etc. We are now in the process of trying to improve our methods of evaluation through a system of gross measurements, correlating the subjective with the objective findings.

Trusting this is the information you desire, I am

Sincerely,

DONALD F. HILL, M.D.

THE UNIVERSITY OF IOWA,
Iowa City, Iowa, April 22, 1968.

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

DEAR DR. TISHLER: I am enclosing two of the Bulletins that we have written giving our experience with indomethacin.[1] You will notice that the last one was written in 1965.

Since that time we have continued to use indomethacin, particularly in rheumatoid arthritis, and are of the same opinion, namely, that this drug is a safe and effective anti-inflammatory medicament in the management of rheumatoid arthritis. Over the years we have used this drug only in conditions in which we could make a definite diagnosis, and from our past experience knew that it would be effective. These conditions were rheumatoid arthritis, gout, Reiter's disease, and a few cases of degenerative arthritis. We have not prescribed this drug in the conditions that are difficult to accurately diagnose, or in which we are limited only to the patient's response. These include low back pain, fibrositis, painful shoulder, and pains in elderly individuals which are, unfortunately, classified as osteoarthritis.

Most physicians are very impatient and think that an anti-inflammatory drug should relieve or cure a chronic ailment such as rheumatoid arthritis in a short period of time. We have found many patients who were on adequate treatment but still continued to have mild degrees of synovitis. The swelling caused by the synovitis results in pain which is difficult to control. When these people are given indomethacin, in addition to the treatment they are receiving, the synovitis gradually decreases, and improve clinically. This, however, may take several weeks rather than a few days. By the same token when we see a new rheumatoid we usually start them on salicylates and if we cannot hold them with this drug, we usually add indomethacin. A high percentage of the patients that we have do well, but a few continue to show intermittent exacerbations and must be given other drugs as well, including steroids, or gold, etc. If one of our patients has been on steroids, we will add indomethacin in an attempt to reduce the dose of steroids to a safe level. As you know, we believe that rheumatoid arthritics should not receive more than a total of 8 mg. of prednisone, or its equivalent in other steroids, per day. Indomethacin has helped us reduce the steroid dose and prevent many of the side-effects caused by the steroid.

Since 1965, our usual dose of indomethacin is 75 mg. per day. With this dose we see fewer side effects than we reported in the enclosed Bulletin. At times we may give 100 or 125 mg., but cut back as soon as the patient has dizzyness, muzziness, or other irrelevant effects. In our hands, indomethacin is a very safe drug.

I was surprised to hear that a Congressional Committee is investigating indomethacin. I suppose this has been started because of the some of the recent reports on the double blind studies. It is in these studies that one finds many of the loosely defined syndromes being treated, as well as rheumatoid arthritis. Most of these studies depend on the patient's own response to the drug given for a short period of time, usually about two weeks. It is difficult to determine the effect of indomethacin in the ill-defined syndromes. Even in rheumatoid arthritis we have seen severe and relentless progression of the disease despite every type of heroic therapy that we try. It is a well known fact that individuals with a high titer of the rheumatoid factor will have progression despite anything that you do. It is not unusual to see an individual with a very high titer have breakdown of the joints in the wrists and fingers, even though they are getting adequate physical therapy, adequate doses of salicylates, steroids, indomethacin, and/or gold. On the other hand, people who have a low titer may have a remission for long periods of time with little or no destruction of joints. In any double blind study, one has both types of patients, and therefore any drug will not work in

[1] Retained in committee files.