

of 100 mg a day, with the vast majority getting 150 mg per day as the minimal dosage.

15 patients had no help.

17 patients recorded slight help (that is less than 25%).

20 patients had significant help (25 to 50%).

11 patients report great improvement (over 50%).

I have not yet analyzed all of the laboratory data, so I cannot give an accurate statement as yet, however certain things are apparent and might be of interest at this time:

18 patients reported severe headache; all but six were able to continue the medication at lower dosage levels or by adding Benadryl; 8 patients reported severe gastrointestinal upset.

One patient (Mr. Jensen) had a history of a DU, but the pretest X-ray was negative. During the third month of 200 mg per day, he developed an active DU. He was continued on the medication in the same dosage and X-rays two and four months later show the ulcer healed.

Another patient (Mrs. Rose) with a known active DU was started on Indocin 150 mg per day and was continued on this for two months because of the marked relief she obtained. At this time however, her GI symptoms increased, the X-ray showed the still active DU and the Indocin was stopped.

A third patient (Mr. Rardin) with a known history of a DU and with signs of activity was given a two month trial of Indocin 75 mg per day. His ulcer symptoms also increased on the medication and the X-ray showed an active DU. All of the other patients had negative X-rays.

I will start going over the charts for the detailed analysis of the laboratory data and will let you know of the results. The work with MK715 is too early to make any comments on except that it seems at least as potent as 615 in the two to one dosage ratio.

I am enclosing the laboratory charges for March and April. Again would you have this made out to St. Barnabas Hospital, Arthritis Research.

I shall soon be enlarging the facilities for out-patient care at the Kenny Institute and we will be in a position to utilize extra funds for our project there. If Merck can make an additional contribution of \$3,000 toward this work, it will be useful and appreciated.

Sincerely,

PAUL J. BILKA, M.D.

THE COLUMBUS MEDICAL CENTER,
Columbus, Ohio, May 11, 1964.

NELSON H. REAVEY CANTWELL, M.D., Ph. D.,
Merck Sharp & Dohme Research Laboratories,
Division of Merck & Co., Inc.,
West Point, Pa.

DEAR NELSON: The enclosed letter is from a very fine patient, a 45 year woman who is a Ph. D. and teaches at Dennison University. She is quite intelligent, immensely cooperative and completely un-neurotic. I thought you would be interested in her very vivid and articulate description of the adverse symptoms which she encountered with Indomethacin.

I would emphasize that these do not alarm me nor indicate any evidence of organic damage but I am afraid they will offer some practical problems in marketing this drug.

Needless to say, I am very grateful for all of your kind efforts in regard to my trip to Japan.

I'll look forward to seeing you on my return. I think we must get together and plan on publishing some of the data which we have collected. Best regards always.

Sincerely,

NORMAN O. ROTHERMICH, M.D.

P.S. I sent a copy of Dr. Shepard's letter to Elmer.