paratively short-term observations. The present report will describe clinical experiences with indomethacin which began in November 1961. Our attention was given mainly to its effects on patients with rheumatoid arthritis, but other rheumatic diseases were also treated. Because this was the first trial of indomethacin in the human, small amounts were given initially and effective dosages were not reached until late January 1962. For this reason, the present report deals with experiences during a 42-month period from Feb. 1, 1962, to Aug. 1, 1965.

Materials and Methods

The treatment sample comprised 216 patients and 234 patient-trials. This does not include 23 patients on whom therapy was begun but for one reason or another became "dropouts." These will be discussed later. It is noteworthy that 26 patients have been on continuous therapy for 30 months or more, the longest being 42 months. In the treatment sample, there were 147 females and 69 males, and all were adults with the exception of three children ages 9, 11, and 13 years. There were 117 patients with probable, definite, and classical rheumatoid arthritis as defined by the Committee on Diagnostic Criteria of the American Rheumatism Association (ARA); all cases of "possible" rheumatoid arthritis were listed under nonspecific polyarthritis. There were 22 cases of ankylosing spondylitis and 14 cases of chronic gouty polyarthritis (ie, the chronic polyarthritis having characteristics similar to rheumatoid arthritis, but associated with a negative latex titer and a high serum uric acid level and occurring in an indivdual who has been diagnosed as having gout). In addition, there were 15 cases of osteoarthritis, 29 cases of fibrositis, and 19 cases of other miscellaneous rheumatic diseases as follow: 10 "possible" rheumatoid, 3 juvenile rheumatoid, 2 psoriatic arthritis, and 1 each of Reiter's disease, pseudogout, villonodular synovitis, and Tietze syndrome.

In the initial trials, patients were selected with moderately severe rheumatoid arthritis which was fairly well controlled with the standard basic program of therapy consisting of increased rest, physical therapy, salicylates, and sedation, as well as small doses of corticosteroids and sometimes gold or phenylbutazone therapy or both. The first step was to discontinue administration of all therapeutic agents except salicylates and corticosteroids, or as many as possible consistent with the patient's continued good management and control of the disease process. Indomethacin therapy was initiated in small doses and gradually increased according to the patient's ability to tolerate higher levels. At the same time, a gradual reduction of corticosteroid therapy was begun. If and when corticosteroid therapy could be discontinued entirely, gradual reduction of salicylate therapy was attempted. In some cases all therapeutic agents were withdrawn and control of the disease was continued at the same level on indomethacin alone. (Withdrawal of salicylates was for experimental purposes and is not to be construed as recommended clinical procedure.)

The evaluation of clinical results was based on those factors described in a previous report.[6] Greatest emphasis was placed on the patient's own gradation of his disease from 0 (no symptoms or disability) to 4+ (severe pain, morning stiffness, and total disability) based on his past experience with his disease. In addition, a separate evaluation of disease activity and disability was made by the physician. It is believed that accuracy and objectivity of such gradations can be greatly enhanced and made more secure by liberal use of placebo substitution and by quantitation of the steroid and aspirin requirements of the individual. When used by a clinician interested in the management of rheumatoid arthritis, these criteria can often be as accurate and precise as the many criteria which have more formalized physical and arithmetical indices.

The well-recognized decisively beneficial effects of corticosteroids (and to a much lesser degree of aspirin) provide an excellent base for reference in therapy of rheumatic diseases. Any new agent therefore must be able to reduce materially or eliminate the need for corticosteroids in an appreciable number of cases. After such elimination, therapy may be further evaluated by the ability to reduce the dose of or discontinue salicylate therapy. These have been important criteria in our evaluation of a favorable response to indomethacin. In all cases listed as having had an excellent response to indomethacin, either of these two or the clear-cut, unequivocal placebo relapses have been a required criterion.

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[6] Rothermich, N. O.: Clinical Experiences With Indomethacin in Rheumatic Diseases, *Proceedings of the Eighth Congress of the Japan Rheumatism Association, Okayama, Japan,* 1964, pp. 159–163.