Patient Preference.—This is shown in Table V. All three patients who were withdrawn from the trial because of severe side-effects on one drug completed 2 weeks of treatment on the other drug and are shown as preferring that drug.

TABLE V.—*Patient Preference*

Preference:	*Number of cases*
For soluble aspirin	21
For indomethacin	13
None	7
Total	41

DISCUSSION

The anti-inflammatory action of indomethacin has been demonstrated convincingly under experimental conditions. Winter, Risley, and Nuss (1963) showed that the drug had a powerful effect in inhibiting granuloma formation in rats. In addition, inflammatory oedema induced by carrageenin was suppressed. Boris and Stevenson (1965) found that indomethacin was the most powerful of a group of five anti-inflammatory agents in inhibiting the inflammatory reaction induced by carrageenin in rats, the others being flufenamic acid, mefenamic acid, oxyphenylbutazone, and phenylbutazone in order of decreasing potency. Under clinical conditions, Hart and Boardman (1963) confirmed this anti-inflammatory action using 150–300 mg. of the drug daily. In view of the high incidence of side-effects with this range of dose we wished to study the effect of indomethacin in a dose not exceeding 100 mg. daily in the in-patient treatment of rheumatoid arthritis and to compare it with soluble aspirin in a dose commonly used in these patients. Studies had already been carried out by Hart and Boardman (1965) and Thompson and Percy (1966) and the drug was found to have considerable therapeutic value in patients with a variety of rheumatic diseases.

In recent years salicylates have been shown convincingly to have anti-inflammatory properties in experimental animals. Spector and Willoughby (1963) showed that systemic sodium salicylate has an inhibitory effect on the volume of exudate in turpentine-induced pleurisy in the rat and causes a non-specific suppression of the action of many substances that increase vascular permeability. Kelemen (1963) studied acute inflammatory oedema in rats using I^{131} serum albumin. He considered that there were two components to the inflammatory response. One was inflammatory swelling which was diminished by salicylate. The other, a possible tissue component, preceded visible swelling, persisted after the oedema had disappeared, and was unaffected by salicylate. In view of this work on salicylates in experimentally-induced inflammation, it must be borne in mind that doses of 4 g. daily in patients with rheumatoid arthritis may have anti-inflammatory activity of the same order of magnitude as that shown by indomethacin in low dosage.

In this study we have used strength of grip and improvement in swelling of the proximal interphalangeal joints measured by jeweller's rings to assess the weekly improvement throughout the trial period. Analysis of mean strength of grip during periods of treatment with soluble aspirin and indomethacin has shown that drug effect was approximately one half of the effect attributable to spontaneous improvement. It has also been shown that indomethacin had a greater effect than aspirin in improving strength of grip and that this difference was just significant at the 5 per cent level. On the other hand, there was no difference between the two drugs in their effect in reducing swelling of the proximal interphalangeal joints and most of the improvement which occurred was the result of spontaneous improvement.

There was a greater preference of patients for soluble aspirin than for indomethacin in this trial. The incidence of headache during soluble aspirin treatment was surprisingly high, so that the patient preference can hardly be due to indomethacin headaches unless these were qualitatively different from the headaches reported during aspirin treatment. Greater pain relief from aspirin in the dosage used may have been important. Hart and Boardman (1963) stated that indomethacin had no analgesic action in the mouse or rat using methods then in use. The manufacturers claim, as a result of controlled clinical studies, that 50 mg. indomethacin is equal in analgesic effect to 600 mg. acetylsalicylic acid. If this is so, then the analgesia produced by aspirin in this study was much greater than that produced by indomethacin.