

reported by "statisticians" or "full time" physicians who treat a small number of patients with rheumatic diseases. While I admit that "double blind" studies are desirable, there are many possible errors that are not included in the statistical analysis of these studies and the results are used only to depreciate the potential values of the drug under test. This is especially true in the case of patients with rheumatoid arthritis, where the disease process is extremely variable from day to day, or week to week status; where short term evaluation of drug effect is inaccurate (in a few weeks); when patients are allowed to use a variable amount of aspirin; and where only objective measurements of joints are the decisive criteria. In the majority of rheumatoid patients in any one study, whether "double blind" or "uncontrolled," irreversible changes that determine size of joints, range of motion, and discomfort, have already occurred and do not improve particularly in a period of a few weeks. Such changes are not due to the active inflammatory process of the disease but are the result of long continued disease. The resultant "mechanical" disturbance of joint components cannot be corrected by anti-inflammatory drugs, whether they are salicylates, anti-malarials, phenylbutazone, or indomethacin. However, the statisticians and the "purists" decry the lack of objective measurements of improvement and completely disregard the subjective response of the patient. I will admit that none of the anti-inflammatory drugs mentioned above, have the prompt, dramatic response as the cortico-steroids but they do not have the serious toxicity associated with their "long term use."

After more than 20 years of experience in the exclusive treatment of rheumatic patients, I do not subscribe to the conclusions of Short & Bauer that 50% of rheumatoid patients improve with the most conservative treatment. Another frequently quoted "double blind," "cross over" trial with an anti-malarial drug, which was regarded as a masterpiece of drug testing and demonstrated the unquestionable response to the drug, is no longer considered as a "drug of choice" by most clinical rheumatologists. This decision has been determined by the nebulous response of most patients both subjectively and objectively, plus the possible occurrence of irreparable eye damage which was impossible to determine during the short period of the study.

I have used Indomethacin in the therapy of the rheumatic diseases in more than one thousand patients in the past 6 years. In my experience, it has been an effective drug in the majority of these patients and has contributed one more effective drug to the treatment of various rheumatic conditions, which have been a most difficult problem, not only to the physician, but more importantly to the patient. On the basis of carefully controlled animal experiments in the laboratory and also by reduction of fever and inflammation clinically in the patient with acute arthritis, there can be no dispute that Indomethacin is a potent anti-inflammatory drug. There is no question throughout the world that Indomethacin is one of the most effective drugs in relieving such conditions as acute gouty arthritis, acute tendonitis, ankylosing spondylitis, and degenerative (osteoarthritis) joint disease of the hip. The only dispute has centered about the question of response in patients with rheumatoid arthritis, which even the "statisticians," the "purists" and the "reviewers" admit is subject to remissions and exacerbations, difficult to evaluate, and that Indomethacin is at least comparable to phenylbutazone and aspirin.

Indomethacin is of benefit to a variable degree in at least 66% of the patients in my experience. Subjective response has been better maintained with this drug than with either phenylbutazone or salicylates in the chronic arthritic patients (either rheumatoid or degenerative joint disease). The majority of these patients have continued to use the drug (many since 1962) for more than 3 years, which I believe in itself is a testimonial that the drug is effective. Many of this group have been challenged with a placebo or have voluntarily discontinued the drug, even replacing it with a high salicylate dose. However, they have reported a prompt flare of their symptoms and have resumed Indomethacin therapy in practically all instances. The drug has produced functional improvement in many patients, even in patients with mechanical damage to their joints. In early rheumatoid patients with inflammation and joint swelling, I frequently observe decrease (and even complete subsidence in some patients) of the joint inflammation. The results of long term administration in this group of patients will be published in the proceedings of the 2nd Laurentian Conference on Rheumatology (Nov. 1966) which I understand is in press at this time.

It has also, been my experience that 50% of rheumatoid patients on corticosteroid therapy have been able to reduce the steroid when Indomethacin has been added to their therapy. Toxicity remains within tolerable limits in my experience