STUDIES ON THE MAMMARY GLAND

V. THE EFFECTS OF INANITION ON THE DEVELOPING MAMMARY GLANDS IN MALE AND FEMALE ALBINO RATS FROM BIRTH TO TEN WEEKS OF AGE *

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In a previous work¹ attention was called to the fact that the postnatal development of the milk ducts probably depends to some extent on the body weight of the animal. The present work is an attempt to show: (1) to what extent the postnatal development of the milk ducts may be altered by changes from the normal body weight of the animal; (2) the effect of severe inanition on the development of all parts of the mammary gland; (3) the recovery of the mammary gland in animals on refeeding after inanition.

MATERIAL AND TECHNIC

The material used in this study was kindly presented to me by Dr. C. A. Stewart,² who made a study on the central nervous system of the same animals. The series of rats used included more than twenty males and females ranging in age from birth to 10 weeks (one or two individuals being somewhat older). The control rats were allowed to grow normally while the test animals were held at or near birth weight for various periods of time. This was done by removing the test rats from the mother at successive periods. To restrict the weight after weaning the rats were fed small amounts of whole wheat (Graham) bread, soaked in whole milk. After such periods of starving, a few females were refed until they reached the weight of the normal or control animal at the time of killing.

In most cases comparisons were made from test and control rats of the same litter. However, in some cases the glands in a control rat of the same litter as the test animal were not available; hence it became necessary to compare the glands of the test rats with those of apparently normal animals of other litters of the same age. In both test and control animals some of the glands were sectioned serially, the sections being 10 microns in thickness, and stained in Heidenhain's iron hematoxylin stain or Mallory's connective tissue stain.

So far as possible the glands were removed from the epidermis with the connective tissue layers of the skin and cleared according to the method used

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1. Myers, J. A.: Studies on the Mammary Gland. III. A Comparison of the Developing Mammary Glands in Male and Female Albino Rats from the Late Fetal Stages to Ten Weeks of Age, *Anat. Rec.* **13**: 1917 (Abst. in *Anat. Rec.* **11**: 1917).

2. Stewart, C. A.: Weights of Various Parts of the Brain in Normal and Underfed Albino Rats at Different Ages, *J. Comp. Neurol.* **25**:511, 1918.

by Lane-Claypon and Starling.³ In rats held at slightly above birth weight, however, it was extremely difficult to remove the connective tissue layer of the skin without tearing it or injuring the mammary glands.

OBSERVATIONS

1. *Effects of Inanition.*—*Newborn.*—In a normal new-born female albino rat of about 4.5 gm., the mammary glands (Fig. 1) show a considerable branching of the milk ducts. (Only two of the six glands on each side are shown in the figure. For complete description, see Myers.⁴) Quaternary ducts are present in all of the glands examined

Fig. 1.—Drawn from a cleared preparation (internal view) of a new-born female albino rat (weight 4.5 gm.) to show distribution and relations of ducts of right abdominal gland (A), and right first inguinal gland (B) $\times 5$. A.n., abdominal nipple; I.n.I., first inguinal nipple; p.d., primary duct; s.d., secondary duct; t.d., tertiary duct; tr.d., terminal duct; e.b., end-bud.

Fig. 2.—Same as Figure 1, but from animal that was starved so as to weigh only 3.6 gm. at eight days, $\times 5$. The greater part of the first inguinal gland (B) was lost in making the cleared preparation.

and in most individuals the fifth, sixth and even the seventh divisions of the ducts have occurred. Terminal end-buds are fairly prominent. Collateral ducts (short side branches) are present in small numbers and are chiefly located near the free end of the ducts of a gland. They are very rare on any of the main ducts nearer the nipple than

3. Lane-Claypon, Miss J. E., and Starling, E. H.: An Experimental Inquiry Into the Factors which Determine the Growth and Activity of the Mammary Glands, *Proc. Roy. Soc. M. and S., Series B* **77**: 1906.

4. Myers, J. A.: Studies on the Mammary Gland. I. The Growth and Distribution of the Milk Ducts and the Development of the Nipple in the Albino Rat from Birth to Ten Weeks of Age, *Am. J. Anat.* **19**: 1916 (Abst. in *Anat. Rec.* **10**:20, 1916). Myers, J. A.: Studies on the Mammary Gland. II. The Fetal Development of the Mammary Gland in the Female Albino Rat, *Am. J. Anat.* **22**: 1917 (Abst. in *Anat. Rec.* **11**:390, 1917).

the quaternary ducts. The branching of the milk ducts in the new-born male is essentially the same as in the female.

It was previously shown⁵ that the nipple of the new-born female albino rat is only slightly elevated above the surface of the surrounding epidermis, and that in some cases there is around the nipple a shallow sulcus, which was regarded as a remnant of the mammary pit of the fetus. The epidermis covering the nipple is considerably thickened. Deep in the sulcus surrounding the nipple lies the projection of the "epithelial hood." Near the highest part of the nipple may be seen a slight excavation which represents the position of the future milk pore and intra-epidermal part of the primary duct. The lumina

Fig. 3.—Same as Figure 1, but from a normal female of 3 weeks (weight 30 gm.), $\times 5$.

of the milk ducts are not completely formed, being best developed from the secondary or tertiary ducts to the free ends of the terminal ducts. As the primary duct is approached the lumen presents an irregular outline, while nearer the attached end of the duct it is represented by isolated lacunae. Near the surface there appears at this stage no trace of a lumen. From the secondary ducts to the end of the terminal ducts the epithelial walls are composed of two fairly definite layers of cells. From the secondary ducts toward the surface the cells gradually show an irregular arrangement until near its attached end the primary duct is represented by a solid cord of epithelial cells.

5. Myers, J. A.: The Histology of the Mammary Gland in the Male and Female Albino Rat from Birth to Ten Weeks of Age, *Am. J. Anat.* To be published (*Abstr. in Anat. Rec.* **14**:46, 1918).

Eight Days (Held at Birth Weight).—In a female that was held at birth weight for eight days the milk ducts (Fig. 2) show considerably less branching than those in a normal rat of seven days. They show, however, a slightly greater tendency to branch than the ducts of the normal new-born rat. The new branches are confined chiefly to the free end of the gland; however, an occasional collateral duct appears on the secondary and tertiary ducts.

When examined macroscopically the nipples appear more prominent than in the new-born. The nipple has, therefore, grown somewhat in spite of the fact that the gross body weight remains the same as at birth, or has even decreased.

Eighteen, Twenty and Twenty-One Days (Held at Birth Weight).—Figure 3 shows the milk ducts of the abdominal and first inguinal glands of a normal female albino rat of twenty-one days. When compared with Figure 1 it will be noticed that from birth to twenty-one days a considerable proliferation and growth of the ducts has taken place. Figure 4, drawn from a female albino rat held at birth weight for eighteen days, shows that the proliferation and growth of the milk ducts have been retarded to a marked extent. The ducts show very little or no development beyond those of the animal held at birth weight for eight days (Fig. 2), or the normal at birth (Fig. 1). The milk ducts in the male rat held at birth weight for eighteen days show approximately the same degree of retardation as those in the female. The ducts in a female held at birth weight for twenty days (Fig. 5) show about the same extent of development as those in the eighteen day stage.

Microscopic sections through the glands of a female show that in spite of the fact that the animal was held at birth weight the nipple has developed beyond the new-born stage. Its development has been considerably retarded, however, as it is much less prominent than the nipple of normal animals of corresponding age. The stimulus that causes the rapid growth of the nipple in normal rats about the second week has apparently been affected by the inanition, as the rapid growth of the gland at this stage has been inhibited. The nipple is considerably elevated above the surface (Fig. 12) of the surrounding epidermis. Partially surrounding the basal part of the nipple is the sulcus, deep in which may be seen the projection of the epithelial hood. This projection shows very little or no further development than appears in the new-born. The processes which appear on the projection of the normal animals of eighteen to twenty-one days (similar to those shown in Fig. 14) are very small in the starved rat. The external opening or milk pore appears near the highest part of the nipple, the lumen leading from this into the intra-epidermal

part of the primary duct is quite shallow and is not continuous with the lumen of the primary duct proper. A cord of epithelial cells separates these two lumina, as is the case in normal animals until the second week of postnatal life is reached. The part of the attached end of the primary duct deep to the intra-epidermal portion is, therefore, without a lumen, but as one follows the sections toward the

Fig. 4.—Same as Figure 1, but starved so as to weigh only 5 gm. at 18 days, $\times 5$.

free end a lumen appears which is more regular in outline than in the new-born state, but is less well developed than in normal or control animals of same age as the test rats. Traced from the primary duct toward the free end of the system of ducts, the lumen presents the same general appearance as in normal animals of the same age except that it is somewhat smaller in caliber. The walls of the milk ducts beyond the primary duct possess the two layers of epithelial cells found in normal animals. Through the free end of the primary duct the cells are more irregularly arranged.

Fig. 5.—Same as Figure 1, but starved so as to weigh only 5 gm. at 20 days, $\times 5$.

Thirty-Three Days (Weight Restricted to 9.4 Gm.).—The female control animal reached a weight of 49 gm. at the end of the thirty-third day. The milk ducts, as shown in Figure 6, have grown and proliferated very rapidly since the 21-day stage (Fig. 3). While there is no overlapping between the ducts of adjacent glands, the ducts of the second thoracic gland are very nearly in apposition with those of the first and third thoracic glands. As seen in Figure 6, the ducts of the abdominal and first inguinal glands very nearly meet. Only a small interspace exists between the ducts of the first and second

Fig. 6.—Drawn from a cleared preparation (internal view) of a normal female albino rat of 33 days (weight 49 gm.) to show distribution and relations of ducts of right abdominal gland (A), and right first inguinal gland (B), $\times 5$. A.n., abdominal nipple; L.n.1, first inguinal nipple; p.d., primary duct; s.d., secondary duct; t.d., tertiary duct; tr.d., terminal duct; e.b., end-bud; L., lymph node.

inguinal glands. An examination of the glands of the underfed test animal, whose body weight never exceeded 9.4 gm., reveals the fact that the milk ducts are still in a very primitive state of development (Fig. 7). In spite of the fact that the body weight of this animal was allowed slightly to exceed that of a normal animal of one week, the milk ducts do not show as extensive proliferation and growth as those in a normal animal of one week. In fact some of the glands of this animal appear very slightly or no better developed than those in normal animals at birth.

Fig. 7. Same as Figure 6 but from test animal of same litter which was starved so as to weigh only 9.4 gm. at 33 days, $\times 5$

The study of microscopic sections shows the nipple slightly more elevated above the surface of the surrounding integument than in test animals of 18 to 21 days of age. The sulcus around the nipple presents approximately the same depth as in the preceding stage. The projection of the "epithelial hood" is in a rudimentary state of development. The sections show rather numerous projections extending

Fig. 8.—Same as Figure 1, but starved so as to weigh only 10 gm. at 38 days, $\times 5$.

inward from the epidermis covering the nipple. The lumen of the intra-epidermal part of the primary duct has deepened somewhat, but is not quite continuous with that of the primary duct proper.

Thirty-Eight Days (Weight Restricted to 10 gm.).—In a female of 38 days, whose body weight never exceeded 10 gm., the milk ducts show a very slight increase in length over those in the normal newborn. In Figure 8 it will be observed that there is an occasional col-

lateral duct branching from the secondary and tertiary ducts. Generally, however, collateral ducts are not numerous on any part of a system of ducts. Compare this and preceding with normal at 1 week (about 10 gm.).

Fig. 9.

Fig. 9.—Drawn from a cleared preparation (internal view of a male albino rat of 58 days, weight 96 gm.) to show distribution and relations of ducts of right abdominal gland (A), and right first inguinal gland (B), $\times 5$. In the illustration p.d.=primary duct; s.d., secondary duct; t.d., tertiary duct; tr.d., terminal duct; e.b., end-bud; L., lymph node.

Fifty-Eight Days (Weight Restricted to 10.9 gm.).—The male control animal weighed 96 gm. at the age of 58 days. The milk ducts (Fig. 9) show about the normal amount of branching for males of this age, there being a failure of the ducts to respond to the puberty

Fig. 10.

Fig. 10.—Same as Figure 9, but from test animal of same litter which was starved so as to weigh only 10.9 gm. at 58 days, $\times 5$.

changes occurring in the female.¹ In the test animal with a body weight of 10.9 gm. the milk ducts (Fig. 10) show approximately the same degree of retardation as those of the female. In other words, the ducts show about the same number of branches, and are, in general, of the same size as at the time of birth, notwithstanding the fact that the body weight of the test animal is more than double that of the new-born.

Fifty-Eight Days (Weight Restricted to 15.5 Gm.).—This animal was allowed to reach a body weight equal to that of a normal rat of 2 weeks. The increase in weight over the last stage, however, had no apparent effect on the growth or proliferation of the milk ducts, as they do not appear noticeably different from those of an animal of the same age with a smaller body weight.

The nipples in microscopic sections show no greater elevation than in animals held at 9.4 gm. for thirty-three days. Normal rats with a body weight of 15.5 gm. possess nipples much more elevated than underfed animals of the same weight. It appears, therefore, that during underfeeding very little of the weight added to the body between the 33 and 58-day stages is accompanied by growth of the mammary glands. The systems of milk ducts in the 58-day underfed rats show the same structure as earlier described stages. The lumina do not communicate with the exterior, owing to the cord of epithelial cells persisting between the lumen of the intra-epidermal part of the primary duct and that of the primary duct proper. The lumen of the intra-epidermal part of the primary duct contains débris derived from the process of desquamation and delamination in the formation of the lumen.

Sixty-Five Days (Weight Restricted to 8.5 Gm.).—It was shown earlier[†] that the milk ducts of the normal female albino rat undergo a tremendous proliferation during the eighth or ninth week—the time when puberty usually appears. The control animal used in the present study had reached a body weight of 82.5 gm. on the sixty-fifth day, the time of killing. The ducts of the mammary glands have developed to such an extent that there is a decided overlapping of the ducts of adjacent glands. The ducts of the thoracic glands have overlapped so as to form on each side a continuous arborization of ducts which extends from the cephalic portion of the first thoracic to the caudal part of the third thoracic gland. The ducts of the abdominal and inguinal glands on each side likewise show a continuous arborization which extends from the cephalic part of the abdominal to the most caudal ducts of the second inguinal gland. In the test animal, which was held at 8.5 gm. by underfeeding, no such development has occurred. The milk ducts are somewhat longer than those in the new-born, but otherwise there is no apparent difference.

Microscopic sections through the nipples of test and control animals show a considerable contrast. The nipple of the control has reached a considerable elevation and has taken on a somewhat conical form. The projection of the "epithelial hood" presents numerous processes, while in the central part of the attached end of the projection degenerative changes are in progress. The system of milk

ducts communicates freely with the exterior through the milk pore. The nipple of the test rat, on the other hand, is only slightly elevated and does not present a conical form. The projection of the "epithelial hood" is very rudimentary. There is a very slight communication of the system of milk ducts through the milk pore, the lumen of the intra-epidermal part of the primary duct not being completely formed.

Seventy Days (Weight Restricted to 16.5 Gm.).—The milk ducts of this female rat show nothing different from that which has been described in the foregoing stages. The ducts remain in a very poorly developed state.

Fig. 11.—Same as Figure 1, but from a test animal which was starved so as to weigh only 8.5 gm. at 65 days, $\times 5$.

Fig. 12.—Drawn from a section through the nipple of a female albino rat. Starved so as to weigh only 5 gm. at 18 days, $\times 66\frac{2}{3}$; ep., epithelium; ep.in., epithelial ingrowth or hood; n., nipple; p.d., primary duct; s., sulcus around base of nipple.

Fig. 13.—Drawn from a section through the nipple of a female albino rat. Starved so as to weigh only 16.5 gm. at 70 days, $\times 66\frac{2}{3}$. Compare with Figure 14. ep., epithelium; ep.in., epithelial ingrowth or hood; n., nipple; p.d., primary duct; s., sulcus around base of nipple.

Microscopic sections (Fig. 13) show the nipple remaining at about the same degree of elevation as in the 33-day underfed rats. The projections of the "epithelial hood" have failed to develop beyond the stages previously described. A slight communication has appeared between the lumen of the intra-epidermal part of the primary duct and that of the primary duct proper. Therefore, the lumina of the system of ducts have a common opening to the exterior through the milk pore. This condition normally is present in the rat at the end of the second week of postnatal life; however, it is usually not until the fifth or sixth week that this communication has attained its normal caliber. The two-layered arrangement of the epithelial walls of the milk ducts persists. No parts resembling developing alveoli have been observed, and there is no indication of lobulation. The mantle layer

(which immediately surrounds the milk ducts) of the stroma is thinner than in normal rats of the same age. The true stroma which normally contains such an abundance of fat is nearly or quite free from fat. The entire stroma appears much more cellular and less vascular than in normal animals of the same age.

2. *Effects of Refeeding.*—This part of the present article should be regarded only as a preliminary report, as further work now in progress will be presented at a later time.

Fig. 14.—Drawn from a section through the nipple of a normal female albino rat of nine weeks, $\times 66\%$. Labeling same as in Figure 13. Compare with Figure 13.

Seventy days (weight restricted to 10 gm. for nineteen days, then placed on normal diet. Weight 42 gm.): The glands of the control animal show the normal extensive development which occurs about the time of puberty described in an earlier article.⁴ From the gross body weight of the test rat one might expect to find the milk ducts in a stage of development nearly equal to those of a normal rat of 4 or 5 weeks. This, however, is not the case. As shown in Figure 15, the ducts have grown and proliferated considerably beyond those in animals of 18 to 21 days held at approximately birth weight (Figs. 4 and 5). The ducts of this animal are quite comparable in their extent of development with those of a normal rat of about 3 weeks (compare with Fig. 3).

Microscopic sections show that the nipple in the re-fed animals possesses a diameter somewhat greater than that of the underfed animal of 70 days. The elevation is approximately the same. The refeeding has apparently had an effect on the development of the projection of the "epithelial hood," as this projection now presents a somewhat greater diameter than in animals before the refeeding; besides, it possesses a number of processes, as does also the inner surface of the epidermis covering the nipple. These processes are somewhat larger than those seen in the starved rats (Figs. 12 and 13).

Fig. 15.—Drawn from a cleared preparation (internal view) of a female albino rat to show distribution and relations of ducts of right abdominal gland (A), and first inguinal gland (B), $\times 5$. This animal was starved so as to weigh only 10 gm. at the nineteenth day of life, after which it was placed on normal diet until 70 days old, when it weighed 42 gm. A.n., abdominal nipple; I.n.t., first inguinal nipple; p. d., primary duct; s.d., secondary duct; t.d., tertiary duct; tr.d., terminal duct; e.b., end-bud.

The milk ducts have increased somewhat in diameter, but the epithelium of the walls is arranged in the two usual layers except the intra-epidermal part of the primary duct, which is lined with the stratified squamous type. The epithelial cells appear somewhat larger than in animals that have not been re-fed and mitotic figures are not uncommon. The stroma does not appear as cellular as when the animals were being starved. Moreover, a considerable amount of fat has made its appearance in the true stroma.

One hundred and twelve days (weight restricted to 10 gm. for nineteen days; then placed on normal diet until gross body weight reached 85 gm., that of control killed at 70 days): This female rat was from same litter as the preceding. Figure 16 shows that the milk ducts have undergone a considerable development beyond those of the sister killed at 70 days, with a body weight of 42 gm. They

have not, however, reached the same degree of development as those of the control killed at 70 days with a corresponding body weight. In the control animal, the ducts of the thoracic glands overlap so as to form a continuous arborization on each side. The abdominal and inguinal glands also form on each side a continuous mass of gland tissue. In the test rat, the ducts of the abdominal and inguinal glands are nearly in apposition and only rarely is there an overlapping. Collateral ducts are much more numerous on the secondary, tertiary and quaternary ducts than on those milk ducts nearer the free end of a system. In many cases the collateral ducts present many branches. The milk ducts as a whole appear to have a diameter smaller than those of normal animals and the terminal end-buds are not so numerous. Those present, however, stand out very strikingly (Fig. 16).

One hundred and twenty-five days (weight restricted to 10 gm. for twenty days; then placed on normal diet until time of killing. Gross body weight 97 gm.): In this female specimen the ducts show an arborization very similar to that of a normal rat of about the age of puberty. Several individuals subjected to similar treatment and killed at approximately the same age as this animal show the milk ducts in a condition similar to those of this specimen. Therefore, we can conclude that in animals subjected to severe inanition during the first three weeks of life the mammary glands are so retarded that it is not until near the eighteenth week that the glands have attained a development equal to that of normal animals of about 9 weeks. Along with the growth of the milk ducts the nipples have developed so that they, too, have reached a stage similar to that reached in normal animals about the age of puberty.

Similar refeeding experiments have been carried out on male individuals with results very similar to those obtained in females except that the male ducts do not reach such a high stage of development. The ducts are retarded in the male as in the female; on refeeding, however, they apparently only keep pace with the growth of the body of the animal.

DISCUSSION AND CONCLUSIONS

The test rats used in the first part of this paper may be divided into three classes. In the first class we have those animals that were held at birth weight and killed at various intervals up to about 3 weeks of age. In the second class are included animals which were starved from birth but were allowed to reach a weight approximately double that at the time of birth. These animals were killed at various stages, the oldest being 65 days of age. The third stage includes animals starved from birth, but whose body weights were allowed to increase

Fig. 16.—Same as Figure 15, but animal was placed on normal diet at end of period of starvation until 112 days old, at which time it weighed 85 gm., $\times 5$. Compare this figure with Figures 12 and 13 of an earlier paper (Am. J. Anat. **19**:385, 1916.

to approximately three or four times the birth weight. The oldest animal in this class was underfed for seventy days before killing.

In the first class it was noticed that the milk ducts grew very little during the first week, after which time growth apparently ceases. However, the nipple becomes somewhat more elevated above the surface than normally at the time of birth.

It has been shown (Stewart⁶) that in animals held at birth weight by underfeeding for various periods, the integument increases about 25 per cent. in weight. There is normally a strong tendency for the integument to grow during the first week of life. Jackson and Lowrey⁷ and Jackson⁸ showed that during this first week of life the integument increases from 20 per cent. to 26 per cent. of the body weight. In Stewart's test animals a fair coat of hair developed. It is therefore possible that the hair and follicles play a considerable rôle in increasing the weight of the integument. As shown in the present article, the mammary glands increase in size but little, however, and therefore scarcely participate in the increase of the weight of the integument during the underfeeding period. Further histologic study of the integument is necessary to ascertain whether parts other than the hair and mammary glands increase in size during this severe inanition.

In the second class, where the body weight in the underfed rats doubled that at the time of birth, the milk ducts show a slight increase, but are not equal to those of a normal animal of the same body weight. These animals are considerably older than those in Class 1, all being killed after the third week. In rats similarly underfed from birth, the body weight being retarded so as to reach only 10 gm. at 3 weeks of age, Stewart⁹ found the weight of the integument about equal to that of normal controls of the same body weight. In rats underfed at a later period, beginning at three weeks of age, Jackson¹⁰ has shown that there is a marked loss in the relative weight of the integument.

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6. Stewart, C. A.: Changes in the Weights of the Various Parts, Systems and Organs in Albino Rats Kept at Birth Weight for Various Periods, *Am. J. Physiol.* **48**:67, 1919.

7. Jackson, C. M., and Lowrey, L. G.: On the Relative Growth of the Component Parts (Head, Trunk and Extremities) and Systems (Skin, Skeleton, Musculature and Viscera) of the Albino Rat, *Anat. Rec.* **6**:449, 1912.

8. Jackson, C. M.: Postnatal Growth and Variability of the Body of the Various Organs in the Albino Rat, *Am. J. Anat.* **15**:1, 1913.

9. Stewart, C. A.: Changes in the Relative Weights of the Various Parts, Systems and Organs of Young Albino Rats Underfed for Various Periods, *J. Exper. Zool.* **25**:301, 1918.

10. Jackson, C. M.: Effects of Acute and Chronic Inanition on the Relative Weights of the Various Organs and Systems of Adult Albino Rats, *Am. J. Anat.* **118**:75, 1915; Changes in the Relative Weights of the Various Parts, Systems and Organs of Young Albino Rats Held at Constant Body Weights by Underfeeding for Various Periods, *J. Exper. Zool.* **19**:99, 1915.

The effect of inanition at various ages on the weight of the integument is discussed by Jackson¹⁰ and Stewart.¹¹ They state that the loss in weight of the integument in young rats during underfeeding is probably due largely to loss of fat.

In a study (uncompleted) on the subcutaneous fat of the albino rat I have been able to demonstrate the presence of considerable amounts of such fat deposit in fairly definite pads in the subcutaneous tissues of the rat before three weeks of age. In the underfed rats used by Jackson and Stewart the fat deposited in the subcutaneous fat depots was of course soon consumed. In my preparations the starving began at the time of birth, but extended far beyond the three week stage. In such rats the body weight increased somewhat during which time the mammary glands showed a very slight increase. No observations have been made to determine whether the mammary glands remain stationary or (like the weight of the integument) actually undergo a decrease in size when the inanition begins at the third week of age or later.

The mammary glands of the rats in the third class (although subjected to less severe inanition) do not show anything essentially different from those of the second class just described. In general, the development of the mammary glands in rats thus stunted by underfeeding is retarded in proportion to the body weight.

It is generally believed that there is such a close relationship existing between the mammary glands and the ovaries that when important changes take place in the ovaries the mammary gland might also be affected. In view of this fact it is interesting to compare the growth of these organs in starved animals. Stewart⁸ showed that in animals held at birth weight for sixteen days the ovaries increase about 5 per cent. The mammary glands from these same animals here described under Class 1 show only a very slight increase. Therefore, one may conclude that the two organs undergo a somewhat parallel development under these conditions. In those animals underfed from birth to 3 weeks, body weight 10 gm., and those underfed from birth to 10 weeks, body weight 15 gm., Stewart⁹ found the ovaries increased in weight 83 per cent. and 54 per cent., respectively. My Figures 7 and 8 show a much smaller increase in the mammary glands under the same conditions. There is, therefore, apparently no close correlation between the growth of the mammary glands and that of the ovaries in underfed young rats.

As shown by the present study, the mammary glands apparently respond somewhat slowly when the animals are refed after under-

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11. Stewart, C. A.: Growth of the Body and of the Various Organs of Young Albino Rats after Inanition for Various Periods, *Biol. Bull.* **31**:16, 1916.

feeding from birth to about 3 weeks of age. In fact, the response was so delayed that the mammary glands did not reach the stage of development ordinarily attained at the time of puberty (about 8 or 9 weeks) until the refed rat had reached an age of about 18 weeks. Stewart¹¹ showed that in rats on which the underfeeding was begun at the time of weaning (3 weeks) or later, and underfed for short periods, the integument and ovaries recovered very rapidly when the animals were refed. Later, however, Jackson and Stewart⁹ showed that when the underfeeding is begun at birth and continued three weeks or longer, a permanent stunting of the body usually occurs. In view of the great individual variation in the development of the mammary glands at any given age or body weight (as shown by Myers⁴), it is hazardous to draw any final conclusions from the relatively few cases observed in the present study. Apparently, however, the mammary glands in the underfed young rats, though temporarily lagging somewhat behind the body weight when the rats are fully refed, ultimately may attain a normal degree of development.

SUMMARY

1. Severe inanition retards the growth of the milk ducts of the female rat during the first week, but apparently does not completely stop their growth. In animals held at birth weight for a longer time the ducts cease to grow, and remain in a condition slightly more developed than at the time of birth. If after the first week the gross body weight of the animals is allowed to increase so as to correspond with that of a normal animal of one week, the milk ducts fail to develop to the same extent as those of a normal animal of corresponding body weight. This also holds true if the body weight of the underfed rat is allowed to equal that of a normal animal of two weeks.

2. The lumen of the primary duct in underfed rats does not communicate with the exterior through the milk pore until the tenth week.

3. The growth of the milk ducts of male rats is retarded by inanition in a manner similar to that of the female.

4. The nipple grows very little during inanition, being elevated above the surface only slightly in young rats starved severely for eight to ten weeks. The epithelial processes fail to develop much beyond the stage reached at birth, and the sulcus around the base of the normal nipple remains shallow.

5. The subcutaneous fat that appears very early in the neighborhood of the milk ducts soon becomes greatly decreased after the amount of food is reduced to a minimum.

6. In all, the retardation in the development of the mammary gland is roughly proportional to the retardation in body weight (at least within limits of normal variability).

7. Severe inanition for a short time at an early age thus temporarily stunts the mammary glands. When the animal is refed the glands respond slowly. When the body weight during refeeding reaches that of a normal rat at the age of puberty, the milk ducts are far behind those of the normal rat at corresponding body weight. That this stunting is not permanent is shown by the fact that the ducts ultimately attain the same stage of development as those of a normal animal, but at a much later period.