Ichthyosis and other skin changes. There are reports of skin reactions ranging from dryness, itching, and scaling to severe exfoliation, and ichthyosis. Some of these changes were also associated with hair loss and cataracts. It is recommended that MER/29 therapy be stopped immediately if such skin changes occur.

Depression of Adrenocortical Function. Adrenocortical function depression as shown by reduced output of adrenal steroids has been produced by MER/29 in animals, and in man at high dosage levels. This effect has not been ruled out in humans at recommended dosage levels. Appropriate precautions should be observed if MER/29 is employed in patients with suspected borderline adrenocortical function or in patients who are subjected to stress.

Other Adverse Effects. Other adverse clinical effects reported include 4 possible cases of leukopenia and scattered cases of abnormal liver function tests, impotence, diminished libido, veginal smear alterations, nausea, vomiting and urine test changes simulating proteinuria. At a level of 25 mg/kg per day of MER/29 deaths have occurred in some dogs within 35 days, with liver damage in some animals. It has caused abortion and prevented conception in rodents, diminished spermatogenesis in dogs, stopped egg laying in chickens, and was assumed to cause acute intravascular hemolytic episodes in some dogs in one study.

The side effects of all types reported to us to date total substantially less than one percent of the patients treated. This includes a number of patients who have been treated with MER/29 in clinical research studies for continuous periods of more than a year, including a few in excess of three years.

In view of all reports concerning adverse effects, it is recommended that MER/29 be used only in patients who can be maintained under very close supervision and frequent observation. Dosage should never exceed 250 mg. per day.

Further studies are under way to assess more fully the incidence and seriousness of adverse effects, with a view to a re-evaluation of the conditions and indications for use of MER/29. We will appreciate any information you may contribute from your clinical experience with MER/29.

Sincerely,

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

(Whereupon, at 4:20 p.m. the subcommittee was adjourned to reconvene at 10 a.m., Tuesday, November 28, 1967.)