LOS ANGELES, CALIF., *April 22, 1968.*

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

DEAR DR. TISHLER: It is my understanding that there are to be some congressional hearings related to the use of indomethacin in the treatment of rheumatoid arthritis. We are all cognizant of the difficulties involved in the evaluation—even double blind studies—of indomethacin or any drug in a disease such as rheumatoid arthritis which is characterized by exacerbations, remissions and the emotional component. However, I have found indomethacin to be a very useful drug in the treatment of rheumatoid arthritis, particularly in milder cases or in patients where one is reluctant to use corticosteroids as patients in the older age group and in those with diabetes, osteoporosis, etc. Furthermore, in the concomitant use of indomethacin with corticosteroids, the dosage of corticosteroids has been reduced in some patients.

Indomethacin has also been a very useful drug in the treatment of other types of rheumatic disease, i.e., episodes of acute gouty arthritis, bursitis, and osteoarthritis. In degenerative arthritis of the hips—for which we have so little to offer therapeutically—I have seen dramatic results from the use of indomethacin.

Sincerely yours,

NATHAN E. HEADLEY, M.D.,
*Associate Clinical Professor of Medicine,*
*U.S.C. School of Medicine.*

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UNIVERSITY OF COLORADO MEDICAL CENTER,
*Denver, Colo., April 22, 1968.*

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

DEAR DR. TISHLER: I understand that hearings currently in progress, under the chairmanship of the Honorable Gaylord Nelson, are considering the drug Indomethacin (Indocin) and its value in the management of patients with rheumatoid arthritis.

I first undertook clinical investigation of this non-cortisone, anti-inflammatory agent in 1963, and first published our clinical studies of this drug in 55 rheumatoid patients in 1965 in the journal, Arthritis and Rheumatism. These clinical investigations were based upon the best objective measurements of rheumatic activity and at that time it was concluded that, "Indomethacin suppresses joint inflammation and improves function but may require up to 2 to 4 months to obtain maximum therapeutic effects". With three additional years of experience with this drug in more than 100 patients under rigid clinical observation and using similar methods of evaluation, I am still of this opinion.

To state how frequently favorable therapeutic effects occur based upon objective tests, and how often this drug is clinically beneficial is difficult, but in my opinion, between 20 to 25 percent do show objective changes; an additional 20 to 30 percent report subjective benefits.

Among the toxic reactions reported with the use of Indomethacin, the frequency of peptic ulceration has been of major concern to critical, clinical observers. An analyses of more than 700 patients treated with Indomethacin at the University of Colorado hospital and its clinics indicates that this complication seldom occurs. These patients had previously received other anti-inflammatory and analgesic drugs including aspirin, corticosteroids, and phenylbutazone. The incidence of peptic ulcers during the Indomethacin period of therapy was actually less than during similar periods of other anti-inflammatory, anti-rheumatic agents. In my experience, the occurrence of peptic ulceration is not a major obstacle to the clinical use of this drug in patients with rheumatoid arthritis.

In my five years experience based on the practical use of Indomethacin and a careful analysis of the results in all of our patients treated by a staff experienced in the management of patients with rheumatoid arthritis in this University Hospital, I am of the opinion that Indomethacin benefits some patients with rheumatoid arthritis. At present no reliable tests are available to predict which