

time of implantation of the pellet the right testis was removed in half the number of animals of each group. Marked atrophy occurred in the testes and related genital organs when the pellet was present in the subcutaneous tissues or in the transplanted ligated spleen. No changes occurred in these organs when the pellet was present in the normally situated spleen, indicating that when the absorbed estrone passes through the liver of normal adult male rats before reaching the organs it specifically affects, it is inactivated.

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Death of Embryos in Guinea Pigs on Diets Low in Vitamin E.

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The need of vitamin E for the successful completion of pregnancy in rats is well known.¹ More recently it has been shown to be essential in mice also.^{2, 3} We have found no reference in the literature describing resorption of the embryo due to vitamin E deficiency in guinea pigs. The failure to demonstrate this heretofore has been due undoubtedly to the fact that guinea pigs on vitamin E-low diets usually die of muscular dystrophy before the onset of sexual maturity.

It seems worthwhile, therefore, to place on record certain observations which indicate that the guinea pig, like the rat and mouse, requires an abundant supply of vitamin E, and that an inadequate intake results in death of the embryo *in utero*.

Experimental. The basal diet V consisted of:

Casein (commercial)	200
Sucrose	150
Cornstarch	360
Yeast	50

¹ Evans, H. M., and Burr, G. O., *Memoirs of the Univ. of Cal.*, 1927, No. 8.

² Bryan, W. L., and Mason, K. S., *Am. J. Physiol.*, 1940, **131**, 263.

³ Goettsch, M., and Pappenheimer, A. M., *Proc. Am. Inst. Nutrition*, 1941, Chicago.

Salt mixture	40
Lard	80
Cod liver oil	20
Cellulose	200

This was supplemented by 5 cc of tomato juice and 25 g of fresh lettuce daily. Lettuce was added to supply a necessary water soluble growth factor, the need for which in guinea pig nutrition has been indicated by the work of Kohler, Elvehjem and Hart,⁴ and of Cannon and Emerson.⁵ The amount of vitamin E contained in this amount of lettuce has been found by us in previous experiments inadequate to protect against muscle dystrophy.

Of 3 controls on this basal diet, 2 died after 101 and 312 days with severe muscular dystrophy. The third died at 286 days without muscle lesions.

Confirming our previous experiences, the addition of 25 g of lettuce daily did not provide sufficient vitamin E to protect 2 of the 3 animals against muscular dystrophy, nor to ensure a successful pregnancy.

Fifteen guinea pigs received a weekly supplement of 5 or 10 mg of alpha-tocopherol acetate (Hoffman-LaRoche). Ten of these had to be discarded from the experiment for various reasons. A brief history of the remaining 5 follows:

Guinea Pig No. 63, receiving 5 mg of alpha-tocopherol weekly, was operated upon on the 30th day after mating, having had a bloody vaginal discharge for 2 days, and a partially resorbed fetus removed from the right uterine horn. This animal is alive and has again been mated, receiving 25 mg of alpha-tocopherol, 2 days after being placed with the male.

Guinea Pig No. 47, which also received 5 mg of alpha-tocopherol weekly, was mated unsuccessfully 6 times. Twenty-nine days after the 7th mating a bloody vaginal discharge was observed. An operation, which resulted in death on the following day, disclosed 4 dead fetuses, 28, 30, 25, and 20 mm in length.

Guinea Pig No. 54, also receiving 5 mg of alpha-tocopherol weekly, became pregnant after her 5th mating. Bloody vaginal discharge was noted 26 or 27 days after mating, and the animal was sacrificed. One living fetus 15 mm in length, was found in the left uterine horn, and a dead fetus, partly macerated, in the right horn.

Guinea Pig No. 46, receiving 10 mg weekly, became pregnant after the first mating. It was found dead on the 47th day; at autopsy,

⁴ Kohler, G. O. Elvehjem, C. A., and Hart, E. B., *J. Nutrition*, 1938, **15**, 445.

⁵ Cannon, M. D., and Emerson, G. A., *J. Nutrition*, 1939, **18**, 155.

2 well preserved fetuses, which microscopically showed subcutaneous and intramuscular oedema, were present in the uterus.

Guinea Pig No. 52, received 10 mg weekly. Sixty days after the first mating, it gave birth to a single healthy infant which survived for 53 days without becoming dystrophic, and died from traumatic accident. The mother was again mated; 33 days after being placed with the male, a bloody vaginal discharge lasting 2 days was noted. Probably resorption took place at this time, but the presence of a dead fetus was not confirmed by operation.

Thus, in these 5 guinea pigs, the tocopherol protected the animals against muscular dystrophy, but the amount was not adequate to insure successful pregnancy. Those receiving 5 mg had resorption at about 30 days, or midway in the term of pregnancy. Of the 2 receiving 10 mg, one gave birth to a living young, followed by resorption (initial fertility); the other went considerably beyond mid-term, dying on the 47th day.

It will be necessary, before definitely ascribing the fetal deaths to vitamin E deficiency, to carry the experiments further, and to establish the minimal dose of alpha-tocopherol required for successful completion of pregnancy. It may be said provisionally, however, that on a low E diet, supplemented by lettuce and weekly doses of 5-10 mg, resorption of the embryos does occur in a high proportion of cases. This amount is sufficient to prevent muscular dystrophy.

Examination of the dead fetuses has not given a clear explanation of the cause of death. Aside from oedema and early autolytic changes, nothing of significance was detected. Sections of the placenta of the living fetus of guinea pig No. 54 showed extensive areas of hemorrhagic and anemic necrosis; the placenta of the dead fetus, and that of the other fetuses, were the seat of complete hemorrhagic necrosis. It will be necessary to have further observations before concluding that the placental lesions are of primary importance.*

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