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DEAR DR. CANTWELL: The results of our experiences with the capsular form of 'Indocin' are contained in detail on the enclosed summary tables.

There can be no doubt that 'Indocin' does have clinically observable antirheumatic effect. This effect is uniformly consistent at comparatively low dosage levels in the rheumatoid spondylitic. It is in this particular disease that phenylbutazone and derivatives have been particularly effective but it would appear that 'Indocin' is equally effective at a slightly lower dosage level and, of course, without any of the life-threatening adverse effects which so often complicate therapy with the former compounds. In other words, it is my belief that in rheumatoid spondylitis, 'Indocin' can do as much for the patient as phenylbutazone but do it with comparative safety.

In the peripheral rheumatoid arthritis, there is considerable variation from one patient to the next and sometimes in the same patient from one time to another in the ability of 'Indocin' to exert a consistently and significantly beneficial effect. There is no doubt that higher dosage levels are required than in the case of the rheumatoid spondylitic. As higher dosage levels are approached, it is to be expected that the incidence of cerebral toxicity goes up proportionately and this, in my opinion, represents a not insignificant disadvantage to the drug for it reduces the number of arthritics who can be benefited by the drug and also reduces the degree of benefit in a given arthritic because it necessarily puts a ceiling on maximum maintenance dosage. This is particularly frustrating because I am personally convinced that this cerebral toxicity does not threaten the life of the patient nor does it leave any permanent residuals. In fact, there is usually prompt subsidence of the cerebral toxic symptoms within comparatively few hours (usually 12 to 24) after the drug has been discontinued. Most of the time, the drug can be resumed at a lower dosage level without a recurrence of the cerebral toxicity. It is quite apparent from the chart that we have been able to carry some patients on a comparatively high maintenance dose and, of course, this implies that these patients did not have enough cerebral toxicity for them to wish to be taken off the drug or have it reduced in dosage.

On the other hand, some patients have developed disabling cerebral toxicity usually in the form of severe vertigo, lightheadedness or violent headaches on comparatively low doses. One patient tried on three separate occasions to take a 25 mg. capsule but just on the one dose developed such a violent headache that he could not continue it. On the other hand, another patient had been on 50 mg. and h.s. for at least a year when his vertigo and lightheadedness had increased to a disabling degree and required him to discontinue the drug temporarily. One other patient developed a violent toxic reaction after only one week of therapy and had to be confined to bed, more or less continuously, for four or five days. One patient while on a ladder working became dizzy and fell off suffering a fractured arm. Another busy executive became so dizzy and lightheaded that he feared crossing the street against all traffic.

It would seem worthwhile to list the various manifestations which I have chosen to lump together under the designation of cerebral toxicity:

1. Headache.
2. Vertigo (usually not true room-spinning).
3. Lightheadedness.
4. Feelings of fogginess in the head.
5. Sometimes difficulty in concentration.
6. Occasional feelings of unreality.
7. Marked stimulation with resultant insomnia. Very similar in designation to caffeine effect.
8. In higher doses, some ataxia and even personality change, more toward a paranoid state, were observed.

It is my belief that the capsule is superior to the tablet only in that it permits for a more consistently reliable rapidity of absorption whereas the tablet form varied greatly in its rate and degree of absorption. However, it cannot be said that the capsule has reduced the incidence of cerebral toxicity.

At the same time, "Indocin" is notably free of other toxic effects. A few patients complain of some stomach pain but these were rarely consistent and reproducible. There were no deleterious effects on the formed elements in the peripheral blood including the red and white corpuscles and platelets. There were no alterations of