As you know, aspirin has been the backbone of drug therapy in the rheumatoid patient for many years. Therefore it is natural that indomethacin would be compared with aspirin in rheumatoid arthritis, just as any new drug would be compared to an accepted standard therapy of the day. Aspirin is generally accepted by both the medical and lay public as safe. However, there is a great deal of history with aspirin which has never been written. Only in recent years has this drug come under closer scrutiny. In thinking about aspirin, one finds that it really is two drugs—the one that most people take for minor aches and pains in one-, two-, or three-tablet doses, and the second a drug which must be taken in massive doses up to 20 or more tablets (4 to 8 grams a day) to effect a therapeutic benefit in a disease such as rheumatoid arthritis.

In the case where only a few tablets are taken occasionally, as needed, there are few side effects. Most people are able to tolerate aspirin in these amounts, but even with these small doses there are patients who experience gastrointestinal irritation.

However, when one approaches the therapeutic doses of aspirin needed to treat rheumatoid arthritis, there are definite side effects—some very similar to those with indomethacin—which need to be watched carefully by patient and physician. Many patients either cannot tolerate these high doses of aspirin or just will not swallow that many tablets.

On the other hand, most rheumatoid patients who can tolerate aspirin will take it whether it is prescribed or not. If they respond to aspirin and the pain disappears, no further medication, no matter how effective, can make that pain disappear any further. If motion of a joint is allowed up to its maximum by aspirin, then indomethacin, phenylbutazone, or the steroids are unlikely to increase that motion any further. If grip strength, swelling of a joint, and inflammation, for example, have improved in a patient who responds to aspirin, an additional drug, no matter how effective, would probably not provide further improvement in the physical status of the patient.

Although we cooperated in setting up the cooperating clinics study, we did not participate in the design of the study—this was up to the committee. However, I understand there were wide differences of opinion on the study design within the committee itself, particularly with respect to whether or not those patients who were to receive indomethacin should continue to receive aspirin, in the amount the patients desired, as a basic background medication. Obviously the majority of the patients included in the study were responsive to aspirin, and it was decided to allow them to continue to take it. Whether this was the right decision is a matter of opinion, but for the reasons I cited earlier I am not surprised that neither these patients nor the physicians could determine the effect of a second active drug that was being given on top of an already "treated" patient. These studies may not have shown that indomethacin is an effective drug in rheumatoid arthritis by the rigid criteria used, but neither have they shown that it is ineffective. They show nothing as to the effectiveness of indomethacin in patients who do not respond to aspirin or cannot tolerate it in large doses. They do show that during treatment with indomethacin many patients were able to decrease the amount of aspirin they were taking, and when indomethacin was discontinued some of