Laboratory and clinical evaluation of 11 patients with mild active rheumatoid arthritis (group A) and of seven patients with severe active rheumatoid arthritis (group B). Results are given as means (SD)

	Start of treatment	After 14 days	After 28 days
Group A			
Ferritin ($\mu\text{g/l}$)	30.40 (25.80)	22.00 (15.60)	26.10 (21.00)
ESR* (mm/h)	56.16 (28.20)	57.20 (30.10)	59.08 (34.50)
IgG (g/l)	14.30 (5.75)	15.51 (5.81)	16.02 (6.24)
β_2 Microglobulin (mg/l)	2.24 (0.84)	2.97 (0.88)	2.82 (0.78)
Ritchie index	22.66 (14.01)	15.58 (10.63)	13.08 (9.23)
Grip strength	67.91 (23.32)	90.83 (29.49)	91.66 (28.30)
Morning stiffness (min)	49.16 (15.15)	10.83 (6.76)	8.33 (6.05)
Group B			
Ferritin ($\mu\text{g/l}$)	368.30 (147.9)	405.5 (124.7)	379.1 (110.0)
ESR (mm/h)	90.16 (37.80)	95.10 (30.20)	102.3 (24.30)
IgG (g/l)	19.82 (4.13)	24.00 (5.60)	23.35 (5.84)
β_2 Microglobulin (mg/l)	3.70 (1.38)	4.83 (1.40)	3.05 (0.60)
Ritchie index	26.00 (10.64)	15.00 (6.80)	12.00 (5.88)
Grip strength	51.66 (32.99)	82.50 (23.76)	85.83 (20.08)
Morning stiffness (min)	68.33 (29.45)	53.33 (13.84)	49.16 (25.41)

*ESR=erythrocyte sedimentation rate.

Desferrioxamine, a metal chelating agent with high affinity for iron, has been found to suppress tissue injury in animal models of inflammation.⁸ Few studies have been performed in humans, and these have given conflicting results. Giordano *et al* showed an improvement of clinical conditions and a significant increase of serum iron and haemoglobin with a marked progressive decrease of serum ferritin in patients with RA with hypsideraemic anaemia in a short desferrioxamine treatment.⁹ Fudman *et al* by intra-articular administration of desferrioxamine noted predominantly systemic effects with decreased serum ferritin and decreased serum concentrations of lipid peroxidation products.¹⁰ Blake *et al* treated patients with RA with larger doses of desferrioxamine and found serious side effects consisting of loss of consciousness and of pigmentary retinopathy.¹¹ Pall *et al* observed ocular toxicity after a low dose of desferrioxamine.¹² Polson *et al* found no significant changes in rheumatological indices or in immunological markers of disease activity of patients with RA refractory to conventional treatment and receiving desferrioxamine for six months.¹³

Recent studies have shown that desferrioxamine affects lymphocyte function. It can inhibit proliferation of human lymphocytes, probably by inhibition of ribonucleotide reductase and DNA synthesis.¹⁴ It is found that desferrioxamine treatment impairs the expression of interleukin 2 binding receptors on lymphoid cells in response to mitogen¹⁵ and markedly reduces interleukin 2 production by mitogen stimulated cells.¹⁵

In this study we noted a statistically significant improvement of clinical indices in the patients with RA at the 28th day. Patients had no side effects. A notable increase of serum β_2 microglobulin concentrations was noted in all patients at the 14th day followed by a statistically significant decrease at the 28th day in patients with more active disease. This increase in β_2 microglobulin at the end of desferrioxamine administration (14th day) without a worsening in clinical indices has not been explained. It may be due to a polyclonal B lymphocyte activation effect in these patients determined by desferrioxamine displacement of iron or other metals. Polyclonal B lymphocyte activators are mitogens that non-specifically stimulate lymphocytes to secrete immunoglobulins, and both groups of patients had significantly increased concentrations of immunoglobulins after desferrioxamine treatment.

High serum ferritin concentrations seem to

correlate with the severity of arthritic involvement. In this study patients with more active RA had higher serum ferritin concentrations than patients with less active disease. On the other hand, low serum ferritin concentrations may be connected with iron deficiency and in this study patients with RA and low serum ferritin concentrations had lower serum iron and higher transferrin and iron binding capacity than patients with higher serum ferritin.

In patients with severe active RA the association of raised concentrations of ferritin and β_2 microglobulin suggests that conspicuous iron deposits may play a part in the stimulation of lymphoid cells. Desferrioxamine seems to reduce lymphocyte activation and function, probably by inhibiting DNA synthesis and interleukin 2 action in these patients. In patients with less active RA and low or normal serum ferritin concentrations the desferrioxamine effects do not seem to influence lymphocyte activity.

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Azathioprine and warts

Sir: In 1963 we began treatment of patients with rheumatoid arthritis with azathioprine,¹⁻⁵ and we are still following up six patients who have been treated with this drug for more than 25 years. At the start we used a dose of 2.5 mg/kg daily and now we use 50 mg a day. Aspirin was added for pain relief when necessary.

The course of their disease has been quite satisfactory with a minimum of discomfort and they have led a fairly active life. The treatment has not prevented the appearance of classical bone deformities, however.

During the past two years, four of our six patients, whose ages range from 60 to 83 years, developed skin lesions on hands and feet, which were diagnosed as warts. To confirm that diagnosis one patient was biopsied. The anatomical diagnosis was 'hyperkeratotic seborrheic wart' (Professor La Chapelle, University of Louvain).

Hyperkeratotic warts are fairly common among old people. It is impossible to draw any conclusion from a group of only six patients but we wonder if the high incidence of warts among our azathioprine treated patients is related to their treatment.

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