TABLE 2.—SYSTEMIC MANIFESTATIONS OF ANKYLOSING SPONDYLITIS DEVELOPING DURING INDOMETHACIN TRIAL AVERAGING 33 MONTHS

Systemic manifestations	Number of cases before indomethacin trial	Number of cases during indomethacin trial
Iritis	[1] 6	3
Angina pectoris	2	0
EKG conduction changes	10	4
Aortic insufficiency	2	1
Foot and ankle ulcerations	0	1
Vasculitis	1	0
Cauda equina lesion	1	0
Total	22	9

[1] 1 patient had 3 bouts of iritis during the indomethacin trial, but had had recurrent iritis before this trial while receiving other antirheumatic agents. Two other patients experienced their first bouts of iritis while receiving indomethacin.

RESULTS

Indomethacin proved an effective suppressive agent of the articular manifestations of AS in the present study, as judged by the following:

1. After treatment for an average period of 33 months, 21 of our 28 patients were in the most favorable functional class I,[19] as compared with only one of 28 before utilization of indomethacin (Table 1). Of 5 patients in functional class III before the drug trial, 3 improved to class II, and 2 to class I.

2. Analysis of each of the four selected parameters revealed a decrease in joint pain in 25 of 28 patients (89 per cent), a decrease in the duration of morning stiffness in 22 (79 per cent), delay in the onset of fatigue in 17 (61 per cent), and an increase in joint mobility in 17 patients (61 per cent) (Table 1). Joint pain and morning stiffness diminished promptly after indomethacin was started, usually in 48 hours, or within one to 7 days. Alleviation of fatigue and improvement in joint mobility was less dramatic, taking from one week to 3 months, and occurring on the average within 4 weeks.

After an average treatment period of 33 months with indomethacin, the over-all therapeutic rating of all four parameters was good in 21 of 28 patients (75 per cent), fair in 5 (18 per cent) and poor in 2 (7 per cent) (Table 1).

3. The average daily maintenance of indomethacin required for suppression of articular disease was 100 mg., the lowest was 25 mg. and the highest 200 mg. (Table 1). Only 7 patients needed more than 100 mg. daily, 5 with active hip or other peripheral joint disease, 2 because of marked axial (spinal) involvement.

4. When indomethacin was withdrawn, severe axial pain and morning stiffness recurred on an average within 48 hours in 24 of the 28 patients. Symptoms were promptly alleviated in all 24 patients when indomethacin was readministered.

Of the remaining four patients, two (Table 1, patients no. 25 and 28) did not respond to the drug and therefore exhibited no symptoms when indomethacin was withdrawn. Two patients (patients no. 15 and 17) had achieved remission.

5. The average Westergren ESR values for all 28 patients decreased during the drug trial from 39 mm. to 26 mm. (Table 1). The p value obtained from Student's t table is statistically significant at the <0.01 level after testing the average paired differences against zero for the ESR values before and after indomethacin.

ESR values were normal (15 mm. or less) initially and remained so in 8 patients (29 per cent). Eight other patients (29 per cent) attained normal ESR values by the end of the trial. Thus, normal ESR values were noted in 16 patients (58 per cent) while on indomethacin (Table 1).

Only 4 patients had marked ESR values after the trial. Response to indomethacin was good in 2 patients, fair in one and poor in one (Table 1).

6. While articular manifestations of AS were generally controlled with indomethacin, certain systemic manifestations of the disease were not (Table 2). During long-term maintenance on indomethacin, iritis occurred in 3 patients, and multiple recurrent ulcerations of the left foot and ankle in one patient. The murmur of aortic insufficiency developed in one patient, while EKG conduction disturbances developed in 4 patients. Cauda equina involvement of three years' duration in one patient, manifested by nocturnal incontinence, poor stream and diminished bladder and rectal sensation, did not improve with indomethacin.