the same six-week period, but were held without additional drug therapy for an additional six weeks and then sacrificed. The following summarizes the results of the study:

Of particular interest in this study is the fact that MER–29 given in dose of 5 mg/kg/day for six weeks did not produce the characteristic adrenal changes observed in the monkeys that had received MER–29 at a dose of 20 mg/kg for 16 months.

In a dose of 5 mg/kg/day for six weeks, MER–29 does not significantly affect the number of primary follicles, maturing follicles or matured follicles in the ovary of the monkey. However, in studying serial sections from both ovaries of the four monkeys so treated, no evidence was found of recent ovulation. By this, we mean that there were no corpora hemorrhagica observed, nor were there any evidence of recent corpus lateum formation. Although we cannot be sure that ovulation did not occur, there was no morphologic evidence to show that ovulation did occur in either of these monkeys.

There was no quantitable changes observed between the two groups of monkeys. Those ovaries examined at the end of six weeks of administration were very similar morphologically to those ovaries that had been off the drug for six weeks before the ovaries were examined.

Conclusions: 1) MER–29, at a dose of 5 mg/kg in the monkey, does not affect maturation of the primate ovary. 2) There is negative evidence to suggest that MER–29 administration of this dose prevents ovulation.

MARCH 26, 1960.

JOHN G. FREEMAN, M.D.,
Nebraska Psychiatric Institute,
Omaha, Nebr.

DEAR DR. FREEMAN: I hope eventually to be able to get caught up on my accumulated correspondence which has resulted from chronic absence from the office. I hope you will excuse the delay in acknowledgement of your kind letter of March 11 and the accompanying data sheets on the patients to whom you and your associates are administering MER/29.

The nicely detailed information you have given us will be of considerable value in our compilation of the assay of cholesterol response and side effects to be expected from MER/29 administration. I might add that most of the side effects you have reported have been unusual ones in that they have not been reported by other investigators. I refer specifically to patient V. H. who apparently developed a leukopenia while taking MER/29 and to patient M. H. who complained of blurred vision and headache after eight to ten weeks of therapy. I shall naturally be interested in any follow up information you may acquire in these instances. Patient I. W., who complained of edema and eye-watering during his first course of MER/29, will also be of interest, especially since he has been restarted on the medication. In reading down through the list, I notice also that patient R. S. had a leukopenia during two periods of administration of MER/29 and that patient I. W. was again forced to discontinue the drug because of watery eyes and edema.

Is it possible that the side effects such as those noted above could have been coincidental with the administration of drugs other than MER/29 concurrently? I would most certainly not ask such a question as this had there been similar reports from elsewhere. On the other hand, if these are indeed potential side effects of MER/29, I think we need to be completely aware of them and to assess them as carefully as possible. I shall look forward to your further reports when you feel them to be justified.

Sincerely yours,

R. H. MCMASTER, M.D.

NEBRASKA PSYCHIATRIC INSTITUTE,
THE UNIVERSITY OF NEBRASKA COLLEGE OF MEDICINE,
Omaha, Nebr., April 7, 1960.

Re: MER–29

R. H. MCMASTER, M.D.,
Department of Medical Research,
The Wm. S. Merrell Co.,
Cincinnati, Ohio

DEAR DR. MCMASTER: Following is a more complete description of the side effects noted in three patients, about which I have written you earlier: