

again and the other form of the drug given. After one month on placebo and one month on indomethacin, all patients were started on known drug for the long-term evaluation. All of the examinations were repeated at monthly intervals, or as close thereto as possible. With the long-term evaluation, dosage of indomethacin was varied according to the patient's response and/or side effects.

The following parameters of disease activity were evaluated at each visit. The patient's evaluation of the amount of pain he had had in the previous month, graded on a scale of no pain, slight pain, moderate or severe pain. The number of aspirin taken; the duration of morning stiffness; the amount of corticosteroids or other medication. A cuff compression test of hand grip and a ring size of each finger were taken each visit. Swelling and tenderness of the shoulders, elbows, wrists, fingers, toes, ankles, knees and hips were evaluated according to the following scales: swelling was graded 1 for slight synovial thickening; 2 for swelling that changed the contour of the joint; 3 was swelling that obliterated the normal joint contour; 4 was the presence of a demonstrable effusion. Tenderness was graded 1 for the patient says it hurts when pressure is applied; 2, the patient says it hurts and winces; 3, the patient tries to withdraw from the stimulus. It was possible for the same observer to evaluate the patients greater than 90% of the time. Sub-totals of the swelling, the tenderness, the grip strength, the ring size, the duration of morning stiffness, the amount of pain, the number of aspirin and the milligrams of prednisone or equivalent were obtained for each visit. The difference between the individual parameters and its base line was obtained so that a negative score indicated worsening of the arthritis, whereas a positive score indicated improvement. In the parameters of swelling, tenderness and number of aspirin (300 mg. tablets) a change of 1 was reflected as a change of 1 in the score. A change in the amount of prednisone was scored as the number of milligrams times two. The duration of morning stiffness, a change of $\frac{1}{2}$ hour was scored as a change of 1. The grip strength was scored as the change in total score of both hands divided by 20, or in other words, a change of 20 mm. of mercury was scored as a change of 1. The sub-totals of the changes in each parameter were then totalled to determine a numerical figure for improvement or worsening of the arthritis. By inspection of the changes in the total score of arthritis, we have evaluated the response to indomethacin as good, fair and none. A good response was considered a response of clearly significant improvement, while on indomethacin, with little or no response while on placebo. A grade of fair was given when there was moderate but definite improvement while on indomethacin, again with little or no response to placebo. The grade none represents either worsening of the arthritis while on indomethacin, or no difference between response to placebo and indomethacin.

We had 31 patients who started the double blind study. Of these, 4 were unable to complete the double blind part of the study because of uncontrollable side effects. The side effects requiring cessation of the study were nausea, vomiting and headache in 2 patients; nausea and headache in 1 patient; and dizziness with nausea and headache in 1 patient. Thus, in the short-term double blind experiment, 68% of the patients had a favorable response; 19% had no demonstrable response; and only 13% had side effects requiring stopping the medication.

The long-term evaluation study has now been under way for ten months, with observations on patients ranging from seven months to ten months in length.

Of the 27 patients finishing the double blind part of the study, 2 were withdrawn before long-term evaluation could be done. One of these was for side effects of the drug, specifically nausea and vomiting, and one patient with a history of bronchial asthma expired with an episode of asthma refractory to all treatment. Of the 25 patients left in the study, 15 had a good response; 9 had a fair response; and 1 showed no response. Of this group, 8 patients have had to stop taking 'Indocin' because of side effects that exceeded the benefit they were receiving. These side effects were dizziness in 5 patients; nausea and dizziness in 1 patient; severe refractory ulcer-type symptoms in 1 patient; giddiness and mental fuzziness in another.

In addition to the double blind study, we have used 'Indocin' in 12 additional patients. Two of these patients had progressive systemic sclerosis; 1 has the fibrositis syndrome; and 1 has an unusual form of hereditary degenerative joint disease. The remaining 8 patients have a diagnosis of either definite or classical rheumatoid arthritis, and were started on the known drug because of severity of the disease process. Four of these were hospitalized because of their arthritis at