

TABLE I.—OVERALL CLINICAL RESPONSE IN 99 PATIENTS TREATED WITH INDOMETHACIN

| Disease                                 | Number of patients | Clinical improvement | No clinical improvement | Inconclusive |
|-----------------------------------------|--------------------|----------------------|-------------------------|--------------|
| Gout.....                               | 15                 | 13                   | 1                       | 1            |
| Ankylosing spondylitis.....             | 14                 | 11                   | 0                       | 3            |
| Rheumatoid arthritis:                   |                    |                      |                         |              |
| Measurable soft-tissue swelling.....    | 15                 | 8                    | 3                       | 4            |
| No measurable soft-tissue swelling..... | 37                 | 14                   | 14                      | 9            |
| Osteoarthritis.....                     | 7                  | 6                    | 1                       | 0            |
| Miscellaneous.....                      | 11                 | 6                    | 5                       | 0            |
| Total.....                              | 99                 | 58                   | 24                      | 17           |

At the beginning of the trial patients were started blind on either the drug or placebo. It was soon apparent that on the high initial dose of 300 mg. daily by mouth patients developed marked symptomatic improvement or side-effects, and, with few exceptions, were able to differentiate the true tablet from placebo. It was felt that a comparison against placebo would therefore provide less information than against other potentially anti-inflammatory agents such as phenylbutazone or the corticosteroids. In the absence of side-effects patients received a minimum of 14 days' therapy, and some have been on treatment for up to one year.

Indomethacin was used for the treatment of acute gout, ankylosing spondylitis, osteoarthritis, and rheumatoid arthritis.

#### Gout

Fifteen patients (14 male, 1 female) with gout received indomethacin for the acute attack. It was given orally in high initial dosage and gradually reduced as symptoms and signs improved. The first four subjects received indomethacin 400–500 mg. in the first 24 hours, dosage then being reduced by 100 mg. every second day. This dose was found to require modification because side-effects occurred not infrequently and most acute attacks responded satisfactorily to a smaller amount of the drug. Subsequently 200–300 mg. was given in the first 24 hours in divided dosage, and this was gradually reduced to 100–150 mg. daily for five days, or longer if symptoms persisted. Patients were not given a maintenance dose between attacks. Plasma uric-acid estimations were performed during and after the acute attack, but these revealed no significant changes. Patients were asked to record their impression of the effect on the acute attack, the rate at which relief ensued, the extent of relief, the occurrence of side-effects, and the presence or absence of symptomatic rebound on cessation of therapy. An attempt was made to compare the response with that previously obtained from phenylbutazone, oxyphenbutazone, or colchicine.

#### Ankylosing Spondylitis

Fourteen patients with ankylosing spondylitis were treated with indomethacin. These patients had all suffered from the disease for at least two years and six had a history longer than 10 years. All had characteristic x-ray changes. All experienced considerable pain and had taken different analgesics for a long time. Ten of these patients received indomethacin 300 mg. daily in divided doses for 14 days and four received 200 mg. daily. When a steady baseline was obtained this was changed blind to placebo and rebound noted. Some patients received the placebo first. They were asked to assess their symptoms during this time and to compare the relief obtained from indomethacin with that previously obtained from phenylbutazone.

#### Osteoarthritis

Seven patients with osteoarthritis were treated with indomethacin: three of them had involvement of the hips, one severe disease in the knees, and three involvement of the cervical spine. They received indomethacin 150–300 mg. daily in divided doses for 14 days. They were asked to note any change in symptoms while on the drug and to compare this with the effect of phenylbutazone taken immediately before. Withdrawal symptoms on cessation of therapy were also noted.

#### Rheumatoid Arthritis

Patients with rheumatoid arthritis were treated with indomethacin and assessed not only on their symptomatic response but also by reduction of joint-