THE ANATOMY AND HISTOPATHOLOGY
OF THE OVARIES OF INFERTILE
CATTLE

by

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INTRODUCTION

In recent years there has been a considerable increase of interest in the age-old problem of bovine infertility. This is not due to the fact that the syndrome has become worse in recent years, or that the methods of handling it have deteriorated; rather, it is because the livestock owners are becoming aware of the economic importance and extent of the problem. (22, p.1)

The reasons for this increased awareness are manifold. At the present time, neither the dairy nor the beef producer can tolerate the losses in production and efficiency that are the direct result of infertility. The increasing use of artificial insemination, the growth of breed and herd improvement associations and the increasing effectiveness of federal and state agricultural and livestock programs have produced a more widespread and detailed amount of record-keeping by the farmers. One of the results of these records has been to bring the infertility syndrome to the attention of the cattlemen and dairymen. The increased costs of feed, labor and management have also contributed to the realization of how much it costs when high priced cattle fail to reproduce efficiently.

It is unfortunate that the failure of reproductive
ability is due to a number of causes. The problem would probably be much more easily solved if there were only a single entity or predisposing factor involved. Unfortunately, numerous predisposing factors and etiological agents which include a whole spectra of pathogenic micro-organisms and viruses, heredity, nutrition, anatomical, physiological and psychological abnormalities all have their recognized place in the infertility syndrome. Each of these has been shown by investigators to exert a greater or lesser effect upon reproductive ability.

Despite the rising interest in infertility, it is still questionable whether the problem is being given the attention it deserves. Although infertility is well recognized, there is still a tendency on the part of the laity to class perfectly normal animals as infertile after the failure or apparent failure of a few routine attempts at breeding. Far too many valuable animals are sent to slaughter as non-breeders because of simple failure to recognize a fertile or a pregnant animal.

Undoubtedly, the percentage of needless slaughter could be reduced by proper examination and diagnosis. The increased utilization of professional assistance would certainly save livestock owners much unnecessary loss and would result in the saving of a considerable amount of money. Despite this, there seems to be a reluctance on
the part of both the farmers and the veterinarians to use the techniques of pregnancy diagnosis and reproductive organ examination which are presently applied to cattle (16, p.655). This is possibly due to the fact that rectal and recto-vaginal palpation is the most effective means of diagnosis. Besides being esthetically obnoxious, palpation for pregnancy cannot be applied with any degree of certainty by the average practitioner until some forty-five days after conception; although it may be used at any time as an aid to diagnosis of disease.

The lack of a simple, readily applied and accurate chemical or biological test for pregnancy, has been a decided handicap in dealing with bovine reproduction problems. The lack of basic information pertinent to the anatomical and physiological function of the bovine reproductive apparatus, has been one of the greater handicaps in perfecting some convenient form of pregnancy test. The same statement also holds true for reproductive organ diseases.

Medawar (32, p.637) has said, and with good reason, "that anything dealing with mammals in general needs a long string of qualifying clauses before it can be made applicable to cattle". It is the qualifying clauses which make the study of bovine reproduction a special problem. Too little is known about basic facts. The histological
anatomy and the histopathology attendant upon infertility are particularly obscure. It is the object of this work to provide some data which may possibly be of value in future studies of the infertility syndrome. The work makes no pretense of being complete, it is merely a partial contribution to an enormous unexplored field.

REVIEW OF THE LITERATURE

Considerable material has been published on the mammalian ovary over the past three hundred years since Reijnier de Graaf (37, p.17) first reported on the follicular structures which bear his name. However, the bovine ovary has received relatively little attention in proportion to the vast amount of work expended upon the human and other animals. Such work as has been done, is for the most part, clinical or therapeutic in nature, with the pathologic and histopathologic considerations subordinated to a relatively minor role. Little has been written on these particular aspects of ovarian study in the bovine, although there are several good works dealing with normal gross and microscopic aspects.

One of the earliest accurate anatomical descriptions of the bovine ovary is referred to in the foreword of Ellenberger and Mueller (14). The description (14, pp.555-556) made its original appearance in the first edition of
the book, published in 1821 under the authorship of E. F. Gurilt.

The earliest significant clinical work found dealing with bovine infertility was that of Zschokke in 1900, cited by Hammond (19, pp.184-185). Zschokke advanced both mechanical and nutritional theories as to the cause of certain aspects of the infertility syndrome. The cases cited, however, were based upon clinical observation and not on controlled experiment.

Hans Rabl in 1893 (40, pp.109-220) published the first accurate histological study of the development of the bovine follicle and corpus luteum, based in part upon actual study of the bovine ovary. A considerable proportion of the work, however, dealt with human specimens.

George W. Corner in 1919 (10, pp.117-181), working with the sow, completed the observations of Rabl and corrected some of the erroneous minor details. He presented an accurate and informative picture of the formation of the corpus luteum that has persisted essentially unchanged to the present day.

Elder (13, pp.349-363) in 1925, conscious of the lack of material on the bovine, examined several hundred abattoir specimens and made some excellent original observations on the so-called "red bodies" and their relationship to infertility, as well as some pertinent
observations on cystic corpora lutea.

McNutt (30, pp.79-122) in 1926, published a detailed and generally accurate investigation of the gross and microscopic aspects of the corpus luteum in relation to the estrus cycle. Except for relatively minor details, his observations stand as a milepost in bovine ovarian histology.

Stieve (50, pp.951-963) in 1927, made a comprehensive study of the relationships between environment and reproductive glands, and came to the conclusion that the ovaries of higher animals were unable to regenerate after suffering injury due to the fact that additional primary follicles were not formed after birth.

Hammond compiled a monumental work on the various aspects of the bovine reproductive process (19, pp.1-266) and gathered together into one volume most of the significant observations of the late Nineteenth and early Twentieth Centuries.

McNutt (31, pp.286-289) published additional material on the corpus luteum of pregnancy in the bovine and determined that regressive changes in the yellow body occurred around the fifth month of the gestation period. Kaay (23, pp.73-82) did further work with the period of initial regression of the corpus luteum of pregnancy.

With the discovery of progesterone by Corner in
1928 and the recognition of the effect of this and other hormones, the orderly development of bovine ovarian investigations was markedly slowed. Instead, there appeared in the literature a host of hormonal treatments and experiments which overshadowed histological and histopathological studies. Only recently has it been recognized that hormone therapy might be doing as much harm as good in promoting sexual health and normality (49, p.470) (55, p.376). However, like stray bits of driftwood in the flood of hormones, one can find a few references to basic studies which improve our knowledge of the organs with which we so blithely tamper.

Kupfer (24, pp.1211-1270) worked on the sexual cycle of the bovine female and on the periodicity of estrum. Quinlan (39, pp.553-573) investigated tubal and vaginal diseases in cattle. Westman (59, pp.290-306), Cole (8, pp.39-97), Pines (38, pp.373-390), Salazar (43, pp.1182-1183), Bourg (2, pp.911-913), Seiferle (44, pp.421-475), Chapman (6, pp.417-435), Reece and Turner (41, pp.37-39) and Mitchell (34, pp.508-517) have reported on various other phases of ovarian anatomy and physiology, and represent most of the significant work accomplished with the bovine from 1928 to 1942.

Only eight pieces of work of any great significance concerning the infertility syndrome in the bovine were
found during the decade 1942-1952. Nalbanov and Casida (36, pp.39-98) made a useful discovery concerning the relationship of ovulation to estrus. Kaay (23, pp.73-82) has been previously mentioned. Venzke (56, pp.347-352) made some good observations on the relation of hormones to fertility and described their clinical effects. Thygesen (53, pp.261-272) discusses an enormous experiment in ovarian adhesions and their relationship to infertility. Tanabe and Casida (52, pp.237-246) bring out clearly the concept of embryonal death in the bovine. De Lange (11, pp.125-334) published a long term experiment on the influences of delayed breeding upon the fertility of heifers. Van Es (55, p.376) brought home fully in a brief report the dangers in the promiscuous use of hormone therapy. Lombard, Morgan and McNutt (26, pp.69-74) performed some very useful pathologic and histopathologic investigations of the bovine oviduct.

Other works (20, pp.131-133), (12, pp.258-266), (25, pp.12-15), dealt with the bacteriology of the reproductive tract, while still other works were, in essence, mere guides for examination and diagnosis of possible infertility, or lists of possible causes of infertility (58, pp.404-410) (43, p.156) (16, p.655) (3, pp.773-777) (35, p.413) (5, pp.128-132) (21, pp.397-406).
It is worthy of note that none of these investigators, with the exceptions of Thygesen, De Lange and Lombard et al., indulged in any marked amount of histopathological studies, and only those of Thygesen and De Lange dealt with the histopathology of the ovary.

Certain texts mentioned in the body of this work and in the bibliography have been of considerable help. Although these books do not deal specifically with bovine structures, they have proven to be valuable in the organization of the studies which follow. The actual data, however, was obtained mainly from gross and microscopic examination of organs obtained at local abattoirs, as it was felt that only through study of the normal bovine structures could any proper evaluation of pathology be made. Gross and microscopic examinations of normal bovine ovaries during this phase of the study revealed considerable agreement between the texts and the tissues.

ANATOMICAL CONSIDERATIONS

The bovine ovaries are plump, solid, bean-shaped structures, which vary from grayish to yellow-pink in color in the living animal. They are somewhat pointed at the uterine end and possess no ovulation fossa. Each ovary is attached at the hilus by a double fold of peritoneum, the mesovarium, to the broad ligament of the uterus.
Elsewhere, the surface of the ovary projects into the peritoneal cavity. According to Sisson and Grossman (46, p.615) and Kämpfer (24, p.1217) they measure 35-40 millimeters in length, 25 millimeters in width and 15 millimeters or more in thickness in their largest part. The weight of each ovary ranges from 15-20 grams. These measurements are for adult cows; the measurements of heifers being considerably smaller and in the neighborhood of 20x15x10 millimeters. The size of the immature ovary is quite inconstant, so the figures listed must be considered as a mean average and not representative of all young animals. Reece and Turner (41, p.38) state that the right ovary is larger, heavier and functionally more active than the left 66.1 per cent of the time. This finding was generally confirmed in the examination of specimens during this study.

Quoting Sisson and Grossman (46, p.615), "They (the ovaries) are situated usually near the middle of the lateral margin of the pelvic inlet in front of the external iliac artery in the non-pregnant subject, but may be further forward, especially in cows which have been pregnant. They are thus about 16 to 18 inches (ca. 40-45 cm.) from the vulvar opening in a cow of medium size. The greater part of the surface of the gland is covered with germinal epithelium, the peritoneal epithelium being limited to a narrow zone along the attached border."

The ovaries are held rather firmly in position by pressure of the abdominal and pelvic viscera, but can be
moved readily by manipulation per rectum. The ovary is associated indirectly with the remainder of the reproductive tract by the dilated proximal end of the fallopian tube (salpinx, oviduct) which lies along the pouch formed by the mesovarium. The dilated end of the oviduct, the pavilion, is attached at one point on its free margin to the peritoneal zone at the hilus of the ovary near the pointed end. The free border is extended by finger-like projections, the fimbriae, which completely invest the free border of the pavilion and surround the ovary. There is no direct tissue contact between the ovary and the remainder of the reproductive tract. (Figure 1)

HISTOLOGICAL CONSIDERATIONS

The surface of the ovary which projects into the peritoneal cavity is covered by a so-called germinal epithelium (Figure 34a) which is composed of a layer of cuboidal cells. This germinal epithelium ends abruptly at the hilus where it is replaced by peritoneum. In calves, the germinal epithelium consists of definitely cuboidal cells, but with advancing age the cuboidal structure is gradually lost, the cells becoming flattened or spindle-shaped and losing their regular arrangement. No basement membrane can be demonstrated separating the germinal epithelium from the underlying layer of relatively
avascular connective tissue, the tunica albugenia (Figure 34b), which surrounds the ovary.

The ovary is composed of two distinct zones, a thick peripheral layer; the cortex or zona parenchymatosa, and a more loosely organized central portion; the medulla, or zona vasculosa (54, p.279). The medulla is covered by the cortex, except at the hilus. The two zones are not separated by a distinct line of demarcation, but blend together at the cortical margin which is filled with a variety of cells, principally fibroblasts, lutein cells and argentophil fibers (57, pp.402-403).

The cortex is composed of a compact layer of highly cellular connective tissue which contains the ovarian follicles and the corpora lutea. The connective tissue is arranged in a folded or whorl-like pattern and is composed principally of spindle-shaped cells with elongate dense nuclei somewhat resembling smooth muscle fibers (Figures 34d and 35). These cells are held near the medulla in a network of fine collagenous fibrils and many small blood vessels. Yellow elastic tissue is practically absent except in the walls of the blood vessels. (47, pp.595-596)

The medulla is composed of a loose connective tissue stroma rich in yellow elastic fibers, and containing large numbers of complexly convoluted blood vessels, lymphatics and nerve fibers. At the hilus, strands of fibrous tissue
and smooth muscle fibers penetrate the medulla, apparently arising from the broad ligament of the uterus. (29, p.544)

The hilus is principally a medullary structure. It is covered by the mesovarium and contains certain vestigial structures and accessory organs. The epoophoron, the female remnant of the male epididymis, arises blindly in the hilus as a series of roughly parallel tubes, which unite outside the ovary to form a longitudinal canal (Gartner's canal), which lies beside and in close proximity to the oviduct. Gartner's canal may extend almost to the uterine tips, although it is usually somewhat shorter. A number of cytons arranged in ganglia have been reported in the hilar region of the bovine ovary by Pines (38, pp.385-386). These cells were observed lying along the nerve fibers entering the ovary at the hilus and, presumably, function in maintaining local reflex arcs within the ovary. The structures were not demonstrated in the tissues examined during this study.

The nerve supply to the ovary, according to Sisson and Grossman (46, pp.855-856) is derived chiefly from the utero-ovarian plexus which envelops its homonymous artery. This plexus in turn arises from the aortic plexus and the posterior mesenteric ganglion, and is composed of adrenergic (sympathetic) fibers. A second and somewhat inconstant supply, is derived from the middle uterine
plexus, which in turn arises from the pelvic plexus. A few medullated fibers can sometimes be found which are probably visceral sensory and motor, but the principal innervation is adrenergic. (34, p.516)

The majority of the nerve fibrils entering the ovary pass to the muscularis of the blood vessels. The remainder of the fibrils ramify through the entire ovary. Pines (38, pp.384-385) states that primitive end bulbs can be found in the medullary stroma and that a smaller number of fibrils penetrate the cortex and form plexuses around the follicle walls. A still smaller number penetrate the tunica albugenia and end in the germinal epithelium.

The vascular system arises at the hilus from an anastomosis of the middle uterine and utero-ovarian arteries (46, pp.729-730). The vessels enter the medulla at the hilus and branch repeatedly to form a tortuous mass of relatively large vessels, the helicene arteries, which ramify throughout the medullary tissues. Around the periphery of the medullary region these vessels form a plexus which gives off radicles that penetrate the cortex. These radicles in turn give off capillaries which supply the follicles and form dense networks in the theca interna. A lesser number of capillaries supply the non-follicular tissues of the cortex. Veins accompany the arteries, becoming large and complex in the medulla and forming a
tortuous plexus at the hilus. (29, p.580) (47, p.609) (54, pp.287-288)

The great majority of the follicles found in the cortex of a normal ovary are so-called primary follicles (Figures 34d, 35a, 36a). Williams (60, p.439) states that three months after birth the female calf possesses some 75,000 of these follicles which are reduced to 21,000 at three years of age. The primary follicles are generally found immediately beneath the tunica albugenia (Figure 34). They are spheroidal bodies averaging about 45 microns in diameter, with an average range from 30-55 microns. The center of the follicle is occupied by the ovum which is about 20 microns in diameter at this stage. Sections through the nuclei of these immature ova show that the nucleus occupies a slightly eccentric position and is composed of a well defined nuclear membrane filled with a loose meshwork of linin threads and a large chromatin nucleolus (Figure 35a and c). Smaller chromatin bodies may also be observed at the junction of the linin threads (Figure 36c). The ovum is apparently devoid of a cell membrane and is separated from the adjacent layer of connective tissue by a single layer of flattened follicular cells. The cytoplasm of the ovum takes stain poorly, and appears faintly granular. (Figure 35) Mature ova develop from certain of these primary follicles, others become
atretic and disappear, and still others grow for variable periods and then atrophy and degenerate.

The process of development begins as the primary follicle sinks deeper into the tissues of the cortex, expanding toward the more loosely organized medulla. Maximow and Bloom (29, pp.546-548), although working with human material, give an excellent description of the development of the Graafian follicle. No disagreement with their report was found in studies made with bovine ovaries.

"The progressive development of a primary follicle consists in growth and changes in the ovum, follicular cells, and the adjacent connective tissue.

As the egg increases in size its nucleus enlarges and the mitochondria become more or less evenly distributed in the cytoplasm. Later yolk granules of two kinds appear. When the ovum reaches a diameter of 60 to 80 microns, a refractile, deeply staining cell membrane appears. It is called the zona pellucida and is probably elaborated by both the ovum and the surrounding follicular cells. It gradually gains in thickness. (Figures 35 and 36)

The growing follicle enlarges mainly through mitotic proliferation of the follicular cells. The few squamous cells of the primary follicle turn first into a layer of columnar cells surrounding the ovum and then into a stratified epithelium which thickens more rapidly on one side of the ovum. The follicle assumes an oval form with the ovum in an eccentric position. Follicles in the deeper zones of the cortex are the first to develop and they expand toward the medulla.

When the follicle is about 0.2 millimeters in diameter, several irregular spaces filled with the clear liquor folliculi appear between the follicular cells. The increase in amount of this liquid causes a further increase in the size of the follicle which is now a graafian follicle."
With the increase of fluid in the follicle, the ovum becomes a polar structure and is embedded in one portion of the follicular wall within a mass of follicular cells called the cumulus oophorus or discus proligerous (Figure 37). This cell mass and the included ovum project into the liquor filled cavity. The remaining follicular cells form an even layer of epithelium 10 to 20 cells thick covering the inner surface of the follicle and called the membrana granulosa (Figure 37f). The granulosa is separated from the ovarian connective tissue by a well defined basement membrane (47, p.599). The follicular cells immediately surrounding the ovum become columnar and are known as the corona radiata (Figure 37d).

During this period of development, the cortical connective tissue has become differentiated into a capsule, the theca folliculi, which surrounds the developing follicle. At about the same time the liquor folliculi appears, the theca folliculi becomes differentiated into two layers, an inner layer of rather loosely organized connective tissue containing a rich capillary bed, the theca interna and an outer layer of denser connective tissue called the theca externa. Both these layers can be easily differentiated from the surrounding ovarian connective tissue. (Figure 37a and b)
The ovum itself also undergoes considerable change during this period of growth of the follicle. The main observable features are enlargement in size and development of the zona pellucida (Figure 37c). However, other less observable changes may be noted. The nuclear membrane becomes denser and the chromatin threads and nucleolus more well defined. The cytoplasm becomes two-layered, revealing a central layer of coarse yolk granules (deutoplasm) and a peripheral finely granular layer.

As the follicle becomes fully mature, it bulges to the surface of the ovary, becoming thin walled at its free surface and relatively gigantic in size (Figure 1h). Hammond (19, p.186) states that the size of a normal ripe follicle is in the neighborhood of ten millimeters. However, mature normal graafian follicles having diameters as great as 20 millimeters have been observed in this study. The follicular fluid becomes less viscous in consistency shortly before ovulation, an avascular area appears on the ovarian surface of the follicle and the follicle ruptures approximately 14 hours after estrum (36, p.192), releasing the ovum into the pavillon of the oviduct.

Upon rupture of the graafian follicle, the follicular walls shrink and become complexly folded. Unlike man and some other animals, there is little or no extravasation of blood into the follicle cavity. (30, p.81) A corpus
hemorrhagicum, therefore, is not formed in the bovine under normal conditions and the cells of the ruptured follicle proceed directly into the metamorphosis connected with the formation of the corpus luteum.

The corpus luteum, or "yellow body" (Figures 11, 13a and 15a), is one of the striking features of the bovine ovary. Frequently it may be considerably larger than the ovary itself. A nipple or protrusion of lutein tissue is usually formed at the spot where the graafian follicle ruptured (Figures 5a and 13a). This lutein papilla varies considerably in size but often reaches eight millimeters in diameter and four millimeters in height. According to McNutt (30, p.83) the color of the corpus luteum varies with its age, from a brownish yellow in recently formed corpora lutea, through gold, yellow, orange and finally to brick red in aged and regressed specimens (Figure 33a and d). This "red body" stage may persist for months or even years. As far as could be determined in this study, the color variations listed by McNutt were accurate. The hormonal function of the corpus luteum seems to be correlated with its color changes. Williams (60, p.466) states, and was confirmed in one instance in this study (Figure 31c), that occasionally a color variant called the corpus luteum nigrum appears, wherein the functional lutein tissue is reddish black in color. The color appears to have no
pathological significance and micro sections examined reveal no difference from other lutein cells.

The views of Rabl (40, pp.104-220), amplified by Corner (10, pp.117-181) and MoNutt (30, pp.79-122) form the accepted basis of corpus luteum formation. They state essentially that the cells of the corpus luteum are derived from the membrana granulosa and the theca interna of the follicle, with the granulosa cells being the ones of greatest functional importance. According to Westman (59, pp.290-306) the true lutein cells which are derived from the granulosa are the ones particularly concerned with the formation of the corpus luteum, as their partial or total removal results in partial formation or absence of a definite corpus luteum. The lutein cells derived from the theca interna remain generally at the periphery of the corpus luteum, extending only a short distance into the body of the structure as they follow the initial infolding of the ruptured follicle wall. These cells are called theca lutein cells to differentiate them from the true lutein cells derived from the granulosa.

Blood vessels penetrate the developing corpus luteum from the theca interna, giving the tissue a stringy appearance. Kaay (23, p.81) states that after a period of growth which varies from 12 days to three and one-half months de-
pending upon whether or not the ovum is fertilized, the corpus luteum regresses. McNutt (31, p.295) places the time of initial regression during pregnancy at five months. Regression of the corpus luteum is accompanied by shrinkage and atrophy, finally resulting in the formation of a non-functional mass of scar tissue called the corpus albicans.

As was previously mentioned, Williams (60, p.439) states that the ovary of a three-month old calf contains approximately 75,000 primary follicles. At the age of three years, the number of follicles has been reduced to about 21,000 and at ten years of age, the number is in the neighborhood of 2,500. At the maximum, about 160 fertile ova will be shed during this period if no pregnancies occur. The loss of some 72,340 primary follicles then must be due to another cause than loss through the normal ovulation cycle. The process of atresia or degeneration of the follicles is the means by which this loss occurs. Grollman (19, p.506) further states that atresia has been shown to begin in intra uterine life. The process is continuous throughout the fertile life of the animal and only a small fraction of the primary follicles possessed by a female ever reach maturity. (Figures 34c, 35b, 38, 39, 40, 41, 42, 43, 45, 52c, 53b and 54b)

Atresia may occur at any stage of development of
the follicle (54, p.287). In the immature female it generally involves the primary follicles, but in the mature animal even fully developed graafian follicles may be affected. In the early stages of follicle development the process of atresia is direct and rapid. There is no mitosis or metamorphosis of the follicular cells. The ovum merely shrinks and degenerates followed by the degeneration of the follicular cells and the theca folliculi (43, p.1183), the area fibrosing to form a tiny scar without the production of a false corpus luteum. (Figure 35b)

The process of atresia (29, pp.557-559) becomes increasingly complex after the follicle has become graafian. In such a follicle the process of atresia begins with the ovum. (Figures 41, 42 and 43) The cytoplasm of the ovum becomes uniformly coarse and granular and filled with fat droplets, the zona pellucida collapses and the cells of the corona radiata separate from the degenerating ovum and float free in the follicular fluid. Frequently large chromophilic granules are seen within the follicle. The ovum itself may lose its attachment to the cumulus oophorus and float freely in the liquor folliculi. (Figure 42)

Connective tissue elements and blood vessels from the theca interna invade the basement membrane and the follicular cells (54, p.287), penetrate the degenerating
ovum and destroy it (Figures 39 and 41). The granulosa de-
generates and is absorbed (Figures 42 and 43), as is the
follicular fluid. The cavity of the follicle collapses,
but remains marked to a greater or lesser degree by persis-
tent sections of the basement membrane. The collapsed
cavity becomes rapidly filled with fibroblasts and blood
capillaries. (Figure 44) The folded and collapsed zona
pellucida of the ovum generally resists disintegration for
some time and persists among the connective tissue elements
(47, p.601) (Figure 39b).

The theca interna becomes greatly modified as it
expands into the follicle cavity. The cells become larger
and arranged in cords, each cell having the appearance of
a theca lutein cell. The microscopic aspect of such a
follicle is similar to that of an old corpus luteum, and
is called a corpus luteum atretica. It has the character-
istic yellowish, and later reddish color of a true corpus
luteum on gross examination. The essential difference is
revealed microscopically by the lack of true lutein cells
and the presence of degenerated remnants of the zona
pellucida and basement membrane.

The atretic follicle ultimately is invaded by
fibrous connective tissue, shrinks and becomes a small
scar. The hypertrophied theca interna cells which
surrounded and penetrated the ovum are broken up into cell islands of various sizes by the invading strands of fibrous tissue. These cell islands form the so-called interstitial cells of the ovary. According to Seiferle (44, p.474), these cells presumably fulfill trophic functions by supplying lipoid to the cells of the granulosa. Also, evidence seems to indicate that they produce a tissue loosening ferment which may possibly function in initiating rupture of the graafian follicle, and in initiating the degenerative changes marking the regression of the corpus luteum.

MATERIALS AND METHODS

The material used in this work was obtained at local abattoirs and through palpation of living specimens at the Oregon State College dairy barns. A total of 155 cases were examined postmortem, involving 310 ovaries. One hundred of these cases were examined for the purpose of determining normal morphology and structure and the remaining 55 because of reported "sterility". Twenty-three of these cases were from the Oregon State College herd and the John Jacob Astor Experiment Station at Astoria, Oregon and had been subject to periodic examinations by veterinarians. The remaining 32 cases were obtained from slaughter specimens obtained at random from farms and dairies in
the Willamette Valley. Arbitrarily, the owner's definition of the status of fertility of these latter animals was accepted, as it was felt that this was the only proper way of assessing the overall aspects of the sterility problem.

Histories of each animal were obtained in as great detail as possible and, whenever possible, the animal was examined antemortem for any visible or palpable changes from normal. After slaughter, the entire reproductive tract was removed, measured and examined for any evidence of gross pathology. Selected organs and those showing lesions were photographed intact.

The ovaries were freed from their attachments by cutting through the hilus, measured and washed in 10 per cent formalin solution to free them of blood, debris and surface contamination. They were then fixed in 10 per cent formalin and divided into sections which were embedded in paraffin after Bensley's (1, pp.51-52) technique (see appendix). Sections were made at eight microns and stained with modified hematoxylin-eosin technique (see appendix) and Pollak's trichrome (18, p.175) for cellular and connective tissue differentiation (see appendix).

Photographs were made of representative gross and microscopic sections of the ovaries and tables were constructed to consolidate the data gained from the
examinations.

Bacterial assay was attempted on the ovaries whose reproductive tracts showed inflammatory or pyogenic lesions. With one exception (Case 18), the results were uniformly negative. Smears were made on nutrient agar, blood agar and beef agar plates; and stab cultures into beef broth media and thiol media.

RESULTS

The results of the examinations of the specimens reportedly infertile are shown in Table I, II, III and IV, and in the remarks section which follows. It would be neither appropriate nor convenient to give detailed pathology reports for each specimen examined, so the major associated lesions found are briefly accounted for in the remarks section, while the tables and later discussion cover the ovarian pathology.
<p>| Case                  | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 32 | Total |
|----------------------|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| Pregnant             | L | R |   |   |   |   |   |   |   | X  | X  | X  | X  | X  | X  | X  | X  | X  | X  | X  |   |   |   |   |   |   |   |   |   |   |   |   | 10 |
| Not Pregnant         | X | X | X  | X  | X  | X  | X  | X  | X  | X  | X  | X  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 22 |
| No Visible Lesions   | X | X | X  | X  | X  | X  | X  | X  | X  | X  | X  | X  | X  | X  | X  | X  | X  | 16 |
| Cystic Follicle      | L | R |   |   |   |   |   |   |   |   | X  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 8  |
| Without CL           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4  |
| Cystic Follicle      | L | R | X |   | X  | X  | X  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 5  |
| With CL              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4  |
| Infantile            | L | R | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2  |
| Senile               | L | R |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 0  |
| Atrophic             | L | R |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  |
| Many Atretic         | L | R |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 0  |
| Follicles            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  |
| Normal Corpus        | L | R | X |   | X  | X  | X  | X  | X  | X  | X  | X  | X  | X  | X  | X  | X  | X  | 19 |
| Luteum               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 7  |
| Cystic Corpus        | L | R | X |   | X  | X  |   | X  | X  | X  | X  | X  | X  |   |   |   |   |   |   |   |   |   |   |   |   |   | 3  |
| Luteum               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  |
| Persistent Corpus    | L | R |   |   | X  | X  | X  | X  | X  | X  | X  | X  | X  | X  | X  | X  | X  | X  | 19 |
| Luteum               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 6  |
| Multiple Corpora     | L | R |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2  |
| Lutea                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 8  |
| Adhesion             | L | R | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  |
| Abscess              | L | R | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  |
| Anomaly              | L | R |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2  |
| Case                     | L | R | 33 | 34 | 35 | 36 | 37 | 38 | 39 | 40 | 41 | 42 | 43 | 44 | 45 | 46 | 47 | 48 | 49 | 50 | 51 | 52 | 53 | 54 | 55 | Total |
|-------------------------|---|---|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|-------|
| Pregnant                |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 0     |
| Not Pregnant           | x | x | x  | x  | x  | x  | x  | x  | x  | x  | x  | x  | x  | x  | x  | x  | x  | x  | x  | x  | x  | x  | x  | x  | 22    |
| No Visible Lesions     |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 4     |
| Cystic Follicle        | L | L |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 5     |
| Without CL             |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 6     |
| Cystic Follicle        | L | L |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 1     |
| With CL                |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 2     |
| Infantile              |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 0     |
| Senile                 |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 1     |
| Atrophic               |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 2     |
| Many Atretic Follicies | L | L |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 8     |
| Normal Corpus Luteum   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 6     |
| Cystic Corpus Luteum   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 1     |
| Persistent Corpus Luteum| L | L |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 3     |
| Multiple Corpora Lutea |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 5     |
| Adhesion               |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 2     |
| Abscess                |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 0     |
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# TABLE IV

PERCENTAGE COMPARISON
COMPILED PATHOLOGY

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Remarks

The following brief remarks on each case are appended to the preceding tables in order to round out the picture of the general pathology encountered.

1. **Case 1.** The entire reproductive tract was normal in size and shape. The right ovary measured 29x27x22 millimeters and presented a somewhat yellow pitted appearance. Ten small "red bodies" two to five millimeters in diameter could be observed in the ovary, together with numerous follicles two to three millimeters in diameter, many of which were atretic. The left ovary measured 32x25x23 millimeters and possessed a medium sized corpus luteum with a diameter of 16 millimeters. Two cysts seven and ten millimeters in diameter, eight "red bodies" two to five millimeters in diameter and numerous peripheral atretic and developing follicles were observed.

2. **Case 2.** The reproductive structures were essentially normal. A two-month (approximately) fetus was found in the right horn of the uterus. The corpus luteum of pregnancy was found in the right ovary.

3. **Case 3.** The reproductive structures were essentially normal. A three-month (approximately) fetus was found in the right horn of the uterus. The corpus luteum of pregnancy was found in the right ovary.
4. Case 4. The uterine wall was thickened and edematous. Pericaruncular ecchymoses and petechiae were observed in both horns. Small organized blood clots three to four millimeters in diameter were found in the lumen. The cervix showed one rosette. The right ovary measured 41x25x20 millimeters and presented a yellowish, lumpy appearance. Twelve small "red bodies" were visible, together with a regressing corpus luteum five millimeters in diameter, three small cysts two to five millimeters in diameter and numerous atretic follicles. The left ovary measured 35x25x22 millimeters and possessed a yellow, indurated, regressing corpus luteum ten millimeters in diameter, two cysts six and eight millimeters in diameter, nine "red bodies" and numerous atretic follicles.

5. Case 5. The reproductive structures were essentially normal. A two months (approximately) fetus was found in the left horn of the uterus. The corpus luteum of pregnancy was found in the left ovary. A regressed corpus luteum was found in the right ovary.

6. Case 6. There were excessive fatty deposits around the uterus and vagina. The right horn of the uterus was slightly enlarged, with many black pigmented areas in the intercaruncular mucosa of both horns. The cervix showed one rosette. There was considerable cloudy mucus in the vagina and a black pigmented area in the region of
the vestibular fold. The right ovary measured 42x32x23 millimeters and possessed two large cysts 22 and 25 millimeters in diameter, several smaller cysts three to five millimeters in diameter and some developing follicles under a millimeter in diameter. The left ovary measured 49x34x23 millimeters and presented two large cysts 19 and 24 millimeters in diameter, several smaller cysts four to five millimeters in diameter and some developing cysts. No corpus luteum was visible in either ovary.

7. Case 7. The reproductive structures were essentially normal. A three months (approximately) fetus was found in the left horn of the uterus. The corpus luteum of pregnancy was found in the right ovary.

8. Case 8. The cervix showed one rosette. There was excessive mucus in the vagina, associated with mild hyperemia. The right ovary measured 43x33x23 millimeters and showed one large cyst 20 millimeters in diameter and numerous smaller cysts about four millimeters in diameter. The tunica albugenia was thickened. The left ovary measured 33x28x21 millimeters and showed numerous cysts five to eight millimeters in diameter. The tunica albugenia was thickened. There was no corpus luteum in either ovary.

9. Case 9. The reproductive tract was essentially normal. The right ovary measured 31x24x16 millimeters and was normal in structure. A normal corpus luteum, 18
millimeters in diameter and a regressing corpus luteum eight millimeters in diameter, were present. The left ovary measured 19x13x9 millimeters and was shrunken, brownish and atrophic with no visible follicle development.

10. Case 10. The reproductive tract was essentially normal. A one month (approximately) fetus was found in the right horn of the uterus. The corpus luteum of pregnancy was found in the left ovary.

11. Case 11. The reproductive tract was essentially normal. The right ovary measured 31x20x18 millimeters and possessed a well developed normal corpus luteum 17 millimeters in diameter. The left ovary measured 25x18x14 millimeters and possessed a graafian follicle 18 millimeters in diameter.

12. Case 12. The reproductive tract was essentially normal. The right ovary measured 32x21x18 millimeters and was yellowish and lumpy in outline. Seven "red bodies", one regressing corpus luteum six millimeters in diameter and numerous pinpoint follicles, were visible. The left ovary measured 34x19x19 millimeters and possessed a large soft corpus luteum 19 millimeters in diameter, numerous pinpoint follicles and six "red bodies".

13. Case 13. Petechiae were observed in the vaginal mucosa. The remainder of the reproductive tract was
normal. The right ovary measured 27x14x11 millimeters and possessed a large follicle 13 millimeters in diameter, a regressing corpus luteum 12 millimeters in diameter and a few, small atretic follicles. The left ovary measured 18x13x8 millimeters and appeared shrunken, yellow and lumpy. Six small follicles were found along the periphery.

14. **Case 14.** The reproductive tract was essentially normal. The right ovary measured 37x22x20 millimeters and showed a large, well developed corpus luteum 17 millimeters in diameter, a large follicle 13 millimeters in diameter and numerous small follicles one to two millimeters in diameter. The left ovary measured 32x17x16 millimeters and presented a regressing corpus luteum and many follicles, some of which were atretic.

15. **Case 15.** Faint pericaruncular hyperemia and slightly excessive vaginal mucus were observed. The right ovary measured 37x24x20 millimeters and showed an old corpus luteum 17 millimeters in diameter and five "red bodies", together with numerous peripheral follicles and two cysts six millimeters in diameter. The left ovary measured 30x22x17 millimeters and showed a regressing corpus luteum nine millimeters in diameter, numerous peripheral follicles, two cysts six millimeters in diameter and twelve "red bodies".
16. **Case 16.** The reproductive tract was essentially normal. A one month (approximately) fetus was found in the right horn of the uterus. The corpus luteum of pregnancy was found in the right ovary.

17. **Case 17.** The cervix showed one rosette. The right ovary measured 38x25x20 millimeters. Multiple peripheral atretic follicles were observed, together with considerable reduction of the cortex. The left ovary measured 49x32x30 millimeters and showed a large persistent corpus luteum 22 millimeters in diameter, with multiple peripheral atretic follicles.

18. **Case 18.** The reproductive tract showed unilateral pyosalpinx and pyometra with focal abscessation. Fibrinous adhesions joined the corpus uteri to the abscessed right ovary, right and left oviduct and peritoneum. Caruncular necrosis, atonic uterus and extensive fatty periuterine deposits were also observed. The right ovary showed extensive abscessation which involved the right oviduct. The ovarian architecture was lost. The abscess measured 145x208 millimeters and possessed a capsule 24 millimeters thick composed of fibrous tissue. The left ovary showed multiple adhesions to the broad ligament of the uterus, a persistent corpus luteum 20 millimeters in diameter with two associated cysts four and six millimeters in diameter and numerous peripheral atretic follicles.
19. **Case 19.** (Figures 9 and 10) The uterine walls were thin and atonic, with the caruncles raised and necrotic on the surface. There was apparent erosion of the uterine mucosa and some hyperemia in the submucosa. The vagina possessed excessive cloudy mucus and the vulvar regions were swollen. The right ovary measured 70x43x34 millimeters and showed two large cysts 42 and 22 millimeters in diameter, together with several smaller cysts and developing follicles. The left ovary measured 66x38x27 millimeters and showed two large cysts 36 and 32 millimeters in diameter, together with several smaller cysts and follicles. No functional corpus luteum was observed in either ovary; a small regressed corpus luteum was present in the right ovary.

20. **Case 20.** The reproductive tract was essentially normal. The right ovary measured 41x29x24 millimeters and showed a large follicle 22 millimeters in diameter, a considerable number of smaller follicles one to three millimeters in diameter and four "red bodies". The left ovary measured 32x23x15 millimeters and showed two regressing corpora lutea, numerous developing follicles one to two millimeters in diameter and eight "red bodies".

21. **Case 21.** (Figures 7 and 8) The reproductive tract showed a dilatation or cyst on the distal portion of
the right oviduct which measured 27x10 millimeters. The uterus was slightly atonic and the mucosa was dark in color. The caruncles were apparent. The right ovary measured 33x25x21 millimeters and showed a large follicle 18 millimeters in diameter and numerous small developing follicles. The left ovary measured 28x21x21 millimeters and showed a regressing corpus luteum nigrum seven millimeters in diameter and many small follicles.

22. **Case 22.** (Figures 5 and 6) The reproductive tract was somewhat small. The horns of the uterus were tightly coiled and folded. The vagina showed a considerable amount of cloudy mucus. The vulvar opening was tiny, measuring but 35 millimeters in length. A persistent hymen was noted. The right ovary measured 32x23x18 millimeters and appeared yellow and pitted, showing a regressing corpus luteum and many pinpoint follicles. A developing follicle eight millimeters in diameter was observed near the hilus. The left ovary measured 34x23x20 millimeters, possessing a large normal corpus luteum 22 millimeters in diameter. A buried cyst-like follicle was observed near the hilus and a few small follicles along the periphery.

23. **Case 23.** The reproductive tract was essentially normal. The right ovary measured 34x23x16 millimeters, possessing a large well formed corpus luteum 17
millimeters in diameter, numerous small follicles and four "red bodies". The left ovary measured 34x20x15 millimeters and showed a large graafian follicle 15 millimeters in diameter, numerous developing follicles and five "red bodies".

24. **Case 24.** The walls of the uterus were thickened and edematous, particularly in the left horn. The distal end of the left oviduct was thickened, but the lumen was patent. The uterus contained a quantity of yellowish brown slimy mucus. The vagina showed excessive mucus of similar consistency. The right ovary measured 32x28x16 millimeters and showed numerous developing and atretic follicles and eight "red bodies". The left ovary measured 41x38x24 millimeters and possessed a large cystic corpus luteum 24 millimeters in diameter, with a central cyst eight millimeters in diameter. A few small peripheral follicles and one cyst 11 millimeters in diameter were observed.

25. **Case 25.** The reproductive tract was essentially normal. A two months (approximately) fetus was found in the right horn of the uterus. A corpus luteum of pregnancy was found in the right ovary.

26. **Case 26.** The reproductive tract was essentially normal. The right ovary measured 24x18x10
millimeters and showed a regressing corpus luteum five millimeters in diameter, and a number of peripheral follicles one to four millimeters in diameter. The left ovary measured 31x25x13 millimeters and showed a large normal corpus luteum and a few peripheral follicles.

27. **Case 27.** The reproductive tract was essentially normal. The right ovary measured 24x20x13 millimeters and showed a regressing corpus luteum, numerous corpora atretica and a number of peripheral follicles many of which showed atresia. The left ovary measured 44x37x24 millimeters and contained a large cystic persistent corpus luteum 21 millimeters in diameter with a central cyst five millimeters in diameter. A number of peripheral atretic follicles and numerous corpora lutea atretica were observed.

28. **Case 28.** The reproductive tract was essentially normal. A two months (approximately) fetus was found in the right horn of the uterus. The corpus luteum of pregnancy was found in the right ovary.

29. **Case 29.** The reproductive tract was essentially normal. A three months (approximately) fetus was found in the left horn of the uterus. The corpus luteum of pregnancy was found in the left ovary.

30. **Case 30.** The reproductive tract was
essentially normal. A three months (approximately) fetus was found in the right horn of the uterus. The corpus luteum of pregnancy was found in the right ovary.

31. **Case 31.** The reproductive tract was essentially normal. The right ovary measured 35x22x13 millimeters and possessed numerous small follicles and corpora lutea atretica. The left ovary measured 51x44x21 and showed a large corpus luteum 23 millimeters in diameter. Numerous peripheral follicles and corpora atretica could be seen.

32. **Case 32.** The walls of the uterus were thin, with blackish pericaruncular pigmentation. The vaginal walls were also thin and showed irregular spotting with black pigment. The entire reproductive tract, although within normal limits of measurement, gave the appearance of being small and undeveloped. The right ovary was small, smooth, pale yellowish-white and featureless, measuring 21x6x4 millimeters. No apparent evidence of follicle development or differentiation into cortical and medullary portions. Few microscopic follicles were revealed on histologic examination. The left ovary measured 21x8x4 millimeters and was identical in all major respects to the right.

33. **Case 33.** The reproductive tract was
essentially normal. Historically the animal showed failure to come in heat and persistent recurrent corpora lutea. The right ovary measured 33x20x20 millimeters and showed an old persistent corpus luteum and many small follicles one to three millimeters in diameter. The scar of an old expressed corpus luteum was visible. The left ovary measured 32x20x18 millimeters and showed one cyst 12 millimeters in diameter and many peripheral atretic follicles one to four millimeters in diameter.

34. Case 34. Excessive mucus slightly cloudy in appearance was observed in the vagina and excessive fatty deposits around the vagina and uterus. Historically, the cow showed symptoms of nymphomania. The right ovary measured 52x33x30 millimeters and showed two large cysts 22 and 23 millimeters in diameter and several smaller cysts four to eight millimeters in diameter. The left ovary measured 57x34x29 millimeters and showed one large cyst 32 millimeters in diameter and several smaller cysts four to ten millimeters in diameter.

35. Case 35. There was a considerable deposit of fat around the uterus and vagina. The adrenals were enlarged with necrotic medullas. The right ovary measured 37x22x20 millimeters and showed a large normal corpus luteum and several developing follicles. The left ovary
measured 34x23x18 millimeters and showed a graafian follicle ten millimeters in diameter as well as several smaller follicles two to four millimeters in diameter.

36. Case 36. A mummified fetus of about five months gestation was found in the right horn of the uterus, together with considerable amounts of grayish, slightly odorous fluid. Both horns of the uterus were swollen and atonic. Considerable fatty deposits were found around the entire reproductive tract. The ovaries were essentially normal. The right ovary measured 34x23x19 millimeters, possessing a normal corpus luteum and several developing follicles. The left ovary measured 31x19x17 millimeters and showed many developing follicles.

37. Case 37. There was a slight mucus exudate in the vagina, together with some vaginal hyperemia. The remainder of the reproductive tract was essentially normal. Historically, the animal showed some nymphomania symptoms but little gross physical change. The right ovary measured 47x33x26 millimeters and showed two cysts 18 and 20 millimeters in diameter, together with several cysts five to seven millimeters in diameter. The ovary was removed surgically several months prior to slaughter. The left ovary measured 42x31x29 millimeters and showed one cyst 18 millimeters in diameter and many smaller cysts four to seven
millimeters in diameter. No corpus luteum was visible.

38. **Case 38.** The vagina showed excessive amounts of cloudy mucus. The cervix revealed one rosette. The uterine wall was edematous and slightly atonic, the caruncles were apparent and the mucosa was darker than normal with a brownish tinge. Historically, the animal showed symptoms of nymphomania and failed to respond to treatment. The right ovary measured 54x40x38 millimeters and showed two large cysts 26 and 30 millimeters in diameter, with several smaller cysts three to six millimeters in diameter. The left ovary measured 51x41x37 millimeters and showed one large cyst 28 millimeters in diameter and several smaller cysts five to ten millimeters in diameter.

39. **Case 39.** The reproductive tract was essentially normal. Historically, the animal was affected with maxillary actinomycosis of the left maxilla and showed no heat for the last three periods prior to slaughter. The right ovary measured 42x34x20 millimeters and possessed a large, soft, embedded corpus luteum 20 millimeters in diameter, accompanied by a small number of follicles one to five millimeters in diameter. The left ovary measured 30x22x15 millimeters and showed many atretic follicles one to four millimeters in diameter.

40. **Case 40.** The reproductive tract was
essentially normal except for the proximal portion of the right oviduct and the right ovary, which were missing. Historically, the right ovary was removed surgically several months prior to slaughter after a diagnosis of persistent cystic ovaries. The left ovary returned briefly to normal and then developed persistent cystic corpus luteum which was treated without result. The right ovary measured 51x40x30 millimeters and showed two large cysts 22 and 24 millimeters in diameter and several smaller cysts. The left ovary measured 37x24x22 millimeters and showed a large pedunculated corpus luteum 22 millimeters in diameter. Numerous atretic follicles were present at the base of the corpus luteum.

41. Case 41. The cervix showed one rosette. The right ovary measured 46x25x22 millimeters and revealed two persistent cystic corpora lutea 14 and 20 millimeters in diameter. There was scant evidence of follicle development and numerous corpora atretica. The left ovary measured 31x22x15 millimeters and presented a yellow pitted appearance, revealing many atretic follicles and corpora atretica.

42. Case 42. The reproductive tract was essentially normal. The right ovary measured 35x22x17 millimeters and possessed a normal corpus luteum of recent
origin 19 millimeters in diameter. Few developing follicles were observed. The left ovary measured 28x21x16 millimeters and showed a large graafian follicle 15 millimeters in diameter associated with many smaller follicles.

43. **Case 43.** The reproductive tract was essentially normal. The right ovary measured 39x25x22 millimeters and possessed a large cystic corpus luteum 22 millimeters in diameter with a central cyst seven millimeters in diameter. There were considerable numbers of atretic follicles and corpora atretica. The left ovary measured 33x22x16 millimeters and presented a yellow and pitted appearance, with numerous atretic follicles.

44. **Case 44.** The reproductive tract was essentially normal. The right ovary was 26x18x14 millimeters and showed a yellow irregular surface that was moderately pitted. There was some slight evidence of long standing atresia of developing follicles. There was no evidence of a corpus luteum. The left ovary measured 27x19x13 millimeters and presented an appearance similar to the right ovary.

45. **Case 45.** The reproductive tract was essentially normal. The right ovary measured 34x21x18 millimeters and showed a persistent soft corpus luteum 18 millimeters in diameter, two follicles five millimeters in
diameter and numerous atretic follicles. The left ovary measured 25x21x16 millimeters and presented a yellowish pitted appearance. The surface was studded with numerous small atretic follicles and corpora atretica.

46. **Case 46.** The vagina contained an excessive amount of cloudy mucus. The cervix showed two rosettes. The uterus was affected with a low grade chronic endometritis accompanied by considerable intercaruncular endometrial erosion and scattered petechiae. Salpingitis was present accompanied by thickening of the right oviduct. There were adhesions of the mesovarium to the broad ligament of the uterus. The right ovary measured 39x27x20 millimeters and was adherent to the broad ligament of the uterus. A corpus luteum 19 millimeters in diameter was present. There was no evidence of bacterial infection. The left ovary measured 32x21x16 millimeters and showed one graafian follicle 11 millimeters in diameter and numerous developing follicles.

47. **Case 47.** The vagina contained an excessive amount of cloudy mucus. Historically, this animal was born twin to a bull calf and freemartinism could be suspected. At maturity the animal exhibited persistent heats, cystic ovaries and nymphomania which did not respond to treatment. The right ovary measured 43x32x24 millimeters
and contained two large cysts 18 and 21 millimeters in diameter and several smaller cysts four to eight millimeters in diameter. The left ovary measured 54x37x32 millimeters and presented two very large cysts 24 and 27 millimeters in diameter and three smaller follicles two to eight millimeters in diameter.

48. **Case 48.** The reproductive tract was essentially normal. Historically, the animal showed persistent cystic ovaries and symptoms of nymphomania. The right ovary measured 41x32x24 millimeters and possessed two cystic persistent corpora lutea 16 and 19 millimeters in diameter. There was scant evidence of follicle development and many corpora atretica. The left ovary measured 30x20x16 millimeters and presented a yellow, irregular pitted appearance with numerous peripheral atretic follicles one to three millimeters in diameter.

49. **Case 49.** The reproductive tract was essentially normal. The right ovary measured 31x20x15 millimeters and showed several developing follicles four to five millimeters in diameter and numerous smaller follicles one to three millimeters in diameter. The left ovary measured 39x22x18 millimeters and possessed a normal corpus luteum 18 millimeters in diameter and a few developing follicles.
50. **Case 50.** This animal was diagnosed as pregnant but was recommended for slaughter because of anatomical abnormality. The uterus was monocornuate. There was no connection between the left ovary and the uterine horn. A two-month old fetus was present in the single horn. The right ovary measured 39x25x18 millimeters with a well formed corpus luteum of pregnancy 23 millimeters in diameter. The left ovary measured 22x17x11 millimeters and apparently was nonfunctional as the ovary was not connected to the uterus. Considerable evidence of early atresia was present.

51. **Case 51.** The reproductive tract was essentially normal. Historically, this animal registered suspect to the brucellosis test. The right ovary measured 35x22x17 millimeters and possessed a graafian follicle ten millimeters in diameter and many developing follicles. The left ovary measured 37x24x18 millimeters and possessed a well formed normal corpus luteum 18 millimeters in diameter. There were few developing follicles.

52. **Case 52.** The reproductive tract was normal except for slightly excessive vaginal mucus. The right ovary measured 34x23x17 millimeters and showed a cyst 12 millimeters in diameter, two smaller cysts four and six millimeters in diameter and many smaller follicles. The left
ovary measured 41x24x22 millimeters and possessed a cystic corpus luteum 22 millimeters in diameter associated with many small atretic follicles.

53. **Case 53.** The reproductive tract showed a severe granular vaginitis and a cervicitis with two rosettes. The right ovary measured 32x23x20 millimeters and presented a very rough and lumpy appearance, with many atretic follicles and seven "red bodies". The left ovary measured 33x26x21 millimeters, with one active corpus luteum 17 millimeters in diameter and one regressing corpus luteum nine millimeters in diameter, together with numerous atretic follicles and five "red bodies".

54. **Case 54.** The reproductive tract showed mild chronic granular vaginitis. The right ovary measured 33x21x18 millimeters and had a yellow pitted appearance. Many small follicles and corpora atretica were present as well as four "red bodies". The left ovary measured 40x26x21 millimeters and possessed a large embedded persistent corpus luteum, with many associated atretic follicles, corpora atretica, developing follicles and six "red bodies".

55. **Case 55.** The reproductive tract showed vaginal, cervical and uterine edema; with excessive cloudy mucus in the vagina and grayish slimy mucus in the uterus. The
right ovary measured 43x35x30 millimeters and showed a single large cyst 23 millimeters in diameter and three smaller cysts four to ten millimeters in diameter. The left ovary measured 33x34x27 millimeters and showed two cysts 18 and 23 millimeters in diameter and numerous developing follicles two to five millimeters in diameter.

**DISCUSSION**

The pathology of the ovaries studied, fell into three major categories; (a) pathology of the ovarian follicle, (b) pathology of the corpus luteum and (c) pathology of the ovarian stroma. Frequently there was an overlapping of the lesions and associated pathology of other portions of the reproductive tract. However, in the interests of logical study the lesions were broken down into groups as shown in Tables III and IV. It was thought that such consolidation would give a more accurate picture than individual discussion of 55 individual cases covering 110 ovaries.

The most obvious fact that presents itself in this study is that 31.25 per cent of the animals sent to slaughter for infertility by persons not employing veterinary personnel, were actually pregnant. This figure is probably somewhat high, as the number of animals studied is not too
large, but it serves as an indication that possibly much of the infertility problem is due to the simple fact that fertile animals are not recognized by their owners. After the elimination of the fertile animals, however, the pathologic picture is much more uniform, varying but slightly in the major categories.

Pathology of the Ovarian Follicle

Essentially, the pathology of the ovarian follicle in the cases studied consisted of the following lesions: (a) nonfunctional, or failure of development of the follicle and (b) cystic follicles.

The failure of follicle development is shown in Figures 52, 53 and 54 and is essentially due to three causes: senility, infantility and atrophy of the ovary. Fortunately, in the cases examined there was a representative example of each of the above subtypes (Cases 44, 32 and 9).

Senility

Failure of normal development in the senile specimen involved only the ovaries. Examination of other aged specimens not in connection with this particular study has revealed that the reproductive tract is apparently normal in size and shape in those animals which were not diseased. The ovaries of the specimen examined in this study,
however, showed a functional failure apparently due to the exhaustion of the reproductive capacities of the animal.

The ovaries presented a waxy, yellowish appearance which was rough and pitted upon the surface. The ovaries were smaller than normal and there was no external evidence of either developing follicles or corpora lutea. The only evidence of follicles to be seen were numerous pinpoint depressions in the roughened yellowish surface. The cut surface revealed a firm partially fibrosed interior interspersed with numerous bands of fibrous connective tissue. There was a visible demarcation of the cortical and medullary regions, with the cortical region somewhat reduced. The follicle structures were not visible to the naked eye. Both ovaries, however, showed numerous "red bodies" indistinguishable except for their smaller size from the "red bodies" formed by old regressed corpora lutea. Most of these "red bodies" were covered and concealed by the thickened tunica albugenia and the yellow pigmentation.

Microscopically, the germinal epithelium was almost completely missing. In the few places where it remained, the cells had entirely lost their cuboidal character and had become flattened and pyknotic. The tunica albugenia was thickened and the cells were denser than in young
specimens. The cortical area was reduced and the thin fibrous connective tissue strands separating the whorl-like portions of the cortical connective tissue had become more prominent. Few primary follicles could be demonstrated, there being less than two follicles per field when examined under low power of the microscope (Figure 54). Such follicles as were demonstrated showed various features of atresia in the great majority of cases. There were considerable numbers of corpora lutea atretica, but no evidence of corpora lutea except for greatly degenerated foci closely approaching scar tissue.

According to Bourg (2, p.913), evidence gained from a study of the ovaries of rats indicated that numerous corpora lutea atretica in the ovaries produced similar modifications of the reproductive tract to those found in pregnancy, including an inhibition of follicle development in the ovaries. This might possibly have been the case here, although exhaustion of the reproductive capacity of the ovary was probably the primary factor. However, it does seem odd that the follicles which remained did not develop into graafian follicles in at least one or two instances.

Infantility

In the infantile case (Figures 21, 22 and 53), gross
examination revealed the exterior of the ovaries to be very smooth, yellowish white in color, considerably laterally compressed and showing no areas or protrusions indicative of either follicle or corpus luteum development. The cut surface revealed a homogenous and apparently fibrous structure that showed no grossly apparent divisions into cortex and medulla. The capsule appeared to be thickened and the intense vascularization of the hilar portions was inapparent. There were no grossly apparent follicular structures.

Microscopically, it was shown that the designation of infantile could only apply to the gross aspect of the ovary. Indeed, the microscopic aspect was one of almost complete lack of any follicular structures although ovigerous cords were present, a condition which is certainly not encountered in the normal immature animal.

The germinal epithelium could not be demonstrated. The tunica albugenia was thickened and extensive, forming a well demarcated capsule that was strongly eosinophilic. The cortical and medullary connective tissues showed no essential difference from normal with the exception that the thickness of the cortex was quite reduced when compared with the general size of the ovary, and the vascularization of both cortex and medulla were reduced. Ovigerous cords were present but there was a virtual absence of primary
follicles, there being less than ten per section, and those follicles that could be found showed early degeneration. Those ova which had become differentiated into primary follicles showed early atresia. In no case was a follicle found that exceeded 150 microns in size (Figure 53b).

Atrophy

The one case of atrophy encountered presented no remarkable features. Grossly the entire ovary was shrunken and wrinkled and brownish yellow in color. The cut surface revealed a homogenous fibrous inner structure with no apparent demarcation into cortex and medulla. There was no excessive thickening of the tunica albugenia and no follicular structures could be seen (Figure 52).

Microscopic examination revealed extensive shrinking and pyknosis of the cellular constituents. The germinal epithelium appeared as a thin flattened layer of pyknotic cells. The tunica albugenia was palely eosinophilic. The cortex showed extensive pyknosis of the connective tissue cells and no demonstrable follicular structures. There was a reduction of vascularization of both the cortex and the medulla and the nerve tracts lacked prominence. The medulla was considerably compacted, the apparent numbers of the connective tissue fibers being
reduced and the blood vessels compressed into a solid mass. Some obliteration of the lumens of the medullary and hilar vessels was observed. There was no evidence of bacterial invasion, the general picture being one of simple cell failure and shrinkage due to reduced blood supply. However, no evidence was found to indicate either thrombus or embolus in the vessels entering or leaving the ovary.

Atresia

At this point it may be well to mention another condition which could possibly affect the reproductive ability of the ovary. While normally not considered pathological, follicle atresia may be so extensive that it can possibly prevent ova from maturing. Excessive follicle atresia was noted in 15 cases among those studied (Figures 38-45), but always in connection with some other abnormality, principally persistent corpora lutea; so it cannot be said with certainty that atresia is of itself pathologic. Case 44, previously mentioned, might be indicative of the fact that atresia can be a self-perpetuating process, but with a senile ovary under consideration, any conclusions derived therefrom would be doubtful at best. However, it is felt that the condition should be taken into consideration in the making of any postmortem examination of infertility.
Follicle atresia is present in both normal and abnormal ovaries. The essential points in the consideration of the possible pathogenicity of this particular condition are the relative frequency of occurrence of atretic follicles as compared with the development of normal follicles and the presence of a normal functioning corpus luteum. As has been previously stated, follicle atresia may occur at any stage of follicle development. Usually, however, it occurs prior to the development of a zona pellucida by the ovum and thus fails to result in the production of a corpus luteum atretica. After this stage, the presence of large numbers of atretic follicles and the presence of large numbers of corpora lutea atretica should be looked upon with suspicion. Unfortunately, this study was not designed to fully develop this phase and only arbitrary and probably inexact correlations can be drawn regarding its relationship to the infertility syndrome.

Arbitrarily, it was decided that the presence of more than ten grossly recognizable atretic follicles per midline section was excessive. This may not actually be the case and will have to await further study. However, all ovaries with persistent corpora lutea showed this condition, while the normal ovaries did not, except for those associated with early pregnancy.
The microscopic aspects of the process of atresia are shown in Figures 34-45. Figures 34c and 35c show atresia in a primary follicle, while Figures 36-45 deal with atresia in follicles of greater maturity.

It can be theorized that the atretic follicle can play a part in the development of infertile ovaries. Assuming that the process of involution of the atretic follicle can be halted after the ovum has been destroyed, it is quite possible that the theca interna can continue to secrete follicular fluid, in which case the atretic follicle could become a cyst (11, p.219).

Corpora lutea atretica can also exert a possible detrimental action on the ovary if they exist in great enough numbers. Since these structures are cellurally similar to the normal corpus luteum and their hormonal action has been indicated (2, p.913), it is possible that their combined activity may be such that they can suppress production of LH and FSH by the anterior pituitary and thus promote the further formation of atretic follicles as well as supersede the functions of the normal corpus luteum (13, p.506) (18, p.537). Furthermore, through their hormonal activity they may further the retention of normal corpora lutea which may be present in the ovary, thus producing a condition of persistent corpus luteum. This
condition is reasonably common in large animal practice. It has been noted during this study that there is a marked increase in the number of recognizable atretic follicles and corpora lutea atretica in the ovaries of animals possessing persistent corpora lutea. It is reasonably certain that these corpora atretica are the result of the presence of the persistent corpus luteum, as similar conditions can be observed in the normal ovaries of early pregnancy. However, there may be a good, but still incompletely investigated possibility, that these corpora atretica may exert a pathologic influence in ovaries which have lost the critical endocrine balance essential to normal functioning.

A diagram of the interactions and origins of the various hormones, insofar as they are known, which directly affect the reproductive tract is shown in Figure 55. It will be noted that the whole process is one of extremely delicate balance, which can be thrown into complete confusion by the excess or diminution of one or more of the hormonal substances. By substituting a cystic follicle, a persistent corpus luteum, or perhaps multiple corpora atretica for the normal structures, we find that there can be set up in the ovary a vicious cycle of events which conspire to support and maintain pathologic conditions.
Venzke (56, p.351) states that there is a definite relationship between the endocrine system and lowered fertility, and Van Es (55, p.376) presents evidence that abnormality in hormone levels can produce difficult conception or infertility.

The significance of the corpora lutea atretica in abnormal ovaries is well worthy of further investigation. The studies of Bourg (2, p.913) seem to indicate that they may have effects which have not been thoroughly explained.

Cystic Follicles

The condition commonly known as cystic ovaries is one of the principal pathologic conditions associated with the infertility syndrome. In this study, 16 of the 55 cases examined had a greater or lesser degree of cyst formation.

Follicular cysts have been mentioned by many authors as a cause of infertility and secondary symptoms of nymphomania and abnormal estrus in cattle (6, p.431) (60, pp.441-451) (5, p.130) (21, p.400) (39, p.558) (49, p.471). However, most of the articles deal with the condition from a clinical standpoint and are relatively useless from a pathological point of view. Hammond (19, p.188) states that the symptoms of nymphomania, other than continuous
"bulling", are swollen vulva, high tail head and sinking of the pelvic ligaments. Further symptoms which can be noted are heaviness in the forequarters and a masculine variation in voice (5, p.130). Masculine qualities gradually become more prominent during the course of this condition.

De Lange (11, pp.211-219) states that in his work with unbred cattle, the cystic ovaries found were of two types: (a) those possessing a granulosa and (b) those consisting merely of a fluid filled sac of fibrous tissue. Both types as described by De Lange were found in this study (Figures 49, 50 and 51).

In this study, however, a somewhat different method of classifying cysts was used: (a) cysts which were associated with an active corpus luteum and (b) cysts which were not. Six ovaries showed cysts associated with an active corpus luteum. Only one mention of this particular condition has been found in the literature reviewed. Hammond (19, p.194) lists the following compiled figures derived from the work of Stalfors:
This report is particularly interesting in that it recognizes the fact that cysts may be associated with corpora lutea.

The cysts in this study existed in the form of follicles ranging from four to twelve millimeters in diameter, with an average diameter of six millimeters. Grossly, the ovaries were essentially normal in size and color, with the exception of Case 18; and all possessed one or more active well developed persistent corpora lutea. In three cases the corpus luteum occurred in the same ovary as the cyst (Figure 17). In two cases the corpora lutea were found in the opposite ovaries and in one case cysts were found in both ovaries. Three of the corpora lutea were normal, two were cystic and one case showed two cystic corpora lutea (Figure 27) in the same ovary. The corpora lutea were relatively poorly attached to the underlying tissues, having a definite, grossly visible capsule, poor vascularization and the characteristic yellow to yellow orange color of old corpora lutea.
Considerable numbers of "red bodies" (Figure 33a, d and i) were also found upon cutting, as many as twelve being counted in a single midline section in Case 15. According to McNutt (30, p.84) the presence of these "red bodies" is an indication of regressed corpora lutea and a possible criterion of infertility, as well as being a time index to the duration of infertility. However, some of the smaller bodies were marked before examination and it was discovered that two out of the five, so marked, showed definite evidence of being corpora lutea atretica rather than regressed corpora lutea.

This fact aroused suspicion that the cysts might actually be either normal or atretic follicles and a careful check of the ovaries was made to prove or disprove this. The follicles showed a well defined granulosa surrounding a deeply staining eosinophilic fluid which had coagulated during the fixation process. The theca interna was well supplied with blood vessels, and in two cases a number of erythrocytes had penetrated the granulosa and were laying along the periphery of the liquor folliculi. Occasional spherical chromophilic granules (Figure 49e) were observed lying on the inner surface of the cellular lining of the follicle. These granules were never demonstrated in normal graafian follicles. Serial sections
through the cysts and examination of the cut surface under the dissecting microscope revealed no sign of cumuli oophori. Remnants of the zona pellucida were demonstrated in three of the specimens.

The above evidence was considered sufficient to discount the possibility that these structures were normally developing follicles, but did not discount the possibility of their being atretic follicles.

Further examination revealed that the granulosa was well formed and intact. No evidence was observed of any extensive vascularization, inward proliferation of connective tissue or theca interna cells, or loosening of the cell membrane of the granulosa. In the absence of these characteristics, the follicles were considered to be cystic (Figure 50).

There would be considerable difficulty in differentiating these cysts from normal or atretic follicles in the living animal, or in a postmortem specimen without microscopic diagnosis. Hammond (19, p.189) cites a physical criterion for differentiation of cysts from normal follicles. If the follicle exceeds 15 millimeters in diameter it should be considered to be cystic. He further states that smaller cysts are very similar to normal follicles but their fluid content tends to be more yellowish.
While this may be true in many cases, functioning graafian follicles as large as 20 millimeters in diameter have been observed in several specimens during this study. Size alone, therefore, cannot be considered to be diagnostic. The criterion for accurate diagnosis is microscopic examination.

The condition of cysts occurring together with persistent corpora lutea allows a possible explanation for those rare cases encountered in practice where a cow exhibits symptoms of nymphomania, yet reveals a persistent corpus luteum on examination, and for those cases of persistent corpora lutea which develop cystic ovaries after the yellow body has been removed. Hammond (19, p.190) lists one case where a persistent corpus luteum was expressed and the animal then developed cystic ovaries on the following heat. Clinical cases examined by the author have shown the same symptoms and lesions. These cases serve as clinical indications that cysts and persistent corpora lutea can possibly occur together.

The second and more common type of cyst was found in 16 of the 56 cases examined (Figures 9, 10, 19, 20, 33g and h). They consisted of large, tense, fluid-filled cavities ranging from five to 42 millimeters in diameter and were not accompanied by a functional corpus luteum in
either ovary. These cysts are easily recognizable in the living animal by their large size and characteristic feeling when palpated. The outer wall and tunica albugenia are stretched almost to the point of rupture in most cases. Puncturing or rupturing these cysts leaves a shrunken flabby sac consisting principally of the medullary stroma, fibrous connective tissue and blood vessels. Fixed specimens, in which the cyst fluid has been coagulated, can be cut with reasonable assurance of retaining the internal architecture of the ovary more or less intact (Figures 19 and 20). Such specimens revealed other smaller cysts associated with the larger ones. Some of these small cysts were deeply buried in the connective tissue separating the bases of the larger cysts. In the cases examined here and in others examined in the course of routine practice, usually not over two large cysts were found per ovary. Possibly the sheer size and pressure of the large cysts prevents the smaller ones from developing (11, p.219). These smaller cysts probably are the source of recurring cyst formation in affected animals after the contents of the larger cysts have been expelled by manipulation or surgery (49, p.476).

Microscopically, the cysts may or may not show the presence of a granulosa as illustrated in Figures 49, 50
and 51. Hammond (19, p.189) states that the presence of a normal granulosa in large cysts is surprising, but that some usually remains. In cysts of long standing the granulosa may be completely absent, degenerating and disappearing in the later stages of untreated cases (Figure 51).

The theca externa is thickened and fibrosed and the normal structure of the ovary is so distorted that it is impossible to find any clear demarcation between cortex and medulla. The cortical portion of the ovary is greatly reduced and the medulla is compressed and distorted by the pressure of the cysts. The germinal epithelium is present, if at all, only in that portion of the ovary which is not incorporated into the dome of the cyst. The tunica albugenia is thickened and in the cyst region is incorporated indistinguishably into the cyst wall. The cyst fluid reveals much the same characteristics as the fluid found in the follicular cysts associated with persistent corpora lutea, being markedly eosinophilic in character and showing the presence of chromophilic granules on the inner surface of the wall.

In four instances in this study, cysts were found in which the granulosa was missing, the cyst wall being formed of fibrocytes derived from the tunica albugenia, theca externa and theca interna. Considerable numbers of
chromophilic granules were found lying in close conjunction with the inner wall. The vascularization was considerably reduced, the theca interna apparently losing its function and being incorporated into the cyst wall.

The majority of the cases, however, showed more or less normal structure of the wall, with the granulosa being variably affected by erosion or disintegration. All stages from a thick layer of cells to a single flattened layer were encountered. The vascularization of the theca interna also showed great variation in the number and size of the vessels.

Pathology of the Corpus Luteum

The pathology involving the corpus luteum is relatively uncomplicated as far as this study is concerned. Essentially, it revolves around two general manifestations: (a) persistent corpora lutea and (b) cystic corpora lutea. Figures 17 to 18, 26 to 30 and 46 to 48 illustrate some of the phases of this condition.

Persistent corpora lutea

A persistent corpus luteum is one which remains in a functional condition beyond its normal involution time. Such corpora lutea are characterized generally by
relatively large size, yellow to yellow orange color, soft or doughy feel and looseness of attachment to the underlying ovarian stroma. The diagnosis of persistent corpus luteum is made by a study of the animal's history and examination of the ovaries and reproductive tract. Historically, the affected animal will show persistent failure to come in heat and on examination a large, soft and usually easily expressed corpus luteum will be found in one or both ovaries.

A number of authors have published excellent articles on the clinical aspects of persistent corpora lutea and the histological aspects of normal corpora lutea, but the literature contains little about the pathology and histopathology of this structure. McNutt (30, pp.85-100) and Hammond (19; pp.35-41, pp.78-85, pp.121-128) in particular have excellent descriptions and references pertaining to normal corpora lutea. Zschokke, quoted by Hammond (19, pp.184-185), states that persistent corpora lutea are produced by the use of certain foods such as rye, malt, brewer's grains and sugar beet silage. He did not, however, obtain this information from experiment, but based it on experience in practice. Hammond (19, p.185) reviews the differences between various forms of corpora lutea and states that the histological structure of the
normal forms showed no essential difference from the ab-
normal, except that degeneration of the corpora lutea of
estrum and its overgrowth by connective tissue occurs at a
much earlier date.

This latter statement was not confirmed by the re-
sults obtained in this study. Eighteen cases of various
forms of pathologic corpora lutea were examined during the
course of this study, and while they showed no marked
variation from normal on cursory examination, three marked
characteristics of internal form and structure served to
separate them from normal. The color tended toward orange,
the cut surfaces of fresh specimens showed only a slight
extravasation of blood and the development of the fibrous
capsule separating the corpus luteum from the ovarian
stroma was so extensive that it could be observed grossly.
The normal ovaries on the other hand showed either a preg-
nant uterus in cases of corpora lutea of pregnancy, or
color ranging from brownish to old gold for the fully
formed corpora lutea of estrum. In addition, the corpora
lutea of estrum showed considerable extravasation of blood
from the cut surface and a lack of development of the fi-
brous connective tissue capsule. Older corpora lutea of
estrum showed definite regression and shrinkage and might
be considered similar to persistent corpora lutea except
for the fact that a functional graafian follicle occurred either on the same or on the opposite ovary, while the persistent forms showed marked follicular atresia as shown in Figure 45.

Microscopic inspection of persistent corpora lutea revealed the presence of considerable amounts of fibrous connective tissue breaking up the lutein tissue into irregular cell masses (Figures 25 and 26a). The vascularization was considerably reduced. The lutein cells retained their regular outline, but mild regressive changes are apparent. Small vacuoles were present in the cytoplasm of the cells in contrast to the larger vacuoles found in normal corpora lutea. The nuclei stained more lightly and frequently no distinct nuclear membrane was visible. The blood vessels were reduced in number and appeared to be somewhat thicker walled. There was a more clear cut demarcation of the lutein tissue from the underlying connective tissue stroma of the ovary, the base of the corpus luteum being enclosed in a thick connective tissue capsule. Figures 25, 26, 46 and 47 show some of these variations.

Cystic corpora lutea

Cystic corpora lutea are generally similar in structure to persistent corpora lutea, with the exception of the
central cyst which is enclosed in a fibrous connective tissue capsule lined with a thin layer of modified connective tissue cells. Figure 43 illustrates this structure. The central cyst in the specimens studied varied from one millimeter to twelve millimeters in diameter. According to Williams (60, p.461), Runnels (42, p.430) and Elder (13, p.362), the presence of a cystic corpus luteum in the bovine is an indication of infertility. McNutt (31, pp.291-292) states that it remains apparently without interfering with normal development and involution and Hammond (19, p.186) states that although cystic corpora lutea have been described by many investigators, it has not been shown that they are associated with sterility, derangement of the estrus cycle or pregnancy. Furthermore (19, p.215) he classes Williams' contention as invalid, stating that cystic corpora lutea are essentially physiological rather than pathological.

The cases examined during this study tend to confirm the findings of Williams and Elder, as no cysts were found in the examination of corpora lutea of pregnancy and estrum, while eight cases of single or multiple cystic corpora lutea were found in specimens which were reportedly infertile. The associated lesions in the ovaries tended to confirm the diagnosis. It seems reasonably safe to assume
that the presence of a cyst in the middle of a corpus luteum is an indication of abnormality and infertility.

The cellular structure of the cystic corpora lutea examined was essentially similar to that of persistent corpora lutea without cysts. Two cases, 41 and 48, showed two well-developed cystic corpora lutea on one ovary as illustrated in Figure 27. The opposite ovaries showed multiple atretic follicles, as illustrated in Figure 45.

The apparent mechanism by which persistent and cystic corpora lutea produce infertility is tied up in the hormone complex previously mentioned and shown in Figure 55. The lutein cells, while apparently reduced in efficiency as shown by their microscopic aspect, still produce enough progesterone to inhibit the normal functioning of the ovarian-pituitary hormonal complex, thus resulting in the formation of atretic follicles and more rarely in the formation of follicular cysts.

Pathology of the Ovarian Stroma

The pathological processes involving the ovarian stroma are apparently few in number and rare of occurrence. Thygesen (53, p.272) cites an incidence of less than one per cent. In the 55 cases studied, only Cases 18 and 46 showed lesions involving tissues other than the follicle
or the corpus luteum. The two cases involving three ovaries showed either adhesions or abscess or both. Of the two ovaries which showed simple adhesions one was complicated by other lesions involving the follicle and the corpus luteum, while the other, except for the adhesions, was essentially normal. Both were associated with infections elsewhere in the reproductive tract, although bacterial infection could not be demonstrated in either specimen. The ovaries were adherent to the broad ligament of the uterus by cords of fibrous connective tissue. One of the two ovaries is shown in Figures 29 and 30. The other case was essentially similar as far as the adhesions were concerned.

The third ovary showed an abscess complicated by adhesions to the broad ligament of the uterus and the pelvic peritoneum. The abscess was so extensive that at the time of examination the exact point of origin could not be determined. The abscess was of bacterial origin and contained a mixed group of microorganisms, principally Micrococcus pyogenes, var. aureus (4, p.236) (33, p.234). It measured 145 by 208 millimeters and possessed a fibrous capsule 24 millimeters in thickness. The abscess not only involved the right ovary, but also the right oviduct and both horns of the uterus. Over two liters of foul-smelling
grayish fluid, pus and solid cheesy material were obtained from the affected organs. A considerable amount of fat was deposited around the ovaries and uterus, concealing much of the extent of the lesions. The condition was apparently an ascending infection, arising from metritis or pyometra subsequent to the birth of a calf.

Microscopic studies were not made of the abscess, but the adhesions were examined and showed bundles of fibrocytes and their processes adhering intimately to the tunica albugenia of the affected ovary and the fibrous portions of the broad ligament of the uterus.

Other conditions affecting the ovarian stroma have been reported, but were not seen during the course of this study. They are chiefly neoplastic in nature and are also remarkable for their rarity. Since none were found it would serve no useful purpose to discuss them.

CONCLUSIONS

The lack of proper diagnosis resulted in the needless sacrifice of ten pregnant animals out of 32 sent to slaughter for infertility reasons by farmers, or 31.25 per cent of the total. Animals which were under constant veterinary supervision showed no such percentage of loss. Only one animal out of 23 sent to slaughter for fertility reasons was pregnant, only 4.55 per cent of the total, and
that particular animal was diagnosed as pregnant before slaughter. A program of education in the use of veterinary service for examination for pregnancy in the living animals would undoubtedly reduce the incidence of needless loss of fertile and normal animals.

Of the several conditions encountered in the 44 cases of possibly infertile animals, ten cases or 22.73 per cent of the total number showed no visible lesions. Whether or not these animals were functionally infertile could not be determined, but it can safely be assumed that some of these cases could have been salvaged with proper veterinary attention. The condition of functional infertility needs further study and research, as it appears to be one of the larger factors composing the infertility syndrome. The remaining 34 animals showed one or more lesions associated with infertility. Assuming, in the absence of proof to the contrary, that the entire 44 animals not pregnant were infertile, it was found that the frequency rate of the individual conditions encountered ran as follows:

<table>
<thead>
<tr>
<th>Type</th>
<th>Cases</th>
<th>Per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistent Corpus Luteum</td>
<td>18</td>
<td>40.91</td>
</tr>
<tr>
<td>Cystic ovaries</td>
<td>16</td>
<td>36.36</td>
</tr>
<tr>
<td>Follicle atresia</td>
<td>15</td>
<td>34.09</td>
</tr>
<tr>
<td>No visible lesions</td>
<td>10</td>
<td>22.73</td>
</tr>
<tr>
<td>Non-functional</td>
<td>3</td>
<td>6.82</td>
</tr>
<tr>
<td>Adhesions</td>
<td>2</td>
<td>4.55</td>
</tr>
<tr>
<td>Abscess</td>
<td>1</td>
<td>2.27</td>
</tr>
</tbody>
</table>
Of the four major categories, little is known about either follicle atresia, or those cases showing no visible lesions. Much work needs to be done on these conditions to determine their significance in the infertility syndrome.

Another condition, hitherto generally ignored by investigators into bovine infertility, is the presence of cysts associated with persistent corpora lutea. This condition was recognized in six cases or 13.64 per cent. Since the methods used to identify the cystic follicles were designed to eliminate possible errors in diagnosis, it can be stated with reasonable certainty that this condition does occur and in a much higher number than might be expected. The condition explains some of the puzzling features that occasionally occur as sequelae to the treatment of persistent corpora lutea in routine practice.

The general belief that cystic corpora lutea do not have an adverse effect upon fertility was generally disproved by the results obtained in this study. In none of the pregnant animals were cystic corpora lutea found. They only occurred in cases with histories of infertility which were examined during the second phase of this work. In the first phase examination of a hundred specimens taken from the killing floors of local abattoirs, the condition was observed only four times and occurred in none of the
23 animals that were pregnant. Since there were no means of ascertaining whether the four animals examined during this phase were fertile or not, these animals were excluded from the compilation of normal material. Both cases of multiple and obviously pathologic corpora lutea examined during the course of this study were cystic and the follicular cysts occurring in an additional four cases of cystic corpora lutea, would tend to confirm six out of the eight cases as being pathologic without resort to histories. It can, therefore, be reasonably certain that the condition of cystic corpora lutea is one which is normally detrimental to normal fertility.

The general pathology of the bovine ovary is multiple rather than simple except for the condition of cystic follicles unaccompanied by corpora lutea in either ovary. While a large part of the conditions encountered can be diagnosed in the living animal, postmortem gross and microscopic observations can reveal many of the more obscure ovarian aspects of infertility and produce some basic data regarding the future handling of complicated cases.

The remainder of the observations generally parallel those of other investigators and present no unusual aspects.
1. The reasons for the increasing interest in bovine infertility are reviewed.

2. The infertility syndrome in the bovine is due to a number of causes.

3. The lack of a simple test for pregnancy not involving rectal palpation has been a decided handicap in dealing with bovine reproductive problems.

4. Insufficient basic data is known about the gross and microscopic aspects of the ovaries of infertile cattle.

5. A study of the gross and microscopic anatomy of 100 animals was made to determine normalcy and to serve as a basis for the study of the pathology associated with infertility. The findings are described.

6. The materials and methods used in this study are described and the results of the examination of the ovaries and genital tracts of 55 animals presented for slaughter for infertility reasons are described and tabulated.

7. The pathology of the infertile ovary is multiple rather than simple and falls, in general, into three major categories: (1) pathology of the follicle, (2) pathology of the corpus luteum and (3) pathology of the ovarian
stroma. Each of these conditions and their several sub-headings are described and discussed in the light of the recorded knowledge and the information obtained during the course of this study and from practice.

8. Certain conclusions dealing with the effect of inadequate professional service, examination and diagnosis prior to slaughter are developed, and three hitherto neglected aspects of ovarian pathology are reviewed.

9. Charts, diagrams, photographs and details of techniques used in the making of examinations of the ovaries are given.
EXHIBITS

Figure 1. (a.) Ovaries, (b.) Pavilion, (c.) Oviducts, (d.) Horns of uterus, (e.) Body of uterus, (f.) vagina, (g.) Vulva, (h.) Graafian follicle, (i.) Corpus luteum.

Figure 2. (a.) Uterine mucosa, (b.) Body of uterus, (c.) Cervix, (d.) Vagina, (e.) Vestibular fold, (f.) Clitoris.

Figure 3. (a.) Pregnant horn of uterus.

Figure 4. (a.) Fetus, (b.) Amnion, (c.) Chorion, (d.) Cervix.

Figure 5. (a.) Corpus luteum, (b.) Forceps inserted into tiny vulvar opening.

Figure 6. (a.) Excessive vaginal mucus.

Figure 7. (a.) Horn of uterus slightly atonic, (b.) Cyst on oviduct.

Figure 8. (a.) Cervix showing one rosette, (b.) Oviduct cyst, (c.) Persistent hymen in vestibular fold region.

Figure 9. (a.) Flaccid atonic uterus, (b.) Body of uterus, (c.) Cystic ovaries.

Figure 10. (a.) Fluid in uterine cavity, (b.) Apparent uterine caruncles, (c.) Cystic ovaries, (d.) Cervix showing two rosettes.

Figure 11. Right and left ovary of Figure 1. (a.) Corpus luteum, (b.) Graafian follicle, (c.) Developing follicles.

Figure 12. Gross appearance of Figure 11 before sectioning.

Figure 13. Normal Ovaries. (a.) Recently formed corpus luteum of estrum, (b.) "Red bodies" (regressed corpora lutea).

Figure 14. Gross appearance of Figure 13.

Figure 15. Pregnant ovaries. (a.) Corpus luteum of pregnancy, (b.) Developing follicle.
Figure 16. Gross appearance of Figure 15.

Figure 17. Pathologic ovary. (a.) Regressed corpus luteum, (b.) Cavity of corpus luteum, (c.) Cystic corpus luteum, (d.) Cyst.

Figure 18. Gross appearance of Figure 17. (a.) Expressed cystic corpus luteum.

Figure 19. Pathologic ovaries. (a.) Ovarian cyst.

Figure 20. Gross appearance of Figure 19.

Figure 21. Pathologic ovary, infantile.

Figure 22. Pathologic ovary, gross appearance of Figure 21.

Figure 23. Pathologic ovaries. Left ovary, (a.) Persistent corpus luteum. Note thickness of capsule. Right ovary shown in detail in Figure 45.

Figure 24. Pathologic ovary, gross appearance of Figure 23.

Figure 25. Pathologic ovary. (a.) Persistent, pedunculated corpus luteum. (b.) Atretic and developing follicles.

Figure 26. Pathologic ovary. Note development and vascularization of capsule.

Figure 27. Pathologic ovary. (a. and b.) Persistent cystic corpora lutea.

Figure 28. Pathologic ovary. Note double persistent corpora lutea.

Figure 29. Pathologic ovary. (a.) Persistent corpus luteum, (b.) Multiple small cysts.

Figure 30. Gross appearance of Figure 29. (a.) Adhesions.

Figure 31. (a.) Cyst on right oviduct Figure 7b and 8b. (b.) Graafian follicle. (c.) Corpus luteum nigrum, partially regressed.

Figure 32. Gross appearance of Figure 31. (a.) Cyst on right oviduct.
Figure 33. A group of pathologic ovaries. (a.) Numerous "red bodies", (b.) Cystic follicle, (c.) Persistent corpus luteum, (d.) Numerous "red bodies", (e.) Developing corpus luteum, (f.) Regressing corpus luteum, (g.) Follicular cyst, (h.) Follicular cyst, (i.) Numerous "red bodies", (j.) Persistent corpus luteum.

Figure 34. Photomicrograph of normal ovary, hematoxylin-eosin, 120x. (a.) Germinal epithelium, (b.) Tunica albugenia, (c.) Atretic primary follicle, (d.) Normal primary follicle, (e.) Ovigerous cords.

Figure 35. Photomicrograph of normal, Pollak's, 400x. (a.) Primary follicle, (b.) Atretic primary follicle, (c.) Primary follicle.

Figure 36. Photomicrograph of normal ovary, Pollak's, 400x. (a.) Primary follicle, (b.) Developing primary follicle, (c.) Ovum, note developing cell membrane and chromatin threads in nucleus, (d.) Follicular cells, (e.) Basement membrane.

Figure 37. Photomicrograph of developing graafian follicle, hematoxylin-eosin, 80x. (a.) Theca externa, (b.) Theca interna, (c.) Ovum and zona pellucida, (d.) Corona radiata, (e.) Basement membrane, (f.) Membrana granulosa, (g.) Coagulated liquor folliculi.

Figure 38. Photomicrograph of atretic follicle, hematoxylin-eosin, 80x. (a.) Atretic follicle.

Figure 39. 400x enlargement of Figure 38. (a.) Follicular cells, (b.) zona pellucida of collapsed ovum.

Figure 40. Photomicrograph of atretic follicle, hematoxylin-eosin, 400x, similar to 39 above except that zona pellucida has disappeared. (a.) Atretic follicle.

Figure 41. Photomicrograph of degenerating ovum, hematoxylin-eosin, 400x. (a.) Ovum, note degeneration of cytoplasm and enlargement of lipoid droplets.
Figure 42. Photomicrograph of atretic follicle, hematoxylin-eosin, 80x. (a.) Cumulus oophorus, (b.) Ovum, (c.) Chromatin granule formed of condensed nuclear material. Note the proliferation of the granulosa into the follicle cavity.

Figure 43. Photomicrograph of atretic graafian follicle, hematoxylin-eosin, 80x. (a.) Degenerating granulosa, (b.) Degenerating ovum, note partially collapsed zona pellucida, (c.) Degenerating cumulus oophorus and corona radiata.

Figure 44. Photomicrograph of corpus luteum atretica, hematoxylin-eosin, 50x. (a.) Corpus luteum atretica. Note continued presence of theca externa.

Figure 45. Multiple corpora atretica, hematoxylin-eosin, about 2x. (a.) Corpora lutea atretica, (b.) Atresia of developing follicle.

Figure 46. Persistent Corpus luteum, hematoxylin-eosin, about 2x. (a.) Small central cyst in corpus luteum, (b.) Thickened capsule of corpus luteum, (c.) Developing follicle.

Figure 47. Photomicrograph of base of persistent corpus luteum in Figure 46, hematoxylin-eosin, 120x. (a.) Lutein tissue, note theca lutein cells, (b.) Blood vessel, (c.) Fibrous capsule.

Figure 48. Photomicrograph of Cystic corpus luteum, hematoxylin-eosin, 120x. (a.) Cyst fluid, (b.) Layer of flattened cells lining cyst, (c.) Fibrous connective tissue cyst wall, (d.) Lutein cells.

Figure 49. Photomicrograph of follicular cysts showing variations in lining of cyst wall, hematoxylin-eosin, 120x. (a.) Coagulated cyst fluid, (b.) Granulosa, (c.) Coagulated cyst fluid, (d.) Theca interna, (e.) Chromophil granule.

Figure 50. Photomicrograph of follicular cyst, showing granulosa and theca interna, hematoxylin-eosin, 120x.

Figure 51. Photomicrograph of follicular cyst, hematoxylin-eosin, 120x. (a.) Cyst fluid, (b.) Theca interna, (c.) Theca externa.
Figure 52. Photomicrograph of atrophic ovary, hematoxylin-eosin, 120x. (a.) Tunica albugenia, (b.) Cortex, (c.) Atretic follicle.

Figure 53. Photomicrograph of infantile ovary, hematoxylin-eosin, 120x. (a.) Tunica albugenia, (b.) Atretic primary follicle, (c.) Ovigerous cords.

Figure 54. Photomicrograph of senile ovary, hematoxylin-eosin, 200x. (a.) Tunica albugenia, (b.) Atretic primary follicle, (c.) Old corpus albicans.

Figure 55. Chart of hormone relationships.

Figure 56. Chart of the ovarian cycle.
Figure 2
Figure 23

Figure 24
Figure 29

Figure 30
Figure 31

Figure 32
Figure 44

Figure 45
HORMONE RELATIONSHIPS OF PITUITARY AND GENITAL ORGANS

FSH (follicle stimulating hormone) which stimulates development of ovary.

LH (luteinizing hormone) which stimulates production of corpus luteum.

PROLACTIN (lactogenic hormone) which inhibits formation of mammary gland.

OXYTOCIN which stimulates lactation of mammary gland.

OVARIAN FOLLICLE which produces estrogen.

CORPUS LUTEUM which produces progesterone.

MAMMAE which stimulates growth of mammary gland.

UTERUS which stimulates development of myometrium and endometrium.

PARTURIENT UTERUS AND BIRTH CANAL which stimulates contractions of uterus.

1. CHORIONIC GONADOTROPIN which produces myometrium.

2. RELAXIN which relaxes myometrium.

Figure 55
THE OVARIAN CYCLE OF THE COW

Diameter in Millimeters

Days

- heat
- ovulation
- developing corpus luteum (subject to variation)
- follicle growth
- corpus luteum
- heat
- ovulation
- regressing corpus luteum

Figure 56

adapted from McNutt (p. 10)
BIBLIOGRAPHY


APPENDIX
APPENDIX

Standard Fixation Technique

1. Fixation: 10% Neutral Formalin\(^1\) (4% Formaldehyde) or Bovin's Fluid 10-24 hours

2. Wash: Tap water 2 hours

3. Dehydrate:
   a. 50% ethyl alcohol 12-24 hours
   b. 70% ethyl alcohol\(^2\) 12-24 hours
   c. 95% ethyl alcohol 2-24 hours
   d. 100% ethyl alcohol 2-24 hours
   e. 100% ethyl alcohol 2-24 hours

4. Clear:
   a. Xylol-C. P.\(^3\) 4-24 hours
   b. Xylol-C. P. 4-24 hours

5. Infiltrate:
   a. Xylol-Paraffin\(^4\)@37°C. 2-24 hours
   b. Pure Paraffin m.p. 58-60°C. 2 hours
   c. Pure Paraffin m.p. 58-60°C. 2 hours

6. Imbed: Pure Paraffin m.p. 58-60°C.

\(^1\)Optimum size of tissue 1 cm. x 1 cm. x 5 mm., although larger pieces can be used.

\(^2\)Tissues if properly fixed and washed can be left in 70% ethyl alcohol indefinitely, after making two changes of 70% alcohol at 24-hour intervals.

\(^3\)The time limit for clearing tissues in Xylol depends upon a number of factors such as the size of the tissue, its composition, the temperature of the clearing solution, and general considerations of technique. Under normal circumstances, the smaller the piece of tissue, the shorter the clearing time. With tissues of optimum size and average density clearing is usually accomplished in four hours. Tissues should not be left in Xylol over 24 hours as excessive hardening and shrinkage will result.

\(^4\)This mixture is composed of equal parts of pure paraffin and C. P. Xylol. Tissues are placed in corked bottles and incubated at 37°C. in a bacteriological oven.
Staining Techniques

I. Modified Hematoxylin-Eosin Technique. Note: This stain works best with material fixed in 10% formalin.

1. Xylol C. P. 8 dips (20 seconds)
2. Xylol C. P. "
3. 100% alcohol "
4. 100% alcohol "
5. 95% alcohol "
6. 50% alcohol "
7. 0.85% NaCl in H₂O "
8. Harris Hematoxylin 3-6 min. ⁶
9. 0.85% NaCl in H₂O 8 dips
10. 2% Phospho tungastic Acid 4-6 dips (10-15 sec.)
11. 0.85% NaCl in H₂O 8 dips
12. 2% NaCitrate in P. S. S. "
13. 0.85% NaCl in H₂O "
14. 5% Eosin in 50% ROH 30 sec. - 1 ½ min.
15. 90% alcohol 6 dips
16. 100% 8 dips "
17. 100% "
18. Xylol C. P. "
19. Xylol C. P. "
20. Mount in balsam or clarite

⁵When using chrome-sublimate fixed material (ex. formol-zenker solution) run sections through
1. Strong Iodine solution in 90% alcohol 30 sec.
2. Saturated Na Thiosulfate in 70% alcohol 15-30 sec. (until bleached)

Place these solutions between the 95% and 50% alcohols.

⁶Formula for Harris hematoxylin stock
Hematoxylin crystals 1 gm.
Absolute Alcohol 10 cc.
Ammonium or Potassium Alum 20 gm.
Distilled water 200 cc.
Red Oxide of Mercury 0.5 gm.

Directions: Dissolve hematoxylin in absolute alcohol. Dissolve alum in water by heating. Combine hematoxylin and alum solutions. Bring rapidly to a boil. Add mercuric oxide carefully, too rapid addition may cause foaming or explosion. When boiling solution turns purple cool rapidly by plunging container into cold
water bath. The stain is ready to use when cool. In the event the stain is too strong, it can be diluted to any desired strength by the addition of distilled water.

When kept in a tightly stoppered bottle away from light the stain can be used for six months.

II. Pollak's Trichrome Technique

Use with 10% Formalin fixed material only.

1. Xylol C. P. 8 dips (20 seconds)
2. Xylol C. P. 
3. 100% ethyl alcohol 
4. 100% ethyl alcohol 
5. 95% alcohol 
6. Weigants Iron hematoxylin 7 min.
7. Wash running tap water 2 min.
8. Pollak's trichrome 7 min.
9. Differentiate in 0.2% CH₃COOH 10 sec.
10. 95% ethyl alcohol 6 dips
11. 100% ethyl alcohol 8 dips
12. 100% ethyl alcohol 
13. Xylol C. P. 
14. Xylol C. P. 
15. Mount in balsam or clarite

7Formula for Weigerts Iron Hematoxylin
Solution A.
1. Hematoxylin, ripened, 10% solution in 100% alcohol 10 cc.
2. 95% ethyl alcohol 90 cc.
Solution B.
1. Ferric chloride 29% aqueous solution 4 cc.
2. Water, distilled 96 cc.

Directions: Mix equal parts of Solutions A and B for use. The mixture blackens immediately through the formation of iron hematoxylin. Keep the solutions separate. Keep in stock a solution of 10% ripened hematoxylin. This solution requires at least 10 days exposure to sunlight to ripen and 3 months to reach maximum staining qualities. It can then be kept in the dark for at least one year.

8Pollaks stain purchased from Will Corporation and used without dilution.