

Before the drug was put on the market, dryness, or scaliness, or a rash-like condition had been reported in a certain number of patients. This was listed under the term dermatitis as a side effect in the original literature. We have heard of a few cases since, most of them recently, where this dermatitis has been of a very severe nature and in some instances referred to as ichthyosis. In the few which we were able to track down through the maze of rumors and have examined by dermatologists the term ichthyosis was found to be incorrect. Also it became apparent that some of these were not related to drug. At any rate, we are recognizing that if mild cases of dermatitis can occur, an occasional rare case will be severe. The two most severe cases which we have tracked down are the least likely to be drug-related. One was the case reported by Corday and which he has been ballyhooing around the country as if it had been an epidemic. This patient was on at least three other drugs known to produce allergic cutaneous reactions and had a previous history of neurodermatitis. The other one also had a history of neurodermatitis, and there is some question whether the dermatitis developing under MER/29 started before that therapy began.

We had further reports that MER/29 affected coagulation time of blood; some reports had an increasing coagulation time, some a decreasing coagulation time, and in some the comments were referred to prothombin time. Studies had been initiated in this direction before the drug reached the market and another was set up when the first reports came in. The data from these studies definitely show that MER/29 has no effect on any of the known factors related to the clotting of blood. There is a suggestion that it may actually decrease platelet stickiness, and this we are investigating further.

The only other complaint that we have received in more than six instances, which we use as our arbitrary number for being watchful, is the loss of libido. I defy anyone to make any sensible pattern out of these complaints. Almost 100 per cent of the complaints come from men, whereas about 80 per cent of the complaints on hair loss come from women. Some clinicians with more than 100 men on MER/29 have no complaints of loss of libido, whereas someone with 15 or 20 cases will report 2 or 3. One must always keep in mind that the majority of cases treated with this drug are middle-aged or beyond. Many have had recent infarcts and have fear of sexual activity as well as other activities, such as roller-skating or whatever you wish to choose. Again, we are not finding this complaint in those patients receiving the larger doses of drug, and if it occurs at all at the 250 mg dose level, it ought to be much more frequent at the higher doses, if it is a truth. I have a strong enough background in pharmacology to be suspicious of any drug action that deviates from some semblance of a dose-response curve.

The above is as accurate a summary and interpretation of our total experience with MER/29 toxicity as I can give you at this time. I will say that if you use the large doses you should exert extra precautions, especially in looking for the earliest manifestation of those side effects that now appear to be drug-related. Most specifically these are: a type of dermatitis, loss of hair, and change in hair color.

You are free to use this letter as you see fit, as it is only what I would comment to anyone asking me about the subject. We have somewhere around 3,000 case reports of unpublished data in our files and some 3,000 or more represented by published reports. In addition, Dr. McMaster and I have had personal interviews or frequent correspondence with at least 300 reliable investigators working with MER/29.

CARL A. BUNDE, Ph. D., M.D.,
Director of Medical Research.

[Inter-Department Memo, July 5, 1961]

To: Dr. H. W. Werner,
From: R. H. McMaster,
Subject: William Hollander, Boston, Consultation Fee.

Hollander mentioned the matter of his consultation fee. You will recall that we have had him on a personal retainer amounting to \$2,400 per year payable in 2 semi-annual installments. If we wish to maintain this relationship (which is apart from Wilkins' grant), a payment of \$1,200 is now due. My own feelings is that we can't afford to chance alienation of Hollander just now (perhaps I shouldn't regard this as blackmail).

Certainly we need his help and counsel.