swelling. This group of 52 patients was divided into those exhibiting measurable inflammatory features (15) and those with less active but painful disease (37). Initially, 300 mg. was given daily in divided dosage, but subsequently 50–150 mg. daily was found to produce similar change with a lower incidence of side-effects.

The patients with inflammatory features all suffered from classical rheumatoid arthritis, 7 out of 11 having positive sheep-cell-agglutination titres ranging from 1 : 32 to 1 : 512. The method of assessment varied according to whether the patient was seen regularly as an out-patient or was admitted to hospital. In-patients were assessed by their own daily record of pain, stiffness, and morning limbering-up time. Twice weekly the size of proximal interphalangeal joints was measured by standard jewellers' rings by one observer at the same time of day. Joint tenderness over proximal interphalangeal and metacarpophalangeal joints was recorded, as was the strength of grip, using a soft cuff inflated to a pressure of 30 mm. of mercury. A Westergren erythrocyte sedimenation rate (E.S.R.) was estimated each week. In addition, four in-patients with swollen knees were assessed by daily clinical examination. Out-patients were seen weekly and the severity of symptoms was recorded, as was their range of activity. Their disease was also assessed by joint size, tenderness, and grip strength. Anti-inflammatory effect was assessed by weekly change in swelling of the proximal interphalangeal joints.

No change in the basic rest-exercise therapy was made during the trial. The patient was started on an identical placebo and observed until a steady baseline assessment was obtained; the genuine tablet was then substituted and when the new baseline was established indomethacin was withdrawn and identical placebo restarted. In assessment of the patient's condition not only an improvement on introduction of the drug was required but also deterioration when the drug was withdrawn before the clinical response was considered positive. In addition to patients with rheumatoid arthritis and inflammatory disease, 37 without measurable soft-tissue swelling were treated with indomethacin and the same parameters assessed. These patients had classical rheumatoid arthritis and the sheep-cell-agglutination titre was positive (1 : 32 to 1 : 2,048) in 22. Eight were in-patients and 29 out-patients.

Miscellaneous

Eleven patients with miscellaneous disorders were treated with indomethacin to assess its influence on fever, as in glandular fever and Reiter's disease, and pain from noninflammatory lesions such as bony metastases.

RESULTS

Gout

Of 15 patents with gout, 11 noted a dramatic and rapid response with full symptomatic relief, two noted a moderate analgesic response without complete alteration of symptoms, one patient noted no effect, and one developed immediate side-effects. The following case histories demonstrate the rapid response that may occur.

Case 1.—A man aged 52, who was diagnosed as having gout in 1956 and had acute episodes several times each year, developed an acute attack in May, 1963. Indomethacin 100 mg. t.d.s. was started. After 100 mg. he noted a dramatic improvement, and within 24 hours pain and inflammatory features had settled completely. Colchicine had produced relief in previous attacks only after several days and diarrhea had always followed. Phenylbutazone 500 mg. in 24 hours had produced some improvement, but with this drug full symptomatic control occurred only after four days or more. The patient felt indomethacin was quicker and more effective. Not all patients noted such benefit (see Case 6).

Case 2.—A man aged 62, who had suffered from gout since 1941, developed an acute attack involving the right carpus, the right elbow, and the left hand. After indomethacin 100 mg. he noted complete relief within four hours and was able to sleep the following night. The attack had previously been treated for four days with colchicine and phenylbutazone with little effect, and he had been kept awake at night by the pain.

Case 6.—A man aged 64 developed acute gout. Indomethacin 100 mg. t.d.s. resulted in mild symptomatic relief, but the joint remained painful and inflamed, and after 48 hours he developed acute gout in another joint. There were no side-effects. This may represent a failure of response, or it may that indomethacin absorption from the gastro-intestinal tract was impaired. Response in previous attacks to phenylbutazone had been entirely satisfactory.