

None of these subjects had evidence of meningeal involvement.

Comment. The results of this study, which has demonstrated that viomycin was rapidly absorbed and that high concentrations were achieved in the serum after intramuscular injection, may bear only a very loose relationship to the successful utilization of the drug in antimicrobial therapy. It has been encouraging to note, however, that the serum concentrations of viomycin which were attained in the present study were well in excess of the minimal inhibitory concentrations of viomycin required *in vitro* to suppress strains of *M. tuberculosis* isolated from patients with active tuberculosis(4). The pattern of absorption and urinary excretion of viomycin was similar to that of streptomycin, and the serum concentrations which were attained following the intramuscular administration of viomycin have compared favorably with the concentrations of streptomycin which have

been achieved following comparable doses of the latter drug(6).

Summary. A study has been made of the absorption and excretion of viomycin following intramuscular administration in humans. Maximum serum concentrations of 82 to 125 μg per ml were attained within 2 hours after a single dose of 25 to 50 mg per kilo. Reasonably high concentrations were achieved in the serum of patients receiving daily maintenance doses of the drug. Small concentrations of viomycin, 10 to 12.5 μg per ml, were detected in the cerebrospinal fluid in the presence of high serum concentrations of the drug, 100 to 125 μg per ml. Viomycin was excreted in the urine in high concentrations, and from 65 to 100% of the administered dose was recovered in the urine within 24 hours.

6. Adcock, J. D., and Hettig, R. A., *Arch. Int. Med.*, 1946, v77, 179.

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Abnormalities of the Eye Occurring in Young Vitamin E-Deficient Rats. (18468)

ELIZABETH CROFTS CALLISON AND ELSA ORENT-KEILES.

*From the Bureau of Human Nutrition and Home Economics, Agricultural Research Administration,
U. S. Department of Agriculture, Washington, D.C.*

In the course of some studies with vit. E-deficient rats, unusual abnormalities of the eye were observed in the young of mothers deficient in this vitamin. Such lesions had not been encountered before in this laboratory, and have not been mentioned by other investigators to our knowledge.

Although the data are limited, it seems of importance to report them, in view of the recently published studies of Owens and Owens(1) indicating that vitamin E may play an important role in the prophylaxis of retrolental fibroplasia, a disorder which appears frequently during the early months of life in small, prematurely born infants. This condition has been recognized for many years,

and has been ascribed to a variety of etiological factors; however, Owens and Owens (2) are the first investigators to follow the progress of the disease from the initial stages of dilatation of the retinal arteries and formation of fibrous bands extending into the vitreous to the final fusing of these bands with folds of the swollen retina to form the characteristic membrane behind the lens. The membrane may be complete, causing total blindness or it may be partial, allowing some vision to be retained. Symptoms accompanying this condition noted by these and other workers(3) were eyeballs smaller than normal and hemorrhages behind the lens. Once the

1. Owens, W. C., and Owens, E. U., *Am. J. Ophthalm.*, 1949, v33, 1631.

2. Owens, W. C., and Owens, E. U., *Am. J. Ophthalm.*, 1949, v32, 1.

3. Krause, A. C., *Arch. Ophthalm.*, 1946, v36, 387.

TABLE I. Summary of Data on Abnormalities of the Eye in Young Rats from Vitamin E-Deficient Mothers.

Maternal history				Eye abnormalities of young
Rat No.	Started E-free diet at, days	Litter No.	Age at birth, days	
1079	14	1	85	2 young weaned, both with small eyes; 1 young, eyes unopened
1199	7	1	75	Large blood clot behind pupil in 1 young
1427	14	1	84	Small eyes in all young (6) of litter; died before weaning
		2	141	White membrane behind pupil in 1 young; small eyes in 1 young; 5 young weaned
1518	7	1	72	White membrane behind pupil in 1 young of 5 weaned
1792	7	3	176	Eyes of all young (4) unopened at weaning
2083	7	1	71	Small eyes in 1 young of 7 weaned
2086	7	1	73	Small eyes in 2 young of 7 weaned

changes occur, they are irreversible, but Owens and Owens have been successful in preventing their appearance almost entirely in a series of premature infants by the administration of dl alpha tocopheryl acetate, starting soon after birth.

In our experiments, female rats that had had access to a vit. E-deficient diet* from either 7 or 14 days of age, and had been weaned at 21 days to the same deficient diet, were mated with normal males as soon as the vagina was patent and regular oestrus cycles had been established. On the fifth day after sperm were found in the vaginal smear, a single dose of 3.0 mg alpha tocopherol acetate (Merck) in olive oil was given. With this treatment, the majority of these animals, when they were from 70-90 days of age, gave birth to first litters of normal size and weight; many of the young died before the 21st day, and the incidence of paralysis was high in the young weaned. The paralyses, which were often severe, were of both the flaccid and spastic type, and affected either fore or hind limbs, rarely both in the same animal. Subsequent matings of the same females, employing the same dose of tocopherol, resulted in a very high percentage of resorptions or in litters consisting of only a few animals.

It was also observed that the eyes of a

number of the paralyzed young exhibited abnormalities which suggested the symptomatology of retrolental fibroplasia, as it has been described. These symptoms in the rats were: Eyeballs smaller than normal, eyelids which failed to open, an opaque white membrane visible behind the pupil, and in one instance a large clot of blood completely filling the pupil. These observations, together with data about the mother which have a bearing on these observations, are summarized in Table I. Unfortunately, it was impossible to follow the studies further at the time and to make a systematic histological study of both the abnormal eyes and eyes which appeared to be normal in littermates of these animals; such a study would have revealed beyond a doubt whether or not we were dealing with a disease in rats similar to human retrolental fibroplasia.

Owens and Owens(1) have pointed out that the large amounts of vit. A with which the diet of the premature infant is supplemented routinely may reduce the available vit. E in the digestive tract, since the tocopherols, by virtue of their antioxidant property, serve to protect vitamin A from destruction in the intestine. The diet is already limited in vit. E because of its low fat content. Increased use of water-miscible vit. A preparations has been demonstrated by Kinsey and Zacharias(4) to show significant correlation with increased incidence

* Casein 24%, dry brewer's yeast 8%, Osborne and Mendel salt mixture 4%, lard 10%, cod liver oil 2%, corn starch 52%.

of retrolental fibroplasia.

In this connection, it is of interest that two water-miscible preparations of vit. A (the alcohol and acetate) have proven, in our laboratory, to be less stable than solutions of the same two isomers in cottonseed oil. Both the oil and water-miscible preparations were secured from the same laboratory at the same time and stored together, unopened, at 0°C. After 18 months, vitamin A bioassays demonstrated that the vit. A potency of the oil solutions was unimpaired, whereas the water solutions had lost so much vit. A activity that even when fed at a level of 3.0 units per day (estimated from original potency), the depleted animals with few

exceptions either died or lost weight during the 4-week assay period. These data suggest that vitamin A is protected from oxidation to a lesser degree in an aqueous medium than in a cottonseed oil medium, and for this reason may render a correspondingly larger amount of vit. E in the digestive tract unavailable for metabolic processes in the body.

These observations are presented with the thought that studies to prevent the occurrence of retrolental fibroplasia in premature infants might be facilitated by further experimentation with vitamin E-deficient rats to develop a standardized technic for the production of a similar abnormality in young rats.

4. Kinsey, V. E., and Zacharias, L., *J.A.M.A.*, 1949, v139, 572.

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Effect of Dilantin and Mesantoin on the Giant Axon of the Squid.* (18469)

SAUL R. KOREY. (Introduced by David Nachmansohn)

From the Department of Neurology, College of Physicians and Surgeons, Columbia University.

The effectiveness of dilantin (sodium diphenyl hydantoinate) and mesantoin (sodium phenyl ethyl methyl hydantoinate) in raising cortical thresholds to electric convulsive shocks(1) and their successful applications in the therapy of convulsive disorders are yet unexplained in terms of mechanism. The present experiments employing the isolated giant axon of squid are an attempt to study the actions of these compounds under simplified conditions and to approach an understanding of their mode of action.

Procedure. The giant axon of squid (*Loligo pealii*) was dissected in connection with its ganglion. The nerve was kept for ½ hour in a solution of artificial sea water to attain ionic equilibrium(2), then it was exposed to various solutions and the electrical signs were

examined periodically. In other experiments the ganglion was removed and the nerve was threaded through a small bore polystyrene tube into which the electrodes had been sealed as described previously(3). The nerve was then perfused continuously and its electrical activity was recorded on a dual beam cathode ray oscilloscope. Stimulation was delivered by a dual square wave monophasic stimulator. The results of the two procedures were similar. A reduction in the content of both calcium and magnesium of the sea water produced spontaneous firing of the giant axon for long periods without showing electrical signs of injury. Omitting either calcium or magnesium did not produce an adequate condition, since the fibers lost their excitability after a brief period of hyperirritability. The concentration of dilantin or mesantoin in the

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1. Merritt, H. H., and Putnam, T. J., *Arch. Neurol. and Psychiat.*, 1938, v39, 1003.

2. Bullock, T. H., Nachmansohn, D., and Rothenberg, M. A., *J. Neurophysiol.*, 1946, v9, 9.

3. Bullock, T. H., Grundfest, H., Nachmansohn, D., and Rothenberg, M. A., *J. Neurophysiol.*, 1947, v10, 63.