The Influence of Delayed Breeding on the Fertility of Beef Heifers.

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Dedicated to the memory of my father, EVERHARDUS DE LANGE.

CONTENTS.

I. INTRODUCTION.

THE close relationship between various environmental factors and normal functioning of the genitalia has been indicated by the foremost authorities on gynaecology. Hence such factors as stabling, restricted exercise, high feeding, high condition and restricted sunlight have been popularly associated with the aetiology of low fertility in cattle throughout the world.

Quinlan (1929) observed that a high incidence of sterility occurred in heifers kept at Onderstepoort Research Institute for the preparation of Redwater and Anaplasmosis vaccine. These heifers kept under conditions of restricted exercise with high feeding became very obese. They were mated after reaching the age of five years and quite eighty per cent. of these animals suffered from functional sterility of a very obstinate nature.

An experiment was conducted by Quinlan and Roux (1936) wherein the influence of dry rations, lack of exercise and lack of sunlight on the reproduction in beef heifers and cows were observed. They found that the factors mentioned above had no unfavourable influence on sexual activity and reproduction.

The above experiment was concluded by Quinlan et al. (1946) and it was found that beef cows kept under the conditions of feeding and management mentioned above, for a period of up to fourteen years, suffered no impairment of sexual functions and reproductive ability, their breeding records comparing favourably with those of bovines kept under conditions generally regarded as optimum for reproduction, thus proving conclusively the fallacy of this theory.

While the above observations were still in progress, it was decided to conduct an experiment in which heifers were kept under similar conditions, to be described in detail later, and wherein a further factor was introduced, namely that of delayed breeding.

Quinlan and Roux (1936) found that the reproductive functions of heifers were not affected when breeding was delayed to the age of 35 months.

The part played by delayed breeding in the production of sterility is recognised by such authoritites as Zschokke (1900), Albrechtsen (1920) and Richter (1926). Craig (1936) observes that where no attempt has been made to breed heifers for four or five years, they are often difficult to get in calf. This also applies to cows in which there has been a long delay in mating after parturition. Hammond (1939) states that it is generally believed that if cows for any reason are prevented from breeding, they become more difficult to get in calf. Williams (1943) mentions nymphomania in cows and mares as sometimes being caused by delayed or irregular breeding.

Babcock *et al.* (1940), working with albino rats, found that when breeding of females was delayed to the age of nine months, this led to the production of small litters at irregular intervals.

The experimental observations to be described in this study, are the results of attempted artificial induction of sterility in beef heifers, by applying methods of breeding and management which are generally regarded as conducive to infertility.

II. PLAN OF THE EXPERIMENT.

The experiment was conducted at the Veterinary Research Laboratory, Ermelo, in the Eastern Transvaal. Twenty-five high grade Sussex heifers, the progeny of cows in the experiment of Quinlan and Roux (1936), were placed under close observation from birth under conditions of restricted exercise and sunlight. With the exception of one animal (No. 6292), the calves were all sired by the same pure-bred Sussex bull.

The earlier treatment of these heifers is described in detail by Quinlan *et al.* (1939), but for the sake of completeness a résumé is given here.

Body-weights were recorded at birth and at monthly intervals. The calves were allowed to suckle their mothers, care being taken not to allow too much milk. During the first month from birth they were allowed to suckle three times daily and thereafter twice. Teff hay and water were available to the calves during the day, and a small supplementary ration of concentrate, to be described later, was fed as the time of weaning approached. They were weaned at the age of six months, when they usually weighed from 350 to 400 pounds. They were dehorned at an early age, inoculated with Anthrax and Quarter Evil vaccine annually, and tested for Tuberculosis and Contagious Abortion at annual intervals.

As the calves grew up and space became restricted in the calf stable, they were drafted into a double row of wood-and-iron and brick-and-iron stables fitted with suitable mangers and hayracks. They were fastened to the former by means of chains and neckhalters. Each animal had a feeding space of $4\frac{1}{2}$ feet. The floors of the stable were of flat stone and concrete. A native was in constant attendance, cleaning the floors and grooming the cattle and they were bedded down at night on the refuse of their roughage. They were confined to the stable day and night.

Due to constant stabling without exercise, it was found necessary to trim the hoofs of the animals periodically. On one or two occasions some of the animals developed panaritium, which was controlled successfully by driving the entire group through a foot bath, containing 10 per cent. Copper Sulphate solution, once daily for a few days.

The two rows of stables opened east and west respectively, in such a way that the cattle were exposed to about one hour direct sunlight in the early morning or late afternoon.

The rations consisted of the following:—

Concentrates.—2 parts by weight of crushed yellow maize and 1 part of wheaten bran. With the wartime shortage of bran, this item was substituted in August 1941 by crushed oats and peanut meal, made up in the following mixture: 5 parts crushed yellow maize, 3 parts crushed oats and 2 parts peanut meal. After weaning the concentrate ration was gradually increased, according to requirements, until the heifers received 2·5 pounds per head per day at the age of 18 months, fed in equal portions morning and evening. As they matured they were consuming 4·5 pounds of concentrate ration daily.

Roughage.—This consisted of teff hay *ad lib.* and it was found that the adult animals consumed 25 to 30 pounds per head per day. During the three winter months, June, July, August, the cattle received, in addition to the above, maize silage at the rate of 10 to 15 pounds *per capita per diem.*

No green feed or mineral mixture was given and the animals were not put out to grazing. They were dipped in 14 day strength Sodium Arsenite solution when deemed necessary.

It was found that with due care, the animals remained in excellent general health and in " prime " condition.

The cattle were let out to water twice daily and this walk to water was the only exercise they obtained. At these times, 8:30 a.m. and 4:30 p.m., oestrous observations were made. The animals were let out into an enclosure 13 by 38 yards, from which they were driven into a farm yard to the water trough. It was estimated that each animal walked a total distance of about three hundred yards daily.

Heifers showing oestrus were easily observed on being released from the shed. In most instances individuals in oestrus tried to mount their companions, and during mounting a clear mucous discharge issued from the vulva. Prior to mounting the heifer depressed the back, while standing alongside the heifer it intended to mount. The heifer showing oestrus stood and allowed herself to be mounted by her companions. They showed excitability and frequently bellowed. In some cases a mucous discharge was noticed 36 to 48 hours prior to the onset of heat. Accurate observations were not made to determine the duration of oestrus, but it had usually disappeared inside 24 hours, while heifers were young. As they grew older the tendency was for the duration of oestrus to lengthen up to 36 hours, and in some cases even up to 48 hours. Some heifers invariably showed oestrus of longer duration and greater intensity than others. " Menstruation " (i.e. the appearance of blood in the genital secretions) sometimes followed oestrus within 36 to 48 hours, but was not consistently present in these heifers.

Occasionally when doubt existed whether a heifer was showing oestrus, a young, vasectomised, " teaser " bull was brought up to her and their reactions noted. Coitus was usually prevented, in order to avoid any possible psychological and physical influence of mating, the possibility of conception being precluded.

It was originally intended to breed from these heifers after they reached the age of five years. As the experiment was progressing, and the older heifers were

approaching that age, it was noted that some of them were beginning to show irregularities of the oestrous cycle, with ovarian cysts and symptoms of nymphomania. Hence it was decided to mate some of the animals at an earlier age, and they were divided into two groups. Group A, consisting of 14 animals, was to be bred after reaching the age of five years, and Group B, consisting of 11 heifers, to be mated after becoming four years old. Table XXI (Appendix II) shows, in the second column, that some heifers in both groups were served for the first time some months after attaining the requisite age for their respective groups. This could not be avoided as the decision to mate them at the ages stated was taken too late to ensure, in all cases, mating on the first oestrus after reaching the requisite age.

The heifers to be served were separated from the rest of the animals in the enclosure, the latter being driven into their stables. The bull was then brought and usually double services were given, the second following about 15 minutes after the first. In a few cases heifers would accept only one service. At first it was endeavoured to give service at about 12 hours after the onset of oestrus, but in some instances it was found that when oestrus was first observed, say at 8:30 a.m., it had passed off at 4:30 p.m. of the same day. Hence it was decided to give service to each animal as oestrus was observed, e.g. at 8:30 a.m., at 4:30 p.m. and again the following day, if oestrus was still present. All females were returned to their stables after service.

In the beginning a young Sussex bull was used for service, but being of a very stocky build and somewhat short on the leg, he experienced great difficulty in serving some of the heifers, which were very big and broad. On some occasions he failed entirely and was soon replaced by a more suitable bull, No. 8056 (see Fig. 75).

The bulls were stabled at night and let into small grazing paddocks during the day. They received the same rations as the heifers, but had access to green pasture. Semen examinations were carried out at regular intervals to ensure maximum fertility, and Bull No. 8056 remained fully fertile throughout the experiment.

Individuals showing recurrence of oestrus after mating, were again served during the following heat. In the case of abortions, service was usually delayed for one or two cycles, while after calving, cows were mated three months after parturition.

All services given during one oestrus period were recorded, but were regarded as "one service" for statistical purposes, irrespective of the actual number given.

The animals were kept under close observation during pregnancy, and, when due to calve, were transferred to a loose box or semi-open shed. Assistance was required at parturition in a few cases and afterbirths were removed in cases of retained placenta. These cases are dealt with individually in Appendix I.

With a native attendant constantly present during the day, and the animals being tied up fairly short, it was possible to observe any abortions which took place, however small the foetus and membranes were at times. The aborted foetus and membranes were carefully examined and any abnormalities recorded. It will be shown later that, in spite of the above precautions, cases of very early foetal death (and possibly expulsion) probably passed over unobserved.

Examinations of genitalia (palpation *per rectum* and *vaginam*) were carried out periodically and any changes in the various organs, including the mammary glands, were recorded. Treatment of any of the cases of sterility encountered was purposely withheld, as this was considered outside the scope of the experiment.

As soon as an animal was considered completely sterile, beyond hope of spontaneous recovery, or had borne one or more calves and thus had served its purpose, it was sold by auction to butchers in the Ermelo Municipal area and slaughtered immediately at the municipal abattoir. Live weight, prior to slaughter, and " dressed " weight were recorded and a postmortem examination was conducted.

The genitalia were trimmed, mounted and photographed in the fresh state and thereafter examined macroscopically, weights and measurements being taken, and specimens of each part were placed in ten per cent. Formalin solution for preservation. The endocrine organs, including the pituitary, epiphysis, thyroid, both adrenals, and portions of the thymus and pancreas, were similarly collected, examined and preserved.

In recording the measurements and weights of the genitalia and endocrines, the system of Sisson (1930) was accepted as standard and measurements were taken in the following way: —

Vulva.

Length—from the ventral commissure to the meatus urinarius.

Width—the distance from the dorsal to the ventral commissure.

Vagina.

Length—from the meatus urinarius to the fornix.

Width—the internal diameter (unopened) midway between the meatus and the fornix.

Cervix.

Length—from the external to the internal ostium uterinum, including the portio vaginalis.

Width—the external diameter, near its middle.

Uterine Body.

Length—from the internal ostium uterinum to the internal (true) bifurcation of the cornua.

Width—the external diameter unopened. The length of the body of the uterus could only be determined accurately after the organ had been opened.

Thickness of wall—the actual thickness, including the layers.

Uterine Cornua.

Length—the distance from the internal (true) bifurcation, along the mid-dorsum, to the apex.

Width—the external diameter, at the level of the external (false) bifurcation of the cornua.

Thickness of wall—as in the case of the Uterine Body, taken at the level of the external bifurcation.

Fallopian Tubes.

Length—from the uterine extremity to the infundibulum, after the tube was freed from the mesosalpinx and the flexures straightened out.

Width—the external diameter taken near the middle.

Ovaries.

Length—from the anterior to the posterior extremity.

Breadth—from the attached to the free border.

Width—the diameter between the lateral and medial surfaces.

Weights.

The individual weights of the ovaries were recorded and, in addition, the total weights of the genitalia, *including* the cervix, uterus, tubes and ovaries, but *excluding* the vulva, vagina and broad ligaments. The vulva and vagina showed little variation in size in the different animals and while these structures and the broad ligaments contained greatly varying amounts of adipose tissue, it was considered that the total weights of the genitalia would be erroneously influenced by the inclusion of these appendages.

Pituitary.

Length—from the anterior (rostral) to the posterior (caudal) extremity.

Breadth—the diameter between the dorsal (cranial) and the ventral (oral) border.

Width—the transverse diameter between the lateral surfaces. The weight was also recorded.

Epiphysis and both Adrenals.

Were similarly measured and weighed, after removal of all traces of covering connective and adipose tissues.

Thyroid.

Length, breadth and width (thickness) of each lobe were measured, as well as the total length of the organ, including the isthmus and the total weight, after removal of as much as possible of the adjacent adipose tissue.

Thymus and Pancreas.

These organs were not weighed or measured, but suitable pieces preserved for microscopic examination.

It should be pointed out that in order to minimise as far as possible, post mortem shrinkage, autolysis and desiccation of the organs, the macroscopic examination was carried out as expeditiously as possible and the organs were, in the meantime, kept moist with warm physiological saline solution.

Frozen sections of all the above organs were prepared and stained with Sudan III, whereas paraffin embedded sections were stained with Haematoxylin-eosin. In addition, various staining techniques were tried out on the Pituitary, for the purpose of differentiation of the three main types of cells in the pars anterior. As the organs were fixed in 10 per cent. formalin solution for periods up to three years, the choice of stains was necessarily limited, as the majority

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of specialised pituitary staining techniques require preliminary fixation in various specified fixatives. It was also found that paraffin embedding did not give very satisfactory results and celloidin-paraffin embedding was then applied successfully. One half of the pituitary was embedded and sectioned sagitally as near the median plane as possible.

Eventually a slight modification of the method evolved by Berblinger and Burgdorf (1935) for staining of the human pituitary, was selected with eminently satisfactory results. These authors also claim good results when this method is applied to the bovine pituitary. This was confirmed by Rodriguez (1937), who had excellent results in staining the pituitaries of pigs, bovines, horses, sheep, dogs and various small laboratory animals.

It was found that preliminary mordanting with 3 per cent. potassium bichromate solution improved the results. In the Berblinger-Burgdorf method the following stains are used: — Cresofuchsin (Weigert), Alum carmine, Orange G and Anilin blue. The cytoplasm of the chromophobe cells, which is barely stained, takes on a pale mauve colour. The acidophiles (alpha cells) are stained orange-yellow to deep orange, with granulations showing up prominently. The basophiles (beta cells) are stained in various shades, from deep purplish-blue to pale blue. The nuclear chromatin and nucleoli usually stain bright red, sometimes with a tinge of orange. The negative images of the Golgi apparatus in the cytoplasm of the alpha and beta cells, show up clearly with this method, but the mito-chondria are not visible. Connective tissue fibres take an intense blue colour, thereby clearly revealing the acinous structure of the anterior pituitary and considerably facilitating the counting of the various cells in the microscopic field.

The cells of the pars intermedia stain light purple, while the pars nervosa takes on a bluish-grey colour. The colloid in the hypophysial cleft is stained in various shades of orange or blue, while the erythrocytes appear orange.

Differential cell counts were made of the anterior pituitary in the following way: — The sections were examined under Zeiss × 90 oil immersion objective and × 10 oculars. Commencing at the dorsal border of the pars anterior, all the cells in every tenth field of every tenth row were counted, until the whole section had been worked through. Using the above magnification, an average of about 140 cells per field (depending on the size of the individual cells) was counted. It must be added that only cells showing nuclei were counted, thereby avoiding over emphasis of large acidophiles. In this way an average of about thirty fields per section (depending on the surface area of the sagittal section) was counted, giving a total of about 4,000 cells per section. In the majority of cases duplicate sections were counted, and it was considered that by taking the sum total of these sections a reasonably representative count was obtained. The final result of these differential counts was expressed in percentages of the total in the usual way. The individual variations in number of the three types of cells in two successive sections were usually in the neighbourhood of a fraction of one per cent. and never greater than three per cent. This was considered sufficiently accurate for the purpose of this study.

Microscopic examination of the genitalia and endocrines of each individual animal was carried out, details of which will be found in Appendix I. Micro-photographs were taken with a 35 m.m. "Leica" camera, mounted on a Zeiss monocular microscope. Camera lucida coloured plates of the anterior pituitary were made in a few cases.

III. THE RESULTS OF EXPERIMENTAL OBSERVATIONS.

A. BODY WEIGHTS.

Hammond (1927) mentions that there is a wide belief that heifers in the early stages of pregnancy fatten more easily than non-pregnant animals, and that this is probably due to the fact that in such animals oestrus with consequent excitement and consumption of energy does not occur. Craig (1930) notes that the appetite of animals increases during pregnancy and that there is a tendency to fatten. He further mentions that this tendency should be guarded against as it may retard the development of the foetus, induce abortion, cause difficult parturition, or give rise to " serious after-consequences ".

Quinlan and Roux, (1936) found that cows kept under similar conditions to those described in the present study, gained weight during gestation, the majority being in prime condition during the latter part of pregnancy. They lost weight while suckling their calves, but gained in weight rapidly after the calves were weaned. Hammond (1939) states that fat heifers and animals kept in show condition were difficult to get in calf.

It is well known that animals suffering from nymphomania lose condition, eventually becoming emaciated with rough and lustreless coat—Williams (1943), Quinlan (1929), Richter (1938).

Table I (Appendix II) shows the individual weights of animals in the experiment, taken at birth and thereafter at six-monthly intervals until the animals were slaughtered, the " live " and " dressed " weights being included. In the final column the dressed weights are expressed in percentages of live weight.

It was found that under the experimental conditions described, the animals showed uninterrupted rapid growth and increase in weight up to the age of 4 to $4\frac{1}{2}$ years, after which the rate of increase slowed down gradually, the majority of animals attaining their maximum weight between the ages of six and seven years, when they were considered to in prime condition. Further information of statistical value is not available after this age, as a number of animals were then slaughtered. Furthermore, many animals had by this time conceived and calved or aborted, with consequent fluctuations in weight, making a true comparison with the weights of sterile heifers at corresponding ages impossible, hence also the comparatively lower " percentage dressed weight " of the former animals.

During pregnancy the majority of animals maintained, and even gained in weight. Abortion during the earlier months of pregnancy caused no appreciable loss of weight and condition. Abortion after advanced pregnancy, calving and lactation in many cases caused a sharp fall in body-weight. After the calves were weaned the cows again showed a rapid gain in weight. Cow No. 6292 weighed 1,358 pounds at the time of conception and increased in weight to 1,400 pounds at the time of calving. Subsequent to parturition she suffered from paresis of the hindquarters for a period of six months, and was in very unthrifty condition during this time. At the end of this period she weighed 1,075 pounds, but showed a slight gain in weight after recovery. In spite of this loss of condition, the sexual cycle was undisturbed for a period of 14 months after recovery from the paresis.

While the experiment was in progress, a number of animals developed ovarian cysts and symptoms of nymphomania, yet failed to lose condition or become unthrifty in appearance. This is graphically represented in Graph A, where the average rate of increase in bodyweight of nymphomaniac animals is compared with that of fertile animals in the same experiment. This may be

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explained by the fact that in the present study the animals were closely confined in their stables and were unable to follow the abnormal inclinations, resulting from ovarian dysfunction, i.e. continuous mounting of other animals, wandering about restlessly, etc., these manifestations probably being to a great extent responsible for the loss in condition encountered in practice.

B. AGE OF SEXUAL MATURITY.

Of the heifers in this experiment, 18 were included in observations made by Quinlan *et al*. (1939) on the age of sexual maturity and the duration of the sexual cycle in beef heifers kept under conditions described in detail in Part II of the present study. These authors concluded that the average age of first oestrus was 528·5 days. Heifers born during the warm season showed oestrus for the first time at an average age of 553 days, while those born during the cold season at 496 days. This difference of 57 days was not regarded as significant. They found a striking difference in the age of sexual maturity of heifers born in different years, for which no explanation could be offered.
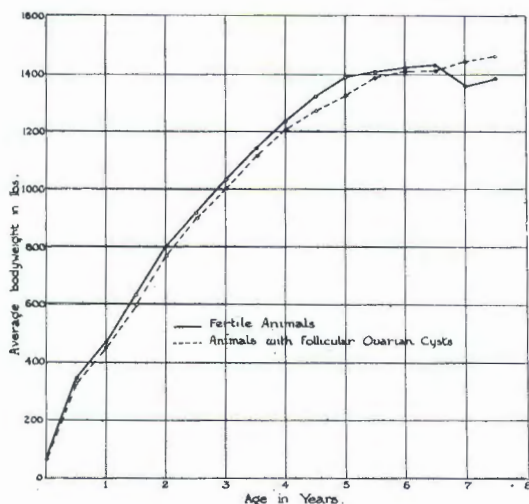
GRAPH A.

Hammond (1927) states that the age of puberty for all breeds under normal conditions of feeding is about 9 months, but may vary from 5 to 15 months. Stoss (1928), quoted by Quinlan *et al*. (1939) observes that heifers reach sexual maturity at nine months; Craig (1930), 12 to 18 months; Williams (1943), 6 to 8 months; Dechambre (1922) and Curot (1921), both quoted by Hammond (1927), 21 months.

Africander cattle under the usual South African veld conditions are stated by Du Toit and Bisschop (1929) to calve for the first time at three years. These authors also found that feeding of bonemeal to cows running on phosphorus deficient veld, resulted in calves (also bonemeal fed), which attained sexual maturity at an earlier age than "control" calves from "control" mothers. Williams (1943) states that the age of sexual maturity depends largely on feeding and housing.

Quinlan and Adelaar (unpublished experimental records), working with various breeds on phosphorus deficient veld, observed that bonemeal-fed heifers became sexually mature at the following average ages: Africanders 577 days; Sussex 503 days; Redpolls 497 days and Frieslands at 535 days. They also found that control heifers which received no bonemeal matured at a much greater age than the bonemeal-fed heifers.

Quinlan (personal communication) observes that heifers at the Onderstepoort Laboratory become sexually mature soon after reaching the age of 12 months.

In the present experiment seven heifers were added to the eighteen used by Quinlan *et al.* (1939). Table II (Appendix II) shows in column 4, the age at first oestrus of individual animals in the experiment. The average age at first oestrus or sexual maturity of the 14 heifers in Group A is $534 \cdot 0$ days. The corresponding figure for the 11 heifers in Group B is $480 \cdot 8$ days. The average for both groups is $510 \cdot 6$ days. No significance can be attached to the difference between the two groups, as they are probably due to individual variations.

When comparing these observations with those made by the authorities quoted above, it is concluded that in heifers kept under conditions of restricted exercise and dry rations, sexual maturity is attained considerably later than in animals under normal conditions of environment and feeding.

C. The Periodicity of Oestrus.

Hammond (1927) states that the length of the normal oestrous cycle in the cow is on an average about $19\frac{1}{2}$ days, but varies from $17\frac{1}{2}$ to 24 days. He also observes that Jerseys usually have a rather longer period than Frieslands and Devons. Wester (1921), Küpfer (1928) and Craig (1930) state that oestrus in the cow recurs every three weeks. Zietschmann (1921-'22) quoted by Hammond (1927), states that the average cycle lasts 21 days. Schmid (1902), quoted by Hammond (1927), found that the variation of the cycle in cows may be much greater than the "average two to four weeks", the limits of variation quoted by most authorities; the majority, he observes, have periods of 18 to 24 days.

Struve (1906, 1911), quoted by Hammond (1927), observed that the majority of cycles fell between seventeen and twenty three days with limits of variation between eight and thirty days.

Weber (1911), quoted by Hammond (1927), found that the cycle was three weeks for cows with intense heat periods, that it varied from $2\frac{1}{2}$ to 4 weeks in cows with average heat periods, and from three to four weeks in cows with feeble heat periods. Barker (1930) indicates that the duration of the cycle in English cattle varies between 19 and 21 days.

Chapman and Casida (1937), working with Friesland cows, observed that out of a total of 690 cycles in clinically normal cattle, $60 \cdot 3$ per cent. fell in a 17-27 days range, with a mode of 21 days. They found no definite seasonal effect in the duration of the cycle, and state that extreme variations in the length of the cycle not only indicate disturbances, such as the presence of cystic follicles and retained corpora lutea, but also serve as a warning of their occurrence in later calving intervals in those animals not known to be abnormal at the time of these extreme cycle length variations.

Anderson (1936), working with Zebu cattle in Kenya, found that the duration of the sexual cycle varies from $17 \cdot 9$ to $24 \cdot 2$ days, with a mean of 20 days, and that there appeared to be no correlation between the periodicity of oestrus and rainfall, temperature and seasonal variations in the pasture constituents.

Quinlan *et al.* (1939) found that the average length of the oestrous cycle in high grade Sussex × Africander heifers, kept under conditions of restricted exercise and dry rations, was 20·3 days, with a range of 18 to 23 days in 91 per cent. of cases.

In the present study the periodicity of oestrus of individual animals between the ages of 1 and 2 years is recorded in Table II (Appendix II), while Tables III to X show this information for the ages of two to ten years, respectively. Tables XI to XIX show the frequency of the periodicity of oestrus of individual animals, at the ages stated above, while this information is summarised in Table XX. When perusing these tables, it should be borne in mind that the numbers of cattle constituting the two groups decreased with advancing age, as the animals were not all slaughtered at the same age. Hence the tables recording the information after the age of seven years, especially for Group B, are of little statistical value, as the number of individuals in the Group is so reduced that individual variations are overemphasized in the summarised results. These latter tables are merely included for the purpose of recording the complete sexual history of every animal in the experiment.

Thus it was found that between the ages of one and two years, out of a total of 127 cycles observed in the Group A heifers, the length of the cycles varied from 14 to 44 days (the latter figure probably representing a double cycle, due to " silent " or unobserved oestrus), with a mode of 21 days and with 92·9 per cent. of cycles falling within the normal range of 18—23 days. In the Group B cattle, with 135 cycles observed, the range was 16 to 46 days, with a mode of 20 days and 91·0 per cent. of cases falling within the normal range of 18—23 days.

Hammond (1927) and Chapman and Casida (1937) found that the length of the cycle in cows increases slightly with age, and that the periods were shorter in fat than in lean animals. Küpfer (1928) states that after a certain number of times, the normal cycle may show aberrations, may be suppressed or may undergo alterations in character. He explains this on the basis that the continuous functioning of the ovaries renders them incapable of producing mature follicles in the normal time, and thus the formation of corpora lutea is interfered with.

In the present study the following variations in the length of the cycle were noted as age advanced: —

Age. (Years).	Group A. Mode (Days).	Group B. Mode (Days).
1– 2	21	20
2– 3	21	19
3– 4	21	19
4– 5	21	21
5– 6	21	—
6– 7	20–22	20
7– 8	21–22	—
8– 9	21	—
9–10	23	—

It therefore appears that very slight, if any, variation in the length of the cycle occurred in these animals.

Quinlan and Roux (1936) found that as the ages of cows kept under special environmental conditions advanced the percentages of oestrous cycles falling between 18 and 23 days decreased.

The following variations in the percentage of cycles falling in the range 18—23 days were noted in the present study, as the ages advanced:—

Age. (Years).	Group A. (Per Cent.).	Group B. (Per Cent.).
1– 2	92·9	91·0
2– 3	94·3	89·7
3– 4	89·7	77·7
4– 5	72·0	63·9
5– 6	49·6	50·0
6– 7	54·0	60·0
7– 8	62·5	25·0
8– 9	66·7	—
9–10	63·2	—

This is in agreement with the findings of the above authors.

D. The Duration of Oestrus.

Hammond (1927) observes that the duration of oestrus varies from 6 to 30 hours with a mean of 17 hours, and that cows show a slightly longer duration than heifers. Also that fat animals are inclined to exhibit shorter duration of heat. Weber (1911), quoted by Hammond (1927) found that in cows with intense heat it varied from 12 to 36 hours, in cows with average heat periods from 6 to 36 hours and in cows with feeble heat periods from 3 to 36 hours.

Craig (1930) states that the duration of oestrus varies from 8 to 24 hours. Chapman and Casida (1937) observe that the duration of oestrus increases with increasing age. Williams (1943) mentions that the duration of oestrus is shortest in the healthiest individuals of the species, that the maturation of the follicle is rapid and its rupture prompt. Wester (1921) gives the duration as 12 to 30 hours; Quinlan (1929), 17 to 24 hours.

Anderson (1936) observes that in Zebu cattle in Kenya, the duration of oestrus is remarkably short, varying from 0·2 to 2·9 hours with a mean of 1·3 hours. He further found no correlation between duration of oestrus and seasonal variation in rainfall, temperature and pasture constituents, but some indications of a possible relationship between sunshine and duration of oestrus. The significance of this relationship is enhanced by the fact that in Britain oestrus in cattle is longer in summer than in winter, and that light stimulates reproduction in other animals.

Quinlan et al. (1941) made observations on the duration of oestrus in summer in heifers of various breeds, kept under environmental conditions prevailing in the North Western, semi-arid, summer rainfall areas of the Union of South Africa. They found that the average duration of oestrus proper in Africander heifers was 7·88 hours; in Frieslands 11·67 hours; in Redpolls 14·00 hours and in Sussex 9·00 hours. They concluded that the environmental conditions mentioned above shortened the duration of oestrus significantly when compared with the accepted standard range of 18 to 24 hours.

In the present study accurate observations were not attempted to determine the duration of oestrus. While the heifers were young, it was found that the duration was usually less than 24 hours. As they grew older the tendency was for the duration to lengthen up to 36 hours, and in some cases to 48 hours. Some heifers invariably showed oestrus of longer duration than others. Menstruation sometimes followed oestrus within 48 hours, but was not consistently present in these animals.

E. Results of Mating.

For the purpose of discussion, the heifers in the experiment which conceived may be divided into two groups, as follows:—

	Groups.	
	A	B
(a) Those in which gestation terminated in normal parturition	2	3
(b) Those in which gestation, at some time or other, terminated in abortions or still births	5	3

1. *Pregnancy Data.*

The details on pregnancies have been summarised in Table XXI, Appendix II, and this Table has been further analysed in Table XXII. The following deductions may be made from these tables:—

(a) The average number of services required to establish pregnancy does not materially differ in the Group A and Group B animals.

(b) The average number of services required to establish pregnancy in both groups, decreased with second, third and fourth calvings. Quinlan and Roux (1936) obtained similar results.

(c) The average number of services required to establish pregnancy was higher than is normally recorded in cows. Quinlan and Roux (1936) in their experiment recorded 1 to 2 services, and considered this as normal. Williams (1943) considers 1 to 2 services as normal.

(d) Seven animals out of 14 in Group A eventually conceived, i.e. 50 per cent. Six animals out of eleven in Group B conceived, i.e. approximately 55 per cent.

(e) The 7 animals in Group A experienced a total of 18 conceptions, with the following results: 6 abortions, 3 still births, 7 normal calves and 2 pregnancies terminated by slaughter. The latter two may be considered as pregnancies which would probably have terminated normally, bringing the total of normal pregnancies to nine. Hence in Group A, out of 18 conceptions 9 normal pregnancies resulted, i.e. 50 per cent.

(f) The 6 animals in Group B experienced a total of 13 pregnancies with the following results: 2 abortions, 1 still birth, 7 normal calves, 3 pregnancies terminated by slaughter. Of the latter, 2 may be considered as normal pregnancies, while the third would probably have terminated in abortion, had the animal been kept alive. Hence in Group B, out of 13 conceptions 9 normal pregnancies resulted, i.e. approximately 69 per cent.

(g) The above differences between the two groups are due to the significantly higher incidence of abortions and still births recorded in Group A than in Group B, the actual figures being: Group A, 6 abortions, 3 still births; Group B, 2 abortions, 1 still birth.

(h) It is significant that no abortions or still births occurred in either group with the third pregnancies.

(i) The average number of services required to establish pregnancies terminating in full term parturitions (including still births) was 3·17.

The average number of services required to establish pregnancies terminating in abortions was 4·25. These differences are considered significant and serve to indicate that potentially degenerate pregnancies are heralded by reduced fertility.

2. *Gestation periods.*

Quinlan and Roux (1936) found that in cows bred at the normal age, but kept under similar conditions as those in the present study, the gestation periods fell within the range of 264-289 days, while the mode was 281 days and the average 279·6 days. Eighty-one per cent. of the periods fell between 276 and 286 days. They found no tendency for the gestation periods to alter with advancing age, or any difference between the periods for male and female calves.

Craig (1930) mentions that the duration of gestation is longer for male than for female calves and that weakly animals have shorter periods than strong, wellfed ones. Out of 1,062 observations he found the mean to be 283 days. He also quotes the following authorities:— Colin, 280 to 285 days; Dieterichs, range 210 to 353 days, average 286 days; Baumeister and Reuff, range 240 to 330, average 285 days; Earl Spencer 284 to 285 days.

Hammond (1927) states the average duration to be 40 weeks, but slightly longer with bull calves and slightly shorter with heifer calves. Wellman (1910), quoted by Hammond (1927) found that Hungarian cows averaged 285 days, while Simmenthalers averaged 291 days. Wilhelm, quoted by Hammond (1927), states that the period of gestation in the Hungarian cow is some ten days longer than in the Dutch cow.

Williams (1943) states that abnormalities in the duration of pregnancy are inseparably linked with abortion, retained placenta, dystocia and other interferences with reproduction. He observes that with twin calves the gestation is usually abbreviated and is followed by a high death rate among the young and the parturient females.

In the present study details on the gestation periods in individual pregnancies will be found in Table XXI, Appendix II, while this information is summarised in Table XXIII, both for full term calvings and abortions.

The following deductions may be made from these tables:—

(a) The range of gestations in calvings is significantly wider in the Group A than in the Group B cattle.

(b) The range for all calvings falls within the period 261 to 291 days, with a mode of 283 days and an average of 278·8 days. Fifty per cent. of all periods fall within the range 276 to 286 days.

(c) The average of gestation periods of calvings in the Group A cattle is 275·8 days, while that of the Group B cattle is 282·9 days. This difference is considered significant, indicating that the earlier bred group had gestation periods approaching normality, while the later bred group was inclined towards short gestation periods.

(d) Eight female calves were born after an average gestation period of 278·25 days, while ten male calves were born after an average gestation of 279·5 days. This difference is not considered significant.

(e) There is no correlation between the ages of the cows and the duration of gestation.

(f) Of the four still births, two were male and two female calves with respective gestation periods of 277, 290, 291 and 264 days. The only twins born in the experiment were a pair of still-born females. Twin foetuses were aborted after 97 days gestation in one case.

(g) The range of gestation in abortions is considerably wider in the Group A than in the Group B cattle. This difference is not considered significant.

(h) Seven out of eight abortions occurred at less than five months gestation.

3. *Birthweights and viability of Calves—Parturition and Lactation.*

Quinlan and Roux (1936) found that unrestricted sunlight and exercise do not reflect any advantage upon the weights of calves produced. Few calves in their experiment weighed less than sixty pounds, while weights up to ninety-nine pounds were recorded. They found a considerable difference in the birth weights of calves sired by different bulls. Cows maintaining a higher condition throughout gestation, lactation and rest were likely to produce calves which were small and light in weight.

Craig (1930) states that the weight and dimensions of the calf at birth vary considerably according to the size, breed and condition of the parents, and other circumstances which more or less influence growth. The calf at birth varies in weight from 31 to 55 Kilograms, with an average of 32·5 Kilograms.

Hammond (1927) states that fat cows frequently produce undersized calves and also that first calf heifers usually have smaller offspring than matured cows.

Williams (1943) observes that the bovine foetus grows continuously with prolonged gestation and that this frequently results in foetal giantism with dystocia.

The majority of cows in the experiment, which eventually calved, showed improper relaxation of the cervix, vagina and vulva at parturition. This frequently resulted in protracted births with uterine inertia, dystocia and retained placenta, the animals often requiring assistance in the form of traction. While the majority of cases of uterine inertia may be attributed to hormonal dysfunction, some of these could, however, be ascribed to myometrial hypoplasia, the expulsive efforts being feeble from the commencement of parturition. The four cases of still births and the numerous cases of retained placenta could be definitely ascribed to prolonged parturition, through the above abnormalities. Undue adhesion between the foetal and maternal cotyledons was not encountered.

The birth-weights of male calves (including still births) ranged from 40 to 92·5 pounds, with an average of 65·9 pounds. That of females ranged from 32 to 83 pounds, with an average of 61·1 pounds. The stillborn calves weighed less than the average, their weights at birth being 52, 40 and 56 pounds, while the stillborn twin females weighed 32 and 34 pounds respectively.

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Of the fourteen live calves born, one was a weakling and died after 19 days. The remainder showed surprising vitality and made rapid progress in weight and growth. Two cows showed poor lactation, being incapable of rearing their calves, the latter having to receive supplementary milk from other cows.

4. *Abortions.*

Quinlan (1929) states, in connection with Brucellosis, that if abortions occur at the third or fourth month the afterbirth is usually expelled with the foetus and the uterus cleans up quickly. When the foetus is carried to seven or eight months before abortion takes place, the afterbirth is retained as a result of incarcerating placentitis of abortion.

Williams (1914) quoted by Hammond (1927) states that when abortion takes place before the foetus is about 30 cm. long, it is expelled enclosed in the foetal membranes but after this period it is born naked and the membranes are expelled as an afterbirth.

Hammond (1927) states that at the end of the first month of pregnancy the foetal membranes lie over the surface of the cotyledons, but no projections are present interlacing the two. In the second month the membranes have become fairly firmly-attached to the cotyledons by finger-like downgrowths, which eat their way into the tissues of the cotyledons. The maternal cotyledon responds to this stimulus by growth of the connective tissue and interlocking lamellae are formed. At three months a larger and more complete system of branching in both the maternal and foetal projections occurs, which increases as pregnancy advances. Hammond (1927) further observes that " cases of sterility are known to occur where the cow is served and, after showing no signs of heat for several months suddenly comes on heat again, although no abortion has been seen. Such cases are frequent after outbreaks of Contagious Abortion or Granular Vaginitis, and are believed by some to be due to persistent corpus luteum or to unobserved abortion; it is more probable, however, that in these cases foetal atrophy has taken place and resorption *in situ* has occurred ".

Craig (1930) states that " in the simplest cases oestrus appears in the cow in from one to two weeks after abortion and conception may then take place ".

Winters, Green and Comstock (1942), quoted by Laing (1945) state that the bovine embryo becomes attached by its membranes within the uterus at about 12 days *post oestrum.*

Laing (1945) observed that in a proportion of apparently normal cows the ovum may be fertilised and then die early so as not to influence the regression of the corpus luteum, oestrus recurring at the first expected time; or death may occur after implantation and the return of oestrus be delayed till some time beyond three weeks from the date of service. He further remarks that this may account for the occurrence of infertility in clinically normal animals served by potentially fertile bulls, including those animals which return for service at six weeks, or between three and six weeks.

Browne, Henry and Venning (1939) formulated the following theory of endocrine mechanism in threatened and habitual abortions in humans:— " The evidence suggests that the ovary and placenta are two sources of progesterone and oestrogen during pregnancy. They interpret the rise in pregnandiol excretion, which occurs from the seventieth to ninetieth days in most normal cases, as being due to the beginning of secretion of progesterone by the placenta. The

time at which the transfer of function occurs from the ovary to the placenta varies in different individuals and in the same individual in different pregnancies. If, however, the corpus luteum ceases to produce progesterone for any length of time before the placenta begins to secrete it, abortion will follow. The time at which a deficiency of corpus luteum hormone is most likely to occur is in the transition period between the ovarian and placental phases (late second and third months). This is a critical period of pregnancy. The cause of many abortions is a faulty gestation from the first; the chorion partakes in this abnormality and produces an amount of gonadotropic substance inadequate to prolong the corpus luteum beyond a certain point. Of other patients whose gestation is less abnormal, the function of the corpus luteum may be prolonged for the usual time and the embryo develop normally, but the placenta may be slow in taking over. Patients in whom either of these conditions occurs repeatedly abort habitually."

As stated previously, seven of the eight cases of abortion observed in the experiment occurred at less than five months gestation. The eighth case occurred after 232 days gestation. With the exception of the latter, the foetuses were expelled in their intact membranes, which showed not the least indication of cotyledon formation. In two cases the foetuses and membranes showed signs of maceration, the remainder being perfectly fresh.

In these seven cases the abortion occurred without premonitory indications. The abortion was sudden and expulsion effortless, without visible disturbance of the health of the cow.

The XXI, Appendix II, shows the periods between abortions and first oestrus. A significant feature is the fact that, with the exception of one abortion which occurred at 232 days (Cow 6423) all cows showed oestrus in from 1 to 3 days after abortion. In one case (Cow No. 7269) the animal showed oestrus on the day *prior* to abortion.

Cow No. 6423 first aborted after 232 days gestation. Dystocia due to breech presentation of the foetus occurred. This was rectified and the foetus delivered, but the placenta was retained as a result of uterine inertia and had to be removed the following day. Recovery was uneventful and the cow showed normal oestrus after 24 days. She again conceived after four services and abortion of twin foetuses occurred after 97 days gestation, followed by oestrus within 24 hours.

5. *Interval between calving and first oestrus.*

Quinlan and Roux (1936) state that in their experiment restriction of sunlight and exercise tended to shorten rather than lengthen the period between calving and first oestrus. Under these circumstances they found that oestrus could occur as soon as 15 days after calving, while some animals showed a period of inactivity of over 100 and even 200 days. In the majority, however, it was in the vicinity of 60 days. They also found that the period of inactivity tended to shorten as the ages of the cows advanced.

Hammond (1927) found that the period varied from 9 days to 6 months, the usual time being 3 to 4 weeks if the cow is milked and about 3 months if the calf is suckled. He states that poor feeding and heavy milking lengthen the period of inactivity. Weber (1911), quoted by Hammond (1927) found that the period varied from 3 to 7 weeks.

Küpfer (1920), quoted by Hammond (1927), states that after parturition the corpus luteum of pregnancy degenerates in the same way as does the periodic corpus luteum and the cow ovulates again 16 to 21 days after calving.

Craig (1930) observes that the period varies from 4 to 9 weeks and that oestrus may be deferred by a suckling calf. This latter view is shared by Williams (1943) who further states that the first oestrus after calving in dairy cows is very erratic and in many cases may be classed as pathological; if bred at less than 70 days after calving, this may result in unrecognised conception, the ovum perishing and disappearing unseen after damaging the uterus and upsetting rhythmic ovulation. He observed similar results in beef cows.

Burger (1946) found in sows that the first oestrus *post-partum* was anovulatory and, therefore, sterile. He observed no correlation between the length of nursing period, litter size and the interval between weaning and post-weaning oestrus.

Table XXI, Appendix II, shows the periods recorded in the present study. After the first calvings the periods varied from 25 to 132 days, with an average of 76·4 days. After the second calvings the range was 30 to 94 days, with an average of 62·0 days, while after the third calvings the range was 59 to 188 days, with an average of 135·6 days. After the single fourth calving (still birth) in the experiment, oestrus was recorded after 43 days.

There is no significant difference between the Group A and B cows in this respect. In general the period of inactivity was shorter following still births than following the birth of viable calves, which suckled their dams up to the age of six months.

F. Functional Sterility.

Some of the heifers as a result of delayed breeding were considered to be suffering from functional sterility. Before describing this condition as encountered in these animals, the literature on the subject will be reviewed.

Quinlan (1929) and Quinlan and Roux (1936) discuss at some length the subject of functional sterility and enumerate the various factors which may be considered as contributory towards the cause of this condition. They point out that housing, insufficient exercise, high feeding, high milk production, controlled and delayed breeding, vitamin and mineral deficiency, obesity and undernourishment are factors which tend to induce a deviation from the normal physiological activities of the female genitalia and that these factors appeared to upset the balance of the hormone secretions connected with the normal functioning of the genital tract. Quinlan (1929) furthermore states that he found no constant pathological change, either macroscopic or microscopic, in the ductless glands outside the ovary in cases of sterility due to pathological lesions in the genitalia. He urges the necessity of further study of the endocrine organs in cases of functional sterility.

Frei (1934) attempts to explain the aetiology and pathology of disturbed reproduction on the basis of neuro-endocrine interrelationship. He first considers the possibility that the genital centre, believed to be located in the diencephalon, and which, being closely interrelated with the hypophysis, may in some manner be the active or passive cause of reproductive disturbances. Whenever the hypophysis or diencephalon is diseased one must expect corresponding disturbances of the reproductive system. Conversely, when no morbid anatomical lesions are to be found in cases of disorders of the reproductive system, the diencephalon and hypophysis must be looked upon as the source of the disorders. Thus sexual infantilism and senescence may have their origin in the diencephalon-hypophysis

system. Various conditions, such as eclampsia, the sagging of the uterine broad ligaments, failure of the cervix to open with the advent of parturition and the disorders incident to parturient paresis may be caused by a possible derangement of the tonus relationship between the sympathicus and parasympathicus.

Linkies (1935) shares the views of Frei (1934) concerning the significance of the vegetative nervous system in the causation of sterility, namely, the antagonism between the sympathicus and parasympathicus. He assumes that sterility due to starvation and that due to overfattening correspond to vagotonia and sympathicotonia respectively. He discusses the influence of seasons on the sexual processes. In spring increased vagotonia stimulates the reproductive functions, while in autumn sympathicotonia is prevalent. Under natural conditions autumn is the principal time for pregnancy, while the period of increased vagotonia favours parturition and development of the young. For best results, he concludes, this normal seasonal rhythm should be followed in the breeding of domesticated animals.

Richter (1936) shows on the basis of numerous data for horses, cattle, goats and pigs, that inbreeding cannot be regarded as a cause of sterility. He further states that the percentage fertilization in domestic animals is considerably lower than in that of the corresponding wild forms, owing to changes in sexual life. He observes that fertility in domestic animals is greatly influenced by various environmental factors such as insufficient light (lack of Vitamin D), excessive, deficient or unbalanced diet (protein, phosphorus or calcium deficiency, lack of Vitamin A and D). These may cause reduction in the percentage of fertilization or sterility through disturbance of oestrus, as these deficiencies impair the functions of the pituitary and gonads.

Craig (1936) discusses the problem of functional and structural sterility. He states that in functional sterility no structural changes or morbid lesions can be detected, but that it is not always possible to make a clear-cut line between the two forms. Production of the pituitary gonadotropic, as well as the follicular and luteal hormones may be affected by a number of extrinsic factors such as drought, inadequate diet, mineral and vitamin deficiencies, over-fattening as seen in beef heifers fed for show or sale. In such cases no anatomical defect can be found and oestrus is sometimes regular. He points out the possibility of thyroid deficiency in these cases. He also mentions confinement and lack of exercise, and that under such circumstances oestrus is not well marked and passes off undetected. Delayed breeding is mentioned by him in heifers (up to the age of 4 or 5 years) and in cows in which service is delayed after parturition, and he observes that in these cases atrophy of the uterine mucosa and cotyledons may exist.

Wooldridge (1938) stresses the importance of Vitamin E deficiency in the causation of sterility, abortion and placental and foetal degeneration, the necessity of this vitamin in lactation and its association with the synthesis of anterior pituitary hormone.

Fossum (1938) states that there are no adequate diagnostic methods of drawing a sharp line of demarcation between the condition of functional sterility and that involving demonstrable genital causes, or between curable and incurable sterility. He enumerates the following causes of functional sterility: Malnutrition (" hunger sterility "), high milk yield and obesity. He mentions that with fattening " a deposition of fat in the ovaries takes place at the expense of the generative tissues."

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Stockklauser (1938) in a brief review on the influence of high milk yield and feeding on sterility, concludes that high milk yield in dairy cows is not a cause of sterility. This review is shared by Eckles (1929).

Lehmke (1938) successfully treated the following cases of sterility with injections of wheat germ oil: —

(a) Animals showing irregular oestrus without clinical changes in the genital apparatus.

(b) Animals with a normal cycle and no clinical changes in the genitalia.

(c) Anoestrus animals.

(d) Animals showing follicular cysts in the ovaries.

In the latter cases he applied genital massage and rupture of the cysts prior to the oil injections.

McIntosh (1938) classes as functionally sterile those animals which fail to ovulate or manifest oestrus, those which fail to conceive when oestrus does occur, early abortions after conception and nymphomania. The latter is not regarded as a no-lesion form of functional sterity but often occurs without any preceding phenomena. Failure to ovulate is often due to persistent corpus luteum. It usually occurs during the colder season with a Vitamin A and phosphorus deficient diet and in cows which are milked close up to the following lactation.

Hammond (1939) found that "fat heifers, animals kept in show condition and cows, which for any reason are prevented from breeding for some time, are difficult to get in calf. The reason for this is probably that luteal tissue accumulates in the ovaries from successive ovulations and upsets the delicate balance of the cycle, leading to less marked physical symptoms of oestrus, although the psychological symptoms appear as usual. Be this as it may, there is a very large number of sterile cows which have quite regular heat periods and in which no abnormal anatomical or pathological condition exists. Many of these cows can be cured of this sterility by removing the corpus luteum. Under the influence of progesterone, the cervix becomes tightly closed and the secretions of the mucosa become dry and sticky, rendering the conditions unfavourable for the ascent of sperm ".

Clark (1937) successfully treated cases of functional sterility with physiological saline douches (vaginal and uterine) and ovarian massage.

Boyd (1934) found that animals fed on a diet low in calcium reproduced equally well as those receiving a high or medium calcium intake. The rhythm of the oestrus cycle continued undisturbed in cows on a phosphorus deficient diet. Evidence, however, indicated that a low phosphorus intake may interfere with normal reproduction, which was manifested by occasional abortions with subsequent sterility.

Kingman (1933) classes under functional sterility hypophyseal dysfunctions which become manifest in the related ovarian disturbances. He includes follicular cystic degeneration as probably being chiefly caused by a disturbed endocrine balance—" a hyper-hypophyseal (Prolan A) stimulation "—in conjunction with various mineral and vitamin deficiencies and nervous disturbances. He further discusses the part played by persistent, cystic and prematurely atrophic corpus luteum and static ovaries, their possible causes and treatment. Schöttler (1934) reports good results in the treatment of ovarian hypofunction with Prolan.

Sorenson (1937), quoted by Hammond (1939), found that by artificial insemination he obtained a rather higher percentage fertility than by normal matings. Siebenga (1938) also quoted by Hammond (1939) has successfully overcome sterility in a number of cows by artificial insemination.

Malan (1935) quoted by Quinlan and Roux (1936), concludes from the results of his observations at this Institute that Vitamin A deficiency in the ration of pregnant ewes and cows produces abortion or weakly young that are often blind and unable to rise. He observed further that the absence of this vitamin in the diet is in some way associated with the absence of the psychological symptoms of oestrus. Both ewes and cows on a dry ration containing a minimum of vitamin A show oestrus only very infrequently and even then, if mated will become pregnant only in a very small percentage of cases.

Müller (1938) reports successful results in the treatment of cases of disturbed oestrus, chronic endometritis and retained placenta with injection of the Vitamin A containing preparation " Multigen ".

Sutton and Brief (1939) found that Vitamin A deficiency in rats exerts a direct damage on the gonads. Histological study of the anterior pituitary revealed a marked increase in the basophile cells similar to that encountered in castrate animals. They also found that the gonadotropic activity of the pituitary increased with Vitamin A deficiency and that these anatomical and physiological alterations represent compensatory changes similar to those following castration.

Madsen, Hall and Converse (1942) found that young beef and dairy cattle, suffering from either Vitamin A deficiency or with a history of early severe Vitamin A depletion, almost invariably had cystic pituitary glands. The cysts occurred either in the residual lumen or within the posterior lobe, often causing compression of the gland and injury to the glandular parenchyma. No evidence of repair in a cystic pituitary was found in an animal that was Vitamin A deficient early in life but fed adequate amounts of carotene, suggesting that the injury to the gland may be permanent.

In the present study, under the heading " Functional Sterility " are included, in its narrower sense, only those heifers which showed no gross clinical abnormalities of the genitalia and which, in spite of repeated matings, failed to conceive. Only three may be classed under this heading, namely Nos. 6358, 6442 and 7469. In its wider sense, those heifers which conceived after an abnormally large number of services (see Table XXI), whether followed by abortion or calving, could also be included in this group, and also those animals which, after repeated services, failed to conceive and eventually developed nymphomania (Nos. 7172 and 7346). However, these latter cases for convenience are grouped under the appropriate headings and will not be discussed here.

Cow No. 6358 received 46 services over a period of 32 months during which she experienced normal sexual cycles which were interrupted at intervals by 3 long periods of 44, 41 and 31 days respectively. Two of these periods may be regarded as multiples of normal cycles, and are probably manifestations of " silent " oestrus or observational failures. Frequent clinical examinations revealed a firm infantile cervix and uterus, while the ovaries remained functionally active. At post mortem examination gross and microscopic cystic degeneration and atrophy of the endometrium, including the cotyledons were present.

Much the same history is shown by Cow No. 7469 which received 21 services over a period of 14 months with failure to conceive. Clinical and post mortem examinations revealed similar changes to those found in the above animal.

Cow No. 6442 received 25 services over a period of 29 months. Shortly after the commencement of mating at the age of 5 years she began to show irregularities of the sexual cycles, which tended to become longer with periods up to 81 days. During these long periods she was carefully observed but no abortions were noted, although this possibility is not precluded. In this connection foetal atrophy and resorption must also be borne in mind, (Hammond, 1927; Laing, 1945). Clinical examination revealed an infantile uterus and cervix but functionally active ovaries. Post mortem and microscopic examination showed cystic degeneration and atrophy of the endometrium, including the cotyledons, unilateral (right-sided) salpingitis and a uterine fibroid in the left horn. None of these changes was clinically demonstrable and the tumour was not considered of any importance in the causation of sterility. The salpingitis undoubtedly contributed to the infertility, although the left tube was normal. The most obvious cause, however, was the endometrial change. The changes in the genital tract and endocrine system in relation to sterility will be discussed in greater detail in a later chapter.

G. Disturbances in the normal Rhythm of the Oestrous Cycle and the Duration and Intensity of Oestrus.

In a previous chapter it was concluded that the duration of the normal oestrous cycle in the cow varied from 18 to 23 days. Any periods falling outside this range must be regarded as abnormal. Ovarian function is controlled by the activities of the anterior pituitary, and the cyclic changes may be disturbed by various extrinsic and intrinsic factors . The rhythmic recurrence of oestrus is dependent on a delicate balance of the internal secretions produced by the corpus luteum and the ripening follicle, through the mediation of the anterior pituitary gonadotropic hormones.

In the present study it was found that the disturbances in the normal sexual cycle occurred in a large percentage of cases and that this resulted in extensive changes, both morphological and physiological, in the sexual and endocrine organs of the individuals involved.

The most common disturbance encountered was that of prolonged oestrus, accompanied by short interval cycles, due to cystic degeneration of the Graafian follicle. This condition is commonly known as nymphomania and has been described in detail in almost every publication on sterility studied during the course of these investigations.

In studying the literature on nymphomania it was found that the gross symptomatology coincides largely with that to be described in the experimental animals. There exists however, a wide difference of opinion on the fundamental cause of follicular cystic degeneration.

Williams (1943) observes that it is most common in dairy cows with high milk production, but he has encountered it also in dairy heifers not known to have been pregnant and in Hereford heifers. W. W. Williams, quoted by W. L. Williams (1943), has observed nymphomania in dairy heifer calves six to eight months old, arresting the growth of the calf and producing early senility. W. L. Williams also states that it is sometimes seen in animals after repeated unsuccessful services and in cows which have been held out of breeding for prolonged periods. Frequently the cow has aborted, or has suffered from retained

afterbirth or metritis, while in numerous cases the parturition and puerperium have been considered as physiological. He concludes by stating that the fundamental cause of follicular cystic degeneration is unknown. Hypothetically it is attributed to an endocrine disturbance, but it is not known which of the endocrine glands is at fault.

The frequency with which cystic degeneration of the ovary is found to exist concurrently with inflammatory changes of the cervix, uterus and fallopian tubes has led most authors to the conclusion that ovarian disease is secondary to that of the genital tract. This view was held by Albrechtsen (1921), Wester (1921), Opperman (1924), Hammond (1927), Quinlan (1929) and Richter (1938).

Frei (1927) offers the following explanation. He agrees with the view held by the majority of German and American authorities, namely, that endometritis is the primary and most usual cause of cystic follicular degeneration, either through direct ascending micro-organismal infection via the tubes or through damage to ovarian function by bacterial toxins resorbed in the endometrium. He, however, recognises the probability that the endometrium is profoundly influenced by the follicular cysts to such an extent that changes resembling those found during oestrus may occur. These changes can so strongly resemble those found in endometritis catarrhalis that no distinction is to be made. Thus, when endometritis and cystic follicular degeneration are encountered concurrently, the changes in the endometrium may be primary or secondary to the ovarian changes.

Hess (1922), quoted by Quinlan (1929), maintains that the pathological changes found in the endometrium of nymphomaniac cows were probably secondary to the cystic degeneration of the ovaries.

Boyd (1934) states that the aetiology of cystic degeneration of the ovary is still obscure and controversial, but that the present trend of thought is gradually swinging to the support of those who believe that dysfunction of the endocrine system is the most common causative factor.

Hammond (1939), in discussing the cause of cystic follicular degeneration, states that if for some reason not known, luteinising hormone (Prolan B) is not secreted by the anterior pituitary when the follicle is ripe, ovulation does not occur and then either (a) the ripe follicle may go on growing and form a large cyst, or (b) other follicles may ripen and form a number of small cysts in the ovary. In the first case the cow usually fails to exhibit any further psychological symptoms, although the physical symptoms such as swollen vulva, relaxed and open cervix and raised tail and head—all symptoms of the action of oestrin— are intensified. In the second case of small multiple cysts the principal symptoms are similar, but the psychological symptoms of heat appear every few days as each follicle ripens.

Moore (1946) succesfully treated 17 out of 18 cows suffering from cystic follicular degeneration with one or two intravenous injections of 1,000 I.U. of chorionic gonadotropin (pregnant mare's serum). Twelve of the animals showed the presence of corpora lutea within eleven days after the administration of the hormone.

In human gynaecology the same importance is apparently not attached to cystic follicular degeneration as in bovines. Blair Bell (1919) states that " follicu- lar cysts rarely reach the size of a walnut and are only occasionally of clinical importance. There are sometimes several of these cysts in the same ovary. The

condition is not uncommonly seen in married women after prolonged sexual abstinence and in middle-aged spinsters. In these circumstances the patient may suffer from menorrhagia. When examined microscopically the cysts are seen to be lined by cells of the membrana granulosa, which is supported by the theca interna and externa, in the former of which may be seen cells of the lutein layer. Blood cysts occur as a result of pelvic infection which encloses the ovary in adhesion. In many cases the infection is of a mild type and proceeds from the bowel. The sequence of events is as follows: — the follicle ripens and haemorrhages occur into it, with detachment of the cells of the membrana granulosa. Rupture cannot occur so the blood is confined within a cyst whose walls are lined by lutein cells—the condition is in fact a lutein retention cyst. The symptoms are similar to those of pelvic infection; the patient complains of dysmenorrhoea, menorrhagia and backache. The treatment consists of laparotomy with partial excision of the ovary or ovaries ".

Shaw (1936) groups under the term " metropathia " cases of irregular and excessive uterine bleeding in which no local abnormality can be detected by pelvic examination. He states that in the past years the aetiology of these cases was attributed to inflammation of the myometrium or endometrium, and the tendency was to group them under such terms as chronic metritis, fibrosis uteri and delayed subinvolution. The modern tendency is to regard them as being determined by ovarian dysfunction, which leads to irregular menstrual rhythm and prolongation of the period of menstrual discharge. In metropathia haemorrhagica the endometrium is thick and polypoidal and one or other ovary contains a cystic follicle. The disease is most prevalent in women over the age of 40, but cases are occasionally encountered in girls under 20. Microscopically the endometrium shows the characteristics of cystic glandular hyperplasia, many glands showing cystic dilatation, the larger ones being visible to naked eye. The epithelium is high columnar with a few large degenerate cells lying in the cavity of the cyst. The glands show hyperplasia but no secretory hypertrophy. One or other ovary always contains a cyst which is seldom more than 2 inches in diameter, while the opposite ovary is usually atrophic. Recent corpora lutea are never found. The cyst has the characteristics of a cystic ripening follicle, but it is not uncommon for both granulosa and theca interna cells to show some degree of luteinisation. The changes therefore indicate that ovulation and corpus luteum formation are inhibited. He concludes by stating that the disease shows an association between ovarian dysfunction and an abnormal condition of the endometrium, but that little is known of the factors which determine the development of the disease. With regard to treatment he mentions that good results have been reported from the administration of anterior pituitary sex hormone.

Turner (1943) reports on a case of bilateral microcystic degeneration of the ovaries in a woman of 23 years as follows: — microscopic examination revealed cystic follicles with a well-defined narrow granulosa layer and much wider theca interna showing distinct luteinisation. There were also clusters of luteinlike cells in the stroma some distance away from the follicles. The endometrial glands were small, poorly defined with a tendency towards secretory activity. The patient showed masculine features such as hirsutism, small breasts, atrophy of the labia and hypertrophy of the clitoris. Complete recovery took place after removal of two thirds of both ovaries and rupture of the follicles.

Allen, Doisy *et al.* (1924) working on rats found that marked atrophic changes accompanied by leucocytic infiltration occurred in the uterus six days after the removal of the ovaries. After several injections of oestrogen the

leucocytes disappear, the organ becomes hyperaemic and oedematous, glandular growth and secretion causing distension of the uterus. Similar changes were brought about in immature mice and rats. Later Allen, Smith and Gardner (1937) found that mitotic division of the uterine and glandular epithelium is greatly accelerated by oestrogen, which results in extensive cellular hyperplasia. The deeper parts of the glands begin growing first, then cell division stops and secretion begins, while mitoses continue in the surface epithelium.

Similar mitotic acceleration was observed in the tubal epithelium of the rat, mouse and monkey with oestrogen injections (Allen, 1938).

Witherspoon (1933), quoted by Nelson (1937), describes the frequent association of cystic ovaries in women with uterine fibroids, and strongly urges the possibility that the latter may be due to a stimulation of the uterine muscle and connective tissue by oestrogenic hormone.

Gardner, Allen and Strong (1936), and others conclude that excessive oestrogenic stimulation probably renders the uterus more susceptible to infection, resulting in bacterial pyometra.

Nelson (1937) found that administration of oestrone or oestradiol in oil to guinea-pigs for a period of two to six months caused cystic glandular hyperplasia of the endometrium and metaplastic downgrowths of the cervical epithelium. Longer treatment induced adenomatous hyperplasia of the endometrium and the appearance of sub-peritoneal fibromatous growths. Similar cystic hyperplastic changes have been produced by experimental injection of oestrogens by Burch, Williams and Cunningham (1931) in rats; Wolfe, Campbell and Burch (1931) in guinea-pigs; Parkes (1935) and Gardner, Allen and Strong (1936) in mice; Lacassagne (1935) and Zondek (1936) in rabbits, and by Zuckerman and Morse (1935) and Zuckerman (1937) in monkeys.

Kaufman and Steinkamm (1936) found that excessive administration of oestrone or oestradiol benzoate to female rats over several months caused the transformation of the endometrial and cervical epithelium into stratified epithelium, while some of their animals developed pyometra.

Selye and Friedman (1940) observed that desoxycorticosterone acetate inhibited the development of the immature rat ovary and produced atrophy of the stroma and cystic atresia of the follicles in rats and mice. Testosterone also produced stromal atrophy and follicular cysts.

Korenchevsky and Hall (1940) found that simultaneous injection of oestradiol, androsterone and testosterone into normal female rats for a period of 53 to 146 days, produced severe metaplasia of the uterine epithelium, adenoma-like over-growths of the uterine glands, cystic glandular hyperplasia of the uterine mucosa and the formation of cysts, sometimes very large, in the ovaries. They concluded that the changes were histologically of the same kind as the similar pathological conditions which occur in women and that it is reasonable to suggest that certain forms of these diseases in women may be caused by a disturbance of the normal balance of male and female hormones.

Cleveland, Phelps and Burch (1941) produced glandular cystic hyperplasia in the endometrium of castrated macaques by the action of oestrogenic substances. They found that the hyperplasia resulted in those animals from which

substantial amounts of endometrium had been removed prior to commencement of the injections, indicating that the ratio of oestrogenic material to the amount of endometrial tissue present may be an important factor in producing the condition.

In view of the changes encountered in the genital tract in the cases of nymphomania, presently to be described, the above results are all considered to be in support of the concept that the aetiology of cystic glandular hyperplasia lies in the action of oestrogenic substances on the endometrium.

That the endometrium is an organ of internal secretion which may influence the ovary both functionally and structurally is supported by the experiments of Mishell and Motyloff (1941) on hysterectomised rabbits. They concluded that:— " The removal of the uterus in the rabbit produces changes in the ovaries which can be demonstrated within three months of the time of operation. These changes consist of a precocious atrophy of the follicular apparatus, abnormalities in the growth of the follicles, atypical development and degeneration of the corpora lutea, and compensatory hypertrophy in the interstitial glands terminating in cellular degeneration. These changes are modified by the administration of endometrial extract prepared from cows' endometrium, which seems to regulate the process of follicular proliferation, protect the functional elements of the ovary and retard the process of atrophy."

In the present study it was found that the condition of nymphomania developed gradually in some animals. Its appearance was usually heralded by gradually decreasing intervals of ovulation, without unduly prolonged duration of oestrus at first, sometimes interrupted by several normal or long sexual cycles, after which the usual manifestations of nymphomania appeared, accompanied by symptoms of almost continuous oestrus. After a further variable period the symptoms of oestrus gradually became less marked, the animal usually refusing coitus but still exhibiting the inclination to mount her companions and the bull. This whole sequence of events may take months, or in some cases even years. In some animals the symptoms developed suddenly without prior warning.

In a few cases no symptoms of nymphomania were exhibited or these were present only for some days or weeks, after which the subject showed no further interest in its companions or the bull, thus becoming completely anaphrodisiac. Periodic examination of the genitalia in these cases invariably revealed an abrupt transformation from normal to cystic ovaries, coincident with the cessation of the sexual cycle. It is difficult to interpret the peculiar behaviour of these animals, in view of the usual clinical manifestations which accompany cases of cystic follicles. Subsequent gross and histological examination of the ovaries, to be described in the following chapter, failed to reveal a satisfactory explanation for this sudden transition from the normal to the state of anaphrodisia. In cases of long standing it was found that the ovarian stroma was reduced to thin strands in the septa dividing the cysts, as a result of pressure atrophy. In the cases under discussion it can hardly be conceived that this process of atrophy could take place within the short space of a few days or weeks.

No attempt was made to treat these animals and, with the exception of one case (No. 7385) no spontaneous recoveries occurred.

In many of the animals the symptoms developed before they had reached the requisite age for mating, i.e.. five years and four years for Groups A and B respectively.

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The following table briefly summarises the condition as encountered in the animals in the experiment:—

Group and No.	Age at Commencement of Nymphomania.		Period of Nymphomaniac Symptoms.	Period of Anaphrodisia (before slaughter).
A.	Years.	Months.	Months.	Months.
6362	3	10	26	22
6363	5	5	5	25
6423	6	7	none.	9
6495	4	7	5	23
6496	4	7	5	23
7157	8	4	1	none.
7172	6	—	2	4
B.				
7277	4	4	2	17
7346	5	2	none.	$8\frac{1}{2}$
7355	2	11	9	23
7385	3	7	6	19 (recovered).
7470	3	8	2	13

From the above table it will be noted that the age of onset of nymphomania varied from two years 11 months to eight years four months. The animals may be classed in the following age groups:—

Age. Years.	Number of Cases.
2–3	1
3–4	3
4–5	3
5–6	2
6–7	2
7–8	0
8–9	1
TOTAL	12 cases.

The period during which short cycles, accompanied by prolonged or continuous oestrus, were exhibited varied from nothing to 26 months. In the majority of cases the period of nymphomania was remarkably short. In general, it was found that the longer the symptoms prevailed, the more pronounced the well-known physical signs of masculinity, elevation of the root of the tail, etc., became. This is clearly shown in the photographs of the animals taken at various stages after the commencement of symptoms.

The animals usually pass over into the stage of anaphrodisia rather suddenly. During the transition, which lasts only a few weeks, symptoms of oestrus gradually become less exaggerated, the animal refusing coitus but still showing the inclination to mount its companions. After a further period even this inclination disappears, the animal becoming quite passive, sometimes with occasional relapses at intervals of months, lasting only one or two days. During this period of anaphrodisia no further alteration in the physical appearance of the animal takes place. Once the animal is settled in this state, apparently no reversion to the original state of nymphomania ever occurs, except as stated above, for occasional relapses of short duration.

Frequent examinations of the ovaries (by rectal palpation) during the period of active symptoms, revealed that the formation of follicular cysts was taking place in fairly rapid succession, the size and shape of the ovaries continually changing as old cysts ruptured spontaneously and new cysts were formed. During this stage also, it was found that the cysts were sometimes ruptured accidentally by slight manipulation, indicating that fibrosis of the walls had not yet reached an advanced stage.

In the later stages of anaphrodisia, the ovaries remained unchanged in size and shape over long periods, supporting the view that the formation of new cysts had been slowed down, the older cysts in the meantime becoming progressively more tough and fibrous.

Palpable changes in the uteri were usually only noted after the commencement of follicular cyst formation.

Of the twelve nymphomaniac animals in the experiment, 10 developed follicular cysts without previous pregnancies having occurred. Of these, eight had never been mated prior to the onset of symptoms.

Only two of the animals had conceived prior to the onset of nymphomania. Cow No. 6423 had aborted twice (after 232 and 97 days gestation) and nymphomania developed suddenly two months after the second abortion. It may be added that with the first abortion dystocia due to malpresentation occurred, followed by retained placenta, while the second abortion was uncomplicated.

Cow No. 7157 calved normally and this was followed by irregular long interovulation periods of 26 months, during which time she was served at every appearance of oestrus but failed to conceive. During this period clinical examination revealed ovarian hypofunction, while the genital tract appeared normal. One month prior to slaughter she suddenly developed symptons of nymphomania with bilateral large cystic ovaries.

Postmortem and microscopic examination of the genitalia and endocrines of these animals revealed extensive changes which will be described in detail in the following chapter.

At this stage, however, it may be concluded from the literature quoted and the results of the present investigation that the development of follicular cysts *in these heifers* was the result of hormonal disturbance of the anterior pituitary-ovarian interaction, the changes in the remainder of the genital tract being *secondary* to those in the ovary.

Arguments in support of this hypothesis are:—

1. Eighty-three per cent. of the animals which suffered from cystic follicles had never conceived prior to the onset of the condition. Of these, 80 per cent. had never been mated. The chances of infection of the genital tract in these cases were, therefore, extremely remote.
2. Of the remaining 17 per cent. of animals (2 animals), one had bred normally, resulting in normal physiological parturition, prior to the onset of the disease.
3. No evidence of either old or recent macroscopic or microscopic inflammatory changes could be found in or near the ovaries or genital tract of a single case of nymphomania encountered.

That the formation of follicular cysts does occur in practice as a sequel to genital infection is readily accepted. The instances described in the large volume of literature on the subject are indeed numerous, the circumstantial evidence being so strong that this is beyond question. Whether in such cases the ovarian changes are the result of direct ascending infection via the tubes or lymphatics, or through resorption of bacterial toxins by the endometrium (Frei, 1927), or through hormonal dysfunction of the endometrium resulting from inflammatory alteration, are questions which cannot be answered at this stage.

With regard to the latter question we have to point out that in human gynaecology it is a common clinical observation that following hysterectomy premature menopause may occur—Burford and Diddle (1936); Marx, Catchpole and McKennon (1936), quoted by Allen, Hisaw and Gardner (1939). The latter authors describe instances where attempts had been made to study this question in laboratory animals with varying results. The observations of Mishell and Motyliff (1941) on rabits have already been mentioned (page 151). Suffice it to state, at this stage, that the subject of hormonal influence of the endometrium on the ovary is still largely controversial.

In the description of the macroscopic and microscopic changes in the endometrium, in the following chapter, the term "endometritis" has been purposely omitted, as no definite changes of an inflammatory nature were encountered. That oestrogen stimulates mitotic division in the endometrial and tubal epithelial cells, has been proved by the work of Allen, Smith and Gardner (1937), Allen (1938), Kaufman and Steinkamm (1936) and many others quoted earlier in this chapter. It was further found that the mitoses commence in the fundus of the glands and from there the process continues towards the surface epithelium. In the meantime cell division in the depth of the gland ceases and secretion commences. Under these circumstances it can be visualised that with accelerated cell division in the neck of the gland, cells may become extruded or desquamated into the lumen, with consequent occlusion, accumulation of secretion and cystic dilatation.

That the condition of nymphomania renders the genital tract more susceptible to bacterial invasion is probable, when one considers the state of the genitalia, so well described by Quinlan (1929) as follows: "The clinical examination of the genitalia of the nymphomaniac bovine is characteristic. The vulva is enlarged, flabby and admits the hand without difficulty. The vagina usually contains a quantity of tenacious opaque mucus. The first cervical fold is frequently ectopic, swollen and ragged. The second cervical fold may also be visible through the ostium uterinum externum. The ostium uterinum is usually open and admits the finger to its entire depth. It contains a characteristic opaque tenacious mucus. The uterus is enlarged and its wall flabby. It is lacking in tone and responds slowly or not at all by contraction to palpation. The horns are also flabby and hang well forward in the abdomen as a result of stretching of the broad ligaments. One or both ovaries are enlarged and cystic. Hydrosalpinx is not an uncommon occurrence. Our experience proves that the cystic degeneration of the ovary associated with nymphomania is concurrent with macroscopic or microscopic change in the tube ".

In this connection also the work of Allen, Gardner and Strong (1936) and Kaufmann and Steinkamm (1936) quoted earlier, where laboratory animals developed pyometra after oestrogenic stimulation, should be borne in mind.

At the end of this study the various stages in delayed breeding leading up to abortion, functional sterility and nymphomania will be discussed and an attempt will be made to find an explanation for these conditions, as encountered.

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IV. MACROSCOPIC AND MICROSCOPIC CHANGES IN THE GENITALIA AND ENDOCRINE ORGANS.

A. VULVA.

Quinlan (1929) states that in nymphomaniac cows the vulva is enlarged and flabby and admits the hand with ease. He also encountered cases of retention cysts in the Bartholin glands and considers these to be caused by occlusion of the openings of the glands, due to inflammatory lesions in the vagina or vulva extending to the ducts and concludes that usually they play no part in the causation of sterility. This view is shared by Richter (1938).

Hess (1921), quoted by Hammond (1927), frequently found cystic Bartholin glands in nymphomaniac cows.

Hammond (1927) states that the vulva becomes congested during oestrus. He found swelling of the epithelial cells during heat, and accumulation of leucocytes in the sub-epithelial tissue, their penetration of the epithelium being probably responsible for the whitish colour of the mucus towards the end of oestrus.

Murphey (1926), quoted by Cole (1930), described cornification and desquamation of the superficial epithelium of the vestibule, beginning at pro-oestrum and continuing to the fifth or eighth day of the new cycle.

Cole (1930) found congestion of the blood-vessels and oedema of the stroma of the vestibule during pro-oestrum and oestrus. A series of changes occurred in the epithelium suggesting preliminary stages of cornification, extending from oestrus to the ninth day post-oestrum. He also finds extensive leucocytic infiltration of the mucosa during oestrus, disappearing again two days after heat. Some animals, however, showed large accumulations of leucocytes at 9 and 11 days post-oestrum.

Table XXIV (Appendix II) shows the measurements of the vulvas of the animals in this experiment. The dimensions show some increase in the pregnant animals and in those which had given birth to calves. There is no significant difference between the measurements of the vulvas of nymphomaniac and functionally sterile animals, or those which had aborted. In general the nulliparous animals had a narrow vestibule which did not permit the passage of the hand for examination of the vagina.

In one case (Cow No. 7045) a retention cyst was encountered at post mortem in the right Bartholin gland. This animal was 183 days pregnant at the time of slaughter.

In Cow No. 6442 the vulvar orifice, instead of being vertical, was inclined to the horizontal (see fig. 51). This at times gave great difficulty with service, the bull often requiring assistance with introduction of the penis.

The cyclic changes in the vulvar mucosa in animals with normal sexual cycles are in accordance with those described by Hammond (1927) and Cole (1930). Insufficient animals were, however, available to follow closely the changes which occurred at various stages of the cycle.

At two days after the commencement of oestrus the epithelial layer is high, while the cells are swollen and show no indication of cornification. There is moderate leucocytic infiltration in the stroma and epithelium, the former being congested and oedematous.

At five days post-oestrum the epithelial layer is moderately high, while the mucosa still shows slight congestion and oedema. The leucocytes have almost completely disappeared except for a few scattered lymphocytes. Cornification is absent.

At ten to thirteen days the epithelial layer is generally low with small compact cells, the superficial squamous layer showing variable degrees of cornification. The stroma is dense and avascular and variable numbers of leucocytes are present. At fifteen days little change from the above has taken place.

The cyclic changes in the vulvar mucosa are so slight and variable that microscopic examination of this part of the genital tract is of little value in determining the exact stage of the cycle at which the specimen is examined.

In the nymphomaniac animals the changes, as was to be expected, simulate those observed during normal oestrus in a somewhat exaggerated form. In addition, some animals showed various degrees of cornification of the superficial squamous cells, this feature being very distinct in some individuals. Usually the stroma was markedly congested and oedematous and showed the presence of variable numbers of lymphocytes, plasma cells and polymorphonuclear leucocytes.

B. Vagina.

A large volume of work on the cyclic changes of the vaginal mucosa of rodents has been done but need not be reviewed here. The striking transformations encountered in the vaginal mucosa of these animals and the possibility of accurately following these changes in the living animal by an examination of the cell content of vaginal smears, provided a good test for oestrogenic hormones. During oestrus or in response to injections of oestrogens in ovariectomised subjects, the superficial epithelial layers become cornified. As the effect of hormone stimulation wears off the cornified layers are desquamated into the lumen in masses and are easily found in the smears. Allen, Smith and Gardner (1937) demonstrated that oestrogenic hormones stimulate growth of the vaginal epithelium by employing the colchicine technique of arresting mitotic cellular division in the metaphase.

Very few descriptions of the cyclic changes in the larger domestic animals can be found in the literature.

Hammond (1927) found that the vaginal mucosa of the bovine consists of three distinct areas : (1) next the os, (2) above the urethra and (3) next the vulva. There exists, however, no hard and fast line of demarcation between the three zones, the character gradually changing from vulva to os, the thickness of the epithelium decreasing as the os is approached. He describes the secretion of mucus from the superficial epithelial cells during oestrus, particularly in the region of the cervix, while more towards the urethra there is extravasation of blood from the congested vessels into the sub-epithelial stroma and leucocytic infiltration into the latter. Forty-eight hours after the beginning of heat extravasated blood is present on the surface and in between the epithelial cells, while there are numerous leucocytes in the epithelial layers and stroma. At seventy-two hours nearly all the blood has been set free on the surface while the leucocytes persist in the sub-epithelial stroma. He regards this blood as largely responsible for the so-called " menstrual flow " noted from the vulva 45 to 80 hours after the commencement of oestrus.

Retterer (1892), quoted by Hammond (1927), states that heat produces no marked changes in the cells, but that changes occur in the last half of pregnancy when the cells become cylindrical owing to the accumulation of mucus.

Cole (1930) found that the infiltration of leucocytes in the posterior region of the vagina reaches its greatest intensity at 9 to 11 days post oestrum, in some cases disrupting or destroying the structure of the epithelium. He found the changes in the vagina near the cervix to be more striking and clear-cut than in any other part of the vagina. Large, wide, mucus-secreting cells constitute the superficial epithelium during pro-oestrum. Beneath this layer there are two or three layers of poly-hedral-shaped epithelial cells. At the time of active heat the epithelium has been reduced to one or two layers in some manner not yet determined. The superficial epithelium at this time consists of extremely tall, narrow, columnar mucus-secreting cells. At two days post-mortem the vaginal epithelium near the cervix is again composed of several layers. The superficial layer is variable in form and only slightly differentiated from the layers beneath. At 8 to 11 days post oestrum the epithelium is lower and appears vacuolate and somewhat degenerate in character. The vaginal mucosa near the cervix undergoes marked changes during pregnancy. It is often reduced to a single layer of deeply staining columnar cells. However, variations do occur at irregular intervals during this time and he found in two cases of cows killed on the 110th and 240th day of pregnancy, the mucosa somewhat resembling that during oestrus. He concludes that although the changes in the vagina are distinct in bovines, these changes cannot be detected by a study of the vaginal smear by methods successful in other species.

Similar changes were found by Brown (1944) in 400 examinations made of 38 dairy cows, although he encountered the maximum leucocytic invasion at two to five days post-oestrum. He also found the vaginal pH to be remarkably constant, 87 per cent. of his total readings falling between $6 \cdot 5$ and $7 \cdot 5$, the range for all readings being $6 \cdot 2$ to $8 \cdot 3$. Conditions such as cystic ovaries, persistent corpus luteum, retained placenta and metritis did not effect the constancy of the pH. He found no apparent correlation between failure to conceive and the pH of the vagina.

Hammond (1927) describes a cyst of Gärtner's canal in the cow and also quotes other authors describing this condition. Quinlan (1929) encountered cysts and abscesses in these canals and observes that usually they appear to be of no importance in the causation of sterility, but when much enlarged may interfere with copulation and cause retention of oestral secretions. He also encountered remnants of the median walls of the Müllerian ducts in the shape of thick bands of tissue, covered with mucosa passing vertically across the portio-vagina of the cervix, and being attached at either extremity to the floor and roof of the vagina. In most cases this apparently did not interfere with conception. This view is shared by Richter (1938) who describes similar bands of tissue at various levels in the vagina.

Williams (1943) regards these arrests in the development of the Müllerian ducts as largely hereditary and advises that such animals should not be used for breeding.

Nieberle (1931) also describes cysts in Gärtner's canals and vertical fibrous bands in the vaginal canal. He also mentions the occurrence of fibromata in the vagina, especially in the dog.

Joest (1925) cites a number of authors who have encountered vaginal fibromata in bovines, horses and dogs. He further states that, when small, they are of no consequence while large tumours may interfere with conception or parturition or cause vaginal prolapse.

The cyclic changes encountered in the vaginal mucosa of animals with a normal sexual cycle are largely in accordance with those described by Hammond (1927), Cole (1930) and Brown (1944), although as stated before, insufficient

normal animals were available to follow completely the changes throughout the cycle. Brown (1944) examined biopsies of the vaginal mucosa from living animals and was thus able to follow the changes occurring throughout the cycle in individual animals, which is considered by far the most satisfactory method.

At two days after the commencement of oestrus the epithelium consists of 3 to 5 rows of polyhedral cells (see fig. 1) supporting a superficial layer of swollen, columnar mucus-secreting cells, with small basally situated pycnotic nuclei. The stroma and epithelial layers show moderate lymphocytic and neutrophilic infiltration, while the stroma is moderately congested and oedematous.

At five days (fig. 2) the epithelial layer is thick, consisting of 6 to 7 rows of large, well-defined polyhedral cells with large, pale, rounded nuclei showing a delicate chromatin network. The superficial columnar mucus-secreting row of cells has collapsed and the cells are becoming flattened but have retained their small pycnotic nuclei. These cells give the surface a somewhat serrated appearance. Infiltrating lymphocytes and neutrophiles are present in fair numbers and are more numerous in the epithelial layers than in the stroma. The latter is dense and avascular.

At 8 to 13 days (Fig. 3) the epithelial layer is thin and consists of several rows of small, polyhedral cells with ill-defined cytoplasmic membranes, dark-staining cytoplasm and small dark nuclei, while the surface row of the cells is flattened. Infiltration of lymphocytic cells reaches its maximum at 11 days, while at this time the stroma is dense and avascular.

At 15 days (Fig. 4) the polyhedral cells are becoming somewhat larger and better defined, with large, pale, rounded nuclei. The superficial layer is still mostly flattened, but in some places swollen, columnar mucus-secreting cells with basal nuclei are becoming evident in preparation for the next oestrus. Leucocytic infiltration is at its lowest ebb at this stage, while the stroma is dense and avascular.
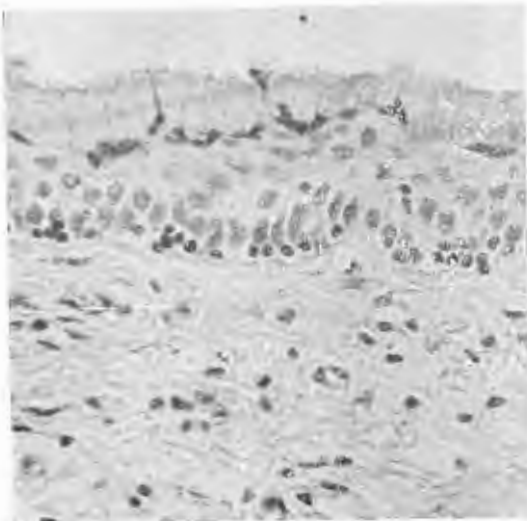
FIG. 1.—Vagina at two days post-oestrum.
Cow 7269.   × 350.
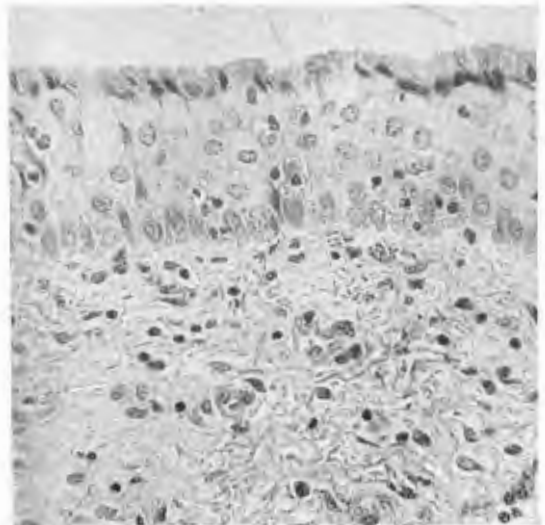
FIG. 2.—Vagina at five days post-oestrum.
Cow 6452.   × 350.
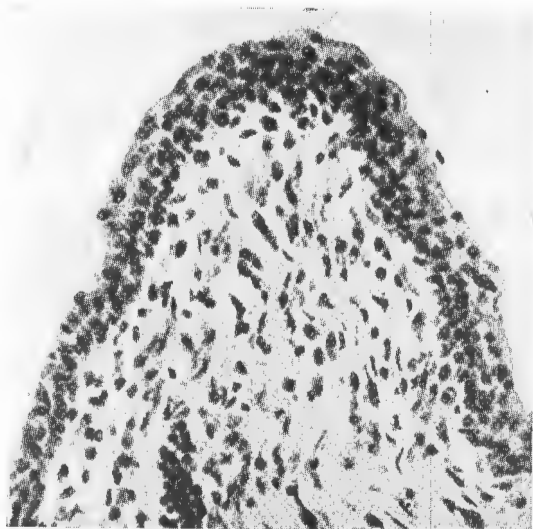
FIG. 3.—Vagina at 11 days post-oestrum.
Cow 6358.   × 350.
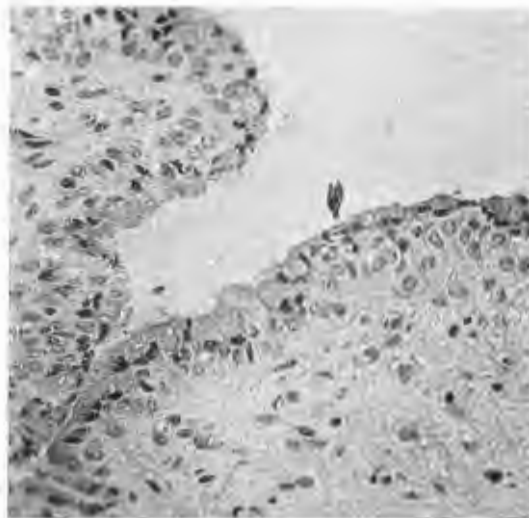
FIG. 4.—Vagina at 15 days post-oestrum.
Cow 6292.   × 350.
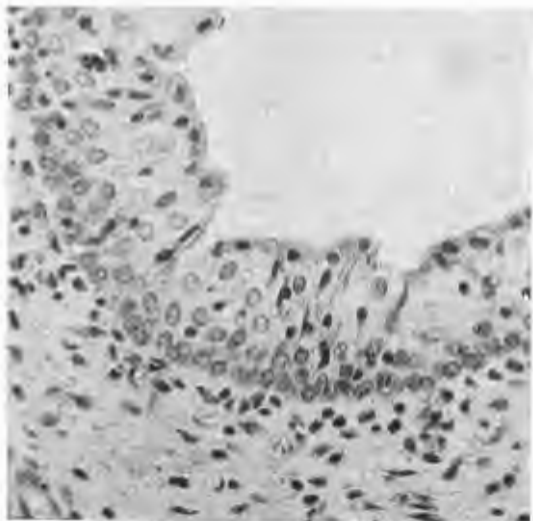
FIG. 5.—Vagina at 26 days pregnancy.
Cow 7385.   × 350.
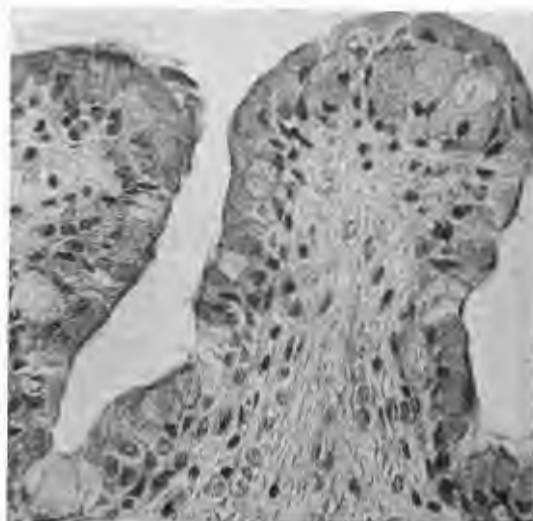
FIG. 6.—Vagina at six months pregnancy.
Cow 7045.   × 350.

At 26 days pregnancy (Fig. 5) the epithelial layer strongly resembles that encountered on the 5th day of the cycle, suggesting that the cyclic changes may persist to some extent after the commencement of pregnancy. Schulz (1946) found indications of a similar persistence of the cyclic changes in sheep in the early stages of pregnancy.

At six months pregnancy (Fig. 6) the mucosa is much folded and the epithelial layer consists mainly of swollen goblet cells, similar to those encountered at 2 days post-oestrum, alternating with areas consisting of thin layers of stratified poly-hedral cells. A few lymphocytes are present in the stroma and the latter is dense and avascular. The question arises whether these changes are indications of oestrogenic stimulation.

At 8 months pregnancy (Fig. 7) the changes are similar to those described at 6 months, but the stroma is becoming moderately congested and oedematous.

In nymphomaniac animals (Figs. 8 to 11) the mucosa is thrown up in folds, the superficial cells are swollen and actively secreting mucus. The cytoplasm is light staining and finely granular, while the nuclei are small, pycnotic and basally situated. The deeper lying cells are small and polyhedral shaped. Figure 8 shows the vaginal mucosa near the os, consisting of a single layer of columnar cells, strongly resembling the cervical epithelium, while figures 9 and 10 show the characteristic alternation of areas of squamous stratified epithelium with those showing superficial columnar cells. There is moderate lymphocytic and neutro-philic infiltration in the epithelium and stroma, while the latter is congested and oedematous. These changes are suggestive of intense oestrogenic stimulation.

In the functionally sterile animals showing normal oestrous periods, the cyclic changes do not deviate from those observed in normal animals.

It is significant that at no stage was there any indication of cornification of the superficial epithelial cells, so characteristic of many other species including man, observed in the vaginal mucosa of these cows.

Small, single retention cysts were found in Gärtner's canals, as well as multiple cysts resembling strings of beads (figs. 50 and 57) in two animals. These cysts are either simple or multilocular cavities, filled with clear, gelatinous secre-tion and lined by a single layer of flattened or cuboid epithelial cells. The multilocular cavities are sub-divided by thin septa of connective tissue, containing blood vessels and covered with epithelium. They were considered of no impor-tance in the causation of sterility.

Cow No. 6423 showed a number of cysts up to 4 mm. in diameter in the vaginal mucosa, containing a mucoid, milky white secretion. Microscopically they were found to be lined with a single layer of flattened epithelial cells and the contents consisted of epithelial and leucocytic debris mixed with slightly granular acidophilic secretion. These cysts are probably formed through occlusion of the crypt-like folds of mucosa, with retention of secretory products. The animal in question was suffering from nymphomania but the cysts were regarded of no consequence.

Persistence of the median walls of the Müllerian ducts in the form of fibrous bands were encountered in five animals, Nos. 6358, 6442, 7346, 7385 and 7471, (Figs. 24, 25, 46, 49 and 50). In four of these cases the band stretched from the floor of the vagina, immediately anterior to the urinary meatus, to its roof and varied in thickness from four to seven mm. One animal (6358) was wont to show a small quantity of fresh blood on the vulvar lips immediately after coitus,
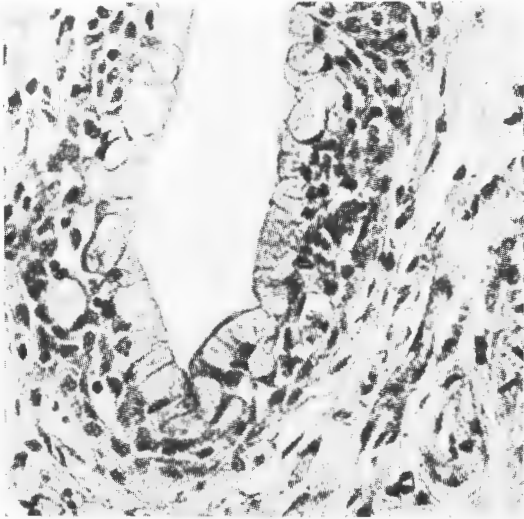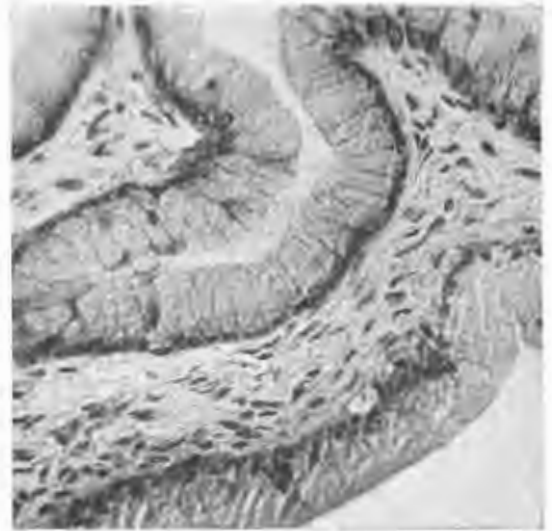
FIG. 7.—Vagina at eight months pregnancy.
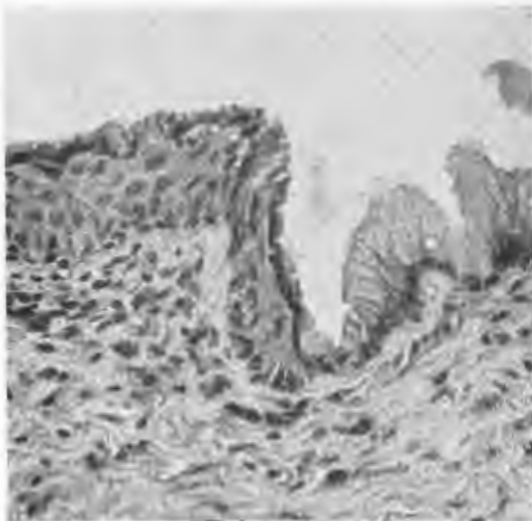Cow 7276. ×350.

FIG. 8.—Vagina, nymphomaniac. Cow 6495.
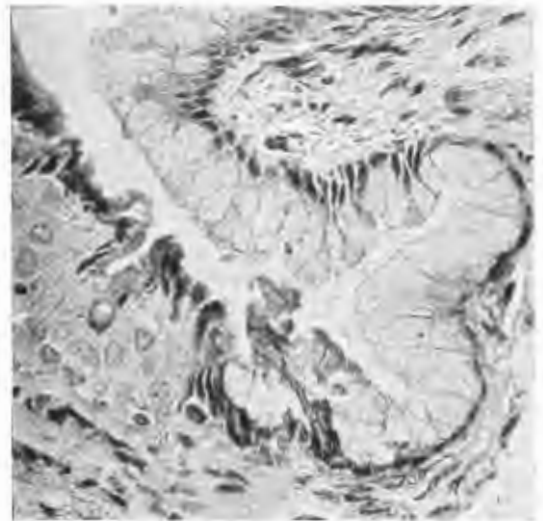×350.

FIG. 9.—Vagina, nymphomaniac. Cow 7277.

FIG. 10.—Vagina, nymphomaniac.
Cow 6496. ×350.

and it is possible that this was caused through injury to the fibrous band. These animals were all nulliparous and the band was intact at post mortem. Cow No. 7471 showed remnants of a similar band in this region in the form of two thin fibrous projections covered with mucosa, directly opposed from the floor and roof of the vagina. In this case the band had obviously broken down with parturition. It was thus found that the band was present in twenty per cent. of the animals in the experiment. It is not known how closely their dams, which originated from one herd, were related, but when one considers that the above heifers were all sired by one bull, the possibility of hereditary causation seems very real (Williams, 1943).

Fibromata were encountered in the vaginas of two cases (Nos. 7355 and 7470; figures 34 and 54). In both cases the neoplasm was situated in a shallow diverticulum near the middle of the vagina and was not covered with epithelium. The tumours were small and considered to be of no consequence.

Table XXIV (Appendix II) shows the measurements of the vaginas in the experimental animals. There is no significant difference in the lengths, while the width in the case of nymphomaniacs was significantly greater than in normal and functionally sterile animals, suggesting a definite state of relaxation.

C. Cervix.

Allen *et al*. (1939) state that in the monkey the cervical glands elongate, coil and secrete mucus under oestrogenic stimulation and that the cervix enlarges, probably as a result of stromal hypertrophy as well as epithelial proliferation. Following castration the epithelium of the cervix and cervical glands is reduced in height and becomes atrophic.

Hammond (1927) states that during the greater part of the cycle, from about three days after the commencement of oestrus, until just before the commencement of the next heat period the cells of the cervical mucosa are cubical in shape. During heat the cells become slightly longer and by twenty four hours after heat are columnar and their length is still further increased after 48 hours, but by three days after the commencement of heat they have almost returned to their cubical form. He further states that the cervix becomes congested and oedematous during oetrus and secretes large quantities of fluid mucus. From three days after oestrum to three days before the next heat the mucus produced is thick, viscid and small in amount, probably as a result of the action of the corpus luteum.

Krupski (1917) found in cows killed at the time of oestrus that the os was open and contained clear fluid mucus.

Cole (1930) describes similar cyclic changes in the glandular epithelium of the bovine cervix as those described by Hammond, (1927). He further states that during pregnancy the structure before the 85th. day is similar to that encountered during the middle of the cycle, but after the 85th. day to the end of pregnancy, the cells seem to be more active and become taller.

Quinlan (1929) states that in the nymphomaniac cow the ostium uterinum is usually open and admits the finger to its entire depth and that it contains a characteristic opaque, tenacious mucus. He also describes the formation of cysts in cases of chronic cervicitis and observes that they are sometimes encountered in conjunction with cystic degeneration of the uterine mucosa. He also describes a case of cervix duplex in which the division did not involve the uterine body.

Richter (1938) describes cervical cysts and observes that they are of no importance in the causation of sterility.

Williams (1943) describes cases of double cervix and uterus and expresses the view that the defect is probably hereditary as in the case of fibrous bands in the vagina, and that the involved individuals should be discarded.

In the present study the cyclic changes found in the cervical mucosa are similar to those described by Hammond (1927) and Cole (1930).

At two days after the commencement of oestrus the glandular epithelium (Fig. 12) is high columnar, swollen, with basally situated, small, flattened nuclei. The stroma is oedematous and congested and shows the presence of a few lymphocytes, while there is some mucus present in the lumen.

At five days post oestrum the epithelium is still moderately high columnar (Fig. 13) while the nuclei are somewhat larger than at two days and oval in shape, but still basally situated. The stroma is moderately oedematous and shows an increase of lymphocytic cells.

At ten to twelve days the glandular epithelium is cuboid to low columnar (Figs. 14 and 15) with large, oval nuclei, situated more or less centrally in the cells, the cytoplasm of which stains deeply. The stroma is dense and avascular and variable numbers of lymphocytes are present. The lumen contains a small amount of stringy mucus.

At 15 days the glandular epithelium and stroma show little change from the above (Fig. 16), while the number of lymphocytes has decreased. In some parts the cells are becoming columnar and the nuclei are moving towards the base of the cells but are still oval in shape.

On the 26th. day of pregnancy the epithelium is moderately high and swollen (Fig. 17) with deeply staining cytoplasm and basally situated, oval to flattened nuclei. There is distinct formation of stringy mucus—the early stages of the plug of pregnancy. The stroma is moderately congested and there are few lymphocytes present.

At six months pregnancy (Fig. 18) the lumina of the glands are greatly distended by the plug of pregnancy and strings of acidophilic mucus are seen to be streaming from the greatly swollen cells which have small, flattened basally situated nuclei. The stroma is dense and leucocytes are absent.

At eight months pregnancy (Fig. 19) the cells are beginning to recede to the cuboid shape, while in some the cell membrane has collapsed and the secretion of mucus has ceased. There are indications suggestive of commencing dissolution of the mucus plug. The stroma is still dense and moderately congested, while the connective tissue fibres have a hyaline appearance.

In the nymphomaniac animals (Figs. 20 to 23) the glandular epithelium resembles that observed at two days post-oestrum, in a somewhat exaggerated form.

The cells are greatly swollen and actively secreting mucus. The nuclei are small, flattened and basally situated while the stroma is oedematous and congested. Moderate numbers of lymphocytes are present. The changes are suggestive of intense oestrogenic stimulation.

In the functionally sterile animals the changes are similar to those observed in the normal animals at the corresponding stages of the cycle.

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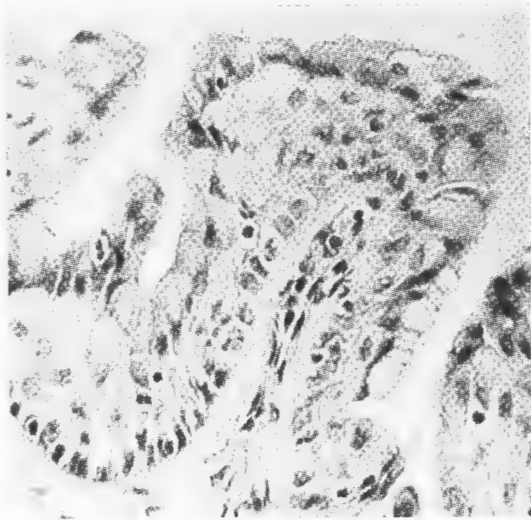
FIG. 11.—Vagina, nymphomaniac.
Cow 6362. ×350.

FIG 12.—Cervix at two days post-oestrum.
Cow 7269. ×300.
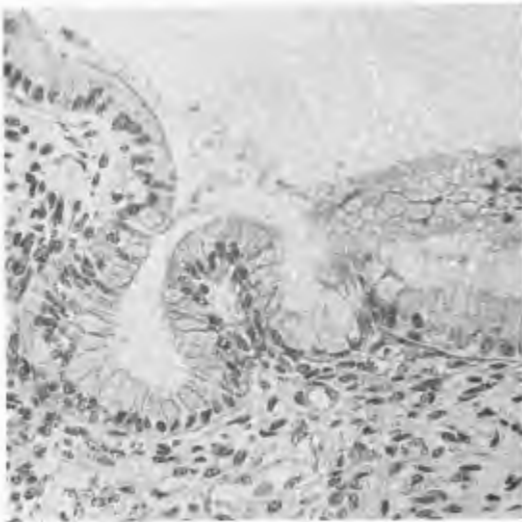

FIG. 13.—Cervix at five days post-oestrum.
Cow 6452. ×300.
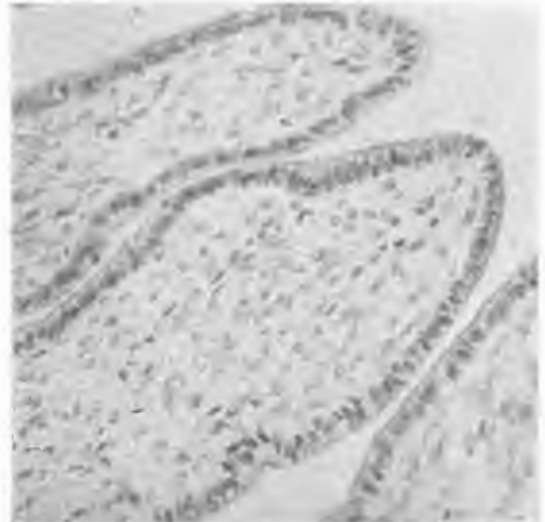

FIG. 14.—Cervix at ten days post-oestrum.
Cow 7469. ×300.
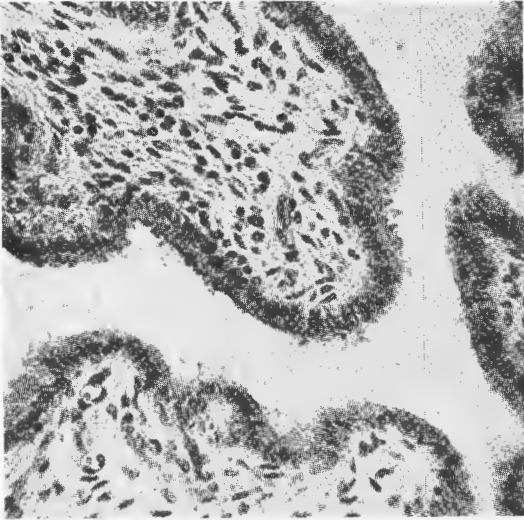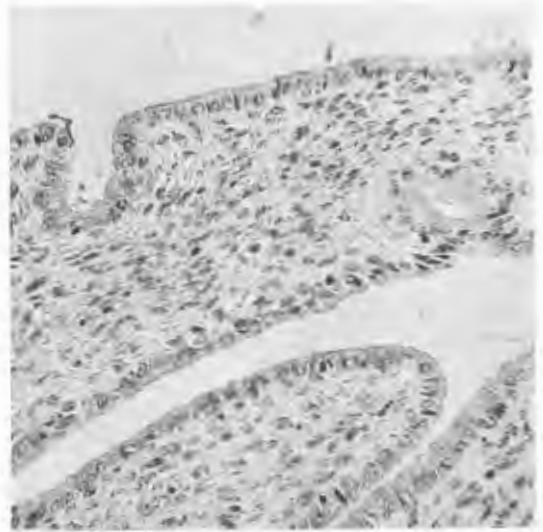
FIG. 15.—Cervix at 12 days post-oestrum.
Cow 7378.   ×300.

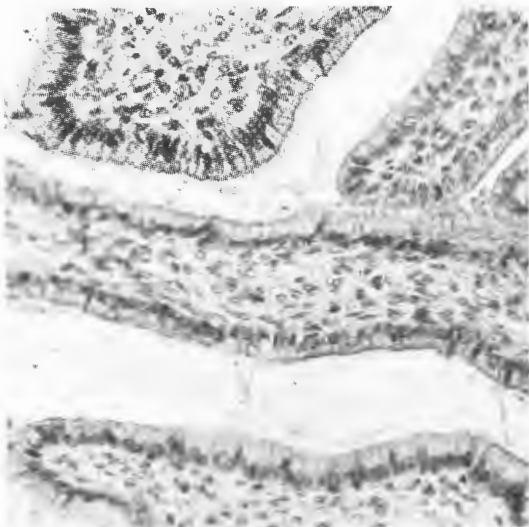FIG. 16.—Cervix at 15 days post-oestrum.
Cow 6292.   ×300.

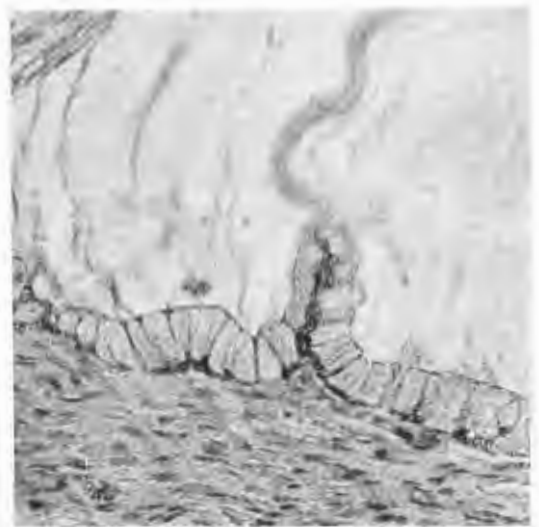FIG. 17.—Cervix at 26 days pregnancy.
Cow 7385.   ×300.

FIG. 18.—Cervix at six months pregnancy.
Cow 7471.   ×300.
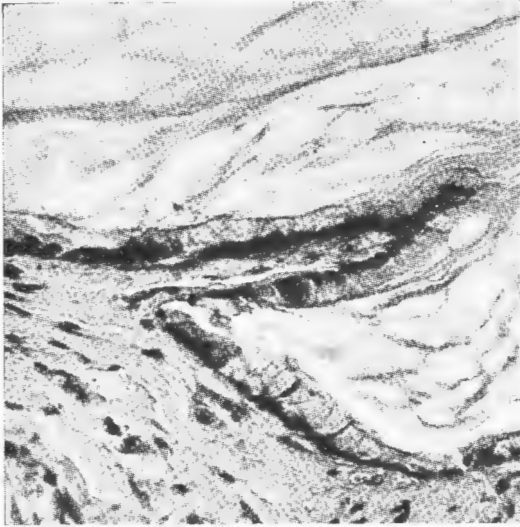
FIG. 19.—Cervix at eight months pregnancy.
Cow 7276.   × 300.
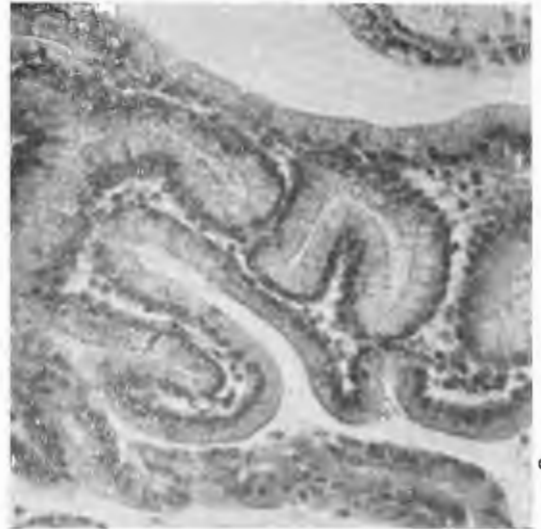
FIG. 20.—Cervix, nymphomaniac.
Cow 7470.   × 300.

FIG. 21.—Cervix, nymphomaniac.
Cow 6363.   × 300.
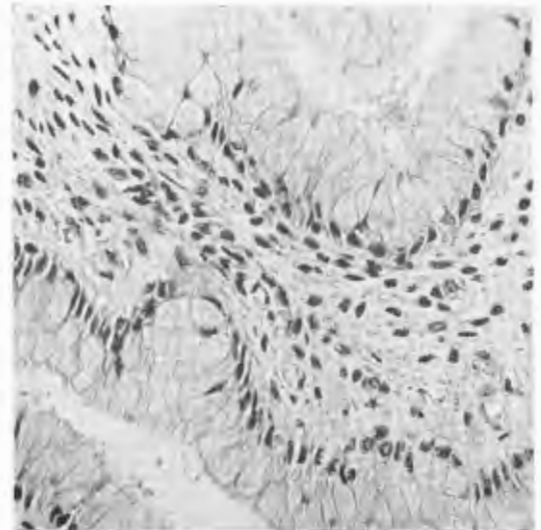
FIG. 22.—Cervix, nymphomaniac.
Cow 7157.   × 300.
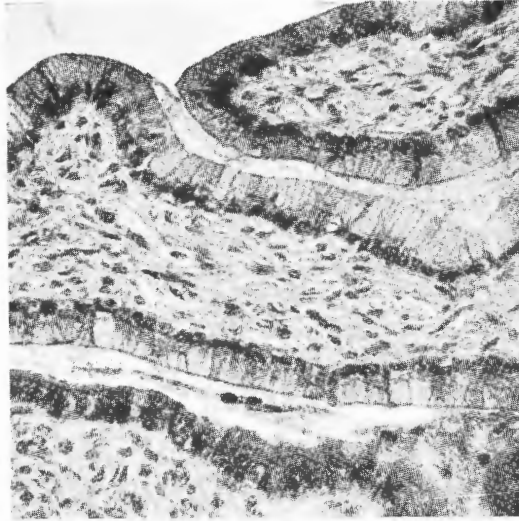
FIG. 23.—Cervix, nymphomaniac.
Cow 6496. × 300.

In those animals which had calved the canal admitted the passage of one finger, irrespective of the stage of the cycle in which she was examined or slaughtered. The nymphomaniac animals in some cases showed a relaxed cervix while in others the canal was tightly closed, allowing the passage of a thin probe only.

The three functionally sterile animals had infantile, tightly closed cervices, (Figs. 45, 49 and 50). No case of cervical stenosis was encountered. In three animals suffering from nymphomania, cysts up to four cm. in diameter were found in the cervical mucosa, filled with thin watery fluid. In one case a large cyst had penetrated the fibrous wall of the cervix and was visible as a rounded, semi-transparent elevation under the serosa on the dorsal surface. (Fig. 54). The cysts were lined by cuboid to flattened epithelium and in most cases surrounded by a thick fibrous capsule.

One case of cervix duplex was encountered (Figs. 24 and 53) coincident with a fibrous vaginal band (Fig. 25) and a completely divided uterus, the division of the cervix extending forward to the bifurcation of the cornua. The right horn contained about 15 cc. of fluid, while the left horn was empty. The animal was nymphomaniac and nulliparous. The malformation of the cervix and uterus was not considered incompatible with conception.

Table XXIV (Appendix II) shows the measurements of the cervices of the various individuals. A notable increase in the length takes place in the later stages of pregnancy, without a proportionate increase in diameter. There is no significant difference in the dimensions of the cervices of sterile and normal animals.
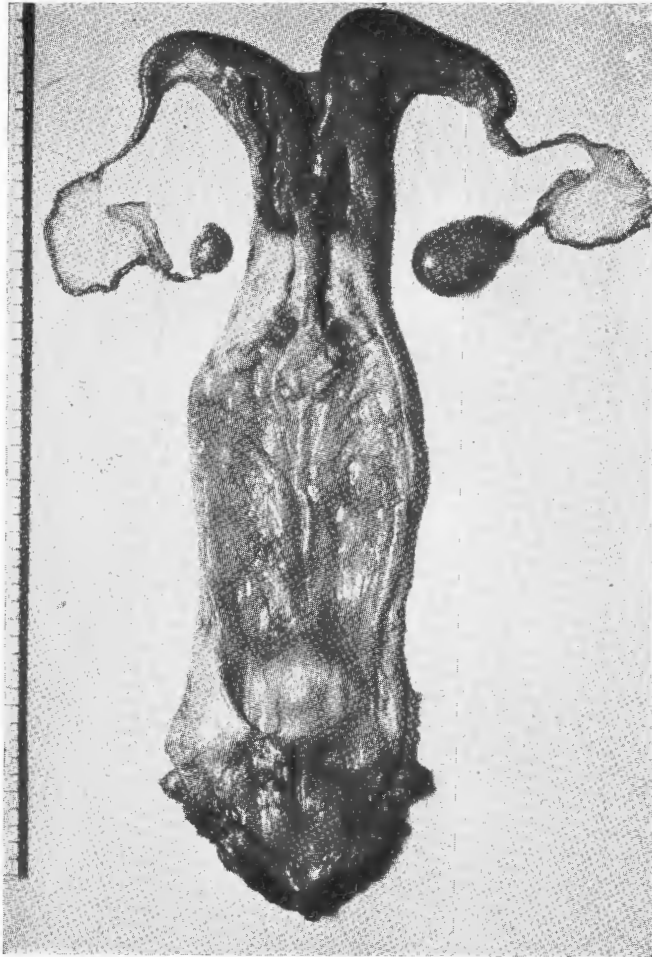
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FIG. 24.—Cervix duplex with divided uterus. Cow 7346.
Scale: Centimetres.

D. UTERUS.

The changes occurring in the endometrium of small laboratory rodents under various conditions have already been referred to (pp. 149, 150 and 151).

Hammond describes the cyclic changes in the endometrium of the cow. He states that during oestrus the stroma is oedematous and congested and that glandular hypertrophy begins three days after with the development of the corpus luteum.

Similar changes have been described by Cole (1930) who also states that the changes in the surface epithelium are not clear-cut, the epithelium being found columnar and pseudo-stratified at all times.

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Quinlan (1929) states that in old animals which have suffered from functional sterility since heiferhood or which have not been mated, the mucosa and cotyledons become atrophied and that there is a tendency for these animals to abort if they do conceive.

He expresses the view that this atrophy may be due to disuse. He further observes that atrophy of the cotyledons is also commonly encountered in cases of metritis chronica catarrhalis.

FIG. 25.—Vertical band in vaginal passage, anterior to the meatus urinarius. Cow 7346.

Craig (1936) also expresses the view that in heifers and cows in which breeding is delayed, atrophy of the mucosa and cotyledons may occur.

The frequent concurrence of cystic ovaries with inflammatory changes in the endometrium has already been referred to. (p. 148).

Quinlan (1929) describes various types of endometritis chronica and also a case of hydrometra with cystic degeneration of the uterine wall. He observes that the latter condition appears to be rare in bovines and in the case described by him the cause would appear to have been cervical deformity, which rendered the escape of oestral debris through the ostium uterinum impossible. Usually the corpus luteum of the last ovulation is found to be present.

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Frei (1925) and Nieberle (1931) mention the occurrence of uterine fibromata and fibroleiomyomata in the cow. Williams (1943) states that benign tumours of the uterus are rare in the larger domestic animals. He describes cases of fibroma in the cow and myoma in the mare, and states that such tumours may or may not bar fertility in a mechanical way according to the size and location.

In the present study the cyclic changes encountered in the endometrium of the normal non-pregnant animals are similar to those described by Hammond (1927) and Cole (1930).
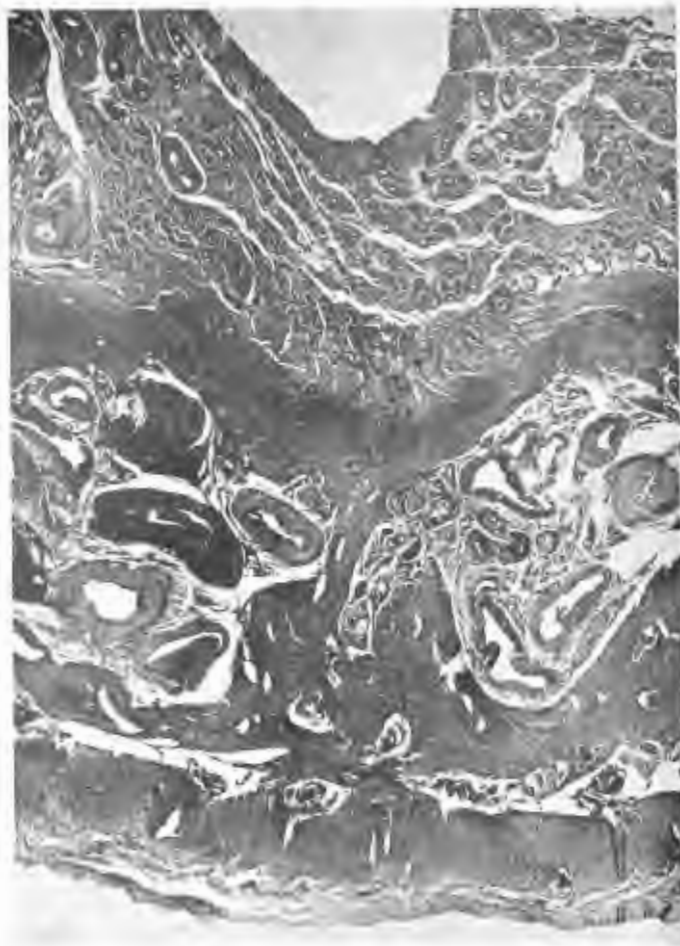
FIG. 26.—Normal uterine wall, multiparous, five days post-oestrum. Cow 6452. × 12.

At two days after the commencement of oestrus the surface epithelium is high columnar, pseudo-stratified. The glandular epithelium is high columnar and the lumina of the glands are small, showing the presence of small amounts of secretion only. The stroma is oedematous and congested.

At five days the epithelium is in a non-secretory phase, while the congestion and oedema of the stroma have passed off, the latter appearing dense and avascular, (Fig. 26).

At eight to thirteen days the glands are hypertrophied and the epithelium shows secretory activity, while the stroma is moderately congested.
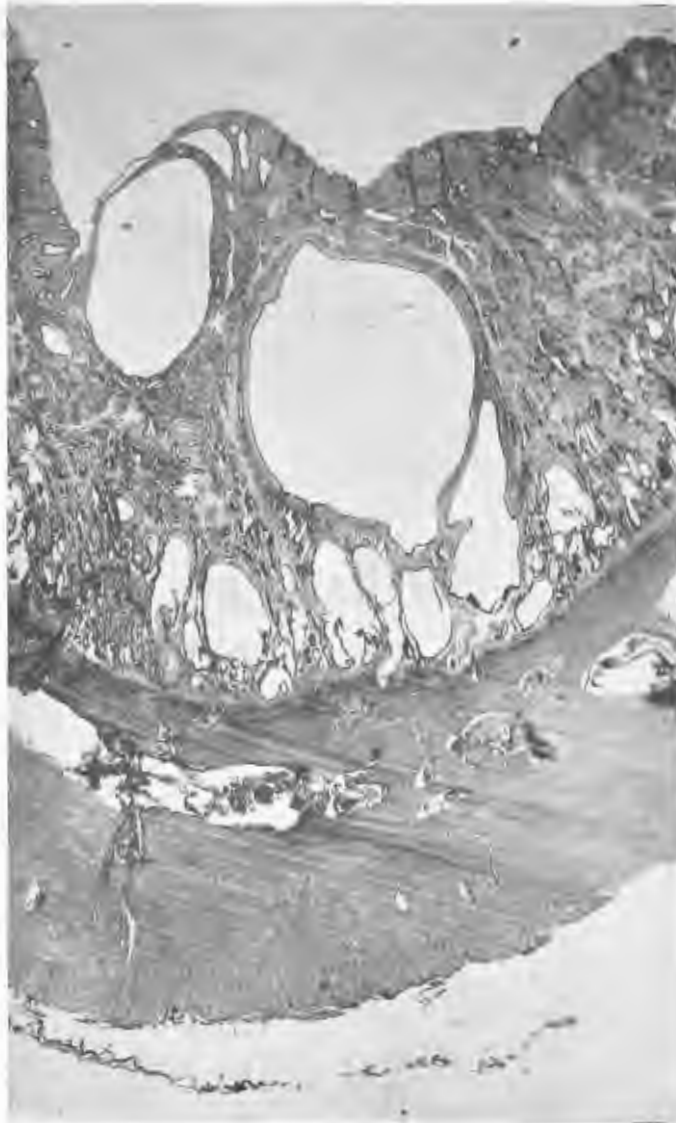

Fig. 27.—Uterine wall, nymphomaniac. Note cystic glandular hyperplasia of the mucosa and atrophy of the myometrium. Cow 6496.   × 12.

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At 15 days the surface epithelium and that of the glands is low columnar, while the lumina of the glands are small and contain little secretion. The congestion and oedema of the stroma are less than that seen at eight to thirteen days.

It is agreed with Cole (1930) that the changes in the uterine mucosa are not as marked and clear-cut as those observed in the vaginal and cervical mucosa.

The animals suffering from functional sterility and the majority of those suffering from nymphomania showed varying degrees of atrophy of the mucosa, cotyledons and musculature, accompanied by cystic degeneration of the glands (Figs. 26 to 32). This is in agreement with the changes observed by Quinlan (1929) in cases of delayed breeding. These changes, it should be emphasised, were not the result of inflammation, for, as stated in a previous chapter, not a single case of endometritis was encountered.

Among the nymphomaniac animals three cases of hydrometra (Figs. 33 to 38) with cystic degeneration of the mucosa and marked atrophy of the entire uterine wall, including the muscular layers, were encountered (Figs. 30 to 32). In these cases the cervical canal was found to be closed, allowing the passage of a thin probe only, but no deformity of the canal with complete stenosis, which could account for the accumulation of fluid, was present. In these cases it is suggested the prolonged oestrogenic stimulation (of ovarian dysfunction) led to fatigue and atony of the already atrophied musculature, resulting in gradual distension of the uterus with secretory products. This distension in its turn was responsible for further pressure atrophy of the mucosa and musculature.

Thus the whole process acted in a vicious cycle resulting in extensive and irreparable damage to the uterus. Two of the animals had never been mated, hence the occurrence of hydrometra can not be explained on the grounds of foetal death and absorption. In all three cases the fluid consisted of thin, watery, almost clear, odourless mucus showing on microscopic examination the presence of traces of desquamated cellular debris only. The ovaries contained cystic follicles, while corpora lutea were absent.

Table XXIV (Appendix II) shows the dimensions of the various components of the uteri. It will be noted that the nymphomaniac animals (with the exception of the three with hydrometra mentioned above) as well as those suffering from functional sterility all had uteri of more or less infantile proportions (Figs. 42, 45, 46, 49, 50, 53, 54, 57, 60, 61 and 64). In these cases the cornua were small and firm in consistence. The total weight of the genitalia (including the cervix, uterus, tubes and ovaries) is show in the last column of Table XXIV, and these figures are even more striking than the measurements.

In those nymphomaniacs suffering from concurrent hydrometra, the uterus being distended with fluid, the dimensions were naturally greater than those mentioned above. After drainage of the fluid the weights of the genitalia approximate those referred to above.

In the group " Pregnant " (Table XXIV) cow No. 7385 which was slaugtered on the 26th. day of pregnancy and had suffered from nymphomania and functional sterility for some time prior to conception the genitalia were small and weighed only 275 grams (Fig. 46). In addition she showed cystic degeneration of the uterine mucosa and atrophy of the cotyledons, which showed no indication of macroscopic or microscopic response to the presence of the embryo. It is suggested, therefore, that early abortion would have terminated this gestation had the animal been allowed to live.

FIG. 28.—Uterine wall. Cow 6495. × 12.

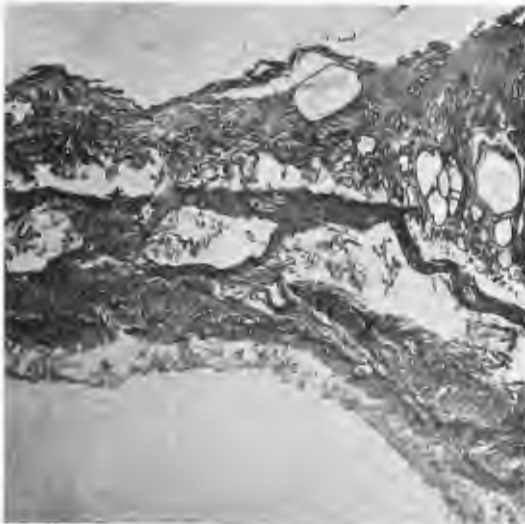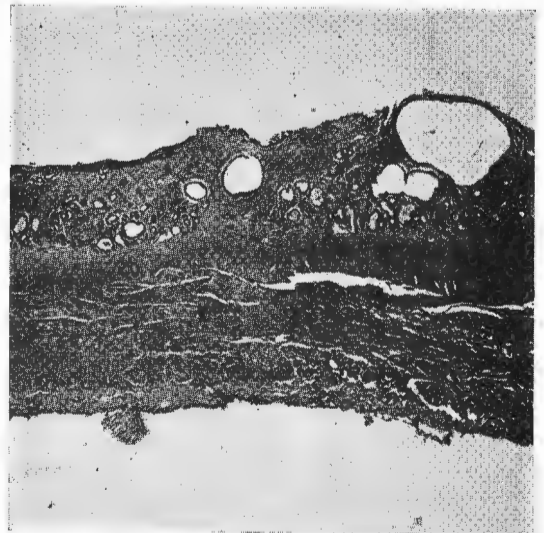FIG. 29.—Uterine wall. Cow 6363. × 12.

FIG. 30.—Uterine wall. Cow 7470. × 12.
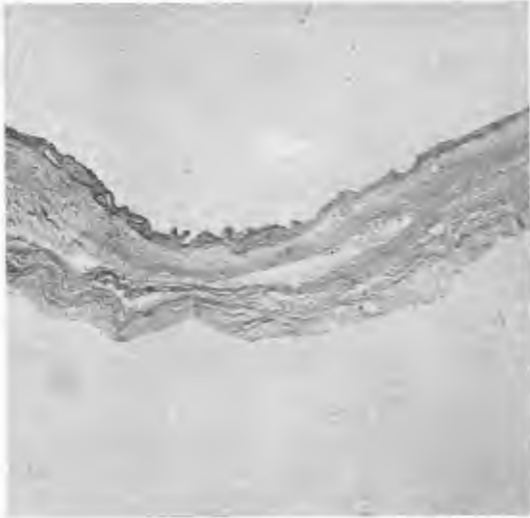
FIG. 31.—Uterine wall. Cow 7277. × 12.

FIG. 32.—Uterine wall. Cow 7172. × 12.

FIGS. 28-32.—Varying degrees of atrophy of all layers of the uterine wall, with cystic degeneration of the mucosa, in cows suffering from follicular ovarian cysts. Note extreme atrophy of mucosa and muscularis in figs. 31 and 32.

FIG. 33.—Cow 7470, four years eight months old.