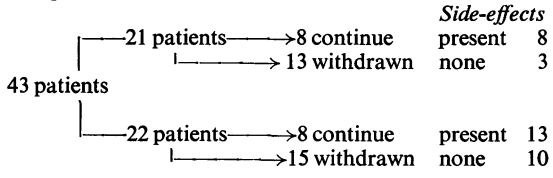
*Group 1. Dose increments of 250 mg every 2 weeks to a maximum of 1500 mg daily*

Of the 21 patients, 2 developed anorexia and stopped treatment before attaining a dose of 750 mg. Of the remaining 19, disease activity decreased in 18, the drug being ineffective in only 1 patient. 3 patients with vasculitis all improved, skin lesions disappeared, and the extent of the peripheral neuropathy decreased. One patient died from a cerebrovascular accident unrelated to treatment. Side effects were common, only 3 patients had none (Table). Only 8 patients continue, 2 maintained at 100 mg; 1 relapses if the dose is dropped below 1500 mg.

*Group 2. Dose increments of 250 mg every 4 weeks to a maximum of 750 mg*

The 22 patients on this regimen had fewer side effects, a total of 13 being recorded, but all 13 have been withdrawn (Table). Active synovitis has decreased in all these patients but the response has been less dramatic than in Group 1. 6 have been successfully maintained on 750 mg, but in 2 the maintenance dose is 1250 mg.

Six patients with vasculitis improved and skin lesions have disappeared or are less numerous, the extent of the peripheral neuropathy has decreased in 3 patients who had this additional manifestation of vasculitis. In particular gastrointestinal upsets have been rare, 1 patient reported mild vagaries of taste and 1 transient nausea with vomiting. Results in both groups are shown in the Figure and the Table.




**Table**

| *Side effects* | *Group 1 (21 patients)* | *with-drawn* | *Group 2 (22 patients)* | *with-drawn* |
|---|---|---|---|---|
| Thrombocytopenia (platelets < 100 000 withdrawn if < 70 000) | 6 | 3 | 2 | 1 |
| WBC < 3000 | 1 | 1 | 0 | 0 |
| Proteinuria (withdrawn when > 2g/24 h) | 3 | 2 | 10 | 9 |
| Rash | | | | |
| Early (all temporarily withdrawn, all restarted without recurrence of rash) | 1 | 1 | 0 | 0 |
| Late | 2 | 2 | 4 | 4 |
| Oral ulcer | 2 | 1 | 0 | 0 |
| Recurrent nausea and diarrhoea | 1 | 0 | 0 | 0 |
| Severe anorexia | 2 | 2 | 0 | 0 |
| Transient nausea | 0 | 0 | 1 | 0 |
| Severe dyspepsia and recurrence of peptic ulcer | 2 | 2 | 0 | 0 |

Penicillamine is a potentially hazardous drug and thrombocytopenia and proteinuria occur in a significant number of patients. Thrombocytopenia may occur in the early or late months of treatment but proteinuria has been more common after 6 or more months of therapy, hence continued vigilance is essential. Gastrointestinal side effects, some sufficiently severe to enforce withdrawal of penicillamine, were common in group 1 as were withdrawals for thrombocytopenia. The lower incidence of side effects in group 2 suggests that monthly increments are associated with fewer side effects, but the optimum maintenance dose must be found for each patient according to clinical and laboratory indices of activity.

**References**

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HILL, H. F. H. (1974) *Curr. Med. Res. Opin.*, **2**, 573 (Selection of patients with rheumatoid arthritis to be treated with penicillamine and their management)

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**Trial comparing azathioprine and penicillamine in treatment of rheumatoid arthritis.** H. Berry, S. Liyanage, R. Durance, C. G. Barnes, and L. Berger (*The London Hospital and St. Mary's Hospital, Colchester*)

A 'single blind' external observer trial has been carried out in two centres to compare penicillamine and azathioprine in the treatment of rheumatoid arthritis. One person supervised all patients in the trial and one 'blind' observer was employed in each centre. The length of the trial was 1 year.

65 outpatients were admitted to the trial. All had erosive, seropositive disease at a stage where gold therapy would conventionally be considered. If the patients were receiving corticosteroid therapy, a stable dosage for the previous 6 months without alteration during the trial was the accepted policy. The patients had to remain on constant anti-inflammatory-analgesic therapy, the only other drug allowed being paracetamol.

Azathioprine 2·5 mg/kg body weight dispensed on ordinary prescription as 50 mg tablets and penicillamine 250 mg tablets were similarly prescribed; penicillamine tablets were initially taken 1 a day, increasing by 1 tablet every 2 weeks to 1 g., *i.e.* 4 tablets a day. 33 patients received azathioprine, 32 penicillamine tablets.

Assessments were carried out on admission to the trial, then every 3 months. Articular index (Ritchie), early morning stiffness, 'Geigy' ring size, and grip strength were measured and pain was evaluated using the visual analogue scale (VAS) and the 4-point scale. Investigations included a full blood count, ESR, and weight. *X*-rays were taken on admission to the trial then at 3, 6, and 12 months. These were assessed by 2 'blind' observers, a clinician (C.G.B.), and a radiologist (L.B.). Toxic effects were sought by direct questioning; a check list was not used.

The initial values and change at 6 months (as a + or − figure) for each measure is as follows (a = azathioprine; p = penicillamine):

*Pain*

| VAS | | 4-point | |
|---|---|---|---|
| a | p | a | p |
| 10·1 | 12·0 | 2·92 | 3·44 |
| −1·9 | −5·6 | −0·07 | −0·89 |

Grip strength

| a | p |
|---|---|
| 415 mm | 415 mm of Hg |
| +55 | +60 |

Articular index

| a | p |
|---|---|
| 15·4 | 13·2 |
| −5·7 | −4·7 |

Geigy ring size

| a | p |
|---|---|
| 592·5 | 596·9 |
| −11·7 | −18·9 |

Early morning stiffness

| a | p |
|---|---|
| 116·5 mins | 126·4 mins |
| −33·7 | −101·1 |

ESR

| a | p |
|---|---|
| 54·2 mm | 55·8 mm |
| −9·8 | −27·3 |

Latex

| a | p |
|---|---|
| 6·95 | 7·17 |
| −1·30 | −2·00 |

Weight

| a | p |
|---|---|
| 63·2 kg. | 6·2 kg. |
| −1·99 | +0·10 |

Hb

| a | p |
|---|---|
| 11·85 g | 12·03 dl |
| +0·27 | +1·13 |

All parameters showed a highly significant change ($P<0·01$) in the penicillamine-treated group except for weight change. Improvement in articular index, latex, and reduction in Geigy ring size were highly significant, grip strength was significant ($P<0·05$) on azathioprine: changes in other parameters were not significant. There was a deterioration in *x*-ray appearance.

Analysis between the two treatment groups showed a significantly greater fall in ESR and rise in Hb in the penicillamine-treated group compared with the azathioprine-treated group. No other difference between the two treatment groups was detected.

A total of 61 toxic effects were encountered (33 on penicillamine, 28 on azathioprine). 30 were gastrointestinal—15 on each treatment. 8 patients had early transient proteinuria on penicillamine and 6 lost their taste temporarily. 8 patients had to be withdrawn from azathioprine therapy, 6 due to extreme nausea and 2 due to lack of response. 3 stopped penicillamine, 2 due to flare-up of disease necessitating admission to hospital and 1 due to severe sickness.

**Effects of local steroid injection for supraspinatus tears. Controlled study.** E. N. Coomes and L. G. Darlington (*St. Stephen's and St. Mary Abbot's Hospitals, London*)

Shoulder pain is common but a minority of patients are referred to hospital. Diagnosis can be difficult and the criteria for treatment uncertain. We investigated supraspinatus tears by arthrogram correlating with the clinical findings and then assessed the effects of local Depo Medrone injection. 40 patients with clinical supraspinatus tears entered the trial. Those with successful arthrograms were separated into two groups, the first treated with local steroid injection, the other with a local anaesthetic injection. All had Conray mixed with the injection checking the site radiologically.

The two groups were similar with respect to age, sex, and ruptures of the shoulder capsule shown on the arthrogram. They were assessed over 5 weeks and seen weekly. Shoulder movement was recorded and patients volunteered the effect of the injection. None knew what the injection contained.

In our clinic shoulder pain referrals accounted for 3% of new patients over the years 1970–74. Of the 40 patients, 37 had successful arthrograms (93%). 81% had the anterior approach, 19% the posterior approach. The anterior approach hurt more but was more successful for the arthrogram. All 37 patients had clinical supraspinatus tears, arthrograms confirmed ruptures in 73%. Pain relief in the Depo Medrone group was significantly better for the first 3 weeks but there was little difference at a month. Movement range and the presence of painful arcs were unaffected by the steroid injection; however, resisted abduction was painful in only 6% of the Depo Medrone group at week 3 compared to 56% of the other group.

(1) Arthrography can be a useful adjunct in shoulder pain diagnosis. (2) The majority of the arthrograms confirmed the rupture of the supraspinatus. (3) Local steroid injection gives pain relief initially but after a month there is little difference between the two groups. (4) Apart from initial pain relief on resisted abduction there is no objective evidence to show local steroid improves the condition.

**Rheumatic disorders in primary biliary cirrhosis.** A. K. Clarke, R. M. Galbraith, E. B. D. Hamilton, and Roger Williams (*King's College Hospital, London*)

In the past 5 years 56 patients with primary biliary cirrhosis have been seen. Diagnosis depended on prolonged pruritis, a serum alkaline phosphatase in excess of twice normal, the presence of mitochondrial antibodies, and compatible histological features on liver biopsy. Of these patients, 11 showed features of scleroderma, 7 showed evidence of the so-called CRST syndrome which is characterized by soft tissue calcification (1 patient), Raynaud's phenomenon (6 patients), sclerodactyly (7 patients), and telangiectasia (2 patients). 4 patients showed evidence of systemic involvement, 3 with oesophageal disease and 2 with lung involvement. In those patients tested there appeared to be an increased frequency of the histocompatibility antigens 1 and 8. In contrast to the very high incidence of scleroderma, other rheumatic disorders were relatively uncommon but did include 6 other patients of whom 3 had an unusual destructive large joint arthritis.