



Dairy Integrated Reproductive Management

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As early as 1831, abnormally large ovarian follicles that failed to ovulate (release an egg) were reported to result in altered cyclic activity, abnormal sexual behavior and reduced fertility. This condition, termed cystic ovarian disease, occurs in 5 to 10% of dairy cows nationally.

In a study of 2532 health records in West Virginia, 7% of the cows had cystic ovaries. Cows that experienced cystic ovaries had calving intervals nearly 2 months longer than herdmates without cysts. Each day a dairy cow remains open past day 85 postpartum represents an estimated loss of \$2.50 to \$3.00. Thus, approximately \$180.00 of potential income is lost per year for each cow that develops an ovarian cyst—over \$1200 per year for a 100-Cow herd. Occurrence in one West Virginia herd is 28%. This herd loses an estimated \$5000 each year because of cystic ovarian disease.

Because of financial consequences associated with ovarian cysts in dairy cows, scientists have studied the disease for over 100 years. Future research may determine why some follicles develop into cysts, factors or traits that make a cow more likely to develop cystic follicles and methods for treatment of cystic cows to minimize extra days open. The following is a brief summary of current knowledge concerning cystic ovarian disease in dairy cattle.

Ovarian cysts are characterized by rectal palpation as structures greater than 2.5 cm (approximately 1 inch) in diameter remaining on an ovary for more than 10 days. Major categories of cysts include follicular cysts, luteinized follicular cysts and cystic corpora lutea.

Follicular cysts result from failure of ovulation and luteinization. (Luteinization is the structural and biochemical changes that occur in cells and tissues of a follicle when it releases the egg. Follicular cells that once produced estrogen change into luteal cells of the new corpus luteum (CL, also called a yellow body) that secrete progesterone. Follicular cysts are blister-like structures, flaccid to the touch.

Luteinized cysts apparently fail to ovulate, but some luteinization occurs. Because of the varying degree of luteinization, luteinized cysts are firmer to the touch than follicular cysts though not as solid as CL.

Cystic CL are CL with a fluid filled center. Several early researchers did not find cystic CL in pregnant cows and reasoned that cystic CL could not support pregnancy. However, researchers at Cornell University report that a CL needs to produce only approximately 100 μ g of progesterone to support pregnancy. Therefore, a cystic CL could maintain pregnancy. In the absence of pregnancy, cystic CL regress and are considered nonpathological.

Symptoms

An abnormal pattern of estrous behavior is the most noticeable sign of cystic ovarian disease. A cow with an ovarian cyst might exhibit "constant" estrus (nymphomania), no estrus (anestrus) or an erratic combination of estrus and anestrus. Ratios of estrus to anestrus vary among studies from 74%:26% to 17%:83%.

Detection of cysts in the early postpartum period might account for the reported predominance of anestrus behavior. Sexual activity does not normally accompany follicular maturation during this time. A predominance of nymphomania was reported in many early studies when more bulls were present on farms. A greater proportion of cows with cystic ovaries will be classified as nymphomaniac where good estrous detection practices are used.

Other general symptoms of cystic ovarian disease include: 1) lack of muscle tone in the vulva, vagina, cervix and uterus; 2) passive prolapse of the vagina and/or excessive discharge of mucus; 3) relaxation of sacroiliac and sacrosciatic ligaments of the pelvis (resulting in the "sterility hump" appearance

of the tail head); 4) changes in general metabolism; 5) erratic changes in milk production; 6) rough dry hair coat; 7) nervous tension; 8) disturbed feeding and rumination and 9) progressive emaciation.

Etiology

Numerous studies have determined the anatomical, physiological and biochemical changes that occur during normal development and ovulation of follicles. With this knowledge, it should be possible to determine what went wrong when a cyst develops. However, many events leading to the rupture of a follicle and release of an egg depend on small changes in molecules within cells that line the inner (granulosa cells) and outer (theca cells) tissue layers of the follicle. These changes occur rapidly, and timing of these events varies among cows. Research in this area has awaited development of new techniques sensitive enough to study these minute cellular and biochemical changes.

Cyclic development and ovulation (rupture) of follicles requires proper timing of release of several hormones from both the ovary and brain. See Fig. 1 for the known general interactions of these hormones. When properly timed, these changes result in release of an egg approximately every 3 weeks in cattle.

Briefly, ovarian follicles begin to develop and enlarge rapidly under the influence of follicle stimulating hormone (FSH) from the pituitary gland. As follicles grow, they secrete an increasing amount of estrogen into the blood. The increased estrogen concentration is necessary for the display of estrus. In addition, the elevated estrogen level causes the brain to release gonadotropin-releasing hormone (GnRH).

GnRH causes the pituitary to release a surge of luteinizing hormone (LH) and FSH. This surge of LH is responsible for ovulation of the follicle and luteinization of the cells lining the follicular wall. Cells that once provided estrogen now secrete progesterone, and the resulting structure is called a CL.

Circulating progesterone from the CL reduces uterine contractions and inhibits the surge release of FSH and LH. If pregnancy does not occur, prostaglandin $F_{2\alpha}$ from the uterus causes the CL to regress on about day 16 or 17 of the cycle. As the CL regresses, progesterone decreases and FSH and LH again are released in greater amounts, culminating in an estrogen induced ovulatory surge of gonadotropins, and the initiation of a new cycle.

See Fig. 2 for known hormonal and biochemical changes that occur within the preovulatory follicle after stimulation with LH. Cystic follicles could develop if any of the steps shown in Figs. 1 or 2 fail. The actual cause(s) of cystic ovarian disease is (are) unknown. However, the apparently successful treatment of cystic cows with GnRH (discussed later) suggests that ovarian cysts result from an inadequate or improperly timed release of GnRH from the brain.

Predisposing Causes

Development of cysts has been associated with many factors. In the late 1800s, it was proposed that occurrence of cysts was influenced by genetics or occurred secondary to uterine infection. Subsequent studies discredited the uterine infection theory and further supported a genetic predisposition.

Estimates of heritability vary considerably from 5% to as high as 43% when the data set is limited to dams and daughters with at least four service periods each. Estimates of repeatability range from 6 to 27%; recurrence varies from 15 to 75%.

Cystic ovarian disease was more common in Holstein-Friesians than in Jersey, Guernsey or Ayrshire cows and varied among sire-lines within breed. Culling bulls whose daughters had a high incidence of cystic ovaries reduced occurrence of cysts in Sweden from 10.8% in 1954 to 5.1% in 1961.

In several studies, more cysts were found in high producing cows compared to their herdmates. Higher levels of peripheral estrogen were found in cows with cysts. Furthermore, cows fed diethylstilbestrol (a synthetic estrogen) produced more milk compared to their identical-twin controls. These findings suggest that an elevated level of estrogen in cows with follicular cysts might cause higher milk yield.

In at least one study, however, cows with cysts averaged 1.2 years older than cows without cysts and, therefore, would be expected to produce more milk. Other studies have found no relationship between cystic ovarian disease and level of production. Some cystic follicles continued to grow without producing estrogen, and less estrogen was found in follicular fluid from cystic follicles compared to normal follicles.

In another study, there was no relationship between content of estrogen in fluid from cystic follicles and behavior of the cow. In addition, lower milk yields were found in nymphomaniac cows (having presumably more estrogen) than in anestrous cows. Thus the relationship between ovarian cysts and level of production of milk still is not well documented.

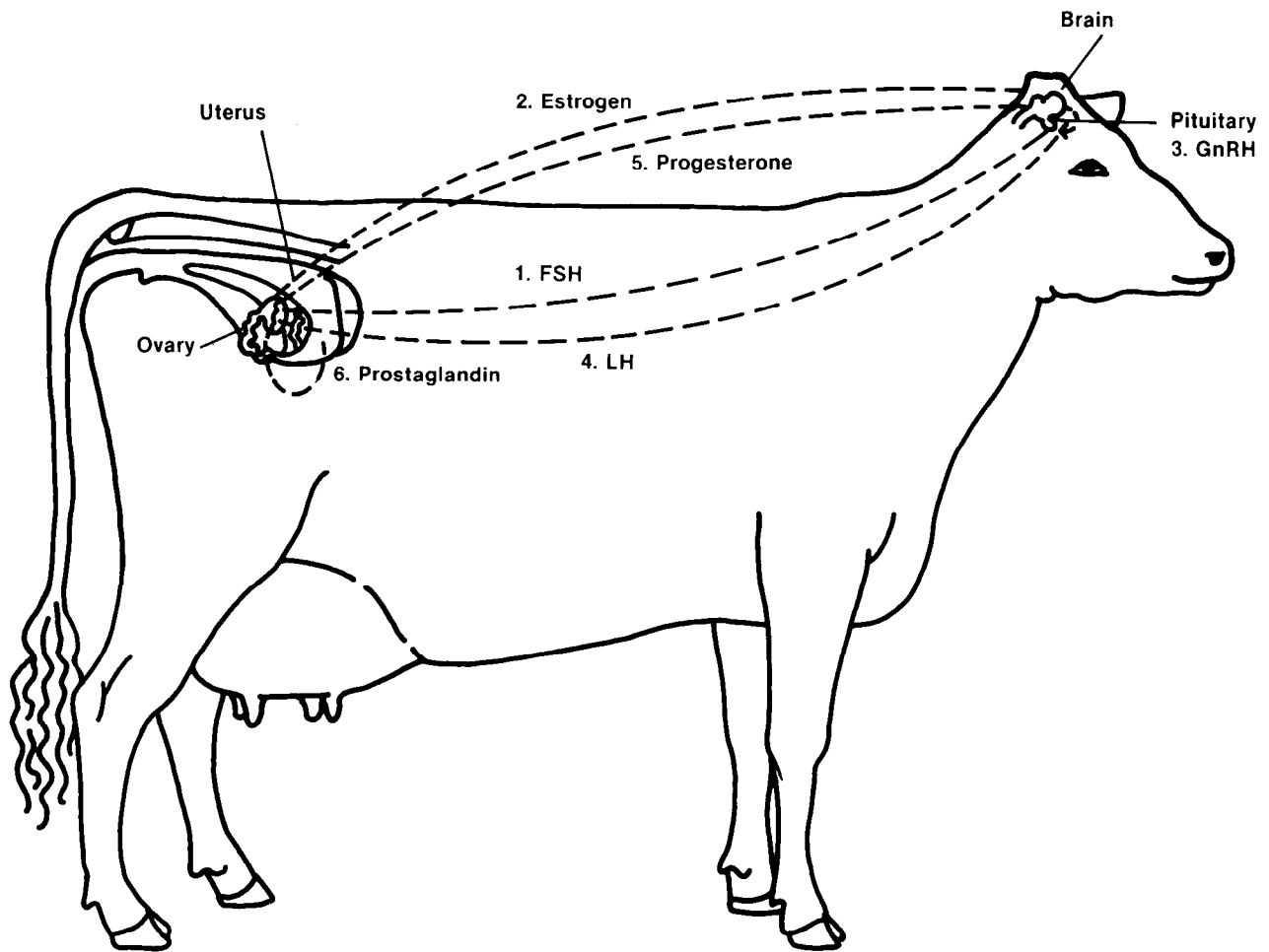


Fig. 1. Hormonal interactions between the ovary and brain.

Older cows have a higher incidence of ovarian cysts with a cumulative rate of 50% over 11 years. Incidence increases up to the fourth or fifth lactation in dairy cows. Beef cows develop cysts after 4 to 6 years of age even if never bred. Yet, no relationship was found between lactation number and incidence of cystic ovaries in 324 cows in the university herd in another study. Presumably, different culling practices for reproductive inefficiency removed many cows predisposed to cystic development before it occurred.

The greatest incidence of ovarian cysts occurs within the first 45 to 60 days postpartum and during October through February.

Treatments

Manual rupture of cysts was practiced by Scandinavian veterinarians in the late 1800s. This “crushing” of the ovary, repeatedly if necessary, was promoted in the United States at the beginning of the century. However, because of frequent excessive hemorrhaging and possible adhesions, manual rupture of cysts is not presently recommended.

The functional relationship between the ovaries and the pituitary gland was established in the 1920s. In 1942, 11 of 13 nymphomaniac cows cycled normally after treatment with an extract of the anterior pituitary gland or with pregnant mare’s serum gonadotropin (PMSG) which contains a similar compound. Conception was reported in 9 of 10 cows that were bred. Shortly thereafter, Wisconsin researchers reported 49 of 71 nymphomaniac cows with normal genital tracts began cycling after treatment with unfractionated pituitary extract from sheep; 38 of the 49 became pregnant.

Following characterization and purification, human chorionic gonadotropin (hCG) also was used successfully to treat cows with cystic ovaries. However, frequent treatment of cows with hCG or PMSG resulted in development of antibodies to these large molecules, and many cows would not respond after a few treatments.

Isolation, characterization and synthesis of the naturally occurring brain molecule GnRH in the early 1970s provided a substance capable of inducing a surge release of LH without inducing

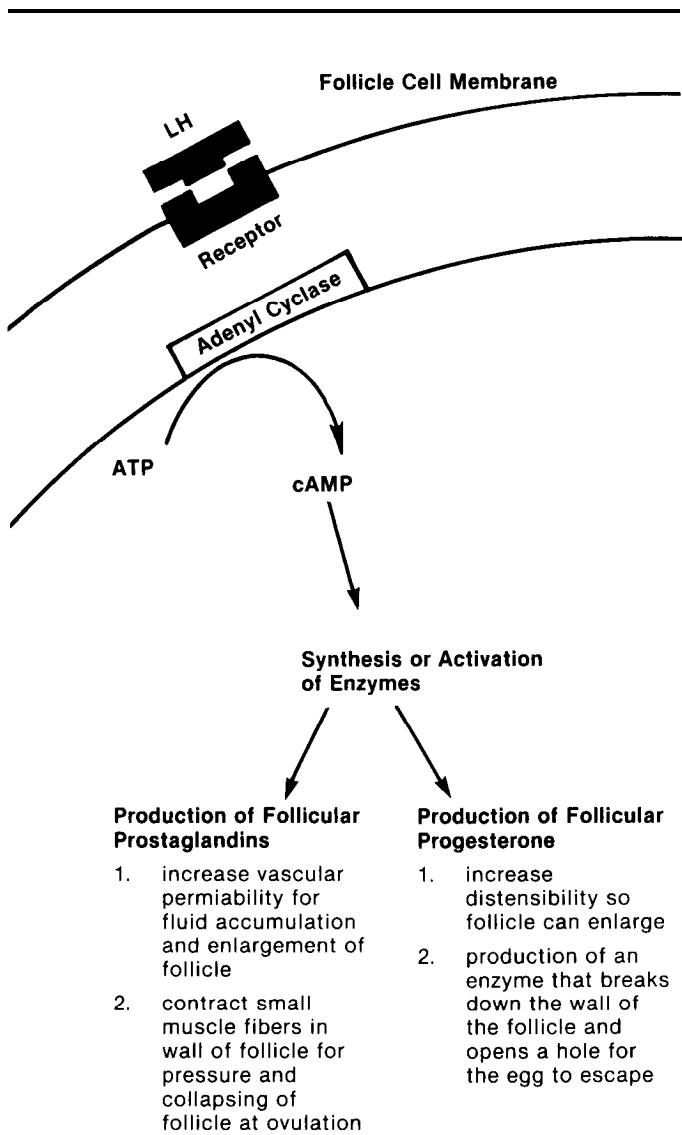


Fig. 2. Effects of LH on cells that line the preovulatory follicle.

an immune response. The surge of LH caused cysts to luteinize and then regress after an interval similar to the lifespan of a normal CL.

Experimental results obtained at Columbia, Missouri, indicate that approximately 75-80% of cows treated with GnRH recover from the cyst and begin cycling within 23 days. Combining manual rupture with hormonal therapy has no additional benefit, and administration of drugs by intravenous and intramuscular routes is equal in effectiveness. Treatment of cows with progesterone or estradiol has had few benefits. Treatment with adrenal corticoids can result in development of additional ovarian cysts.

Prophylactic administration of GnRH at approximately 2 weeks postpartum reportedly decreased calving interval by stimulating ovarian activity early postpartum. This also resulted in lower occurrence of cystic ovaries and less culling of cows with no detrimental effect on services per conception or days open. However, other investigators found no benefit with routine prophylactic treatment.

Many cows with cystic ovaries recover spontaneously without treatment (range 30-71%). Herds that were examined every 2 weeks were found to have a greater incidence of cysts than herds examined at intervals of 4 weeks. This suggests that some cysts develop and then regress spontaneously in less than 30 days. Development of and self-recovery from cystic ovarian disease is more common early in the postpartum period.

A major factor in assessing actual or perceived cystic ovarian disease is the expertise of the person palpating the cow's ovaries. As early as 1919, W.L. Williams wrote on the difficulty of distinguishing by rectal palpation cystic ovarian follicles from normal ovarian structures near the time of ovulation. In a recent field study involving 28 herds and the 10 veterinarians who regularly served the herds, there was no benefit of treatment with GnRH over saline in 40 cows diagnosed as cystic from a single examination. The study pointed out possible inaccuracies of some individuals when diagnosing ovarian cysts by a single rectal palpation. Using a milk progesterone assay to determine hormonal activity of ovarian structures, Japanese researchers found a high incidence of unnecessary or inappropriate treatment of misdiagnosed "cystic" cows.

Recommendations

Based on current knowledge of cystic ovarian disease and on a computerized economic decision analysis system, it is recommended to wait until approximately one month post-calving before attempting to diagnose cystic ovarian disease. After this time, cows diagnosed by an experienced palpater as having an ovarian cyst should be treated with GnRH at first diagnosis. Cows should be palpated a second time within 7 to 10 days if possible and retreated if necessary.

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