patients with this chronic disease which is marked by spontaneous remissions and exacerbations, will respond favorable to this drug.

Until more potent and less toxic anti-inflammatory agents are made available for clinical use, I strongly recommend that Indomethacin continue to be available for use in this most crippling of all arthritic conditions. I would not discard a valuable tool although it might have a sharp edge.

Sincerely yours,

CHARLEY J. SMYTH, M.D.,
Professor of Medicine,
Head, Division of Rheumatic Diseases.

NORTHWESTERN UNIVERSITY,
Chicago, Ill., April 22, 1968.

DR. MAX TISHLER,
Merck Research Laboratories,
Merck & Co., Inc.,
Rahway, N.J.

DEAR DR. TISHLER: As you know, we have been engaged during the last year in evaluating the efficacy of Indocin in patients with generalized osteoarthritis. In addition, we have used Indocin in the treatment of patients with other forms of arthritis particularly those of rheumatoid arthritis.

Although we do not have the results from our osteoarthritis study tabulated as yet, I would like to recall for you some of the difficulties that emerge from this type of work.

First, the cause of these types of arthritis is unknown. This means that one must utilize the symptoms the patient shows as clues concerning the response of the patient to treatment. It is not possible to state that a given causative feature has or has not been altered or changed by the treatment program. Such a statement concerning drug evaluation would of course be the best evidence for determination of an effective program.

This difficulty is further compounded by the variability of the course of these illnesses. It is very difficult to interpret the exact response of the patient to a drug or to no drug.

Therefore, to properly reach a conclusion about the efficacy of a drug requires a careful assessment of a number of signs and symptoms present in the disease and sufficiently large number of patients who are being evaluated.

Although gold treatment for rheumatoid arthritis has been used for almost four decades, it was only in the last few years that a carefully controlled drug study on the efficacy of this compound was completed by a group of British workers.[1] Even here considerable difficulty was encountered. I do not take the view that proper assessment is impossible but it certainly is difficult.

I think that it can be said that Doctor Mainland reached similar conclusions in his careful assessment of role of Indocin in rheumatoid arthritis. He did find it had a beneficial effect although no greater than aspirin. He also points out the real problems that beset any one who does drug evaluation studies.

In ordinary practice in our clinic we have been impressed by patients' response to Indocin in rheumatoid arthritis and other forms of arthritis, including osteoarthritis. We use the drug to help provide relief for patients who require additional medication besides aspirin.

It would be a tragic event if the demands for precision outstrip the methodology available. In our present state of ignorance one must accept less than optimal measure of effect. However, one constantly must try to improve the state of the art.

Sincerely yours,

FRANK R. SCHMID, M.D.,
Associate Professor of Medicine,
Chief, Arthritis-Connective Tissue Section.

TUCSON, ARIZ., *April 22, 1968.*

MAX TISHLER, Ph. D.,
Merck Research Laboratory,
Merck Sharp & Dohme,
Rahway, N.J.

DEAR DOCTOR TISHLER: This is a testimonial letter in regard to Indomethacin (Indocin).

---

[1] Annals of Rheumatic Diseases, 19:95–117, 20:315–334, 1961.