disease, and a repeated pulmonary HRCT after 12 months showed a further progression of pulmonary fibrosis.
Conclusion—Autologous PBSC transplantation associated with Campath-1g treatment was safe and well tolerated in all patients and resulted in marked and sustained clinical improvement in two of the three patients.

11 Treatment of paediatric rheumatic diseases

11.1 Cyclosporin A treatment in chronic recurrent uveitis in JIA

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Uveitis is a serious cause of morbidity in pauciarticular onset juvenile idiopathic arthritis (JIA), the prognosis of which is otherwise good. To assess the efficacy of cyclosporin A in the treatment of chronic recurrent JIA uveitis, where local steroids failed, cyclosporin A was given to 4 patients (2–14 years old). The initial dose was 3–5 mg/kg/24 h by mouth, followed by a 3 mg/kg/24 h maintenance dose after inflammatory suppression. Cyclosporin levels and side effect parameters (blood pressure, WBC, Cr, AST, ALT, UT) were estimated. Patients were receiving non-steroidal anti-inflammatory drugs and one of them was receiving methotrexate also. The rate and severity of recurrences were recorded before and after cyclosporin. Before cyclosporin there were 6 (range 4–7) recurrences/child, 1 recurrence/month, of mean duration 2.5 (0.5–4) months, Tyndall 3+/recurrence. After cyclosporin, there was 1 recurrence/child with Tyndall 1+/recurrence, which was the result of non-compliance. Inflammatory suppression was achieved in a mean of 25 days. Mean follow up time was 12 (6–12) months. Cyclosporin side effects were: hirsutism (3), gum hyperplasia (1). Cyclosporin A is an effective and safe treatment in persistent, refractory uveitis of JIA.

11.2 Exceptional therapeutic response to infliximab treatment in recalcitrant Crohn's spondylitis

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At age 8 years in December 1990 a white boy presented to us with limp and an erythrocyte sedimentation rate of 70 mm/1st h, a value that would not go below 60 mm/1st h for the next 9 years. The cause could not be initially established. A year later he developed ankle synovitis. 15 months later magnetic resonance imaging confirmed bilateral sacroiliitis. A negative HLA-B27 in the presence of sacroiliitis made us suspect Crohn's spondylitis,[1] but intestinal disease was not obvious until 1999. Although clinically he had only mild diarrhoea his colonoscopic and histological findings were classic of Crohn's disease. His systemic symptoms, sacroiliac pain, peripheral arthritis, and weight loss continued to deteriorate over the years despite sulfasalazine 2500 mg/d, prednisone 20 mg/d, methotrexate 17.5 mg/w, and naproxen 500 mg/d. In January 2000 he received his first dose of infliximab 250 mg. The results of the intervention were astonishing. A month after the infusion he was able to attend school and to work part time, had no pain, no morning stiffness (previously up to 90 minutes), and his stamina normalised. There was no evidence of synovitis on examination, though lumbar mobility is still unchanged (Shober 12 cm). His response has been sustained and a second dose was given 2 months later (table 1).

Table 1

	12/90	*7/99*	*10/99*	*4/00*
Haemoglobin (g/l)	114	111	103	132
ESR (mm/1st h)	76	85	ND	11

Infliximab in this case was indicated for the skeletal and systemic but not gastrointestinal manifestations of Crohn's disease. A prospective study on the use of infliximab in paediatric ankylosing spondylitis/spondyloarthropathies is critical at this point.

1 J Rheumatol 1998;25:S1–49.

11.3 Nitrous oxide analgesia for intra-articular injection in children

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Background—Intra-articular injection of corticosteroid is commonly used in the treatment of inflammatory arthritis in children. Often the procedure is carried out under general anaesthetic or using sedation with agents such as benzodiazepines. Entonox, a mixture of 50% nitrous oxide and 50% oxygen, is widely used in paediatric practice for the alleviation of procedural pain. We report our experience with Entonox for intra-articular injection.
Results—Intra-articular injection was carried out in 70 patients. 69 of the patients had juvenile idiopathic arthritis and one had juvenile dermatomyositis. 64 patients (91%) tolerated the procedure well without any distress and 82 joints were injected, with a maximum of 2 joints injected each session. The joints injected were knees 73 (89%), ankles 3, wrist 1, elbow 1, metacarpophalangeal joint 1, and proximal interphalangeal joint 3. All patients who had had previous injections under general anaesthetic or with midazolam indicated that they would prefer Entonox in the future. Patients who tolerated the procedure had an age range 4 years 8 months to 17 years 7 months. There were no complications in any patient and all were fit for discharge within 30 minutes of the procedure. In 6 (9%) of the patients the procedure was not well tolerated, and 3 of these children completed the procedure in the same session using intravenous sedation. 3 of the children who did not tolerate the intra-articular injection using Entonox were aged less than 6 years.
Conclusion—In selected patients Entonox is a safe analgesic agent that may facilitate rapid and well tolerated intra-articular injection to treat inflammatory arthritis in children.

11.4 Infliximab in the treatment of persistently active refractory juvenile idiopathic (chronic) arthritis

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An open prospective trial was carried out in a young population affected by severe, refractory, polyarthritic juvenile idiopathic arthritis (JIA) to evaluate the efficacy and safety of infliximab (Remicade). We enrolled 10 female subjects, mean age 21.9 years (range 11.3–32.5), mean onset age 3.3 years (1.1–10), mean disease duration 18.6 years (9.8–31.4). All patients had been previously treated with more than one disease modifying antirheumatic drug (DMARD) (mean number 3.8/patient, as mono or combined treatment). All patients still had active disease: number of active joints (mean 5.9), erythrocyte sedimentation rate (ESR; mean 60 mm/1st h), C reactive protein (CRP; mean 39.2 mg/l), physician global evaluation (mean visual analogue scale (VAS) 52), Health Assessment Questionnaire (HAQ; mean disease index 1.43). 8 patients were still receiving corticosteroids (mean 0.1 mg/kg). All patients discontinued any other DMARD aside from subcutaneous methotrexate (mean weekly dose 12.5 mg, range 5–25) and continued with previous non-steroidal anti-inflammatory drugs and corticosteroids. Infliximab was given as a single infusion of 3 mg/kg at time 0 and at weeks 2, 6, 14, and 22. Until now 1 patient has received 5 infusions, 4 patients 4 infusions, 3 patients 3 infusions, and 2 patients 2 infusions. One patient withdrew because of a severe adverse event (hypersensitivity reaction at the third infusion). After the second infusion, 8 out of 10 patients achieved a very good response (50% reduction in number of active joints, ESR, CRP, VAS, HAQ). A significant improvement was also observed at the third infusion: number of active joints (mean 1.3), ESR (mean 21 mm/1st h), CRP (mean 1.5 mg/l), VAS (mean 13.8), HAQ (mean 1.06). An 11 year old girl with chronic active uveitis showed a great improvement of the visus. These data suggest that infliximab can significantly and promptly reduce disease activity and improve the quality of life in patients affected by persistently active and refractory JIA. However, more data are needed to evaluate its efficacy and safety as a long term treatment.

11.5 FK-506 (tacrolimus) treatment in severe juvenile idiopathic arthritis (JIA)

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FK-506 safety and efficacy were retrospectively tested in a reduced number of unresponsive patients with JIA
Patients and methods—The treatment of 12 children affected with JIA (4 systemic, 6 polyarticular, and 2 oligo with severe eye disease) was switched from cyclosporin A to FK-506, because of lack of response and/or unacceptable side effects. Median age was 10.45 (6.33 (14.49)), time from diagnosis 4.75 (2.21 (9.7)), and the female to male ratio was 3/1. All patients completed one year of treatment. FK was used at 0.1–0.3 mg/kg to maintain whole blood concentrations

between 5–10 ng/ml. Informed consent was signed by the parents before treatment was started.
Results—6/12 patients improved clinically by both medical and parent global assessment (3 systemic, 2 polyarticular, and one with eye disease). There were no major side effects. Minor side effects were seen in fewer than 25% of cases and included: abdominal discomfort, vomits, diarrhoea, headache, and insomnia. Steroid treatment was reduced in all responders except one. Biological data showed no changes in renal and liver function and no haematological abnormalities were recorded.
Conclusion—FK-506 has been shown to be safe, with only minor side effects, when monitored correctly. It could be considered in the treatment of patients with severe JIA, when cyclosporin A has failed.

11.6 Treatment of iridocyclitis in juvenile idiopathic arthritis

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Juvenile idiopathic arthritis (JIA) represents the most common cause of anterior uveitis. An early diagnosis of iridocyclitis, frequent ophthalmological examinations, and an aggressive treatment of the anterior uveitis are strongly recommended. The charts of 171 patients with JIA were reviewed retrospectively. Ophthalmological examination identified uveitis in 17 patients. 13/17 were female, 15/17 were affected by pauciarticular form, 15/17 were antinuclear antibody test positive, 16/17 had had onset of the articular disease before the age of 5. We followed the "step ladder" approach to treatment, described by Foster and Barret,[1] that takes care of the evolution and seriousness of eye disease. This strategy is divided into five steps: topical steroids, regional injection of steroid, oral non-steroidal anti-inflammatory drug treatment, systemic steroids, and chemotherapy. The patients examined had an ocular disease at the same time or soon after the onset of arthritis. All 17 patients were treated with topical steroid treatment, 7/17 needed steroid subtenonian injections, 5/17 received systemic steroids, 3/17 received methotrexate. In one patient treated with cyclosporin in association with topical and systemic steroids, treatment failed after one year to improve the intraocular inflammation. Three patients treated with systemic steroids needed cataract surgery. Systemic immunosuppresive/immunomodulatory treatment represents a step forwards in the treatment of anterior uveitis associated with JIA.

Foster CS, Barret F. Ophthalmology 1993;100: 809–17.

11.7 Bone density evaluation with calcaneal ultrasound in children with chronic rheumatic diseases: a 2 year follow up study

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Calcaneal ultrasound is a useful tool to evaluate bone density in children with chronic rheumatic diseases. We evaluated prospectively broadband ultrasound attenuation (BUA) in 40 patients (27 female, 13 male) affected by juvenile arthritis (28), dermatomyositis (6) and systemic lupus erythematosus (6). Mean (SD) age at onset of the study was 9.9 (3.6) years (range 3.2–15.8), mean disease duration was 5.1 (3.2) years. BUA was determined with a paediatric contact ultrasound bone analyser (CUBA). Seventy healthy subjects matched for sex, age, pubertal stage, and weight acted as controls. Mean (SD) BUA Z score in the total group of patients did not change over a 2 year period (from −0.68 (0.96) to −0.85 (1.64), p = NS). Patients treated with non-steroidal anti-inflammatory drugs (NSAIDs) only (18) showed a similar trend (from −0.34 (0.93) to −0.29 (1.50), p = NS). Patients treated with corticosteroids (13) showed a marked decrease in the Z score already during the first year of follow up (from −1.09 (1.08) to −1.66 (1.62), p<0.001), and more so during the second year (to −2.18 (1.49), p<0.001). Patients treated with alendronate (9) showed a significant increase in BUA Z score after the 2 year follow up (from −0.86 (0.48) to −0.02 (0.65), p<0.05). In the whole group of patients the mean rate of change of BUA values over 2 years ((observed value − baseline value)/baseline value) × 100) was about +10% (+5% in both years). Patients treated with alendronate showed a mean rate of change of about 15% during the first year and about 30% during the second year. In conclusion, BUA as determined with calcaneal ultrasound can be useful in monitoring bone status in children with rheumatic diseases; patients treated with corticosteroids, but possibly also with NSAIDs, seem to have a progressive decrease in bone mass.

11.8 Use of etanercept in the treatment of systemic JIA in the USA: results of a survey

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Objective—This study aimed at determining use and response to etanercept among patients with systemic JIA.
Methods—Surveys of the use of etanercept in individual patients with systemic JIA were sent to all paediatric rheumatologists in the USA.
Results—59 of 122 surveys were returned. Data were obtained on 45 patients (19F, 26M) who had been treated for a mean (SD) of 7.6 (4.9) months (range 1–27). The mean age at onset was 4.8 (4.9) years. The mean age at the start of treatment was 9.7 (5.4) years. 11 patients (24%) showed little or no improvement (4F, 7M), while 21 patients (47%) improved by >60% (11F 9M). 20 patients responded within 1 month, 11 patients took 2 months, and 6 patients took 3 months or longer to show improvement. There was no difference in the age of onset or disease duration between responders and non-responders. Systemic features (fever, rash, serositis) resolved in 21 of 28 patients who had symptoms at the start of treatment. 10 patients had been treated with high doses (up to 3 times the recommended dose). Only 2 appeared to have a better response to the higher dose. There were no major adverse reactions reported.
Conclusions—Etanercept seems to be well tolerated by patients with systemic JIA. These patients may have a lower rate of response than has been reported in patients with other types of JIA. Male subjects seemed to be less responsive than female subjects, but otherwise there were no features which distinguished responders from non-responders.

11.9 Movalis in the treatment of patients with juvenile chronic arthritis (JCA)

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Objective— This study aimed at assessing the efficacy of Movalis (Boehringer Ingelheim) in patients with JCA.
Methods—The drug was given in the form of 7.5 mg tablets to 20 patients (13 girls, 7 boys), They were aged from 10 to 18 years (mean (SD) 14.5 (1.94)), and had JCA with articular (17 patients) as well as systemic (3 patients) onset. A follow up period of 3 months was planned.
Results—Two patients dropped out of the study—one because of a lack of therapeutic effect (patient with JCA complicated with amyloidosis), the second because of adverse side effects (headache and somnolence). A considerable clinical improvement was seen in 71% of the 18 patients who completed the 3 month study. Movalis had a beneficial effect on fever, joint pain and swelling, and morning stiffness. A significant decrease in laboratory indices of the acute phase was seen in 83% of these patients.
Conclusion—The study results indicated that the treatment with Movalis in patients with JCA aged >10 years is useful and safe.

11.10 Alternative treatments in paediatric rheumatology: psychosocial factors influencing their use

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In paediatric rheumatology an increasing number of patients are using alternative treatments. However, little is known about the motivation and psychosocial factors influencing the use of these treatments.
Methods—A questionnaire based study was conducted to investigate motivations to the use of alternative treatments, conceptions of disease, coping strategies, compliance and satisfaction with conventional treatment in paediatric rheumatology patients and their families.
Results—Of 57 patients (40M/17F) and families who answered the questionnaire, 50.9% had used alternative treatments. Treatments most commonly used were homoeopathy (32%) and vitamins (18%). Most common reasons for their use were "to do everything possible for the child" (93%) and "alternative treatment as important supplement" to conventional treatment (70%). Patients with experience of alternative treatments were significantly more content with conventional treatment than those without. Patients currently using alternative treatments were rated by their doctors as significantly more compliant with conventional treatment. There were no significant differences in parent education, social status, coping strategies, and control conceptions between users and non-users of alternative treatment. Although 89% of users stated that they had informed their paediatric rheumatologist, doctors only knew in 23% and suspected in 10% that alternative treatments were being used.

Conclusion—In accordance with other studies, alternative treatments are also widely used in this study group. The use of alternative treatments is not a confrontation, but rather seen as supplementary to conventional treatment. Areas mostly in need of improvement are information and communication about disease and treatment, both conventional and alternative.

11.11 Treatment with etanercept in intractable juvenile idiopathic arthritis

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We treated with etanercept, a soluble tumour necrosis factor (TNF) receptor, 7 patients with intractable juvenile idiopathic arthritis, two (female subjects, aged 8 and 11 years) with a systemic form and five (one male and four female subjects, average age 14 years) with a polyarticular form. All patients received etanercept 0.4 mg/kg subcutaneously twice weekly. The patients were evaluated with the Child Health Assessment Questionnaire clinical score and inflammatory indexes.

The two systemic forms showed only a mild and transient clinical improvement with a steroid reduction of 3 mg/d in one case and 15 mg/d in the other. Neither reached remission and in neither case was it possible to withdraw steroid treatment.

On the other hand, the five patients with polyarticular form experienced a rapid response. There was a significant improvement in the clinical score and in the laboratory data within one month from the start of treatment. The drug was well tolerated and no important collateral event was reported. The only side effect in the two cases was a reaction at the site of injection.

In our experience the TNF inhibitor is useful in inducing remission in polyarticular forms, as reported in a recent study,[1] but the benefit in the systemic forms was too mild. The long term efficacy of etarnecept should be assessed, as well as its ability to induce a stable remission in these severe conditions.

1 Lovell DJ, *et al*. N Engl J Med 2000.

11.12 Efficacy of local treatment with triamcinolone hexacetonide in oligoarticular forms of JIA: clinical and laboratory correlations

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We studied 37 patients (30 female, 7 male) with juvenile idiopathic arthritis (JIA) oligoarticular forms, affecting only knees in 31 subjects. The average age was 3.6 years. Twenty one patients (57%) were antinuclear antibody (ANA) positive. The mean duration of follow up was 31.3 months.

Eighteen subjects were treated within 6 months from the first clinical manifestation while 19 patients were treated during relapses, 6 months after the beginning of the disease. The average remission time was 13.9 months, if the disappearance of all clinical signs of inflammation in the affected joint is considered as remission, relapsing after 6 months as prolonged remission, and a long stability period without relapsing as stable remission. Twelve patients (32%) (7 ANA positive, 5 ANA negative) went into stable remission after only one infiltration (average follow up 41.8 months). Thirteen patients (35%) (3 ANA positive, 10 ANA negative) went into prolonged remission but relapsed after an average of 19.4 months. Twelve patients (11 ANA positive, 1 ANA negative) relapsed within 6 months from treatment, and repeated infiltration or started oral treatment. Twenty five patients (67%), altogether went into stable or prolonged remission.

Our data show that the presence of ANA correlates with a reduced probability of maintaining a long remission ($p<0.01$). As far as timeliness of treatment is concerned, we found a positive significant correlation with the duration of remission ($p<0.03$). Furthermore, we found that in patients treated within the first 6 months the disease had a good evolution independently of ANA positivity. By contrast, relapses occurred before six months in patients who were infiltrated after 6 months from the onset of disease, particularly if they were ANA positive (8/11 ANA positive *v* 1/6 ANA negative). We found no correlation between age at onset and duration of remission. In conclusion, early local treatment and ANA negativity are the principal factors correlating with long term remission in patients with oligoarticular JIA.

11.13 Fludarabine based conditioning for autologous lymphocyte infusion in idiopathic juvenile arthritis

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We treated two patients with intractable forms of systemic juvenile idiopathic arthritis (JIA) with autologous lymphocyte infusion, using a new schedule for the conditioning regimen. We substituted fludarabine for cyclophosphamide because it is at least as effective in inducing immunosuppression, but has fewer adverse effects. Fludarabine is the base for the so called "mini-transplants" or "non-myeloablative transplants" in allogenic settings.

The patients received immunosuppressive treatment as follows: on day 7, for 5 consecutive days, they received IV fludarabine 30 mg/m^2/d; from day 5, 5 vials/m^2/d of lymphoglobulin (Inst. Merrieux) were given for 5 days; autologous lymphocytes were infused on day zero. Cyclosporin A was given intravenously from day 1 at doses of 4 mg/kg on the first day, then of 3 mg/kg up to the 7th day when it was given orally; from day 5 up to day 1, betamethasone 0.2 mg/kg was given intravenously, followed by an oral dose of prednisone 1 mg/kg/d for 1 month.

Both our patients (a 15 year old boy and a 14 year old girl) achieved a remission that was maintained even after steroid reduction. After one year from autologous infusion the boy is still in remission, receiving cyclosporin A as his only treatment. The girl maintains the remission while receiving cyclosporin A and low doses of steroids (prednisone 5 mg/d). In conclusion, we suggest that our procedure might be proposed for intractable systemic JIA because it can induce remission, allows a reduction of steroids with regain of growth, and is well tolerated.

In comparison with other conditioning regimens, the morbidity and mortality of our regimen is surely safer.

11.14 Alendronate in the treatment of osteoporosis in rheumatic diseases of childhood

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Alendronate is an aminobisphosphonate widely used in the treatment of corticosteroid induced osteoporosis in adults, but few studies have been carried out on the use of bisphosphonates in children. This study aimed at assessing the efficacy and safety of alendronate in the treatment of corticosteroid induced osteoporosis in 6 children (5F, 1M), mean age 15.7 years (range 10.9–18.1), with systemic lupus erythematosus (5 patients) and dermatomyositis (1 patient). Patients were receiving chronic corticosteroid treatment; the steroid mean dose was 0.2 mg/kg/d, and the cumulative dose was 21.15 g (range 10.9–27.2 g). Alendronate was given at 10 mg/d (after an overnight fast, with water) for at least 12 months. Bone mineral density (BMD) of the lumbar spine at the L1-4 level was evaluated by dual energy *x* ray absorptiometry (DEXA Hologic QDR 2000) every 6 months. In all the patients the BMD increased (mean 19.1%; range 4.9–38%) after 12 months' treatment. Four patients continued to receive a stable dose of steroid, 1 patient relapsed so the steroid treatment was increased from 0.2 to 0.5 mg/kg/d after the first 3 months of treatment, and in 1 patient disease improved, allowing a reduction in steroid treatment from 0.5 to 0.3 mg/kg/d. In 4 patients, in whom alendronate treatment has been continued for 24 months, lumbar BMD has improved (mean 6%). In 2 patients, alendronate treatment was stopped after the first 12 months because of a low dose of steroid (less than 0.1 mg/kg/d) and disease inactivity; in these patients BMD evaluation after a year showed a 3% reduction in lumbar BMD in one patient and a 0.4% increase in the other one, whose improvement after alendronate treatment had been 20.6%. After 24 months the drug was withdrawn in a further 4 patients and in 2/4 BMD worsened after 12 months. No relevant side effects were seen during the treatment. Alendronate seems to be effective and safe in the treatment of steroid induced osteoporosis in paediatric connective tissue diseases, but its effect is not always long lasting even after 24 months' treatment.

11.15 IV Solumedrol pulsing in new onset systemic JIA

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Consistent with the experience of most paediatric rheumatologists, a recent review of systemic juvenile idiopathic arthritis (JIA)[1] indicated that despite the aggressive use of disease modifying antirheumatic drugs, most patients (74/80) required steroids, resulting in significant morbidity, especially growth failure.

Retrospective chart review disclosed 19 new patients with systemic onset JIA seen in the arthritis clinic at TSRH between August 1997 and September 1999 and followed up for 7–35 months. Patients with persistent systemic features after 4 weeks of therapeutic non-steroidal anti-inflammatory drugs were offered the choice of daily prednisone or pulse IVCS. Low dose daily prednisone was

Table 2

Treatment	*No*	*Func Class*	*Current status*	*Disease activity (mo)*	*Growth*
NSAID only	4	I	Remission	5.4	Normal
MTX	1	I	Inactive	27	Normal
Pred	2	I	Remission	7	Abnormal
Pred/MTX	1	II	Controlled	16	NA
IVCS	3	I	Inactive	4.3	Normal
IVCS/MTX	3	I	2 Inactive	18	Normal
		II	1 Controlled	8	Normal
IVCS/MTX/Pred	5	I	1 Remission	9	Normal
		I–II	3 Controlled	14.7	Normal
		III	1 Active	16	Normal

required between pulses in 5 patients and methotrexate added in 9 (table 2).

These preliminary data seem to indicate that IVCS are effective, well tolerated, and help preserve normal growth curves in most patients despite active disease variables.

1 Lomater. J Rheumatol 2000;27:2.

11.16 Etanercept in the treatment of juvenile idiopathic arthritis

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Methods—We report here the results of 6 months' treatment with etanercept in 21 patients (16 girls, 5 boys, mean age 10 years (SD 3.5), disease duration mean 6.6 years (SD 3.2)) with juvenile idiopathic arthritis. All patients had active disease (14 polyarthritis, 5 extended oligoarthritis, 2 Still's disease) despite treatment with systemic prednisolone every 2nd day (median dose 10 mg (range 5–41 mg)) and disease modifying antirheumatic drug(s) (DMARDs; median number 2.0 (range 1–4)).

Results—2 patients (10%) developed adverse events leading to discontinuation (allergic rash after 3 weeks and 2 months, respectively). The results are given for the 19 patients completing the 6 month treatment. During the treatment there was a significant decrease in the number of days within 3 month periods treated at hospital (median 7.0 *v* 9.0 *v* 5.0, p=0.009). Also, the dose of prednisolone, number of DMARDs used, number of intra-articular glucocorticoid (GC) injections decreased, and the laboratory variables reflecting inflammation ameliorated (table 3).

Conclusion—Except for rash, etanercept was well tolerated. The treatment resulted in excellent clinical response. During the 6 month course, the dose of oral prednisolone and the number of local GC injections decreased, and the numbers of DMARDs used could be reduced. In addition, the numbers of days treated at hospital because of active disease was reduced in comparison with the 3 month period before the start of the treatment.

11.17 Hip injection in juvenile idiopathic arthritis (JIA): long term follow up

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Sixty two hips were injected with triamcinolone hexacetonide (TX) in 16 patients with systemic JIA (S), 11 with polyarticular JIA (Po), 8 with extended oligo (EO), and 2 with ERA. Mean age at disease onset was 5.15 years (range 0.25–15), mean age at injection was 9.1 years (2–17.5). Hips were injected with 10–40 mg TX under general anaesthesia with image intensifier. Bilateral injection was performed in 15 S, 9 Po, 1 EO, unilateral injection was performed in 1 S, 2 Po, 7 EO, 2 ERA. Injections were followed by three days immobilisation and a programme of non-weightbearing activity either at home (17 patients) or in a rehabilitation centre (20 patients). Four hips underwent a second injection. Functional results were evaluated according to an adapted Postel Merle d'Aubigné scale, grading pain, joint range, walking from 18 (normal) to 0 (worst). Hips were assessed after one year (T1) and at final examination (Tf: mean 7 years for S and Po, mean 3 years for EO). The results were considered as excellent or good (gain of >6 points), no change, or worse (loss of >6 points) (table 4).

Both patients with ERA had good results. Further surgical procedures were arthroplasties in 16 hips and 3 osteotomies.

Table 3

Variable	*At entry Mean (range)*	*At 3 months Mean (range)*	*At 6 months Mean (range)*	*p Value**
Prdn, dose (mg)	14 (5–40)	10 (0–30)	9 (0–20)	<0.001
DMARDs (n)	2.4 (1–4)	2.0 (0–4)	1.7 (1–3)	<0.001
GC injections (n)	10 (0–30)	4 (0–34)	2 (0–7)	<0.001
ESR (mm/1st h)	38 (7–115)	20 (3–54)	20 (6–115)	<0.001
CRP (mg/l)	22 (0–159)	7 (0–65)	13 (0–170)	<0.001

*Friedman's test.

Table 4

	Systemic		*Poly*		*Ext oligo*	
	T1	*Tf*	*T1*	*Tf*	*T1*	*Tf*
Excellent, good (%)	**82**	40	**66**	37	**55**	30
No change (%)	12	20	27	13	22	30
Worse (%)	6	**40**	7	**50**	23	**40**

11.18 Antibody response to influenza vaccination in children with chronic rheumatopathies and long term immunosuppressive treatment

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This study aimed at assessing seroconversion after influenza vaccination in children with rheumatic diseases (RD) who were receiving long term (1–5 years) immunosuppressive treatment. 70 patients with JIA, systemic lupus erythematosus, systemic vasculitis, or other RD, aged 4–18 years (mean (SD) 11.6 (6.5)) and 5 healthy children (aged <11 years), siblings of the affected ones, were studied. Patients were assigned to one of 4 groups according to the drug regimen: (*a*) prednisone (PS), (*b*) PS +1 disease modifying antirheumatic drug (DMARD), (*c*) PS + 2 DMARDs, (*d*) 1or 2 DMARDs without PS. All children received a split influenza vaccine (Fluarix SB). Blood samples were drawn before immunisation, before the 2nd dose (mean (SD) 34 (5) days) and about one month later. Antibody titres to the influenza antigens contained in the vaccine were measured—namely, to strains A/Beijing/262/95(H1N1), A/Sydney/5/97(H3N2), and B/Beijing/184/93. It was found that before vaccination 31% of patients had a protective antibody titre (≥40) to A(H1N1), 99% to A(H3N2), and 55% to B. After vaccination (1st dose) a protective antibody titre developed in 87% of patients to A(H1N1), in 100% to A(H3N2), and in 77% to B. No protective titre to A(H1N1) and B was found in 12% and 23% of patients respectively. As a whole, the antibody response of patients to all strains of influenza vaccine was similar to that reported for healthy children. Comparison of the mean geometric titre before and after vaccination between patients and healthy children as well as among the 4 groups of patients did not show any significant difference for the 3 antigens studied. Additionally, no association was detected between the absence of antibody response and the age of patients or the drug combination. In conclusion, immunosuppressive treatment in standard doses does not affect the antibody response to influenza vaccine in children with chronic rheumatic diseases.

11.19 Use of cyclic etidronate in patients with juvenile chronic rheumatic diseases receiving long term treatment with steroids

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An open prospective study to evaluate the efficacy of etidronate in preventing corticosteroid induced osteoporosis was carried out in children with chronic rheumatic diseases. We considered 25 patients (6 M, 19 F); mean onset age 10.1 years (range 1.5–16.2), mean age at the start of treatment 15.6 years (7.8–25.0), mean disease duration 5.6 years (0.6–12.8). 22 patients were affected by juvenile chronic arthritis (7 systemic, 11 polyarticular, 4 pauciarticular) and 3 by systemic lupus erythematosus. At the start of treatment all patients were receiving steroids: mean dose

0.20 mg/kg/d pred. eq. (0.04–0.69). All cases were receiving 25OH-D3. Etidronate was given by mouth at a dose of 150–300 mg/d for 15 days followed by calcium citrate 0.5–1 g/d for 75 days on a cyclic course. Lumbar bone mineral density by DEXA was periodically checked to monitor the mineralisation status of the patients with time. The mean (SD) annual bone mineral density percentage (BMD%) change in the year preceding the start of treatment was −6.5% (5.0) (range −17.9–3.4), after 6 months it was 3.4 (4.7)% (−7.5–10.2) (p<0.0001), after 12 months (20 patients) it was 3.5 (6.1)% (−4.4–19.2) (p=0.005), after 24 months (14 patients) it was 13.8 (11.8)% (−1.2–29.6) (p=0.004), after 36 months (11 patients) it was 4.5 (11.8)% (−16.1–15.5) (p=0.05). No statistically significant variation in steroid dose could be seen during this period. Finally, comparing the annual BMD% changes observed with the expected values matched for sex and age, a statistically significant difference could be seen in the preceding year, while such a difference was lost after 6, 12, 24, and 36 months of treatment. These data suggest that cyclic etidronate can prevent osteoporosis and increase the BMD in children affected by chronic rheumatic diseases receiving long term treatment with steroids.

11.20 Improved articular and systemic disease in a boy treated with anti-TNFα monoclonal antibody (Remicade) for refractory systemic JCA

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Evidence indicates a key proinflammatory role for tumour necrosis factor α (TNFα), interleukin 1 (IL1), and IL6 in the pathogenesis of juvenile chronic arthritis (JCA). Remicade (infliximab, Centocor), a neutralising anti-TNFα monoclonal antibody emerges as a new drug for refractory rheumatoid arthritis (RA), possibly JCA. We report the use of Remicade in a boy aged 10 with systemic onset JCA and severe polyarthritis, unresponsive to non-steroidal anti-inflammatory drugs, steroids, and high dose methotrexate. Remicade was given at 3 mg/kg (cf RA and juvenile Crohn's disease trials), resulting in clear but transient improvements of general well being and morning stiffness. Dose increase to 5 mg/kg induced manifest improvement of articular disease. Systemic symptoms and inflammatory parameters clearly responded after the 4th infusion. After one infusion of 10 mg/kg both arthritis and systemic disease activity went into remission. The 10 month treatment course was associated with (*a*) a decrease of active and limited joints (9 to 0, resp. 12 to 2); (*b*) a decrease of visual analogue scale scores (pain 50 to 20, global 65 to 25), but no change in Child Health Assessment Questionnaire score (1.1), possibly related to previously existing mechanical hip problems; (*c*) disappearance of systemic symptoms, decrease of C reactive protein (CRP; 410 to 150 mg/l) and erythrocyte sedimentation rate (46 to 31 mm/1st h). IL6 serum levels paralleled systemic disease activity and serum CRP levels and declined after the 4th dose of 5 mg/kg. Importantly, steroid dose was tapered from 12 to 9 mg daily. Possible adverse events of Remicade were fever (once) and upper airway infection (twice). Remicade holds promise for the treatment of refractory systemic JCA. However, important dissociation in response was noted of articular and systemic disease: cytokine networks in systemic JCA may differ from those in RA and high doses may be required for control of systemic JCA.

11.21 Treatment of refractory juvenile systemic arthritis (JSA) with cyclosporin A and methotrexate : an open study of 5 patients

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Objective—To evaluate the safety and efficacy of cyclosporin A (CyA) with or without methotrexate (MTX) in refractory JSA.
Methods—5 patients (2 boys, 3 girls) with JSA fulfilling Durban classification criteria were studied retrospectively. JSA was considered as refractory on 2 criteria: severe disease during the first 6 months requiring prednisone ⩾1 mg/kg/d and MTX; persistent active disease despite this treatment after 4 months. Efficacy was evaluated by clinical parameters: presence of morning stiffness, daily fevers, number of synovitis, dose of steroids. Laboratory monitoring of disease activity and drug toxicity included: haemogram, erythrocyte sedimentation rate (ESR), serum C reactive protein (CRP), and creatinine level. CyA was given at a dose of 2.5 mg/kg/d and then, if necessary, increased to 3.5 mg/kg/d.
Results—The mean (SD) age at onset of JSA was 5.6 (3.)5 years and at initiation of CyA 5.8 (2.8) years. Mean duration of CyA treatment was 1.9 (0.7) years and mean dose 3.2 (0.7) mg/kg/d. Mean dose of MTX (4 patients) was 0.6 (0.2) mg/kg/week. At one month all patients had improved: lack of fever and morning stiffness, decreased number of synovitis. At 3 months ESR and serum CRP level decreased respectively from 72 mm/1st h (range 34–99) to 9 mm/1st h (2–20) and from 127 mg /l (66–200) to 14 mg/l (5–39). At 6 months the mean number of synovitis decreased from 6.2 (4–>10) to 2 (0–4), with mean ESR 11 mm/1st h (10–12) and CRP 2.8 mg/l (1.6–4). Prednisone dose was decreased from 0.9 mg/kg/d (0.5–1.5) at baseline, to 0.6 (0.4–0.8) at 6 months. No patient developed hypertension; in 1 case serum creatinine rose above 30% of the baseline level, requiring a decrease in the CyA dose.
Conclusion—These data suggest that combined treatment with MTX and CyA might be effective in controlling disease activity and reducing steroid treatment and is well tolerated.

11.22 Varicella-zoster infection and immunity in patients with juvenile chronic arthritis treated with methotrexate in northern Norway 1985–99

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Children with juvenile chronic arthritis (JCA) treated with methotrexate (MTX) are at risk of developing severe illness and complications on exposure to varicella-zoster (VZ).

We retrospectively investigated VZ immunity, the use of VZ immunoglobulin (VZ-Ig), and the incidence of VZ infection among children with JCA from northern Norway (Troms and Finnmark counties, mean child population 48 488 children, aged <16 years) in the years 1985–94. Cases were identified from the hospital files of the University Hospital of Tromsoe, the only hospital in the study area treating JCA, using the European League Against Rheumatism criteria for JCA. From 1995 cases from the same area were prospectively studied, from 1997 as part of a multicentre study from the Nordic Study Group of Paediatric Rheumatology (NSGPR).

Of 162 patients with JCA, 66 were treated with MTX during the study period. As many as 37 of the 66 patients were non-immune, or probably non-immune, to VZ. Nine were given VZ-Ig as prophylaxis on exposure to VZ, one or several times. Eight developed VZ infection during MTX treatment despite efforts to avoid such infections. No serious complications or very severe illness was seen.

There are no established guidelines on avoidance of VZ infections in children with JCA treated with MTX. Also, lack of data about the risk of severe illness versus level of immunosuppression and dosage of MTX, makes it difficult to decide what strategies to follow. Further investigations on this topic are needed.

11.23 Autologous stem cell transplantation in two patients with juvenile SLE

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Autologous stem cell transplantation (ASCT) has recently been described as a possible treatment for severe chronic autoimmune diseases refractory to conventional treatment. Some 20 adults with systemic lupus erythematosus (SLE) treated with ASCT have been described with varying results. We report ASCT in a 15 year old girl and a 14 year old boy with SLE.
Cases—A girl presented at the age of 9 with a malar rash, polyarthritis, oral ulcers, acrocyanosis, severe skin vasculitis, nephritis, and severe pneumonitis. Her SLEDAI was 28. In the following 5 years she was treated with prednisone, azathioprine, cyclophosphamide (CY) pulses, and methotrexate, but remission was never achieved. The second patient was diagnosed with SLE at the age of 9 with haemolytic anaemia, polyarthritis, lymphadenopathy, a malar rash, and retinal vascultitis. In the following years he developed a severe glomerulonephritis that remained active despite glucocorticoids, azathioprine, and CY pulses.
Methods—Unprimed bone marrow was taken 1 month before ASCT and T cell depletion was performed. The conditioning regimen consisted of antithymocyte globulin (20 mg/kg), CY (200 mg/kg), and low dose irradiation (4 Gy). Prednisone was tapered after ASCT.
Results—Engraftment occurred at 25 and 30 days after ASCT. A mild pericarditis occurred in one patient. The girl has a drug free remission (SLEDAI 0) at an 18 month follow up. Her nephritis has disappeared, complement is normal, the anti dsDNA is now negative, and her antinuclear antibody titre has decreased. Her immune reconstitution was rather slow to normalise the number of T cells at 12 months. The second patient is now in a drug free remission 12 months after ASCT, his SLEDAI is 8.
Conclusion—ASCT may be an option for children with SLE refractory to conventional treatment and who have severe side effects. Long term follow up will be necessary to show whether the remission will persist.

Table 5 Number (%) of responders juvenile arthritis

	Response criteria Juvenile arthritis	*ACR 20 response*	*ACR 50 response*	*ACR 70 response*
2 Weeks	8 (88)	5 (56)	2 (22)	2 (22)
6 Weeks	5 (71)	4 (57)	4 (57)	2 (28)
14 Weeks	1 (50)	1 (50)	1 (50)	1 (50)

11.24 Sulfasalazine in the treatment of juvenile idiopathic arthritis

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Objective—To assess the efficacy and tolerance of sulfasalazine (SAS) in the treatment of patients with juvenile idiopathic arthritis (JIA).

Patients and methods—Nineteen patients with JIA (11 girls, 9 boys) were enrolled into this study. Their average age was 11.9 years (range 4.58–18), duration of the disease was 4.53 years. Twelve patients with oligoarthritis, 3 with extended oligoarthritis, 3 with rheumatoid factor negative polyarthritis, and 1 with arthritis and enthesitis were studied. Treatment with SAS was started with a daily dose of 50 mg/kg. The efficacy was evaluated by monitoring the following variables: morning stiffness, number of swollen joints, number of total affected joints, erythrocyte sedimentation rate, and haemoglobin. At 3 months 17 patients were evaluated, at 6 months 12 patients, and at 12 months 11 patients. Patients were carefully monitored for side effects.

Results—All assessment measures, except haemoglobin, were significantly improved at 3, 6, and 12 months, but significance decreased during the treatment (from $p<0.001$ to $p<0.01$). The haemoglobin values during the treatment did not differ from baseline. Side effects were noted in 7 patients. Two patients were withdrawn (owing to urticaria and headache) a month after the start of the SAS treatment. Mild anaemia was seen in 3 patients, gastric intolerability in 1, and dizziness as well in 1 patient.

Conclusion—Sulfasalazine as a second line drug is effective for the treatment of JIA during 12 months, side effects are mild, and the drug is well tolerated. However, it is necessary to assess the long term efficacy and tolerableness.

11.25 Juvenile chronic polyarthritis treated with infliximab

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Objective—Infliximab is an effective drug in the treatment of rheumatoid arthritis (RA). Etanercept has been shown to be effective and well tolerated both in RA and juvenile arthritis (JA). We wished to test the efficacy and tolerance of infliximab in treatment resistant JA.

Methods—Children with active polyarticular JA and poor response to methotrexate (MTX) treatment were invited to be treated in an open study with infliximab, 3 mg/kg, at baseline, 2 weeks, 6 weeks, and thereafter every 8th week.

Results—To date 11 patients have been included. One patient was withdrawn because of Quinke oedema and another because of spiky fever. These adverse events occurred in both patients within 30 minutes after the first infusion was initiated. In the remaining patients no significant adverse events were seen. Nine patients have been followed up for 2 weeks, 7 patients for 6 weeks, and 2 for 14 weeks (table 5).

Conclusion—Treatment with infliximab led to significant improvement in the majority of severely ill patients with JA previously resistant to MTX treatment. Two patients were excluded because of adverse advents early during first infusion. Infliximab was well tolerated in all remaining patients.

11.26 Pharmacokinetics and clinical outcome of Meloxicam in juvenile rheumatoid arthritis

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The pharmacokinetic profile as well as efficacy and safety of Meloxicam, a new COX-2 non-steroidal anti-inflammatory drug, were investigated in children with juvenile rheumatoid arthritis.

Thirty six patients (mean age 8 years) were treated once daily with a Meloxicam oral suspension (0.25 mg/kg) for up to 12 weeks. Efficacy and safety were assessed at baseline, every two weeks, and at the final visit. Venous blood for determination of plasma concentrations was collected in 18 patients after first administration up to 72 hours.

Table 6 summarises key pharmacokinetic results for the younger (2–6 years, mean age 3) and the older (7–14 years, mean age 11) age groups and gives historical data of healthy adults (mean age 35).

Evaluation of efficacy showed increasing improvement over time, reaching a plateau at week 6 and a further increase up to week 12 when 71% of the patients were considered to be responders according to the definition by Lovell. Global efficacy was judged to be good or satisfactory in 90%. Nausea, abdominal pain, and diarrhoea in four patients (11%) were the only adverse events judged to be drug related. Overall, adverse events were reported in 67% of the patients. Global tolerance was rated as good or satisfactory in almost 95%.

Meloxicam suspension was well tolerated and effective in the treatment of juvenile rheumatoid arthritis. Differences in C_{max} and AUC are not considered clinically relevant and no dose adjustment is considered necessary based on the clinical outcome of this trial.

Table 6

	Young children (n=7)	*Older children (n=11)*	*Adults (n=16)*
Cmax (µg/ml)	1.2 (47)	1.8 (27)	0.9 (28)
AUC (µg.h/ml])	25 (83)	34 (23)	30 (34)
NCL/f (ml/min/kg)	0.17 (83)	0.12 (23)	0.11 (43)
t_ (h)	13 (54)	13 (21)	19 (31)

Number in brackets denotes coefficient of variation.

11.27 Early sequential intensive treatment (SIT) in EOPA-JIA: a prospective long term observation study

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In children presenting with EOPA-JIA, early diagnosis and immediate intensive combination treatment induces in most cases a complete and continuous clinical remission (CCR). In 21 children (14 female, 4 male), all antinuclear antibody positive, disease began at an average age of 48.7 months. Diagnostic procedures were completed within 3.8 months after onset and treatment with methotrexate (MTX) was started in all patients. Treatment had to be intensified using a combination of MTX/sulfasalazine in 19 of 21 patients after 4 months (mean). In 3 cases, treatment with additional immnunosuppressive drugs, such as cyclosporin A or azathioprine was necessary. In all cases complete remission was achieved after an average period of 9.4 months. During this period of remission no relapse was seen except for some short flares in 3 children. We discontinued treatment in children who completed two years of CCR. However, 3 of the 5 children relapsed during a treatment pause. Two children are still in CCR and now 4 respectively 30 months without treatment. We observed a second group of seven EOPA-children, treated by MTX only: Treatment was started on average 5 months after the onset of disease. Remission was reached late (17.4 months mean time) and three of these children have relapsed under MTX treatment until now.

11.28 Enbrel (etanercept) in juvenile idiopathic arthritis (JIA)

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Treatment with etanercept leads to significant improvement and good tolerance in children with polyarticular juvenile idiopathic arthritis (JIA)[1]. This drug is not yet available in France, but can be used according to the French legislation as individual "Temporary Authorisation for Use" delivered by the National Drug Agency. We currently are treating 14 children with chronic rheumatic diseases (5 systemic onset JIA, 8 non-systemic onset JIA, one CINCA). Inclusion criteria were age above 4, polyarticular course, erythrocyte sedimentation rate (ESR) >20 mm/1st h, and failure or intolerance to methotrexate. Etanercept was administered subcutaneously twice a week at 0.4 mg/kg/injection. The response was defined as an improvement of 30% or more in at least 3 of 6 indicators of disease activity, with no more than one indicator worsening by more than 30% (that is, global assessment by the physician, global assessment by the patient/parents, number of active joints, number of joints with limited motion, functional ability

(Child Health Assessment Questionnaire), ESR). The results obtained in 8 children (4 systemic, 4 non-systemic) who were treated for more than 3 months are available. Mean (SD) age at disease onset was 6.6 (3) years, mean age at treatment was 13 (2.9) years. Four patients (3 non-systemic and one systemic) improved, four patients did not improved (3 systemic and one non-systemic). In conclusion, these preliminary results tend to show that patients with systemic onset JIA respond less to etanercept than patients with non-systemic onset JIA.

1 N Engl J Med 2000;342:763–9.

12 Vasculitis

12.1 A series of childhood microscopic polyangitis and classic polyarteritis nodosa: the significance of ANCA

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We aimed at evaluating the distribution and features of classic polyarteritis nodosa (PAN) and microscopic polyarteritis (MPA) and the importance of antineutrophil cytoplasmic antibody (ANCA) in childhood PAN. Classic PAN was diagnosed by aneurysms on angiography in 10 patients and by the presence of necrotising vasculitis in mid-size arteries in 5, adding to a total of 15 patients. MPA was diagnosed in 10 patients; by characteristic findings in renal biopsy in 6 and by the small and/or medium sized necrotising arteritis in 4. ANCA was studied by indirect immunofluorescence (IIF) and subsequently an ELISA test for MPO.

The mean (SD) ages of the patients with classic PAN and MPA were 11.33 (3.69) and 9.55 (2.94) respectively. None of the patients in the classic PAN group had renal failure. However, 60% of the patients with MPA presented with renal failure and 40% progressed to chronic renal failure. Clinically evident pulmonary renal syndrome was present in 3 of the 10 patients with MPA. IIF for ANCA in classic PAN showed negative staining in 9, mild staining patterns in 6, and one MPO-ELISA was mildly positive. On the other hand, IIF for ANCA in MPA showed very strong p-ANCA staining in 9 and atypical staining in 1. In MPA, the median MPO-ELISA level was 42.5 EU/ml (range 20–250).

In conclusion, treatment of childhood PAN is satisfactory with effective treatment; however, relapses have occurred. ANCA is important for the diagnosis and follow up of MPA.

12.2 Epithelial cell-derived neutrophil activator levels in Henoch-Schönlein purpura in childhood

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Epithelial cell-derived neutrophil activator (ENA-78) is a recently discovered chemokine, which is one of the most important chemotactic cytokines for neutrophil chemotaxis. Pathogenesis of vasculitis is complex and not yet fully elucidated, but neutrophils play a major part. Henoch-Schönlein purpura (HSP) is also leucocytoclastic vasculitis. ENA-78 was measured by ELISA using samples obtained from 11 patients (10 boys and 1 girl), aged 2.5–17 years (mean (SD) 11 (4.3)) with HSP in this study. Patients were grouped according to renal, intestinal, and joint disease. Mean ENA-78 level was found to be 2832 (1893) ng/ml at the acute stage. Levels of ENA-78 in patients with HSP and renal disease were lower than in those without renal involvement (1793 (1497) ng/ml *v* 2580 (1646) ng/ml, p>0.5). Similarly, patients with joint disease had lower ENA-78 levels than those without intestinal disease (1666 (996) ng/ml *v* 2732 (1998) ng/ml, p>0.05). ENA-78 levels in patients with more than one system affected were lower than in those with one system involved (1343 (248) ng/ml *v* 3120 (1925) ng/ml, p>0.5). However ENA-78 levels were similar in patients with and without intestinal disease. Contrary to expectation, we found lower ENA-78 levels in systemic disease than in those without systemic disease. We speculate that increased tumour necrosis factor α may suppress ENA-78 by downregulating chemokine receptor 2 (CXCR2) in severe cases. Additionally, ENA-78 may be produced locally rather than systemically and may be lost with urine. Further investigation is needed to explain this pathogenesis.

12.3 Familial vasculitis : a new Georgian disease ?

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Familial vasculitis is rare and only a few families with polyarteritis nodosa (PAN) have been reported. We report here on 2 unrelated families of Georgian-Jewish origin with PAN.
Family 1—A 7 month old boy presented with painful nodular livedoid rash, anaemia, raised erythrocyte sedimentation rate (ESR), and normal immunological profile. At the age of 14 months he had generalised seizure with right paresis with normal brain computed tomography (CT). Two years later, he deteriorated with right paresis, hypoventilation, and hypertension. Brain CT and magnetic resonance imaging showed thalamic and cerebellar lesions. Renal angiogram disclosed multiple PAN-like aneurysms. One year later, he is doing well receiving oral cyclophosphamide and prednisone. His 5 year old sister has had leg pain, livedoid rash, anaemia, and a raised ESR for 4 years.
Family 2—Two sisters presented at the age of 1.5–2 years with fever, myalgia, livedoid and purpuric rash. Their cousin died in infancy of systemic vasculitis with cerebral haemorrhage and mesenteric aneurysms on angiogram.

As opposed to other reports of familial vasculitis, our group was uniformly Georgian-Jewish and if enough probands are identified, we will be able to look for genetic markers. Familial atrophie blanche has been reported by Suster (1986) in 4 Georgian-Jewish adolescents who had recurrent refractory leg ulcers but no systemic features of vasculitis.

12.4 Multicentre data collection of 250 patients

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The epidemiology of Kawasaki disease (KD) varies in different countries, and genetic factors may have an influence on disease expression. We have retrospectively reviewed the charts of 250 white patients with KD seen in tertiary referral hospitals of northern Italy and followed up for a mean period of 3 years (range 1–120 months). The male:female ratio was 1.8:1. Mean age at diagnosis was 37 months. Fever lasted for a mean period of 9 days; in most of the cases the erythrocyte sedimentation rate (ESR) was performed during this period, with a mean value of 76 mm/1st h. Other laboratory findings included mean IgG and IgM values of 8.27 and 1.48 g/l, respectively, and thrombocytosis (mean platelet count 430×10^9/l). Only one patient had a low platelet count (15×10^9/l at the 8th day of illness). Clinical criteria reported (in decreasing order) were rash (221/246), oral mucosal alterations (219/245), conjunctivitis (208/245), extremity changes (185/246), and lymphadenopathy (176/246). About a third of the patients fulfilled all criteria. Most of our cases (196/250) were treated with IV immunoglobulin, from day 1 to day 51 of illness (mean day 8). Coronary aneurisms were reported in 40 patients (22 male, 18 female). Their mean age was 29 months (range, 3–112). Mean fever duration and ESR value in these patients were no different from those of the whole group. IV immunoglobulin had been given in 35/40 patients with coronary aneurisms, no later than in the whole group. Other complications included pericardial effusions (37 cases), abdominal pain/diarrhoea (11), arthritis (10), hydrops of the gall bladder (6), myocardial infarction (5), cardiomyopathy (5), DIC (1), hemiparesis (1).

A statistical model to evaluate possible risk factors for coronary aneurisms in this large cohort is currently being tested.

12.5 Role for vascular endothelial growth factor in Henoch-Schönlein purpura

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Vascular endothelial growth factor (VEGF) is a multifunctional growth factor. It increases vascular permeability, interstitial collagenase production, von Willebrand factor release, and enhanced procoagulant activity. Henoch-Schönlein purpura (HSP) is the most common small vessel vasculitis in childhood, which is the result of a complex series of inflammatory and immunological processes. We aimed at investigating the possible role of VEGF in the pathogenesis of HSP. Thirty four children with HSP were enrolled in the study and 10 age matched healthy children served as controls. Plasma VEGF levels were determined by ELISA. VEGF expression was evaluated by immunohistochemistry within the vasculitic lesion as well as the non-affected skin and in skin specimens after resolution of the disease. Mean (SD) plasma VEGF levels were significantly higher during the acute phase (407.8 (64.92)) than during the resolution phase (202.17 (26.6), p<0.002) and higher than in healthy controls (135 (22.8), p<0.001). Further analysis of data showed a correlation with erythrocyte sedimentation rate, C reactive protein, and white blood cell (WBC) count. VEGF expression by the vascular bed was more intense in resolving lesions than in acute vasculitic lesions