Cystic ovarian degeneration is a pathologic condition of dairy cows that results in formation of ovarian cysts secondary to anovulation of preovulatory follicles.1 The incidence of cystic ovarian degeneration is approximately 15%2-6 and ranges from 9.5% to 25%.3 The condition can occur at any time during the lactation period, but the incidence reportedly is higher between 40 and 150 days after parturition4 or between 31 and 60 days and between 120 and 210 days after parturition.4 Factors such as metabolic disorders, stress,9,10 uterine infection,11 and lameness12 are associated with a high incidence of cystic ovarian degeneration. In addition, a genetic predisposition may be involved.13,14

It has been reported that in cows with ovarian cysts, the positive feedback of estradiol on release of gonadotropin-releasing hormone (GnRH) is compromised.15-19 Therefore, although the pituitary gland is compromised,15-19 therefore, although the pituitary gland is able to release luteinizing hormone (LH) in cows with ovarian cysts,20,21 function of the hypothalamic-pituitary-ovarian axis is altered.1 After a preovulatory follicle fails to ovulate, a transient increase in follicle-stimulating hormone (FSH) concentration stimulates a new wave of follicular development, which occurs under conditions of low progesterone concentration and high LH concentration, and this causes excessive growth of dominant follicles. These follicles produce large amounts of estradiol and inhibin, which are responsible for a delay in follicular turnover.22,23

Several reports24-26 have described the etiology, dynamics, and pathogenesis of ovarian cysts in dairy cattle. The present review focuses on strategies for the diagnosis and treatment of ovarian cysts that develop in lactating dairy cows after a voluntary waiting period.

**Diagnosis**

On the basis of results of palpation per rectum, ovarian cysts have been defined as follicles > 25 mm in diameter that persist in the ovaries for at least 10 days in the absence of a corpus luteum and are classified as follicular or luteal according to the degree of luteinization and progesterone secretion.27 Although cows with ovarian cysts may have nymphomania and irregular estrous cycles,28 anestrus is a common clinical sign.29

It has been shown that ovarian cysts are not static structures since they may persist, luteinize, or become atretic.1 Similar to cows with normal estrous cycles, cows with ovarian cysts have ovarian follicular waves that may result in spontaneous ovulation or in the formation of another cyst.30 Follicular turnover in cows with ovarian cysts takes 13 to 19 days, whereas in clinically normal cows, it occurs every 8.5 days.31

Because preovulatory follicles range from 14 to 16 mm in diameter following 3 or 2 follicular waves, respectively, a follicle > 17 mm in diameter could be classified as a cyst.32 In addition, ovarian cysts have been defined as a single follicular structure > 20 mm in diameter or multiple follicles > 15 mm in diameter that persist for 7 days in the presence of low progesterone concentrations.33 Therefore, on the basis of information obtained concerning follicular waves and results of ovarian ultrasonography and assays of endocrine hormone concentrations in cows with ovarian cysts, we define this condition as the presence of multiple ovarian follicles approximately 18 to 20 mm in diameter, the absence of a corpus luteum, and a lack of uterine tone. After spontaneous or induced ovulation of a dominant follicle in a cow with ovarian cysts, a corpus luteum is formed and the cow could become pregnant, even though other cysts may remain in the ovaries.

Follicular and luteal ovarian cysts must be differentiated from cystic corpora lutea, preovulatory follicles, postpartum and nutritional anestrus, cysts of the limbus, cysts of the ovarian bursa, and granulosa cell tumors.

**Differentiating between follicular and luteal ovarian cysts**—The sensitivity and specificity of using rectal palpation to differentiate follicular from luteal ovarian cysts are low. Ultrasonography is effective in detecting luteal cysts but has a low specificity for follicular cysts.32 The accuracy of diagnosing ovarian cysts and differentiating follicular and luteal cysts can be increased by combining per rectum palpation of the genital tract to determine that a corpus luteum is absent and the uterus lacks tone;33 ultrasonography to confirm that a corpus luteum is absent, to determine the size of follicles that are present, and to check for luteinization;32,33 and measurement of plasma progesterone concentration to determine the degree of luteinization.34,35 For therapeutic purposes, differentiation of follicular and luteal cysts may not be necessary.
because most of the recommended treatment regimens include administration of a dose of GnRH followed by administration of a dose of prostaglandin F₂α (PGF₂α) and are effective for both conditions.

Differentiating between luteal cysts and cystic corpora lutea—Luteal cysts are pathologic and originate from follicles that fail to ovulate and subsequently luteinize. In contrast, cystic corpora lutea are physiologic and originate from follicles that have ovulated and formed a cavity during corpus luteum development. A luteal cyst can be differentiated from a cystic corpus luteum by palpation per rectum to determine whether the structure has the typical characteristics of a corpus luteum. These include detection of a line of demarcation and distortion in the shape of the ovary. These palpable characteristics are observed with a corpus luteum but not with a luteal cyst.

Sensitivity and specificity of using palpation per rectum to detect luteinization of follicles are low; therefore, ovarian ultrasonography is also often used to detect luteal cysts. However, during ultrasonography, a corpus luteum can still be observed 2 days after regression, when it is already nonfunctional. Therefore, results of palpation per rectum and ultrasonography of the ovaries should be combined to differentiate luteal cysts from cystic corpora lutea.

Differentiating between ovarian cysts and normal preovulatory follicles—Ovarian cysts and normal preovulatory follicles are differentiated on the basis of number and size but mainly on the basis of uterine tonicity. During palpation per rectum, ovarian cysts are identified as multiple follicles that are typically larger-than-normal Graafian follicles with a flaccid uterus in the absence of a corpus luteum. In contrast, cows in proestrus have an erect, turgid uterus. In cows without ovarian cysts that are in proestrus or estrus, luteal oxytocin secreted at the time of luteolysis contributes to the tone of the uterus, with maximal binding to oxytocin receptors in the myometrium at the time of estrus. In contrast, cows with ovarian cysts that are in proestrus or estrus, luteal oxytocin secreted at the time of luteolysis contributes to the tone of the uterus, with maximal binding to oxytocin receptors in the myometrium at the time of estrus. In contrast, cows with ovarian cysts are typically examined after they fail to ovulate, at which time the uterus is flaccid. The number and size of ovarian follicles can be determined by means of ultrasonography. Even though uterine hyperechogenicity is common during proestrus, uterine tonicity should be determined by means of palpation per rectum. Therefore, differentiating ovarian cysts from normal preovulatory follicles involves both palpation of the uterus per rectum and ultrasonography of the ovaries.

Differentiating between ovarian cysts and postpartum nutritional anestrus—The terms noncyclic, anovular, and anestrus have been used to describe anovulatory conditions in postpartum, lactating dairy cows. However, several physiologic (eg, pregnancy), pathophysiologic (eg, postpartum and nutritional anestrus and ovarian cysts), and pathologic (eg, pyometra, hydrometra, ovarian hypoplasia, and granulosa cell tumor) conditions result in a lack of cyclic activity, anovulation, or anestrus. Therefore, we use the term deep postpartum nutritional anestrus to describe a condition that occurs mainly during the early postpartum period under conditions of extreme negative energy balance, lack of gonadotropin support, and nearly complete suppression of follicular development. Similarly, we use the term shallow postpartum nutritional anestrus to describe an anovulatory condition that occurs during the early postpartum period and is characterized by recurring follicular waves yet insufficient basal secretion of LH and insulin-like growth factor I (IGF-I) to support full follicular development and insufficient estradiol secretion to trigger ovulation. In the contrast, the term cystic ovarian degeneration is used to describe a condition that occurs at any time during lactation, usually under conditions of positive energy balance in which follicular development is pronounced but positive feedback of estradiol on GnRH release is altered. During postpartum resumption of ovarian cyclicity, cows may experience deep or shallow anestrus and then resume cyclicity or develop ovarian cysts (Figure 1). Depending on nutritional status and energy balance, cows may alternate between periods of normal cyclicity and shallow or deep anestrus. In addition, cows with normal cyclicity may develop ovarian cysts in response to various conditions that cause stress or low plasma progesterone concentrations because stress blocks the estradiol-induced preovulatory surge in LH concentration. Cows with ovarian cysts can return to normal cyclicity following treatment or spontaneous ovulation.

Differentiating ovarian cysts from deep postpartum nutritional anestrus is not difficult because cows in deep anestrus have low FSH secretion and small ovaries with minimal follicular development. Ovarian cysts are differentiated from shallow anestrus on the basis of the number and size of the follicles, occurrence of follicular waves, body condition score (BCS), and stage of lactation. Shallow postpartum nutritional anestrus is associated

---

**Figure 1**—Dynamics of postpartum nutritional anestrus and ovarian cysts in lactating dairy cows. P₄ = Progesterone.
with a condition of negative energy balance and is characterized by a low BCS (< 3 on a scale from 1 to 5); low concentrations of IGF-I, LH, and estradiol; and, typically, a single nonestrogenic follicle (≤ 18 mm in diameter) and a few small follicles (≤ 8 mm in diameter) in the ovaries. Shallow anestrus is more common in the early postpartum period, when incidence is approximately 20%,48 and less common late in lactation, when incidence is approximately 3%.49 In contrast, ovarian cysts can occur during any stage of lactation, are not necessarily associated with conditions of negative energy balance, and typically occur in cows with a BCS > 3. Cows with ovarian cysts have more pronounced follicular development because of normal FSH concentrations, higher basal concentrations of LH, and follicular waves with a longer turnover period than in cows without ovarian cysts.22,51

In summary, the diagnosis of ovarian cysts can be made on the basis of detection of multiple follicles approximately 18 to 20 mm in diameter, the absence of a corpus luteum, and a lack of uterine tone. These characteristics can be identified by combining results of palpation per rectum and ultrasonography.51,54,55 In addition, cows with ovarian cysts will usually have a BCS ≥ 3. Confirmation of the diagnosis 7 to 10 days later may not be necessary because the lack of palpable uterine tone indicates that luteolysis had occurred at least 7 days ago, the uterus is no longer under the effect of oxytocin, and the follicles have been growing in the absence of progesterone. Moreover, because ovarian cysts and ovarian follicles are dynamic structures, a delay of 7 to 10 days may yield a different stage of ovarian follicular development. During ultrasonography, cows in the follicular phase of the estrous cycle (proestrus and estrus) have high uterine tone with 1 or more large ovarian follicles. However, cows with ovarian cysts or in shallow nutritional postpartum anestrus have a flaccid uterus. Cows with ovarian cysts have pronounced follicular growth and an acceptable BCS. In contrast, cows in shallow anestrus have poor follicular development and low BCSs (Figure 2).

Treatment

Spontaneous recovery (ie, ovulation of a dominant follicle) has been reported in cows with experimentally induced and naturally occurring ovarian cysts,22,23,55 with the rate of spontaneous recovery seemingly higher during the early postpartum period than during the late lactation period.23 Even with spontaneous recovery, development of ovarian cysts, without treatment at the time of diagnosis, can extend the interval from calving to conception by 64 days and cause economic losses of $55 to $160/lactation.7

Treatment of ovarian cysts originally consisted of administration of exogenous compounds with LH activity.24 Similarly, administration of compounds that induce LH release may stimulate luteinization of the cysts and ovulation of mature follicles, resolving the cystic condition.7 Manual rupture of the cysts is not recommended because there is a risk of hemorrhage and formation of adhesions to the mesovarium, which can compromise fertility.55 Administration of human chorionic gonadotropin (3,000 units) and GnRH analogues and agonists (gonadorelin diacetate [100 µg] or buserelin acetate [10 µg]) has been used for the treatment of ovarian cysts.44,45 but GnRH is preferred because it is a small, stable molecule and does not generate any adverse effects or immune response.58 A dose of GnRH induces LH release within 30 minutes, with concentration of LH peaking after 2 hours,56 and this causes luteinization of the cysts or ovulation of a mature follicle.25,54.25 The increase in progesterone concentration results in negative feedback on the hypothalamic-pituitary axis, inhibiting LH pulsatility and contributing to follicular atresia. Moreover, the GnRH-induced increase in FSH concentration causes recruitment of a follicular wave that may restore normal cyclicity.1 In 1 study,54 for instance, cyclicity resumed within 20 days in 72% of cows with ovarian cysts treated with GnRH, compared with 16% of control cows. Administration of PGF2α, 9 days after GnRH treatment induced expression of estrus in 2 to 3 days.55 In cows without ovarian cysts, an interval of 7 days between doses of GnRH and PGF2α synchronizes follicular wave development and induces estrus within 2 to 3 days.55 In cows with ovarian cysts, plasma progesterone concentration is high 5 days after GnRH treatment.55 Therefore, an interval of 7 days can be used in cows with ovarian cysts to obtain high fertility after insemination at estrus.57 However, this approach requires a high estrus detection rate.57 Alternatively, timed insemination may be used to increase pregnancy rate in cows with ovarian cysts.58

Administration of exogenous progesterone has also been successfully used in the treatment of cows

Figure 2—Ultrasonograms of the ovaries and uterus of 4 cows. A—Ultrasonograms obtained during proestrus or estrus. A single dominant follicle can be seen in the left ovary (thin arrow); the uterine horn has high echogenicity (thick arrow). B—Ultrasonograms obtained during presumed shallow nutritional anestrus. Notice the poor echogenicity of the uterine horn (thick arrow); 2 follicles (14 and 8 mm in diameter) can be seen in the ovary (thin arrow). C—Ultrasonograms obtained during proestrus or estrus. High echogenicity of the uterine horns can be seen. D—Ultrasonograms of a cow with ovarian cysts. Notice that several cysts can be seen in both ovaries (arrows).
with follicular cysts. Similarly, various progesterone-releasing intravaginal devices, such as the progestosterone-releasing intravaginal device (PRID), and the controlled internal drug-releasing insert (CIDR), have been used. The CIDR is approved for use in lactating dairy cows in the United States, but the PRID and norgestomet are not approved for use or available in the United States.

A method for synchronizing ovulation (ovsynch) in dairy cows has also been advocated for treatment of cows with ovarian cysts. With this method, a dose of GnRH is given, followed by a dose of PGF$_{2\alpha}$ 7 days later. A second dose of GnRH is given 2 days after the dose of PGF$_{2\alpha}$, and the cow is artificially inseminated at a predetermined time (typically, 16 to 20 hours later), regardless of whether signs of estrus are seen.

In a study of whether this ovulation synchronization protocol could be used to treat cows with ovarian cysts, the pregnancy rate for cows with ovarian cysts treated with this protocol (18/76 [24%]) was not significantly different from the pregnancy rate for cows with ovarian cysts that received a single dose of GnRH and then a dose of PGF$_{2\alpha}$ 7 days later and were artificially inseminated when signs of estrus were seen. Separate studies in Florida and Wisconsin also found acceptable pregnancy rates following use of the ovulation synchronization protocol to treat cows with ovarian cysts.

A follow-up study of dairy cows with ovarian cysts that were routinely given bovine somatotropin (bST) every 14 days evaluated whether administration of a dose of bST, GnRH, or both at the time ovarian cysts were identified, followed by the ovulation synchronization protocol 7 days later, would affect pregnancy rates. In that study, there was no effect of pretreatment with GnRH, but pretreatment with bST reduced the pregnancy rate, possibly because the additional dose of bST increased the number of cows with ovarian cysts. The CIDR increased pregnancy rate in cows with ovarian cysts, but not in cows in proestrus. Approximately 25% of the cows with ovarian cysts had a BCS < 3, and cows with a BCS < 3 had a lower pregnancy rate than did cows with a BCS ≥ 3, despite use of the CIDR. Thus, it was assumed that cows with a BCS < 3 were in shallow nutritional anestrus. This is in agreement with findings of a previous study in which cows in early lactation with low BCSS were more likely to be anovulatory, to have smaller follicles, and to have a lower pregnancy rate following use of the ovulation synchronization protocol, compared with cows that were cycling. Moreover, previous studies in which plasma progesterone concentration was used to determine cyclicity during the early postpartum period (ie, day 50) reported low pregnancy rates in cows with low BCSS subjects to the ovulation synchronization protocol.

Taken together, results of these studies suggest that the ovulation synchronization protocol is more effective than the estrus synchronization protocol for treating cows with ovarian cysts, that administration of bST to cows with ovarian cysts that are routinely (ie, every 14 days) treated with bST reduced the pregnancy rate associated with the ovulation synchronization protocol, that pretreatment with GnRH 8 days prior to use of the ovulation synchronization protocol increased pregnancy rate in cows with ovarian cysts, that cows with ovarian cysts were detected 30 days after insemination were treated with the ovulation synchronization protocol with or without pretreatment with GnRH 8 days earlier. Pregnancy rate was higher for cows that received the GnRH pretreatment than for cows that did not. Pretreatment with GnRH may have induced formation of a corpus luteum or a follicular wave that permitted induction of a corpus luteum when the first dose of GnRH was given with the ovulation synchronization protocol.

Finally, in a study in which cows with ovarian cysts and cows in proestrus were treated with GnRH, a CIDR, or both, followed by administration of PGF$_{2\alpha}$ 7 days later, administration of GnRH 2 days after that, and artificial insemination 16 hours after administration of GnRH, pretreatment with GnRH significantly increased the number of cows with ovarian cysts that had a corpus luteum 7 days later but did not have any effect on the number of cows in proestrus. Use of the CIDR increased pregnancy rate in cows with ovarian cysts but not in cows in proestrus. Approximately 25% of the cows with ovarian cysts had a BCS < 3, and cows with a BCS < 3 had a lower pregnancy rate than did cows with a BCS ≥ 3, despite use of the CIDR. Thus, it was assumed that cows with a BCS < 3 were in shallow nutritional anestrus. This is in agreement with findings of a previous study in which cows in early lactation with low BCSS were more likely to be anovulatory, to have smaller follicles, and to have a lower pregnancy rate following use of the ovulation synchronization protocol, compared with cows that were cycling. Moreover, previous studies in which plasma progesterone concentration was used to determine cyclicity during the early postpartum period (ie, day 50) reported low pregnancy rates in cows with low BCSS subjects to the ovulation synchronization protocol.

Taken together, results of these studies suggest that the ovulation synchronization protocol is more effective than the estrus synchronization protocol for treating cows with ovarian cysts, that administration of bST to cows with ovarian cysts that are routinely (ie, every 14 days) treated with bST reduced the pregnancy rate associated with the ovulation synchronization protocol, that pretreatment with GnRH 8 days prior to use of the ovulation synchronization protocol increased pregnancy rate in cows with ovarian cysts, that cows with ovarian cysts were detected 30 days after insemination were treated with the ovulation synchronization protocol with or without pretreatment with GnRH 8 days earlier. Pregnancy rate was higher for cows that received the GnRH pretreatment than for cows that did not. Pretreatment with GnRH may have induced formation of a corpus luteum or a follicular wave that permitted induction of a corpus luteum when the first dose of GnRH was given with the ovulation synchronization protocol.

Finally, in a study in which cows with ovarian cysts and cows in proestrus were treated with GnRH, a CIDR, or both, followed by administration of PGF$_{2\alpha}$ 7 days later, administration of GnRH 2 days after that, and artificial insemination 16 hours after administration of GnRH, pretreatment with GnRH significantly increased the number of cows with ovarian cysts that had a corpus luteum 7 days later but did not have any effect on the number of cows in proestrus. Use of the CIDR increased pregnancy rate in cows with ovarian cysts but not in cows in proestrus. Approximately 25% of the cows with ovarian cysts had a BCS < 3, and cows with a BCS < 3 had a lower pregnancy rate than did cows with a BCS ≥ 3, despite use of the CIDR. Thus, it was assumed that cows with a BCS < 3 were in shallow nutritional anestrus. This is in agreement with findings of a previous study in which cows in early lactation with low BCSS were more likely to be anovulatory, to have smaller follicles, and to have a lower pregnancy rate following use of the ovulation synchronization protocol, compared with cows that were cycling. Moreover, previous studies in which plasma progesterone concentration was used to determine cyclicity during the early postpartum period (ie, day 50) reported low pregnancy rates in cows with low BCSS subjects to the ovulation synchronization protocol.
cysts treated with GnRH at the time of diagnosis are more likely to have a corpus luteum 7 days later, that insertion of a CIDR on the day of diagnosis and removal 7 days later increased pregnancy rate in cows with ovarian cysts treated with the ovulation synchronization protocol, and that cows with ovarian cysts that had low (<3) BCSs had low pregnancy rates when treated with the ovulation synchronization protocol, compared with cows with higher (≥3) BCSs.

Conclusions

Previous research has shown that 2 approaches could be considered in the diagnosis of cystic ovarian degeneration. First, the diagnosis could be made on the basis of detection of multiple follicles approximately 18 to 20 mm in diameter, the absence of corpora lutea, and a lack of uterine tone, as determined during a single clinical examination by means of per rectum palpation and ultrasonography of the genital tract. This approach could be used in clinical trials evaluating pharmacologic treatments or in clinical practice. Second, a more specific diagnosis could be made by means of detection of multiple ovarian follicles ≥18 to 20 mm in diameter and ovarian follicular waves during a period of 7 to 10 days in the absence of ovulation, corpora lutea, and uterine tone. Determining the presence of ovarian follicular waves during a 7- to 10-day period with follicles that reach ovulatory size (12 mm) could be used to retrospectively differentiate ovarian cysts from shallow nutritional anestrus in cows with low BCSs.

Strategies for treatment of ovarian cysts (Figure 3) should include induction of ovarian follicular turnover and an increase in progesterone concentration, which can be achieved by use of an ovulation synchronization protocol. However, cows should be evaluated at the time of PGF2α injection to determine the presence of a corpus luteum. If a corpus luteum is present, cows can be treated with PGF2α and inseminated when estrus is detected, if the estrus detection rate is high, or be treated with a second dose of GnRH to synchronize ovulation for timed insemination. However, if a corpus luteum is not present, cows should be retreated with GnRH. Use of a CIDR may eliminate the need for evaluation of the presence of a corpus luteum at the time of PGF2α treatment.

References

32. Parin FW, Youngquist RS, Parfet JR, et al. Diagnosis of luteal...