(PS) 0.8—0.3 mg/kg/d for 4 months and then on alternate days, methotrexate 15 mg/m² and indomethacin 2 mg/kg/d. At the time the pain occurred she was receiving indomethacin, PS (20 mg/kg/d), and cyclosporin A (3 mg/kg/d). There was no previous history of trauma to the affected limb. Her imaging work up showed the following: X-rays of knees and femur—skip lesions in the right femur, one sclerotic in the middle shaft with heavy periarticular reaction and another one mainly lytic with destruction of the cortical bone and periosteal reaction. Magnetic resonance imaging showed skip lesions localised in the middle third of diaphysis and in the distal metaphyseal region of the femur. The lesions destroyed the cortical bone, infiltrated the bone marrow, and produced a periosteal reaction without extension to the soft tissues or in the epiphyseal. These lesions were indicative of a possible bone solid tumour—that is, osteosarcoma or Ewing's sarcoma. However, a thallium scan was not indicative of malignancy. Her haematological and biochemical findings, including alkaline phosphate and lactate dehydrogenase, were also within normal limits. An open bone biopsy was then performed and ruled out the chance of malignancy; it showed aseptic necrotic lesions in the femur. The case is presented because of the unusual location and imaging appearance of the aseptic necrosis.

8.2 Disabement by untreated systemic juvenile idiopathic arthritis

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Background—We commonly only know the final state of systemic juvenile idiopathic arthritis (sJIA) from pictures in medical textbooks. Nowadays effective drugs exist which can stop the inflammation preventing disability.

We present an 8 years 3 months old girl who had had sJIA since the age of three.

Case report—Personal history: 1994 diagnosis of sJIA. 1995 begin treatment with non-steroidal anti-inflammatory drugs, 1995 additional treatment with steroids. 1996/97 tapering of steroids and discontinuation in November 1998. January 1998—99 treatment with growth hormone because of impressive growth retardation. January 1999 exacerbation of sJIA. A trial of treatment with methotrexate was discontinued after two weeks. Since then only homeopathic treatment has been given by the parents. Clinical examination December 1999: bad health, all joints are extremely swollen, very painful on movement and palpation, severe limitation of motion, and functional loss in every joint. The girl can nearly walk; she cannot stand up or sit down or lie down when in sitting position. She is not able to lie flat on her back or to dress or undress, her neck is fixed in a flexion contracture and she cannot look up or turn her head at all. Growth retardation, retardation of the Ray: very severe destruction of the atlanto-occipital joint.

Conclusion—sJIA is a severe chronic illness, which untreated can lead to most severe destruction despite its mostly favourable prognosis. In most cases sJIA can nowadays be treated effectively with drugs to prevent disability. Children with sJIA therefore must be treated effectively and in time.

8.3 Pain in arms and legs in childhood

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Objective—To describe the different causes and characteristics of a group of children with referred pain in the arms and legs.

Materials and methods—We studied, from 1995 to 1999, 208 school age children from Tenerife island, with referred pain in arms and legs. The diagnosis was made from clinical, physical examination, blood tests, and radiological study in all of them; additional tests were need for some of them (bone gammagraphy, computed tomography, or magnetic resonance).

Results—Of the 208 children, 102 presented organic causes and 106 were diagnosed as growth pains. In the group with organic pains, 38 were diagnosed as arthritis (17 were septic arthritis and 21 juvenile chronic arthritis, 12 oligoarticular, and 9 polyarticular), and 64 as myositis. In the group with arthritis the joints most commonly affected were the knees (in 12 children, right knee in 6). In the group with myositis 80% of the children had had an enteric or upper respiratory infection previously. In the group labelled as growth pains, additional tests (bone gamma scintigraphy, bone scan, and enzymes) were carried out in 8 children to rule out organic causes. The course was favourable in all the patients with growth pains and myositis. In the arthritis group, treatment was started in all of them and the outcome was favourable in only 29.

Conclusions—Pain of arms and legs, particularly growth pain, in childhood is common, though few reports exist in the current literature. Moreover, they are an important cause of absence from school, causing concern to parents. The results of our study confirm this assumption.

8.4 Cemmentless total hip arthroplasty in juvenile idiopathic arthritis

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From 1975 to 1997 40 patients with juvenile idiopathic arthritis (JA) had 68 cementless hip replacements. Prostheses used were used for 16 children and Zweymuller protheses. Autotopic bone grafts were used for important acetabular defects.

The average age of the patients at the time of surgery was 17.5 years (range 11—29). JA was systemic in 12 cases, polyarticular in 28 cases. Sixteen hips had had a surgical synovecmy with triamcinolone hexacetonide previously and JA was active in 16 cases. Functional results were evaluated according to the Postel Merle d’Aubigné scale for the hip, and the Steinbrocker classification was used for global function. Mean follow up was 7 years (range 3—15). 6 patients required revision: one for infection, three for acetabular loosen- ing with Endler component, one femoral shaft fracture and a loosening of the Zweymuller acetalubar cup owing to a bad primary fixation.

Results for the hips were rated excellent and good for motion and pain. However, functional results observed were quite different because of the location of arthritis, and 8 patients needed another reconstructive procedure to recover good function. A radiographic review showed good bone integration of the components despite early migration in cases of bad primary fixation. It showed the thickness of the femoral shaft bone around the femoral piece. Use of cementless prostheses appears to be a good solution in this disease, preserving bone stock and showing good radiological and functional results.

9 Rare diseases

9.1 Urinary glycosaminoglycan in the course of FMF

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Familial Mediterranean fever (FMF) is characterised by recurrent fever and serositis. The most important complication of the disease is amyloidosis, which is diagnosed by biopsy. Cheaper and non-invasive methods would be important in the early diagnosis of amyloidosis. We have attempted to study the role of urinary glycosaminoglycan (GAG) in the early diagnosis of amyloidosis. The study group included 123 patients with FMF without attack and 11 patients with FMF secondary amyloidosis. Patients with acute attack were excluded. Eight healthy children and 10 patients with primary nephrotic syndrome served as controls. Microalbumin was also measured in patients with FMF. In patients with amyloidosis, urinary GAG levels were lower than in patients with FMF, those with nephrotic syndrome, and controls. In 49 patients with FMF with a low GAG level, urinary GAG levels increased significantly with incremental increase in the colchicine dose (p<0.05). In some patients with low GAG levels, microalbuminuria was also detected. In these patients, microalbuminuria also decreased along with the increase in urinary GAG, when the colchicine dose was increased. These results suggest that in patients with FMF, monitoring urinary GAG and microalbumin levels may be important in the regulation of the colchicine dose and prevention of amyloidosis. We suggest that effective colchicine dose may be monitored by following urinary GAG levels.

9.2 Epithelial cell-derived neutrophil activator (ENA-78) levels in patients with FMF

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The exact mechanism triggering acute attacks in familial Mediterranean fever (FMF) is unclear. Neutrophil is the effector cell of the inflammatory response at the serosal surface.

Epithelial cell-derived neutrophil activator (ENA-78) a recently discovered chemokine, is one of the most important chemotactic cytokines for neutrophil chemotaxis. We have examined plasma ENA-78 levels in 63 patients with FMF. Thirty one patients had acute attacks and 32 patients had remission. Mean (SD) ENA-78 levels were greater in patients with acute attacks than in attack-free patients (2186.45 (774.93), p<0.05). The ENA-78 level correlated with erythrocyte sedimentation rate and
fibrinogen levels. Our results suggest that ENA-78 may be an important factor in the pathogenesis and activity of FMF disease.

9.3 Five cases of juvenile idiopathic arthritis and the velocardiofacial (22q11) syndrome

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Introduction—The association between juvenile idiopathic arthritis (JIA) and the velocardiofacial syndrome (VCFS) has recently been described in two separate groups in a total of eight cases. We report a further five cases, all of whom have deletions at the 22q11 locus.

Results—All five patients had a history of congenital heart disease (CHD) and velo-pha-ryngeal insufficiency (VPI). 4 have significant learning difficulties. None had a history of recurrent infections but two have a selective IgA deficiency and one has abnormal T cell function with a defective phytohaemagglutini- n response. In all patients the arthritis is polynuertic onset or extended pauciarticular in nature, progressively requiring treatment with disease modifying agents and indistinguishable from true JIA. Three of our patients were diagnosed with VCFS in the first years of life as a result of the combination of CHD and VPI. In the other two the syndromic diagnosis was made at 17 and 21 years after rheumatology review. The immu- nomological profiles of the 13 total cases of VCFS with JIA are reviewed: 5 are antin- clear antibody positive, 3 rheumatoid factor positive, 5 have T cell deficiencies, and 4 (2/5 of ours) have selective IgA deficiency. The increased incidence of both IgA deficiency and JIA in the 22q11 deletion syndrome pro- vides further evidence for possible genetic factors in the pathogenesis of JIA. In addition, the presence of demonstrable T cell defects in 5/13 patients adds further weight to the hypothesis that JIA is a T cell related dis- ease.

Conclusions—The severity of the arthritis in VCFS may reflect underrecognition of milder cases of joint disease in this syndrome and it is important for clinicians to be aware of the association. In addition, the possibility of VCFS should be considered in any patient with JIA in the presence of other features of the syndrome, such as CHD, speech prob- lems, and learning difficulties.

9.4 Effects of colchicine on neutrophil adhesion molecules in familial Mediterranean fever (FMF)

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Objective: We aimed at elucidating the role of L-selectin of neutrophil adhesiveness in patients with FMF in acute attack than in remission (p<0.05). Furthermore, patients with acute attack and receiving colchicine had a higher CD18 expression than those with acute attack but not receiving colchicine (p<0.05). No significant difference in CD62 and CD11 expression, both on neutrophils and lymphocytes, was seen between patients with acute attack and in remission and the patients not receiving colchicine. APC, which may upregulate the proinflammatory cyto- kines interleukin 6 (IL6) and IL8 in human endothelial cells, remained at normal levels both in patients with acute attack and those in remission. Our results suggest that as one of the neutrophil adhesion molecules CD18 appears to have an important role in the FMF attacks. Further studies are needed.

9.5 SAPHO syndrome and hemiparesis in a child

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SAPHO syndrome is uncommon in children. It is sometimes associated with inflammatory bowel disease and ophthalmological condi- tions. We present the case of a child with acute transitory hemiparesis as presenting symptom of SAPHO syndrome.

An 8 year old boy was referred for a right faciocranial hemiparesis and painful, warm, and erythematous mass over the right sternoclavicular joint. The past medical history included only primary enuresis. On admiss- ion, neurological examination showed decreased strength in the right upper and lower extremities, claudication but normal pain, thermal and light touch sensation. Labora- tory tests showed erythrocyte sedimentation rate 47 mm/1st h, while C reactive protein, antinuclear antibody, rheumatoid factor, co- agulation tests, and fungal, bacterial, and viral culture were normal. Standard x ray and computed tomography (CT) of the osteoor- ticular lesion were compatible with osteoperi- ostitis. Cerebral CT and magnetic resonance imaging (MRI) were negative; MRI of the spinal cord showed thoricacic syringomyelic cavity between D5-D6 and D10-D11. An open biopsy of the sternoclavicular mass showed fibroinflammatory tissue with rare lymphocytes and plasma cells. On follow up the neurological problems completely recovered in a few weeks while the sternoclavicular lesion persisted with intermittent symptoms of pain and swelling.

The diagnosis of SAPHO syndrome is supported by the sternoclavicular involve- ment, the insidious clinical course, and the histological picture. Skin lesions in children can be absent at onset or appear later on dur- ing the course of the disease. A neuropathic arthropathy has been ascribed to the basis of the level and severity of the syndrome, the preservation of pain, thermal sensation and cutaneous tropism, and the histology. How- ever, the coincidence between the onset of SAPHO syndrome and acute transitory hemiparesis is peculiar and not previously reported.

9.6 Puzzling problems for the diagnosis of inflammatory diseases

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The diagnosis of inflammatory disorders remains a challenge for the physicians. Indeed, each separate entity can mimic another one clinically and there are few biological tests to help the diagnosis. Moreover, a number of these diseases may aggregate in the same patient or in the same family.

Case 1—A 6 year old girl with periodic fever syndrome and ulcerative gastroenteritis and vascular purpura (HLA-B1+), one mutation of the gene responsible for FMF (MEFV: M694V), BD have been reported in 1% of patients with FMF. We could document 2 MEFV muta- tions (true genetic FMF) in our case 2 (pseudo-PAN) that we consider as prolonged febrile myalgia syndrome. The presence of MEFV mutations in the other cases (VCFS) with BD (HLA-B1+) and JIA in this patient suggests that a true genetic FMF (true genetic FMF) that may upregulate the proinflammatory cyto- kines interleukin 6 (IL6) and IL8 in human endothelial cells, remained at normal levels both in patients with acute attack and those in remission. Our results suggest that as one of the neutrophil adhesion molecules CD18 appears to have an important role in the FMF attacks. Further studies are needed.

Case 2—An 11 year old Algerian boy with prolonged fever, myalgia, purpura, and orchitis (2 MEFV mutations M694V, HLA-B1+), final diagnosis: febrile myalgia syndrome showing FMF.

Case 3—A 3 year old boy with recurrent fever, oral ulcers, oedemas, and sacroiliitis (HLA-B51−), grandmother: ulcerative colitis (HLA-B1+).

Case 4—A 20 year old woman with periodic fever, complete BD features and antiphos- pholipid syndrome (HIDS).

This report suggests that a true genetic link may exist between inflammatory disor- ders. Inflammatory bowel diseases, PAN and BD have been reported in 1% of patients with FMF. We could document 2 MEFV muta- tions (true genetic FMF) in our case 2 (pseudo-PAN) that we consider as prolonged febrile myalgia syndrome. The presence of MEFV mutations in the other cases (VCFS) with BD (HLA-B1+) and JIA in this patient suggests that a true genetic FMF (MEFV: M694V).

9.7 Hyper-IgD syndrome: case report

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Hyper-IgD syndrome (HIDS) is character- ised by attacks of spiking fever, which last for 1–7 days preceded by chills and rigor and accompanied by a number of symptoms—lumphadenopathy, abdominal distress, skin manifestation, arthritis, splenomegaly, etc. In the 1999 the gene for mevalonate-kinase was discovered as the gene responsible for HIDS. Our patient is a girl who came to our depart- ment with recurrent fever at the age of 4 years and 7 months. Her fever appeared every week and lasted for 3 days. It was accompanied with cervical lymphadenopathy, abdominal pain, arthralgia, and raised inflammatory proteins and erythrocyte sedimentation rate. Infection and malignancy were excluded. Repeatedly, the IgD level was over 140 mg/l.

The patient was treated with prednisone and the fever disappeared. On the first day of steroid treatment the fever appeared again and IgD reached its maximum—198 mg/l. The patient is now 9 years old, takes 2.5 mg prednisone daily, is without any symptoms, and her IgD concentration remains high.
Currently, DNA analysis for MVK gene is being performed.

9.8 Chronic joint pain in tricho-rhino-phalangeal syndrome type I

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Tricho-rhino-phalangeal syndrome type I (TRPS) is an autosomal dominantly inherited syndrome characterised by hypotrichosis of the scalp hair, bulbous tip of the nose and skeletal abnormalities including cone-shaped epiphyses of the phalanges and hip.

Our patient is a girl, the first child of three healthy parents. No consanguinity. Gross motor development was slightly delayed, but intellectual development has been normal. She was bald until the age of two. She developed a facial impression of TRPS: the scalp hair was thin and sparse, protruding ears, a long broad philtrum, and a pear-shaped nose. She has pronounced hypermobility in both small and large joints and laxity of the skin. She has swelling of the proximal interphalangeal joints of both hands with bilateral ulnar deviations in the middle phalanges of the index fingers. Radiological examination of the hands has shown cone-shaped epiphyses of both second indices. Bone age development is retarded. There are no malformations in the hips.

Combined conventional cytogenetic banding analysis and molecular cytogenetic analysis disclosed a pathogenic aberration showing a complex, apparently balanced, translocation t(7;13)(p51;q21;q24.1)de8(q24.1). The breaking point on chromosome 8 (8q24.1) has resulted in an interstitial deletion of at least 3 Mb covering most of the TRPS1 gene region that has recently been cloned.1

9.9 X-linked lymphoproliferative syndrome with intracranial and pulmonary aneurysms

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X-linked lymphoproliferative disease (XLP) is an inherited immunodeficiency to Epstein-Barr virus (EBV) infection that has been mapped to chromosome Xq25. The most common presentation is fulminant infectious mononucleosis (IM), but more than 10% of boys have problems, usually infections or lymphoma without EBV infection. Our patient was born in 1985 as the second of three healthy unrelated parents with no consanguinity. Gross motor development was slightly delayed, but intellectual development has been normal. She was bald until the age of two. She developed a facial impression of TRPS: the scalp hair was thin and sparse, protruding ears, a long broad philtrum, and a pear-shaped nose. She has pronounced hypermobility in both small and large joints and laxity of the skin. She has swelling of the proximal interphalangeal joints of both hands with bilateral ulnar deviations in the middle phalanges of the index fingers. Radiological examination of the hands has shown cone-shaped epiphyses of both second indices. Bone age development is retarded. There are no malformations in the hips.

Combined conventional cytogenetic banding analysis and molecular cytogenetic analysis disclosed a pathogenic aberration showing a complex, apparently balanced, translocation t(7;13)(p51;q21;q24.1)de8(q24.1). The breaking point on chromosome 8 (8q24.1) has resulted in an interstitial deletion of at least 3 Mb covering most of the TRPS1 gene region that has recently been cloned.1

9.10 CINCA (chronic, infantile, neurological, cutaneous, and articular) syndrome: report on three new cases

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CINCA (chronic, infantile, neurological, cutaneous, and articular) syndrome, a rare multisystemic inflammatory disease of unknown cause. In all cases the typical rash was present and within the first days of life; thereafter the disease progressively affected other organs.

In the first case the rash was associated with papillodea, spiking fever, transient arthritis, and persistent lymphadenopathy, identified by biopsy as a reactive lymphadenopathy with mixed hyperplasia.

The second case showed recurrent arthralgia and patellar hypertrophy. At direct immunofluorescence examination, the skin biopsy showed an urticaria-like vasculitis affecting the small and medium vessels of the dermis with XLP deposits in the dermis-epidermis junction.

The third case was characterised by transient arthritis, perceptive deafness, patellar overgrowth, papillodea, morphological facial modifications, and spiking fever. Skin biopsy showed a leucocytoclastic vasculitis with IgM and complement deposits.

None of our cases had mental retardation (though described as a constant feature).

In all 3 cases laboratory findings showed leucocytosis, increased serum immunoglobulin levels, and raised C reactive protein and erythrocyte sedimentation rate.

In 2 cases the neutrophil activation markers were studied: XLP CD11b and CD18 being greatly raised. These surface antigens have a role in the production of interleukin 8 and in the response to this cytokine. Chronic activation of both circulating and tissue neutrophils, suggesting a primitive defect of this cell line and of osteoclastic cells, which share the same staminal cells, may have an important role in the pathogenesis of CINCA.

9.11 Primary SJÖGREN’s syndrome (pSS) in children and adolescents: clinical, immunological, and immunogenetic characteristics

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We followed up five girls with average age 14.6 years (range 14–15). All patients had recurrent infections of upper airways, sustained fever, and persistent symptoms included arthralgia (5/5), Raynaud’s Phenomenon (3/5), dental decay (3/5), hair loss (3/5), abdominal pain (3/5). Only two patients had sicca syndrome, detected by Schirmer’s test and stimulated parotid secretion.

In immunologically, we found polyclonal hypergammaglobulinaemia (4/5), positivity of rheumatoid factor (4/5), presence of antinuclear antibodies (3/5), ant–Ro/La antibodies positivity (3/5). Immunogenetic HLA typing showed that three of five patients had antigens B8/DR3, especially with anti–Ro/La antibodies. The association HLA-B8/DR3 with pSS in adults and anti–Ro/La is typical for the Slovak population. All patients had idiopathic changes typical for Sjögren’s syndrome.

Diagnostic criteria for adult pSS are not fully applicable in children and adolescents, because laboratory autoantibody positivity in these patients precedes signs of sicca syndrome. Although arrhythmia, fatigue, and other symptoms, and immunological changes may suggest a diagnosis of pSS, sialography may be decisive for the diagnosis in childhood.

9.12 Primary juvenile SJÖGREN’s syndrome: a rare disease in childhood

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Primary SJÖGREN’s syndrome is rare in children. The disease affects mainly older women and only a few cases of primary SJÖGREN’s syndrome in children have been described.

We report the case of a five year old girl, whose initial manifestation of disease was Raynaud’s phenomenon. After 6 months, arthritis, polyarthalgia and peripheral polyarthritis developed. Two years later recurrent swelling of the parotid glands (mainly right side), dry cough, and vasculitis were additionally seen, dental caries progressed. Raynaud’s phenomenon, sedimentation rate, positive rheumatoid factor test, positive antinuclear antibody test, pulmonitis shown by a chest x ray, oestosclerosis of distal phalanges in a hand x ray were found. An ophthalmologist showed conjunctivitis with lachrymal hypersecretion. In a biopsy of the salivary glands plasmaic cell infiltration in the glands and in hypertrophied epithelium of ductuli, paracelagogenic amyloid concentration around capillaries. Typical for the diagnosis of SJÖGREN’s syndrome with secondary amyloidosis was made. Corticosteroid treatment and basic treatment with Leukeran (chlorambucil) improved the general status of the patient. After 6 months laboratory findings were normal. Mild signs of inflammation, were found, but disorder of the peripheral blood circulation and acrocyanosis was present. Typical dry mouth and eyes syndromes and symptoms of other systemic autoimmune disease did not develop during the period of the observation.

This clinical case report suggests, that primary juvenile SJÖGREN’s syndrome can manifest without sicca features, typical in adults. Early diagnosis and treatment relieves the course of the disease and, probably, protects dysfunction of the exocrine glands.

9.13 Thrombosis associated with antiphospholipid antibody in paediatric systemic lupus erythematosus

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Antiphospholipid syndrome is a disorder of recurrent arterial or venous thromboses, thrombocytopenia, and the presence of circulating antiphospholipid antibodies. Recurrent fetal loss is a common manifestation of the syndrome and frequently occurs in women with no history of thrombosis. Thrombocytopenia occurring during the course of

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Antiphospholipid syndrome is usually mild. If the clinical syndrome occurs in a patient with systemic lupus erythematosus, or less commonly in other disorders, such as systemic sclerosis, rheumatoid arthritis, or Behçet’s syndrome, antiphospholipid syndrome is regarded as secondary. In primary antiphospholipid syndrome there is no evidence of other underlying disease.

We report the case of a 14 year old boy, whose initial manifestation of disease was arterial occlusion. Results of clinical manifestations of antiphospholipid syndrome is so wide that it includes virtually all medical specialties.

9.14 Remission of haemophagocytosis upon treatment with an anti-TNFα antibody

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Haemophagocytosis is a severe disease characterised by inappropriate macrophage activation resulting in pancytopenia and excessive inflammation, it can occur as a familial inherited form or in association with diseases such as juvenile idiopathic arthritis.

At the age of 1 month, a girl presented at our hospital with a first episode of haemophagocytosis, which was induced by using intravenous immunoglobulins (IVIG), cyclosporin A (CSA), and steroids. Haemophagocytosis was reactivated at the age of 7 months. The patient was treated with IVIG, intravenous steroids, and intravenous CSA. However, the patient deteriorated further and had to be transferred to the intensive care unit.

In diseases such as rheumatoid arthritis and Crohn’s disease, characterised also by an exaggerated secretion of an array of proinflammatory mediators, application of anti-TNFα antibodies has proven beneficial. This led us to treat our patient with a monoclonal anti-TNFα antibody (infliximab), rather than using more toxic drugs such as antithymocyte globulins or etoposide. Other treatments (steroids, CSA) remained unchanged. After 1 year of spaced PGE1 courses (4 weeks), permanent closure of the skin defects was seen. Side effects of treatment were pain and erythema on PGE1 infusion.

Conclusion—In this girl with CINCA syndrome severe skin necrosis developed, which might be a consequence of the vasculopathy. The effect of intermittent PGE1 on healing of the skin lesions may include inhibition of platelet aggregation, vasodilatation, and/or angiogenesis.

9.16 Mistakes of, and obstacles to, recognition of neoplastic and haematological disorders mimicking juvenile chronic arthritis

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The present paper is the summary of our observations on neoplastic and haematological disorders of both malignant and benign origin that developed with pronounced rheumatological manifestations and were not identified on early stages.

The most rare case of Asekin’s tumour (from FNET group malignancies) in a 6 year old girl was presented as systemic juvenile rheumatoid arthritis (JRA) (so-called subependymal glioma) followed by vasculitis-like disease, suspected to be Wegener’s granulomatosis. Asekin’s tumour was diagnosed after death by histology and immunohistochemical analysis, whereas oncological examination was done repeatedly during the course of disease with negative results. We also dealt with a case of non-Hodgkin’s lymphoma (Ki1-), presenting as a vasculitis-like syndrome with asymmetrical polyarthraly in an 11 year old girl. We observed a series of different neoplastic and haematological disorders mimicking juvenile spondyloarthropathies (JSA) owing to the localisation of peripheral arthritis, the presence of enthesitis, sacroilits and axial disease (1 melanoma, 1 mediastinal neuroblastoma, 1 Ewing’s sarcoma, 2 acute leukemias, and 2 patients with heritable spherocytic anaemia). One more case of JSA mimicking was found in a teenage boy who had back pain due to exostosis of the lumbar spine (not detected previously by x ray) and talagia accompanied by ankle arthralgia due to an orthopaedic problem. We also observed 3 cases of secondary knee monarthritsis due to atypical localisation of osteoid oseomas, exostosis, and haemangioma.

In all reported cases the mistaken diagnosis was caused by (α) pronounced rheumatological manifestations; (β) inclusion of different disorders under a single title; (γ) an overestimate of the negative results of the previous diagnostic procedures. Our experience proves that in all doubtful cases differential diagnostic research should be continued.

9.17 Familial Mediterranean fever (FMF) presenting with unusual musculoskeletal manifestations

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FMF is characterised by recurrent episodes of peritonitis, pleuritis, and synovitis. Although the most common musculoskeletal manifestation of the disease is acute recurrent monarthritis other manifestations have been described, including chronic joint disease, spondyloarthropathy, myopathy, and the “febrile myalgia syndrome”. The diversity and non-specificity of these clinical features are often an obstacle to the diagnosis of FMF. We describe a group of patients who displayed a variety of non-specific musculoskeletal symptoms and in whom genetic screening showed homozygosity for the FMF gene.

Ten patients were Sephardic Jews and 3 were Israeli Arabs. Nine were homozygous for the M694V mutation and the rest were homozygous or compound heterozygous for one of the other 4 mutations (V726A, M680I, M694I, E148Q). Six patients had the “febrile myalgia syndrome”, 2 had recurrent episodes of calf pain and pretilial swelling, 2 had non-specific myopathy, 1 had recurrent episodes of thigh swelling, 1 had chronic knee arthritis without any other features of FMF, and 1 had spondyloarthropathy.

Conclusion—Our observations indicate that genetic screening for FMF should be included in an investigation of recurrent or unexplained episodes of musculoskeletal symptoms among children of Mediterranean extraction.

9.18 Treatment of hyper-IgD syndrome: a question unanswered

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A long term follow up of a child affected with hyper-IgD syndrome (3 years) is reported, with particular emphasis on the treatment of this disease. A male child, born on March 1996 from unrelated, healthy parents, developed recurrent fever spikes associated with chills, severe malaise, short term diarrhoea from December 1996. Between disease flare
ups, he was well. Three months later, a widespread enlargement of mesenteric lymph nodes and a thickening of colonic walls were shown. In the following months we noted (a) high IgA plasma concentration (9.45 g/l); (b) increased mevalonate urinary excretion; (c) strongly reduced activity of mevalonate kinase (5.4 vs 347 pmol/min/mg). Familial Mediterranean fever was ruled out by genetic analysis. On this basis, we suggested the diagnosis of hyper-IgD syndrome. The patient was treated with colchicine (1 mg/day continuously), prednisone (0.5 mg/kg), and naproxene (15 mg/kg) only at the beginning of flare up. Table 1 shows the results obtained.

Table 1

<table>
<thead>
<tr>
<th>Flare ups (days)</th>
<th>Mean (SD)</th>
<th>Follow up (months)</th>
<th>Flare ups</th>
</tr>
</thead>
<tbody>
<tr>
<td>No treatment</td>
<td>17 (8.2)</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Colchicine</td>
<td>33 (25)</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>Prednisone</td>
<td>14 (6.2)</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>Naproxene</td>
<td>18 (7)</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>

Although our one case does not permit statistical analysis, our data seem to suggest that colchicine gives better disease control, reducing fever flare ups, whereas prednisone and naproxene sharply stop the fever attack at the beginning.

We thank RA Wanders for the mevalonate-kinase assay.

9.19 Joint involvement in eosinophilic gastroenteropathy in childhood
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Eosinophilic gastroenteropathy (GE) is an uncommon disease characterised by eosinophilic infiltration of the gut wall. The disease may have different clinical presentations. Joint involvement is likely an underestimated complication of GE.

We report on 13 patients seen during the period 1992–99. Their mean age at the presentation of the disease was 8 months (range 1–4). All patients underwent gut endoscopy with multiple biopsies. We considered the gold standard to be villous containing >20 eosinophils infiltrating the epithelium.

The heralding symptoms were severe iron deficiency anaemia in 5 patients, which was associated with oedema due to loss of protein through diarrhoea in a further 5 patients; and haematochezia in 5 patients. Two patients presented severe bloody diarrhoea. The remaining patient came to us because of exudative ascites.

Four patients developed non-erosive arthritis in both the knee (2) and at the tibiotarsal joints. This symptom occurred after 12–19 months from the diagnosis. Arthritis was treated with sodium naproxene in 2 patients and intra-articular steroid infiltration in 1 patient. Interestingly, 1 patient developed a good response to an exclusive monomeric diet; when this schedule was modified arthritis flared up. No patient needed steroids or immunosuppressive drugs for the control of arthritis.

Our experience suggests that (a) arthritis is a relatively common complication of GE; (b) the feeding treatment using monomeric dietary schedule may be effective in the treatment of GE related arthritis.

10 Scleroderma

10.1 Thermography in juvenile localised scleroderma assessment
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To evaluate the clinical use of infrared thermography in localised scleroderma (LS) in disease activity assessment and management.

Methods—We retrospectively reviewed thermal images of children with LS obtained between 1993–2000. Thermographs were included only when a contemporary detailed clinical description of the lesion(s) was available. Lesions were classified as “active” (new or extended) or “quiescent” according to clinical description (colour, skin texture, measurements). Thermographs were considered positive when the area temperature was >0.5°C higher than the surrounding skin or the opposite site. Two clinicians (GM and KJM), blinded to the clinical description and thermography report, reviewed the thermal images independently. Full agreement in scoring was achieved in 86%, and discordant results were resolved by mutual examination.

Results—40 patients were included in the study (26 F, 14 M). The most common diagnosis was a combination of morphea and linear scleroderma (M+LiS, 14 patients), followed by isolated LS (11 patients), en coup de sabre (6 patients), and M (5 patients). 68 lesions were examined: 35 affecting the legs, 16 the arms, 10 the face/scalp, and 9 the trunk. We reviewed 130 separate thermal images, 34 lesions having multiple thermographic examinations. There was complete agreement between the clinical description and thermography in all new lesions (table 1). Of the clinically inactive lesions positive on thermography, most were “old” lesions with the presence of severe atrophy and subcutaneous fat loss.

Table 1

<table>
<thead>
<tr>
<th>Thermography</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinically active</td>
<td>47/51 (92%)</td>
<td>4/51 (8%)</td>
</tr>
<tr>
<td>Inactive</td>
<td>25/79 (32%)</td>
<td>54/79 (68%)</td>
</tr>
</tbody>
</table>

Conclusions—Infrared thermography is a potentially reliable tool for assessing the activity of LS lesions in conjunction with clinical activity, particularly for clinically suspicious new and extending lesions. Further evaluation is needed to determine whether thermography can predict future progression of lesions, particularly those which are equivocal clinically.

10.2 An unusual type of scleroderma with neurological disease
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We describe the case of a 14 year old boy who started with a linear scleroderma and presented later a neurological disease.

At the age of 11 years the boy developed a marked hypotrophy and hypoplasmy of the right forearm apparently owing to prolonged immobilisation. Over a period of few months the disease progressed to affect the skin and muscles of the right arm, hand, and fingers with a sclerotic evolution. All laboratory and radiological examinations (x rays and magnetic resonance imaging (MRI) of the arms, x rays of the chest and of the gastrointestinal tract), spirometry, and a nailfold capillaroscopy were normal, except for a high antinuclear antibody titre (1/1280).

Borrelia infection (IgM and IgG low titre) was suspected and the patient began treatment with penicillin 15 000 000 U/d for 10 days, without any improvement.

Two years later he had uveitis and seizures (abnormal EEG, cranium asymmetry at x ray examination, microvascular ischaemic encephalopathy at MRI, negative cerebral arteriography).

Recently, facial haemiatrophy with a contralateral hemisyndrome is evident and skin and muscle atrophy have worsened.

Whether this form is an evolution of linear systemic scleroderma or is linear scleroderma with neurological disease, which has already been described, cannot be stated for sure.