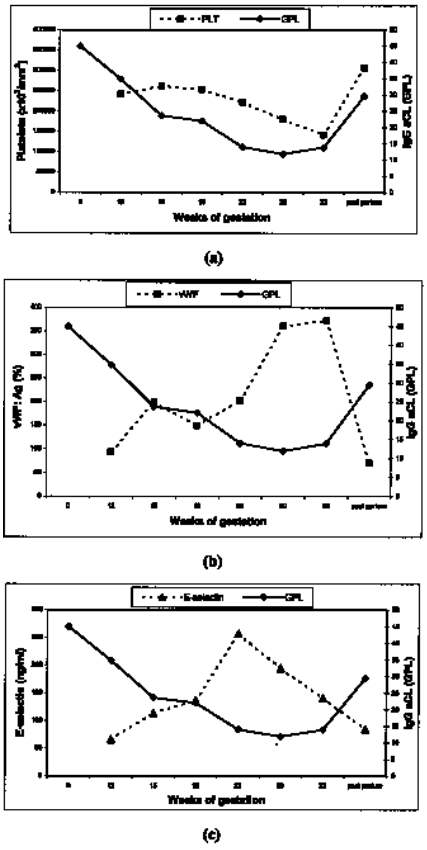

Fig. 1. (**a**) Pattern of IgG aCLlevels and platelet number; (**b**) pattern of IgG aCL levels and von Willebrand values; (**c**) pattern of IgG aCLlevels and E-selectin values.

parameters and antibodies to platelet factor 4-heparin complex were within the normal range. At the 32nd week of pregnancy, vaginal bleeding associated with abdominal pain manifested unexpectedly. Ultrasonography showed a large area of placental separation with a number of retroplacental clots and fetal heart activity was absent. The patient was thus delivered by uncomplicated caesarean section of a dead fetus. The placenta weighed 370 g and a retroplacental haematoma on the maternal surface without villous tissue damage was observed. Histological examination confirmed that the blood clot was situated outside the intact placental wall. The fetus was a normal male, weighing 2040 g (65th percentile). Available stored sera were retrieved and some markers of endothelial perturbation including von Willebrand factor antigen (vWF:Ag), intracellular cell adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), E-selectin and antibodies to endothelial cell (AECA) were tested for. ICAM-1, VCAM-1 and AECA were within the normal ranges in all serum samples, while the highest levels of vWF:Ag and E-Selectin were found at the 22nd, 29th and 32nd weeks, when the lowest values of IgG aCLwere noted (Fig. 1).

Spiral artery changes are generally considered to be important to the pathogenesis of retroplacental haematoma (2). This endothelial cell disorder may lead to several alterations, including vessel ruptures followed by retroplacental haemorrhage (3). Antiphospholipid antibodies (aPL) have been considered a cause of abnormal physiological changes in the spiral arteries of the placental bed (4). Using *in vitro* studies Di Simone *et al*. (4) demonstrated that either β_2-GPI-dependent or β_2-GPI-independent aCL bind to trophoblast cells. They thus postulated that this binding might represent a potential pathogenetic mechanism for a defective placentation in women with APS. Chamley *et al*. (5) observed that antibodies to human cardiolipin alone, to β_2-GPI alone or to cardiolipin/β_2-GPI complexes inhibit the proliferation of human choriocarcinoma cells. They therefore speculated that proliferation of endovascular trophoblast cells could be inhibited in women with aCL. In accordance with these studies we hypothesize that the decreases in IgG aCL titers occurring in our patient as the pregnancy progressed might be a consequence of aCL binding to trophoblastic cells during placentation. The occurrence of some signs of endothelial perturbation such as a rapid increase in vWF:Ag and E-selectin levels along with a decrease of platelet number, when the lowest values of IgG aCL were observed, might be indicative of endothelial damage causing spiral artery rupture and placental abruption.

Moreover, the absence in our patient of anti-endothelial antibodies and abnormalities in ICAM-1 and VCAM-1 levels during pregnancy would exclude the presence of endothelial activation with an inflammatory response. This later mechanism has been described by several authors (6-8) who report endothelial activation by anti-β_2GPI or β_2-GPI-dependent aCL through the adherent cofactor β_2GPI. Enhanced levels of ICAM-1 and/or VCAM-1 were correlated in these studies with increased adhesion of leukocytes to endothelium and with vascular thrombosis.

Our data suggest that in APS women with a history of placental abruption and positivity for IgG aCL, monitoring aCL, platelet, vWF:Ag and E-selectin levels might be a useful procedure during pregnancy. A steady fall in aCL titers associated with a decrease in the platelet count and an increase in vWF:Ag and E-selectin might in fact predict placental abruption.

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Pulse steroid treatment of polymyalgia rheumatica

Sirs,

Corticosteroids are the standard treatment for polymyalgia rheumatica (PMR). Their clinical response is dramatic. However, the total dose of steroids used by PMR patients is high and associated with side effects in as

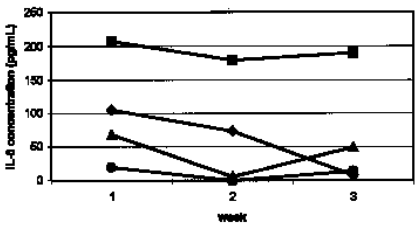

Fig. 1. IL-6 concentration before (week 1) and after 2 and 3 weeks from the administration of i.v. steroid boli in the 4 patients with recent onset polymyalgia rheumatica. The mean IL-6 concentration plus 3 standard deviations in 43 healthy age- and sex-matched controls was < 4 pg/mL.

much as 65% of patients (1). Therapeutic approaches proposed to reduce the incidence of steroid-related side effects include different administration schemes of steroids or alternative drugs with a possible steroid-sparing effect. Steroids have been used by shoulder injection (2) or weekly depot injections (3). Steroid-sparing therapies studied so far include methotrexate (4), azathioprine (5), and tenidap (6), but their efficacy is not clear.

Our hypothesis was that steroid pulses administered in the early phase of the disease could induce remission by aborting inflammation. The recently described mechanisms of action, such as inhibition of nuclear factor-κB resulting in decreased transcription for expression of pro-inflammatory genes (7) and non-genomic physicochemical actions (8), are probably active only when steroid pulses are used. Steroid pulses are not associated with the side effects commonly reported with chronic administration. In this pilot study, administration of pulse steroids to PMR patients, at doses roughly equivalent to those assumed in the first 2 months of standard therapy, was attempted. Four patients affected by untreated PMR (9) (mean disease duration 64.8 days, range 49-90 days) were studied. The study was performed according to the declaration of Helsinki and was approved by the relevant ethical committees. PMR recurrences and relapses were defined as signs or symptoms of the disease associated with increased ESR or CRPappearing, respectively, during treatment or after its discontinuation.

ESR, CRP, and IL-6 (R&D Systems, Minneapolis, MN, USA) were evaluated before treatment and after 7 and 15 days from the first corticosteroid bolus. Bolus i.v. injections of methylprednisolone (250 mg in 250 cc of saline) were administered on 3 consecutive days. If PMR relapsed, oral prednisone was given with the rapidly decreasing dosage previously used in a controlled trial on the efficacy of methotrexate as steroid-sparing agent (4). End points of the study were the time between the last steroid bolus and the relapse of PMR, if any, as well as the dosage of steroids eventually needed after the 3-day course. In addition, the number of recurrences and relapses occurring during and after oral steroid treatment respectively was calculated and compared with those of the control group of the previously cited therapeutic trial, consisting of 31 patients with PMR treated with prednisone alone (4).

PMR symptoms disappeared and laboratory signs of inflammation improved in 3/4 patients during i.v. treatment, but recurred in all patients after a mean time of 6.4 days (range 3-14 days) from the last steroid bolus. The mean dosage of oral prednisone taken after the boli was 2237 ± 213 mg, a value which was not different from the 2832 ± 750 mg taken by controls. Recurrences were seen in 1 out of 4 (25%) patients in the first group and in 22 out of 31 (71%) patients in the second group (ns). The median follow-up period after the initiation of steroid treatment was 19 months (range 12-22 months). After completion of the treatment, no pulse-treated patient suffered relapses in comparison with 10/31 (32.3%) controls (ns). IL-6 concentrations dramatically decreased after the bolus treatment but returned to the initial values 2 weeks later in all but one patient (Fig.1). This patient did not improve after the boli and therefore received oral steroids earlier than the other patients, a fact that probably kept the IL-6 concentration low.

In conclusion, 3 pulses of i.v. methylprednisolone failed to induce remission in PMR and to show any steroid-sparing effect in our small, uncontrolled study. Similarly, no significant corticosteroid-sparing effect has been described after a single pulse with 240 mg of methylprednisolone in patients with GCA(10).

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β-thalassaemic trait and systemic lupus erythematosus

Sirs,

The coexistence of haemoglobinopathies and connective tissue disorders has rarely been investigated and published data relating to this matter are only anecdotal. In 1975 we demonstrated that the incidence of the β-thal trait in patients with RA coming from an area in which haemoglobinopathy is endemic, such as Ferrara and Rovigo (the Po Delta, northern Italy), is higher than would be expected based on its occurrence in the general population (19.8% vs 13.1% of a random population from the same two areas) (1).

In SLE, varying degrees of anaemia are quite a common finding but only rarely has the issue of concomitant haemoglobinopathies been addressed. To the best of our knowledge 16 reported cases have describ-