trend in each group suggested that this parameter improved specifically on indomethacin. The magnitude of the response obtained depends not only on the anti-inflammatory effect of the administered drug but also on the amount of soft-tissue inflammatory swelling present that is potentially capable of exhibiting reduction of size. It is unlikely that optimal conditions existed in these patients, for reduction of joint size; they were selected from the regular attenders at the out-patient clinic and had disease of moderately long duration. That indomethacin was associated with reduction of joint size, as compared with the baseline, was demonstrated in the patients admitted to hospital.

Indomethacin was initially available in the form of tablets. These proved to be unsatisfactory and gelatin-coated capsules were substituted. The patients in the long-term studies received both preparations. These results are not given separately, except for side-effects, because the capsule is the only preparation available; a comparison of the two preparations revealed that the only difference of statistical significance was the incidence of side-effects.

The most consistently satisfactory results from indomethacin were obtained in patients suffering from ankylosing spondylitis (68.7%) and osteoarthritis (65.3%). Results for gout are reported separately (Boardman and Hart, 1965). Excellent results did occur in rheumatoid arthritis, in particular in patients with active disease, but there were also some dramatic failures, and overall benefit was obtained in only 50.5%.

Side-effects were a more frequent cause of therapeutic failure than inadequate drug potency. The change from the tablet to the capsule preparation was associated with a reduction in frequency from 66.3% to 36.6%, together with a decrease in the severity of untoward reactions. The most common pattern of side-effects consisted in headache, giddiness, muzziness, and nausea. These were transient, dependent on dosage, and occurred within the first few days of starting treatment.

Dyspepsia was relatively rare during indomethacin administration. Smyth *et al.* (1964), in a study of 63 patients with rheumatoid arthritis during an 18-month period, found one who developed peptic ulceration on indomethacin and one on placebo. Catoggio *et al.* (1964) had two cases of duodenal ulceration in a group of 33 patients. Clark (1964), in a study of 100 patients with rheumatoid arthritis, encountered peptic ulceration in 10, nine of whom also received corticosteroids; there were three instances of perforation and one of hemorrhage. Bilka *et al.* (1964) reported one patient, out of a total of 61, who developed a small gastric ulcer after 12 weeks of indomethacin therapy. Haemorrhage and perforation do not appear to be serious risks as judged on the figures of this series, in contrast to the findings of Lövgren and Allander (1964). Unlike their six patients with a history of gastric or duodenal ulceration treated in hospital, in our series four of seven patients with duodenal ulceration and four of five with gastric ulcers tolerated indomethacin well, the total period of therapy being 1,566 days. Nevertheless, with certain exceptions, dyspepsia occurring on indomethacin was considered an absolute indication for cessation of therapy. In our series antacids were not used for symptomatic control. Lövgren and Allander (1964) treated their patients in hospital with anticholinergics and antacid agents; it is possible that some of their problems arose as a result of the masking effect of these symptomatic remedies on what should be considered a warning symptom.

The dose probably suitable for most patients is 25 mg. three times a day, administered after food. It is suggested that to overcome the frequent early side-effects the dose should be increased slowly during the first week, from an initial 25 mg. daily. Dyspepsia due to indomethacin is an indication for the withdrawal of therapy.

During the two and a half years that indomethacin has been available to us it is of relevance to note that only three patients with rheumatoid arthritis have been started on long-term corticosteroid therapy or A.C.T.H. The fact that a non-steroid anti-inflammatory agent is now available may well make a profound difference to the present use of corticosteroids in this condition.

SUMMARY

A double-blind cross-over trial was carried out to compare indomethacin, 75 mg. daily, with phenylbutazone, 300 mg. daily, each being given for a period of 28 days to patients with active rheumatoid arthritis. No significant differences were found between the two groups in the relief of symptoms, but the results