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Dr. CALABRO. This article requires comment, since rarely does any one study violate so many basic tenets of a drug evaluation. For instance, Senator Nelson, as part of the drug trial of indomethacin, all patients continued to take their previous medication, such as aspirin, phenylbutazone, or adrenocorticosteroids. In fact, some patients were even receiving two of these other drugs simultaneously.

Now, how do we test a drug if we allow patients to stay on another worthwhile and effective antirheumatic agent at the same time?

But even before undertaking the study—and this is an inherent difficulty of many crossover studies—unnecessary bias was introduced. All 30 patients, the investigators point out "were specifically advised of the side effects which were known to occur with indomethacin."

In fact, the patients were so well advised that half developed indomethacin side effects while on placebo. In table III of their report, 60 percent of the patients had side effects—not ordinary side effects, but indomethacin side effects—while they were receiving placebo.

Predictably, such a poorly conceived and biased study produced inconclusive results. However, even more appalling—for me as a clinical rheumatologist responsible for the care of patients with rheumatoid spondylitis—even more appalling than their obvious errors of methodology are the apparent expectations by Kinsella and associates that indomethacin would provide "objective functional improvement."

Now gentlemen, this is a clinical misconception, since antirheumatic agents are at best palliative. By providing effective relief of joint pain and inflammation, drugs then allow the clinician to utilize important supportive measures, such as therapeutic exercises and other forms of physical therapy.

To illustrate this point, Senator Nelson, if you had rheumatoid arthritis of the right wrist, and I were to give you an antirheumatic agent, be it corticosteroids or for that matter indomethacin, these drugs could relieve the inflammation and pain in your wrist joint. But if this effect required a number of weeks or a number of months, you would then end up with a joint that would have some restricted motion. No drug in the world is going to bring that motion back. The only measures that will correct this deformity, of course, are well-prescribed, regularly performed therapeutic exercises.

I might ask all of you gentlemen to analyze closely the double-blind studies reported by Dr. Mainland and more recently analyzed by Dr.