Blood salicylate levels were determined on Day 1 and Day 8 at six clinics by the method of Brodie, Undenfriend and Coburn.[6] The interpretation of these data is complicated by the variability of the intervals between the last dose of aspirin on Day 8, the time of clinical examination and the withdrawal of blood for salicylate determination. The more detailed report will include this topic.

The data sheets called for the reporting of *undesirable signs and symptoms*, but no check list was provided. Expenditure of much time on this inquiry did not appear to be justified because no valid population estimate of frequencies could be made from a group that was partly selected by exclusion of salicylate reactors.

PATIENTS' CHARACTERISTICS

From the 492 patients who were entered in the trial, the data of 51 (28 on placebo and 23 on aspirin) were omitted from the analysis for the following reasons: ineligible by protocol, 19; drop-outs or late for final examination, 14; change in basic therapy, 15; change in observer, 3. If this had been a trial of a new drug it would have been necessary to handle the data from the drop-outs and late attenders in such a way as to avoid bias in favor of the drug. This hardly seemed necessary, at least in a preliminary report on experiences with aspirin.

The remaining 441 patients were considered eligible in all respects, including the interval between assessments (9 were one day late, 1 was one day early). They were provided by 11 clinics (18 to 86 per clinic). Assigned to placebo: 223; assigned to aspirin: 218. Males: 131; females: 310. Median age: 53; range (middle 90 per cent): 30 to 73. Median duration of disease: 7 years; range (middle 90 per cent): 1–27 years.

THERAPIES

The basic therapies with numbers of patients assigned to placebo (P) and aspirin (A) were as follows: Corticosteroids (P, 59; A, 55); Salicylates (P, 100; A, 93); Antimalarials (P, 14; A, 17); Miscellaneous, i.e., combinations of therapies and some patients who at the beginning of the trial were receiving no antirheumatic therapy (P, 50; A, 53). Thirty-one patients were receiving indomethacin, usually along with another therapy. Except in the salicylate group, all these patients were maintained on their basic therapies during the trial.

In order to permit a search for relationships between intake of the trial therapy and the outcome of the trial, patients were classified rather arbitrarily as "on schedule" if they met all the following criteria: (1) at least 32 capsules during the 5 days following the day of the initial examination; (2) at least 8 capsules on the day preceding the day of the final examination, or 6 capsules if the only dose missed was the breakfast dose; (3) at least 2 capsules on the day of the final examination.

The 117 patients (28% of the P patients, 25% of the A patients) whose reported dosage failed to meet one or more of these criteria were classified as "not on schedule." There was little difference in the proportions of these among the various therapy groups. The data were analyzed as a whole, and also in "on-schedule" and "off-schedule" groups separately. The results from the total 441 patients are shown here, because when a pronounced placebo-aspirin difference in outcome occurred, it did so in spite of the incomplete dosage of some patients.

COMPARISON OF AVERAGE CHANGES IN FIVE MEASURES OF DISEASE ACTIVITY

Table 1 shows the placebo-aspirin contrast in patients who in the initial examination were recorded as having greater than zero readings in the respective measures of disease activity, because the inclusion of initially "inactive" patients would tend to damp the contrast between the two agents. To estimate how frequently the drug-placebo contrasts in the table would occur solely as the result of the random assignments, the data were arranged in fourfold tables (placebo versus aspirin; improved versus not improved, i.e., deteriorated or unchanged), and the chi-square test (with Yates' correction) was applied. In all measures except morning stiffness the differences would rarely occur in random assignment (P values from chi-square less than 0.01). In morning stiffness the P value was 0.12; which means that, even if there were no difference

[6] Hepler, O. E., Manual of Clinical Laboratory Methods, Charles C. Thomas, Springfield, Illinois, 1953.