caused adrenal enlargement with depletion of the steroids in the zona fasciculata. A recent study (Hollozy and Eisenstein, Proc. Soc. Exper. Biol. & Med. *107*, 347, 1961) shows that triparanol feeding to rats results in a reduction in the amount of corticosterone (the main glucocorticoid produced by the rat) secreted by the rat adrenal in response to the stress of surgery and bleeding.

The list of publications cited by the firm to show that a dose of 250 mg. per day has no effect on the adrenals of humans is not convincing. The paper by Melby, et al., New England J. of Med. *264*, 583 (1961) refers to this dose only in a footnote and submits no data although the paper does show that the adrenal function is severely impaired on 1000 mg. per day. The paper by Ford in Progr. Cardiov. Dis. 2, 548 (1960) shows a trend towards adrenal depression but the author says it is not significant. However, the original data was not given for calculation of the significance. In the unpublished paper by Ford, data are presented, and although the author states that the response to ACTH is not significantly changed due to the treatment with 250 mg. of triparanol daily, we have recalculated this data and find it is significant at the 5% level and approaches significance at the 1% level. The paper by Hollander, et al., J.A.M.A. *174*, 5 (1960) states that following treatment of 13 patients with 250 mg. of triparanol daily, there was a non-significant increase in the 17-ketosteroid excretion and a significant decrease in the 17-hydroxycorticosteroid excretion. The patients were not challenged with ACTH or stress in this study. This raises the question as to whether or not the pattern of steroid production by the adrenal may not be altered under triparanol therapy, so that less glucocorticoids are secreted by the adrenals or those that are secreted are less active. So far as we have been able to ascertain whether or not this question has not been studied. The paper by Goodman, Avigon and Wilson presented at the First International Congress of Pharmacology, Stockholm, 1961, may have a bearing on it but the details are lacking. In addition, this paper does not mention the dose of triparanol to the humans nor the period of treatment.

If the NDA is not suspended, we strongly recommend that a caution on impairment of adrenal function be included in the brochure.

E. I. GOLDENTHAL.
ERNEST J. UMBERGER.

MEMORANDUM OF CONFERENCE

WILLIAM S. MERRELL CO.,
Cincinnati, Ohio, November 13, 1961.

William M. Kessenich, M.D.
John. O. Nestor, M.D.
Memo of meeting.

(1) *Eyes.*—Cataracts, Corneal opacities.
(2) *Hair.*—Loss of hair, thinning and changes in color and texture.
(3) *Skin.*—Icthyosis, Urticaria, Drying, scaling, and Itching.
(4) *Reproduction.*—Impotence, Loss of Libido, Reduced Spermatogenesis, Prevention of Ovulation and conception. Abnormal offspring. Vaginal smear alterations, temporary menstrual bleeding.
(5) *Adrenals.*—Reduced production of adrenocorticoids with associated diminished ability to respond to stress.
(6) *Blood.*—Hemolytic Anemia. Leukopenia.
(7) *Liver.*—Fatty Metamorphosis. Transient increase in BSP retention.
(8) *G. I.*—Nausea and vomiting.

JOHN O. NESTOR, M. D.

DRUG WARNING—MER/29 (TRIPARANOL)

DEAR DOCTOR: In cooperation with the United States Food and Drug Administration, we are writing to inform and caution you concerning adverse effects, including some unpublished reports, associated with the use of MER/29 (Triparanol). Although comparatively few serious clinical injuries have been reported to date, their possible significance is emphasized by findings from animal studies.