tuberculous arthritis, to gout, or to a variant of the so-called seronegative peripheral arthritis as seen in Reiter's disease, arthritis associated with gastrointestinal disease, psoriasis, and ankylosing spondylitis. In all these conditions, however, the involvement of the proximal interphalangeal joint is uncommon, with exception of tuberculous arthritis where the tumor albus or spina ventosa are typical examples. Polyarthritis of the small hand joints was seen in four paintings. Polyarthritis was only present or visible in one hand and not with certainty in the other hand. The feet were only visible in one painting and there they were normal. So no convincing evidence of symmetrical rheumatoid arthritis is found. Except for one case, all observed arthritis cases were males, which is in contrast to the male/female ratio of rheumatoid arthritis.

Although I looked for arthritis in the work of Breughel, Vandenbosch, Rembrandt, Rubens, and other painters of the Renaissance, no such deformities were found.

Immunostimulant therapy for rheumatoid arthritis. E. C. Huskisson, P. A. Dieppe, Jane Scott, Jane Trapnell, H. W. Balme, and D. A. Willoughby (*St. Bartholomew's Hospital, London*)

If rheumatoid arthritis is a chronic inflammatory response maintained by a persistent antigen, it is as logical to stimulate the immune system in the hope of removing the antigen as it is to suppress it in the hope of stopping the reaction which follows. Therefore considerable interest has been shown in the possible use of levamisole and a report of its effectiveness in an uncontrolled study (Schuermans, 1975).

34 patients with active rheumatoid arthritis were studied. 12 received at least 3 months' treatment with levamisole (50 mg tds), 12 with penicillamine, and 10 with placebo; treatments were not identical. Before assessment, patients were stabilized on an analgesic and anti-inflammatory regimen which remained constant during the study. Measurements were carried out before and at 3-monthly intervals after the start of the treatment by a 'blind' observer who was unaware of the treatment and with whom the side effects were not discussed. Measurements included pain (visual analogue scale), duration of morning stiffness, articular index, and proximal interphalangeal joint circumference. Weekly measurements of pain relief were made by the patient. ESR, tests for rheumatoid factor, and immunoglobulins were measured at 3-monthly intervals. At these times

delayed hypersensitivity to tuberculin was assessed by skin tests and by leucocyte migration inhibition.

After 3 months' treatment there was significant pain relief in both penicillamine and levamisole groups compared to placebo, and both produced significant reduction in ESR (Table). Both drugs worked slowly. There was a trend towards enhancement of skin tests and greater leucocyte migration inhibition in patients on levamisole than in those on placebo. These changes showed a significant correlation with pain relief ($r=0.44$, $P<0.05$ for skin tests, $r=0.4$, $0.1>P>0.05$ for leucocyte migration inhibition). It is suggested that levamisole has activity of the type shown by penicillamine in rheumatoid arthritis.

Reference

SCHUERMANS, Y. (1975) *Lancet*, 1, 111

Penicillamine in rheumatoid arthritis: comparison of two dose schedules. A. G. S. Hill and H. F. H. Hill (*Stoke Mandeville Hospital*)

The UK controlled trial (Multi-centre Trial Group, 1973) proved the superiority of penicillamine over placebo in a group of patients with advanced persistently active rheumatoid arthritis. It did not attempt to define its use in rheumatological practice, either in terms of selection of patients or dose. Day *et al.* (1974) and Hill (1974) suggested that side effects were less common if the drug was introduced slowly and the maintenance dose was the lowest which produced a satisfactory response.

This study compared two dose regimens in patients with disease which had been persistently active for months or years. Penicillamine (base) was added to the existing anti-inflammatory regimen when the latter had failed to halt disease activity. All patients had polyarticular synovitis and raised sedimentation rate (ESR) and a positive test for C-reactive protein. Vasculitis in the form of skin lesions and peripheral neuropathy were present in some patients and were taken as an additional indication for treatment. Patients were aged between 32 and 67 and the duration of disease was from 9 months to 21 years.

Group 1 In 21 patients the regimen used in the controlled trial (Multi-centre Trial Group, 1973) was adopted, namely 250 mg penicillamine daily increased by 250 mg every 2 weeks until the dose was 1500 mg at which it was held for 6 months. Thereafter the dose was decreased by 250 mg not more often than every 2 months, the final maintenance dose being the lowest which maintained remission.

Group 2 In 22 patients the dose of penicillamine was increased more slowly from the same initial dose of 250 mg. Subsequent increments of 250 mg were made at monthly intervals until the dose was 750 mg at which it was held for a minimum of 3 months. Thereafter further increments of 250 mg were made if disease activity persisted, but always at intervals of not less than 3 months.

The duration of follow-up (October 1975) was 22–30 months in group 1, 12–24 months in group 2.

Table Changes in clinical measurements and ESR after 3 months' treatment with levamisole, penicillamine, and placebo

	Pain	DMS	Joint size	Articular index	ESR
Levamisole	+8.8*	+25.6	+11.3	+5.3	+27.3*
Penicillamine	+6.1*	+116.3*	+14.3*	+5.6	+35.2*
Placebo	+0.3	+10.0	+1.6	+3.4	–1.8

Positive figures indicate improvement. *Denotes statistically significant difference between active drug and placebo ($P<0.05$).