## OTHER PREPARATIONS

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## MEDICAL INTELLIGENCE

THE EVILS OF CAMOUFLAGE AS ILLUSTRATED BY THALIDOMIDE 1

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The abrupt decline in the occurrence of phocomelia in West Germany eight months to the day after the public announcement that thalidomide (Contergan) was suspected as the cause offered conclusive evidence that Lenz (1) and McBride (2) were correct in their belief that the ingestion of this substance in early pregnancy caused phocomelia in the offspring. Indeed, the incidence of phocomelia dropped almost to zero. In September, 1962, I was advised that 1 case had been reported in August; this woman had not heard the warning and had taken thalidomide in early pregnancy. These events show how widespread the publicity was on November 28, 1961.

Lenz and Knapp (3) have emphasized the fact that injury to the fetus occurred only when the drug was taken during the "sensitive period," which was between the twenty-eighth and the forty-second day (inclusive) after conception or the thirtieth to the sixtieth day after the first day of the last menstrual period. In a subsequent careful analysis of his material Lenz (4) has correlated the time during which the mother took thalidomide with the type of abnormality found in the infant. In every case in which the infant was born with an abnormality of the arms the mother had taken thalidomide between the thirtyninth and the forty-first day (inclusive), whereas when the legs were abnormal, the mother had taken the drug between the forty-first and the forty-fourth day after the last menstrual period. This observation is in line with the fact that arm buds appear slightly before the leg buds. When the infant was born with an abnormality of the external ear, however, the mother was found to have taken thalidomide between the thirty-fifth and the thirty-seventh day after the last menstrual period. This is in striking contrast to the fact that the exernal ear is not discernible until after the arms and legs are readily apparent. The early date at which injury occurs to the anlage of embryonic cells destined to form the ear is similar to the effect of the rubella virus on the heart. The commonest cardiac abnormality resulting from an infection with the rubella virus in early pregnancy is persistent patency of the ductus arteriosus, whereas the cells destined to be concerned in the closure of the ductus arteriosus are among the last cells in the heart to be discernible.

The incidence of cardiac abnormalities caused by thalidomide is relatively high. In Lenz's 4 series 17 per cent of the living infants and 50 per cent of those who had died had cardiac abnormalities. Nevertheless, no specific type or

types were apparent.

A wide variety of other malformations have been observed from thalidomide poisoning, but, as yet, the relation of these abnormalities to the time of ingestion

of the drug has not been determined.

The problem remains whether thalidomide alone is responsible for the outbreak of phocomelia or whether other drugs may cause a similar deformity. This question is raised because a history of the ingestion of thalidomide has been obtained only in approximately 50 per cent of the cases. If, however, thalido-mide was responsible for only half the cases, the incidence should have declined markedly, but the outbreak of phocomela would scarcely have come to an abrupt end. In a recent letter Dr. Lenz 5 advised me that during the first six months of 1962 the incidence of phocomelia in Hamburg was 1 or 2 per 1000 births, whereas after August 1, 1962, among the first 5000 births in the city of Ham-

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