LUPUS ANTICOAGULANT (LA) IN A PROSPECTIVE LONGITUDINAL STUDY OF CHILDREN WITH JIA

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Objective: aCL have been frequently detected in juvenile idiopathic arthritis (JIA), but have not been associated with disease activity or the clinical features of the antiphospholipid syndrome (APS). Our aim was to determine the values of aCL, anti- β_2 GPI and LA in serial samples from children with JIA and to investigate the clinical significance of these antibodies.

Methods: The values of aCL, anti- β_2 GPI and LA were prospectively followed in 28 children with JIA from the very beginning of the disease. aCL and anti- β_2 GPI were assayed by an ELISA method. Two monoclonal β_2 GPI dependent aCL (HCAL and EY2C9) were used as calibrators. LA was determined by a modified dilute Russell viper venom time test.

Results: Thirteen (46.4%) children with JIA were positive for aCL already at the first referral to our center. During the follow-up, the frequency of aCL decreased from 46.4% to 28.6%, however, it remained significantly higher as compared with healthy children. In contrast, for anti- β_2 GPI the difference in frequency rate between children with JIA and healthy children was not statistically significant. Serial determination of aPL levels in JIA patients revealed frequent fluctuations. Positive aCL persisted over time in 6 (21.4%) children with JIA, six (21.4%) children were initially positive for aCL, but became later negative, and three (10.7%) children were initially negative for aCL and became later positive. Persistently positive anti- β_2 GPI were observed during follow-up only in one patient, while none of the patients was persistently positive for LA. Associations between aCL, anti- β_2 GPI or LA and disease activity could not be established. No patient with positive aCL, anti- β_2 GPI or LA showed any clinical feature of APS.

Conclusion: The discrepancy between the presence of aCL and anti- β_2 GPI might indicate that production of aCL in JIA is associated with an infectious trigger. Furthermore, the low frequency of anti- β_2 GPI and LA could explain limited prothrombotic potential of aPL observed in JIA. However, we found a distinct group of JIA patients with persistently positive aCL, which are potential risk children and should be monitored carefully.

P037 DIAGNOSTIC VALUE OF FERRITIN AND GLYCOSYLATED FERRITIN IN CHILDREN WITH SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

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We performed a retrospective study of 44 children less than 15-year-old, who had serum ferritin and glycosylated ferritin (GF) assays in our Department of Pediatrics to determine the usefulness of these

measurements in the diagnosis of systemic juvenile idiopathic arthritis (JIA). Patients were classified as having JIA according to the EULAR criteria (15 children) or control diseases, including other systemic diseases: Kawasaki disease, periarteritis nodosa, Castleman's disease, chronic recurrent multifocal osteomyelitis (control group 1: 17 children) or infectious diseases (control group 2: 12 children)

The mean ferritin value was significantly higher in the JIA group (4356,3 ± 4872 µg/l) than in the control group 1 (246 ± 202 µg/l) and in the control group 2 (194 ± 132 µg/l) (p < 0,0001). GF was significantly lower in the JIA group (14,2 ± 10%) than in the control group 1 (22,7 ± 15%) (p < 0,05), but not than in the control group 2 (12,1 ± 9,6%). The combination of ferritin 5 times normal with GF level ≤ 10% produced a sensitivity of 46,6% and specificity of 97,4%. All the ten children with ferritin above 1000 µg/l and GF level of ≤ 20% had JIA.

In children, low levels of GF can be observed in other diseases than JIA, especially in infectious diseases and the combination of ferritin 5 times normal with GF level ≤ 10% had a poor sensitivity for the diagnosis of JIA. However it had a high specificity which may help the pediatrician for excluding differential diagnoses.

P038 SAFETY, EFFICACY AND OUTCOME OF EARLY TREATMENT OF SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS WITH RELATIVELY HIGHER DOSES METHOTREXATE AND GLUCOCORTICOID

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Objective: To investigate the results of early and aggressive treatment.

Patients and methods: Ten consecutive patients (pts) with systemic juvenile idiopathic arthritis between 1993-2001 treated more than 6mo—median 31,5mo (range 7-77) and regularly followed-up more than 2y—median 58mo (range 24-94) are included. The protocol consisted of pulse glucocorticoid (gc) followed by conventional dose and simultaneous start of relatively higher dose oral once weekly methotrexate (mtx) - median 0,775mg/kg.wk (range 0,4—1,04). Two pts received initially mtx alone. Therapy was begun at median 1mo (range 0,5-2,5) after onset of fever and median 0,4mo (range 0,1-0,75mo) after hospitalization. All pts were at onset at median age 5,2y (range 1,7-12,3) except one in first relapse at 5,5y of age.

Results: Fever disappeared after median 0,65mo (range 0,3-2,5mo), esr normalised after median 2,75mo (range 1,5-9). Mtx alone for the pt with relapse was effective and the pt is in remission without therapy for 79mo; for the pt at onset was without effect. Gc were discontinued after median 8,25mo (range 2,5-16). Two patients cannot be weaned off gc with 3-4 flares and follow-up for 39 and 77mo. Mtx was discontinued in 5 pts—one of them had flare of disease 4mo apart, the rest are in remission and without therapy for 45, 66 and 79mo (one died of trauma 6mo thereafter). Four pts are currently with mtx and without gc for 3,15,24 and 38mo. Five pts had nausea (only 1 with regular vomiting) which resolved in 3 of them. Two pts had asat/alat up to 10 times rise which persisted for 5 and 7,5mo and resolved after mtx discontinuation. One pt has persistent asat rise 2 times before/during the treatment. Liver biopsy has not been performed.

Conclusion: Current protocol is safe and effective. Mtx alone also can be effective. Mtx cannot prevent relapse after gc discontinuation in all cases. No predictive factors could be found for gc dependence.

P039 NUTRITIONAL STATUS IN JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Nutritional impairment is a recognised complication of juvenile idiopathic arthritis (JIA). Previous studies have utilised many different anthropometric measures, and the nutritional status data published is confusing and inconsistent. For intervention to be appropriate the aetiology of impaired nutritional status in JIA needs to be better understood. This is a cross-sectional study of nutritional status in JIA in a single centre providing secondary and tertiary paediatric rheumatology care. Weight, height, body mass index (all converted to a standardised (SDS) score), percentage ideal weight for height (%WFH) and mid upper arm circumference (MUAC) were

measured. Nutritional impairment was defined as 2 positive out of the following: weight SDS score less than -1.29 ; MUAC less than 10th percentile; %WFH less than 85%.

Results: 141 children with JIA were screened. Median age was 10.8 years (range 1.3–18.3 years). 25 (17.7%) met criteria for nutritional impairment. Weight, height and BMI SDS score and % WFH in this nutritionally impaired group were significantly lower than those with normal nutritional status ($p < 0.001$). The MUAC was below the 10th percentile in all children satisfying criteria for nutritional impairment. The JIA subtype with the highest prevalence of impaired nutritional state was oligoarthritis (persistent).

Conclusion: This preliminary data indicates that impaired nutritional status is a risk factor in all JIA sub-types. Such a high prevalence in persistent oligoarthritis has not been previously reported and may reflect the representative nature of the sample population. Further work to identify factors associated with nutritional risk has begun.

P040 SJOGREN SYNDROME. AN UNEXPECTED DISEASE OCCURRING FOURTEEN YEARS AFTER OLIGOARTICULAR ONSET JUVENILE IDIOPATHIC ARTHRITIS (JIA)

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Primary Sjogren syndrome (SS) is exceptional in children. It can be observed during the course of autoimmune disease such as systemic lupus erythematosus, or connective tissue diseases. Very few cases were reported during the course of JIA, generally during the course of rheumatoid factor positive forms. We report the observation of a girl who suffered of oligoarticular onset JIA in whom clinical and biological features of SS occurred after fourteen years follow-up.

This 21 year old patient was followed since the age of 18 months for an oligoarticular onset JIA with chronic uveitis and positive antinuclear antibodies. At the age of 9, a trend to extension of the joint manifestations occurred. At 18, salivary gland swelling and adenopathies associated to a relapse of arthritis was observed. At 19, fatigue, vomiting, lumbalgia and dysuria led to the discovery of kidney involvement.

Salivary gland histology showed lesions of focal lymphocytic sialadenitis grade IV (Chisholm and Mason score), kidney histology showed 4 sclerotic glomeruli among 17, mononuclear cell infiltrate in the interstitium with fibrotic lesions, no immunofluorescent deposits.

The retrospective study of frozen serum samples situated the occurrence of specific anti Ro 60 SSA and anti La SSB antibodies at the age of 15. HLA typing was A1-2, B8-65, DRB1*0301-07, DQB1*0202, DPB1*02012-0401, a phenotype not associated to oligoarticular JIA except for HLA A2. This observation represents, to our knowledge, the first case of a typical oligoarticular JIA further complicated with SS.

P041 A CASE OF LYMPHEDEMA AND JUVENILE IDIOPATHIC ARTHRITIS IN A GIRL WITH TURNER SYNDROME

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Turner's syndrome (TS) is frequently associated with autoimmune conditions such as thyroiditis, inflammatory bowel disease and diabetes. Recently, association between TS and juvenile idiopathic arthritis (JIA) has been reported and the prevalence of JIA among girls affected by TS seems to be six times greater than expected if the two conditions were only randomly associated.

Lymphedema is a complication shared by the two diseases, more often in association with TS.

We describe a girl affected by Turner syndrome and mental anorexia who developed JIA with a severe lymphedema of lower limbs.

Her father was affected by alopecia. She herself developed alopecia at 8 years of age. The Turner syndrome was diagnosed when she was 10 years old. Analysis showed cariotype mosaicism 45 X/46XX. (10% / 90%). Mental anorexia developed at the age 14 years.

At age of 16, she was admitted to our hospital for fever resistant to antibiotic treatment, rash, arthritis of knees and elbows and lymphedema of lower limbs.

Laboratory data showed high erythrocyte sedimentation rate (ESR), C reactive protein (CRP), ferritin, fibrinogen, and WBC count with neutrophilia and mild anemia. Antinuclear antibodies and Rheumatoid factor were negative. Deep venous thrombosis was excluded by Doppler ultrasound.

The CT of thorax and abdomen showed peritoneal and pleural effusion and liver enlargement. Juvenile idiopathic arthritis was diagnosed and flurbiprofen treatment was started.

After ten days of treatment, despite improvement of fever and arthritis, the non-steroidal anti-inflammatory drugs was stopped because of hypertransaminasemia. Cortisone (prednisone 2 mg/kg/day) was administered with rapid relief of fever, arthritis and lymphedema.

According to previous observations lymphedema is not consistently associated with the course of JIA and does not respond to the therapy. On the contrary, the patient responded rapidly to cortisone. Lymphedema is a rare extra-articular complication of JIA, reported so far a 33 cases, none with Turner syndrome.

P043 LEVEL OF AGREEMENT BETWEEN PARENT AND CHILD RATINGS OF DISABILITY, PAIN AND WELL BEING IN JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Many studies that report disability, pain & well being in children and adolescents with Juvenile Idiopathic Arthritis (JIA) rely on parents as proxy respondents. We investigated the level of agreement between patient & parent reports of disability, pain and well being by comparing responses from the Child Health Assessment Questionnaire (CHAQ).

Method: 6 fathers, 27 mothers & 33 patients with JIA completed the CHAQ in separate locations on the same day (mean age of patients 12.4 years, range 8–16). The only probe used was an explanation of the term “not applicable.”

Results: Patient & parent disability scores showed moderate agreement, weighted kappa 0.52, whereas pain & well being (categorized data) showed low agreement, weighted kappa 0.36 & 0.31 respectively. Bland Altman analysis further demonstrated some agreement in disability scores, but very little agreement in ratings of pain & well being. The ratings of disability agreed excellently on average (mean difference 0.12). However, 95% limits of agreement ranged from -1.1 to 0.87 indicating that we would expect the difference between patient & parent ratings of disability to differ by < 1 in either direction.

Conclusion: These findings suggest that we should not rely on parents as sole informants for assessment of disability, well being and pain when using the CHAQ.

P044 A PROSPECTIVE, RANDOMISED COMPARISON OF VIDEO-ASSISTED AND COMPUTER-ASSISTED ARTHRITIS EDUCATION FOR CHILDREN

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Children with juvenile idiopathic arthritis (JIA) may have psychosocial difficulties and, as adults, are at risk of depression, unemployment, and functional difficulties. Disease education might influence psychosocial adjustment in JIA. Our aim was to compare computer-assisted learning (CAL) and video-assisted learning (VAL), in JIA, using outcome measures including arthritis knowledge and symptoms, treatment adherence, function, and psychosocial well-being. Parental well-being was also assessed.

Methods: Patients were randomised to the CAL or VAL groups. Quantitative data were collected prospectively by self-administered questionnaires pre- and 4 months post-education. Qualitative data were collected through semi-structured interviews.

Results: Of 204 families enrolled, complete data were available from 86 patients (age 7–17 years). No significant differences in demographics, disease subtype, disease severity or co-morbidity were detected between CAL (n=41) and VAL (n=45). Improvements were

found in arthritis knowledge and hope for both CAL and VAL. Self-efficacy, joint stiffness, pain and anxiety were also significantly improved in the VAL group. *($p < 0.01$).

Table 4

	Knowledge (median)		Hope (median)		Efficacy (median)	
	Pre	Post	Pre	Post	Pre	Post
CAL	7/28	12*/28	23/36	27*/36	5.2/10	6.6/10
VAL	6.3/28	13*/28	26/36	31*/36	6.1/10	7.2*/10

Conclusion: Both CAL and VAL were effective sources of disease information; VAL as a disease introduction and CAL during disease progress.

P045 CHRONIC ANTERIOR UVEITIS IN JUVENILE IDIOPATHIC ARTHRITIS (JIA): AN ASSOCIATION WITH EXTENDED OLIGOARTHRITIS

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There is a well recognised association between chronic anterior uveitis (CAU) and oligoarthritis. The ILAR classification identified 2 subgroups of oligoarthritis, persistent (PO: cumulative arthritic joints ≤ 4), and extended (EO: oligoarthritis accumulating >4 joints after the first 6 months). Our aim was to determine the frequency and clinical associations of CAU in EO.

Methods: 925 children listed with the UK paediatric rheumatology registry, were grouped into the 7 ILAR JIA subgroups. For all patients, 30 clinical and laboratory variables were documented, as well as HLA type. Statistical analyses included multivariate analysis, and the unpaired t-test.

Results: 87 of 925 subjects (9.4%) had CAU. Three subtypes of JIA covered 94.3% of CAU: PO (43, 49.4%), EO (27, 31.10%) or polyarthritis RF- (12, 13.79%). In each group, ANA+ was significantly associated with CAU. Of 129 subjects with EO, 27 (20.9%) had CAU. EO subjects with CAU were significantly younger (34.60 ± 28.72 months) than those without CAU (56.08 ± 43.91 months; $p < 0.001$). There was no female predominance; EO girls with CAU = 21, 80.8%, EO girls without CAU = 77, 76.2%. There were no other features specifically associated with the presence or absence of CAU. The frequency of CAU in the PO group was lower than the EO group; 43/261 patients (16.4%), had CAU. Unlike the EO group, there was a greater proportion of PO females with uveitis (32: 74.42%), than those without (139: 64.65%), but this difference was not statistically significant. No significant HLA differences were found.

Conclusion: Children with extended oligoarthritis are at least at similar risk of developing CAU as children with persistent oligoarthritis.

P046 CLINICAL AND TOMOGRAPHIC FEATURES OF THE TEMPOROMANDIBULAR JOINT (TMJ) INVOLVEMENT IN PATIENTS AFFECTED BY JUVENILE RHEUMATOID ARTHRITIS (JRA)

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The involvement of the TMJs in JRA is an underrated problem. The aim of this study was to evaluate the incidence of the TMJ involvement in the different subtypes of JRA and the statistical correlations between symptoms, clinical signs and tomographic changes of the TMJs. Our series included 56 patients older than 10 years (42 F, 14 M), mean age 17.3 yrs (range 10-25), mean onset age 7.0 yrs (range 1-16), mean disease duration 10.4 yrs (range 2-22). Each patient was evaluated according to the Helkimo protocol (assessment of anamnestic dysfunctional index, clinical dysfunctional index and occlusal index) and, when indicated, a tomographic study was performed (32 patients). Tomographic features were assessed according to the Rohlin-Petersson scale (grade 0-5 according to the severity

of erosive changes). Radiological alterations were observed in 94% of patients (bilateral in 75%). All patients with systemic and polyarticular onset JRA showed a tomographic TMJ involvement, TMJ changes were present also in 84% of pauciarthritic subtype. No significant correlation was found between subjective symptomatology and clinical dysfunctional signs, in particular the severity of symptoms was generally lesser than that of the clinical dysfunctions. Moreover, no correlation was found between clinical dysfunctional signs and morphological alterations in the TMJ tomograms: the severity of dysfunctional signs was lesser than that of the morphological alterations. In conclusion these results confirm the importance of clinical examination in patients affected by JRA even if they are asymptomatic and the usefulness of TMJ tomograms in patients even with only moderate clinical dysfunctions.

P047 INVOLVEMENT OF THE TEMPOROMANDIBULAR JOINT IN JUVENILE IDIOPATHIC ARTHRITIS (JIA)

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Involvement of the temporomandibular joint (TMJ) in JIA is often underdiagnosed. This may lead to significant dysfunction of the masticatory apparatus. We wanted to evaluate a diagnostic test to improve clinical diagnosis of TMJ arthritis. 102 patients referred to the section of pediatric rheumatology were analyzed prospectively using the Helkimo diagnostic index which includes the history (Da) and function (Di) of the masticatory apparatus. Patients with signs of TMJ involvement were further diagnosed by X-rays of the masticatory apparatus (orthopantomogram- OPG) which were analyzed using Rohlin's and Petersson's method. In addition Manly's functional test of the masticatory apparatus was performed (Yurkstas' modification). 28 of 102 patients (27%) diagnosed with JIA showed signs of TMJ involvement in the Helkimo index (Da ≥ 1 and/or Di ≥ 1) including chewing sounds (71.4%), asymmetric mouth opening (17.8%) and pain of the TMJ (17.8%). X-rays (OPG) were performed in 11 of 28 patients, 4 of these showed severe destruction of the TMJ (grade IV). In addition, Manly's functional chewing test revealed significant dysfunction in all 28 patients.

Introduction of the Helkimo index and Manly's functional chewing test into the diagnostic standard of the outpatient clinic improved early diagnosis of TMJ involvement.

P048 2Q37.3 DELETION AND OLIGOARTICULAR-ONSET JIA: A FORTUITOUS ASSOCIATION?

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2q37 deletion syndrome is a rare chromosomal abnormality, phenotypically resembling Albright's hereditary osteodystrophy, that is, association of short stature, facial dysmorphism, epilepsy, mental retardation and brachymetaphalangism. For the first time, we describe a very terminal deletion of the long arm of chromosome 2 associated with typical extended oligoarthritis in a little girl. C.G. had a cleft palate repair at birth time. Umbilical hernia and anal ectopy were also noted. At the age of two, the child was diagnosed with a typical positive antinuclear antibody oligoarticular-onset juvenile idiopathic arthritis, further evolving into its extended form. Facial dysmorphism with round face, flat nose and hypoplastic alae nasi, hypertelorism and epicanthus, down-turned corners of the mouth, as well as brachymetaphalangism, short stature, mental retardation and behavioral disturbances became evident with aging, prompting to a karyotype realization. High resolution banding analysis revealed a (46XX del(2)(q37.3->qter)), that could be concordant with the phenotype findings due to its very terminal localization. However autoimmune manifestations had never been reported along with 2q37 deletion syndromes. The presence yet of a potent down-regulator of immune responses, namely PD-1, within the 2q37.3 region might, when deleted, contribute to autoimmune disease pathogenesis, as demonstrated in PD-1 knockout mice. Precise determination of the deleted region in C.G. is currently investigated and might be particularly helpful to both her diseases understanding.

P049 RECURRENT BICIPITAL CYSTS IN SEVERE SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

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Objective: To describe the clinical presentation and treatment of bicipital synovial cysts in patients with juvenile idiopathic arthritis (JIA).

Methods: A clinical description of the JIA subtype, activity of concurrent arthritis and biochemical inflammatory parameters. The cysts were visualized by ultrasonographic examination.

Results: The bicipital cysts were observed in 4 out of 49 patients with systemic JIA 2 months to 7 years after disease onset. All patients were boys (aged 3½ -8½ years) and had a systemic onset JIA with a severe polyarticular course. The cysts presented as a painful swelling on the flexor aspect of the upper arm. At time of presentation all patients had active disease with systemic features in 3 patients. None of the cysts regressed spontaneously. Ultrasonography showed a cystic structure. In one patient the cyst disappeared after initiation of systemic corticosteroids. In the other patients already receiving systemic corticosteroids aspiration of fluid from the cysts was followed by injection of triamcinolone hexacetonide having a marked effect. However, recurrent swelling of the cysts led to reiteration of the procedure in 3 patients. None of the patients were operated.

Conclusion: Bicipital synovial cyst is a rare manifestation that may be attributed to systemic JIA. Diagnosis is easily confirmed by ultrasonography. Although recurrence is frequent treatment with corticosteroid injections is preferred.

P050 INCIDENCE AND SPECTRUM OF CIRCULATING AUTOANTIBODIES IN FAMILIES OF CHILDREN SUFFERING FROM VARIOUS RHEUMATIC DISEASES

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Objective: To investigate the incidence and spectrum of autoantibodies in 1st degree family members of pediatric rheumatic patients.

Subjects and methods: 32 families (143 individuals) with probands and at least one 1st or 2nd degree relative suffering from RD (1st group), 36 families (149 individuals) with only probands suffering from RD (2nd group) and 15 families (56 individuals) without probands or other family members with history of RD (3rd group). Serum antinuclear antibodies (ANA, dsDNA, ENA) were detected using three different techniques: indirect immunofluorescence (IFA), semiquantitative enzyme immunoassay (ELISA) and immunoblotting. Autoantibodies non specific for RD such as antithyroid (ATA), anti-parietal cell (PCA), anti-smooth muscle (SMA), anti-liver/kidney microsomal (LKM) and anti-reticulon (R1) were detected using IFA. Antineutrophil cytoplasmic (PR3-ANCA and MPO-ANCA) and anticardiolipin (aCL) antibodies were measured by ELISA. Rheumatoid factor (RF) was measured by enhanced rate nephelometry using a BNA equipment.

Results: The incidence of ANA and RF was significantly higher in the 1st group (14,8% and 12.03%) compared with the 2nd (6,2% and 1,77%) and 3rd (4,8% and 2.3%) groups ($p < 0.05$). Positivity was not always related with the presence of a RD. Thus, 4.8% of ANA and 2.3% of RF were found in apparently healthy family members. The mean titer of ANA was significantly higher in the 1st group compared with the two others. Coexistence of ANA/ENA was found very rarely in all groups studied. The incidence of ATA, PCA, LKM, ANCA and aCL was comparable between the groups studied. Anti-SMA and anti-R1 were found more frequently in the 1st and 2nd groups than in the 3rd one.

Conclusions: These findings indicate that autoantibodies commonly found in RD (ANA and RF) as well as other non specific for RD autoantibodies (anti-SMA, anti-R1) are frequently present in family members of children with various RD regardless they express clinically a RD or not.

P051 PULMONARY FUNCTION IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Objective: To investigate whether JIA subgroup, disease activity, disease duration or therapy influence pulmonary function tests (PFT).

Methods: A total of 44 children with JIA, age 5-19, (6 Oligoarthritic, 6 Oligoarthritic ext., 5 Polyarthritic-rheumatoid factor negative, 5 Polyarthritic-rheumatoid factor positive, 8 Systemic arthritic, 3 Spondylarthropathic (enthesitis-associated), 4 Psoriatic arthritic and 7 others) without clinical and/or radiologic pulmonary findings were examined. Spirometry, body plethysmography, determination of diffusion capacity (DLCO) and blood gas analysis were performed in all patients (T0). Systemic disease activity was rated by clinical examination and laboratory parameters (ESR, CRP). After 6-9 months pulmonary function tests were repeated in 36 children (T1) as follow-up part of the study.

Results: Peak expiratory flow (PEF; 76,4%), Mean expiratory flow (MEF75; 83,4%) and DLCO (84,2%) were reduced significantly compared to normal values. In 21 out of 44 patients (47,7%) DLCO was reduced below 80% of normal. FEV1, MEF50, MEF 25, FVC, TLC, FRC_{pleth}/TLC and RV were without significant changes. Airway resistance was increased (151%). There was a significant difference in airway resistance ($p < 0,001$) when patients with or without active disease were compared. Diagnosis (JIA subform), duration of disease, therapy and examination time point were without significant influence on PFT.

Discussion: JIA patients without pulmonary disease had impaired pulmonary function, mainly a reduced diffusion capacity and obstructive changes. There were no restrictive changes. Follow up examination 6-9 months later showed no additional changes. Only airway resistance was correlated to disease activity. JIA subgroup, disease duration and therapy had no correlation to reduced PFT.

P052 COGNITIVE COPING, HEALTH-RELATED QUALITY OF LIFE (HRQOL) AND EMOTIONAL PROBLEMS IN ADOLESCENTS WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA)

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The first objective of the present research was to study the differences between an early- (12-14 years) and late JIA adolescent sample (15-18 years), in the use of cognitive coping strategies.

The second objective was to study whether these two age groups differed in the extent that certain cognitive coping strategies are related to emotional problems and HRQoL.

The early-adolescent sample consisted of 30 adolescents (mean age 12,97; 44% male; 56% female) and the late-adolescent sample (mean age 16,00; 45% male; 55% female) consisted of 29 adolescents. During their visit to the outpatient clinic the adolescents filled out three questionnaires by personal computer: the Cognitive Emotion Questionnaire (CERQ), the DUX-25 (HRQoL) and two subscales (Depression and Anxiety) of the Symptom Checklist-90 (SCL-90).

The results revealed that more cognitive coping strategies (except 'Refocus Positive') were used and more emotional problems were reported by the late adolescents sample compared to the early adolescent sample, in combination with more problems in their HRQoL. The results also showed that in the early adolescent sample no cognitive coping strategy was significantly related to HRQoL and only one cognitive coping strategy ('Acceptance') was related to depression. In the late-adolescent sample three cognitive coping strategies ('Self-blame', 'Rumination' and 'Catastrophizing') were significantly related to HRQoL and anxiety and depression.

P053 PROGRESSIVE PSEUDORHEUMATOID ARTHROPATHY OF CHILDHOOD AS AN IMPORTANT DIFFERENTIAL DIAGNOSIS OF JUVENILE IDIOPATHIC ARTHRITIS

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Progressive pseudorheumatoid arthropathy of childhood is an autosomal recessive inherited skeletal dysplasia and can simulate juvenile idiopathic polyarthritis. The frequency is estimated 1:1.000.000 in UK but is likely higher in the Middle East. This disorder of ossification typically starts in early childhood with muscular weakness and a striking gait. During course an increasing stiffness of the spine, fingers, hips and other joints develops together with osseous swelling especially of the proximal and distal interphalangeal joints, and finally a disproportionate short stature. Radiology reveals

dysplastic changes with a platyspondylia, irregularities of the acetabulum and widened ends of tubular bones with generalized osteoporosis. Blood test and synovial histology are normal. There is a lack of response to disease modifying antirheumatic drugs. We present 5 children seen in our hospital with PPAC. Patients 1 and 2 are brother (6 years) and sister (8 years) of German origin, patients 3 and 4 brother (13 years) and sister (12 years) of Turkish origin, patient 5 a boy (6 years) of Turkish origin. A consanguinity of the parents is found for patients 3,4 and 5. No other family members were affected. The first symptom of all patients was a striking gait at the age of 2 to 3 years with varus deformity of the lower leg and/or muscular weakness. During course all had an involvement of the spine, elbows, hips, knees, wrists with progressive decrease in the range of motion, osseous joint swelling and finally contractures, mimicking JIA. Patient 3 had a transient synovial effusion of the hips. All had typical radiologic findings like platyspondylia, enlarged epiphyses at metaphyses, especially around the proximal and distal interphalangeal joints, dysplastic changes of the hips without destructive signs. All patients were negative for ANA, HLA B27 an RF. Body length was diminished, with an especially short trunk. **Conclusion:** PPAC is a rare differential diagnosis to polyarticular JIA. Early diagnosis is important to protect the children from ineffective drug therapy.

P054 CONCENTRATION OF PLASMA ERYTHROPOETIN (EPO) IN CHILDREN WITH JUVENILE CHRONIC ARTHRITIS (JCA) - A PILOT STUDY

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Microcytic anaemia often accompanies the acute period of JCA with the correlation between the severity of anaemia and severity of JCA. It is assumed that the main role is played by cytokines elevated during the active phase of arthritis, which are responsible for decreasing serum EPO.

Aim: The aim of this study was to find the relation between the anaemia and serum EPO in JCA in children.

Material and Method: Serum samples were collected from 33 patients suffering from JCA/13 boys and 20 girls/Age of the onset of JCA was 18 months to 16 years/mean 8,45y/Duration of the disease ranged between 1 month and 12,5 years. In 15 patients oligoarticular, in 8 -polyarticular and in 8 general onset of JCA was diagnosed. In 2 children data concerning the onset of the disease were lacking. 9 children were on NSAID,16 on steroids,4 on cytostatics, 3 on Arechin,1 on Plaquenil during the EPO estimation.8children were without treatment. EPO serum level was estimated simultaneously in all patients.

Results: In 20 patients EPO serum level was decreased. In 6 was within the norm ranges and in 5 was above upper norm limit.4 patients with elevated serum EPO were treated longer than 4 years because of JCA with generalised onset. In these patients induction of the remission was very difficult.

Conclusions: 1. In 60,61% of children with JCA decreased serum EPO levels were observed. 2. The group of JCA patients with decreased or normal serum EPO levels is in homogenous.

P055 BURDEN OF ILLNESS FOR CHILDREN AND ADOLESCENTS WITH JUVENILE CHRONIC ARTHRITIS (JCA) AND JUVENILE SPONDYLOARTHROPATHY (JSPA)

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Background: Since 1992, data of patients with chronic arthritides seen at the three pediatric rheumatology units in Berlin have been annually recorded.

Methods: From 1992 to 1999, 989 patients with JCA and JSpA were recorded at these units. 183 of them had been seen over at least 4 years. Their clinical and patient questionnaire data were analyzed.

Results: The subgroup distribution in the patient sample reflects the selection of more severe cases with a higher amount of systemic (19%) and polyarticular JCA (20%) cases and a lower amount of those with oligoarticular JCA (44%) and JSpA (14%), compared to population-based cohorts. At first registration 51% of the patients reported having had pain, 45% limitations in functioning, and 68% in overall well-being. Over the follow-up the number of patients with pain and limitations decreased by 5–12% in the whole group. Patients with a short disease duration (≤ 12 months) improved best, with 25% vs. 50% reporting limitations in functioning and 22% vs.

52% pain at follow-up, but patients with a disease duration of ≥ 6 years also improved over time. Patients seen earlier in their disease course (≤ 12 months) at the rheumatology unit had a better functional baseline status than those seen later, however, this difference had almost disappeared at follow-up. Over the years nearly all patients had received treatment, with NSAIDs (80%), DMARDs (67%) and/or physiotherapy (68%).

Conclusion: Data suggest that specialized rheumatology care can decrease burden of illness and hold up functional loss in juvenile chronic arthritides.

P056 DOWNS SYNDROME AND JUVENILE IDIOPATHIC ARTHRITIS: A COHORT OF 11 CASES WITH SEVERE ARTHRITIS, REQUIRING, AND RESPONDING WELL TO DMARD THERAPIES

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Aims: The association of Down Syndrome with a chronic inflammatory arthritis or Juvenile Idiopathic Arthritis (JIA) has been reported only occasionally. We sought to identify all cases of this association from our prospectively collected database and included if they had been followed in the unit between 1990-2000.

Methods: Cases were included if they had a definite diagnosis of Down syndrome based on chromosomal analysis, and had sufficient clinical data available. We documented nature of onset, course, erosiveness and joint deformity, together with serological characteristics (ANA, RhF and B27 where relevant).

Results: We report 11 cases further confirming this true association. Seven were male and 4 female, at aged 3-16 yrs at onset with delay to diagnosis of 0.25 to 6 years (Ave 1.3 yr). The arthritis was chronic, polyarticular in onset (9/11, 2 oligoarticular) and course (11/11) and symmetrical (9/11) in nature all cases reported here (and most in the literature) affecting both small and large joints. Complications of the arthritis were common including joint contractures 9/11, and subluxation of joints in 8/11 (including 3 with definite atlanto-axial subluxation and one with cord compression). 2/11 were ANA positive and one had anterior uveitis, but none were RhF+. ESR was only moderately elevated at diagnosis (Ave. 22mm/hr) or throughout the course. 9/11 required DMARD therapy (8 on MTX) and most continued on this successfully with considerable therapeutic benefit.

Conclusion: Our findings support an increased risk of JIA overall in Down Syndrome, which is often delayed in recognition and treatment. Overall the arthritis responds well to disease modifying treatment. Early recognition and treatment should be considered in all cases prevention of serious complications.

P057 AGE ASPECT OF AXIAL INVOLVEMENT IN JUVENILE ANKYLOSING SPONDYLITIS

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Aim of the study: To determine the clinical features and terms of axial involvement in JAS.

Patients: Among 2140 pts with juvenile idiopathic arthritis treated in our clinic from 1988 to 2000 yrs 132 pts (114 male and 18 female, aged 14-24 yrs) were found who developed classical clinical picture of JAS (according to the New York criteria). The mean disease's onset age was $10,2 \pm 0,3$, range 1,2-15,1). The average disease duration comprised $6,2 \pm 0,3$ (range 3,8-14,7) yrs. All pts were divided into 4 groups according to age at onset: I - < 7 yrs (19 pts); II - 7 to < 10 yrs (28 pts); III - 10 to < 13 yrs (52 pts), IV - 13-16 yrs (33 pts).

Results: In 117 pts (87%) the disease started with peripheral arthritis or SEA-syndrome. Sacroiliac joints involvement and lumbar pain and/or stiffness were present in all cases, cervical spine involvement—in 43 pts (33%). The time appearance of axial involvement was in strong inverse correlation to the age at onset ($r = -0,81$, $p < 0,001$). Lumbar and cervical spine pains were observed within 1st year of the disease in most of pts from 3rd and 4th groups (70% and 79% respectively) and at anybody from 1st ($p < 0,01$). X-ray evidence of sacroiliitis was found with the delay of 8,2; 4,8; 2,4 and 2,7 yrs in 1-4 groups. Syndesmophyte formations were observed in 8 (6%) pts (average disease duration 6,2 yrs) on X-ray examination and in 21 pts (16%) on MRT. There were no significance differences in the incidence and terms of apophyseal joints ankylosis occurrence between the 4 groups.

Conclusion: Our results showed that the appearance of typical axial damage (gold standard in JAS) does not depend on disease duration and start to develop only in certain (later than 14 yrs) age.

P058 DELAYED MENARCHE AND BONE MASS PEAK IN JUVENILE RHEUMATOID ARTHRITIS (JRA)

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Osteoporosis is a serious problem in JRA. Delayed onset of pubertal spurt and age at menarche increase this defect. The aims of this study were to determine if girls with JRA present a delay in menarche age and if the delayed menarche can influence the bone mass peak. Our investigation consisted in a transversal and a longitudinal study. In the first one we considered 63 girls with JRA (13 systemic, 24 poly, 26 pauci) (26 on long term steroid treatment), mean disease duration 7.8 yrs. Comparing the age at menarche of the patients (mean 13.4 yrs SD \pm 1.5) with that of their mothers (mean 12.8 SD \pm 1.4) and of the Italian healthy population (mean 12.5 SD \pm 1.5), a statistically significant difference was observed (respectively $p=0.03$ and $p<0.001$). In the longitudinal study we considered 21 prepubertal females with JRA (6 systemic, 10 poly, 5 pauci). 18/21 were on steroids. BMD lumbar spine was monitored every 6-12 months in each patient before and after menarche since the bone mass peak was reached. This series was divided into two subgroups according to the time of menarche in comparison with the healthy population: normal in 12 cases, delayed in 9 cases. Taking into account the BMD % annual change (BMD delta) a statistically significant difference was observed between patients with delayed menarche in comparison with those with normal menarche ($p=0.01$). Patients with delayed menarche present a low annual bone mass increase and can reach bone mass peak several years after puberty.

P059 LYMPHOCYTE SUBPOPULATIONS IN JUVENILE CHRONIC ARTHRITIS

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Objectives: To study absolute counts of peripheral blood lymphocyte subsets in juvenile chronic arthritis (JCA) patients; to compare the results of patients with different disease subtype and duration.

Patients: First analysis was performed in 61 patients diagnosed with JCA in Tartu University Children's Hospital (46 oligoarthritis, 12 polyarthritis and 3 systemic subtype). In forty-eight patients the duration of disease was 0-2 years, in eight 2-5 years, in four 5-10 years and in one over 10 years. Second analysis was performed in 23 patients on average of 17 months after first analysis.

Method: Immunophenotyping peripheral blood lymphocytes by flow cytometry.

Results: In first analysis the most frequent finding was increase in absolute counts of CD19+ B lymphocytes (in 23,3%) and CD8+ T lymphocytes (in 21,3%); 26,7% and 24,4% in oligoarthritis group respectively. In polyarthritis group the absolute count of CD19+ cells was increased in 18,2%. In second analysis there were no significant changes in absolute counts. Concerning the duration of disease the most notable was increase in absolute counts of CD19+ and CD8+ cells in the group of duration of 0-2 years (22,9% and 18,8% respectively) and increase in count of CD8+ cells in 75% of patients with disease duration of 5-10 years.

Conclusions: Increase in absolute counts of CD19+ B and CD8+ T lymphocyte subsets was the most frequent finding in the whole study group, especially in oligoarthritis with disease duration of 0-2 years. Changes in counts of subsets in patients with longer course of disease were inconsistent.

P062 SENSITIVITY TO CHANGE OF THE NORWEGIAN VERSION OF THE CHILD HEALTH QUESTIONNAIRE (CHQ)

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Objective: To assess the sensitivity to change of the Norwegian version of the CHQ in patients with early juvenile arthritis.

Methods: One hundred and thirty children (median 8.4 years, range 4-16 years) with juvenile rheumatoid arthritis (91.5%) or juvenile spondylarthropathy (8.5%) and a mean disease duration of 12.4

months (range 1.5 -30) were included. The CHQ gives summary scores for physical (PhS) and psychosocial (PsS) functioning. The patients were reassessed after a mean of 10 months (range 3-20). Clinical change was defined according to the preliminary ACR definition of improvement in juvenile arthritis. Effect size was computed as the mean change of the PhS from baseline to follow up divided by the standard deviation.

Results: The mean changes of the PhS were: 9.3 (SD:9.7), $p=0.000$, effect size 0.96 in improved patients ($n=43$), 1.1 (SD:6.9), $p=0.249$, effect size 0.16 in unchanged patients ($n= 54$) and - 8.3 (SD:13.8), $p =0.043$, effect size -0.60 in patients who were worse ($n=14$). An effect size of 0.50 is moderate, an effect size above 0.80 is large. Changes in PsS were not statistically significant ($p>0.05$) and effect sizes were small.

Conclusion: These data show that the physical summary score of the Norwegian version of the CHQ is sensitive to clinical changes in patients with early juvenile arthritis. Psychosocial summary score is not sensitive to clinical changes in these patients.

P064 OSTEOPROTEGERIN SERUM LEVELS ARE ELEVATED IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Skeletal complications of Juvenile Idiopathic Arthritis (JIA) include focal bone erosions and juxtaarticular osteopenia at sites of active inflammation, as well as systemic osteopenia. Osteoprotegerin (OPG) has been identified as a novel molecule which inhibits differentiation and activation of osteoclasts. The aim of our study was to evaluate serum levels of OPG in patients with JIA and healthy controls.

Subjects and Methods: Eighty-four patients (66 girls and 18 boys) with JIA (30 pauciarticular and 84 polyarticular RF negative) and 20 sex and age-matched controls were enrolled in our study. Patients were further divided in four groups: 21 without therapy, 12 on corticosteroid therapy, 26 on metrotrexate, and 25 on the association of corticosteroid and metrotrexate. Serum OPG was measured using an enzyme-linked immunosorbent assay. Statistical analyses were performed using Mann-Whitney U test, Ancova analysis and Tukey's test, as indicated.

Results: We observed that JIA patients had significantly higher serum levels of OPG than controls (mean 0.866 ± 0.31 ng/ml vs 0.652 ± 0.14 ; $P=0.001$). Moreover, we observed a statistically significant difference in the amount of serum OPG between patients with and without therapy (ANCOVA, $P=0.002$). In particular, patients on steroid therapy had higher serum OPG mean levels than patients without any therapy (1.10 ± 0.57 vs. 0.67 ± 0.22 ng/ml; $P=0.01$). Finally, no significant differences in the amount of OPG were observed between patients with and without bone erosions.

Conclusions: In conclusion, JIA patients have elevated serum levels of OPG. This might reflect a compensatory response to degeneration of bone and cartilage.

P065 WRIST MAGNETIC RESONANCE IMAGING (MRI) FINDINGS IN JUVENILE IDIOPATHIC ARTHRITIS (JIA)

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Aim: Our study was performed in order to assess the role of a diagnostic imaging MRI technique in the identification of synovitis induced anatomical damage in JIA.

Subjects and Methods: Fourteen girls and two boys (mean age: 10.9 yrs, range 4-21 yrs; mean disease duration: 7.6 yrs, range 6 months-1 yrs) entered our study. Thirteen of them were affected by polyarticular arthritis (2 of whom RF-positive), and 3 by oligoarticular onset disease. Twelve patients were taking methotrexate, while four were only taking nonsteroidal antiinflammatory drugs. MRI of the wrist joints (radio-carpal, intra-carpal, and carpo-metacarpal) was performed in 16 patients (total, 96 anatomical sites) with a 1.5 Tesla superconducting magnet system before and after i.v. contrast gadolinium DTPA infusion. MRI were scored for the presence of marrow edema, cortical abnormalities, synovial effusion, and articular pannus.

In 12/16 cases conventional radiographs, performed during the same 4 weeks, have been evaluated by a different radiologist, who was blinded to the MRI findings.

Results: The MRI abnormalities detected were the following: cortical defects (78%), marrow edema (65%), synovial pannus (61%), effusion (57%). In three patients abnormalities detected with MRI were not present at X-ray evaluation. In a 3-year old girl MRI findings were abnormal already after 6 months of disease, with diffuse marrow edema. In all cases swelling on clinical examination was concordant with MRI findings.

Conclusions: MRI may be a useful tool in the early diagnosis, management and response to treatment of childhood arthritis, can complement conventional radiographs in selected situations, but availability and cost issue limit its use.

P066 FASTING SERUM LEPTIN LEVELS IN JUVENILE IDIOPATHIC ARTHRITIS

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Aim: To assess the possible role of Leptin, a proposed key hormone mediating the cytokine-dependent anorexia and cachexia in chronic inflammatory diseases, in Juvenile Idiopathic Arthritis (JIA).

Subjects and Methods: In 68 JIA patients (25 M and 43 F, mean age 111.9 ± 52.9 month) body weight (kg) and height (cm) were measured by the same operator to calculate Body Mass Index (BMI). Thirty healthy children (11 M and 19 F; mean age 107.5 ± 45.5 month), age and sex matched, served as controls. Patients and controls venous blood samples for serum leptin measurements were collected at 08:00 AM after an overnight fast. Sera were kept frozen until analysis performed by a radioimmunoassay.

Results: Patients and controls differ for BMI (17.3 ± 3 and 19 ± 3.1, respectively; $p = 0.009$, Student's *t* test). Serum leptin levels were significantly lower in patients than controls (8.14 ± 4.8 vs 10.7 ± 7.5 ng/mL; $p = 0.04$, Student's *t* test). JIA female showed significantly higher concentrations in serum leptin than boys (10.18 ± 6.4 vs 6.75 ± 4.1, $p < 0.005$, Student's *t* test), independently to BMI differences. In JIA, serum leptin levels correlates positively with BMI ($r: 0.55$, $p < 0.0001$) and age ($r: 0.40$, $p < 0.0005$), while in controls leptin correlates only with BMI ($r: 0.75$, $p < 0.0001$). A multiple regression analysis, performed to exclude collinearity, showed that BMI and gender are the best predictor of serum leptin levels in patients ($r: 0.65$, $p < 0.001$) and controls ($r: 0.83$, $p < 0.0001$).

Conclusions: These results suggest that in JIA, as well as in adult rheumatoid arthritis, decreased leptin levels seem not mediate typical anorexia of chronic inflammatory diseases and might induce an impaired host defence against TNF- α sustained chronic inflammatory process.

P067 INCREASED MYELOID RELATED PROTEIN 8 AND 14 SECRETION REFLECTS PHAGOCYTE ACTIVATION AND CORRELATES WITH DISEASE ACTIVITY IN JUVENILE IDIOPATHIC ARTHRITIS TREATED WITH AUTOLOGOUS STEM-CELL TRANSPLANTATION

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Aim was to analyse whether Myeloid Related Proteins (MRP8/MRP14), a complex of two S100 proteins related with neutrophil and monocyte activation, could be used as a marker for disease activity, and as an early indicator for relapse or Macrophage Activating Syndrome (MAS) in Juvenile Idiopathic Arthritis. We studied a group of 12 patients that underwent an autologous haemopoietic stem cell transplantation (ASCT) for refractory JIA. MRP8/MRP14 serum concentrations were determined using a sandwich ELISA as described (ref Frosch). Definition of improvement used to assess disease response employs a core set of criteria as described previous by Gianinni. We used these criteria in analogy with the criteria from the American College of Rheumatology (ACR) to describe improvement from baseline.

After ASCT, MRP8/MRP14 serum concentrations in JIA showed a positive correlation with the CHAQ ($r = 0,80$) and ESR ($r = 0,45$). Mean MRP8/MRP14 serum concentrations dropped dramatically in the first three months post ASCT ($p = 0,0039$) together with a marked

improvement of the clinical parameters of disease activity such as CHAQ ($p = 0,0039$). During transient relapse there is an increase in MRP8/MRP14. MAS, a serious complication in systemic onset JIA, occurred in 3 patients 1-5 months after ASCT, was not found to induce significant changes in MRP8/MRP14 serum concentration. In conclusion, MRP8/MRP14 serum concentration can be used as a marker for disease activity in patients that received an ASCT for refractory JIA. This indicates a possible role of macrophage activation in the pathogenesis of systemic onset JIA.

P069 AGGREGATION OF RHEUMATIC DISEASES IN FAMILIES OF PEDIATRIC RHEUMATIC PATIENTS

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Objective: To investigate the incidence of rheumatic diseases (RD) in the family members of pediatric rheumatic patients.

Subjects and methods: In this case-control study 304 families of probands affected by various RD with an age of onset <16 years were included. A number of 203 families of children hospitalized for respiratory viral infections without a RD in their history served as controls. Of the 304 children with RD 253 had juvenile idiopathic arthritis (JIA), 19 systemic lupus erythematosus (SLE), 15 systemic vasculitis, 4 juvenile dermatomyositis, 4 mixed connective tissue disease, 2 Behcet syndrome, 2 ankylosing spondylitis, 2 systemic scleroderma, 1 recurrent erythema nodosum, 1 myositis and 1 overlapping syndrome. Detection of RD in the 1st and 2nd degree relatives of pediatric patients and controls was attempted by interviews using a preformatted questionnaire. Confirmation of the diagnosis in the diseased members was achieved by retrospective study of the medical records, by contacting the attending physicians and/or by performing appropriate additional analyses.

Results: The incidence of RD was found to be significantly higher in the families of pediatric rheumatic patients (11.84%) than in control families (2.46%) (OR=5.319, 95%CI=2.05-13.8). The RD most commonly affecting the patients' first degree relatives were found to be rheumatoid arthritis (RA) (9/20), ankylosing spondylitis (6/20) and SLE (3/20). Accordingly, the commonest RD among patients' 2nd degree relatives were SLE (7/21), RA (6/21), scleroderma (3/21) and JIA (3/21). In both groups the commonest non-rheumatic autoimmune disease was found to be psoriasis (48.24% and 6.41% respectively). In the control group, the following RD were found: SLE (2), RA (1), Scleroderma (1) and s. vasculitis (1).

Conclusion: These findings indicate that there is an aggregation of various RD in certain families. Further studies will show if this aggregation is due to a genetic background.

P070 NITRIC OXIDE LEVELS IN SYNOVIAL FLUID OF PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA)

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Nitric oxide (NO) is directly involved in the pathogenesis of rheumatoid arthritis, however there are no studies in children with JIA.

Objective: determine the nitrite/nitrate (NO₂/NO₃) levels in the SF collected and correlate it with inflammatory parameters

Methods: We analyzed 39 synovial fluids of children, mean age of 12,6 years (range 4-22 years), mean disease duration of 7,5 years (range 0,3-20 years). Eleven patients were from the systemic type of onset, 10 poliarticular and 18 pauciarticular. The NO₂/NO₃ level was quantified in diluted SF by Griess reaction. The number of each leucocyte population was also determined. A complete clinical and laboratory examination consisting of acute phase reactants, rheumatoid factor and articular radiographs, were evaluated.

Results: Our results shown that NO₂/NO₃ levels are higher in the SF than in serum ($p < 0,01^*$). We did not find a significant difference between synovial NO₂/NO₃ in the three types of onset and in the different groups of treatment. Levels of SF NO₂/NO₃ were higher in patients with hip involvement ($p = 0,03^*$). The number of mononuclear cells in SF correlated with the levels of NO₂/NO₃ ($p = 0,02^*$). No correlation was found between the acute phase reactants or radiological evaluation (Steinbrocker) and the nitrite/nitrate levels in the synovial fluid.

Conclusion: Nitric oxide seems to be produced *in situ* and to be involved in the pathogenesis of JIA.

P071 ANTI-CYCLIC CITRULLINATED PEPTIDE ANTIBODIES IN JUVENILE IDIOPATHIC ARTHRITIS

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Objective: Antibodies against cyclic citrullinated peptide (anti-CCP) are considered to be specific for rheumatoid arthritis (RA). To our knowledge they have not been studied in children; therefore we have assessed their clinical significance in a cohort of patients with juvenile idiopathic arthritis (JIA).

Methods: Anti-CCP were tested by ELISA in sera of 109 children with JIA (52 polyarticular, 51 oligoarticular and 6 systemic disease). Thirty were boys and 79 girls, with a mean age of 9.8 years (range 0.6-20.3 y) and a mean disease duration of 3.9 y (range 4 months-15.6 y). Anti-CCP were also tested in synovial fluid samples of 23 children with JIA, and in sera of 50 adult patients (30 with RA and 20 with SLE).

Results: Positive anti-CCP values were found in sera of 11 patients with JIA (10.9%), 6 with polyarthritis (11.5%) and five with oligoarthritis (9.8%). Statistical analysis showed that anti-CCP were not associated with the presence of erosive disease, rheumatoid factor, or antinuclear antibodies. Elevated anti-CCP levels were found in synovial fluid samples of 7/23 children with JIA (30.4%). In the control group, 73.3% (22/30) of adults with RA and 20% (4/20) of those with SLE were positive for anti-CCP.

Conclusions: Our data show that anti-CCP can be detected also in children with JIA, but are less frequently present than in adults with RA. The higher frequency of anti-CCP positivity in synovial fluid vs. sera of patients with JIA confirms the previous suggestion of local production of these antibodies in the inflamed joint.

P072 THE CLINICAL FEATURES OF SAPHO IN DUTCH CHILDREN

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Introduction: SAPHO-syndrome (Synovitis, Acne, Pustulosis, Hyperostosis and Osteitis) is a rare condition in childhood and adolescence. The aetiology is unknown and many names are used to describe the combination of skin and skeletal manifestations or skeletal symptoms alone (CRMO: Chronic, Recurrent, Multifocal, Osteomyelitis). To investigate the clinical manifestations of SAPHO in Dutch children questionnaires were sent to members of the Dutch Society of Paediatric Rheumatology, with the proposed diagnostic criteria for SAPHO-syndrome as guideline (Chamot and Kahn 1994).

Results: 14 patients were included (7 female, 7 male; mean age at diagnosis 10.7years; range 1,9 to 17). Skeletal manifestations were seen in all patients, skin diseases in 3. Osteitis was present in 13 patients, confirmed by biopsy in 8 and MRI in 3; CRMO was described in 6 patients.

Table 5

Manifestations in 14 patients	
Synovitis	8 (knee joint: 6; sacro-iliacal joint: 2)
Acne	2
Psoriasis	1
Hyperostosis	1 (both clavicles)
Osteitis	13 (axial lesions: 20*, non axial: 26**)

*Vertebrae 9, pelvis 5, sternum 2, clavicle 2, rib 1, scapula 1

**Long bones 18 (a.o.tibia 8), tarsus/metatarsus 8

Conclusion: The diagnostic criteria were useful to get the data and consistency with literature was seen. As in other studies skeletal manifestations were more frequent than skin diseases. 8 Patients with good recovery and short duration of symptoms (3 month to 3 years) were lost from follow up; they might have developed skin lesions. A multidisciplinary approach up to adulthood may give more insight in pathophysiology and outcome.

P073 A COHORT OF CHRONIC RECURRENT MULTIFOCAL OSTEOMYELITIS WITH AN UNUSUAL CASE OF SAPHO SYNDROME (SYNOVITIS, ACNE, PUSTULOSIS, HYPEROSTOSIS AND OSTEITIS)

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Aims and objectives: To demonstrate the severe end of disease spectrum in a young boy with SAPHO syndrome compared with a cohort of six patients with CRMO, and correlate clinical, radiological and laboratory findings in the disease course and outcome.

Methods: We selected all cases of CRMO and SAPHO from a prospectively collected paediatric rheumatology diagnostic index. The temporal relationship between clinical, investigation and response to treatment was demonstrated.

Results: Seven patients were identified with clinical and radiological features considered diagnostic of these related disorders. These cases demonstrated involvement of particular skeletal areas including clavicle, mandible and spine. The SAPHO case had extremely widespread disease with osteitis, hyperostosis and new bone formation involving almost all long bones, together with a distinctive synovitis. His disease onset was before twelve months age and he had not responded to antimicrobial treatment, a feature observed in the CRMO cases. Treatment with steroids and Disease Modifying anti-Rheumatic Drugs was instigated in most cases, with considerable benefit. In the SAPHO case in particular and in the CRMO cases as well, this produced dramatic and sustained improvement which has been maintained.

Conclusion: CRMO/SAPHO syndrome are considered now as part of the psoriatic arthritis spectrum of disorders with enthesitis periostitis and hyperostosis considered the early primary pathology. These inflammatory rheumatic disorders are unlikely to respond to antibiotics. Anti-inflammatory therapy including steroids and DMARDs should be considered in many cases and has been associated with a good outcome in this cohort.

P075 SEROPREVALENCE OF HUMAN PARVOVIRUS B19 IN CHILDREN AFFECTED BY JUVENILE IDIOPATHIC ARTHRITIS

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Recently the role of human parvovirus B19 in the etiology and pathogenesis of adult rheumatoid arthritis has been discussed controversially. Studies analyzing a potential pathogenic role of parvovirus B19 in juvenile idiopathic (rheumatoid) arthritis (JIA) are limited in all ethnic groups. We analyzed the prevalence of anti-parvovirus B19 IgG antibodies in the serum of 382 children who were referred to the section of pediatric rheumatology at the University of Würzburg, Germany. In addition 146 age-matched healthy controls were analyzed. The studies were performed according to policies established by the institutional ethics review board at the University of Würzburg. Patients and controls uniformly were of white caucasian descent. The subgroups were oligoarthritis n= 80, polyarthritis (RF + and -) n=19, systemic arthritis n=12, psoriatic arthritis n= 11, enthesitis related arthritis n=66, reactive arthritis n= 38, Lyme arthritis n=37, "other" arthritis n=28, arthralgias n=85, systemic lupus erythematosus n=4, iridocyclitis n=6. The frequency of anti-parvovirus B19 IgG antibodies were 35% (oligoarthritis), 58% (polyarthritis), 62.5% (systemic arthritis), 63.6% (psoriatic arthritis), 72.2% (enthesitis related arthritis), 39.5% (reactive arthritis), 67% (Lyme arthritis), 57% (other) 62%, 62.5% (arthralgias), 100% (SLE) and 33% (iridocyclitis), respectively. The seroprevalence in the reactive arthritis group was significantly less than expected from the control group (p≤0.05). With inclusion of additional 5 patients with erythema infectiosum and subsequent arthritis (all seropositive) into "reactive arthritis" the difference did not reach statistical significance. All seroprevalence in the different groups did not reach statistical significant difference from the age-matched controls, which were adjusted for the mean of age and the standard deviation of the age distribution.

Analysis of the seroprevalence of anti-parvovirus B19 IgG antibodies in European caucasian children affected with arthritis did not support the hypothesis that human parvovirus B19 is involved in the pathogenesis of JIA.

P077 LACK OF ASSOCIATION OF HEPATITIS C VIRUS (HCV) ANTIBODIES TO JUVENILE ONSET SYSTEMIC LUPUS ERYTHEMATOSUS (JSLE)

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Anti-HCV was demonstrated in 2,4 to 13% of adult onset SLE while no data is available regarding JSLE. In order to analyze the presence and possible association of HCV infection in JSLE we studied 50 patients. All subjects (43F:7M mean age at onset = 13,7 ± 3,4yrs mean disease duration = 5,5 ± 3,1 yrs) met the 1982 revised ACR criteria for SLE with onset ≤ 18 yrs. Twenty acute rheumatic fever patients and 20 healthy children matched for sex, age and social status were included as controls. Anti-HCV was tested using a high sensitive third generation microparticle enzyme immuno-assay (AxSYM HCV version 3.0, Abbott Lab.). All JSLE patients and controls were uniformly negative for anti-HCV. These results are in contrast to adult onset SLE in which there is a higher prevalence of anti-HCV than in general population. Our findings may reflect the absence of risk factors in children for the exposure to HCV infection such as intravenous drug use, repeated administration of blood products and promiscuous sexual activity. In addition, the immunosuppression caused by the disease itself or its treatment, which may require hospitalizations, and invasive procedures did not increase their chance of exposure to HCV. Our data suggest a lack of association between HCV as triggering or perpetuating agent for JSLE and further studies are necessary to determine whether there is any role for HCV in other childhood autoimmune diseases.

P078 VARICELLA VACCINATION IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Varicella is potentially a harmful disease for immunocompromised children. Vaccine against varicella was registered in Finland in 1996. It is not included in the Finnish vaccination programme. We have recommended vaccination for all polyarthritis children with no history of varicella before starting methotrexate and systemic corticosteroids.

Methods: Between May 1996 and February 2000, live attenuated varicella vaccine (Varilrix®, SmithKline Beecham plc, UK) was administered to 14 children suffering from polyarthritis. Methotrexate and corticosteroids were started not earlier than three weeks after vaccination. Because of the relatively high cost of the vaccine only one dose was used.

Results: The mean age of the children vaccinated was 4.4 years (range 2-8.4 years). None of the children got any adverse effects after vaccination. However, six children suffered from clinical varicella infection after a mean period of 1.7 years after vaccination (range 0.4-3 years). The disease was quite mild in all these children.

Conclusions: Varicella vaccine seems to be safe and no severe adverse events were reported after vaccination. Unfortunately, we did not measure antibody responses to vaccination. In this study group vaccination did not prove to be very effective since 6 (43%) of 14 vaccinated children got clinical disease. However, the disease was quite mild and this was probably due to vaccination. It is not known whether a second dose of vaccine could increase the protective effect against clinical varicella.

P080 CARDIAC INVOLVEMENT IN INFANTILE RHEUMATIC DISEASE: ECHOCARDIOGRAPHIC EVALUATION

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The authors retrospectively analysed the clinical files of the patients followed by Paediatric Rheumatology in order to evaluate the cardiac involvement in these patients. All patients were submitted to cardiac evaluation mainly by echocardiography and subsequently followed by Paediatric Cardiology if cardiac lesions were found. Of the 76 patients (47 females, 29 males), 60 had Juvenile Idiopathic Arthritis (JIA) and 16 Rheumatic Fever (RF) defined by Jones criteria. Of the JIA group 18 had systemic-onset, 17 polyarticular-onset and 25 pauciarticular-onset. Seven of this had pericardial effusion with haemodynamic

compromise in 2, all of them with systemic-onset. In the 16 patients (10 females, 6 males) with RF, the mean age at diagnosis was 9.5 years (range: 32 to 179 months). Six of this patients had mitral regurgitation, 1 mitral disease, 2 aortic regurgitation and 3 combined mitral and aortic regurgitation. One case also had moderate pericardial effusion. Four patients had no cardiac involvement. The valvular disease was considered to be moderate to severe in 8 patients, needing medical treatment. Three of the mitral regurgitation and one aortic regurgitation needed surgical repair. All patients resolved completely with proper treatment. We conclude that symptomatic cardiac involvement is rare in the JIA, presenting only with acute systemic-onset. On the other hand, 75% of the patients with RF had cardiac valvular involvement, needing treatment.

P081 VIRUS-ASSOCIATED HAEMOPHAGOCYTTIC SYNDROME IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS—A CASE REPORT

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Haemophagocytosis is one of characteristic diagnostic features of macrophage activation syndrome, which can be triggered by many different events. Children with a systemic course of juvenile idiopathic arthritis (JIA) are highly susceptible to this life-threatening complication.

We present a 10-years-old boy who was diagnosed with JIA four years ago. The systemic onset of the disease was associated with high fever, splenomegaly and abdominal pain leading to appendectomy. Bone marrow biopsy was made and the reactive changes were described. Laboratory findings (ESR, CRP) showed high inflammatory activity. Corticosteroid (Cs) therapy was effective but flares of the disease after interruption of Cs therapy occurred. Therefore a combination therapy with methylprednisolone and methotrexate was used and after establishment of laboratory and clinical remission the therapy was finished after 18 months.

Three months later, the boy was admitted to the hospital with high fever, myalgias and increased ESR, CRP. Cs therapy led to a short-time improvement, but two days later seizures and unconsciousness occurred with a need of artificial ventilation. Bacterial infection was excluded. Despite of HD IVIG therapy, anaemia, leucopenia, thrombocytopenia, raised triglycerides, elevated transaminases and ferritin developed. A new marrow biopsy showed haemophagocytosis. Testing for presence of parvovirus B19 DNA in the bone marrow and cytomegalovirus DNA in leukocytes were positive (PCR analysis). Therapy with protocol HLH-94 was performed and led to the disappearance of HLH symptoms and bone marrow changes. The patient is treated with combination therapy with methylprednisolone, methotrexate and cyclosporin A because a laboratory activity of JIA is still present. Clinical symptoms disappeared.

In our case report we demonstrate a severe course of the systemic JIA complicated by virus associated haemophagocytic lymphohistiocytosis.

P083 AN UNUSUAL CASE OF IDIOPATHIC UVEITIS

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Idiopathic uveitis are difficult to diagnose and may represent an heralding symptom of many rheumatic disorders; hence they represent a challenge for the paediatric rheumatologist. We report the unusual case of a child who came to our observation because of low-back pain.

Davide developed low back pain when he aged 10 years. Two months later he referred dark spots in the visual field. An ophthalmologist pointed out the diagnosis of anterior uveitis. At admission we did not find arthritis/enthesitis. Neither oral nor genital aphthous lesions and/or folliculitis was present. The acute phase reactants were negative; notably he was HLA-B51+ and HLA B27 negative. ANA and angiotensin converting enzyme were negative. Since the ophthalmologist noted bilateral anterior uveitis with granulomatous deposits in the anterior chamber, we planned further investigations: the computerised evaluation of Tyndal was of 5.5 ph/ms in the right eye and of 3.8 ph/ms in the left one. Non retinal vasculitis was present.

On this basis we re-evaluated the clinical history of our patient. Intriguingly, Davide was in a private school 3 years ago where a possible tuberculous infection might be supposed (some children with Mantoux

reaction positivity, a teacher affected with an undiagnosed chronic pneumonia). The Mantoux reaction we performed was frankly positive. No tuberculous X-ray findings were present. On these basis antituberculous chemotherapy was started with a prompt ophthalmologic amelioration.

Tuberculous uveitis usually appears as chronic uveitis or disseminated choroiditis. Mantoux skin test should be considered as mandatory in the initial diagnostic work-up for every patient with idiopathic uveitis. Our experience supports the opportunity to extend Mantoux test in patients with idiopathic uveitis, even in Western people where tuberculous infection incidence seems to be increasing.

P085 RESULTS OF ELUCIDATION OF CHLAMYDIA TRACHOMATIS, UREAPLASMA UREALYTICUM AND MYCOPLASMA HOMINIS IN UROGENITAL TRACT OF GIRLS WITH RHEUMATIC ARTHRITIDES

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Objective: to study the possibility of elucidation and clinical significance of Chlamydia trachomatis (C. trachomatis), Ureaplasma urealyticum (U. urealyticum) and Mycoplasma hominis (M. hominis) in the urogenital tract of virgin girls with rheumatic arthritides.

53 girls at age 2-16 years with no sexual contact were examined for elucidation of urogenital infections: C. trachomatis (by ligase chain reaction in the samples from vagina, external orifice of urethra and urine), U. urealyticum and M. hominis (by the passages of samples from vagina and external orifice of urethra). Patients were divided into 2 groups: 1) 26 girls with arthritis (17—reactive arthritis, 9—juvenile idiopathic arthritis); 2) 27 girls with vulvovaginitis without arthritis (control group). In arthritis group above mentioned infections were elucidated in 5 patients (C. trachomatis—1, U. urealyticum—2, M. hominis—2) when in the control group—only in 1 patient (U. urealyticum). In all cases these infections were clinically symptomatic. C. trachomatis was elucidated in the samples from vagina, orifice of urethra and urine in 7 year old girl with one-month-duration oligoarthritis.

In conclusion, C. trachomatis, U. urealyticum and M. hominis can be a cause of infectious focus in the urogenital tract of virgin girls with rheumatic arthritides.

P087 IDIOPATHIC JUVENILE OSTEOPOROSIS: IS AN EARLY DIAGNOSIS POSSIBLE?

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Case report: A prepubertal 8-year-old girl came to our attention for the finding of bilateral femoral epiphysiolysis. She started limping when she was 7 y 6 m old, apparently after a trauma of the left knee. An X-ray performed on that occasion was normal. Persisting left knee arthralgia, blood samples were taken with the finding of an elevated ASO titer. No therapy was prescribed then. The symptom didn't improve; flurbiprofen was then administered with no benefit. Finally an X-ray of both knee was required, that showed an epiphysiolysis of both femur distal ends; she was treated with a plaster cast. She was then referred to our Centre for further investigations. Physical examination, serum calcium, phosphorus and alkaline phosphatase, renal function, calcium and phosphorus tubular reabsorption, aminoacids urinary excretion, thyroid function, sex hormones, vitamin D metabolites, antigliadin antibodies and IgA-endomysial antibody were normal.

Total urinary calcium excretion and PTH were mildly elevated, but the girl hadn't walked for 1 month before coming to our Centre. Bone mineral density (BMD) was evaluated with DEXA, that showed a reduction of BMD compared with normal subjects matched for age and sex (z-score -2,5). Clinical examination, laboratory and radiologic findings and in particular the exclusion of secondary osteoporosis lead to the diagnosis of idiopathic juvenile osteoporosis (IJO). The radiographic images reminded also of scurvy bone lesions, even if no other signs were present, such as skin involvement, haemorrhages, stomatitis, abnormal aminoacids excretion. Nevertheless, she was asked about assumption of vegetables and fruit, that were quite excluded from her diet. Therefore, in association with calcium,

vitamin D and oral bisphosphonates, a therapy with ascorbic acid was started. However, a new fracture was observed after one month, even if secondary to a trauma, so bisphosphonates treatment was then given i.v..

Conclusion: IJO remains a rare cause of osteoporosis in children. The diagnosis can be made only after having excluded secondary osteoporosis. Nevertheless, an early diagnosis is a key factor in fracture protection and rehabilitation procedure.

P088 CHRONIC RECURRENT MULTIFOCAL OSTEOMYELITIS: DESCRIPTION OF TWO CASES

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Introduction: Chronic Recurrent Multifocal Osteomyelitis (CRMO) is a rare immunomediated inflammatory bone disorder, characterised by recurrent episodes of multiple nonpyogenic osteolytic lesions, involving predominantly long bones, clavicles and vertebral bodies. The lesions remind of infectious osteomyelitis, but no causative agent can be detected from tissue cultures and there is no response to antibiotics. NSAIDs and steroids are beneficial in more than 80% of the patients, even if long term sequelae, such as growth retardation and bone deformities, occur in up to 7% of cases. We described two patients complaining about arthralgias in whom a diagnosis of CRMO was made.

Case 1: A 9-year-old girl with a 1-year history of arthralgias, involving initially the left knee; ESR 34 mm/hr, at the X-Ray an osteolytic lesion in the proximal left femur. She has been given nimesulide for 6 months with partial regression of the bone lesion. Soon after NSAIDs discontinuation, she started referring pain at the left elbow, after a minor trauma experienced a fracture of the left lateral epicondyle that resulted in complete epiphysiodesis. No therapy was prescribed on that occasion. The girl came to our attention referring back pain; ESR 26 mm/hr, normal WBC count. A technetium radionuclide scan of the spine showed an increased uptake at the D4-D6 level and the RMI revealed a reduction in height of the correspondent vertebral bodies. Steroids were started with a pulse regimen, associated with NSAIDs, with immediate relief.

Case 2: A 9-year-old boy with ankles arthritis followed by left clavicle swelling; ESR 50 mm/hr, normal WBC count. He has been given antibiotics for several months without improvement and then ciprofloxacin and flurbiprofen for 3 months with partial regression. A clavicle biopsy was then performed, which showed signs of chronic inflammation, as seen in CRMO, while tissue cultures were negative. Therapy was discontinued two months ago with no flare-up.

Conclusions: CRMO, although rare, must be considered in the differential diagnosis of chronic arthralgias in children, in order to avoid useless antibiotic treatments and to limit invasive procedures, even if in the acute phase a bone biopsy may be necessary to exclude a neoplastic process.

P089 SYSTEMIC INVOLVEMENT IN BRAZILIAN PATIENTS WITH JUVENILE SCLERODERMA

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Juvenile scleroderma (jSc) is a very uncommon childhood rheumatic disease associated to high morbidity and visceral disorders. In order to evaluate major organ involvement in jSc we studied 14 children classified according to preliminary 1981 ACR criteria for systemic Scleroderma (jSSc) followed at our Unit between 09/2000 and 05/2001. Search for systemic alterations including respiratory assessment was performed by high resolution computed tomography (HRCT) and by complete pulmonary function test (CPFT); distal esophageal hypomotility (DEH) was judged by barium contrast radiological examination and cardiac involvement by two-dimensional echocardiogram (ECHO). Five (5/14) children had jSSc (3F:2M, mean age at onset 11,2 ± 4,4yrs; mean disease duration 13,2 ± 10,8 yrs) and 9/14 had localized jSc (jLSc), 6 morphea, 3 linear (7F:2M, mean age at onset 6,8 ± 4,2yrs; mean disease duration 8,7 ± 8,1 yrs). All patients with jSSc had gastrointestinal dysfunction, 3/5 (60%) had restrictive pattern with compromised CO diffusing test on CPFT and 3/5 (60%) had altered HRCT (alveolitis with ground glass opacification (AGGO) in 2 and interstitial fibrosis in 1). Five (56%) jLSc patients without

systemic complains had major organ involvement: 2 DEH (22%), 1 tricuspid valve insufficiency (11%), 2 AGGO (22%), 1 restrictive lung disease (11%) and 1 hyperinflation pattern (11%) at CPFT. Our data indicate a remarkable high prevalence of major organ involvement in both jSSc and JLS. The long-term significance of these alterations in asymptomatic children with prolonged JLS remains to be determined.

P090 JUVENILE SYSTEMIC SCLEROSIS (JSS) IN ITALY: A MULTICENTRE DATA COLLECTION OF 27 PATIENTS

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Aim: To collect data on current practice in the diagnosis, assessment, treatment and outcome of Juvenile Systemic Sclerosis (JSS) in a cohort of Italian patients.

Methods: A retrospective analysis of medical charts of patients with JSS, managed at the Paediatric Rheumatology units belonging to the Italian Paediatric Rheumatology Study Group was performed by sending data collection forms requiring information on demographics, clinical features, laboratory tests, treatment and outcome.

Results: 8 Centres took part of the survey and 27 patients with JSS were included in the study. 18 had the diffuse form, 4 the limited and 5 overlap syndromes. Average age at onset was 8.3 years and disease duration at diagnosis was 13 months. Antinuclear antibodies (ANA) were positive in all but 2 patients. Extractable nuclear antigen (ENA) specificity was checked in 22/25 ANA+ pts.: 13/25 had no specificity, Scl-70 was present in 2, RNP in 5 and ACA in 2 patients. The first symptom at onset was Raynaud's phenomenon in 17/27 patients, in 8 associated with skin thickening, in 6 with oedema of the fingers. The mean follow-up duration was 91.5 months (range 12-324 mo.). Over the follow-up period 6 patients developed pulmonary fibrosis, associated with pulmonary hypertension in 3, gastroesophageal reflux was documented in 10, renal crisis in 2. Treatments included D-penicillamine (13), oral Cyclophosphamide (11), Methotrexate (11), and Prednisone (11). Three patients underwent autologous Bone Marrow Transplantation (ABMT): 2/3 stabilised or improved. 18 patients were stable or improved at last visit, 3 had worsened clinical course, 4 died (2 heart, 1 multiorgan and 1 cardiopulmonary failure) all within the first two years, and 2 were lost at follow-up.

Conclusion: In this cohort of patients JSS is characterised by a high mortality (16%). The retrospective design of the study and the lack of validated outcome measures do not allow a full evaluation of the efficacy of the different treatments. ABMT seems to be a promising therapeutical approach.

P091 JUVENILE LOCALISED SCLERODERMA IN ITALY: A MULTICENTRE SURVEY

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Aim: To collect data on current practice in the diagnosis, assessment, treatment and outcome of Juvenile Localised scleroderma (JLS) in a cohort of Italian patients.

Methods: A retrospective analysis of medical charts of patients with JLS, managed at the Paediatric Rheumatology units belonging to the Italian Paediatric Rheumatology Study Group was performed by sending data collection forms requiring information on demographics, clinical features, laboratory tests, treatment and outcome.

Table 6 (P093)

	Gender	Clinical manifestations	Age	Time to diagnosis	Type	ESR	PPD
1	F	seizures	7 y 3 m	4 m	IV	50	15
2	M	pyoderma gangrenosum	1 y 9 m	5 y 5 m	I	20	05
3	M	fever, claudication, arthritis	7 y 3 m	<1 m	II	61	15
4	F	claudication, heart failure	7 y 1 m	2 m	II	37	14
5	F	headache, paresthesia in upper extremities	6 y 8 m	6 m	III	51	0
6	F	Sweet syndrome, arthritis, fever, heart failure	10 m	11 m	III	57	0
7	F	pyoderma gangrenosum, periostitis, arthritis	1 y 11 m	1 y 2 m	III	54	NR

Results: 50 patients from 8 Centres entered the study. The main clinical forms were linear (27/50), followed by morphoea (12/50), En coup de Sabre (6/50) and generalised morphoea (5/50). Mean age at onset was 6.2 years and the diagnostic delay was 10 months (range 0-48 m). ANA was positive in 26/50 patients. The follow-up duration was 85 months (range 12-276 mo). Main treatments used alone or in combination were: prednisone (48%), D-penicillamine (32%), methotrexate (22%), i.v. methylprednisolone (10%). The long-term outcome included skin atrophy in 64% patients, muscle atrophy in 36%, localised growth failure in 32%, joint contractures in 18%. 19/50 patients developed ≥ 2 deformities. Patients with morphoea experienced a better outcome with 80% having mild skin changes only, while 70% of patients with linear form had moderate to severe local growth failure or contractures. No patient showed internal organ involvement but 1 had gastroesophageal reflux. Simple clinical impression (34%), with serial lesions measurements (68%), clinical photographs (42%), mRodnan skin score (28%) were some of the methods used to measure progression or improvement of the lesions.

Conclusion: JLS, particularly the linear form, is characterised by a high morbidity, related to severe functional defects due to deep tissues involvement. A validated classification of the different subtypes of JLS and outcome measures are needed to better follow these patients and to plan future multicentre clinical trials.

P093 TAKAYASU'S ARTERITIS IN CHILDHOOD

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Introduction: Takayasu's arteritis is a rare disease in childhood, with a high morbimortality. It is very important its early recognition and treatment, what results in a directly impact on its prognosis.

Objective: To describe the clinical and laboratorial findings in seven children with Takayasu's arteritis.

Patients and Methods: The data of seven patients with Takayasu's arteritis were reviewed, followed in the period between 1990 and 2000. The mean age at presentation was 4 years and 8 months (range 10m to 7y3m). The female: male ratio was 2.5:1.

Results: The clinical and laboratorial findings at presentation are described in the table.

At clinical examination, all patients showed decreased pulses and blood pressure differences, 6/7 hypertension and 4/7 arterial or heart bruit. Angiorresonance was performed in all patients and angiography in four. The therapy included: corticosteroid (6), immunosuppressors (4), gammaglobulin (1), tuberculosis therapy (3) and arterial surgery (3).

Conclusions: Takayasu's arteritis may present with different manifestations. The complete clinical examination, including verification of pulses and blood pressure in the four extremities, is extremely important to the suspicion and diagnosis.

P095 FEATURES OF HENOCH-SCHÖNLEIN PURPURA IN CHILDHOOD

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Henoch-Schönlein purpura (HSP) is more common in children than adults. However, current classification criteria were developed in predominantly adult populations in order to distinguish between primary systemic vasculitides, and may have limitations when applied to childhood populations.

Aims: To assess the ACR criteria in defining this population; and to identify the presenting clinical features of HSP in an incidence cohort of children.

Methods: A resident population of 1.1 million children was surveyed over 2 years. Data were collected by monthly questionnaires sent to 321 hospital consultants, a single questionnaire sent to 2860 general practitioners, and review of 406 further case notes with hospital diagnostic codes for vasculitis. Included cases fulfilled ACR criteria. However, children with isolated palpable purpura (PP) were only included when the PP were in the classical distribution.

Results: 463 children fulfilled diagnostic criteria. All cases fulfilled the age criterion, and had PP. Few cases fulfilled biopsy (1%) or gastrointestinal bleeding (2%) criteria. Moderate thrombocytopenia (105-142 x 10⁹/l) excluded 20 children with classical PP, including 12/20 with arthritis +/- abdominal pain. A hierarchy of clinical features was recognised: PP (100%); arthritis (75%); arthritis + PP only (37%); abdominal pain (35%); classical triad (28%); PP only (14%); abdominal pain + PP only (5.6%). The sex ratio (M:F) was 1.2:1 overall, but arthritis was twice as common in boys (2.4:1) unlike isolated PP (1.08:1), or severe disease (1.07:1). Urinalysis was normal in 61%, with significant renal disease on biopsy in 1%.

Conclusions: The data suggest that the current ACR criteria are inappropriate for the paediatric age group. PP was the only ACR criteria identifying >90% of HSP in a childhood population. New criteria for children should be developed for prospective testing. The enormous contribution of all consultants, general practitioners and medical records staff in the West Midlands supporting this study is acknowledged. J Gardner-Medwin is an ARC clinical lecturer.

P096 CLINICAL PRESENTATION AND OUTCOME OF HENOCH-SCHONLEIN PURPURA (HSP): A RETROSPECTIVE ANALYSIS OF TEN YEARS

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Objective and methods: To assess clinical presentation and long term outcome of HSP, a ten-years retrospective analysis of all case records of patients with HSP was performed. All patients with renal involvement over 1-10 years of follow-up were checked at the moment of the study.

Results: 54 children (30 males, 24 females), aged 7 months-12.8 years (5.9 ± 2.5) were identified. A previous infection was reported in 38.8% (with a throat culture for group A Strepto β positive in 13.9%), a previous history of drugs in 14.8%. Purpura was associated to arthritis in 85%, to abdominal pain in 51.8%, to fever in 20%; purpura + arthritis + abdominal pain was present in 38.8%. Purpura was not present at the onset in 28%, preceded by arthritis in 53.3%, arthralgia in 13.3%, abdominal pain in 30.3%. In two patients of these a laparotomy was performed. Relapse of purpura was registered in 18.5%, 7 days-1 year later. Renal involvement, as microhematuria or microhematuria + proteinuria and nephrotic syndrome in one patient, was present in 8/54 (15%), between 0-30 days from the disease onset. At a medium follow-up of 6.8 y., 4/8 normalized renal alterations, 4/8 (with a biopsy-proven membranoproliferative glomerulonephritis in 3 and focal sclerosis in 1) showed a persistence of the initial findings without evolution in renal insufficiency. Between all risks factors analysed, renal involvement correlates only with purpura-relapse, present in 5/8 patient with nephritis versus 5/46 without nephritis (p<0.03).

Discussion: Purpura could follow other manifestations of the vasculitis leading to important diagnostic mistakes. According to our data, there was a lack of serious complication on long term follow-up; renal involvement was present in a percentage smaller than that reported in literature and had usually a benign course as previous reported by others Italian studies.

P097 RETROSPECTIVE ANALYSIS IN TEN YEARS (1990-2000) OF KAWASAKI DISEASE (KD) IN NORTH-WESTERN ITALY: IS IT TIME TO REVIEW THE DIAGNOSTIC CRITERIA?

Collaborative study of the FVG regional group of Italian Pediatric Society (SIP).

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We studied the KD cases occurred in Friuli-Venezia-Giulia (North-Western Italy, population 1,200,000 people) in the last 10 years. Fifty-eight cases have been identified (38 M, 20 F; mean age 41 months; age range 2m-14y), with an incidence of 2.4 new cases/years/

100,000 and seasonal peak in spring. The mean duration of fever at the admission in the hospital was of 6.5 days. At the moment of the diagnosis, the other symptoms included in diagnostic criteria were: hyperaemic conjunctiva 86%, oral lesions 91%, changes of extremities 79%, rash 91%, linfadenopathy (>1.5 cm.) 31%. Related clinical features (not included in the diagnostic criteria) were: irritability 56%, arthralgia 22%, hypertransaminasemia 51%, dropsied gallbladder 8%, diarrhea 23%, bottom desquamation and erythema 36%, uveitis 22%. Cardiac involvement in the acute phase of the disease: 1 case of myocarditis, 5 cases of pericardial effusion. Therapy: IGIV (1gr/kg) 91% (100% within the 10th day); ASA (50-100mg/kg) 96%. Two patients required a second cycle of IGIV therapy because of the persistence of the symptoms. Follow-up: complete recovery of the patients; no coronaric aneurysms occurred. Typical KD was diagnosed in 43 out of 58 patients (74%). The mean age was 47 months in the typical cases and 25 months among the not-complete cases (p<0.05). The children with incomplete KD are younger than the patients affected by typical KD. Considering the preventive effect on the cardiac complications particularly in the youngest patients confirmed by our data, the early treatment with IGIV in a young child with incomplete KD appears justified. A review of the diagnostic criteria should be consider, in our opinion, particularly in young children, where the co-existence of mucositis and changes of extremities may not require any more the persistence of 5 days fever to confirm the diagnosis.

P098 ACUTE HEMORRHAGIC EDEMA IN INFANCY: CASE REPORTS

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Objective: To present the clinical spectrum and outcome of acute hemorrhagic edema of infancy (AHEI) in children admitted to our PED over a 3 year-period. AHEI, a rare leukocytoclastic vasculitis occurring in infants younger than 2 years, has a dramatic onset with abrupt appearance of urticarial plaques, which rapidly become edematous and purpuric. Mild fever and peripheral edema are commonly associated. It usually follows an upper respiratory tract infection.

Case reports: 5 children (4 M, 1 F) aged between 6 to 16 months (median 11 months) having AHEI were diagnosed in our Hospital. In all clinical manifestations at onset included edematous or ecchymotic plaques, with a cockade pattern, on the face (in 3 on pinna), limbs and arms; one child had purpuric lesions of the oral mucosa. Four patients showed feet edema and 1 hand edema. Fever was present in 3 cases; ankle's arthralgia in 2. Medical history revealed a recent pharyngitis in 2 and pneumonia in 1. Mild hepatomegaly was found in 2, but aminotransferases levels were temporarily elevated only in 1. Acute phase reactants were normal or slightly increased in 4; high ESR and CRP levels and mild leukocytosis were found in the boy with pneumonia. Coagulation blood tests, immunoglobulin and complement levels were normal in all of them. Neither renal nor gastrointestinal involvement was found. All these children recovered completely after a mean duration of 16 days (range 7-28 days). No specific treatment was administered. Nobody had relapses or significant long-term complications. **Conclusions:** The clinical spectrum of AHEI and outcome in our cases are the same as reported in the literature; the tendency to recurrence in the short-term referred, however, has not been confirmed by our series. The relatively high number of cases seen in a few years, in contrast to the rarity reported, suggests that AHEI is probably underdiagnosed. The peculiarity of cutaneous manifestations (pattern and localization) in otherwise healthy infants, must suggests such diagnosis. This disorder, in fact, might be confused with severe disease (i.e. purpura fulminans, disseminated intravascular coagulopathy), but good general conditions, with apyrexia or mild fever, without hematological alterations should help pediatrician in differential diagnosis.

P099 NEUROLOGICAL INVOLVEMENT IN POLYARTERITIS NODOSA

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Polyarteritis nodosa (PAN) is a necrotizing vasculitis, rare in childhood; no single pattern of clinical presentation characterizes this pathology. Peripheral or central nervous system (CNS) involvement develops in 50 to 70 % of patients, as reported in other studies.

Aim of this study was to evaluate the involvement of the nervous system in patients affected by PAN. We enrolled 8 patients (5 males and 3 females) mean age 8,1 years (range 0,5-13,2), with a mean follow-up of 5,1 years (range 1,7-12,7 years). At onset all patients had a CNS involvement; clinical findings included migraine in 4 out of 8 pts, seizures and blindness in 3 out of 8 pts, facial nerve palsy in 2 out of 8 pts and a mono-polyneuropathy in 4 out of 8 pts.

All patients had been treated with glucocorticoid therapy and 2, who had a severe form of disease, with intravenous cyclophosphamide. Two patients with peripheral polyneuropathy discontinued therapy 24 months ago and are now in stable remission. The presence of seizures, blindness and migraine in 4 patients, associated in 1 of them with mononeuropathy, conditioned negatively the prognosis, intravenous glucocorticoid and/or immunosuppressive therapy were necessary. The other two young patients showed a transient facial palsy (in 1 associated with migraine and in the other one with polyneuropathy) improved with steroids to remission.

In conclusion these data show that all our patients had neurological symptoms since the onset, and that CNS serious involvement is related to a poor prognosis.

P100 IDENTIFICATION OF T HELPER (TH) SUBSETS IN FAMILIAL MEDITERRANEAN FEVER CONFIRMED BY INTRACELLULAR CYTOKINE STAINING

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Familial Mediterranean fever (FMF) is characterized by recurrent self-limited attacks of fever and serosal inflammation. An outburst of acute phase inflammatory products and some cytokines accompany the clinical inflammation.

Objective: We have aimed to identify the Th subsets in FMF patients to further elucidate the character of the inflammation. Cytokine products of Th1 and Th2 cells were identified by intracellular immunofluorescent staining.

Methods: Mononuclear cells isolated from peripheral blood samples of FMF patients during attacks (Group I; n=8), asymptomatic attack-free FMF patients (Group II; n=13) and healthy controls (Group III; n=7) were stimulated by PMA and ionomycin and stained with appropriate surface-specific monoclonal antibodies for IL-4 and INF- γ . The percentage of IL-4 and INF- γ -positive cells was analyzed by a FACScan (fluorescence activated cell sorter) flow cytometer.

Results: The mean \pm SD production of INF- γ in FMF patients during attack period (Group I) was $27,06 \pm 16,11$ and it was significantly different from attack-free FMF patients (Group II) with a mean \pm SD of $12,36 \pm 12,03$ ($p=0,025$) and from healthy controls (Group III) with a mean \pm SD of $1,20 \pm 1,49$ ($p<0,05$). We also found a significant difference in the production of INF- γ between attack-free FMF patients (Group II) and healthy controls (Group III) ($p=0,008$). We did not find any significant difference in the production of IL-4 between Group I, II and III.

Conclusion: This is the first report showing that the inflammatory pattern in FMF is of Th1 type. The increased levels of INF- γ in attack-free FMF patients compared to controls may reflect the ongoing subclinical inflammation in these patients.

P102 STREAKING LEUCOCYTE SYNDROME: A CASE REPORT

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The so called "Streaking leucocyte syndrome" is a rare form of arthritis characterized by recurrent episodes of sterile pyarthrosis responsive to steroid treatment; in the first description by Jacobs in 1975, random migration of polymorphonuclear leucocytes was reportedly increased and this was thought to account for the sterile pyarthrosis ("Streaking leukocytes"). From 1975 to date, only a few cases have been reported. We describe here a 20 years old male patient whose maternal uncle suffers from spondylitis. At the age of 2 years he was hospitalised because of arthritis of the left shoulder, phlegmon of the ipsilateral arm and high fever. Erythrocyte sedimentation rate (ESR) and levels of C reactive protein (CRP) were high. White blood cell (WBC) counts were also high with neutrophilia. The phlegmon

was drained: fluid was purulent but the culture was sterile. The patient was treated with antibiotics and slowly improved; he remained well up to the age of 7 when he presented similar symptoms with high fever and arthritis of the left ankle; a new episode of arthritis of the right hip occurred one year later. During both episodes ESR, CRP and WBC counts were high but blood and synovial fluid cultures were negative. He was treated again with antibiotics; symptoms slowly resolved over the subsequent months. In the following years, without fever and with mild elevation of ESR, CRP and WBC counts, he had several further episodes of sterile pyarthrosis. Immunological investigations showed normal serum immunoglobulins levels and normal counts of lymphocyte subsets; NBT test, antinuclear antibodies and rheumatoid factor were negative. At the age of 20 years he was admitted for the sudden onset of arthritis of the right hip associated with a large abscess of the quadriceps femoris muscle, without fever and with mildly elevated ESR, CRP and WBC counts. A diagnosis of "Streaking leucocyte syndrome" was made on the basis of recurrent episodes of sterile pyarthrosis unresponsive to antibiotic therapy. Treatment with prednisone (2 mg/Kg/die for 1 month) resulted in rapid and complete remission of symptoms. Since then, he had two other episodes of relapsing arthritis promptly responsive to steroid therapy.

The cellular and molecular mechanisms underlying this syndrome remain unknown. The disease could be the consequence of genetic abnormalities in the chemokine network leading to massive joint and soft tissue inflammation in the absence of infection. Familial cases, with AD disease transmission, have been reported and the responsible gene has been mapped on the long arm of chromosome 15.

P105 VOGT-KOYANAGY-HARADA SYNDROME AND ARTHRITIS. A RARE DISEASE IN CHILDHOOD

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The Vogt-Koyanagy-Harada syndrome was first described in 1940 and then at the beginning of the last century. The etiology is unknown, an autoimmune aspect is suspected. There is an association to HLA-DR 4 and the disease affects persons who are asian and latino and it is a rare or underdiagnosed disease in childhood. It has varied manifestations: I is a uveitis associated with vitiligo and central nervous system and auditory signs. Our patient is a 13 year old whitw boy who presented with uveitis and papillitis including eye pain, redness and blurred vision. Also he had headache and a history of mental and development disorders and arthritis. The CSF showed a pleocytosis, the ANA titer was positive. There was also a focus in the EEG, the MRI was quite normal. Under immunosuppressive therapy and initially corticosteroids the boy is doing well, an uveitis can not be seen. The mental disorders are getting better. In conclusion the Vogt-Koyanagy-Harada syndrome is a interesting differential diagnosis for uveitis.

P106 CHRONIC PAPPILLOEDEMA, ARTHRALGIA AND SKIN RASH IN A 7-YEAR-OLD BOY: CINCA/NOMID SYNDROME

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Objective: To describe an unusual case of CINCA/NOMID (Chronic Infantile Neurological Cutaneous and Articular/ Neonatal Onset Multisystem Inflammatory Disease) syndrome.

Methods: Case report.

Clinical features: A transient generalized skin rash was the first sign noticed 12 hours after birth and recurred regularly. At 6 years, he presented with headache and neck pain since half a year. He always had been less active than his sisters and had regularly unlocalized pains in the legs. No physical or cognitive abnormalities, except for height ($-2\frac{1}{2}$ SDS), bilateral papilloedema with normal vision, uveitis anterior and posterior, and high tone perceptive deafness.

Laboratory investigations: Elevated ESR and CRP, leukocytosis, hypochromic anemia, hypergammaglobulinemia G₁, A and E. Cerebrospinal fluid was normal, except for increased pressure and pleiocytosis with increased B-cells; no intrathecal immunoglobulin production. Normal MRI and EEG.

Treatment and course: CINCA/NOMID syndrome was diagnosed. Naproxen only improved neck pain. Both prednisone and methotrexate improved neck pain, arthralgia and rash; however, not papilloedema. With prednisone ESR and IgG normalised. In the past 3 years, inflammatory parameters and papilloedema remained unchanged. Symptoms are progressive. Since the age of 8½ years, attacks of arthralgia in various joints. Nowadays, he has daily neck pain and rash and, weekly, progressive severe pain in knees or ankles lasting 2 to 3 days but without fever.

Conclusion: In this 7-year-old boy with rash since birth, arthropathy and chronic papilloedema, the diagnosis of CINCA/NOMID syndrome was delayed due to a mild expression of the disease.

P109 TNF-RECEPTOR ASSOCIATED PERIODIC SYNDROME (TRAPS) - A DIFFERENTIAL DIAGNOSIS OF JUVENILE SYSTEMIC ARTHRITIS (JSA)

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Background: TRAPS is a dominantly inherited, chronic inflammatory condition characterized by febrile attacks of musculoskeletal and abdominal pain. There are hints that recombinant human TNF receptor (TNFRSF1B) (p75):Fc fusion protein might be useful in treating TRAPS patients. Here, we describe a German family with the newly identified T50K TNF-R1 (TNFRSF1A) gene mutation.

Methods: The index case and close family members were evaluated with full clinical history, soluble TNFRSF1A assays and genotyping of TNFRSF1A by M.F. McDermott.

Results: The 20 year-old male, index case (A), has had recurrent attacks of fever, skin lesions, myalgia and stiffness since 8 months of age. His symptoms responded promptly to steroids, while other immunosuppressive drugs the patient was receiving because one assumed that he suffers from an atypical course of JSA had showed no benefit. Both his 50 year-old father (B) and his 24 year-old sister (C) have also had features of typical TRAPS, but additionally case C has had suffered from paraesthesia from the age of 22. The MRI of the brain showed bilateral fronto-parietal multiple MS-like lesions, possibly TRAPS related. Patients A-C all had the T50K TNFRSF1A gene mutation and low levels of soluble TNFRSF1A. Treatment was started with etanercept in patient A and C, resulting in a rapid improvement of disease parameters.

Conclusion: In atypical cases of JSA TRAPS has to be considered just as other periodic fever syndromes. In certain TRAPS cases etanercept treatment might be helpful to control disease activity and prevent complications, however, demyelination is crucial in this respect.

P111 MUTATION DISTRIBUTION IN MEFV IN FAMILIAL MEDITERRANEAN FEVER PATIENTS AND HEALTHY CONTROLS IN THE TURKISH POPULATION CONFIRMING A HIGH CARRIER RATE

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Familial Mediterranean fever (FMF) is a recessive disorder characterised by self-limited episodes of fever and serosal inflammation, in the form of peritonitis, arthritis or pleuritis. Most of mutations in the MEFV gene (MEFV) causing the disease have been identified; five of these account for the majority of the cases in the Turkish and non-Askenazi Jewish populations. The aim of this study was to determine the mutation frequency in the clinically diagnosed FMF patients and the carrier rate in the Turkish population.

The distribution of the mutations was as follows: M694V that is associated with the most severe phenotype was found in 51.55% of the patients. The frequencies of M680I, V726A, M694I and E148Q were 9.22%, 2.88%, 0.44%, and 3.55%, respectively. We found a very high frequency of carriers in the healthy Turkish population (20%). The distribution of the MEFV mutations among healthy individuals (M694V 3%, M680I 5%, V726A 2%, M694I 0% and E148Q 12%) were significantly different ($p < 0.005$) from that found in the FMF patients. The high carrier rate is in agreement with those reported from Israel and Armenia. What advantage the heterozygotes for the MEFV mutation had, remains to be defined.

P112 RECURRENT FEVER, PRETIBIAL PAINFUL SWELLING AND HYPERGAMMAGLOBULINEMIA: A CASE OF GOLDBLOOM SYNDROME

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We report a case of Goldbloom Syndrome (GS) in an 8-year-old boy presenting with a few weeks history of recurrent fever, severe pain in the lower extremities and adjacent joints. At times he was not able to walk. Clinically, bilateral diffuse pretibial painful swelling with slight warmth and without alteration of overlying skin was noted. Pain on motion resulted in limited motion of adjacent joints, but there was no arthritis. Physical examination was otherwise normal.

Laboratory tests showed elevated ESR and CrP with moderate anemia. X-rays of the lower legs were normal. Extensive rheumatologic, immuno-hematologic and infectious research including bone marrow aspiration were not contributive, apart from hypergammaglobulinemia and positive Mycoplasma pneumoniae serology. The patient was suspected of having GS (idiopathic periosteal hyperostosis with dysproteinemia). MRI showed extensive periosteal enhancement of both tibiae without intramedullary or soft tissue involvement compatible with GS. GS is a challenging, interesting entity. Its differential diagnosis includes rheumatologic diseases including Still's disease, rare inflammatory syndromes and recurrent/ prolonged fever. The etiology remains unknown, GS is a self-limited disease over a period of months. NSAIDs are the recommended treatment. In our patient, mycoplasma infection was coincident with GS. This finding is questionable in terms of causality, but it should be recognized with regard to the lack of clear etiologic aspects. We hypothesize GS to be of yet unknown parainfectious origin.

P113 FAMILIAL MEDITERRANEAN FEVER (FMF) IN CHILDREN: FROM SYMPTOME TO DIAGNOSIS AND EFFECTIVE TREATMENT

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Familial Mediterranean Fever (FMF) is a genetically transmitted disease characterized by recurrent fever, abdominal pain, arthritis and serositis. In children the diagnosis is often difficult to resolve. All patients diagnosed with FMF seen in our hospital from 1996-2001 are included in this study. We include 6 patients of different ethnic backgrounds (Lebanon, China, Turkey and one armenian-turkish girl), aged 7 to 16 years, mean age at onset 3 years, gender: 3 girls and 3 boys. Clinical features at onset: fever (6/6), abdominal pain (5/6), acute abdomen (1/6), arthralgia (3/6), arthritis (3/6), skin changes (3/6), chest pain (1/6). Lab findings: elevated ESR and increased CRP (6/6). Abdominal ultrasound showed splenomegaly in two patients. Median duration from clinical onset to diagnosis: 2,5 years. Diagnostic tools: metaraminol testing (3/6), genetic testing (3/6). Treatment: Colchicine (6/6), mean dosage after diagnoses 1mg/day, additional therapy with NSAID's (6/6), amyloidosis 0/6. The diagnosis of FMF still appears to be made delayed due to uncharacteristic clinical and laboratory features. At least one girl underwent appendectomy and laparotomy without any significant pathological findings after a long period of unexplained abdominal pain and fever. After confirmation of the diagnosis all our patients received Colchicine therapy and improved within a short period of time. Discontinuation of the therapy leads to clinical relapses implying that lifelong treatment is indicated. Under our monitoring none of the patients has developed amyloidosis so far. As patients with FMF consequently treated with Colchicine have a good prognosis it is important to take this disease into consideration in the differential diagnosis of recurrent abdominal pain, fever and arthralgia.

P114 GENETIC ANALYSIS OF GREEK CHILDREN WITH FAMILIAL MEDITERRANEAN FEVER

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Introduction: Familial Mediterranean fever (FMF) is an autosomal recessive hereditary disease with acute episodes of self remitting fever and serositis. It is common among Sephardic Jews, Armenians, Arabs and Turks but it is also traced in other nations around Mediterranean sea.

Aim: To detect mutations in the gene responsible for FMF in Greek children.

Patients and Methods: Symptoms of 8 patients (3 males, 5 females, age 5-26 years) of Greek origin were recorded retrospectively. All patients were diagnosed as FMF according to diagnostic clinical criteria. All patients had recurrent fever (100%), 7 had acute abdominal pain and one of them had undergone appendectomy, 5 had pleuritis (62,5%), 5 arthritis (62,5%), 2 oral ulcers (25%), 1 cervical lymphadenitis (12,5%) and 1 had skin rash (12,5%). DNA analysis was proceeded for five known classical mutations accoutered in other nations: V726A, M694V, M694I, M680I and E148Q and rare mutations in exon 10, the mutational hot spot for FMF.

Results: Genetic FMF was established in patients with at least two mutations (either homozygosity or compound heterozygosity). Mutations of the MEFV gene were found in 5 children (62,5 %): there was 1 homozygote for E148Q mutation, 1 compound heterozygote for M694V and M680I mutations and 3 patients with only one mutation (all of them with M694V). No classical mutation was found in 3 patients. Both patients with genetic FMF and 2 of the patients with only one classical mutation have also relatives with FMF.

Conclusion: According to our knowledge this is a documentation of the MEFV mutations in Greek children exclusively. Mutations found for FMF in Greece are relevant to the ones in other countries around Mediterranean sea. Other than classical mutations remain to be clarified.

P115 HYPER IGD SYNDROME - ARE WE MISSING SOME?

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Objectives: To look at the profile of all patients who had IgD levels requested in a Regional Children's Hospital between 1993-2000.

Methods: All IgD's done between 1993-2000 were obtained from the computerised immunology database.

Results: IgD levels were done in 13 patients, of which in 3 patients case notes could not be located. The median age of presentation was 5.6 years; M:F ratio was 1.5 : 1 and median age of onset of attacks was 5 yrs of age. The maximum median recorded temperature during an attack was 40 degrees C. Raised IgD levels were noted in 50% (5/10) and only 1 had mevolonate kinase levels and gene mutations done. The median IgD levels was 0.042g/l (Normal 0.015-0.04) and only 10% had IgD levels repeated. 2 out of the 10 patients were treated, of which 1 was treated with colchicine and the other with aspirin. The ESR was raised to >20 mm/hr in 80% of patients (8/10) and raised IgA levels noted in 50% (5/10). 40% had serum cholesterol levels checked (4/10) of whom 10% (1/10) had a raised level.

Conclusions: Our retrospective study with such a high rate of raised levels amongst those looked at (50%), reveals that the diagnosis has not been considered often enough. Also, the test was repeated in only a small percentage of those with raised levels of IgD illustrating the need for greater awareness about HIDS and its features. Since there is a specific gene test for HIDS now it is even more important that the diagnosis is looked for in children presenting with periodic fevers.

P116 IS CINCA A GENETICALLY INHERITED DISORDER?

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CINCA (chronic, infantile, neurological, cutaneous and articular syndrome) was firstly described by AM Prieur (1983). This disease is characterised by the urticaria-like lesions, central nervous and sensorial organs impairment and bone epiphyseal anomalies. The disease seems to be sporadic. We report a girl whose father developed some symptoms of this disease.

G Gloria was born from unrelated healthy parents on 1995. At birth a widespread urticaria-like rash was present associated with a severe neutrophil leukocytosis (WBC count 22.320 mm³ and neutrophils 16.600 mm³); the acute phase reactants were within the normal ranges, C3 and C4 and the chemotaxis tests were normal too. A skin biopsy showed only a mild perivascular aggregation of polymorph cells. At the age of 3 years patella overgrowth and epiphyseal enlargement (elbows and knees) developed. At the age of 6 years, the brainstem evoked response audiometry showed impaired complexes

III and IV. Two years later, a perceptive bilateral deafness was documented. Severe headache attacks were present too, without neurological or ocular symptoms. When our patient aged 7 years, her father started to present hearing loss. Audiogram showed a perceptive bilateral deafness which worsened progressively. Enlarged knees and patella overgrowth were also noted. No other CINCA-related symptoms were present. The genetic background of CINCA is poorly known. Few families have been reported where more than one member is affected, suggesting that CINCA might be a genetically inherited disease. The clinical heterogeneity of CINCA may i) significantly influence the phenotype of the patients of the same pedigree, as that we reported ii) induce to misdiagnosis of the pauci symptomatic patients.

P117 PROXIMAL MYOPATHY WITHOUT SKIN CHANGES IN PAEDIATRIC PRACTICE—A DIAGNOSTIC CHALLENGE

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Background: Within juvenile idiopathic inflammatory myopathies polymyositis forms only a minor part of the disease spectrum. It is characterised by an absence of skin changes and different histopathology findings. Differential diagnosis is complicated by a large number of non-inflammatory causes of proximal myopathy and/or elevation of muscle enzymes. Appropriate evaluation and multidisciplinary approach are inevitable to avoid both therapeutic delay in myositis and unnecessary corticosteroid application in heritable disorders. Retrospective analysis illustrates diagnostic difficulties in 4 cases.

Case reports: Four children had muscle enzyme elevation and no pathologic skin or nailfold capillary changes, three had proximal muscle weakness, all four had pathological muscle MRI and biopsy findings, three myopathic EMG pattern. After complex evaluation diagnosis of polymyositis was made and anti-inflammatory therapy started in three children. In one girl dystrophinopathy Carrier State was revealed and genetic counselling offered to the family.

Conclusion: Myositis other than typical dermatomyositis though extremely rare should be seriously evaluated as a part of work-up for proximal myopathy in childhood. Since non-specific inflammatory activity could be absent more detailed tests might be sought incl. immunoblot techniques for rare autoantibodies and lymphocyte immunophenotyping. Muscle MRI serves not only a diagnostic test but also directs EMG and muscle biopsy. Histopathology examination should include immunostaining for structural proteins in selected cases. Screening tests for inherited metabolic disorders include investigations of carnitines, alanine and fasting and postprandial lactate and pyruvate in blood. Measurements of respiratory chain complexes in isolated platelets or muscle mitochondria and for some diseases DNA analysis are available.

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P118 TREATMENT OF JUVENILE DERMATOMYOSITIS (JDM) WITH HIGH-DOSE ORAL STEROIDS OR WITH STEROID-PULSE-THERAPY PLUS LOW-DOSE ORAL STEROIDS

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Objective: Treatment with oral steroids may control inflammation in the large majority of children with JDM, but is followed by Cushingoid syndrome. Therapy with i.v. pulse steroids may be complicated by flares during the treatment-free intervals.

Methods: Prospective randomized open study with oral high-dose steroids (prednisone 2 mg/kg for 4 weeks followed by gradual decrease) versus repeated pulses (i.v. methylprednisolone 20 mg/kg for 3 days with decreasing frequency of pulses) plus low-dose oral steroids (prednisone 0,2 mg/kg). Patients were evaluated after 8 weeks for initial response and for further 40 weeks for relapse.

Results: Among 24 patients with newly diagnosed JDM (median age 7 years, range 3-17 years, 17 girls) 13 patients received steroid-pulse-therapy plus low-dose oral steroids, 11 high-dose oral

steroids. All patients were considered responders. All patients were followed for ≥ 48 weeks. 7/24 patients had a relapse (3x pulse, 4x oral). Cushingoid syndrome was found in 9/11 patients with oral steroids and in 2/13 with pulse steroids ($p=0.003$).

Conclusion: Treatment of JDM with pulse-steroids plus low-dose oral steroids may be as effective as high-dose oral steroids, but Cushingoid syndrome occurs significantly less frequently.

Participants: Biedermann/ Berlin, Eisenberg/Herford, Häfner/Garmisch, Häfner/München, Haller/Switzerland, Heidemann/Augsburg, Horneff/Halle, Keitzer/Berlin, Lehmann/Bad Bramstedt, Leipold/Erlangen, Leupold/Dresden, Möbius/Cottbus, Queisser/Ludwigshafen, Quietzsch/Plauen, Weißbarth-Riedel/Hamburg. Supported by Aventis for patients' insurance.

P121 WHAT CRITERIA DO PEDIATRIC RHEUMATOLOGISTS USE TO MAKE THE DIAGNOSIS OF JUVENILE DERMATOMYOSITIS (JD)?

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Objectives: The purpose of this study is to determine what criteria pediatric rheumatologists practically use to diagnose JD as the criteria proposed by Bohan and Peter have never been validated.

Methods: 175 pediatric rheumatologists were asked to rate the importance of clinical findings, elevated muscle enzymes, muscle biopsy (MB), EMG, and MRI in establishing the confident diagnosis of JD using a 5 point Likert scale.

Results: The response rate was 59%. More than 85% of respondents rated the classic skin rash and proximal muscle weakness, and 69% elevation of muscle enzymes, as very or extremely important in making the diagnosis of JD. MB and EMG were rated by 54% as somewhat or not important at all. Investigations routinely used by respondents to diagnose JD: MRI (39%), EMG (26%), and MB (25%); 41% used none of these. MB were reported as frequently normal in cases where the classic JD triad was present, which did not influence therapeutic decisions in 55% of respondents. In the absence of the classic JD triad, MB was often found to be diagnostic.

Conclusions: These data suggest that pediatric rheumatologists do not routinely use the Bohan and Peter criteria to diagnose JD. Based on current practice, JD might be diagnosed in the presence of symmetric proximal muscle weakness, elevation of one or more muscle enzymes, and a classic skin rash. Only in the absence of all 3 criteria would MB or EMG be indicated for diagnostic purposes.

P124 EXPRESSION OF ICAM-I AND VCAM-I IN MUSCLE TISSUE FROM PATIENTS WITH JUVENILE DERMATOMYOSITIS

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Objective: To access of ICAM-I and VCAM-I in muscle tissue from patients with juvenile dermatomyositis (JDM) and to compare the expression of these cell adhesion with clinical, laboratorial and histological parameters.

Patients and methods: Thirty-five patients with JDM (Bohan and Peter criteria) were studied. The mean age of disease onset was 6 years 10 month and follow up time was 34 month. The male/female proportion was 1/2,5. The muscle biopsy was performed in the first year of disease onset (median: 4 months) in all children prior to immunosuppressive therapy in 25 patients. Routine histochemistry and immunohistochemistry (StreptABCcomplex/HRP) to ICAM-I and VCAM-I (Dakopatts) were performed on serial frozen sections. Statistical methods used were Chi-square, Wilks, Mann-Whitney, Kruskal-Wallis, Friedman and Mc Nemar tests.

Results: A semiquantitative analysis considering the positivity on vessels in different topography and on muscle fibers showed the following distribution (Table 7):

ICAM-I expression in capillaries of muscle tissue showed statistical significant correlation to muscle weakness ($p=0,005$), pulmonar involvement ($p=0,005$), CK level ($P=0,016$), degree of muscle degeneration on histology ($p=0,019$) and with predominance on females ($p=0,035$). Muscle vessels of all cases showed weak reactions to VCAM-I.

Table 7

	Vessels			
	Endomysial			
	Arterioles	Capillaries	Perimysial	Muscle fibers
ICAM-I	81,1%	94,6%	91,9%	8,1%
VCAM-I	5,4%	5,4%	18,9%	8,1%

Conclusion: ICAM-I expression on muscle vessels mainly on capillaries correlated to the severity of JDM manifestations.

P125 CORRELATION OF EXPRESSION OF MEMBRANE ATTACK COMPLEX EXPRESS TO PERIFASCICULAR ATROPHY AND CLINICAL DURATION OF JUVENILE DERMATOMYOSITIS (JDM)

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Objective: To establish a temporal correlation between the degree of perifascicular atrophy on muscle biopsy and the vascular complement deposits.

Patients and methods: Muscle biopsy specimens of 32 patients with JDM (Bohan and Peter criteria) were studied. Serial frozen sections from each case were stained with HE and for membrane attack complex (MAC) employing a monoclonal antiserum to neoantigens of human C5b-9 by standard streptavidin AB peroxidase method. A quantitative studies of diameter measurement of 500 muscle fibers of at least two fascicles were performed in all cases. All morphological determinations were made by two observers in double blind methods.

Results: 22 patients were submitted to biopsy during the first six months of onset of symptoms, and perifascicular atrophy was seen as soon as one month of disease. The peak of atrophy was observed around four months after onset. MAC deposits were scanty on all cases, being expressed on endomysial and perimysial vessels on 18% and 45% of cases, respectively. Among the 10 cases submitted to biopsy after six months of clinical duration, MAC was detected on endomysial vessels in 10% of cases and 50% on perimysial vessels.

Conclusion: Our findings support the hypothesis that the complement mediated vasculopathy might occur as a primary immunopathogenic event in the evolution of muscle lesion in JDM at the very beginning of the disease.

P126 SEVERE CENTRAL NERVOUS SYSTEM INVOLVEMENT IN JUVENILE DERMATOMYOSITIS

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Juvenile dermatomyositis (JDM) is a chronic autoimmune disease, characterized by myositis leading to proximal muscle weakness, and a typical skin rash. The course of JDM can be complicated by severe vasculitis in the muscles, skin, gastrointestinal tract, lungs, retina and even myocardium. Although irritability is often observed, severe central nervous (CNS) involvement is extremely rare.

We present 3 patients with JDM and severe, (near) fatal, central nervous system complications. All patients had at least 4 positive criteria of Bohan and Peter, which confirmed a definite diagnosis of JDM. Remarkably, they were all male, and had a relative high CK value at admission (1532-4260 U/l). Besides progressive proximal muscle weakness and skin rash, one patient presented with rapid irreversible decline of vision. Ophthalmologic examination showed active vasculitis of the retina. All three patients developed CNS symptoms (generalized tonic-clonic convulsions) while they were already treated for over two weeks with immunosuppressive drugs and being in an improved, relatively stable clinical condition. Other causes of the neurological symptoms could be excluded. In all three patients the course of JDM was fatal.

In conclusion, the clinical symptoms and further investigations in our patients suggest CNS involvement of the JDM. Though rare, CNS vasculitis can be a serious and life-threatening complication of JDM.

P127 OCULAR MANIFESTATIONS IN CHILDREN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Objective: 1. To determine the spectrum and prevalence of ocular manifestations in children with systemic lupus erythematosus (SLE). 2. To examine the correlation of the ocular manifestations with disease activity and the presence of circulating autoantibodies.

Methods: In this pilot study, we performed a comprehensive evaluation including detailed eye examination, measuring circulating autoantibodies (antinuclear, antiphospholipid antibodies) and calculation of disease activity index (SLEDAI) on children with SLE.

Results: Thirty-six consecutive children (32 female) with SLE completed the evaluation. The mean age of the patients was 11.3 years and the mean SLEDAI was 9.5. Twenty-three patients (63.8%) had the disease for more than 1 year. Thirteen patients (36%) had ocular manifestations. Nine eyes of 7 patients had abnormal schirmer's test. Three eyes of 3 patients had retinal vascular lesions. Two eyes of 1 patient had iridocyclitis. Three eyes of 3 patients had optic neuropathy and 7 eyes of 6 patients had visual field defects. Testing for correlation, using fisher exact test revealed positive correlation between optic neuropathy and CNS involvement. There were no correlation among other variables; however, the sample was small.

Conclusion: Ocular manifestations including sight-threatening complications are not uncommon in pediatric SLE. Optic neuropathy has strong prediction for CNS lupus.

P128 RAYNAUD'S PHENOMENON IN CHILDHOOD. IMMUNOLOGICAL FEATURES AND NAILFOLD CAPILLARY PATTERNS

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Objective: To study the immunological features and nailfold capillary patterns in patients with Raynaud's phenomenon (RP) begins under age 16.

Patients and methods: 24 infantile patients were studied, not selected and serial (year 2000), with RF and absence of skin or internal organs manifestations. All the patients were girls (15 mean age; 10-16 years) with mean evolution time of 3.5 years (1-11 years). Nailfold capillary microscopy study, autoantibodies profile were done in every patients.

Results: 45.8% patients developed connective tissue diseases (CTD): 1 SLE, 3 MCTD, 5 Undifferentiated CTD, 2 Pseudoscleroderma. The ANA was positive in 41.7%: 80% speckled pattern, 10% homogeneous and 10% anti-centromere, to superior titles at 1/160. The time of evolution of the FR was superior (mean 4.5 years) in the CTD patients that in those that had RF and ANA negatives (media 2.5 years). The microangiopathic patterns detected were: 29.6% CTD patterns without specific capillary abnormalities of scleroderma, 12.5% with scleroderma-pattern, 20.8% functional pattern with capillary pallor and 37.1% normal. Functional pattern with capillary pallor was observed in 84.6% of PR and negative ANA patients.

Conclusions: RP in childhood prevails in girls with mean age 15 years. In the patients with RP and positive ANA, CTD/scleroderma pattern was observed, confirming the CTD diagnosis in the pursuit. The functional pattern with capillary pallor showed a significant association with FR and negative ANA.

P129 THE FREQUENCY AND CLINICAL CHARACTERISTICS OF SELECTIVE IGA DEFICIENCY (SIGAD) IN CHILDREN AND ADULTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Objective: To determine the frequency of SIgAD in children and adults with SLE and evaluate potential differences in presentation and course of this disorder.

Methods: IgA deficiency was defined as a serum IgA concentration ≤ 0.01 mg/ml on 2 occasions by radial diffusion. SLE was defined by the 1997 revised criteria. 77 children with SLE seen over 20 years and 152 adults surveyed during a 1 year period were assayed for serum IgA levels. Disease characteristics were compared among the deficient patients and the IgA-normal patients.

Results: 12 patients with SIgAD were identified: a) J-SLE: 4 children with juvenile onset (≤ 18 yrs) for a frequency of 5% and 4 others encountered as adults; and b) A-SLE: 4 patients with adult onset for a frequency of 2.6%. No significant differences were found in clinical presentation or course except for a possible increase in recurrent infections ($p < 0.05$) and the observation that there were only 2 African-Americans. Anti-IgA antibodies were present in 7/7: 5 patients had received transfusions with no reactions; 3 had anti-IgA antibodies. One pediatric patient developed levels of IgA up to 1 mg/ml during a follow-up of 2 years. 2 patients died (septicemia, carcinoma) and 1 was on dialysis. For comparison, SIgAD was identified in 4/4134 persons in a midwestern community survey (0.1%); none had SLE; one had arthritis.

Table 8

	Sex F/M	Race W/B	Onset Age (yrs)	Follow-up (yrs)
J-SLE	7/1	6/2	13 (7-18)	18 (1-24)
A-SLE	3/1	4/0	32 (23-42)	5 (2-9)
Malar rash	6	Nephritis		6
Discoid rash	0	Encephalopathy		6
Photosensitivity	2	Serositis		8
Ulcerations	1	Cytopenia		8
Arthritis	11	Serology		12

Conclusions: SIgAD was identified in 2.6% of adults and 5% of children with SLE for a 35-fold increase in overall frequency. This small number of patients did not appear to have an altered clinical presentation or course of SLE.

P130 SWOLLEN LEGS IN PAEDIATRIC RHEUMATOLOGY

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Objective: Unilateral or bilateral swelling of the leg has been a presenting feature of several children to the department of paediatric rheumatology at our institution. This is a retrospective clinical study of selected cases.

Results: The diagnosis in each case is summarised in the table.

Table 9

Case	Sex	Age	Diagnosis
1	F	14	Campylobacter myositis
2	F	4	Osteomyelitis distal fibula
3	F	9	Vascular malformation in left soleus muscle
4	F	15	Idiopathic lymphoedema
5	F	12	Cellulitis left leg
6	M	10	Ruptured popliteal cyst in polyarticular JIA
7	F	10	Panniculitis in undifferentiated connective tissue disorder
8	M	13	Deep vein thrombosis in microscopic polyangiitis
9	F	11	Focal myositis
10	F	5	Popliteal cyst post acute reactive arthritis
11	F	14	Spontaneous deep vein thrombosis
12	M	6	Becker's muscular dystrophy

Conclusions: Unilateral or bilateral leg swelling may develop in children either with a pre-existing rheumatic illness, or be a presenting feature of disease in others. The range of diagnoses highlights the importance of general paediatric expertise within the paediatric rheumatology unit.

P131 CARDIAC ABNORMALITIES IN CONNECTIVE TISSUE DISORDERS IN CHILDREN

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Aim: To identify the nature and incidence of cardiac abnormalities in children with connective tissue disorders

Patients and methods: A retrospective case note review of 60 children (aged 1-16) with a diagnosis of connective tissue disorders attending the Rheumatology clinics in Alder Hey Children's Hospital. This included 28 children with systemic onset juvenile idiopathic arthritis (JIA), 16 Systemic lupus erythematosus (SLE), 9 Juvenile Dermatomyositis (JDM), 6 with other connective tissue disorders.

Results: 13 of 28 children with systemic onset JIA had echocardiography. 8 of the 13 had pericardial effusions (61.5% of those scanned). 8 of 16 patients with SLE had echocardiography and 2 had pericardial effusions (25% of those scanned). One presented with cardiac tamponade. 5 of 9 patients with juvenile dermatomyositis had cardiac problems. 2 had mitral regurgitation; 1 ventricular tachycardia requiring cardioversion; 1 persistent sinus tachycardia. One child presented with tachycardia and heart failure. In total 33 of 60 patients had cardiac assessments. Of these, 15 (45%) had significant cardiac abnormalities.

Conclusion: There is a significant incidence of cardiac involvement in children with connective tissue disorders, particularly JDM. Cardiac assessment should be an essential part of the investigation and management of affected children.

P132 ANTI BETA2-GP1 ANTIBODIES IN JUVENILE AUTOIMMUNE DISEASES (JAD): A MARKER FOR HEMATOLOGIC MANIFESTATION OF THE ANTI-PHOSPHOLIPIDS SYNDROME (SAF)

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Background: Beta2-GP1 is a serum protein necessary for the binding of anti-cardiolipin and cardiolipin and seems to identify patients affected by SAF or its associated clinical manifestations. There is scarce data regarding the presence of a-Beta2-GP1 in JAD.

Objectives: To investigate a-Beta2-GP1 in JAD and to establish its relation to clinical findings.

Methods: a-Beta2-GP1 and anticardiolipin antibodies (aCL) were investigated in 45 pts: 13 LES, 2 primary SAF, 16 JIA, 14 with other connective diseases (CD) (5 JDM, 5 undifferentiated connective diseases, 4 SS). a-Beta2-GP1 antibodies and aCL (isotopes G and M) were detected in the serum with the ELISA (INOVA). Their presence was also investigated in 49 healthy controls. The lupus anticoagulant (LA) was manufactured by the Screen and Confirm method.

Results: Six out of the 13 pts with LES (46%) were found to be a-Beta2-GP1⁽⁺⁾ (associated with aCL in 5 pts); they all presented the clinical manifestations of SAF: 5 with AHA and one Evans syndrome (p=0.01). The remaining 7 pts with LES (54%) were a-Beta2-GP1⁽⁻⁾ (5 were aCL⁽⁺⁾) and one had livedo reticularis with histopathologic thrombosis. The 2 pts with primary SAF presented association of a-Beta2-GP1 and aCL. 3/14 pts (21%) with other CD were a-Beta2-GP1⁽⁺⁾; 2 had association with aCL, and one with SS had Evans Syndrome. Out of the 16 pts with JIA, 3 systemics (19%) were a-Beta2-GP1⁽⁺⁾ (2 pts with aCL); none had the clinical manifestations of SAF. 3/12 pts (25%) were LA⁽⁺⁾ and only one had symptoms and association with a Beta2-GP1 and aCL.

Conclusions: 31% of the population studied were a-Beta2-GP1⁽⁺⁾; 64% of them presented symptoms of SAF (p=0.01): all hematologic. There was correlation between a-Beta2-GP1+aCL (p=0.01). The pts with LES had a stronger association between clinical manifestations and a-Beta2-GP1. The presence of a-Beta2-GP1 in JAD could be useful to identify hematologic involvement related to SAF, pending validation on adequate number of patients.

P133 AGGRESSIVE IMMUNOSUPPRESSIVE TREATMENT FOR PROTEIN-LOSING ENTEROPATHY (PLE) IN A SLE-LIKE PATIENT

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A.C., female. At the age of four severe thrombocytopenia and haemolytic autoimmune anaemia occurred. I.V. methylprednisolone was started with gradual resolution. After 4 months, proteinuria was disclosed. Renal biopsy showed a mesangial proliferative glomerulonephritis. Treatment with steroids and oral cyclophosphamide took to a prompt improvement of renal manifestations.

At the age of six, periorbital and pretibial edema were noted again. Albumin levels were 1.27 gr/dL. ESR was 73 mm/1st hour. Complement consumption was present (C3 11 mg/dL, C4 < 4 mg/dL). ANA were positive (1:160, speckled pattern), whereas other autoantibodies were negative. Proteinuria was absent. Faecal a1-antitripsin showed a severe intestinal protein dispersion (1500-6.500 gr/gr humid faeces, n.v.<200), consistent with the diagnosis of PLE. Abdominal echography showed a diffuse thickening of the submucosal layer of the small bowel. At colonoscopy diffuse purpuric-like

lesions, apparently at the level of the submucosa were also present. At histology, no specific features consistent with frank vasculitis or inflammatory bowel diseases were noted. A presumptive diagnosis of intestinal venulitis was posed. Pulses with i.v. methylprednisolone (10 mg/kg for 5 days) did not alter faecal protein dispersion since the patient required daily infusion of 20 gr. of human albumin. Cyclophosphamide pulses were started at high dosage (1 g/m² every 3 weeks) for a total of 3 infusions. After the first infusion, faecal protein dispersion showed a dramatic decrease and any further i.v. albumin supplementation was needed. After the second infusion, complement serum levels were within the normal range. Control abdominal echography and ileopancolonoscopy showed complete normalisation of the intestinal features. PLE may be a rare cause of severe hypoalbuminemia in the course of pediatric SLE. Even if, a prompt resolution after low doses of oral steroid is generally reported, aggressive immunosuppressive treatment could be necessary to control the gastrointestinal symptoms, especially when immune-mediate pathological process are suspected.

P134 ANTIRIBOSOMAL P ANTIBODIES (ANTI-P) AND NEUROPSYCHIATRIC MANIFESTATIONS IN JUVENILE SLE (JSLE)

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In JSLE, an association between anti-P and neuropsychiatric manifestations (NPM) has not been definitely established despite its association to depression and psychosis in adult onset SLE. In this study, we investigated the prevalence and clinical significance of anti-P in children with JSLE and NPM. Fifty-eight children meeting ACR criteria for SLE with onset ≤ 18yrs (49F: 9M, mean age at onset 13,3 ± 3,6 yrs; mean disease duration 5.5 ± 3,4 yrs) followed between 03/2000—30/2001 were included. Patients' charts were retrospectively reviewed; at the moment of the study, patients were interviewed and psychiatric questionnaires were performed. Anti-P was detected by Western-Blot technique using mouse liver ribosome. Sera from 20 rheumatic fever patients and 20 healthy children sex and age matched were tested as controls. Chi-square test was used for statistical analysis. Half of children (30/58 = 52%) presented NPM: 11 seizures (19%), 9 headaches (16%), 8 behavior alterations (14%), 7 psychosis (12%), 5 depressions (9%), 2 aseptic meningitis, 1 mild humor lability, 1 loss of memory, 1 facial palsy and 1 cerebral vascular ischemia. Anti-P was detected in 13/30 patients (43%) and negative in all controls (p<0,05). Anti-P was strongly associated headache (OR 2,58, p<0,05) mainly in girls (OR 3,63, p<0,005). We found a higher prevalence of NPM in JSLE (79%) than the worldwide average adult prevalence (50%). In contrast to adult onset SLE, anti-P was not associated to psychosis or depression, but to headache.

P135 CARDIAC INVOLVEMENT IN CHILDREN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Objective: To determine the prevalence and the pattern of cardiac involvement in children with systemic lupus erythematosus (SLE), and its relationship with disease activity.

Materials and methods: The medical records of 21 patients (pts) with SLE were reviewed. Inclusion criteria were diagnosis of SLE by the revised criteria of the American College of Rheumatology, and age < 16 years. Standard 12-lead electrocardiograms (ECG) and echocardiograms were analysed. Activity of the disease was measured by the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI).

Results: 19 (90.9%) pts had changes on ECG. The most frequent abnormality was ST-T change. It occurred in 10 pts (47.6%). Other changes were sinus tachycardia, sinus bradycardia, QTC prolongation, first degree AV block, anterior LBBB, atrial and ventricular premature beats. 14 pts (66.6%) had abnormalities on echocardiograms: 10 pts (47.6%) had mitral insufficiency, 3 pts (14.3%) - left ventricular (LV) dysfunction, 3 pts (14.3%) - LV hypertrophy, 2 pts (9.5%) -pericardial effusion. LV dysfunction, LV hypertrophy and pericardial effusion were associated with high disease activity (SLEDAI ≥ 20). Mitral insufficiency and ECG changes were not related to disease activity.

Conclusions: Cardiac abnormalities are frequently found on routine evaluation of children with SLE using ECG and echocardiogram. Our data suggest that ST-T changes and mitral insufficiency unrelated to disease activity are the most common findings. However, further investigations on this topic with larger sample sizes are required.

P136 ACUTE ABDOMEN IN CHILDREN AS SOLE PRESENTATION OF SLE

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A 10 year old girl and a 16 year old boy were admitted to our department for fever and severe abdominal pain. Both underwent emergency appendectomy. The persistence of the symptoms in the girl lead to a second laparotomy that showed necrosis and multiple perforations of the distal ileum and cecum, which were resected. The biopsy was compatible with mesenteric vasculitis. Hypocomplementemia, ANA and anti DNA positivity, and laboratory signs of glomerulonephritis fulfilled diagnostic criteria for SLE. After surgery, the second patient presented episodes of lower gastrointestinal bleeding with severe anaemia leading to a second laparotomy that showed edema and bleeding in final intestinal loop and cecum.. An ileal-cecal resection was required. The biopsy revealed leukocytoclastic vasculitis of the small and medium mesenteric vessels. Laboratory data showed LAC test positive, hypocomplementemia, ANA, ANCA, anti ds-DNA, anti-cardiolipin antibodies positivity. After few days, a malar rash appeared leading to a diagnosis of SLE. Although gastrointestinal symptoms affect 30% of patients with proven SLE, acute abdomen as sole presentation of SLE is quite rare. In a review of SLE patients with vasculitic presentation, only 1 out of 540 had an initial presentation as acute abdomen.

Seventy-five percent of all SLE-patients with gastrointestinal symptoms show biopsy-proved vasculitis with non-specific clinical manifestation. There are no available instrumental tests able to diagnose mesenteric vasculitis. The intraoperative evidence of macroscopic intestinal lesion and intraperitoneal haemorrhagic fluid may suggest intestinal vasculitis and thus require appropriate immunological and coagulation laboratory tests to confirm the diagnosis of SLE and to start early treatment in order to prevent more serious complications.

P137 HLA-DRB1 TYPING AS A PREDICTOR OF SYSTEMIC CONNECTIVE TISSUE DISEASES IN CHILDREN

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Objective: To investigate the frequency of HLA DRB1 alleles with the aim of finding if HLA-typing allows to identify more genetically homogeneous groups of patients in children with systemic connective tissue diseases.

Materials and Methods: The study comprised 64 patients, categorized as: mixed connective tissue disease (MCTD) (n=23), scleromyositis (n=16) and undifferentiated connective tissue disease (UCTD) (n=25), first admitted to the Institute of Rheumatology (Warsaw, Poland) between 1997-1999. As controls, a group of 158 healthy unrelated individuals of Polish origin who have been previously typed genomically for DRB1 alleles was used.

Patients were typed geneticaly for HLA class II alleles using sequence oligonucleotide probing (PCR-SSO).

Results: Patients with MCTD groups showed significantly higher frequency of DRB1*04 compared to the healthy controls (60.9% vs 19%, RR=6.63; p<0.0001). Patients with scleromyositis showed a significant increase in the frequency of DRB1*03 alleles (81.3% vs 20.8%; RR=16.4; p<0.0001) and a decrease in the frequency DRB1*15, DRB1*16 encoding the DR2 molecules. The distribution of DRB1 alleles in patients with UCTD did not differ from the controls. Direct comparison among the investigated three groups of patients showed a significantly higher frequency of HLA-DR*04 in MCTD patients compared to scleromyositis and UCTD (60.9% vs 12.5% vs 8.0%, respectively). Further, HLA-DR3 was more frequent in patients with scleromyositis compared to patients with UCTD (81.3% vs 20%).

Conclusions: The differences in HLA associations observed in studied patients suggest that HLA-DRB1 typing can be very useful, together with clinical presentation, in diagnosis of patients with connective tissue diseases.

P138 SYMPTOMS AND SIGNS IN CHILDREN WITH JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic Lupus Erythematosus is a syndrome, in which immunological events lead to a similar clinical picture. The usual style of reporting lupus is defining the disease by diagnostic criteria. That practice in children lead to ignore the initial clinical manifestations and to a delay in the diagnosis.

Objective: To describe symptoms and signs registered in patients with JSLE at diagnosis.

Methods: Structured medical record review of JSLE cases diagnosed at the Children's Hospital in Costa Rica. Data from 38 JSLE (4 boys/34 girls) were reviewed. They satisfied diagnostic criteria of the ACR for SLE.

Results: Of the cases, 40% were aged less than 10 years, 55% between 10 and 14 years and 5% were older than 15 years. The time from beginning of symptoms and diagnosis was less than 1 month in 45%, between 2 and 4 months in 39% and longer than 5 months in 16% of the cases. General symptoms presented in 26 (68%) patients: fever (n=21), malaise (n=9) and anorexia (n=9). Cutaneous manifestations were registered in 35 (92%) cases: malar rash (n=22), photosensitivity (n=15), edema (n=10), mucous ulcers (n=9), rash (n=9) and alopecia (n=5). Twelve cases (32%) presented neuropsychiatric manifestations: mood disorders (n=6) and headache (n=3). Joint and muscle symptoms were present in 32 (84%) cases: arthritis (n=22), arthralgia (n=17) and myalgia (n=6). Other findings included hepatosplenomegaly (n=5), hypertension (n=3) and serositis (n=7).

Conclusions: JSLE presents a variety of symptoms ignored in the diagnostic criteria. Provided with appropriate information about symptoms, other than the diagnostic criteria of JSLE, an early diagnosis is possible.

P139 CHARACTERISTICS OF MALE PEDIATRIC SYSTEMIC LUPUS PATIENTS

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Purpose: To evaluate the presentation and course of male pediatric systemic lupus (SLE) patients.

Methods: Retrospective chart review of all patients presenting between 1990—2000 with the diagnosis of SLE to the arthritis outpatient clinic identified one hundred and fifteen patients of whom 23 were male. Presentation, course, medications and laboratory values were reviewed. SLEDAI & SLICC scores were calculated

Results: The results are shown in the table.

Table 10

	#	F	M (%)	Renal Disease	Class IV Nephritis	CYC	SLICC* >1
Caucasian	30	27	3 (10)	1/3	0/3	0/3	1/3
African American	39	33	6 (15)	5/6	2/6	5/6	0/6
Hispanic	38	27	11 (29)	11/11	7/11	9/11	5/11
Asian	6	3	3 (50)	2/3	2/3	2/3	0/3

*SLICC by 2 years

CYC—Cyclophosphamide

Conclusion: SLE occurs more frequently in Hispanic males than in Caucasian males. Renal disease is more common and severe in this group. Non-Caucasian male patients were more likely to require Cyclophosphamide therapy.

P140 PROGNOSTIC FACTORS IN JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS

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Objective: The aim of the study was to analyse the prognosis and course of Juvenile Systemic Lupus Erythematosus (JSLE) depending on the clinical, immunological and genetical features seen at the onset of disease.

Materials and Methods: The study population comprised 106 patients admitted to the Pediatric Clinic between 1995-1999. The mean age of the patients at the onset of SLE was 12.7 yrs, and mean disease duration was 4.88 yrs. The onset of the disease was estimated as the first six months from the appearance of symptoms justifying the SLE diagnosis. All the patients met 4 or more of the ACR Classification Criteria. The disease activity at its onset and during its further course was estimated according to the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI). Patients were typed genetically for HLA class II alleles using sequence oligonucleotide probing (PCR-SSO).

Results: Our observations showed an allevation or full remission of the disease course parallel to the decrease in SLEDAI scale in 50% of the pts, while 33% of them demonstrated a progressive character of the disease process. Hypertensive, diffuse proliferative glomerulonephritis associated with profuse proteinuria and early increase in serum creatinine and urea level, presence of serum anti ds-DNA, vasculitis and hypocomplementemia were consecutively the most serious prognostic factors. The mortality rate for the whole group was 5.7%. General bacterial or virus infections were the most frequent causes of death. The results of the genetic tests showed that the presence of the DRB,*03 and DRB,*02 alleles is connected with JSLE but it doesn't have any influence on the course and prognosis.

P142 CARDIAC AUTOANTIGEN PATTERNS IN A PAIR OF MONOZYGOTIC TWIN DISCORDANT FOR CONGENITAL HEART BLOCK

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Objective: We studied if there are differences between cardiac autoantigen patterns in the serums of identical newborn twins discordant for congenital heart block. Patients: A pair of monozygotic twins: a) mother diagnosis of SLE according with the ACR criteria, with antiRo (SS-A) positive and antiLa (SS-B) negative b) infant 1 developed a severe congenital heart block and dead into the first 24 hours after birth. Infant 2 did not develop any typical feature of neonatal lupus and lives healthy c) no differences were found between the autoantibody profiles in the serums of the twins: ANA + homogeneous to 1:80; anti-dsDNA (ELISA) + 138; antibodies to Sm, RNP and SSB/La negatives, SSA/ Ro +; anticardiolipin antibodies negatives.

Methods: In order to check the existence of different autoantigen patterns we performed a battery of parallel western blot in which we ran microsomes from cardiac human tissue. These blots were probed with serum at several dilutions from each of these twins.

Results: The expression patterns of twins showed to be no differences between both infants. These findings drive us to think that, in this particular case, the cardiac antigen differences are not the responsible for the clinical features of these patients.

P144 ANTICARDIOLIPIN ANTIBODIES IN A PAEDIATRIC POPULATION

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Aim: To look at the diagnosis in children in whom anticardiolipin antibodies were done over a 7 year period in a Regional Children's Hospital.

Methods: All cardiolipin antibodies done between 1993-2000 at Royal Manchester Children's Hospital were analysed from the immunology computerised database.

Results: A total of 370 patients had anticardiolipin antibodies requested between

1993-2000. Of these only 54 (14%) showed levels greater than normal at any one point in time. We were able to examine 44 patient records (10 patient notes unable to locate). The median age was 11.5 years. The M:F ratio was 1:1.6. The test was repeated in only 10 patients; of whom in only 4 had the result normalised. The median anticardiolipin level was 20.5 (Normal < 8). 4 patients were commenced on anticoagulant therapy. 30% of patients had SLE, 35% had Vasculitis / Connective tissue disease, 5% Primary Antiphospholipid antibody Syndrome and 35% had Other diagnoses (Encephalomyelitis, renal impairment, prolidase deficiency and glutaric aciduria). ESR (Erythrocyte sedimentation rate) was raised in 44%; 35% had a ESR of more than 25mm of Hg. 48% had a raised ANA

(Antinuclear antibody), dsDNA (double stranded deoxyribonucleic acid) was raised in 18% and ANCA (anti neutrophil cytoplasmic antibody) was raised in 14% of the patients.

Conclusion: Our retrospective study reveals that anticardiolipin antibodies were being done more frequently than we anticipated. However our figures show that in a significant proportion of those who have raised levels the result was never subsequently repeated, and treatment was commenced only in a small proportion of those with persistently raised levels. The role of anticardiolipin antibodies in children is still unclear and currently there is no clear consensus on treatment guidelines. A multicentre prospective study needs to be undertaken to clarify these issues and to develop consensus guidelines.

P145 OUTCOME OF PEDIATRIC PRIMARY ANTIPHOSPHOLIPID SYNDROME (PAPS)

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PAPS is a peculiar clinical entity defined by the presence of ivascular thrombosis the presence of persistent positivity of anticardiolipin antibodies (aCL) and/or lupus anticoagulants (LA) in absence of an other underlying autoimmune disease (particularly SLE). PAPS is extremely rare during childhood and, so far, no data are available regarding its outcome.

Patients and Methods: Case records of 13 pts (8 M, 5 F) under 14 year of age presented as APS according to Sapporo's criteria have been retrospectively evaluated. The clinical outcome during follow-up was compared with the PAPS exclusion criteria proposed by Piette and co-workers (J Rheumatol 20; 1802-4, 1993) and ACR's criteria for the diagnosis of SLE in order discriminate three possible outcomes: i) persistent PAPS, ii) SLE, iii) SLE-like syndrome.

Results: The median age at onset was 9 years (range 5-13). All patients displayed venous or arterial thrombosis concomitantly with positivity of aCL and/or LA at least on two occasions. Deep vein thrombosis was seen in 5 pts, vascular cerebral involvement in 5 pts and arterial occlusion in 3 pt. Three patients displayed thrombocytopenia. The median follow-up was of 6 years (range 1-16). Four pts displayed recurrences of APA-related manifestations (TIA, stroke, deep vein thromboses) before starting warfarin treatment. Two patients developed frank SLE after 9 and 14 months from disease onset, respectively. displayed some PAPS exclusion criteria (high titer ANA positivity, lymphopenia) during follow-up and is currently considered as a SLE-like syndrome

Conclusions: PAPS can be considered as a distinctive clinical entity in the setting of autoimmune disorders also in pediatric age. The careful evaluation of exclusion criteria during follow-up may allow to the prompt identification of patients at risk to develop frank SLE or SLE-like syndrome.

P146 GONADAL FUNCTION IN ADOLESCENTS AND YOUNG MEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Objective: To evaluate gonadal function in adolescents and young men with SLE.

Methods: Four young men with SLE (ACR criteria) were submitted to a clinical (physical examination of the genital) and laboratorial (testicular ultrasound, hormones, antisperm antibodies and semen analysis). All patients were asked to provide 3 semen samples following masturbation after a minimum of 3 days sexual abstinence during period of 3 months. All 4 patients had a severe disease with renal involvement (World Health Organization class IV ou V).

Results: The median follow up after treatment was 6 years and 7 months. The median patients' age for beginning to ejaculate was 13.7 years. All patients were P5 and G5 based on Tanner's pattern of puberal changes, referred a normal erection and libido, and had physical examination including testicular volume and normal testicular ultrasound. One patient azoospermic (with high FSH and LH) and another oligo-eratospermic was in use of cyclophosphamide. Two patients were teratospermic. Antisperm antibodies were negative in all patients.

Table 11

Case/age (y)	Sexual activity/masturbation	Total sperm X 10 ⁶ /motile (%)	Seminal morphology	Cumulative dose P/M/A (gr)	Cumulative dose C (gr)/Time since last dose (y)
1 / 19	- / +	138 / 50	abnormal	40 / 5,1 / 74	11,1 / 6,5
2 / 17	+ / +	0,3 / 50	abnormal	61 / 0,5 / 14	24,6 / in use
3 / 22	+ / +	0 / 0	abnormal	41 / 5,7 / 77	8 / in use
4 / 16	- / +	135 / 64	abnormal	29 / — / 85	—

P=prednisone, M=methotrexate, A=azatioprine, C=cyclophosphamide

Conclusions: Despite the small number of patients, it seems that the immunosuppressive treatment for patients with SLE may damage the testicle function. Further semen analysis will demonstrate if these alterations are transitory or definitive.

P147 GONADAL FUNCTION AND AGE OF MENARCHE IN ADOLESCENTS AND YOUNG FEMALE WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Objective: Analyze the gonadal function and age of menarche of 23 female adolescents and young adults with SLE, and correlate it with clinical and laboratory (SLEDAI) and therapeutic parameters (prednisone, cyclophosphamide, azatioprine, methotrexate, cyclosporin and micophenolate mofetil).

Methods: A coorte study was performed to analyze the gonadal function based on gynecologic background and complementary laboratory assay. The clinical and laboratory parameters used in this study as markers of gonadal function were: regular menstrual cycles with or without dysmenorrhea and/or daily corporeal temperature with biphasic pattern and/or normal cervical mucous lenght and/or normal levels of plasma FSH, LH, estradiol, progesterone, prolactin and testosterone and/or normal uroctograms and/or serial abdominal and pelvic ultrasound compatible with either ovulatory pattern or actual or previous pregnancy. Statistical analysis was determined with Fisher's exact test, Kolmogorov and Smirnov test and Pearson coefficient.

Results: The mean age of menarche (13,5 ± 1,4 years) was greater than that found among 2578 Brazilian healthy adolescents (12,5 ± 1,3 years) (p=0,0002). The mean age of menarche was correlated with the time of duration of the disease (p=0,0085) and the cumulative dose of steroids (p=0,0013) used until the appearance of the first menstrual period. Pregnancy occurred in six patients. Sixteen female (70%) patients were considered fertile and seven (30%) infertile, even with normal plasma levels of FSH in the proliferative phase indicated an appropriate follicular storage in all patients. Fertility was not correlated with clinical and laboratory parameters of SLE.

Conclusions: The results of this study suggest that pediatric female patients with SLE reach adulthood with high chance of fertility.

P149 ULTRAVIOLET LIGHT EXPOSURE IS NOT A REQUIREMENT FOR THE DEVELOPMENT OF CUTANEOUS NEONATAL LUPUS ERYTHEMATOSUS

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Cutaneous neonatal lupus erythematosus (NLE) is a rare disorder, linked to the presence of transplacentally acquired maternal autoantibodies (anti-ENA). NLE skin lesions frequently appear in the second or third month of life, and ultraviolet exposure is thought to be an initiating factor since it can externalize intranuclear autoantigens at the cell surface. We report a baby who was born already with an extensive NLE rash, suggesting that sun exposure is not a requirement for the development of NLE skin lesions. A 31-year-old woman affected with mixed connective tissue disease gave birth to a female after 38 weeks of gestation. Pregnancy was uneventful and no perinatal complications were seen. The mother was positive for anti-RNP, but negative for anti-SSA/Ro and SSB/La autoantibodies. Already at birth, an extensive scarring rash with a few erythematous lesions was present on the baby's face and scalp; this progressed over the following months, and subsequently stabilized. Anti-ENA were

present in the baby's serum. Due to the unusual features of the disease expression, a skin biopsy was performed at age five months: results were consistent with the diagnosis of NLE, showing mononuclear cell infiltration and immunoglobulin deposition. No other features of NLE were detected.

This observation is unusual for 1) the presence of an NLE rash in the absence of anti-SSA/Ro; 2) the scarring and atrophic characteristics of the lesions; and 3) the development already *in utero*. This latter finding argues against the knowledge that sun exposure is necessary for lesion induction.

P150 ETANERCEPT AND JUVENILE IDIOPATHIC ARTHRITIS: ARE THERE CORRELATIONS BETWEEN DRUG EFFICACY AND DURATION OF DISEASE?

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Objective: To describe the effect of Etanercept in four patients with different duration and different Juvenile Idiopathic Arthritis (JIA) onset.

Methods: In our center, four patients with active polyarticular JIA who had inadequate response to methotrexate, received subcutaneous injections of etanercept (0.4 mg per kilogram of body weight twice weekly), for up to six months. There were 2 girls with polyarticular JIA at onset and 2 boys with systemic arthritis at onset; all patients had an average age of 12 years (range 5-27) and average disease duration of 10 years (range 3-24).

The Etanercept response was defined as a 30 per cent improvement or more in at least three of six indicators of disease activity (Lovell at all.2000)

Results: Etanercept was safe and well tolerated; one patient had urticaria after the first dose of etanercept; injection-site reaction occurred in two patients.

Treatment with etanercept for six months led to significant improvement in 3 of 4 patients. Only one patient did not have an adequate response to etanercept; this patient, male, with systemic arthritis at onset, had a disease duration of 23 years; during etanercept treatment he had one episode of flare. Another patient, male, with the same arthritis type at onset but with disease duration of only 3 years, had an improvement up to 30 per cent.

Conclusion: From these data, we observe that disease duration probably plays an important role, more than type of onset, in the efficacy of etanercept. Aggressive therapy in patients with early JIA has greater potential to improve disability but further studies are necessary to investigate its long term effect.

P152 AUTOLOGOUS BONE MARROW TRANSPLANTATION IN TWO CHILDREN WITH SYSTEMIC-ONSET JUVENILE IDIOPATHIC ARTHRITIS AND ONE CHILD WITH SYSTEMIC SCLEROSIS

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Between February 1999 and February 2001, 3 children underwent autologous bone marrow transplantation for severe and refractory systemic-onset juvenile idiopathic arthritis (2 cases) or systemic sclerosis (1 case). Conditioning regimen consisted in ATG 10 mg kg⁻¹ day⁻¹ from D-10 to D-6, cyclophosphamide 50 mg kg⁻¹ day⁻¹ from D-5 to D-2. No irradiation was administered. After bone marrow collection, CD34+ selection was performed (Mylenii, Amgen®) and 2 to 4 x 10⁶ cells/kg were infused.

The first patient, a 10-year-old girl with severe systemic-onset JIA, died 17 days post BMT from disseminated *Toxoplasma gondii* infection (Quartier P, Prieur AM, Fischer A. [letter] *Lancet* 1999;353:1885-6).

The second patient, a boy born in February 1995, started systemic-onset JIA at 11 months. His disease was highly active with both persistent systemic symptoms and polyarthritis that were refractory to prednisone, pulsed methylprednisolone, methotrexate, etanercept and the combination of etanercept 0,8 mg/kg x 2/week + methotrexate 1mg/week. Autologous BMT was performed in December 8th 2000. No complication occurred. Persisting knee joint effusion required intra-articular triamcinolone hexacetonide injection. The

child is well, with normal ESR, under prednisone 0,1 mg kg⁻¹ day⁻¹. Lymphocyte counts has recently reached normal values. CHAQ evaluation confirmed the functional improvement.

The third patient, a girl born in September 1992, had systemic sclerosis with hepatic, pulmonar and cardiac involvement. Autologous BMT was performed on February 1st 2001. No complication occurred. The child is significantly improved according to CHAQ and skin scores.

P153 A SELECTIVE COX-2 INHIBITOR, MELOXICAM (MX), AS AN EFFECTIVE ALTERNATIVE FOR TREATMENT OF PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA)

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MX as a selective COX-2 inhibitor, has already been registered for use adult s with rheumatic arthritis. During our participation in the phase I/II study of MX for children with JIA, a good drug effectiveness and tolerability was observed (Ann Rheum Dis 2000, 59 (Suppl 1): 252, A 824). Encouraged by these results a therapeutic observation was started on January 1, 1999, using the same MX dosage (0.25 mg/kg once a day). Patients participated who either did not tolerate Naproxen (NX) or were the once daily application of this drug was preferred.

Until April 30, 2001 MX-treatment was initiated and followed in 45 patients. 12 were male and 33 female. The mean age was 11.1 year (range 5-19 years). 21 patients had oligoarticular JIA, 5 polyarticular JIA, 1 systemic JIA, 13 enthesitis related JIA and 5 psoriatic JIA. MX was selected in 24 cases due to NX related side effects, and in 21 because of the once daily dosage.

Commercially available tablets containing 7.5 or 15 mg MX were administered, with a daily mean dose of 0.24 mg/kg (range 0.125- 0.3 mg/kg). The mean therapy duration was 5.2 months (range 1-20 months). The number of active joints decreased from 1.7 (range 1-9) before to 0.9 (range 0-2) at the end of the observation. 11 of 45 patients discontinued MX therapy due to side effects. Only one patient had to discontinue MX because of drug ineffectiveness.

In this preselected patient population MX was generally well tolerated and effective in 73% of the patients.

P154 EVALUATION OF DISEASE ACTIVITY, DISABILITY AND QUALITY OF LIFE IN PATIENTS WITH PERSISTENTLY ACTIVE REFRACTORY JUVENILE CHRONIC ARTHRITIS AFTER ONE YEAR TREATMENT WITH MONOCLONAL ANTI-TUMOR NECROSIS FACTOR- α ANTIBODY (INFLIXIMAB)

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An open prospective trial was carried out in a young population to evaluate the efficacy of Infliximab on disease activity, disability and quality of life. We enrolled 20 females, median age at the start of the therapy 21 yrs, median onset age 5 yrs, median disease duration 17 yrs. All patients had active disease: number of active joints (median 7), ESR (median 62 mm/hr), CRP (median 4.8 mg/dL), VAS (median 50), DAS index 4.68, health assessment questionnaire (HAQ) (median D.I. 1.06), Short Form 36: physical DIM 41 and mental DIM 56. 17 patients were still on corticosteroids. All patients discontinued any other DMARD aside from MTX. Infliximab was administered as a single infusion of median 4 mg/kg at time 0 and at weeks 2, 6, 14, 22, 30, 38, 46, 54. Since the 1st infusion, all 20 patients achieved a \geq 50% reduction in number of active joints, ESR, CRP, VAS. 8 patients who completed the 12 months course of treatment showed a statistically significant improvement of the median number of active joints (5 \rightarrow 0), the median value of the DAS index (4.65 \rightarrow 2.81), the median value of VAS (45 \rightarrow 22). The parameters of life's quality improved: HAQ D.I. (1.44 \rightarrow 1.37), physical DIM SF-36 (41 \rightarrow 69) and mental DIM SF-36 (60 \rightarrow 70). Two patients withdrew because of hypersensitivity reactions. Two patients with chronic active uveitis showed a visus improvement. These data suggest that Infliximab can significantly and promptly reduce disease activity and improve the quality of life. The treatment efficacy has shown to persist over time.

P155 CHRONIC RECURRENT MULTIFOCAL OSTEOMYELITIS IN CHILDREN: LONG TERM FOLLOW-UP AND TREATMENT OF RELAPSES

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The time course and clinical severity of chronic recurrent multifocal osteomyelitis (CRMO), an inflammatory disorder of unknown origin, may vary significantly. We followed 27 patients (mean of age 11 years) for a mean of 4.8 years. All patients were diagnosed using a clinical score, in addition to X-rays, MRI and CT. In addition, 17 patients underwent diagnostic biopsy including extensive microbial workup. All bacterial and fungal cultures from native biopsy tissues were negative. Of 27 patients 13 had a single occurrence of CRMO with no relapse, 5 patients had two relapses, one patient had 5 and one had 6 relapses. 7 patients suffered from "chronic" persistent inflammation lasting more than 12 months. A total of 22 patients was treated with naproxen (15mg/kg/day) for a mean duration of 19 months. The mean duration of therapy in 15 patients with one single occurrence or with a relapsing course of disease was 9 months. In general naproxen was sufficient and effective to control signs of inflammation in this group. Mean duration of therapy in the 7 patients with chronic persistent inflammation was 3.4 years and could not be controlled with naproxen alone. In one patient naproxen therapy was successfully switched to meloxicam, another patient was treated successfully by adding sulfasalazin. 5 of 7 "chronic" CRMO patients were treated with oral prednisone for 27 days (2 mg/kg/day over 7 days, followed by 1.5 mg/kg/day over 4 days, 1 mg/kg/day over 4 days, 0.5 mg/kg/day over 4 days, 0.25 mg/kg/day over 4 days, 0.25 mg/kg/day alternating over 4 days) in addition to naproxen. This regimen induced remission in 4 out of 5 patients, which lasted at least 1.5 years. The fifth patient (disease duration of 7.5 years) benefitted substantially during treatment, however signs of inflammation immediately recurred after discontinuation of prednisone treatment. Therapy was well tolerated in all 5 patients.

Oral prednisone treatment should be considered in the treatment of severe persistent CRMO, in addition to treatment with NSAID.

P156 ETANERCEPT TREATMENT IN SEVERE JUVENILE IDIOPATHIC ARTHRITIS FOR TWELVE MONTHS

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Material and methods: We report here the results of a-12-month therapy with etanercept in 22 patients (17 girls and 5 boys, mean age 10 (range 4-15) yrs; mean disease duration 7.7 (range 0.8-13.6) yrs) with juvenile idiopathic arthritis (JIA). All patients had active disease (15 polyarthritis, 4 extended oligoarthritis and 3 Still's disease) despite of therapy with systemic prednisolone every 2nd day (median dose 11 (range 0-45) mg) and DMARDs (median median 2.5 (range 1-4)). Statistical analyses are based on ITT analysis with LOCF.

Results: Reasons for discontinuation of the therapy in five patients were: rash (n=2), lack of efficacy (n=2), and loss from follow-up (n=1). There was a significant decrease in the number of hospitalisation days assessed from the consecutive 6-month periods since half a year before the start of the therapy (median: 14.5 vs 15.0 vs 7.5, p=0.043). A significant change was also found in the prednisolone dose (every 2nd day), number of current DMARDs, number of glucocorticoid (GC) injections needed, and in the level of disease activity markers:

Conclusions: According to this retrospective study etanercept is an effective and well tolerated therapy for severe JIA resistant to conventional drug treatment.

Table 12

Variable	Baseline Median (range)	At 12 months Median (range)	Median change ³ Median (95% CI)	p-value ⁴
Prdn, dose, mg ¹	11 (0-45)	7.5 (0-45)	-5 (-7.5 to -2.0)	<0.001
DMARDs, n	2.5 (1-4)	2.0 (1-3)	-0.5 (-1.0 to -0.5)	<0.001
GC injections ² , n	16 (0-30)	0 (0-12)	-6 (-11 to -3.5)	<0.001
ESR, mm/h	32 (7-115)	14.5 (4-115)	-16 (-26 to -4)	0.009
CRP, mg/l	9 (0-159)	0 (0-12)	-8 (-17.5 to 0)	0.02

¹Every second day. ²Calculated within 3-month periods. ³Rank-based confidence interval for difference in paired medians. ⁴Kornbrot's rank difference test.

P158 THE GERMAN ETANERCEPT JIA REGISTRY

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Objective: Etanercept has been introduced in clinical practice following a single controlled trial in juvenile idiopathic arthritis. Data regarding long term efficacy and tolerability are lacking in these patients. Therefore, in January 2001 the paediatric rheumatology working group of the "Deutsche Gesellschaft fuer Kinderheilkunde und Jugendmedizin" has set up a registry for long term follow-up of all children treated with etanercept.

Methods: The patient's history including diagnosis, pre-treatment, indication for start of etanercept, disease activity and concomitant therapy are documented. Disease activity is prospectively monitored using the PRINTO criteria including the number of tender and swollen joints, the number of restricted joints, patient's/parent's and physician's assessment, the ESA, CRP and the Child Health Assessment Questionnaire. Adverse events and reasons for drop-out are being recorded.

Results: So far, up to 200 children and adolescents are treated with etanercept in Germany. Data regarding the spectrum of diagnoses, pre-treatment, indication for treatment, clinical and laboratory responses, the spectrum of adverse events and reasons for discontinuation will be provided.

Conclusion: A registry is not able to replace prospective long term follow up studies. However, data regarding feasibility, efficacy, reasons for discontinuation, and adverse events allow to estimate the feasibility of etanercept treatment in clinical practice.

The registry is supported by Wyeth Pharma

P159 GROWTH RECONSTITUTION IN JUVENILE IDIOPATHIC ARTHRITIS TREATED WITH TNF-ANTAGONISTS

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Objective: To investigate effects of highly active antirheumatic treatment on growth retardation. Growth failure is a leading problem in uncontrolled juvenile idiopathic arthritis. It also affects the 10% of patients who are not treated with corticosteroids. The influence of proinflammatory cytokines like IL-1 β , IL-6 and tumour necrosis factor (TNF) on the neuroendocrine axis as well as on the production of IGFs has been postulated.

Results: 11 children with highly active refractory JIA were treated with etanercept for at least 9 months. In response to treatment, clinical and laboratory complete remission was achieved in 6 patients while major improvement was noted in 4 patients. Growth charts were reviewed and IGF-levels were determined. Before treatment 6 of the responders had a growth delay resulting into length SDS of -1.6 to -3.9. Upon treatment, growth velocity increased from 3.8 +/- 1.1 to 7.8 +/- 1.6 in these patients. 1 girl presented at the age of 17 (bone age 13, pubertal stage 1, SDS -3.9). This patient was treated with both etanercept and GH.

Conclusions: Intensified anti-inflammatory treatment using etanercept has a beneficial effect on growth in children with so far uncontrolled inflammatory disease. Growth failure should be included in the evaluation of anti-rheumatic treatment.

P160 AUTOLOGOUS STEM CELL TRANSPLANTATION IN A BOY WITH REFRACTORY SYSTEMIC JIA

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ASCT was performed in a 12 y old boy suffering from unremitting systemic JIA refractory to oral and parenteral methotrexate (up to 1mg/kg), cyclosporine, etanercept (up to 1.2 mg/kg twice weekly), methylprednisolone and cyclophosphamide pulse therapy (6x1g/m² monthly). Fever, exanthema, pericarditis and oligoarthritis recurred when prednisone was tapered below 20mg daily (0.8 mg/kg).

Progenitor mobilisation was performed with cyclophosphamide (4g/m²) and G-CSF(10 μ g/kg for 7 days). CD34 selection following the first two cytophereses yielded 19.4x10⁶ CD34 cells/kg. Cryopreservation without purging was performed with a third apheresis product. In response to the mobilisation regimen, the patient underwent clinical and laboratory remission and corticosteroids were

tapered. Three months later ASCT was performed. Methotrexate was discontinued at day -28 and diclofenac at day -3. On day -2 he developed fever and bilateral exudative coxitis responding well to 20mg prednisone. ASCT was performed using the CD34 selected product containing 6.5x10⁶ CD34+ and 4x10³ CD3+ cells/kg. During neutropenia a single febrile period occurred. The patient was discharged on day 28 while on antiinfectious prophylaxis and prednisone 10 mg. To date the patient is in remission 6 months after transplant and is treated with only 5mg prednisone.

The question arises, whether clinical remission can be maintained in children responding dramatically to a single high dose cyclophosphamide pulse or whether high dose conditioning and autologous stem cell transplantation is necessary.

P161 TREATMENT OF PERSISTENT KNEE SYNOVITIS WITH JOINT LAVAGE IN JUVENILE IDIOPATHIC ARTHRITIS (JIA)

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Objective: To assess the efficacy and safety of joint lavage with steroid injection in persistent knee synovitis despite previous steroid injections, in JIA.

Patients: 10 children (2 boys and 8 girls) with a total of 17 knees treated between 1997 and 2000 were retrospectively studied. Mean age was 14 years (10-20), and mean disease duration was 6.3 years (1-17). The diagnoses were: enthesitis related arthritis (1 pt), oligoarthritis (6 pts) with secondary extension for 2/6, systemic arthritis (2 pts) and juvenile dermatomyositis (1 pt). All patients (pts) had failed intra-articular triamcinolone-hexacetonide (THA) injections of the knee (2.3 injections/ pt within 2 years) with relapses occurring in 2 months or less. X-rays were normal except in 2 pts: osteoporosis with hypertrophy of medial condyle in one case. The mean CRP level was 22.8 mg/l (3-95) and the mean ESR was 23.5 mm first hour (8-80). Cytologic analysis of synovial fluid performed in 9 cases showed a mean of 10870 cells/mm³ with predominant PMN cells. 8 patients received disease modifying antirheumatic drugs (DMARDs) : methotrexate (6 pts) with ciclosporine (2 pts/6), or azathioprine (2 pts). The anti-inflammatory treatment was either oral corticosteroid (4 pts) with NSAIDs in 2 pts/4 or NSAIDs alone (5 pts).

Methods: The joint lavage was performed under analgesia (in a 24 hours-hospitalisation) : synovial fluid aspiration was followed by lavage with normal saline (500 to 1500 ml), and completed by steroid injection (THA in 15 knees, betamethasone in two). Articular rest in extension was then applied during 48 hours. The efficacy criteria were : joint effusion, pain, decrease of oral treatment.

Results: All joints responded favorably at one month. At 6 months, 47% (8/17) remained in remission and at one year, 18% (2/11) maintained a good response. Those 2 cases were observed in systemic arthritis. The DMARDs could be tapered in 2 children and oral steroids stopped in 2 others. The beneficial effect of the lavage was not associated with age, sex, disease duration, ESR, CRP, fluid leucocyte count. No side effects were noted.

Conclusion: These preliminary results demonstrate that joint lavage with intra-articular steroids injection is well-tolerated in children. Long lasting improvement occurred in few children ; however joint lavage was indicated in severe cases after previous relapses. Thus, joint lavage may be an option before synovectomy.

P163 SEMICIRCULAR LIPOATROPHY IN A GIRL FOLLOWING S.C. INJECTIONS OF METHOTREXATE

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Objective: Weekly s.c. injection of methotrexate is widely used in pediatric rheumatology, since it is a convenient way of administering and patients or parents can be easily trained to apply the injections, and local side effects have not been described. Lipatrophy semicircularis, a rare entity with atrophic dents, is seen exclusively on the ventral thighs of women, and is supposed to result from physical trauma. Localized lipotrophies are more common both following injection of drugs and in patients suffering from collagenoses. We report on a child who possibly exhibits a combination of these pathomechanisms.

Statement: A 10 year old girl had suffered from SLE for 4 years. Due to progressive disease with mononeuritis multiplex and

transverse myelitis she was treated with i.v. steroid pulses, cyclophosphamide, and s.c. methotrexate 20mg weekly, administered by the parents on the ventral side of both thighs alternately. After 9 months, the girl noticed infiltrations that 4 months later had developed into two semicircular, depressed skin areas, one 4x6-cm on the left anterolateral thigh and a second 2x10cm symmetrically located on the right thigh. A central bluish discoloration was temporarily prominent. Laboratory studies were within normal ranges. Although it cannot be proven, since parents did not give permission for biopsy, we believe this to be the first case of semicircular lipoatrophy resulting from s.c. methotrexate administration.

Conclusions: Young female patients, especially those suffering from collagenoses, should be advised to minimise trauma on the ventral thigh and in particular to avoid s.c. injections in this vulnerable skin area.

P165 UVEITIS, PEDIATRIC BEHCET DISEASE (BD) AND ALPHA INTERFERON

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Ocular disease is a major concern in children with BD, with regards to its frequent uncontrollable course and poor visual prognosis. Steroids give high benefit but result in too many side effects especially on growth velocity. The efficacy of immunosuppressive agents remains controversial. Recent reports have suggested the use of α interferon (α IFN) for severe ocular disease in adults. We report herein our first experience with α IFN treatment in a child with sight threatening ocular BD.

This 7 year-old Turkish boy, HLA B51 positive, presented with large mouth ulcers. and bilateral panuveitis: hyalitis, hypopion, without retinal vasculitis and impaired visual acuity. Oral steroid treatment (60mg/m²) was started with partial efficacy. The addition of azathioprine and colchicine allowed improvement of visual acuity. Unfortunately he relapsed 4 months later when steroids were decreased. Marked obesity and growth retardation lead us to consider α IFN treatment in this child. We used 3 Million steroids could be tapered to 0.5 Mg/kg/d. No side effect was observed during 3 months of α IFN therapy.

This observation confirms the high efficacy of α IFN in ocular BD especially in a corticoid dependant pediatric patient unresponsive to Azathioprine therapy. In adult experience α IFN has shown efficacy in terms of severity of retinal vasculitis, improvement of visual acuity and frequency of relapses. Few data on follow-up of 16 German patients (Kötter I et al), off α IFN treatment during a mean of 13 months, have suggested the possibility of prolonged remission. A multicenter study is needed to define the accurate dosage and duration of treatment in pediatric patients.

P166 HUMAN PROLYL-HYDROXYLASE (HPH) AND TYPE IV COLLAGEN (CL-IV) AS MARKERS OF LIVER FIBROSIS DURING THERAPY WITH METHOTREXATE (MTX)

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The association between long-term MTX therapy in juvenile idiopathic arthritis (JIA) and the development of significant liver fibrosis is controversial. Several studies reported 8% of liver fibrosis, documented by biopsy, occurred in patients treated with cumulative dose of MTX of at least 3 g/m². Several serum fibrosis markers, that can allow an early and not-invasive recognition of the collagen deposition in the follow-up of MTX therapy, have been recognized. Recently CL-IV, the major basement membrane constituent, and HPH, an enzyme involved in collagen synthesis, have been proposed as accurate fibrosis markers. We studied 23 patients (20 affected by JRA, 1 SLE, 1 overlap syndrome, 1 sclerodermia) treated with long term MTX therapy (range of dosage 2.5-17.5 mg/week, mean cumulative dose 994.38 mg, range 162-5753 mg) by measuring the transaminase, HPH and CL-IV levels.

All the patients younger than 15 years old showed normal CL-IV levels, while among the older patients 6 out of 23 presented elevated levels with no correlation with the cumulative dose.

About the HPH level, 20 patients had at least one elevated value but with no correlation with hypertransaminasemia and cumulative dose of MTX. These data are difficult to interpret: they could suggest that long term therapy with MTX at low doses may increase the risk

of liver fibrosis, but other studies are required to confirm the reliability of CL-IV and HPH as liver fibrosis markers. CL-IV elevation in patients older than 15 years of age can suggest the need of more intensive follow-up in selected patients.

P167 SIDE EFFECTS CAUSING WITHDRAWAL OF ETANERCEPT (TNFR:FC; ENBREL) IN PATIENTS WITH INTRACTABLE JUVENILE IDIOPATHIC ARTHRITIS (JIA)

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Etanercept has been showed to be effective in the management of methotrexate-resistant polyarticular JIA. In a recent pediatric study, the drug was safe and well tolerated, only 3 patients out of 69 (4,3 %) withdrew for side effects. We have treated 10 patients suffering from intractable polyarticular JIA, with etanercept (0,4 mg/kg twice a week s.c.). We describe 3 patients with important side effects which induced withdrawal in 3 cases (30%).

Case 1. A boy, affected by JIA since he was 2, started etanercept plus diclofenac at age 11. Three months later, he presented an important elevation of liver enzymes (x10), persisting after diclofenac discontinuation. After excluding other causes of hypertransaminasemia, we stopped etanercept. Quickly transaminase levels fell into normal range. Case 2. A girl, (sister of case 1), affected by JIA since she was 3, started etanercept at age 25 in association with naproxene. Five months later she presented mild elevation of liver enzymes (x3); because of the great benefit of the treatment, we decided to continue etanercept at the usual dosage. After nine months therapy, she experienced episodes of anxiety, sweating and tachycardia, immediately after the injection. Etanercept was discontinued and the symptoms promptly disappeared. Case 3. A boy, aged 22, with intractable JIA since he was 15, started etanercept and one month later he presented an itching, diffused, maculopapular rash resistant to steroid and antihistaminic therapy. The rash subsided upon discontinuation of the drug.

In adult rheumatoid arthritis, hypertransaminasemia occurred only in 16%-24% of patients treated with etanercept and it didn't occurred among the pediatric series described. Severe rash and personality disorder also occurred in our small series and caused the drug discontinuation, suggesting a very careful clinical and laboratory follow-up during etanercept treatment in pediatric patients.

P169 NITROUS OXIDE AS ANALGESIA DURING INTRA-ARTICULAR STEROID INJECTIONS IN CHILDREN WITH JIA

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Purpose: Intra-articular steroid injections are an essential part of treatment in children with juvenile idiopathic arthritis (JIA). N₂O offers a possibility of better pain relief and minimises the need for general anesthesia. We have evaluated N₂O -analgesia during intra-articular steroid injections in terms of pain, side effects and usability in children.

Method: The material consists of 60 children 4-19 years of age. Pain was evaluated with visual analogue scale (VAS) in 44 children during 55 sessions (170 intraarticular injections). A nurse familiar with the procedure performed N₂O-analgesia using an open circular system with a scavenging device. Paracetamol 40 mg/kg up to 1500 mg was given orally 2 h. in advance. Skin anaesthetics in form of EMLA® cream was offered. N₂O 30% was given gradually increased up to 50%. The children inhaled oxygen for 2 minutes after completion of treatment.

Results: Median rating for pain (VAS) before procedure was 8/100 (range 0-85), during procedure 10/100 (range 0-85) and immediately after 7 (range 0-80). Most children wanted to use the same technique next time (49/55). We noticed few side effects except nausea (7/55 before, 6/55 during and 9/55 after treatment) and vomiting (1/55 before, 5/55 during and 2/55 after treatment). All children achieved "street fitness" a short time after treatment.

Conclusion: N₂O as analgesia during intraarticular injections is a safe and efficacious method. Pain relief is adequate in children with JIA even if they had pain before the procedure. This project is supported by grants from AGA Healthcare, Sweden

P171 RISK OF LIVER FIBROSIS IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA) ON LONG-TERM THERAPY WITH METHOTREXATE

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Objective: To determine if the long-term use of methotrexate (MTX) in children with JIA is associated with the development of significant liver fibrosis.

Methods: Needle biopsies (Menghini suction-type needle) of the liver were performed on 200 children with JIA treated with MTX. 177 had a single biopsy, 23 multiple biopsies. The mean cumulative dose of MTX was 2.1g/m² of body surface area.

Results: 1. Patients with a single biopsy: 142 (80%) showed no fibrosis and 35 (20%) a slight fibrosis. 2. Patients with multiple biopsies: 16 (70%) had normal histologic findings in all biopsies, 4 (17%) with a normal first biopsy developed a slight fibrosis and 3 (13%) improved from slight fibrosis to normal. 3. In all 200 patients the liver biopsies were well tolerated without any following complications.

Conclusion: Long-term use of MTX in JIA does not appear to be associated with the development of significant liver fibrosis. Therefore we wouldn't recommend regular liver biopsies in JIA-patients on long-term MTX.

P172 THE POSITION OF AUTOLOGOUS STEM CELL TRANSPLANTATION (ASTA) IN CONCEPTIONS OF TREATMENT IN JCA/JIA AND OTHER INFLAMMATORY CONNECTIVE TISSUE DISEASES

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Based on the concept of the pathogenesis of autoimmune diseases like juvenile chronic arthritis (JCA)/juvenile idiopathic arthritis (JIA) or other connective tissue diseases ASTA is proposed to be a new therapeutic option in cases not responding to conventional treatment.

At the onset of polyarthritis or systemic types with high inflammatory activity and serious progression tendency current approaches for treatment of JCA/JIA favour an aggressive combined drug therapy. Treatment algorithms are including NSAID's, Prednisolone, Sulfasalazine, Methotrexate, intra venous Immunoglobuline, Methylprednisolone pulses and anti-Cytokines (anti-TNF).

The new therapeutical options are improving the overall prognosis markedly, but 5–7 % of patients are non responders. The development of serious handicaps and the persistence of inflammatory activity under combined drug therapy should be indication for treatment with ASTA. The total exploitation of the combined drug therapy in time, composition and dosage is the condition to start ASTA. We want to present the cases of four patients who were not responding to combination therapy and who were referred to the centre of transplantation of the Friedrich-Schiller-University of Jena. The individual indication for the use of ASTA in these cases should be discussed.

P173 ETANERCEPT IN JUVENILE IDIOPATHIC ARTHRITIS THE FRENCH EXPERIENCE

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We initiated in November 1999 an observational study by collecting prospectively data to assess the efficacy and tolerance of etanercept in children with different onset type JIA. Until February 28th 2001, etanercept was administered in 49 children with JIA from 15 French centers. All these patients had a polyarticular course and an inadequate response to methotrexate.

Tolerance to treatment was good in all patients but one who had psychiatric manifestations requiring treatment withdrawal after 31/2 months. No severe side effect occurred in the other patients. After 31/2 months, etanercept efficacy was assessed by using Giannini criteria in 40 patients. Twenty-nine (72%) patients improved. Significant

improvement was observed in 9 out of 17 (51%) patients with systemic-onset JIA (30% improvement: 9, 50%: 6, 70%: 4) and in 20 of the 23 (86%) non systemic patients (30% improvement: 20, 50%: 15, 70%: 8).

Etanercept seems to be less effective in patients with systemic-onset JIA.

P175 THE PLACE OF THE DISEASE MODIFYING ANTIRHEUMATIC DRUGS (DMARD) IN THE TREATMENT OF PATIENTS WITH JUVENILE RHEUMATOID ARTHRITIS (JRA) AND UVEITIS

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The purpose: To determine therapeutic efficiency of (DMARD) in patients with JRA and uveitis.

Materials: It was the comparative retrospective study to evaluate the efficacy of treatment with non-steroidal anti-inflammatory drugs (NSAID) and NSAID with DMARD. 76 pts were included in the study. All patients were receiving NSAID. 1) 21 pts were receiving NSAID + methotrexate (MTX), 2) 22 pts—NSAID + Hydroxychloroquine (HClq), 3) 33 pts—NSAID without DMARD.

Results: The 1st group—after the treatment 38,1 % of pts had not arthritis, 14,3 % of children had polyarticular onset but pauciarticular course of disease. In the 2 and 3 groups the development of pathological process took place despite of conducted therapy, that has found reflex in increasing of number of swelling joints (36,4 % and 42,4 % accordingly). The number of pts without uveitis after the treatment was approximately identical in all three groups (this fact does not exclude a possibility of independent regress of a uveitis without the treatment). However number of children with uncomplicated course of uveitis was much higher with methotrexate (66,7 %) as contrasted to by two other groups: 36,4 % (HClq) and 15,2 % (NSAID) (p < 0,001). 19 % of pts with MTX had the recurrence of uveitis and complications, (36,4 % of pts with HClq, 72,7 % pts with NSAID (p < 0,05).

Conclusions: The therapy with using of the DMARD has shown obvious advantages as for the arthritis, as for uveitis. Pts with JRA and uveitis need the serious treatment with using DMARD, as allows to change the prognosis of disease in the favourable party.

P176 INFILIXIMAB AND ETANERCEPT IN THE TREATMENT OF JUVENILE IDIOPATHIC ARTHRITIS. THE ATHENS EXPERIENCE

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Introduction: Tumor necrosis factor (TNF) has been proved to play an important role in the inflammatory process of juvenile idiopathic arthritis (JIA). Its biological action depends on binding to soluble or cell surface receptors. Anti-TNF factors either inactivate TNF- α (Infliximab) or bind to the TNF receptors (Etanercept).

Purpose: To study the efficacy of anti-TNF factors in treating JIA with polyarticular involvement resistant to conventional therapy.

Patients and methods: Thirteen children, 4 boys and 9 girls, with polyarticular JIA resistant to DMARDs and low corticosteroid dosage were included in the study. The selection of the anti-TNF factor was depended on the availability of the biological product. Infliximab was given to 4 children (30,8% of the patients), 2 boys and 2 girls, at a dose of 3–4mg/kg iv. Etanercept was given to 9 children (69,2% of the patients), 2 boys and 7 girls, at a dose of 0,4–0,6 mg/kg sc. The children's mean age was 9,00 \pm 3,66 years. The mean age of the disease onset was 3,50 \pm 1,90 years and the mean duration of the disease was 4,92 \pm 2,39 years. The mean duration of treatment with anti-TNF factors was 5,00 \pm 2,48 months. Follow-up of the disease was based on the following parameters: Ritchie index, CHAQ, systemic demonstrations, ESR, CRP, Hb, MCV, WBC, platelets, immunoglobulins. Improvement was considered a change of at least 30% in clinical parameters and in three or more laboratory indices.

Results: The response to anti-TNF factors was already obvious since the first month of treatment. Twelve patients presented improvement as this was defined above. The thirteenth patient had a severe allergic reaction during the third infusion of Infliximab which responded to prompt discontinuation of Infliximab infusion. Other side effects were not noticed.

Conclusions: The use of anti-TNF factors, either Infliximab or Etanercept in the treatment of severe forms of JIA is absolutely encouraging

P177 TREATMENT OF JCA AND SLE WITH HIGH-DOSE CHEMOTHERAPY AND AUTOLOGOUS HEMOPOIETIC STEM CELL TRANSPLANTATION (AHSCT)

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AHSCT has been proposed as a new therapeutic option for patients with severe autoimmune disease refractory to conventional treatment. Here, we report three children with a severe form of systemic JCA and one patient with severe systemic lupus erythematoses treated with AHSCT in a phase I study.

Patients: Three patients (age: 5, 9, 14 yrs) who developed severe systemic JCA with high spiking fever, rashes, hepatomegaly, polyarthritis, morning stiffness, ESR > 100 mm/h, CRP > 100 mg/l were refractory to NSAIDs, MTX, cyclophosphamide, steroids, etanercept after 2.5, 13 and 6 yrs. 1 patient (16 y-old) with SLE had a disease duration of 2.5 yrs with arthritis, carditis, pericarditis, hypertension, reduced pulmonary capacity, ANA 1: 5120, anti-ds DNA 485, anti-ss DNA > 200, anti-cardiolipin IgM 13.4, C₄ 0.09 g/l, lupus anticoagulants positive was refractory to steroids, MTX, IVIG, CsA and cyclophosphamide. This patient acquired on day + 45 EBV infection with LPD which was treated successfully with ganciclovir, cidofovir and rituximab. Stem cell harvest: After a priming dose of cyclophosphamide (2 g/m²) and mobilization with G-CSF (10 µg/kg/day) peripheral blood stem cells were collected using of a Cobe separator. Using a Clinimacs device, CD34-positive selection was performed yielding a final CD34⁺ cell amount of 4.2–6.5 × 10⁶/kg contaminated with zero to 3.2 × 10⁴/kg CD3⁺ lymphocytes, respectively. Stem cells were stored in liquid nitrogen. Conditioning regimen: Fludarabine (30 mg/m²): days -7 and -6; cyclophosphamide (50 mg/kg): days -5 to -2; ATG (5-10 mg/kg): days -6 to -2; methylprednisolone (1g/m²): days -4 to -2. On day 0, the frozen CD34⁺ cells were thawed and infused.

Results: Rapid engraftment of neutrophils > 1.0 × 10⁹/l: days +10 to +13; platelets > 20 × 10⁹/l: days +6 to +14; lymphocytes > 1.0 × 10⁹/l: days + 46 to + 66, respectively. Patients were discharged from hospital on day + 24 to + 53, respectively and remained free from active JCA and SLE with no immunosuppressive medication for 3.5, 3.5, 14.5 and 14.5 months, respectively.

P178 COMBINED TREATMENT WITH METHOTREXATE PLUS CYCLOSPORIN IN CHILDREN WITH PERSISTENTLY ACTIVE JIA. AN 18-24 MONTH FOLLOW-UP STUDY

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The aim of this multicentre study was to assess safety and efficacy of combined methotrexate (MTX) and cyclosporin A (CSA, Neoral Sandimmun[®]) in selected cases of persistently active JIA. 31 patients (M/F= 14/17) aged 2-18yrs (mean= 10.8 ± 5.1) with active disease (15 systemic to poly-, 9 polyarticular and 7 oligo-extended) despite treatment with one (at a time) DMARD plus NSAID and/or prednisone (PDN) were enrolled in the study and started treatment with MTX (15mg/m²/w) plus CSA (3-4mg/kg/d). 28/31 patients completed at least 12-months of therapy. The mean time between the onset of JIA and the initiation of the combined MTX-CSA regimen was 70.11 ± 39 months (12-180mo). Safety and efficacy of the MTX-CSA regimen were assessed at 12, 18 and 24 months. For efficacy, the "core set of outcome" of JIannini et al (1997) was used. At the end of 12 months, 54.8% of the patients had a good tolerance of the regimen and 45.2% manifested one or more adverse reactions, namely increase of serum creatinine (7), hyperhirsutism (5), gingival hyperplasia (2), transient hypertension (2) and anemia (1). In no patient signs of hepatotoxicity were found. 28/31 patients showed

improvement and continued the regimen. 23/28 patients completed 18-24 months of treatment (11/23 ≥ 18 mo and 12/23 ≥ 24 mo). At the 18 months, 5/11 patients were withdrawn due to poor response, 2 had moderate and 4 had satisfactory improvement. At the 24 months, 3/12 patients had moderate and 9 had satisfactory improvement. In conclusion, the combined administration of MTX plus CSA in children with persistently active JIA proved to be safe and effective in 18/28 (64.3%) patients.

P179 ANTI-TNF α TREATMENT IN JUVENILE IDIOPATHIC ARTHRITIS (JIA)

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Objective: To evaluate efficacy and safety of anti-TNF α treatment in patients with JIA who had inadequate response to methotrexate.

Patients and methods: Open-label study with 15 patients (7 male/ 8 female) affected by severe, refractory JIA with polyarticular course. Patients over 18 years old were treated with Infliximab (3mg/kg, weeks 0-2-6 and each 8 after), and patients under 18 received Etanercept (0,4 mg/kg, maximum 25mg per dose, twice a week). Improvement was defined as increase of 30 percent or more in at least three of six indicators of disease activity, with no more than one indicator worsening by more than 30 percent (Pavia criteria). Duration of treatment ranges from 3 to 21 months.

Results: After treatment, 14 of 15 patients showed improvement, and corticoid dose was reduced to 50 percent in 7 patients and discontinued in 7. Two patients withdrew because of severe adverse events (anaphylactic reaction during sixth infusion and macroscopic haematuria). Positivation of antinuclear antibodies was observed in patients while in treatment with anti-TNF α .

Conclusions: In our experience, new anti-TNF α treatments lead to significant improvement in patients with polyarticular JIA, and are well tolerated. Wider studies are needed to establish the frequency of adverse reactions and the clinical significance of antibody positivation.

P180 INFILIXIMAB IN JUVENILE IDIOPATHIC ARTHRITIS

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Infliximab (Remicade), a chimeric monoclonal antibody against tumor necrosis factor α (TNF- α), has been recently introduced for the treatment of Juvenile Idiopathic Arthritis (JIA).

Objective: To evaluate the efficacy and safety of infliximab (Remicade) in patients affected by a severe, refractory JIA non responder to traditional DMARDs.

Methods: We enrolled in an open study 9 patients (7 female, 2 male), mean age 13 years (range 5,2-26,2), mean onset age 6,2 years (range 1,7-12,8), mean disease duration 6,9 years (range 2,2-13,4). All patients had been treated with more than one disease modifying antirheumatic drug (DMARD). At every control we evaluated the following parameters: number of active joints, ESR, CRP, TNF α , IL-6, IL-8, physician and parents global evaluation (mean visual analogue scale (VAS), pain VAS, Child Health Assessment Questionnaire (CHAQ)). All patients were receiving non steroidal anti-inflammatory drugs (NSAIDs) and 3 corticosteroids (mean=0,1 mg/kg/die). Infliximab was given as a single infusion of 3 mg/kg at day 0, 15, 45 and then every 2 months. All patients discontinued DMARD aside from methotrexate.

Results: Until now 5 patients had received at least 4 infusions and 4 patients 2 infusions. After the first infusion all patients achieved a very good response. A statistically significant improvement of all parameters was observed (number of active joints, ESR; CRP; VAS CHAQ) at the first infusion and thereafter. At the fifth infusion one patient had an allergic reaction characterised by dyspnea and rash, but none withdrew because of adverse event.

Conclusions: These data suggest that Infliximab appears to be an effective and well tolerated treatment, reduce disease activity and improve the quality of life in patients affected by refractory JIA unresponsive to DMARDs. However, more data needed to evaluate its efficacy and safety as a long-term treatment in children.

P181 THE USE OF HEALTH-RELATED QUALITY OF LIFE (HRQoL) DATA IN THE CARE OF CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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The aim of the present study was to evaluate the use of the DUX-25, a health-related quality of life (HRQoL) measure, in the care of children with juvenile idiopathic arthritis. The DUX-25 (short form of the DUCATQOL = Dutch Children AZL/TNO Questionnaire Quality Of Life) is a generic self-report HRQoL questionnaire for school-aged children (5-16 years). HRQoL was defined as the affective evaluation of children of various aspects of their daily functioning. The items of the DUX-25 (using a five-point Likert scale) cover four domains: physical, emotional, social and home functioning. During their visit to the outpatients' clinic 34 children (mean age 9.01 years, st. dev. 2.02) and their parents were randomly assigned to two groups. In group 1 (n=17) the doctor used the HRQoL data of child and parent and in group 2 (n=17) no HRQoL information was given. Immediately after the visit to the doctor and two weeks later, the satisfaction score of all participants (child, parent and doctor) in group 1 was higher (for children significantly) compared to controls (n=17). However, the most important factor concerning satisfaction after visiting the doctor is HRQoL. The children with a better HRQoL, their parents and the doctor were more satisfied shortly after the visit and two weeks later (F=5,46; p=0,03).

P182 EPIDEMIOLOGY OF JUVENILE IDIOPATHIC ARTHRITIS IN NORD-PAS DE CALAIS REGION OF FRANCE

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Aim: To determine the prevalence of Juvenile Idiopathic Arthritis in the region of Nord-Pas de Calais, according to Durban classification.

Method: During 1999, this retrospective study included sex, date of first sign, date of diagnostic, anterior uveitis history (AUH), presence of antinuclear antibody (ANA), rheumatoid factor (RF), HLA B27. A first questionnaire was mailed to general paediatricians, rheumatological physicians, hospital paediatricians and orthopaedic surgeons in this region.

Results: 109 patients were followed up (67 females, 42 males); 48 oligoarthritis (44 %); 19 polyarthritis RF negative (17.4 %); 4 polyarthritis RF positive (3.7 %); 19 enthesitis related arthritis (17.4 %); 9 systemic arthritis (8.3 %); 10 unclassifiable arthritis (9.2 %); no psoriatic arthritis; 44 had ANA positive; 13 had AU. The prevalence was 11/100000 children, mean-age at the study time was 10.3 +/- 3.8 years; mean-age at the onset of the disease was 7.3 +/- 4.4 years; mean age at the diagnostic was 8.1 +/- 4.5 years.

Conclusion: This study confirms the prevalence described in the literature. The high number of unclassifiable arthritis suggests that Durban classification could not be sufficient to describe JIA.

P184 BACK PAIN IN PORTUGUESE SCHOOLCHILDREN

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Objectives: Calculate the prevalence of back pain in schoolchildren as well as their associated factors and repercussion on daily lives. Then we compared with a control group.

Methods: The study included 767 children from four urban schools. There were 419 girls and 348 boys. Mean age was 10.6 + 2.4 years (6-17). 92.2% were caucasian, 7.8% black and 0,7% Asian. A detailed interview on the basis of a standardised questionnaire was applied. Two rheumatologists performed physical examination. Control group was constituted by schoolchildren with musculoskeletal pain at other location.

Results: Back pain was reported by 61 schoolchildren (8%), 75,4% girls and 24,6% boys. Mean age was 11+2.2 yr (6-16). Back pain was more frequent in children at 10-13 yrs (64%). 43% had pain every day or week. Pain duration was at last 24 hours in 23% of cases and intensity had a mean 3.3 +1.95 (0.4-10), by visual analogue scale.

75% of cases had disability to daily live activities. Sixteen children visited their physician and 6 needed treatment. Back pain was associated with schoolbag carriage, physical activity and posture in 74% of children.

Comparing children with back pain and the control group we observed statistical differences in age, race, height, weight, lower extremities length and puberty (p<0.05).

Conclusion: In Portuguese schoolchildren, back pain was not so frequent as in other countries. However was recurrent and interfered with child lives. Association with schoolbag and practice of sport is an important factor. Back pain was related with anthropometric parameters and puberty.

P185 MUSCULOSKELTAL PAIN IN PORTUGUESE CHILDREN AND ADOLESCENTS

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Objectives: To determine the prevalence and consequences of musculoskeletal pain in urban schoolchildren.

Methods: This study was performed in unselected population of four urban schools. Two Rheumatologists visited 767 children (419 girls and 348 boys) in their school. The survey includes a detailed interview on the basis of a standardised questionnaire and physical examination. Visual analogue scale and a subjective disability index assessed the severity of their pain.

Results: 28.4% of cases had musculoskeletal pain. Pain was located at lower extremity in 59.6% of children. 28% had spinal pain, 8.7% upper extremity pain, 2.3% pain in thorax and 1.4% generalized pain. Severity of pain, by visual analogue scale, had a mean 3.31 +1.9 (0.1-10) and disability was present in 76.6% of cases. Pain relapses daily or weekly in 38.1% and persists part of a day in 78.9% of cases. 29% consulted their physician and 39 children consumed analgesics. Physical activity and schoolbag carriage was associated with pain in 63.8%. There were no statistically significant demographic differences among cases with and without musculoskeletal pain, except for weight and body mass index.

Practice of sports wasn't statistical different within groups, considering the type and time spent by week.

Conclusion: Musculoskeletal pain is a frequent symptom in our schoolchildren. Girls were affected more frequently. A high weight and body mass index was associated with pain. Pain had a relapsing character, determined disability, consumption of medical services and drugs. Children referred the relationship with physical activity.

P186 JOINT HYPERMOBILITY IS RARE IN PORTUGUESE CHILDREN AND ADOLESCENTS

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Objectives: To determine the prevalence of joint hypermobility in urban schoolchildren and it's association with musculoskeletal pain.

Methods: The Beighton criteria for joint hypermobility was applied by two rheumatologists on 767 schoolchildren (419 girls and 348 boys). Mean age was 10.6 + 2.4 years (6-17 years); 92.2% were caucasian, 7.8% black and 0,7% Asian. Children answered a questionnaire for musculoskeletal pain.

Results: 285 children had hypermobility. Only one (0.13%) had a score=5. Localized hypermobility was presented in 37.2% (mean score 2.13 + 0.53). Hypermobility was more frequent from 6 to 11 years (224/285). 55,1% were girls and 44.9% were boys (F:M= 1.2). Race distribution was 94.7% caucasian and 5.3% black.

Musculoskeletal pain occurred in 30.2% of schoolchildren with hypermobility and in 27.4% of the children without hypermobility (p>0.05). Location of pain hadn't correlation with hyperlaxity articular. Visual analogue scale had a mean of 3.04+ 1.7 (0.5-8) and 3.5+2 (0.4-10) in each group (p>0,05). Disability was present in 22.8% and 21.2% of the children with and without joint hyperlaxity, respectively. Children with localized hypermobility hadn't more pain related with trauma. Thirty-one percent of children with hypermobility practice sports and pain was present in 30 cases. This wasn't statistical different from the 56 schoolchildren with hypermobility and pain but without sports activity.

Conclusion: Joint hypermobility is rare in our population with a prevalence of 0.13%. Localized hypermobility wasn't related with musculoskeletal pain. Physical activity wasn't a risk factor to pain in joint with hyperlaxity.

P187 EVALUATION OF THE JIA-UEVITIS SCREENING PROGRAMME AND IDENTIFICATION OF HIGH-RISK PATIENTS REQUIRING URGENT OPHTHALMIC REFERRAL

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The outcome of uveitis is closely related to the severity of disease at diagnosis. Delays in initiating treatment of uveitis are an avoidable source of visual morbidity. We therefore examined the time to ophthalmic referral of JIA patients since 1986 in a single tertiary referral centre and the risk factors for delayed referral as well as severe disease at the time of diagnosis.

369 patients with JIA undergoing ophthalmic screening were included. 82 developed uveitis and had details of first presentation. 16/82 had severe uveitis.

The age at arthritis is 43 m and the age at uveitis is 41 m with a gap from arthritis to uveitis of 7.5 m. The age at diagnosis of uveitis has not changed over 15 yrs. The median gap from joint symptoms to the first slit lamp visit has declined from 9 months in 1990 to 4 months in 2000. Delayed referral was more likely in older children.

There were 12 oligoarticular JIA and 4 polyarticular JIA with severe onset. The risk factors for mild onset uveitis were female sex 0.5 (0.05) and oligo articular onset 0.4 (0.03).

Severe uveitis is more likely at diagnosis in males and polyarticular JIA, however all JIA patients are at some risk and all require an urgent first slit lamp examination. Delays in referral do not closely relate to clinical parameters and are likely to be linked to variations in medical awareness of the urgency of ophthalmic referral. There has been some improvement of referral.

P189 USE OF ALTERNATIVE THERAPIES IN CHILDREN WITH RHEUMATIC DISEASES

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Alternative therapies (AT) are becoming increasingly popular with general public, in particular in chronic conditions. The aim of our study is to determine the frequency of AT use and the type of medicine in children attending a paediatric rheumatology clinic. We interviewed the parents of 23 children, mean age 10.5 years, 13 girls and 10 boys, seen at our consultation of paediatric rheumatology. The diagnosis recorded were juvenile idiopathic arthritis (9), parainfectious arthritis (4), juvenile dermatomyositis (2), familial mediterranean fever (2), systemic lupus erythematosus (1), Behcet (1), non rheumatic conditions (4).

The use of AT was found in 8/23 children (35 %). Four of them had tried more than one AT and homeopathy was the most used (5 children). In the literature, the frequency of AT use varies considerably from 11 % in a general paediatric clinic to 84 % in haemato(c)oncologic patients. This study emphasizes the importance in children with rheumatic diseases to recognize the use of AT, which may interfere with patient care.

P190 SPINAL PAIN IN YOUTH

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Objective: The aim of this study was to analyse the prevalence of the spondylodynia among the population of the youth and to estimate the connection the signs of the disease with the presence of the pain.

Materials and Methods: The investigation was performed in 2498 students in 15 randomly selected higher schools according to the questionnaire based on the diagnostic criteria of juvenile spondyloarthropathies. The age of the examined students ranged from 14 to 21 age.

Results: Spondylalgia was found in 8.8% of cases. Lumbal and back pain occurred the most frequently (respectively 11.9 and 9.3%); the postural pain was the strongest. Limitation of the mobility of lumbal spain was observed significantly more frequent than cervical and dorsal spain (respectively 8.6% vs 2.6% and 3.8%). Scoliosis over 10 was detected in 20.3% of examined students.

Conclusion: In none of the investigated students any kind of spondyloarthropathy was found. Singular symptoms characteristic for inflammatory spondyloarthropathies appearing in the students may be treated as a risk factors for further disease. Posture abnormalities as scoliosis, kyphosis and vertebral insufficiency are frequent causes of the spinal pain.

P191 AUTOIMMUNE DISEASES IN JUVENILE CHRONIC ARTHRITIS (JCA) PATIENTS FAMILIES

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The aim of study was to discover the incidence of autoimmune disease in families of JCA patients.

Methods: Epidemiological, immunology, statistic methods were applied.

Objective: We studied 60 polyarticular onset JCA patients' families. Mean age of patients was 10,2 years at diagnosis, 41 were girls, 19 -boys. The diagnosis corresponded to EULAR criteria. Disease duration was 3,2-10,8 years (mean -7,2).

Results: Among first degree relatives we found out 1 case of systemic scleroderma, 1 case of diabetes, 1 -coeliac disease, 7 relatives of first degree had rheumatoid arthritis, 1 -trombocytopenia, 1 -glomerulonephritis, 2 -Raynaud syndrome. Two siblings had rheumatoid factor positivity. Most of affected relatives were womens (77%). So the incidence of autoimmune diseases in polyarticular JCA patients families was more than one hundred times higher comparing to population. The autoimmune diseases and symptoms were found in families those patients who had very advanced damage of joints and very high activity of disease.

Conclusion: Our data can suggest about shared mechanisms of polygenic inheritance both lupus cluster and diabetes cluster in autoimmune diseases.

P192 UVEITIS PREVALENCE IN JUVENILE CHRONIC ARTHRITIS (JCA) IN NORTHERN NORWAY 1985-1999

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Generally accepted risk factors for developing JCA-associated uveitis are female gender, young age at onset of arthritis, oligoarticular onset type and the presence of antinuclear antibodies (ANA). Ophthalmological screening programs have been directed according to these risk factors.

We have retrospectively investigated the prevalence of uveitis in all children diagnosed with JCA (EULAR criteria) in a total population from Northern Norway in the years 1985-1999. Mean child population 48.488 children <16 year of age.

The study group included 164 new cases of JCA, average annual incidence 22.6 per 100,000 children < 16 years, girls 63.4%, oligoarticular onset type 53.1 %, and median age at onset 7 years. Only 17.6% were ANA positive. At 31st of December 1999, 26 (15.9%) of the 164 had developed uveitis. Among these, 76.9% were girls, 69% had an oligoarticular onset type, 30.8% were ANA positive and median age of onset of arthritis was 2 years. Four of the 26 had a symptomatic acute uveitis, median age at onset of arthritis 12 years. Uveitis was diagnosed at the first eye examination after JCA diagnosis in 9 of the 26 patients. At 31.12.1999 eight patients still had active uveitis, and seven patients had developed sight-threatening complications. Among these seven, there were four with uveitis at their first ophthalmological examination. Young age at onset was the most important risk factor and ANA positivity was of less importance. In spite of our knowledge of risk factors and existing screening programs, uveitis continues to represent a serious threat to the eventual outcome of JCA in children.

P193 JUVENILE IDIOPATHIC ARTHRITIS (JIA) - TRANSITION FROM CHILDHOOD TO ADULTHOOD.

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Juveniles with JIA who are taken up to a transition programme should be able to cope better their disease and less complications of the disease can be expected. In addition adolescence programmes seem to be a great help for parents, too.

The change from the specialised paediatric rheumatism center to the rheumatologist of adulthood is often very difficult for patients with JIA and their parents. Transition is not a short term but rather a long-standing process.

The feeling of being ill, difficult contacts to friends and reduced possibilities in challenge lead to anxiety for the future. It seem not to be enough to hand out documents to the rheumatologist, because he can neither get an overview about the course of the disease, nor he can recognize the individuals burden. In our experience, this dissatisfaction prevents the necessary specialised consultations, and damages can be anticipated. In order to give the same chance to juveniles with arthritis as to healthy juveniles, medical services are required to think about strategies of transition which include the whole family.

From the view of the parents it would be important to guarantee: teamwork between the "paediatric" and the "adult" rheumatologist and a team of advisers and therapists for vocational guidance, education and study, sexuality, pregnancy, furtherance of independence, having intercourse with friends and support in loosening from parents.

P194 ELECTRONIC DATA MANAGEMENT (ARDIS) IN PEDIATRIC RHEUMATOLOGY CLINICS—A STUDY ON FAMILY SATISFACTION

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Objective: An electronic data management system (ARDIS—Arthritis and Rheumatology Documentation and Information System) was implemented in our outpatient clinic. This study evaluated family acceptance and satisfaction with the new form of data management.

Methods: A questionnaire was completed by 53 of 55 (96%) families who were scheduled subsequently for an appointment in clinics after the implementation of ARDIS and who had had appointments before, when paper based data management was used. Questions covered the use of computers in clinics, changes in doctor-patient conversation, doctors attention, atmosphere, duration or topics within the conversation. Answers were scaled from 1 (very positive) through 5 (very negative) or could be given in plain text.

Results: The use of computers in clinics was rated very positive by 50% of families. Doctors attention was rated unchanged by 67%, higher by 18% and reduced by 7%. Atmosphere was rated unchanged by 67%, better by 18% and worse by 10%. Duration of conversation was rated unchanged by 63%, longer by 23% and shorter by 9%. Potential advantages of the system were named by 65% including better and more complete documentation, letter composition, transparency of disease course, independence from paper chart, rapid access to information and reduced waiting time. Potential disadvantages were named by 25% including loss of data, impaired contact to patient, atmosphere of conversation, data security and quality control.

Discussion: The majority of families gave positive ratings for the use of ARDIS in clinics. Apparently the electronic system did not affect critical areas like doctors attention, atmosphere of conversation and duration of visit. The advantages of ARDIS, like facilitated data management, improved documentation of clinical status and easier access to data for scientific studies are matched by good family acceptance and satisfaction.

P195 GAIT ANALYSIS AFTER TREATMENT WITH ETANERCEPT IN JUVENILE IDIOPATHIC ARTHRITIS (JIA)—A CASE PRESENTATION

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Objective: To investigate effects on the gait pattern in a child with JIA., before and after treatment with the TNF-inhibitor etanercept,

Subject and method: An 11-year old girl with polyarticular JIA was tested before and after 6 months of etanercept treatment. Her disease had been active for 5 years and required methotrexate and repeated intraarticular corticosteroid injections (but none after start of etanercept). Gait analysis was performed using a six-camera motion analysis system (Vicon, Oxford, England). The subject walked with a self-chosen speed over two force plates (Kistler). Range of motion was measured by an experienced PT.

Results: The gait patterns showed improvements of the transversal plane kinematics of the ankle, knee and hip six months after treatment. The left foot progression normalised from an external to a more neutral position. In the sagittal plane plantar flexion increased by 11° immediately following toe-off. Increased ankle joint power was generated at toe-off and an improved plantarflexor moment was observed. The stride length was increased from 0.80 m to 0.97 m compared to normal subjects (1.14 m). The velocity increased from 0.86 m·s⁻¹ to 1.15 m·s⁻¹, approaching normal speed of 1.2 m·s⁻¹.

Conclusion: In this case of JIA, etanercept therapy lead to an almost normalized gait pattern.

P196 TEMPORAL AND FORCE PARAMETERS IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Juvenile idiopathic arthritis (JIA) often involves the lower extremities. The disease may result in restricted joint motion and pain, consequently leading to limping, a decreased step length and a reduced walking velocity. The purpose of this study was to compare temporal gait parameters and ground reaction forces during walking in 15 children with JIA and 14 healthy controls. The JIA children were additionally assigned into two groups based upon whether the disease affected one or both legs. Subjects walked along a 7.5-meter walkway at a self-chosen velocity. The mean velocity for the children with JIA was 1.06 m·s⁻¹ while the control group walked faster at 1.28 m·s⁻¹. When velocity was normalised to height, there was a tendency for the children with JIA to walk slower than the controls, although not significantly. A significant negative correlation was found between the level of perceived pain and walking velocity for the children with JIA. A significant decrease in the peak vertical force during heel contact and push-off were also observed in the children with JIA. There were no significant differences for any temporal parameter between the three groups; however, a tendency was seen for the children with unilateral involvement to have a shorter single support time for their affected leg. The results of the present study support subjective observations that we have seen in the clinic. The temporal and kinetic measures made here can provide the clinician additional information to make prudent decisions regarding treatments that include intra-articular steroid injections or physical therapy.

P197 PERCEPTIONS OF PLAY AND LEISURE IN JUNIOR SCHOOL AGED CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Play is recognised as having an important role both in child development and in physical and emotional well being. It is the dominant occupation in childhood, which provides a medium for fun, creativity and self-expression. Past research has suggested that children with disability experience a variety of barriers to engagement in play.

The aim of this research was to explore the perceptions of play and leisure in junior school aged children with Juvenile Idiopathic Arthritis. Twelve children between the ages of seven and eleven were interviewed in order to uncover any barriers to engagement in play, and the implications if any, for occupational therapy practice.

Results showed that all children in the study, reported difficulty engaging in play and leisure activities. Symptoms of the disease, fatigue, treatment regimes and their side-effects, as well as psychosocial factors were all reported to affect play and leisure experiences. Children also reported that play behaviours were often restricted by parents, friends and school personnel. Fear of damage and unclear communication about the effects of activity resulted in self-imposed restrictions, which further limited play experiences. Although children adopted a number of coping strategies to deal with these difficulties, they reported more indoor play and engagement in more sedentary activities, which often gave rise to feeling of sadness, loneliness and feelings of being different.

These findings may have important consequences for occupational therapy practice and provide an important reminder about the importance of assessing play as a vital and distinct area of occupational performance in children.

P198 EVALUATION OF AN 'INDEPENDENCE BREAK' FOR TEENAGERS WITH RHEUMATIC DISEASE

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Parental overprotection and other psychosocial issues, as well as reduced range of movement, muscle weakness, pain and fatigue, can limit the development of functional skills in children and adolescents with rheumatic disease. In the UK, conventional physio and occupational therapy interventions have largely focused on exercise/therapeutic activity programmes, splints, and activities of daily living. These conventional methods do not necessarily meet the needs of the teenage population. The need for an innovative intervention was therefore identified. A four day self-management programme in the areas of self-care, productivity and leisure, - 'The Teenage Independence Break', was developed, in order to try to address some of these needs. Although research has shown the benefits of summer camps for children with chronic disease, the content of the 'Independence Break' was significantly different, and the need to evaluate it was recognised. Twenty teenagers with a rheumatic disease attended the Independence break. Each was given an evaluation form prior to, and after the break. Teenagers identified a number of reasons for attending including; increasing independence levels, meeting similar others and to have fun. Post break questionnaires revealed the majority of

Question 1: What is your main reason for coming on the break?

For a break	1
Fun	7
Rest	1
To increase independence	5
To escape	2
To meet similar others	7
To get away from parents	2
To get away from siblings	1
For a new experience	2
For water activities	1
To participate in activities at own level	1
To feel normal rather than different	1

Question 2: What do you hope to achieve?

To increase function	1
To increase independence	8
Relaxation	1
Feel refreshed	1
Cook	1
Make new friends	3
Talk to others	1
Increase responsibility for own drugs	1
Learn to cope	1
Fun	3
See how others cope	1
Have a chance to do what I want	1

Question 3: Compared to your friends, do you think you can do as much as they can?

Yes 10	No 10	If no, for what reason?
		Unable to keep up
		Weaker
		Slower
		Less active
		Joint contractures

Post break Evaluation

Do you think you gained anything from attending the independence break?

Yes 15	No 3	If yes what
		Peer support
		Increase independence
		Made new friends
		Increased walking

teenagers felt they gained something positive from the experience. Responses included increasing levels of independence, increasing self-confidence, facilitating peer support and decreasing feelings of isolation. All participants felt it would be useful for other teenagers with rheumatic diseases. Although this evaluation supports previous research identifying the importance of psychosocial interventions in the management of young people with chronic disease further research is still needed in this area.

P199 AEROBIC EXERCISE TESTING IN JUVENILE IDIOPATHIC ARTHRITIS PATIENTS

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The purpose of this study was threefold (i) to examine the feasibility of maximum exercise testing in Juvenile Idiopathic Arthritis (JIA) patients, (ii) compute the error of measurement of maximum exercise tests, and (iii) characterize the functional aerobic impairment of these patients.

Twenty-three patients diagnosed with JIA (age 6-14) performed two graded, maximum exercise tests using an electronically braked cycle ergometer and metabolic cart to volitional exhaustion, two months apart.

Forty-six maximum exercise tests from 23 children were available for analysis. We faced no complications during the tests. Standard error of measurement between the first two assessments was 7.3%. The majority of the patients had an impaired physical fitness.

Maximal exercise testing of our study population of JIA patients was feasible. There were large variations in aerobic impairment between JIA patients, which makes a generalization about aerobic fitness in this population difficult. Using maximum exercise tests, JIA patients with a low aerobic fitness can be identified and a physical training program can be initiated.

P200 COMPUTER GAMES DEVELOPED TO EDUCATE CHILDREN ON DISEASE MANAGEMENT

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We have developed a series of computer games to provide exciting, educational experiences for children with juvenile idiopathic arthritis (JIA) and their caregivers. The games were developed to introduce children to the vocabulary, joint anatomy, medical management and coping skills needed to deal with their disease.

Methods: 5 games were developed and tested. Non-violent puzzle games were selected, as they are most appealing to the target population, (primarily girls 9 - 14). The games include: 1) maze; 2) solitaire; 3) memory card flip; 4) slider puzzle; 5) hangman.

Over 300 questions were included introducing self-selected levels of difficulty to each game. Vocal and written instructions addressing different reading levels were used. 17 girls and 8 boys with JIA (ages 7-18 yrs) participate. Children played the games independently and evaluated them at the end. Game scores were also recorded in the program. Each game session lasted 40 - 60 minutes.

Results: All the children enjoyed the educational experience. Greater than 80% liked the maze, solitaire, and memory flip games. 85% of children liked the hangman game; 69% the slider game. They all enjoyed the voice and music components.

Conclusion: Children respond well to educational experiences using computer games. Patients can contribute in the development of relevant, age appropriate materials leading to good acceptance of the information. Knowledge acquisition is yet to be tested.