Even more appalling are the apparent expectations of many investigators conducting short-term studies in RA that indomethacin would provide objective functional improvement. This is a clinical misconception since all antirheumatic agents are at best palliative. By providing effective relief of joint pain and inflammation, drugs allow patients to undertake therapeutic exercise and other supportive measures. These provide objective improvement. Yet, such measures receive scant mention and do not appear to be an integral part of the reported double-blind studies of indomethacin in RA.

In spite of these controlled trials, many physicians have the impression that indomethacin benefits certain patients with RA. As Healey has recently pointed out in the Bulletin of the Rheumatic Diseases (18, 483, 1967), there may be a sub-group of patients with RA that are controlled by indomethacin, a finding that would not be evident when such patients are included in a general drug trial. To my knowledge, this hypothesis has not been tested.

The result of our long-term evaluation of indomethacin in ankylosing spondylitis (AS), a form of rheumatoid disease affecting young men, has recently appeared in the journal Arthritis and Rheumatism (11, 56, 1968).

In this trial of indomethacin averaging 33 months in 28 AS patients who received an average daily dosage of 100 mg., the response to the drug was good in 21 patients, fair in 5 and poor in 2. Of the 28 patients, 21 improved to ARA functional class I. Before the use of indomethacin, only one of the 28 was so rated. Joint symptoms followed temporary withdrawal of the drug in all but four of the 28 patients. These symptoms were promptly relieved when indomethacin was again taken by the patients.

Clearly, our report parallels the experience of others, such as Bilka, Hart, Kass, Pohl, Rothermich and De Seze, that indomethacin is an essentially safe and effective drug in suppressing the articular manifestations of AS.

I sincerely hope, despite the current controversy and confusion, that investigative pursuits of indomethacin will continue. Only then can we more fully understand the role of this extremely useful and valuable antirheumatic agent. Best wishes.

Very truly yours,

JOHN J. CALABRO, M.D.
Chief, Rheumatology Section, Wadsworth Hospital.

ST. LOUIS UNIVERSITY,
SCHOOL OF MEDICINE,
St. Louis, Mo., April 22, 1968.

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

DEAR DR. TISHLER: I understand that indocin is under Federal scrutiny in regard to its effectiveness in rheumatoid arthritis. Since I am presently performing a double blind study with this drug in the treatment of rheumatoid arthritis, I would like to offer the following comments.

The therapy of rheumatoid arthritis, as you know, is very difficult. Fortunately, we have many drugs available today which help the practicing physician control this crippling illness in most patients. Many times we find it necessary to use several medications in the same individual because of a lack of any specific drug which will perform to the degree of satisfaction we desire. Some of these drugs are rather toxic, thereby obviating their routine usefulness. By combining drugs like indocin with some of the more toxic medications, we are thus able to effectively use some of the latter preparations in smaller dosages and, consequently, avoid some of their complications. This would be particularly true of the steroids, the "cortisone-like" drugs. Also, when used alone, indocin may offer significant relief so that the addition of other antiflammatory drugs may not be necessary.

Despite the fact that indocin's value in rheumatoid arthritis has been questioned recently, it is my opinion that this medication certainly has a place in the therapy of rheumatoid arthritis. I do not administer indocin as a drug of first choice; however, I do believe it offers a significant advantage to approximately fifty percent of rheumatoid patients.

Evaluation of any drug for the treatment of rheumatoid arthritis is extremely difficult. Double blind studies, such as those being performed at the present time, seem to be the appropriate method of determining a drug's effectiveness. If a