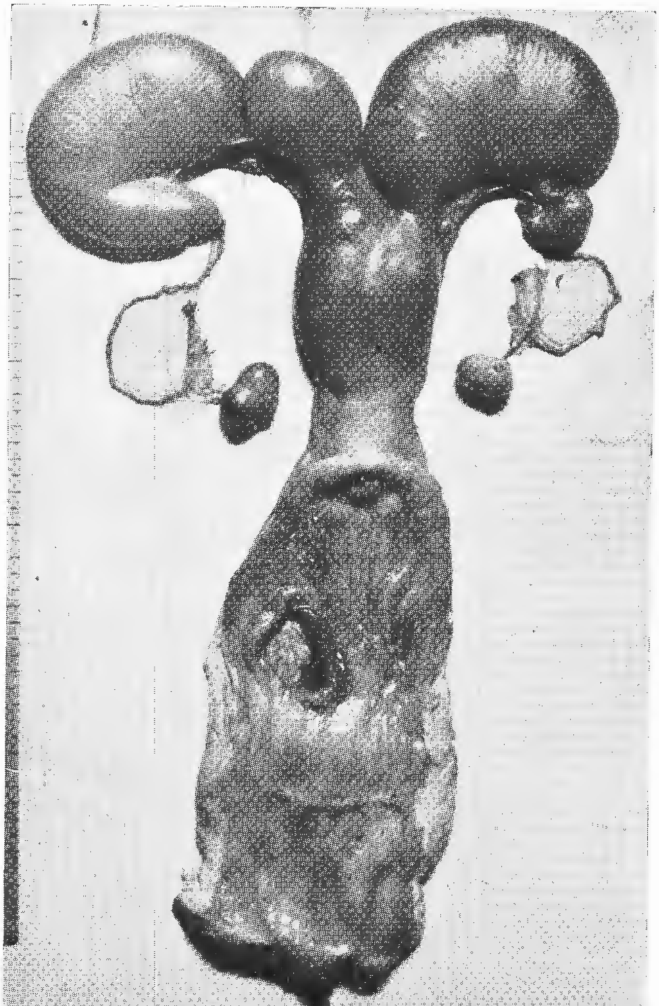

FIG. 34.—Genitalia of Cow 7470. Hydrometra, bilateral follicular ovarian cysts and vaginal fibroma. Scale: Centimetres. (For histological structure of cervix, uterus and fallopian tube see Figs. 20, 30 and 85, respectively.)

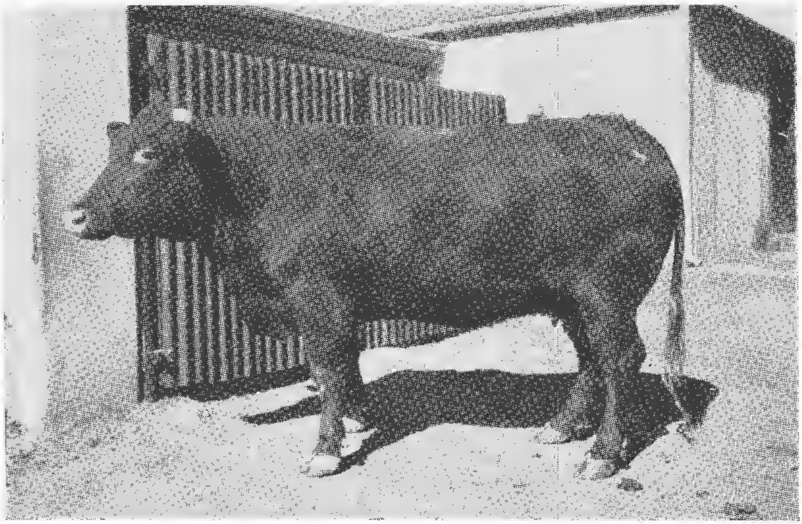

FIG. 35.—Cow 7277, five years eight months old.

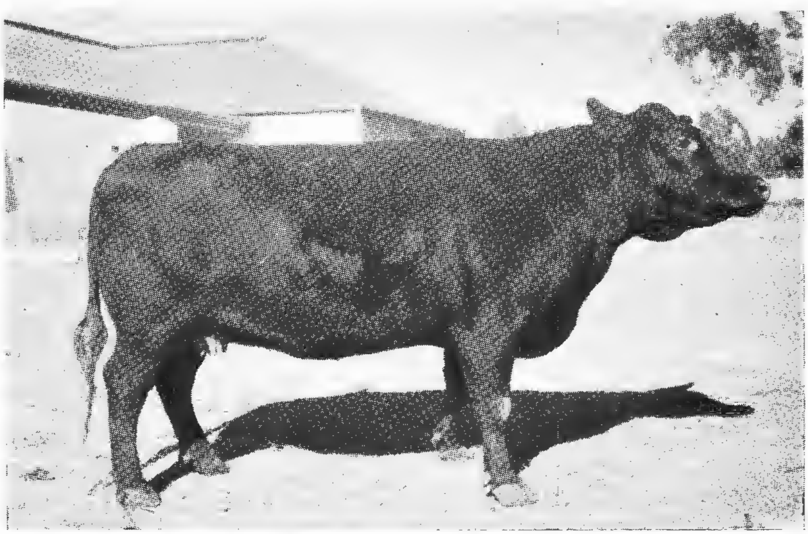

FIG. 36.—Cow 7172, six years two months old.

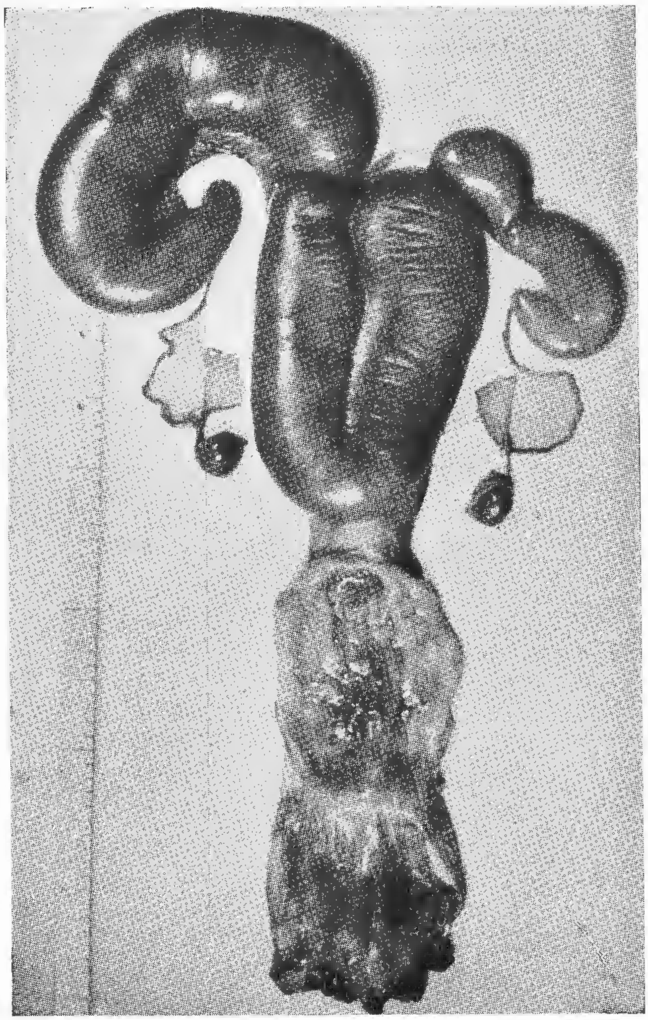

FIG. 37.—Genitalia of Cow 7277. Hydrometra and bilateral follicular ovarian cysts. Scale: Centimetres. (For histological structure of vaginal mucosa, uterus and anterior pituitary see Figs. 9, 31 and 111, respectively.)

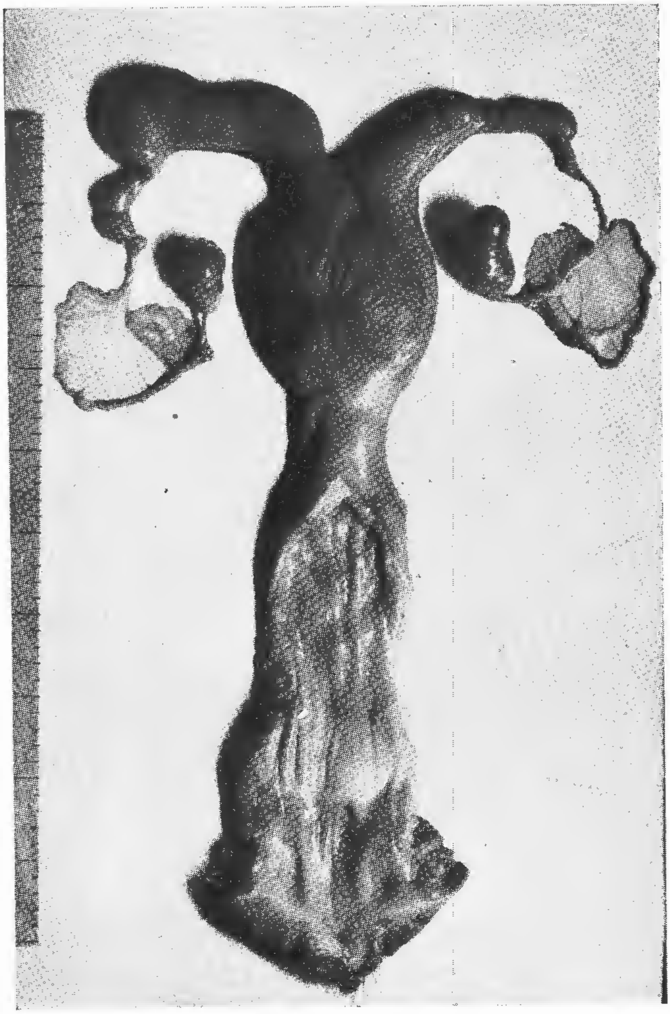

FIG. 38.—Genitalia of Cow 7172. Hydrometra and bilateral follicular ovarian cysts. Scale: Centimetres. (For histological structure of uterus and anterior pituitary see Figs. 32 and 114, respectively.)

FIG. 39.—Cow 7271, five years eight months old, 18 days after first parturition. Calf stillborn.

FIG. 40.—Cow 6495, six years eight months old.

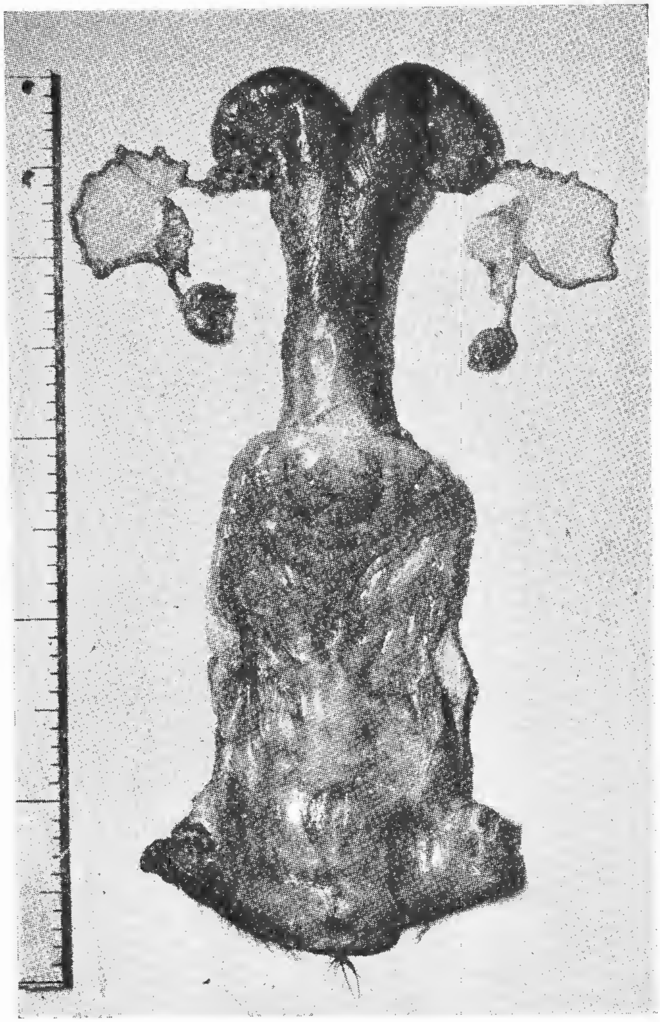

FIG. 41.—Genitalia of Cow 7271, normal, primiparous, at 13 days post-oestrum. Note well developed cervix and thick, muscular cornua. The corpus luteum of last ovulation and a maturing follicle are visible in the left overy. Scale: Centimetres.

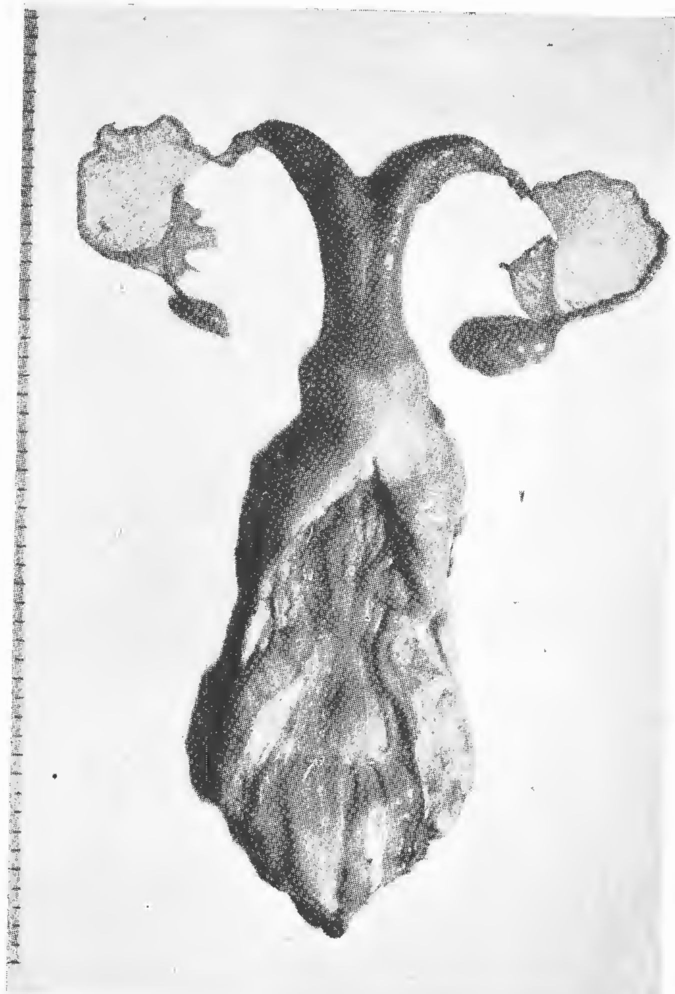

Fig. 42.—Genitalia of Cow 6495. Note infantile uterus and cervix. Left ovary atrophic and contains small, cystic follicles. Right ovary contains three large follicular cysts. Scale: Centimetres. (For histological structure of vagina, uterus and ovarian cysts see Figs. 8, 29, 94 and 99, respectively.)

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FIG. 43.—Cow 7469, four years eight months old.

FIG. 44.—Cow 7385, five years two months old.

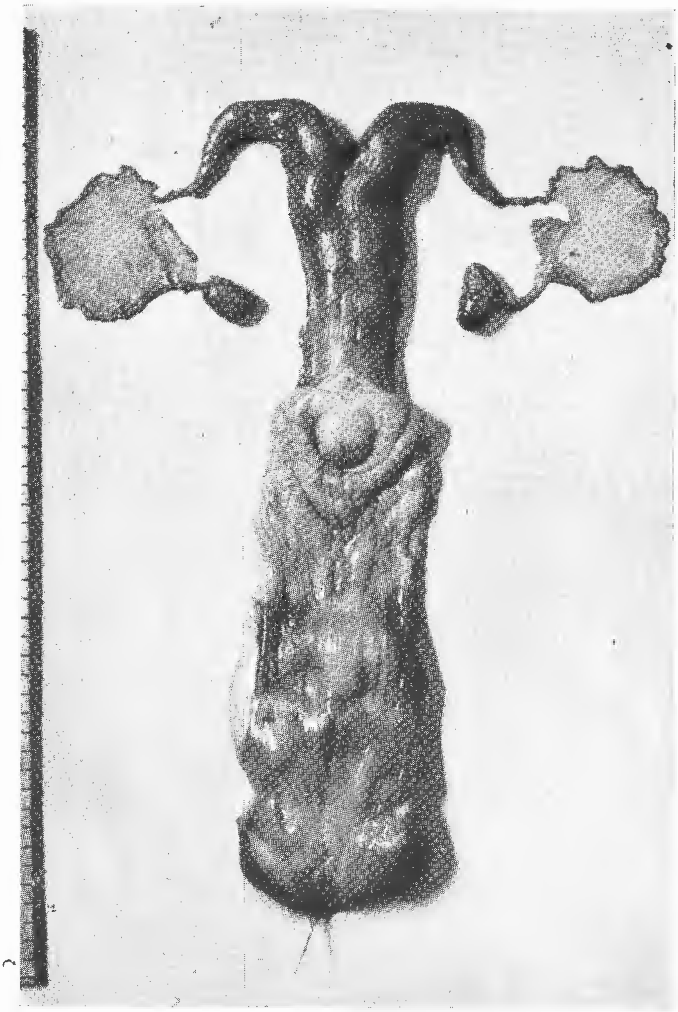

Fig. 45.—Genitalia of Cow 7469, ten days post-oestrum, functionally sterile. Note infantile uterus and cervix. Corpus luteum of last ovulation in right ovary and maturing follicle in left. Scale: Centimetres. (For histological structure of cervix and fallopian tubes see Figs. 14 and 78, respectively.)

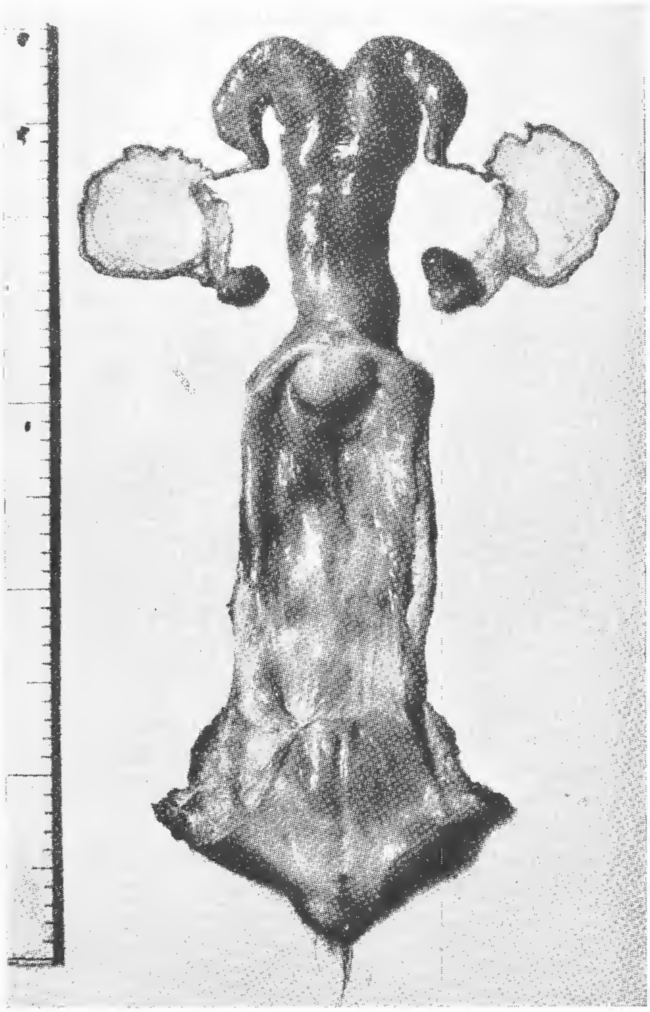

FIG. 46.—Genitalia of Cow 7385, 26 days pregnant, spontaneously recovered from nymphomania. Note infantile uterus and median band in vagina. Corpus luteum of pregnancy in right ovary and mature follicle in left. Scale: Centimetres. (For histological structure of vagina, cervix and fallopian tubes see Figs. 5, 17 and 81.)

FIG. 47.—Cow 6358, seven years six months old.

FIG. 48.—Cow 6442, seven years old.

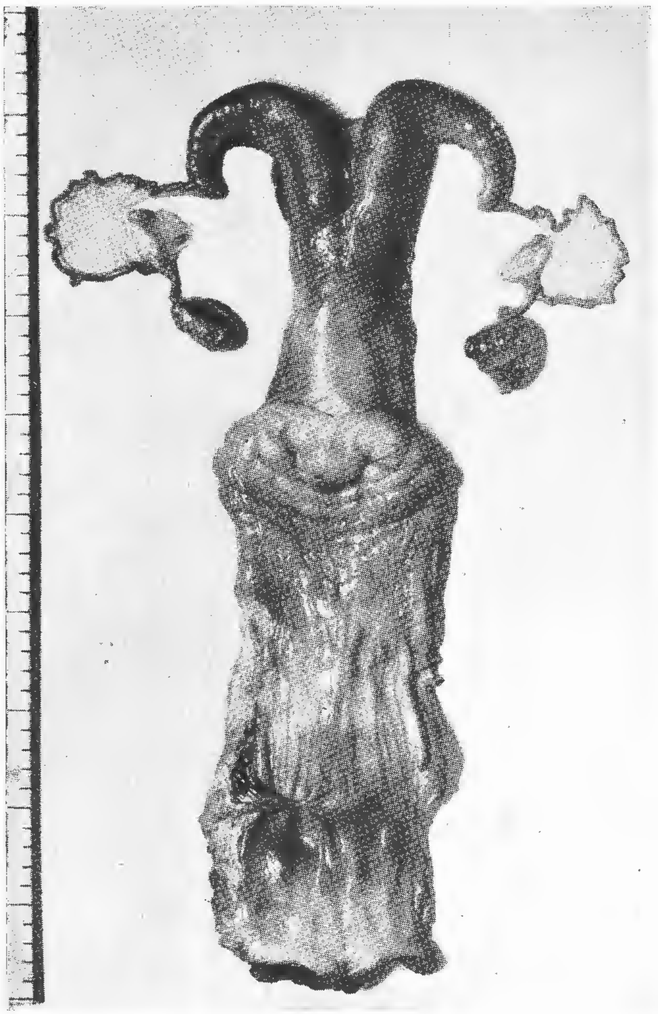

FIG. 49.—Genitalia of Cow 6358, 11 days post-oestrum, functionally sterile. Note infantile uterus and median band in vagina. Corpus luteum of last ovulation and maturing follicle in right ovary. Scale: Centimetres. (For histological structure of vagina, ovary and anterior pituitary see Figs. 3, 100 and 115.)

FIG. 50.—Genitalia of Cow 6442, functionally sterile, 24 days post-oestrum. Note median band in vagina, infantile cervix and uterus. Also beadlike retention cysts in Gärtner's canals behind, and on either side of, the os. The wall of the left cornu, at the bifurcation, contains a fibroleiomyoma. Corpus luteum of last ovulation and mature follicle in left ovary. Scale: Centimetres. (For histological structure of fallopian tube see Fig. 88.)

FIG. 51.—Cow 6442, horizontal vulva.

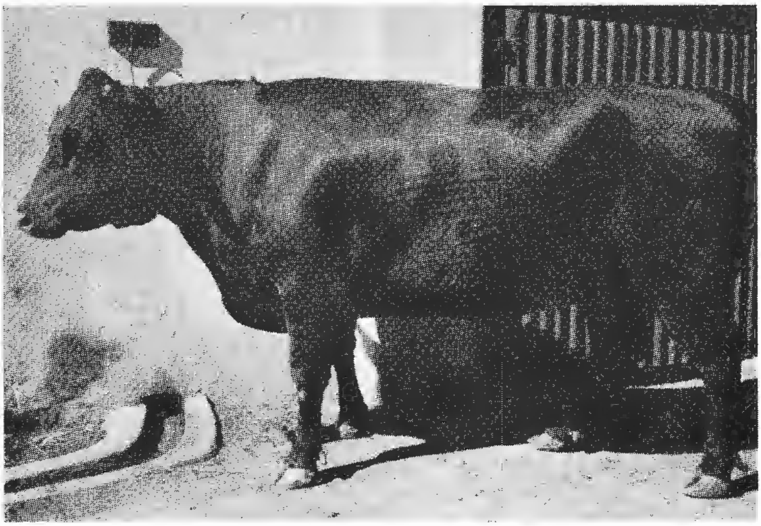

FIG. 52.—Cow 7346, five years five months old.

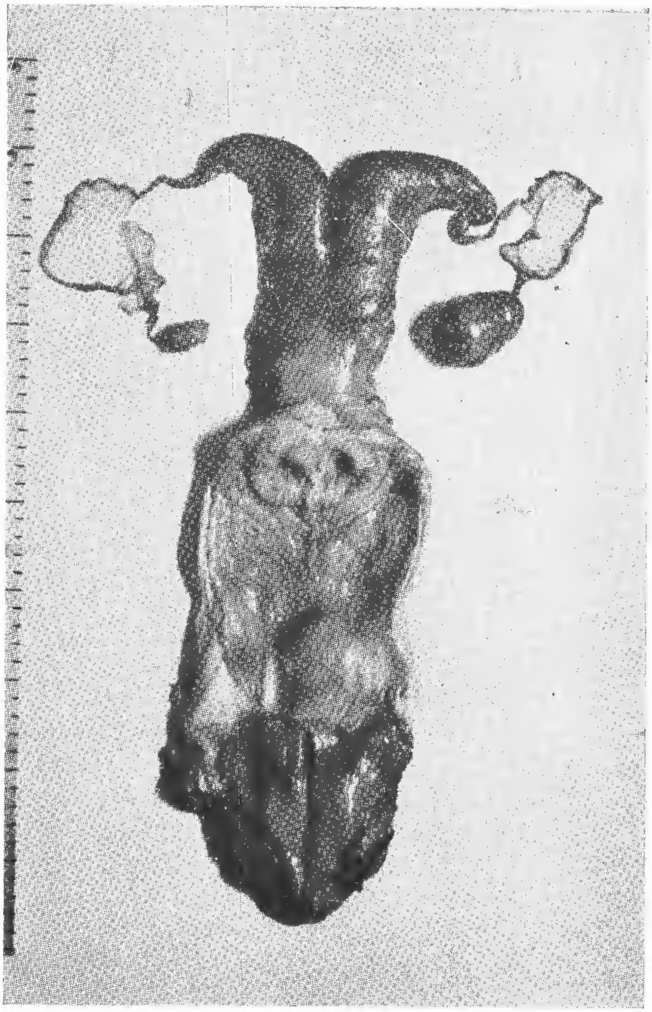

FIG. 53.—Genitalia of Cow 7346. Note median band in the vagina, double cervix and uterus (see also Figs. 24 and 25). Infantile uterus, atrophic left ovary and large follicular cystic right ovary. Scale: Centimetres. (For histological structure of ovary see Fig. 90.)

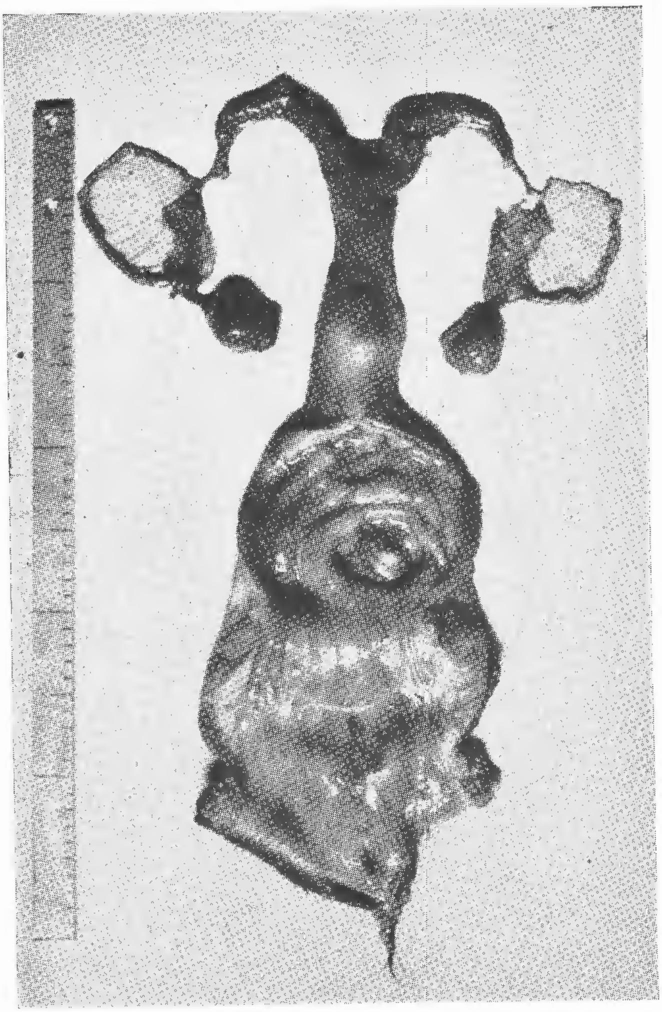

FIG.—54.—Genitalia of Cow 7355. Note vaginal fibroma, cervical retention cyst visible under the serosa, infantile cervix and uterus and bilateral large follicular ovarian cysts. Scale: Centimetres. (For histological structure of ovary see Fig. 91.)

Fig. 55.—Cow 7355, five years four months old.

Fig. 56.—Cow 6363, seven years eight months old.

FIG. 57.—Genitalia of Cow 6363. Note infantile cervix and uterus, cystic endometrium (right cornu opened), and bilateral large follicular ovarian cysts. Scale: Centimetres. (For histological structure of cervix, uterus, fallopian tube and ovary see Figs. 21, 28, 84 and 93, respectively.)

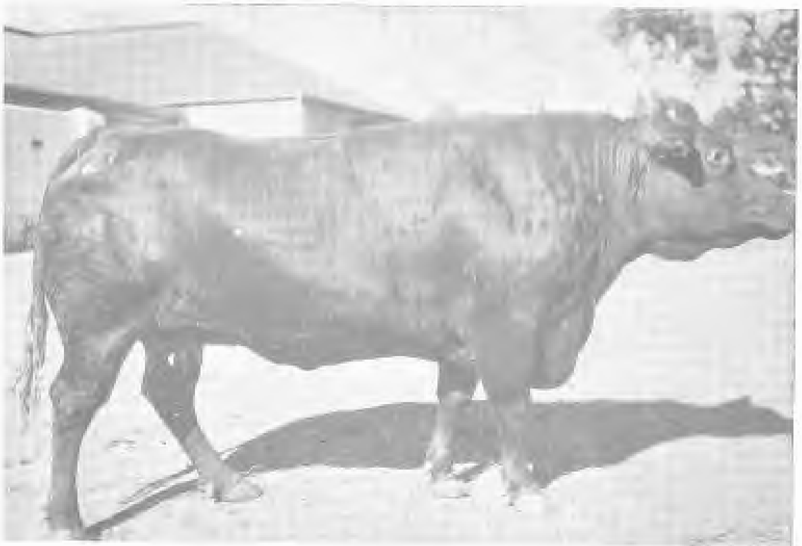

FIG. 58.—Cow 6362, seven years eight months old. Note nymphomaniac characteristics.

FIG. 59.—Hindquarters of Cow 6362. Note elevation of root of tail and relaxation of sacro-sciatic ligaments.

FIG. 60.—Genitalia of Cow 6362. Note infantile cervix and uterus, cystic endometrium (left cornu opened) and bilateral large follicular ovarian cysts. Scale: Centimetres. (For histological structure of vagina and ovaries see Figs. 11, 96 and 97, respectively.)

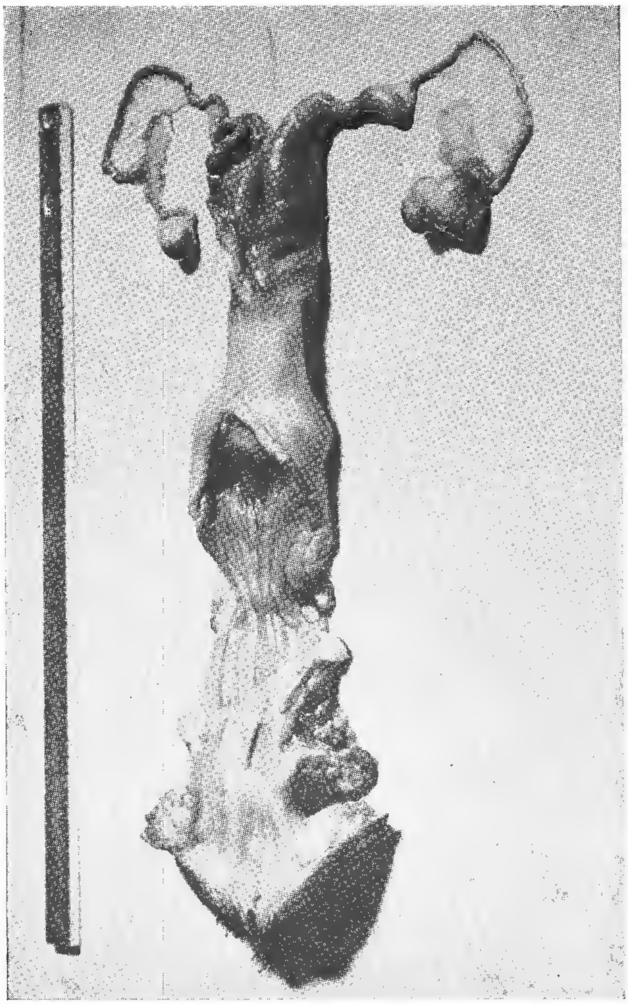

FIG. 61.—Genitalia of Cow 6496. Note infantile uterus and cervix, cystic endometrium (left cornu opened) and bilateral large follicular ovarian cysts. Scale: Centimetres. (For histological structure of vagina, cervix, uterus, fallopian tube and ovary see Figs. 10, 23, 27, 86 and 95, respectively.)

FIG. 62.—Cow 6496, six years eight months old.

FIG. 63.—Cow 6423, seven years one month old.

FIG. 63A.—Hindquarters of Cow 6423. Note elevation of the root of the tail and depression of the lumbar region.

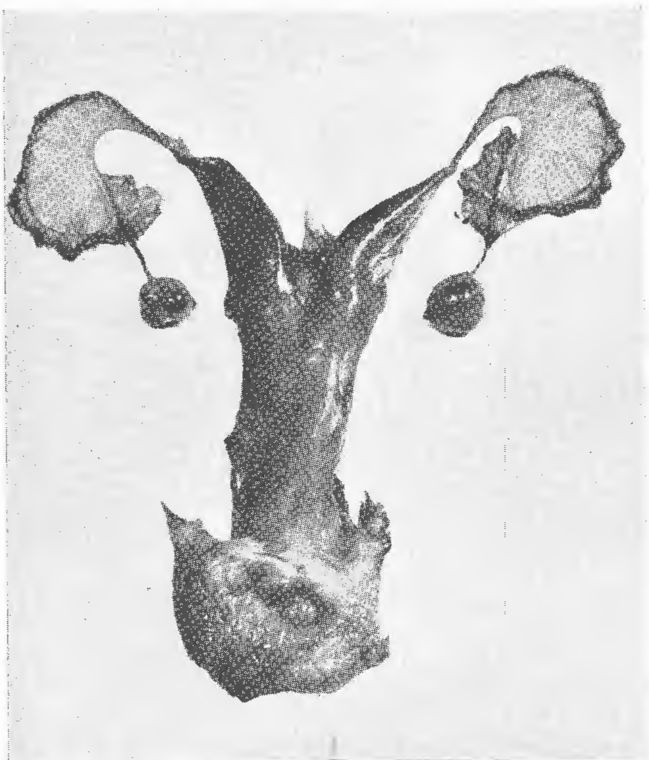

FIG. 64.—Genitalia of Cow 6423. Note infantile cervix and uterus and bilateral large follicular ovarian cysts. (For histological structure of ovary see Fig. 98.)

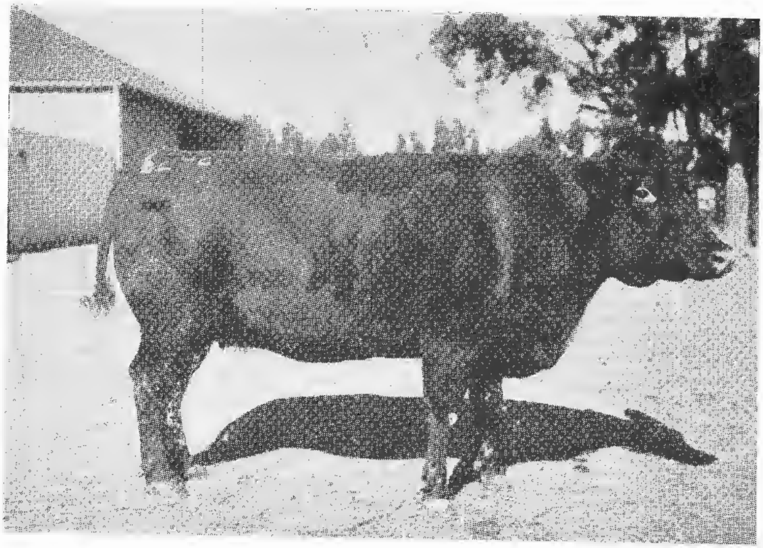

FIG. 65.—Cow 6292, seven years 11 months old. 59 days pregnant —third pregnancy. (Two previous abortions.)

FIG. 66.—Cow 6452, seven years old. 77 days after first parturition—calf stillborn. (One previous abortion.)

FIG. 67.—Cow 7045, six years seven months old, with first calf, five days old.

FIG. 68.—Cow 7157, six years five months old, with first calf 90 days old.

FIG. 69.—Cow 7189, six years one month old. 117 days after first parturition—calf stillborn.

FIG. 70.—Cow 7269, six years old, with first calf, 15 days old.

FIG. 71.—Cow 7276, five years nine months old, with first calf, 35 days old.

FIG. 72.—Cow 7378, five years four months old, with first calf, 79 days old.

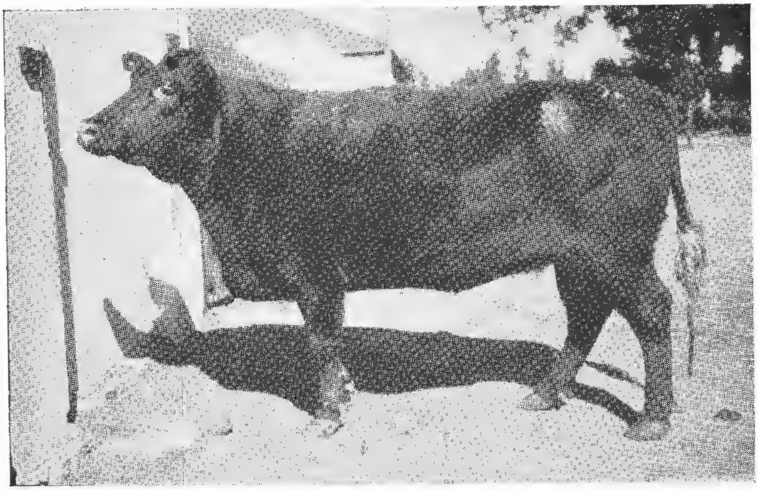

FIG. 73.—Cow 7401, five years old, 54 days pregnant—first pregnancy.

FIG. 74.—Cow 7471, four years eight months old, non-pregnant.

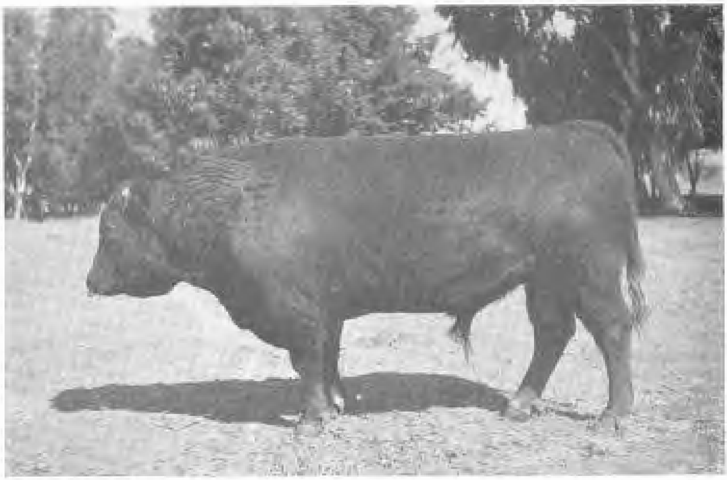

FIG. 75.—Bull 8056, used throughout the greater part of the experiment.

In the group "Fertile Non-pregnant" animals, are included those which had at some time conceived, whether conception had terminated in normal parturition or abortion (Table XXI), but which were non-pregnant at the time of slaughter.

In the group "Pregnant" the uteri of animals in advanced pregnancy were not measured, the greatly distorted components making accurate measurements impossible. In these cases the total weight (minus uterine contents) only were recorded.

Cow No. 6442 had a small fibroleiomyoma in the wall of the left horn of the uterus near the bifurcation, (Fig. 50). Although this animal was suffering from functional sterility, the neoplasm was not considered as being contributory to the causation of the disease.

E. Fallopian Tubes.

Allen (1938), using the colchicine method, has demonstrated that the injection of oestrogenic hormone stimulates extensive cell division in the tubal epithelium of the rat, mouse and monkey.

Extensive degeneration of cells and their extrusion into the lumen of the tubes during met-oestrum in the mouse have been reported by Allen (1923) and Espinasse (1935), both quoted by Allen, Hisaw and Gardner (1939). Degenerative changes in the tubal epithelium have also been observed by Snyder (1923, 1924) in the pig and woman.

In addition to division of the epithelial cells secretory activity of the tubal epithelium is dependent upon hormonal stimulation. Courrier (1924) quoted by Allen *et al.* (1939) found that, following ovariectomy, there is cessation of secretion which can be induced again by the injection of oestrogens.

Kok (1926), quoted by Allen *et al.* (1939) has studied spontaneous contractions of the uterine tubes of pigs, sheep and cows, *in vitro,* and reported peristaltic contractions which were minimal at about the time of ovulation.

Moreaux (1913) quoted by Hammond (1927) has shown that a cycle of secretion exists in the epithelium of the Fallopian tubes of mammals.

Bergmann (1921) quoted by Hammond (1927) found no changes in the length of the fallopian tubes during pregnancy.

Quinlan (1929), in discussing the causes of salpingitis, states that tubal affections do not occur independently, but are due to secondary invasion from existing pathological lesions in the genital tract or peritoneum. He describes a case of hydrosalpinx and cystic pavilionitis in an eighteen months old Friesland heifer which had never been served. This animal was suffering concurrently from cystic ovaries. He observes that salpingitis is frequently associated with follicular or corpus luteum cysts. He describes vacuolation in the epithelial cells lining the cysts in hydrosalpinx and associates this vacuole formation with secretion or regressive changes.

Williams (1943) shares the view held by Quinlan (1929) in that tubal diseases are secondary to uterine and cervical infections. He observed cases of hydrosalpinx in heifers, however, which were not known to have been pregnant. He states that superficially it would appear that hydrosalpinx is regularly a consequence of salpingitis, as adhesions between the pavilion and oviduct and cystic corpus luteum are nearly always present in such cases.

Richter (1938) describes retention cysts in the tubes causing stenosis of the lumen and sterility. He regards them as persistent remnants of the Wolffian ducts, which may be mistaken for hydrosalpinx.

No description of cyclic changes in the tubal mucosa of the cow could be found in the available literature.

In the present study the following changes were noted during the sexual cycle in normal animals. At two days after the commencement of oestrus the epithelium is high columnar (Fig. 76) with scanty ciliation and basal nuclei. Many cells show large basal vacuoles which force the nuclei towards the centre of the cells. The cells are distended with cytoplasmic secretory granules, and the stroma is oedematous and congested.

At five days post-oestrum the epithelium is low columnar (Fig. 77) with basal nuclei which occupy a proportionately larger portion of the cell than at two days, indicating cytoplasmic shrinkage. The stroma is dense and avascular. It will be noted that the cells are devoid of cilia in this animal (No. 6452). As only one case was available at this stage of the cycle, it is not possible to state whether this occurrence is usual. It is not likely that the cyclic changes are accompanied by shedding of cilia and in this case it is probably incidental.

Two types of cells are described in the tubal epithelium of the human by Maximow and Bloom (1938), who state that ciliated cells are especially numerous in the ampulla. The other non-ciliated cells are of glandular nature and contain granules. They express the opinion that these two types of cells are probably merely different functional conditions of the same element. Various authors also describe the progressive disappearance of cilia as the uterus is approached in rodents. In the present experiment specimens of both tubes were taken from halfway between the uterine and fimbriated extremity, unless some abnormality was encountered in an other portion, when this was naturally included in the section, irrespective of the level at which it occurred.

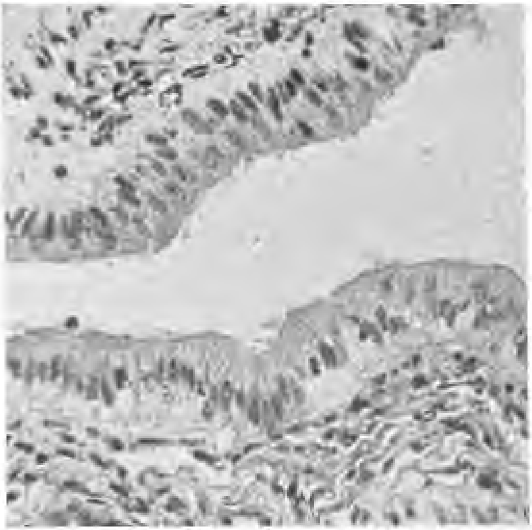

FIG. 76.—Fallopian tube at two days post-oestrum, Cow 7269. ×350.

FIG. 78.—Fallopian tube at ten days post-oestrum. Cow 7469. ×350.

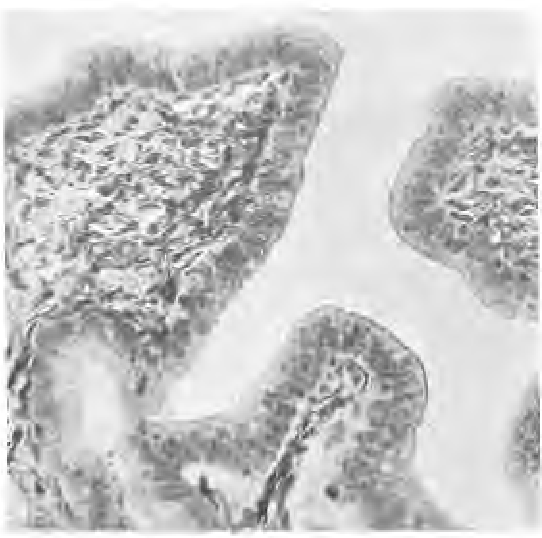

FIG. 77.—Fallopian tube at five days post-oestrum. Cow 6452. ×350.

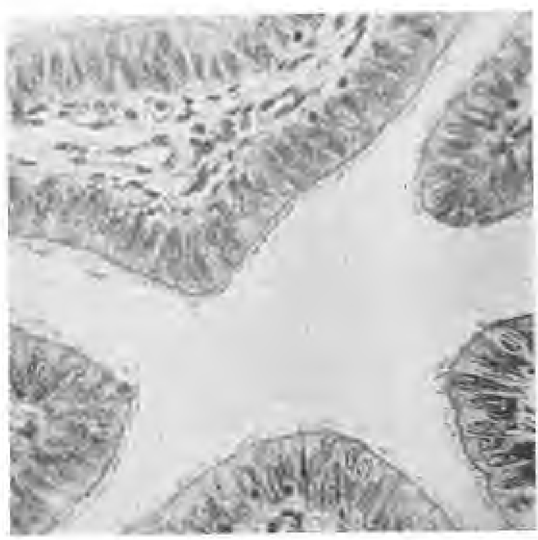

FIG. 79.—Fallopian tube at 12 days post-oestrum. Cow 7378. ×350.

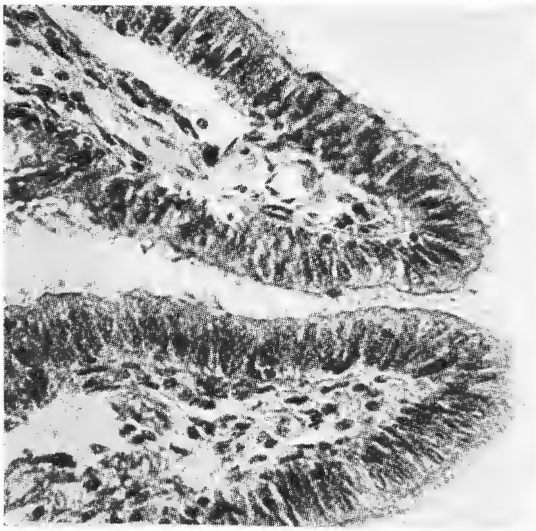

FIG. 80.—Fallopian tube at 15 days post-oestrum. Cow 6292. ×350.

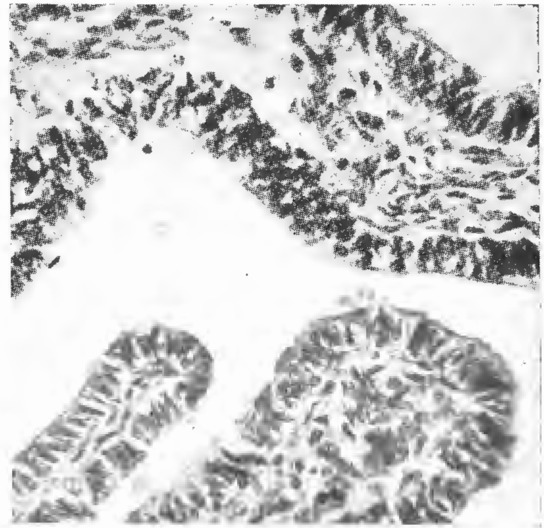

FIG. 82.—Fallopian tube at six months pregnancy. Cow 7471. ×350.

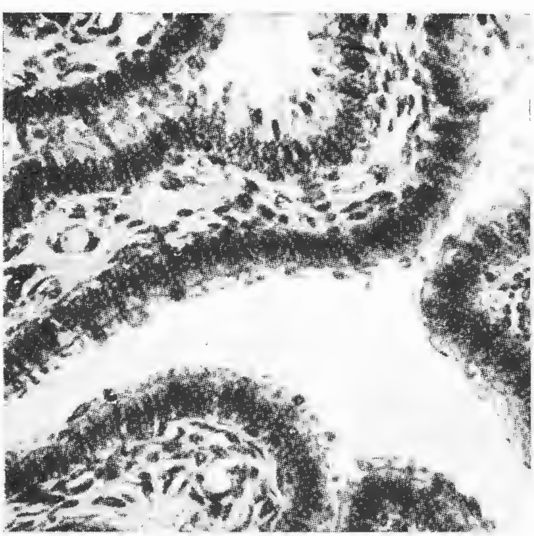

FIG. 81.—Fallopian tube at 26 days pregnancy. Cow 7385. ×350.

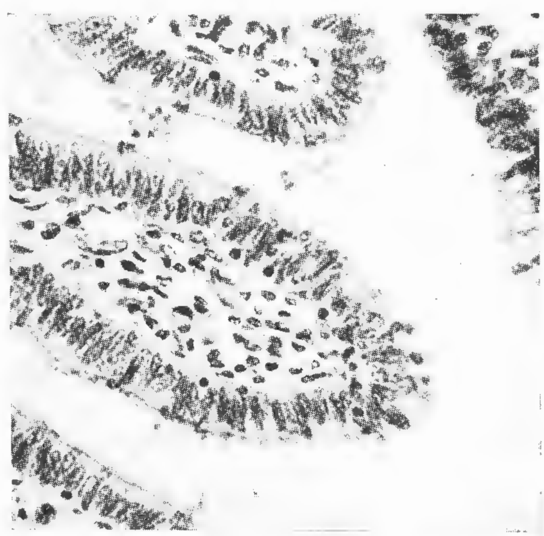

FIG. 83.—Fallopian tube at eight months pregnancy. Cow 7276. ×350.

At ten to twelve days (Figs. 78 and 79) the epithelium is low columnar, profusely ciliated and containing large, oval central nuclei. Peculiar cytoplasmic and nuclear extrusions appear at this stage. The extrusions are thrust out into the lumen from the underlying cells and are usually still attached to the latter by a thin strand of cytoplasm, while many nuclei appear to be lying free on the epithelial surface. These structures give the surface an irregular outline. The stroma is dense and avascular.

At fifteen days (Fig. 80) there is little change from the above, although the extrusions appear to be less frequent.

During pregnancy (Figs. 81, 82 and 83) the epithelial cells are low columnar with large, oval, centrally situated nuclei and a proportionately small amount of cytoplasm. Cytoplasmic and nuclear extrusions, similar to those observed at mid-oestrum, become very numerous, the epithelial surface being irregularly serrated in outline. Ciliated cells are visible in between the extrusions. Globules of cytoplasm are seen apparently free in the lumen. It is suggested that these changes occur under the influence of the corpus luteum hormone, progesterone. In these cases the stroma appears dense and avascular.

In nymphomaniac animals the epithelial cells are large, swollen and columnar (Figs. 84 to 87) with lightly staining granular cytoplasm and small basal nuclei. In a number of cases similar basal vacuoles (Fig. 84) are present, as observed at two days post-oestrum (compare with Fig. 76). In the former cases, however, the vacuolation is more extensive. As other portions of the genital tract show evidence of secretory activity under oestrogenic stimulation (whether during normal oestrus or under the influence of follicular cysts) it is reasonable to suggest that these vacuolations are indicative of active (or hyper-) secretion. The stroma in these cases is almost invariably oedematous and congested.

In those animals suffering from functional sterility but showing normal sexual cycles, the cyclic changes in the tubal mucosa are similar to those encountered in normal animals. One of the functionally sterile animals (No. 6442) showed chronic unilateral (left sided) salpingitis (Fig. 88) on microscopic examination. Macroscopically the tube revealed nothing abnormal. The mucosa showed fibrosis, the normal structure being considerably disturbed, while the stroma and muscular coats show inflammatory cellular infiltration. The lumen is filled with necrotic exudate. It is likely that this condition contributed to the sterility from which the animal was suffering, although the right tube was intact. This animal was nulliparous and showed endometrial atrophy and cystic degeneration. If endometritis had been present this was no longer detectable on microscopic examination. The ovaries showed no evidence of cystic follicles or corpora lutea, although ovarian dysfunction manifested by irregular cycles, had been present for some years before slaughter. A small fibroleiomyoma, described earlier was present in the uterine wall.

Cow No. 7045 presents an interesting case. She had a cyst, 3 mm. in diameter (Fig. 89) in the right tube near the middle, clearly visible and palpable at post mortem. She was 183 days pregnant when slaughtered, with the foetus lying in the right horn and the corpus luteum of pregnancy in the right ovary. Transperitoneal and internal (uterine) migration of the ovum is considered very unlikely in this case. The only acceptable explanation appears to be that the cyst developed subsequent to fertilisation and implantation. Before this the animal had twice calved normally and the final pregnancy followed after two services.

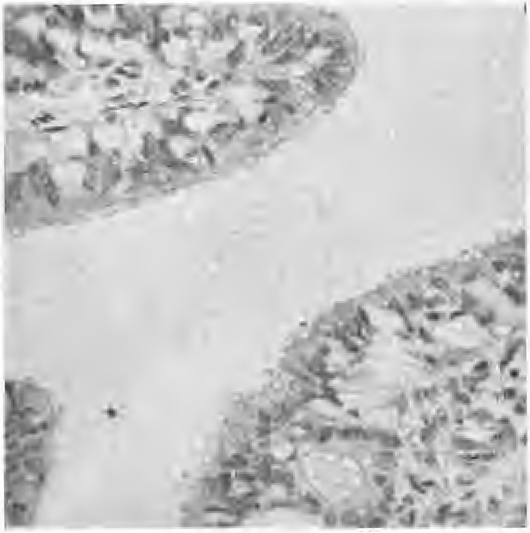

FIG. 84.—Fallopian tube, nymphomaniac.
Cow 6363. ×350.

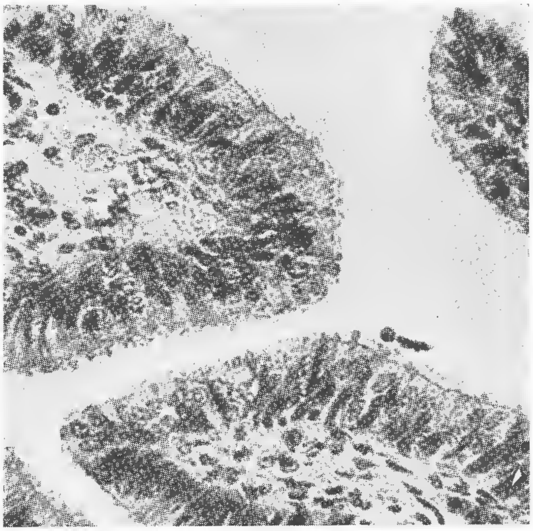

FIG. 86.—Fallopian tube, nymphomaniac.
Cow 6496. ×350.

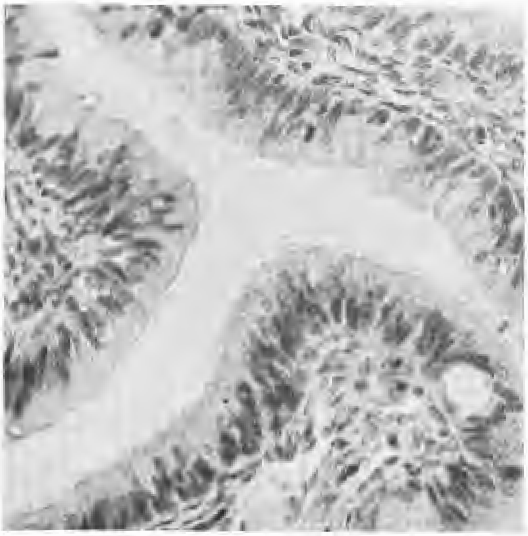

FIG. 85.—Fallopian tube, nymphomaniac.
Cow 7470. ×350.

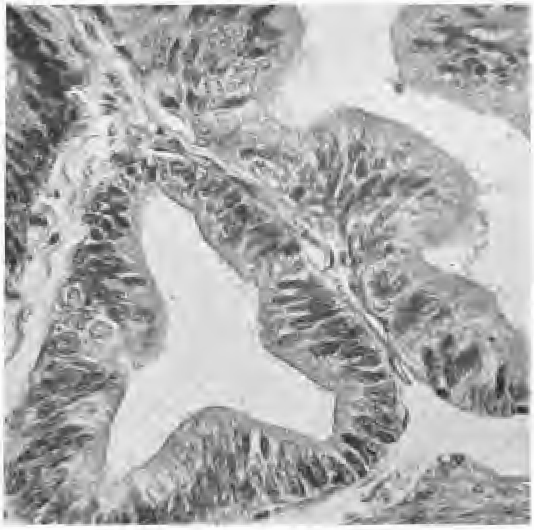

FIG. 87.—Fallopian tube, nymphomaniac.
Cow 7157. ×350.

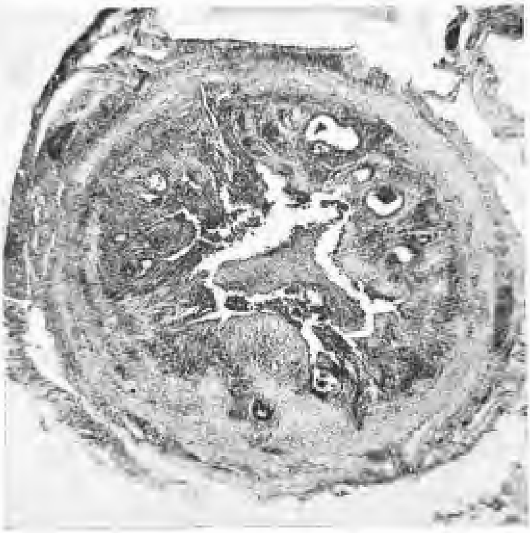

FIG. 88.—Fallopian tube, chronic (unilateral) salpingitis. Cow 6442. ×28.

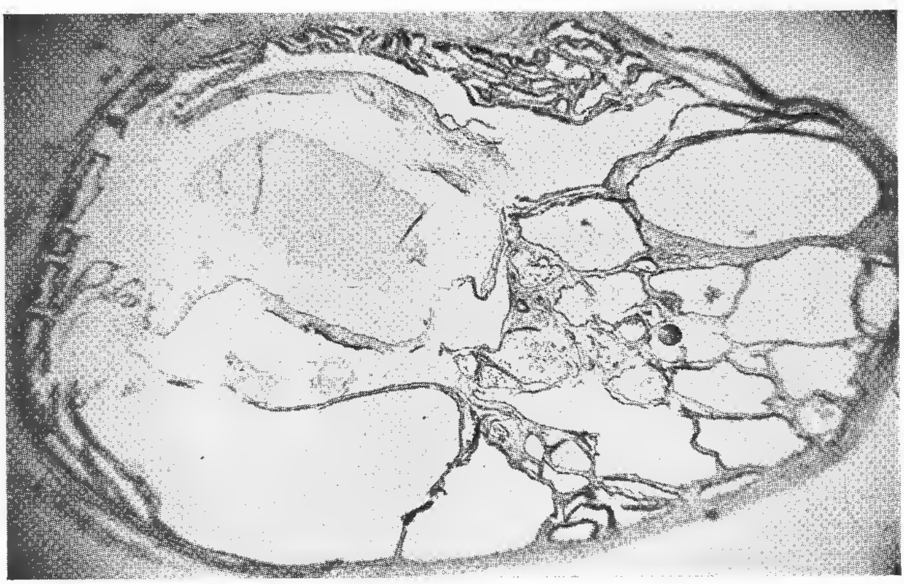

FIG. 89.—Cystic fallopian tube. Cow 7045, six months pregnant. ×28.

Cow No. 7172 showed along the entire length of both tubes minute pinhead cysts penetrating the muscular coats and plainly visible under the serosa. Microscopically these cysts were lined by a single layer of flattened epithelium. They contained clear, colourless fluid. The animal had never conceived in spite of numerous services and at the time of slaughter was suffering concurrently from hydrometra with cystic degeneration and atrophy of the uterine wall, and bilateral cystic Graafian follicles.

Apart from the abovementioned three cases the remainder of the animals showed no structural changes in the fallopian tubes, which could have interfered with the fertility of the individuals concerned. This is remarkable considering the extensive changes encountered in other portions of the genital tract.

Table XXIV (Appendix II) shows the dimensions of the Fallopian tubes. It will be noted that there is no significant difference in the length or diameter of the tubes of animals suffering from nymphomania or functional sterility as compared to normal pregnant or non-pregnant animals. It appears that these structures do not participate in the atrophic or hypertrophic processes which involve the remainder of the genital tract under the various sexual conditions enumerated.

F. Ovaries.

A discussion on the various pathological conditions occurring in the ovaries and a review of the relevant literature are beyond the scope of this article. The only ovarian lesions encountered were follicular cysts associated with nymphomania.

Hammond (1927) states that in follicular degeneration the granulosa is the first layer to break up and that this is attended by decrease in the size of the cyst. He observes that in cysts of long standing the granulosa disappears. He believes that the prevention of ovulation and formation of cysts may occur as a result of any inflammation on the surface or in the depth of the ovary, which leads to the growth of tough connective tissue.

Quinlan (1929) regards follicular cystic degeneration as being secondary to inflammatory changes in the genital tract and does not agree with Hess who states that the ovarian disease is primary. Williams (1943) observes that the fundamental cause of follicular cystic degeneration is unknown and that hypothetically it is attributed to endocrine disturbance.

Quinlan (1929) in describing the microscopic changes in follicular cysts, states that the histological appearance depends upon the stage at which it is examined. He observes that the first change takes place in the ovum which undergoes degeneration. This is followed by degenerative changes in the cumulus oophorus. Thereafter the follicular epithelium degenerates, the inner layer of cells being the first to disappear, and cell debris may be seen in the liquid contents. During this period of changes in the follicular epithelium an apparent increase of connective tissue in the theca interna takes place, but these cells can still be recognised. Later partial or total degeneration of the theca interna takes place and eventually the capsule is entirely composed of fibrous tissue.

In the present study the causation of follicular cysts will be discussed elsewhere.

At the time of slaughter eleven animals were suffering from cystic follicles associated with nymphomania. The microscopic changes in the cysts, in various stages, are in accordance with those described by Quinlan (1929) and the following stages have been recognised:—

1. Cessation of mitotic cellular division in the granulosa and theca interna, not necessarily accompanied by cessation of fluid production.

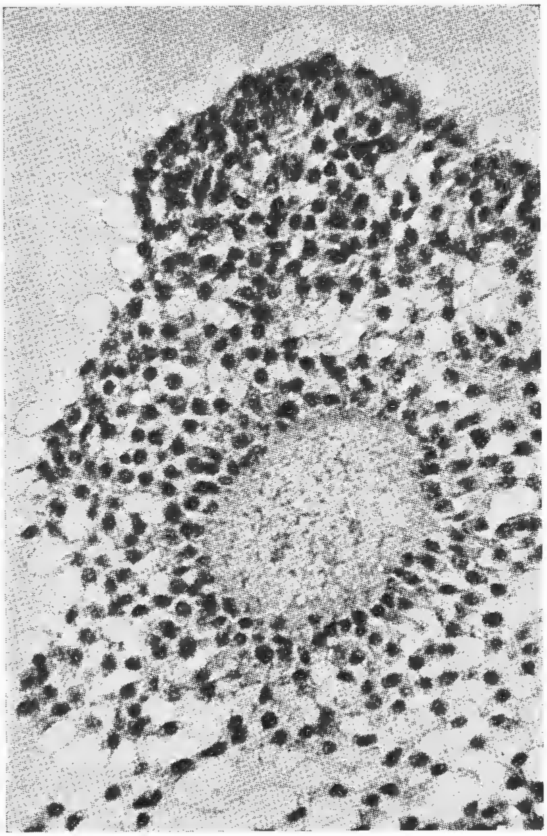

FIG. 90.—Follicular cyst. Degenerative changes in ovum and cumulus oophorus. Cow 7346. ×350.

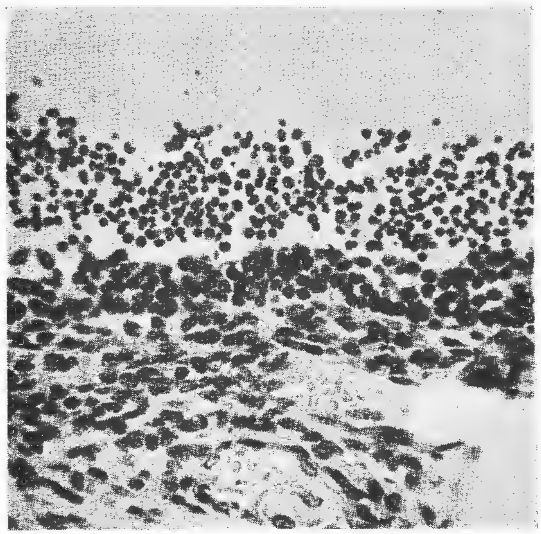

FIG. 91.—Follicular cyst. Pycnosis of granulosa nuclei, dissolution of cytoplasm and casting off of cells into the follicular fluid. Cow 7355. ×350.

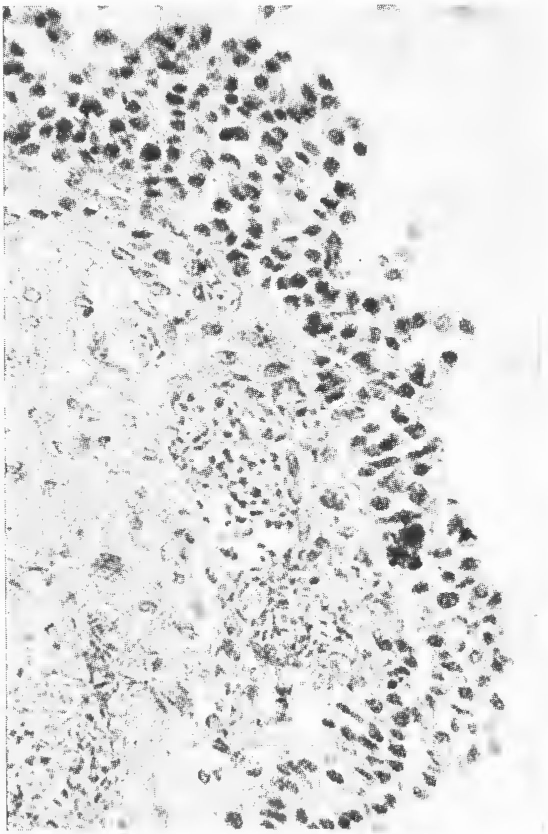

FIG. 92.—Follicular cyst. Thickening, fibrosis and vascularisation of theca interna. The granulosa has partly disappeared. Cow 7157. ×350.

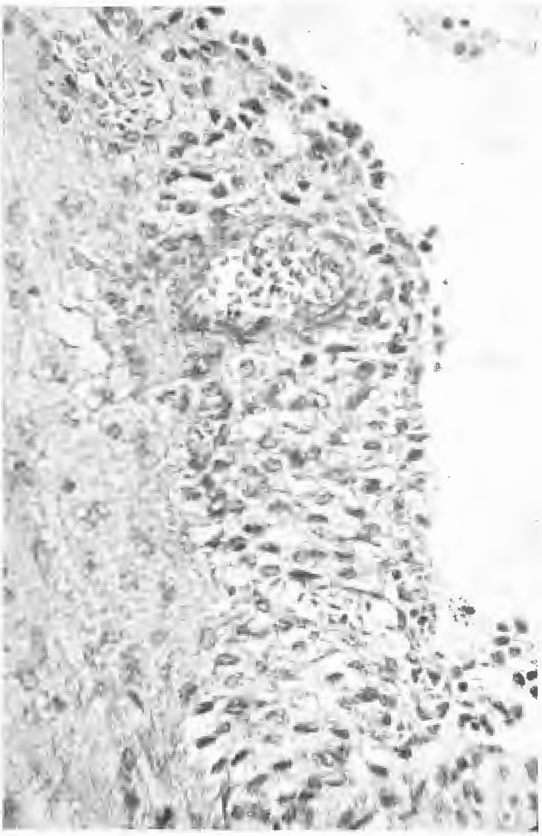

FIG. 93.—Follicular cyst. Changes similar to those seen in Fig. 92. Few cells of the granulosa layer remain. Cow 6363. ×350.

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2. Degenerative changes in the ovum and cumulus oophorus, (Fig. 90).
3. Degenerative changes in the granulosa layer characterised by pycnosis of the nuclei, dissolution of the cytoplasm and casting off of the cells (Fig. 91). In many cases the pycnotic nuclei coalesce and form large globules of nuclear material, freely suspended in the follicular fluid, (Figs. 94 and 95).
4. Thickening, fibrosis and vascularisation of the theca interna take place as stage 3 above progresses, (Figs. 92 and 93).
5. Eventually degeneration of the granulosa is almost complete, and the process of degeneration and pycnosis commences in the theca interna (Figs. 94 and 95).
6. The granulosa disappears completely and the theca interna cells are progressively reduced in number and replaced by fibrous tissue (Figs. 96 and 97).
7. The process terminates with complete fibrosis of the cyst wall, when no further histological changes take place (Figs. 98 and 99).

At no time was luteinisation of the granulosa or theca interna cells observed in the above process of degeneration of the follicle. Apparently this process of luteinisation is frequently observed in cystic follicles in humans; (Blair Bell 1919, Shaw 1936, and Turner 1943), and has been described in the bovine by Krupski (1917), Frei (1927) and others.

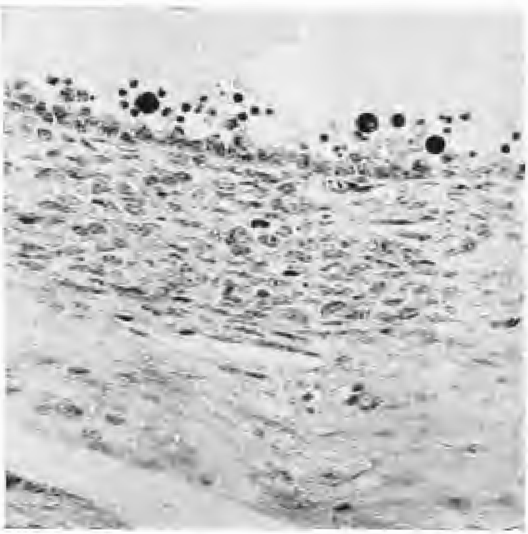

FIG. 94.—Follicular cyst. Note almost complete disappearance of granulosa layer and coalescence of pycnotic nuclear material. Cow 6495. ×350.

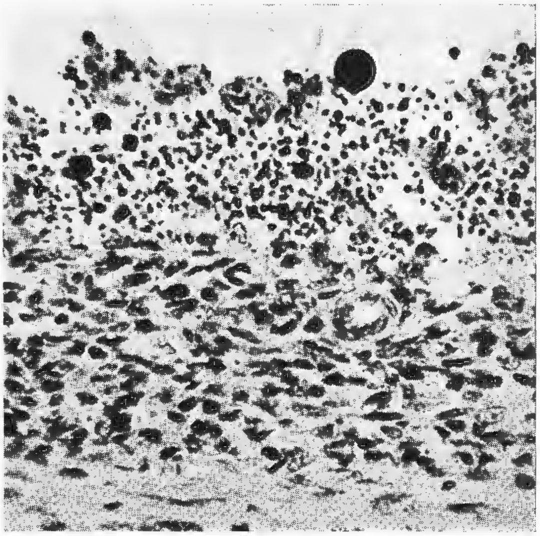

FIG. 95.—Follicular cyst. Complete degeneration of granulosa. Commencing pycnosis of theca interna nuclei. Cow 6496. ×350.

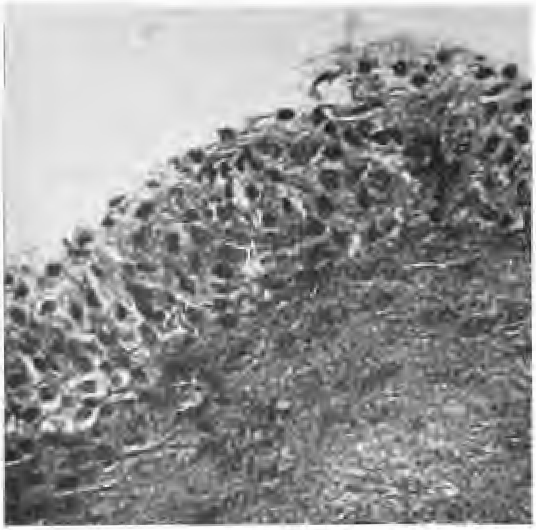

FIG. 96.—Follicular cyst. Granulosa layer completely disappeared. Pycnosis of theca interna nuclei. Cow 6362. ×350.

FIG. 98.—Follicular cyst. Complete fibrosis of the cyst wall. Cow 6423. ×350.

FIG. 97.—Follicular cyst. Similar to Fig. 96, but theca interna cells become progressively reduced in number and are being replaced by fibrous tissue. Cow 6362. ×350.

FIG. 99.—Follicular cyst. Complete fibrosis of the cyst wall. Cow 6495. ×350.

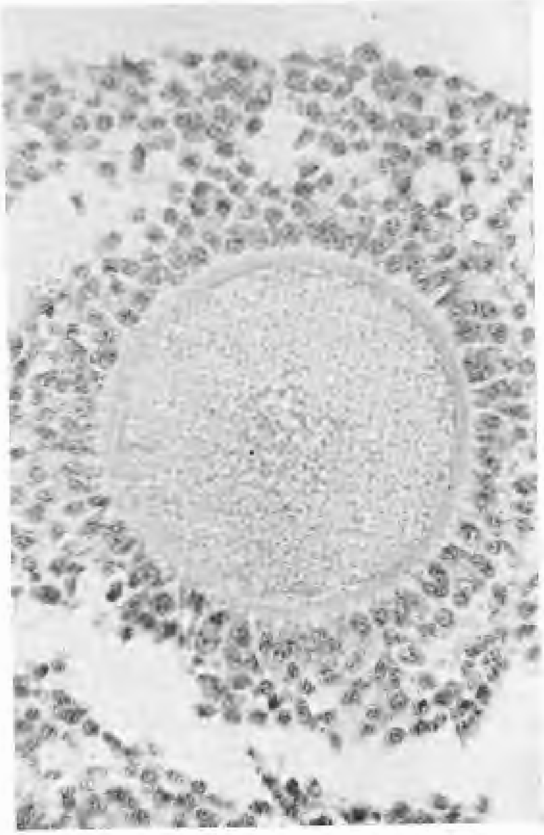

FIG. 100.—Normal ovum and portion of cumulus oophorus. Cow 6358. ×350.

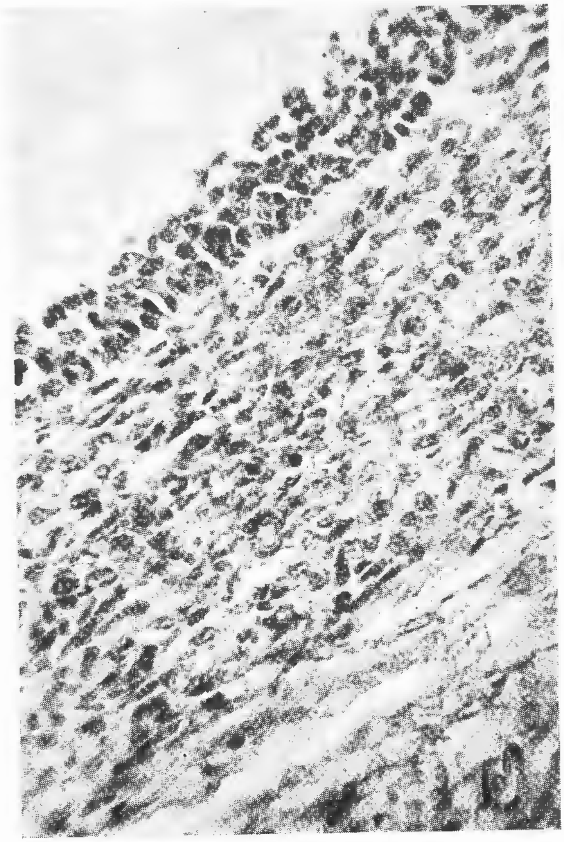

FIG. 101.—Normal mature follicle. Note well-defined granulosa (upper left), and theca interna (middle) and theca externa (lower right) layers. Cow 6292. ×350.

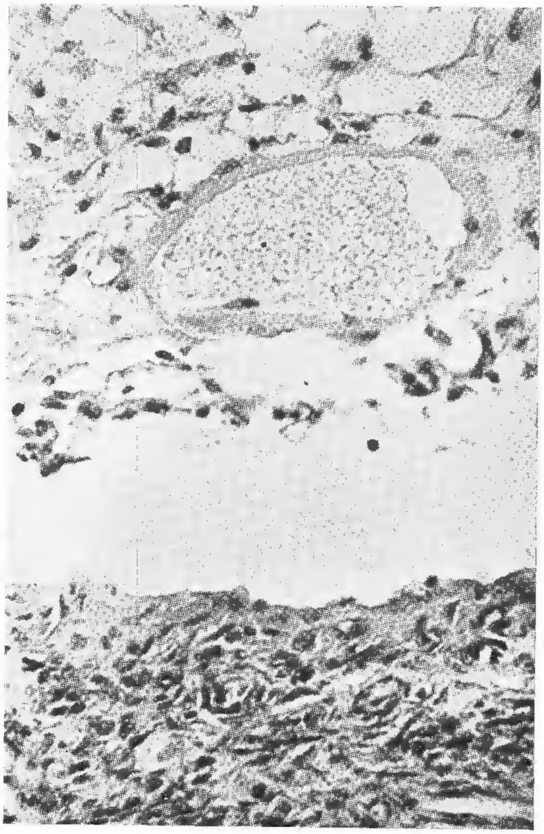

FIG. 102.—Atretic follicle. Degenerative changes in ovum and cumulus oophorus. Cow 6452. ×350.

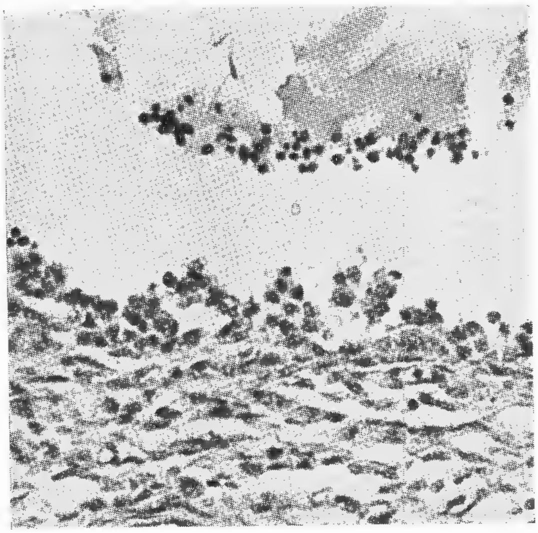

FIG. 103.—Follicle, Cow 7045, six months pregnant. Note nuclear pycnosis and cytoplasmic dissolution of inner layers of granulosa cells. ×350.

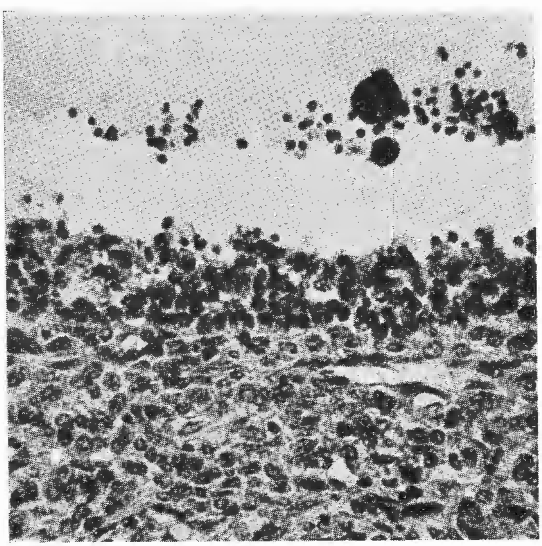

FIG. 104.—Follicle, Cow 7276, eight months pregnant. Similar to Fig. 103, but also showing coalescence of nuclear chromatin. (Cf. Figs. 94 and 95.) ×350.

For comparative purposes a normal ovum with portion of the cumulus oophorus (Fig. 100) and the wall of a normal mature follicle (Fig. 101) are included among the microphotographs. In the latter the three layers composing the follicular wall are clearly defined.

In the process of physiological atresia of the follicle, degenerative changes in the ovum and cumulus oophorus are sometimes observed, similar to those seen in the early stages of formation of cysts (Fig. 102).

During the later stages of pregnancy the larger follicles which were present at the time of fertilisation are also seen to undergo degenerative changes in the granulosa, consisting of pycnosis and cytoplasmic dissolution, (Figs. 103 and 104), identical to those observed in the early stages of cystic degeneration. In the former case, however, the process appears to be abortive and does not appear to reach the stage of complete dissolution of the granulosa and theca interna. The question arises as to the fate of these degenerate follicles. Are they capable of giving rise to oestrus subsequent to parturition, with liberation of viable ova, or does the process of regression merely continue as in the case of physiological atresia?

The dimensions and weights of the ovaries are shown in Table XXIV (Appendix II). The great increase in size and weight of ovaries of nymphomaniac cows is due to the presence of large cysts filled with fluid. When these are ruptured the remaining ovarian stroma is observed to be reduced to thin strands in the septa between the follicles as a result of pressure atrophy. It will be noted that there is no significant difference between the size and weights of ovaries of functionally sterile animals and fertile animals, whether pregnant or non-pregnant.

G. Mammary Gland.

Werner (1942), in summarising the literature on the physiology of lactation, observes that " experimental evidence indicates that growth of the mammary glands depends upon stimulation by the ovarian oestrogenic hormone which produces the pubertal condition, and that both oestrin and the luteal hormone are necessary to prepare the gland for the action of the lactation-inducing hormone of the anterior pituitary ".

From the extensive literature on the subject it appears that while the oestrogenic hormone stimulates development of the glandular ducts, corpus luteum hormone is responsible for the growth and development of the alveoli, after which anterior pituitary lactogenic hormone stimulates milk production and secretion. Variations are, however, evident in different species and Turner (1939) observes that in primates and guinea-pigs complete lobule-alveolar growth follows stimulation with oestrogens alone.

Krupski (1921, b) observed a remarkable degree of development and secretory activity in the mammary glands of nulliparous cows suffering from cystic ovaries, and holds the ovarian hyperfunction responsible for the mammary hypertrophy.

Quinlan (1929) states that with nymphomania the milk yield decreases and that its quality deteriorates.

Espe (1938) observes that many instances of lactation have been recorded in virgin heifers. He also states that in nymphomania the hypersecretion of oestrogen stimulates the duct system to such an extent that lactogenic hormone initiates a secretion in the modified glandular cells of the ducts and that this condition is known as " duct secretion ".

In the present study those cows which calved normally usually produced sufficient milk to rear their offspring. Being of a beef breed this is all that was to be expected. In one or two cases, however, the calves had to receive additional milk as the quantity produced by their dams was obviously insufficient.

The animals suffering from functional sterility had poorly developed udders and teats. This was confirmed by histological examination of the glandular tissue. The nymphomaniac animals in general showed moderately to highly developed udder and teats. On histological examination the ducts as wel as the alveoli revealed a remarkable degree of development and secretory activity. The secretion present varied from a small quantity of yellowish watery fluid to thick creamy secretion resembling colostrum. In some cases the secretion was indistinguishable from normal milk and several hundred cubic centimetres could be drawn off at a time. Cow No. 6362 yielded up to four pints daily of apparently normal milk over a long period.

It is suggested that in these cases the mammary development occurred entirely under oestrogenic stimulation in the absence of corpus luteum hormone. Whether the secretion was initiated by pituitary lactogenic hormone is a question which cannot be answered.

THE ENDOCRINE ORGANS.

H. Hypophysis.

A huge volume of work has been done on the physiology of the pituitary and on the structural changes which occur in this most important of endocrine organs under various normal and abnormal physiological conditions in laboratory animals. Its role in the regulation of many body functions, including sex, is well recognised. The literature dealing with the various aspects of the function and structure of the hypophysis in relation to sexual physiology has expanded enormously during recent years, and a comprehensive review of this work is beyond the scope of this article. Only those aspects which are directly concerned in the present study will be briefly dealt with.

The relationship of the three distinct cell types occurring in the anterior lobe, in correlation with its functional activity, has given rise to much controversy and no agreement has yet been reached in this matter. Severinghaus (1939), in a comprehensive review on this subject states that the majority of investigators maintain that the acidophile and basophile cells are independently related to the chromophobes which are the reserve cells of the gland. He describes in detail the changes occurring in these cells in relation to the sexual cycle and pregnancy, and concludes that the basophiles are probably responsible for the production of follicle-stimulating hormone, while the acidophiles produce luteinising hormone.

Friedman and Hall (1941) produce evidence that the outer, acidophilic zone of the bovine pituitary contains a higher concentration of lactogenic hormone than the remainder of the gland.

Wolfe and Chadwick (1936) by a series of graded doses conclude that oestrogens affect both the basophiles and acidophilic cells. Small doses effect a degranulation of the basophiles, but larger doses over a more protracted period also degranulate the acidophiles and cause an increase of the latter through active mitoses in these cells.

Baker and Everett (1944) injected small doses of diethyl stilboestrol into immature female rats daily for periods up to 14 days and observed an increase in weight of the pituitary, increase in the number of acidophiles through active mitoses and hypertrophy of the Golgi apparatus. The basophiles underwent degranulation and reduction in number, while the chromophobes were also reduced in number. They concluded that diethyl stiboestrol had a stimulative effect on the acidophiles.

Zeckwer (1944), working with parabiotic female and gonadectomised rats, observed that the increased amount of follicle-stimulating hormone secreted by the pituitary of the latter stimulates the ovaries of the former to enlargement of the follicles and secretion of oestrogen. This oestrogen stimulates the pituitary to secretion of luteinising hormone to a stage where exhaustion or inhibition of production of this hormone by the pituitary occurs as evidenced by degranulation of the chromophil cells.

Wittek (1913) quoted by Gilmore *et al.* (1941) found great variations in the weight of the hypophysis in bovines of the same age. A positive relationship existed between hypophysis weight and slaughter weight. He also observed an increase in weight of the gland after castration, and a decrease in weight in aged cows with advanced pregnancy.

Krupski (1921, a) found no alteration in weight of the hypophysis in pregnant and castrated bovines, but observed a marked increase in weight in cows with cystic ovaries.

Quinlan (1929) in studying the endocrines of sterile cows found that the average weight of the hypophysis in such animals was 3·41 grams as compared to 3·261 grams in normal South African cattle.

Rosta (1931) observed no increase in weight of the bovine pituitary during pregnancy but increase in weight after castration. He states that histologically there is no difference in the gland between pregnant and non-pregnant animals.

Blickenstaff (1934) quoted by Boyd (1934) observed a definite hypertrophy of the gland in sterile cows. In these animals an average weight of 3·111 grams was recorded as against 2·868 grams in pregnant cows and 2·505 grams in bulls and oxen.

Gilmore, Petersen and Rasmussen (1941) undertook a detailed study of the normal bovine hypophysis. They found no relationship between the relative weight of the hypophysis and the producing ability. The weights of hypophyses in freemartens tended to be smaller than in normal females.

Severinghaus *et al.* (1932) have summarised the literature for the different species.

While much work has been done on the proportion of the different cell types in the anterior lobe of the human hypophysis and that of various laboratory animals, a search of the available literature revealed only one publication in which definite information on this subject in bovines is given. Gilmore *et al.* (1941) counted the cells of twelve bovine females of an average age of 5 years 7 months and recorded the following mean proportional cell counts: acidophiles 44·3 per cent., basophiles 7·0 per cent. and chromophobes 48·7 per cent. They found no significant difference in the proportions in males and females. They report the presence of two types of acidophiles in the bovine pituitary, crimson and brick-red types, and state that the former appear to be associated with sexual activity as in other species. They observed no effect of castration on the proportional cell distribution.

Schönberg and Sakaguchi (1917) are of the opinion that the eosinophilic cells greatly predominate in the bovine hypophysis. They found more chromophobes in steers than in bulls but fewer in steers than in cows.

Beato (1935) states that in the bovine anterior lobe eosinophiles greatly predominate over chromophobes especially after repeated pregnancies and that basophiles are "entirely or almost entirely absent".

Rodriguez (1937), in studying the hypophysis of various domestic and small laboratory animals, observed that typical granulated basophiles are absent in the anterior lobe of the calf, while in adults these cells are usually infrequent but sometimes occur in great numbers.

In the present study the measurements and weight of the pituitary and the proportional cell counts of the anterior lobe were recorded and are tabulated in Table XXV (Appendix II). From this table it will be noted that the glands of nymphomaniac animals are significantly larger and heavier than those of the remaining groups of animals and that the increase in size is three-dimensional. There is no significant difference in size and weight between the glands of functionally sterile and fertile, non-pregnant animals. The average weight of the glands of pregnant animals is considerably lower than those of the two previous groups, but this is probably purely accidental and considered to be of no significance, the number of animals being insufficient to be of statistical value.

In the fertile, non-pregnant group cellular changes coinciding with the sexual cycle were evident. These changes are summarised by Severinghaus (1939) as follows: "There is cytological evidence of increased secretory activity of the basophiles at the onset of oestrus, as judged by a marked progressive discharge of their granules. Acidophiles later, during the luteal phase, in some instances at least, participate in similar degranulation. These findings are in agreement with experimental evidence of a decreased gonad-stimulating potency of the pituitary gland during oestrus . . . ."

The average proportions of cells in the anterior lobe in this group are: acidophiles 40·0 per cent., basophiles 14·6 per cent. and chromophobes 45·4 per cent. The following changes were observed concurrent with the changes in the genitalia at various stages of the sexual cycle.

At two days post-oestrum, that is shortly after termination of the follicular and commencement of the luteal phase of the cycle, the alpha (acidophile) cells are large, heavily granular, with large delicate nuclei and prominent Golgi apparatus, (Fig. 105), while the beta (basophile) cells are small and degranulated with pycnotic nuclei and indistinct Golgi.

At five days when the corpus luteum is rapidly growing, the alpha cells show great activity, characterised by deeply staining, heavily granular cytoplasm, many cells showing pycnotic nuclei, while others have large delicate nuclei and prominent Golgi apparatus. The beta cells are unchanged from the above and appear to be resting at this stage, (Fig. 106).

At 10 to 12 days, when the luteal phase reaches its height, the alpha cells are becoming degranulated with pycnotic nuclei and indistinct Golgi, changes indicative of spent activity. The beta cells at this stage begin to show increased granulation of the cytoplasm, with large delicate nuclei and prominent Golgi, (Fig. 113).

This evidence of increasing activity of the beta cells is apparently in preparation for the approaching phase of follicular activity.

At 13 to 15 days the alpha cells are unchanged while the basophiles show fair numbers of pycnotic nuclei, (Fig. 107).

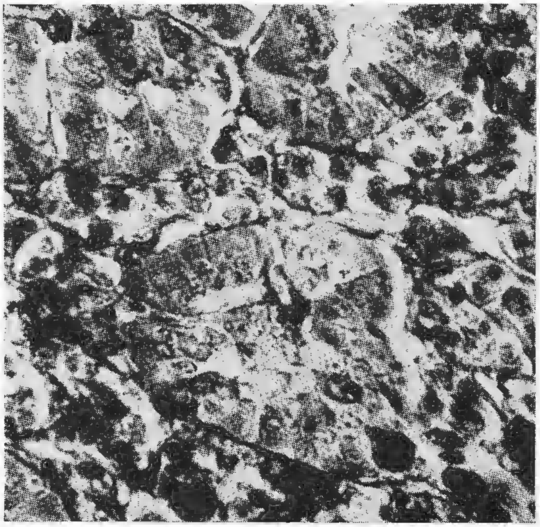

FIG. 105.—Anterior pituitary, Cow 7269, two days post-oestrum. Note acinus in lower centre, composed almost entirely of large, heavily granular acidophiles along the periphery, while the central area of the acinus is occupied by chromophobes. The acinus is surrounded by small, degranulated basophiles. Berblinger-Burgdorf stain. ×450.

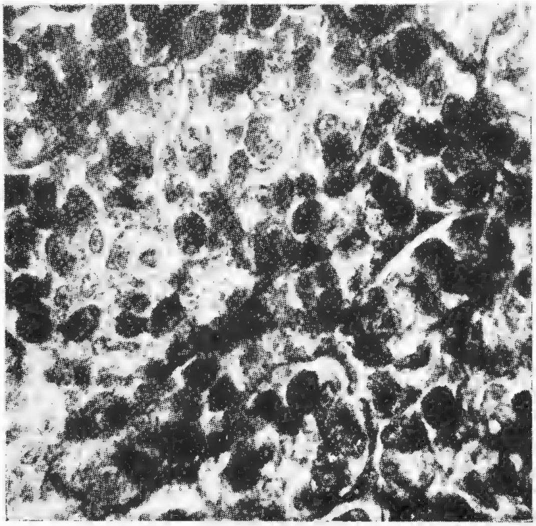

FIG. 106.—Anterior pituitary, Cow 6452, five days post-oestrum. Note heavily granular acidophiles (almost black), with many chromophobes (light grey) distributed in between. A few small, degranulated basophiles are visible in the centre of the microphotograph. Berblinger-Burgdorf stain. ×450.

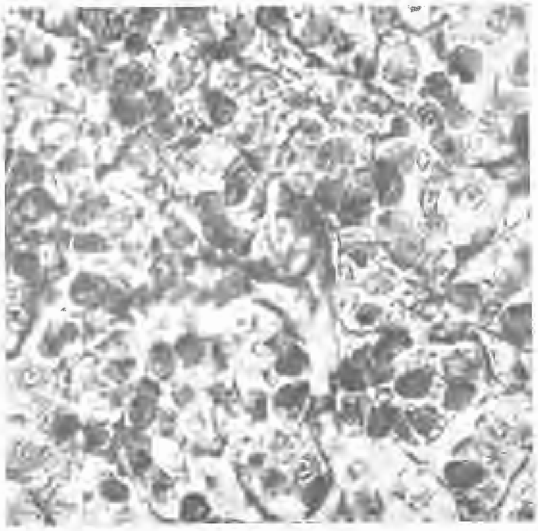

FIG. 107.—Anterior pituitary, Cow 6292, 15 days post-oestrum. Note degranulated acidophiles (grey) with pycnotic nuclei and heavily granular basophiles (almost black) also with pycnotic nuclei. Many chromophobes are visible. Berblinger-Burgdorf stain. ×450.

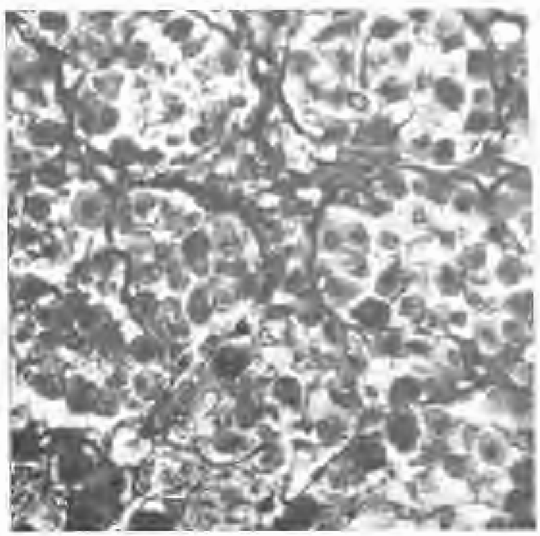

FIG. 108.—Anterior pituitary, Cow 7276, eight months pregnant. Note large numbers of partly degranulated acidophiles with pycnotic nuclei—the so-called "pregnancy cells". Basophiles are present in all stages (shades varying from light grey to almost black). The central areas of the acini are occupied by chromophobes. Berblinger-Burgdorf stain. ×450.

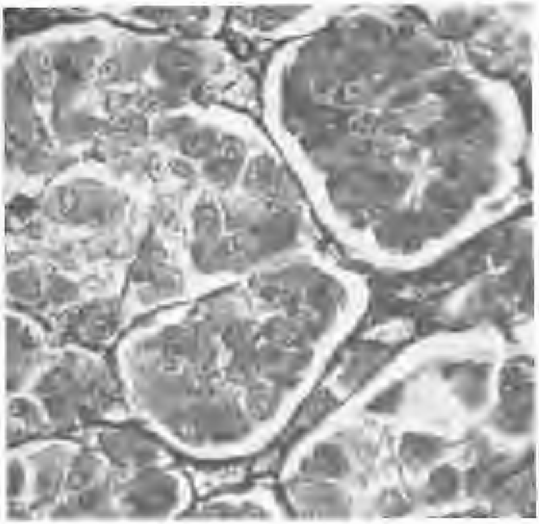

FIG. 109.—Anterior pituitary, Cow 6362.

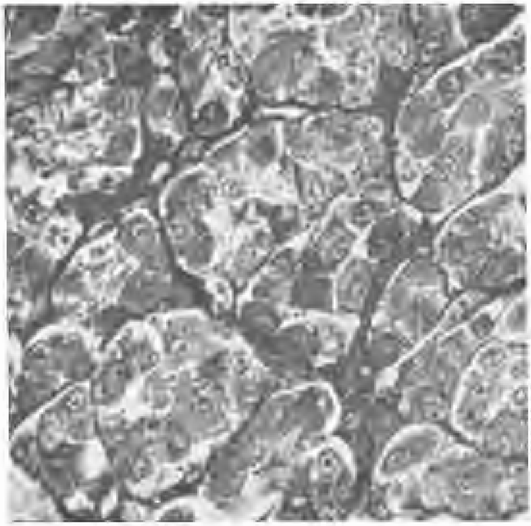

FIG. 111.—Anterior pituitary, Cow 7277.

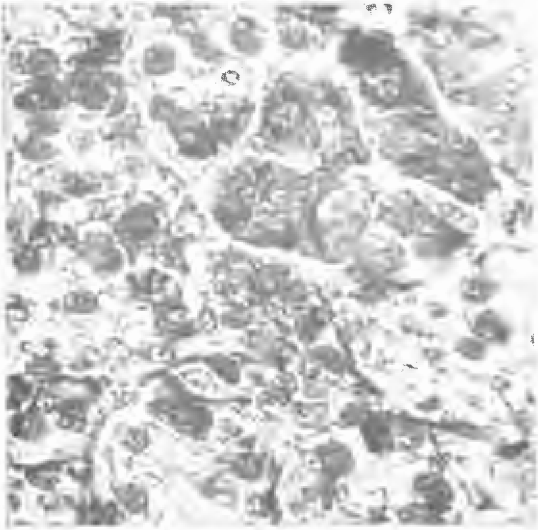

FIG. 110.—Anterior pituitary, Cow 7157.

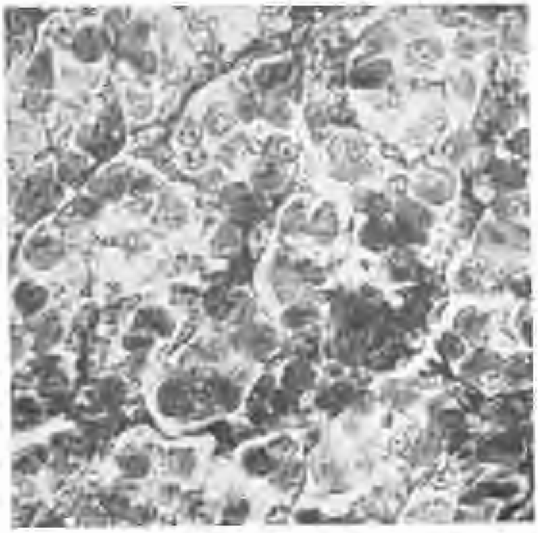

FIG. 112.—Anterior pituitary, Cow 6495.

FIGS. 109-112.—Anterior pituitaries of cows suffering from follicular ovarian cysts associated with nymphomania. Note predom inating large, heavily granular acidophiles, in most cases occupying almost the entire acinus (Cf. Fig. 114). Few basophiles are visible Berblinger-Burgdorf stain. × 450.

The above changes are strongly suggestive of cyclic periodic phases of granulation and degranulation of the chromophile cells, accompanied by changes in the nuclei and Golgi apparatus and presumably of production and release of hormones. Furthermore these changes are in support of Severinghaus' (1939) hypothesis that the basophiles are responsible for the elaboration of the follicle-stimulating hormone (F.S.H.) and the acidophiles for luteinising hormone, (L.H).

No positive correlation could be found between the differential cell counts and the sexual cycle. The changes in the cells appear to be morphological rather than numerical. A correlation, however, appears to exist between normal lactation and the proportion of basophiles, the highest numbers being encountered in those cows suckling their calves at the time of slaughter, insufficient animals being, however, available to make this certain. This appears contradictory to the findings of Friedman and Hall (1941), quoted earlier, that the lactogenic hormone is associated with the acidophiles.

During pregnancy there is a numerical increase in the proportion of acidophiles while the basophiles are slightly reduced in number. The acidophiles consist largely of partly degranulated cells, the so-called "pregnancy cells" of Erdheim, which were already observed on the 26th day of gestation. Basophiles in all stages are present, and this is in agreement with the findings of Severinghaus (1939) who states that during pregnancy both alpha and beta cells are in an active phase of secretion. (Fig. 108).

In the nymphomaniac animals a considerable increase, both in numbers and size of individual cells, took place in the acidophiles (Figs. 109—112 and 114). The cytoplasm usually became heavily granular and showed the presence of a prominent Golgi apparatus, while the nucleus was usually large, with delicate chromatin network.

Very few pycnotic nuclei were seen in the alpha cells of the majority of glands from this group of animals.

A remarkable drop in the proportion of basophiles in the anterior lobe (Figs. 109 to 112) took place in the nymphomaniacs. This is ascribed to active degranulation of the cytoplasm, which shows a prominent Golgi apparatus, the majority of nuclei being large with delicate chromatin network, although many pycnotic nuclei were also present. The changes indicate active production and accelerated release of hormone, without accumulation taking place.

The chromophobes show nothing unusual, pycnotic and large delicate nuclei being invariably in equal proportion. Morphologically, the acidophiles in the nymphomaniac pituitary, evaluated by the standard evolved by Severinghaus (1939), create the impression of active production of hormone the secretion of which is inhibited, leading to accumulation. In spite of their numerical increase, no mitoses were observed in the alpha cells, suggesting that the increase was due to transformation of chromophobes, rather than due to cellular multiplication.

In the functionally sterile animals the acidophiles, although showing a proportionate increase in number above the fertile groups, are of moderate size with degranulated cytoplasm and indistinct Golgi, while a large proportion of pycnotic nuclei is present. These changes are indicative of inactivity and hormone depletion, while the numerical increase in acidophiles may be regarded as an attempt on the part of the animal system to compensate for this inactivity and depletion of individual cells.

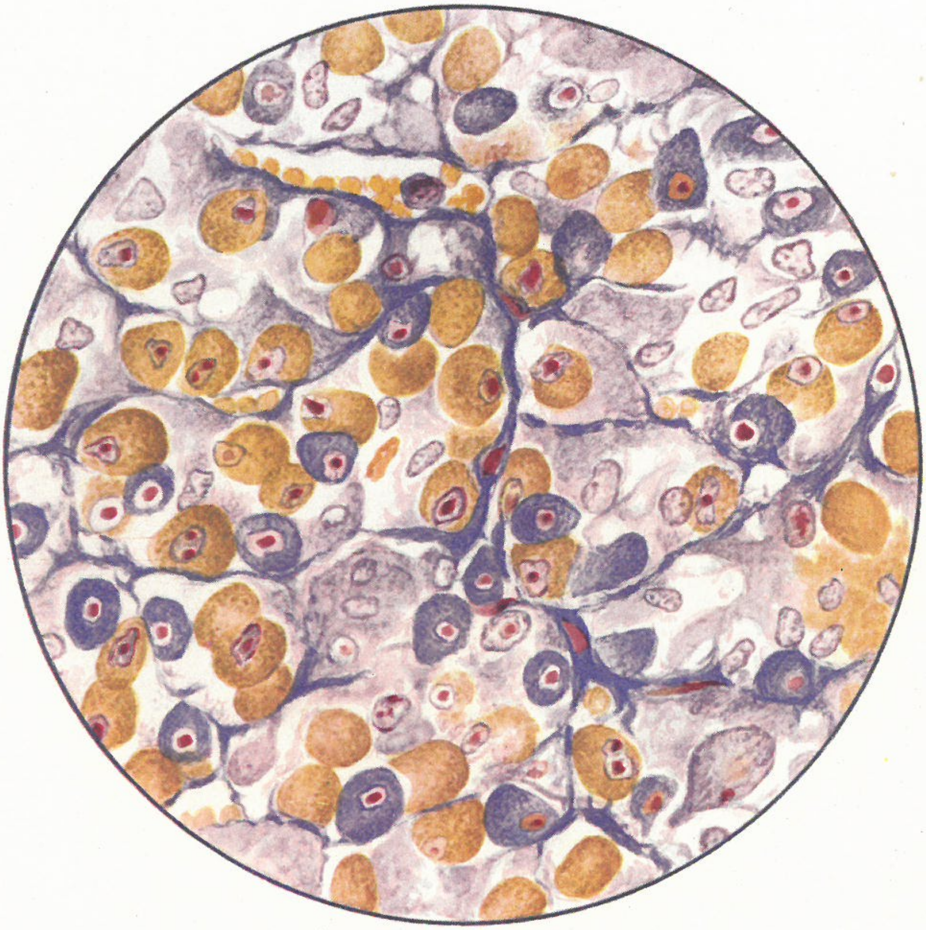

FIG. 113.—Anterior pituitary, Cow 7378 ,12 days post-oestrum. Note degranulating acidophiles (orange) with pycnotic nuclei. The basophiles (purplish blue) show increased granulation. Many chromophobes (pale mauve) are visible. Reproduction of camera lucida coloured plate, C. G. Walker del. Berblinger-Burgdorf stain. ×830.

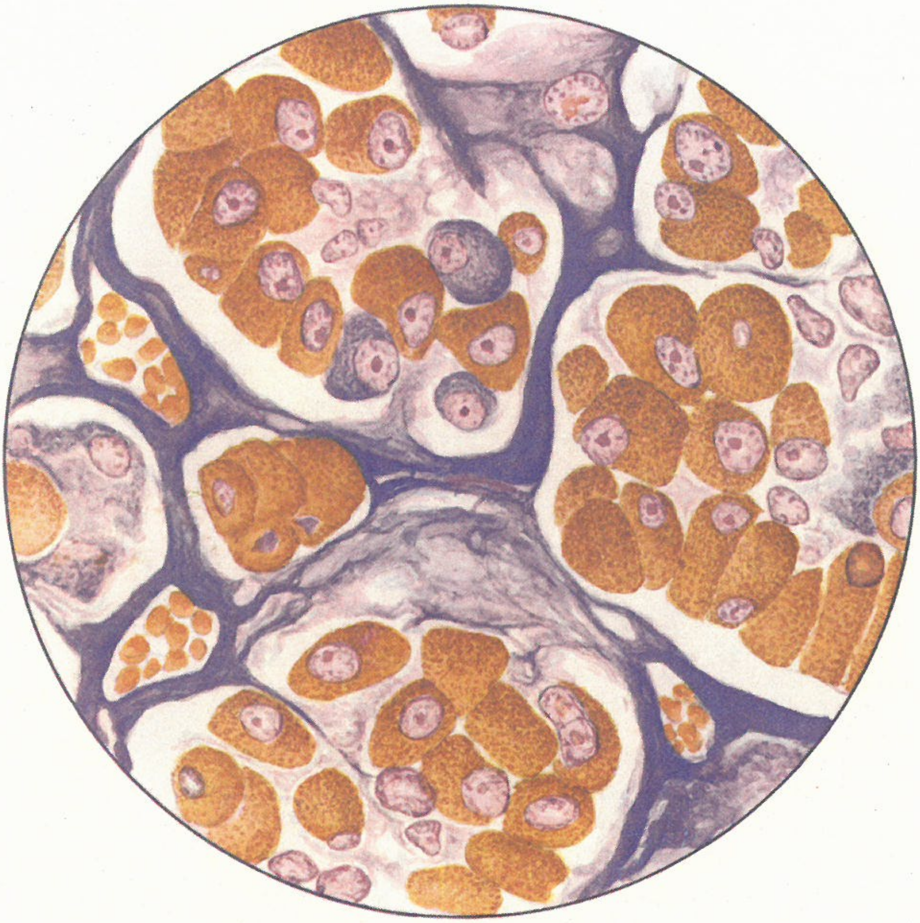

FIG. 114.—Anterior pituitary, Cow 7172, nymphomaniac. Note large, heavily granular acidophiles with large, globular nuclei predominating. Also the proportionate decrease in basophiles. Reproduction of camera lucida coloured plate, C. G. Walker del. Berblinger-Burgdorf stain. ×1100.

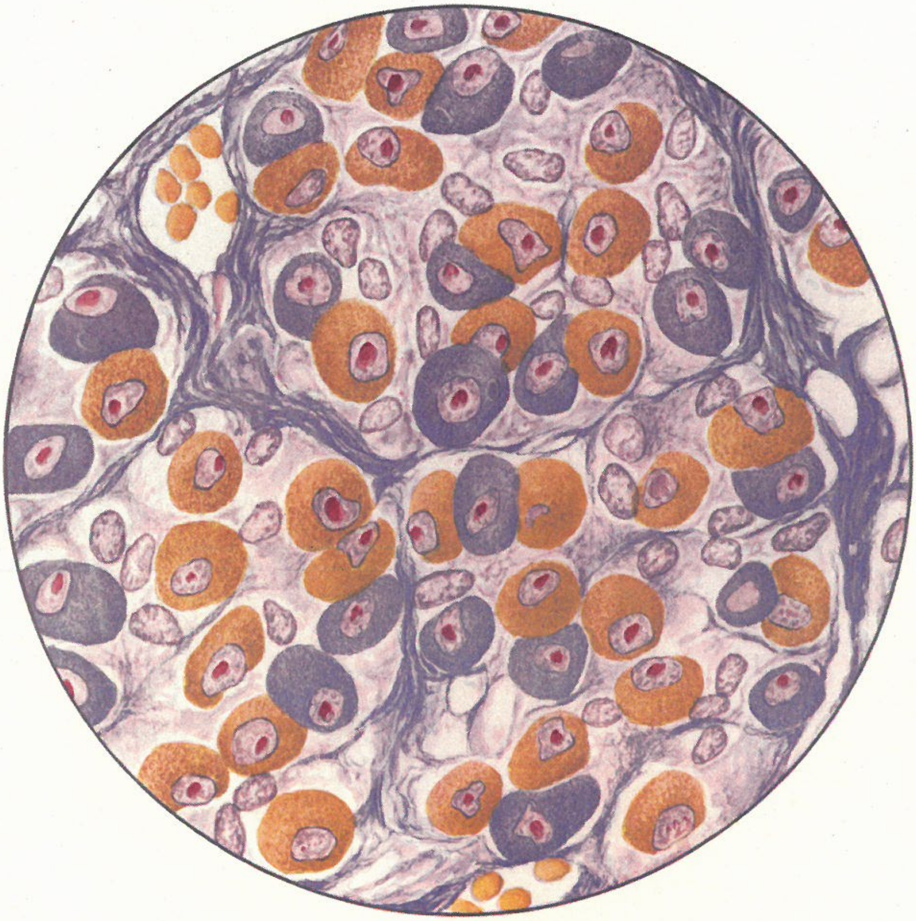

FIG. 115.—Anterior pituitary, Cow 6358, 11 days post-oestrum, suffering from functional sterility. Note the degranulated acidophiles (Cf. Fig. 110), many with pycnotic nuclei, and the heavily granular basophiles. The large basophile near the centre of the plate shows the negative image of the Golgi apparatus in the cytoplasm, to the right of the nucleus. The Golgi apparatus is also visible in the basophiles near the edge in the upper and left sectors of the plate, respectively. Many chromophobes are visible. Reproduction of camera lucida coloured plate, C. G. Walker del. Berblinger-Burgdorf stain. × 1100.