at least partially immune for as long as 43 days after the apparent cure of the first infection. This correlation suggests that residual infection plays an important part in the production of immunity to spirochetal infection in Chinese hamsters.

Comment. (1) Chinese hamsters apparently recovered from infection with a California strain of relapsing-fever spirochetes were resistant to subsequent infection. Treatment did not seem to influence this immunity to any appreciable degree. (2) A suggested correlation between residual infection in the brain and immunity appears in the present experiment.

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Effect of Diethylstilbestrol Dipropionate on Mammary Development and Lactation.

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The prolonged effect of the dipropionate ester of diethylstilbestrol has been shown to maintain rats in estrus 50 days after a single 10 γ injection.[1] The influence of this estrogen upon mammary development and lactation was studied on heifers and rats. Two Jersey heifers, one a castrate at 12 months of age and the other a sterile 3-year-old, were used. Twelve castrate and 14 intact lactating rats were employed to further check the results obtained in the heifers.

The castrate heifer was injected over a period of 9 months with a total of 1560 mg of diethylstilbestrol dipropionate* and 530 mg testosterone propionate† at the end of which time milking was begun. During the first half of the injection period only the estro-

[1] Dodds, E. C., Goldberg, L., Lawson, W., and Robinson, R., *Nature*, 1938, **142**, 211.

* Stilbestryl dipropionate contributed by The Lakeside Laboratories, Inc., Milwaukee, Wisconsin.

† Oreton contributed by Schering Corporation, Bloomfield, New Jersey, and Perandren contributed by Ciba Pharmaceutical Products, Inc., Summit, New Jersey.

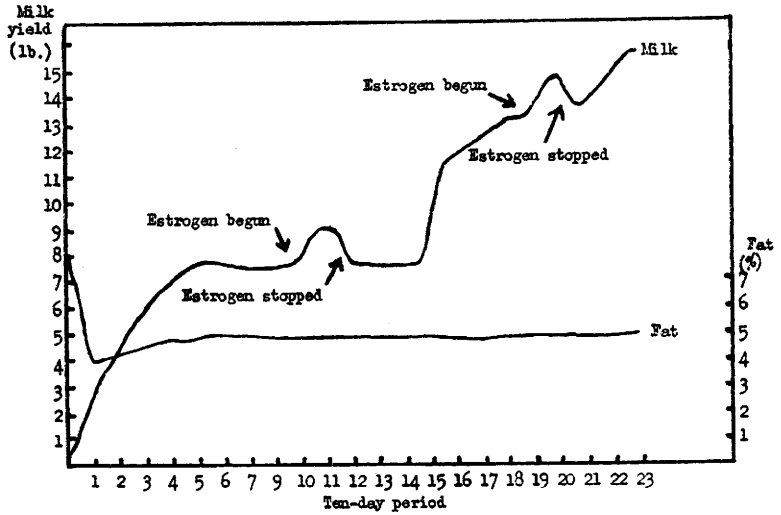

FIG. 1.

Lactation record of a castrate grade Jersey heifer injected with diethylstilbestrol dipropionate.

gen was used. The udder developed slowly under this treatment and reached about one-fourth of its present size. During the latter half of the 9-month period testosterone propionate was added to the estrogen in the proportion of 4 parts estrogen to 1 of androgen. The udder responded by more than doubling its size. All treatment was stopped at the end of 9 months and daily milking was begun. Small quantities of milk were obtained during the first few milkings but the yield increased rapidly and was more than 3 pounds at the end of 10 days. The lactation record of this animal is shown in Fig. 1.

Twice during the lactation period additional injections of diethylstilbestrol dipropionate alone were given. In the first instance 110 mg were given in alternate daily doses of 10 mg each. At the beginning of this series of injections milking had been in progress for 100 days and the daily yield was 8 pounds. The yield immediately increased to 9½ pounds but after 50 mg had been given a sudden decline began which continued during the remainder of the 21-day injection period and carried the production to 7½ pounds. This level was maintained for the next 30 days when the yield increased rapidly and reached a new high level of 13 pounds. The second series of injections was begun on the 180th day of lactation after the 13-pound level had been maintained for 10 days. Sixty mg were given in 10 mg doses on alternate days. The production immediately rose to 15 pounds and again receded to 13 pounds at which time

the injections were stopped. During the following 20 days the yield rose to a new high of 16 pounds per day. It is to be noted that this animal was castrated 10 months before any injections were given and that no progesterone was ever given. It is also worthy of note that the production rose immediately after injections were made during the lactation period. No inhibition ensued until a much higher titer was established. The period of time following the "hump" in the production curve after estrogen administration during which the inhibition continued (recovery time) seems roughly proportional to the dosage. The constancy of the fat percentage during the increased yield seems good evidence that new parenchyma was developed during the recovery period. This would then represent a true growth of the mammary gland and not merely an "enrichment effect" of Folley.[2, 3] The immediate response to the estrogen when the titer is known to be low and the rise occurring at the end of the recovery time when the titer is once again low show that the new parenchyma develops under these titers. Flaccidity of the udder was always noted to accompany the establishment of an injuriously high titer in both lactating and non-lactating glands.

The sterile heifer was injected with a total of 350 mg of diethylstilbestrol dipropionate over a 90-day period and milking was then begun. During the first 30 days of lactation the yield reached 3.7 pounds per day. At this time alternate daily 5 mg doses of diethylstilbestrol dipropionate were begun and continued for 43 days until a total of 85 mg had been injected. During this 43-day period the milk yield rose to 8.1 pounds. At this time the injections were stopped and within the next 17 days the milk production increased to 14 pounds per day. During the 43-day injection period the udder increased markedly in size. It is to be noted in this animal that the titer of estrogen was slowly built up so that no actual inhibition occurred until the very end of the period. Upon cessation of estrogen administration the titer again became low with a consequent increase in udder growth and milk production.

Diethylstilbestrol dipropionate was given in 0.2 mg and 1.0 mg doses to castrate and intact lactating rats, whose litters had been reduced to 6 at parturition. Injections were given daily from the second to the twentieth day after parturition. The average growth rate of the young was used as a measure of the rate of lactation.

The average growth rate of the young of all treated mothers exceeded that of the controls through the second day of the injec-

[2] Folley, S. J., *Lancet*, 1941, **240**, 6124.

[3] Folley, S. J., and Young, F. G., *Lancet*, 1941, **240**, 6134.

tion period. After the second day of treatment, the young whose mothers were left intact gained weight less rapidly than the sucklings of non-castrate controls. On the contrary, the rapid growth rate was continued for 6 days in the young of the castrate mothers which were given 1.0 mg, and for 12 days in the litters of castrate mothers which were given 0.2 mg doses. The suppression of lactation was much more pronounced in intact than in castrate animals. The ovaries, adrenals, and pituitary of those animals that were injected showed a pronounced increase in weight over those of the control mothers.

The premature opening of the vagina which occurred at 12 days after birth in most of the treated litters indicates that large amounts of the estrogen were secreted with the milk and also that this hormone is not readily attacked by any of the enzymes of the rat.

Conclusions. 1. Progestin is not necessary for complete mammary development in cattle. 2. Estrogens will induce mammary development and copious milk secretion in cattle without injection of prolactin. 3. The turgidity of the udder may be used as an indicator of the secretory activity of the non-lactating gland. 4. The titer of estrogen determines its effect on the mammary gland. A low titer induces proliferation of the parenchyma and secretion of milk; a high titer suppresses lactation and brings on involution of the mammary gland.

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Renal Carbonic Anhydrase.

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The presence of carbonic anhydrase in the mammalian gastric mucosa has been reported and discussed by Davenport and Fisher[1] and by Davenport.[2, 3] Although the rôle of carbonic anhydrase in the gastric secretion of hydrochloric acid is not yet

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1 Davenport, H. W., and Fisher, R. B., *J. Physiol.*, 1939, **94**, 16P.

2 Davenport, H. W., *J. Physiol.*, 1940, **97**, 32.

3 Davenport, H. W., *Am. J. Physiol.*, 1940, **128**, 725.