the Committee turned its attention to the scarcity of well-documented information on the clinical effects of aspirin. It decided to study the changes in manifestations of disease activity in patients who were continued on their previously assigned antirheumatic therapies, but were assigned strictly at random to aspirin in a fixed rather high dosage or to placebo, in approximately equal numbers, and were studied by the double-blind technique. In order to avoid excessive distress to patients, and a risk of breakdown of the trial, the period was restricted to seven days.

CRITERIA OF ADMISSION TO THE TRIAL

The patients were to be outpatients (or domiciliary hospital patients), of either sex and any ethnic group, with "classical" or "definite" peripheral rheumatoid arthritis (A.R.A. Criteria, 1958 Revision [4]) which had become manifest after the sixteenth birthday. In addition to the 20 exclusions in the A.R.A. Criteria, patients were not to be admitted if they had experienced severe infection or major surgical operation within one month before the start of the trial, or if they had a history of toxic reactions to aspirin. Patients who were known or suspected to have ankylosing spondylitis were to be excluded, but it was not obligatory to screen all patients by sacroiliac radiography.

THERAPY

The drug, acetylsalicylic acid, was administered in capsules, each capsule containing 7.5 grains (approx. 0.5 gm.) and the prescribed dose of drug or corresponding placebo was 2 capsules 4 times a day for 7 days (total daily dose = 60 grains = 3.9 gm.). Assignment of drug or placebo was performed by random numbers at the Biometrical and Coordinating Center. Except for these assignments, patients were allowed to be on any (or no) therapy for rheumatoid arthritis, but it was stipulated that, if possible, no change be made in the type of therapy during the two week preceding the trial or during the trial itself, and also that dosage changes, especially of corticosteroids, be minimal during the trial. Patients were be urged to refrain from aspirin and other salicylates during the week of the trial. Details of types and dosages of all therapies were recorded in the data sheets for use during analysis. The trial extended from April 5 through November 14, 1963.

METHODS OF EVALUATION

All observations at the initial and final examination (Day 1 and Day 8) were to be made by the same observer who was to have at least the rank of clinical fellow. The maximum allowable departure from the 7-day interval was ±1 day. The following assessments were made in both examinations:

1. *American Rheumatism Association functional classification* [5] with reference to the patient's *usual* occupation.
2. *Duration of morning stiffness*—estimated for an "average" or "typical" day.
3. *Grip strength*—determined by folded blood pressure cuff attached to mercury sphygmomanometer, with patient's arm unsupported. Inflate initially to 20 mm. Hg. Read height of column maintained by squeezing (not initial spurt). Record three successive readings on each hand.
4. *Walking time*—the time required to walk a straight continuous distance of 50 feet as fast as possible (without running) from a standing start.
5. *Number of clinically active joints*—determined by any one of the following: tenderness on pressure, pain on passive movement, swelling other than bony proliferation. Recorded also were heat, redness, ankylosis (determined by clinical examination) and subcutaneous nodules.
6. *Erythrocyte sedimentation rate*—Westergren method; anticoagulant, 3.8% sodium citrate; one hour reading.
7. *Patient's assessment*—the patient's impression regarding his arthritis, recorded as "good," "fair" or "poor"; and as "better," "about the same" or "worse" in comparison with his condition one week previously.
8. *Observer's overall assessment*—recorded in the same terms as the patient's assessment, taking into account not only the impressions gained from the measurement methods (without referring to Day 1 data sheets), but any other available information.

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[4] Ropes, M. W., et al., Bull. Rheumat. Dis., 9:175, 1958.
[5] Steinbrocker, O., Traeger, C. H., and Batterman, R. C., J.A.M.A., 140:659, 1949.