methacin in a clinical study that is now in its fifth year. A battery of laboratory tests was done before and periodically during this drug trial. Thus, we were able to combine a long-term threapeutic evaluation of indomethacin with a continuous monitoring of possible side effects.

MATERIALS AND METHODS

The patient group. Only patients with active AS were selected for this study. They were 25 men and 3 women who attend the arthritis clinics of the Jersey City Medical Center. They have been treated with indomethacin for periods ranging from 5 to 52 months, or for an average of 33 months (Table 1). On alalysis in April, 1967, the age of the patients averaged 41 years, ranging from 20 to 58 years. The duration of disease averaged 19 years, ranging from 3 to as long as 36 years.

The mean age of the patients at disease onset was 24 years. The longest interval between onset and diagnosis was 25 years in one man, but the average interval proved to be 9 years. The mode of onset was insidious in 18 patients and acute in 10. Initial involvement was found to be axial (spinal) in 14 patients, peripheral in 13 and systemic (with recurrent iritis) in one. Of 14 patients with axial onset, 12 had lumbar, one had dorsal, and one had cervical involvement. Of the 13 patients with AS of peripheral onset, 6 had involvement of the hip, 4 of the knee, 2 of the shoulder, and one of the heel.

Serial x-rays have disclosed bilateral sacroiliitis, apophyseal irregularities, and some degree of vertebral demineralization or squaring in all 28 patients. Three patients have associated ulcerative colitis and two have regional enteritis.

Major systemic manifestations in these 28 patients before the indomethacin trial included iritis in 6 patients, aortic insufficiency in 2, angina in 2, while one patient each had vasculitis and cauda equina involvement (Table 2). Persistent EKG abnormalities, chiefly in the form of conduction disturbances, were noted in 10 patients.

Prior to the trial with indomethacin, one patient was in functional class I, 21 in class II, 5 in class III, and one in class IV (Table 1).[19] Previously of the 28 patients, 15 had taken aspirin (daily dosage 1.5 to 6.0 Gm.), 9 had received phenylbutazone (100 to 300 mg.), one oxyphenbutazone (300 mg.), while 3 had taken various types and amounts of adrenocorticosteroids.

Indomethacin dosage. The initial dosage of indomethacin administered to each patient was 100 mg. daily, with 25 mg. capsules given after meals and at bedtime. Daily maintenance dosages were then adjusted to the lowest possible required for individual suppression of active articular disease. Adjunctive measures, such as physical therapy, were encouraged. But no medication other than the test drug was administered except in one patient who was gradually being weaned from adrenocorticosteroids.

The study design. Each patient was evaluated initially, and again at weeks two, six and 12, and then at three-month intervals. At the initial visit, a detailed work-up, including history, physical examination, x-rays, electrocardiogram and a battery of laboratory studies, was performed on each patient. The patient's functional status was then assessed by means of the ARA Steinbrocker criteria.[19]

At each follow-up visit, careful histories were taken and physical examinations were performed on all patients.

In addition four parameters of disease activity were selected for initial and continued assessment. The parameters were: 1) joint pain, 2) duration of morning stiffness, 3) onset of fatigue and 4) joint mobility including spine extension and flexion chest cage expansion and range of motion of peripheral joints.

To serve as a control phase, temporary withdrawal of indomethacin was carried out in all patients after they had been maintained on the drug for a period of at least three months. The drug was promptly readministered once active disease had recurred.

Laboratory studies performed before indomethacin administration and each time we saw the patients included serum SGOT, SGPT, alkaline phosphatase, cephalin flocculation, thymol turbidity, total bilirubin, total protein and A/G ratio, BUN, uric acid, paper electrophoresis, latex fixation and blood glucose. Of the last 8 patients admitted to the trial, serum studies included only a BUN, SGOT, uric acid, paper electrophoresis and latex fixation test.