

**Table I.** Prevalence of Beta-thalassaemic trait in patients with RA and SLE compared to the control population (data referring to the Ferrara and Rovigo areas of Italy).

Total no. subjects	Expected prevalence of -thal in the geographic area studied	Observed prevalence of -thal	Ratio of -thal observed/-thal expected
RA	146	13.1%	19.8%
SLE	177	13.1%	9.6%

ed the coexistence of sickle cell disease (SCD) and SLE (2), but only Kaloterakis *et al.* (3) described a case of sickle cell/ -thalassaemia in a SLE patient.

In a study conducted by Montecucco *et al.* (4) it was stated that the prevalence of the -thal trait in patients with connective tissue diseases and seronegative spondyloarthropathies is similar to that expected for the whole population according to their geographic distribution, but the conclusion was not supported by consistent data.

Previously we observed a markedly lower incidence of the -thal trait among a lupus population born in Ferrara and Rovigo areas compared to a control population coming from the same two areas (5). However, these findings were historical and remained unpublished because of the lack of a rigorous methodological approach to gathering and analysing the data.

We have now prospectively studied the prevalence of -thal minor in 177 consecutive SLE patients from the Ferrara and Rovigo areas (32 males and 145 females, mean age 54 years, range 20-89) diagnosed according to the 1997 revised ACR criteria (6, 7) and followed by our Department from 1998 to the present. Their -thal status was suspected based on findings of a low mean corpuscular volume, low haemoglobin value, and increased number of red blood cells; the condition was confirmed in all the cases by haemoglobin electrophoresis. In this patient population we found 17 SLE patients (all female, mean age 53 years, range 20-88) with -thal minor (9.6% of the cases). This prevalence was 0.7 times lower than the expected rate of 13.1% of the control population and almost half of the prevalence previously observed in RA patients (19.8%) coming from the same areas (Table I).

These data suggest that -thal subjects exhibit a particular immunological reactivity of different circulating lymphocyte T-cells subpopulations. If we consider that RA is a prevalently Th1-oriented disease and SLE is a prevalently Th2-oriented disease, it could be argued that -thal might modify the immunological profile of circulating T cells through a different immune reactivity. Obviously confirmation of this hypothesis will require further studies on T-cell subpopulations and their functioning in

-thal subjects.

On the basis of these data we conclude that the prevalence of the -thal trait is higher in our RA patients and lower in our SLE patients compared with the normal population. The reasons for this different frequency and the way in which the -thal trait interferes with the clinical characteristics of RA and SLE remains a matter of discussion. Large prospective epidemiologic studies will be necessary to determine if the prevalence of serologic and clinical features of immune complex diseases such as SLE is influenced by the coexistence of a haemoglobinopathy.

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## Monolateral coxitis as a unique osteoarticular manifestation of Parvovirus B19 infection

Sirs,

Since its discovery (1), human parvovirus B19 (B19) has been linked with a broad spectrum of clinical syndromes, the most common of which are erythema infectiosum, aplastic crisis complicating chronic hemolytic anemia and hydrops fetalis (2). The articular manifestations, though less commonly recognised, have received increasing attention recently. The recent studies have shown that B19 infection can cause acute arthritis both in children and adults, although its prevalence in adults with arthralgia and acute arthritis has been reported to be 80% (3) while in children it is 21.2% (4) or 21.6% (5). In order to provide further insights into the various clinical manifestations of acute arthritis in children with B19 infection we would like to report a 13-year-old male child with monolateral coxitis.

The patient was admitted to our unit because of remittent fever lasting for 20 days associated with pain and restricted left hip motion. The boy held his left hip flexed and abducted, with no internal rotation and no objective evidence of local inflammation. Laboratory investigations revealed leukocytosis (13,600 cells/ml) with normal neutrophils (60%), high ESR levels (62/hr) and positive C reactive protein CRP(20.7 mg/l; normal range 0-3 mg/l).

ANA, nDNA, HLA-B27, ASO, the Mantoux test and serologic tests for Cytomegalovirus, Epstein-Barr virus, rubella, *Mycoplasma pneumoniae* and brucella were all negative. B19 infection was diagnosed on the basis of the specific presence of IgM antibody (enzyme immunoassay: IgM 92.5 U/ml; normal < 30 U/ml) and was confirmed by seroconversion during a 6-month follow-up. Ultrasound evaluation and computerized tomography of the left hip confirmed the presence of synovial fluid. After 2 days of treatment with Flurbiprofene (5 mg/kg/day) the fever disappeared and the articular symptomatology slowly improved; after 15 days of therapy CRP and leucocytosis were normalized. Flurbiprofene therapy was continued for 3 months, with final normalization of the ESR and complete recovery of hip motion.

According to a very recent pediatric study, the most frequently involved joints associated with B19 infections are the knee, wrist, ankle and interphalangeal joints, whereas the elbow, shoulder and cervical vertebrae are less frequently affected (5). To the best of our knowledge coxitis had never been reported hitherto in the literature. Another atypical finding in the present case is the mo-

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nolateral joint involvement, which have been reported to be very low in the overall literature (5-7). Another unusual feature in our case history was the dramatic clinical picture. The absence of a skin rash, on the contrary, cannot be considered an unexpected finding, since its prevalence in a pediatric population with B19-associated arthritis has been recently reported to be lower than 50% (5).

In this case the overall clinical picture, the laboratory tests demonstrating abnormal indices of inflammation and the rapid response to anti-inflammatory therapy could suggest the hypothesis of a rheumatic-like disease. It is known that both in children and adults B19 infection has been implicated as a possible triggering factor of autoimmune diseases affecting the joints, connective tissue and large and small vessels, thus confirming that B19 may contribute to the induction of autoimmune reactions (8, 9). Therefore, we can underline, on the basis of our atypical case report, the conclusions by Oguz *et al.* (5) that B19 IgM have to be searched for in children who present with acute monoarthritis, whatever the clinical picture and localization.

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## Comparison of serum IgE levels between female and male SLE patients, with reference to gender differences in the incidence of SLE

Sirs,

Several studies have been performed to investigate the importance of the serum IgE level in systemic lupus erythematosus (SLE) (1-3). It has been reported that serum IgE levels are significantly higher in the active stage of SLE when compared with the level during remission (1). Our recent study of 51 patients with SLE (45 women and 6 men) revealed significantly higher IgE levels in SLE patients compared with normal controls ( $450.5 \pm 1136$  IU/ml in 51 SLE patients vs.  $72.7 \pm 87$  IU/ml in 391 controls,  $p = 0.007$ ) independent of disease activity (2). In general, the IgE level in SLE patients does not appear to be related to the development of atopic diseases (3).

As shown in Table I, 7 out of 12 male patients (58%) in our SLE cohort showed high serum IgE levels ( $> 250$  IU/ml) compared with normal controls (normal  $250$  IU/ml). In contrast, 21% (10/47) of our female SLE patients showed high IgE levels ( $> 250$  IU/ml). There was a significant difference in the prevalence of high serum IgE levels between male and female SLE patients ( $p = 0.011$  by the chi-squared test performed with SPSS software; Chicago, USA). In contrast, a significant difference was not observed in the average amounts of IgE levels between male and female SLE patients ( $399 \pm 372$  IU/ml in 12 male patients vs.  $330 \pm 755$  IU/ml in 47 female patients,  $p = 0.66$ ), probably because certain female patients showed extremely high levels of IgE. In our male patients, no significant correlation was observed between IgE and other serum parameters such as immunoglobulins (IgG, IgA, and IgM) and autoantibodies. Thus,

their high serum levels of IgE did not seem to result from polyclonal B cell activation. A history of atopic disease in 12 male patients was only obtained in one patient.

The prevalence of SLE is significantly higher in females than in males, and this is probably due to promotion of the immune response by sex hormones (especially estrogen), including the production of several cytokines (such as interleukin (IL)-1, -6, and -10) and antibodies mediated by these T helper-2 (Th-2) cytokines (4). Estrogens are also reported to contribute to an increase in the transcription of autoantigens (5), such as human endogenous retroviruses (HERV) that may be a plausible causative agent of SLE (6). Thus, female hormones such as estrogen appear to cause a decrease in the threshold for responsiveness to autoantigens and/or production of autoantigens, and that this is related to a higher incidence of SLE in females. In addition, DNA methylation seems to play an important role in the induction of autoimmunity in SLE. Low levels of cytosine methylation (indicated by low activity of DNA methyltransferase-1 (DNMT-1), a methylation-regulating enzyme) in the regulatory sequences of DNA leads to transcriptional activation of genes, and DNA methylation is decreased in both male and female SLE patients (7). DNA hypomethylation (implied by low DNMT-1 activity) is thought to contribute to hyperresponsiveness to autoantigens in SLE patients and to the production of autoantigens, including HERV (7). It has been reported that IgE production is contributed by DNA hypomethylation and is also enhanced by estrogens (8, 9). The levels of IgE production mediated by IL-4 are known to be closely associated with the estrogen level (4). Thus, high IgE levels in male SLE patients may reflect stronger hyperresponsiveness due to DNA hypomethylation that is not related to the influence of sex hormones.

Further precise clinical and/or laboratory investigations of male SLE, as well as female patients with the postmenopausal onset of SLE (10), may make an important contribution to elucidation of the reason for the gender bias of this disease.

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**Table I.** Serum IgE levels in male and female SLE patients.

Sex	No. of pts.	IgE High ( $> 250$ IU/ml)	IgE Low ( $< 250$ IU/ml)	Pvalue (male vs. female)
Male	12	7 (58%)	5 (42%)	< 0.05
Female	47	10 (21%)	37 (79%)	

IgE was measured by chemiluminescent enzyme immunoassay (CLEIA; Fuji Levio Co., Inc. Tokyo, Japan).