APPENDIXES

APPENDIX I

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INDOMETHACIN IN IN-PATIENT TREATMENT OF RHEUMATOID ARTHRITIS

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Indomethacin has been used in the treatment of rheumatic disease for over 3 years. Preliminary reports of the effectiveness of the drug were encouraging (Rothermich, 1963; Norcross, 1963) Katz, Pearson, and Kennedy (1963) also found the drug to be beneficial but treatment had to be discontinued in over 20 per cent of patients because of side-effects. Hart and Boardman (1963) showed that indomethacin produced a measurable reduction in swelling of the proximal interphalangeal joints in patients with rheumatoid arthritis and that, when a placebo and the drug were used alternately, significant rebound effects commonly occurred with the commencement of placebo treatment. Side-effects, principally headache, dizziness, dyspepsia, and mental disturbances, were frequent being observed in over 50 per cent. of patients treated with a dose exceeding 200 mg. A trial of the drug by Wanka, Jones, Wood, and Dixon (1964) showed that indomethacin was effective when compared with a placebo, and a comparative trial against phenylbutazone by Percy, Stephenson, and Thompson (1964) showed that 200 mg. indomethacin was approximately equivalent to 300 mg. phenylbutazone daily, although a decidedly higher incidence of side-effects occurred with indomethacin.

During this period of development of the drug it was supplied in tablet form and the doses used ranged from 150 to 400 mg. daily. Wanka and others (1964), using this preparation and range of dose, reported one case of intestinal haemorrhage and one of perforated gastric ulcer. Lövgren and Allander (1964) used a similar dosage in eighteen patients with rheumatoid arthritis, six of whom had a previous history of peptic ulcer but had negative barium meals immediately before treatment; five patients developed peptic ulcers, two of these having no previous history, and three of the five had severe bleeding.

During the past 2 years indomethacin has been supplied in capsule form and the manufacturers have recommended an initial dose of 50 mg. daily, gradually increasing to a maximum of 150 mg. The incidence of side-effects was stated to have fallen from 50 to 10–30 per cent of all treated patients (Today's Drugs, 1964) as a result of using capsules and more conservative dosage, and Clark (1964) reported satisfactory improvement in many patients of a large group with rheumatoid arthritis using this scale of dosage. Recently Hart and Boardman (1965) have compared 75 mg. indomethacin daily with 300 mg. phenylbutazone daily, in out-patients with rheumatoid arthritis. A double-blind crossover trial was carried out, each drug being given for a period of 28 days. No significant differences were found in the relief of symptoms although there was a greater reduction of morning stiffness with phenylbutazone. There were no significant differences in strength of grip or in improvement in ring sizes of proximal interphalangeal joints, but indomethacin tended to have a greater effect on the latter. The preference of patients was in favour of phenylbutazone. The incidence of side-effects of indomethacin in this short-term trial are not stated, but in long-term studies on patients with rheumatoid arthritis, osteo-arthritis, and ankylosing spondylitis, the authors found that 37 per cent of the patients developed side-effects of drug treatment.

The present study has been carried out to evaluate indomethacin in a dose of 50 to 100 mg. in the in-patient treatment of patients with rheumatoid arthritis. Salicylates are currently the mainstay of drug therapy while the patient is being