

domen was distended showing that, when given intraperitoneally, these preparations were toxic. No signs of hastened maturity of sexual organs were observed, but rather a tendency of the uterus and tubes to atrophy.

Parallel with vitamin E experiments prolan A (from pregnancy urine) and hormone prepared from anterior lobe of hypophysis were tested. The preparations were administered subcutaneously as well as *per os*. In all cases enhanced maturity was observed, *i. e.*, ripening of follicles, opening of vagina and great hyperemia and hypertrophy of labiae vaginalis, uterus and tubes. In case of subcutaneous administration the reaction followed within 80-100 hours and the prolan preparations were active in very small doses, while in cases of peroral administration the reaction followed in 160-180 hours and was not so noticeable and larger doses were required.

We were unable to repeat Verzár's findings, and conclude that vitamin E does not induce sexual maturity as does anterior pituitary hormone and prolan A; this method therefore can not be used for standardization of vitamin E preparations.

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Vitamin E and Pituitary Hormone. II. Failure of Ant. Pituitary Hormone and Prolan A to Substitute Completely Vitamin E.

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In disagreement with reports of Verzár and his collaborators, results obtained by us¹ on young rats indicate that vitamin E has a biological action different from that of gonadotropic anterior pituitary hormone and prolan A. In a different type of test we have used mature female rats which were raised on vitamin E-free diet and have tested the capacity of gonadotropic pituitary hormone and prolan A to induce fertility in them as does vitamin E.

These rats, raised on vitamin E-free diet and all more than 3 months old, were divided (May 30) into 2 groups (I and II); both groups being left on vitamin E-free diet. Group I received twice a week 0.5 cc. of wheat-germ extracts as a source of vitamin

¹ *Proc. Soc. Exp. Biol. and Med.*, 1933, **31**, 58.

E. Since the rats showed no changes this dose was increased (August 3) to 6×0.5 cc. weekly. Even this quantity seemed too small and the dose was again increased (August 19) to 6×1.0 cc. weekly for 3 animals (Nos. 122, 123 and 135). A pregnant female (No. 130) was left on the previous dose (6×0.5 cc.) of vitamin E extract and this animal on August 27 gave birth to 6 healthy young. Nos. 122, 124 and 135 also gave healthy litters of average size, but even at this dose No. 123 resorbed her fetuses.

The rats of group II (on vitamin E-free diet and serving as control for group I) did not produce any young from May 30 to August 9. During this period these rats increased in weight and were fertilized but the fetuses died and were resorbed. From August 9 three animals received (1.0 cc. daily) pituitary gland hormone and the other 3 the same quantity of prolan A (from urine). Both preparations had very high gonadotropic activity as shown by tests on infantile female rats. On August 13 administration of both preparations was temporarily discontinued; from August 20 to September 12 the animals again received 1.0 cc. daily of pituitary hormone and prolan A. All females had become pregnant and increased in weight but none of them had given birth to young. On November 12 this group was transferred to normal Sherman diet; within 10 to 15 days all of them became pregnant, and all gave birth to healthy young, showing that the fertility of the female rats was not destroyed but only suspended by lack of vitamin E.

These experiments show that neither pituitary hormone nor prolan A can completely replace vitamin E; they merely aid the first phase of embryonic development. Evidently the biological action of vitamin E is not identical with that of pituitary hormone and prolan A. The hormone preparations may favor ovulation, implantation of the fertilized egg, and early embryonic development; but vitamin E is necessary for further development of the fetus and the completion of gestation.

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