Managing Anovulation and Cystic Ovaries in Dairy Cows

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Take Home Messages

- Reproductive efficiency is a critical factor in any dairy herd.
- Up to 50% of cows may be anovulatory at 60 days postpartum
- Cystic ovarian disease is a significant infertility problem on many dairy farms
- Hormonal programs, such as Ovsynch and progesterone supplementation, will assist in improving reproductive efficiency by reducing the incidence of anovulation, anestrus and cystic ovarian disease

Introduction

The terms anestrus and anovulation are often used interchangeably but are actually very different conditions. Anestrus is failure of cows to exhibit overt estrus but is more commonly a problem with estrus detection. Some cows exhibit overt estrus for a very short time, have few mounts or show signs of estrus in the middle of the night making estrus detection in these animals difficult. The estrus detection rate on many farms is less than 50%, being a very limiting factor to reproductive efficiency. Many factors, such as footing, management and milk production level, will affect demonstration of estrus. While these cows are not observed in estrus, they have normal estrous cycles and will respond well to ovulation synchronization programs (Wiltbank et al., 2002).

Anovulation

Anovulation is failure of cows to ovulate. These animals have abnormal follicular development and abnormal estrous cycles. Ovulation failure may be classified into three categories.

Anovulation with Follicle Growth to Emergence

This condition is very rare. It may result as a genetic problem with chromosomal abnormalities or in severely malnourished animals. Complete ovarian hypoplasia (underdevelopment or incomplete development) may result from a single recessive autosomal gene with incomplete penetration. These animals have few primordial follicles (Roberts, 1986). Ovarian hypoplasia is also associated with freemartinism. The failure of follicular growth beyond emergence may be due to a deficiency of follicle stimulating hormone (FSH).

Anovulation with Follicle Growth to Deviation

Anovulation with follicular growth to deviation but not ovulatory size is a common occurrence, especially in prepubertal animals and in the postpartum period. The characteristic signs of this condition are small ovaries caused by the absence of a corpus luteum (CL) or ovulatory size follicles. However, daily ultrasound evaluation of the small ovaries of these anovulatory cows has demonstrated the presence of follicular waves. Heifers as young as two weeks have follicular waves. Follicular waves occur throughout pregnancy, and the first postpartum wave begins approximately four days postpartum. Although in dairy cows the first postpartum dominant follicle may ovulate, more commonly the first ovulation occurs approximately 33 days postpartum. Malnutrition, suckling or peripartum disease can prolong the time to first ovulation.

In prepubertal animals the hypothalamus is extremely sensitive to the negative feedback effect of estradiol, resulting in inhibition of luteinizing hormone (LH) pulses. As puberty approaches, the number of hypothalamic estradiol receptors decreases, reducing the negative feedback effect of estradiol. The subsequent LH increase supports the growth of the follicle to ovulatory size resulting in sufficient estradiol to induce an LH surge and ovulation.

The postpartum dairy cow is in negative energy balance until approximately eight weeks. The time to first ovulation is variable but is related to the timing of the nadir in negative energy balance for the individual cow. A return to positive energy balance allows an increased maximal size of the dominant follicle, increased follicular estradiol and an increase in pulsatile LH secretion resulting in ovulation. The state of negative energy balance may be similar to that of the prepubertal animal in which low estradiol level is inhibitory to hypothalamic GnRH secretion.

The serious negative energy balance that accompanies catabolic metabolism affects the time of the first postpartum ovulation. Insulin-like Growth Factor-1 (IGF-1) from the liver regulates maturation of the dominant follicle during the first postpartum follicular wave. Plasma IGF-1 levels during the first follicular wave are higher in ovulatory cows than anovulatory cows. The negative energy state of postpartum cows results in an elevation of growth hormone (GH) secretion and an decrease in IGF-1 and insulin.

Plasma glucose and IGF-1 concentrations are lower, and plasma NEFA, ketone bodies and milk yield are higher in anovulatory cows compared to ovulatory cows (Kawashima et al., 2007).

Beef cows exhibit similar nutritional related effects on ovulation as dairy cows. Additionally, beef cattle are affected by suckling. Suckling increases the sensitivity of the hypothalamic GnRH pulse generator to estradiol negative feedback. The negative feedback effect decreases as the postpartum interval increases. There is also a role of the maternal-offspring bond and suckling frequency.

Resolution of the problem in prepubertal heifers and cows is based on good nutrition. In beef cows limited suckling to once or twice daily, or calf removal for 24-48 hours, may improve the percentage of cows cycling. Milk production level, body condition score, follicular growth and ovulation are interrelated. Cows with high milk production may have shorter overt estrus periods. Poor body condition score (BCS) is correlated with smaller follicles and an increased incidence of anovulation. Good body condition is associated with anovulation resulting in ovarian cysts (Wiltbank et al., 2004).

A small percentage of cows may exhibit ovulation failure following estrus. These animals may have irregular inter-estrus intervals and normal follicular wave pattern. The underlying etiology may be failure of hypothalamic response to estradiol, or small follicles producing insufficient estradiol. GnRH at the time of insemination has been reported to improve the conception rate of repeat breeder animals and will possibly be a good treatment for these animals. These animals will likely respond to the Ovsynch or Ovsynch plus CIDR programs (Rhodes et al., 2003).

Walsh (2006) recently investigated the incidence of postpartum anestrus prior to 60 days in milk (DIM) in 18 Ontario dairy herds. In this study, the prevalence of anestrus was 19.5% with a variation between herds of 5% to 44%. The impact of anestrus diminished after 160 DIM with the pregnancy rate becoming equal to normal herdmates. Subclinical ketosis during the second week postpartum had a major detrimental effect on fertility. Other factors associated with anestrus were obstetrical conditions such as dystocia and twins, periparturient conditions such as retained placenta, displaced abomasum and lameness, and BCS less than 2.75. In this trial, the use of an intravaginal progesterone device (PRID) after 60 DIM reduced time to first insemination by 17 days in primiparous animals and 8 days in multiparous animals, but did not alter first service conception rate.

Treatment

Anovulatory cows may respond to the Ovsynch program but Ovsynch plus CIDR will yield a better response (Gumen et al., 2003; Rhodes et al., 2003; Wiltbank et al., 2004). Many anovulatory cows have ovulatory size follicles but lack an LH surge. The conception rate of anovulatory cows treated with the Ovsynch program averages 25-35%, with a range of 10% to 40%. The Ovsynch plus CIDR program usually results in a better conception rate.

Anovulation with Follicle Growth to Ovulatory or Larger Size

Cystic Ovarian Disease (COD) is a common and economically significant condition of dairy cattle (Johnson and Coates, 2004). It was first described in the early 1900's and is recognized as an important cause of reproductive loss in cattle. Each incidence of cyst formation increases the calving interval by 22-64 days.

Definition

The condition is expressed as two syndromes. Follicular cysts are anovulatory follicles that persist for a minimum of 10 days, have a diameter greater than 2.5 cm and are characterized by either continuous estrus or anestrus. Luteal cysts are anovulatory follicles over 2.5 cm in diameter that are partially luteinized and persist for a prolonged period, and are usually characterized by anestrus. Both follicular and luteal cysts occur in the absence of a CL. However, approximately 40% of cows diagnosed with cysts may also have a CL. This definition has limitations as a cyst is seldom monitored for 10 days prior to diagnosis and the presence of a CL is difficult to determine without the use of ultrasonography. Recent ultrasound data indicates that follicles normally ovulate at approximately 17 mm diameter, suggesting that follicles that persist and have a diameter greater than 17 mm be considered cysts. Follicles destined to become cysts grow at the same rate as those destined to regress or ovulate until approximately 16 mm, following which the cysts continue to increase in size.

The lactational incidence rate of COD is commonly 5 to 15% with individual herds in the 30 to 40% range. There is a bimodal distribution with one peak occurring between 30 and 40 DIM and another between 190 and 220 DIM. The occurrence is higher in high producing cows, usually in the second to fifth lactation and in winter months. The incidence of COD is highest in the early postpartum period but 60% of cows that develop COD before the first ovulation undergo spontaneous recovery. This factor has been overlooked in many COD therapeutic studies where the inclusion of a control group in the experimental design was neglected, resulting in an apparent positive treatment efficacy.

A third ovarian cyst, commonly included in cyst classifications, is cystic CL. Follicular and luteal cysts are pathological structures resulting from ovulation failure, whereas cystic CLs are normal structures, being a normal CL with a central fluid filled cavity of variable size. Inclusion of cystic CLs in the discussion on cysts serves only to confuse the topic as they have no detrimental effects on fertility. However, cystic CLs may have a very similar appearance to luteal cysts, making differentiation difficult.

Diagnosis

A diagnosis of COD is based on behavioural signs, per-rectal palpation and transrectal ultrasonography of the ovaries and uterus, and hormonal determination. Behavioural signs of cows with ovarian cysts will vary from frequent, irregular, prolonged or continuous estrus to anestrus, usually reflective of the hormonal influence. In addition to having palpable cysts on the ovaries, the uterus may be thickened and flaccid with excessive mucous production. Differentiation of follicular and luteal cysts is difficult by per-rectal palpation but transrectal ultrasonography will aid in determination of the cyst type. Progesterone analysis has commonly been used to differentiate follicular and luteal cysts. However, the presence of a CL in addition to the ovarian cyst confounds this analysis. It is also possible to confuse luteal cysts and cystic CLs with a large central cavity. Considerable variation exists among the steroidogenic capacity of cysts. Generally, cows with follicular cysts have greater estradiol concentrations in follicular fluid and serum than normal cows. Cows with chronic COD may develop a raised tailhead.

Etiology

The etiology of COD is multifactorial and controversial (Gumen and Wiltbank, 2002; Hampton et al., 2003; Kaneko et al., 2002; Lopez-Diaz and Bosu, 1992; Peter, 2004; Woolums and Peter, 1994). The basic pathophysiology of COD involves a neuroendocrine dysfunction of the hypothalamic-pituitary-ovarian axis resulting in ovulation failure. Research evidence incriminates each part of the hypothalamic-pituitary-ovarian axis as the causative organ. The hypothalamus may be unresponsive to the positive feedback of estrogen from the dominant follicle resulting in a deficiency of GnRH and a subsequent inadequate or inappropriate timing of the LH surge, resulting in ovulation failure. Anovulation may result from a pituitary deficiency where GnRH fails to induce an adequate LH surge to induce ovulation or luteinization. The pituitary is often normal as exogenous GnRH is able to induce a LH release, however, the release pattern may be different in COD cows from normal cows.

It is possible that the abnormality in COD originates with intraovarian factors. Ovulation failure possibly results from a deficiency of LH receptors in the follicle, not a lack of LH. Extracellular matrix proteins, including vitronectin and fibronectin, appear to be influenced by follicular size, and inappropriate production may interfere with ovulation (Peter et al., 1995). Excessive growth and failure of follicular cyst regression may be attributable to unbalanced control of cell proliferation and cell death. Apoptosis of theca cells decreases in cysts compared to atretic follicles, possibly influencing the delay of follicular cyst regression.

Cows with follicular cysts continue to have follicular growth and turnover (Archbald and Thatcher, 1992; Cook et al., 1990; Hamilton et al., 1995) Follicular wave emergence and FSH secretion are variable with differing cystic conditions. In cystic cows, follicular wave emergence was more variable than in normal cows. Cystic cows that exhibit cyst turnover or spontaneous disappearance have a FSH wave prior to the emergence of the follicular wave, as in normal wave emergence. Cows exhibiting persistence of the cyst lack a FSH wave. The active cyst may produce a substance, possibly inhibin, which inhibits the subsequent wave emergence. Loss of dominance of the cyst may be associated with atresia of the granulosa layer, resulting in loss of function and secretory capacity of the cyst, allowing recruitment of a new wave of follicular growth. A persistent dominant follicle sustains inhibin production longer than a normal dominant follicle and establishes long-term dominance by suppressing emergence of a new follicular wave (Kaneko et al., 2002).

Endocrine profiles of COD cows have shown that serum LH is high or normal, LH pulse frequency and amplitude are higher than normal, serum FSH is low or normal, and serum inhibin is high (Archbald and Thatcher, 1992; Hamilton et al.., 1995). The high baseline LH levels support persistence and growth of the follicle to an abnormally large size (Calder et al., 2001).

Many factors, such as high milk production, uterine infections, endocrine and metabolic conditions, genetics, and nutritional status, have been implicated in the formation of cysts. High milk production and COD have a positive correlation but the cause and effect have not been determined. Possibly high producing cows have a higher incidence of COD, but delayed conception will increase milk production.

Many clinical conditions in the early postpartum period such as retained fetal membranes, hypocalcemia, endometritis and metritis are negatively associated with fertility. Postpartum uterine infections result in abnormal patterns of ovarian activity (Mateus et al., 2002). High uterine bacterial contamination is associated with fewer first and second dominant follicles on the ovary ipsilateral to the previously gravid horn (Sheldon et al., 2002). Postpartum uterine infections may stimulate PGF2α and cortisol secretion that affect the preovulatory LH surge (Peter et al., 1987). While uterine infections have been positively associated with COD, it has not been established if COD prevents the uterus from clearing infections or if uterine disease inhibits normal ovarian function. Cows with persistent uterine infections may have a shortened luteal phase following the first ovulation attributable to increased uterine prostaglandin production causing premature demise of the CL. The resulting intermediate progesterone levels allow development of persistent, large follicles (Hatler et al., 2003). Also, E. coli endotoxin from the uterus may reduce estrogen production from the preovulatory follicle and subsequent pituitary LH production (Peter et al., 1990).

An association between nutritional status and endocrine function has been suggested. Lactating dairy cows have a close correlation between milk production and dry matter intake. The increased feed intake required to meet high production demands results in an increase in blood flow through the liver and an increased rate at which estradiol is removed from the blood. This may result in a more rapid drop and a lower peak of estradiol during estrus, and lower concentrations of circulating estradiol in high producing cows. Low estradiol levels may result in poor positive feedback to the pituitary and hypothalamus, low LH surge levels and ovulation failure.

Many nutritional factors, including low energy balance, estrogen contaminated feeds, selenium and beta-carotene are suspected to influence ovarian function. The nutritional influence on reproduction may be partially mediated by leptin (Maciel et al., 2004; Williams et al., 2002). GnRH and LH pulses are suppressed by acute and chronic malnutrition. Ruminants are less sensitive than monogastrics to short term malnutrition but similar effects are observed in chronic conditions. Prepubertal heifers are more sensitive to malnutrition than mature animals. The effect appears to be mediated at the adenohypophysis, affecting the frequency of GnRH release. Exogenous leptin can prevent fasting-mediated reduction of the frequency of LH pulses and modify GnRH-mediated release of LH in prepubertal heifers. The influence of leptin on the hypothalamus may be mediated by estrogen as feed restriction appears to extend the period of inhibition of estradiol negative feedback on LH secretion in prepubertal heifers. It is also possible that insulin and IGF-1 may mediate the nutritional effect of undernutrition as insulin and IGF-1 decline during feed restriction. Low leptin levels may counteract the effect of feed restriction on insulin and IGF-1 production.

The heritability of COD is low, but a genetic component has been attributed to the etiology of COD as it appears to occur more frequently in certain cow families. The Scandinavian countries have reduced the incidence of COD by genetic selection.

Stress may be another contributing factor (Lopez-Diaz and Bosu, 1992).

Adrenocorticotropic hormone (ACTH) administered during the follicular phase of the cycle results in ovulation failure and cyst formation. Cortisol may impair follicular estrogen production, resulting in absence of the preovulatory LH surge and anovulation. Various stressors may act through endogenous opioid peptide action to block the estrogen induced LH surge.

Treatment

Treatments for COD are numerous and variable, and have changed considerably over the years (Peter, 2004; Roberts, 1986; Woolums and Peter, 1994). Administration of exogenous hormones is the common and accepted method for treatment of COD. The hormone most commonly used for treatment is GnRH, with human chorionic gondatotropin (hCG) also being frequently used. Purified LH is also available. These hormones are equally effective, however, because GnRH is a small synthetic peptide, it potentially causes fewer side effects. The historical rationale for using these therapeutic agents is to induce luteinization of the cyst through the action of LH. Lysis of the luteal tissue will subsequently occur by natural mechanisms, usually within 20 days, or following administration of exogenous PGF2α. There is very little evidence to support the contention that follicular cysts will luteinize following GnRH treatment.

The effect of GnRH on the ovaries of COD cows is not clear. In most studies there is a not a consistent relationship between GnRH treatment, a progesterone increase or return to estrus, questioning the relationship of the events. The use of GnRH as a treatment has been questioned. A recent study (Johnson et al., 1997; Jou et al., 1999) demonstrated no difference in the time to cyst disappearance or CL appearance between a GnRH treated group and a saline treated group. Cystic cows commonly have high LH levels, so treatments that further increase LH are of questionable therapeutic value. The high spontaneous recovery rate confounds many of the early therapeutic studies as the use of untreated control animals was omitted from the experimental protocols.

The accepted treatment for luteal cysts is PGF2α to induce luteolysis, regression of the cyst and return to normal cyclicity. A combination of GnRH followed by PGF2α in 7 to 14 days is a popular treatment regime. This regime will treat both follicular and luteal cysts without differentiation, will shorten the time from treatment to estrus and will induce estrus at a predictable time, allowing accurate detection of estrus and insemination. Many of these cows should also be treated with GnRH during estrus to induce ovulation of the fresh, dominant, ovulatory follicle, thereby preventing a return to the cystic condition. Interestingly, while this protocol has been recommended for many years, it is basically the modern Ovsynch program.

Administration of exogenous progesterone has been used as a treatment regime for cysts (Calder et al., 1999). Progestogens as single or multiple injections, in the form of intravaginal devices (CIDR or PRID) or as ear implants have been used to treat COD. The rationale for their use is to mimic the effect of a CL, allowing a normal ovulation following removal. Progesterone has a dramatic effect on follicular development and ovulation. Intermediate levels of progesterone will inhibit follicular turnover, block the LH surge and prevent ovulation, resulting in persistency of large dominant follicles. Continued follicle growth and absence of ovulation will result from high baseline LH secretion. Progesterone may be present in the fluid of follicular cysts at varying levels. Progesterone concentration in peripheral circulation of cows with cysts is usually in the intermediate range. High levels of exogenous progesterone may restore hypothalamic sensitivity to estradiol in cows with cysts and regulate LH pulse frequency. Progesterone appears to "reset" the hypothalamic surge centre by reinstating the sensitivity of the hypothalamus to estradiol. Progesterone treatment decreased mean LH and LH pulse frequency resulting in regression of cysts and initiation of new follicular growth. It may also have a direct, negative effect on estradiol production by granulosa cells. Cystic cows with high estrogen levels fail to generate a LH surge in response to exogenous estradiol, indicating that cows with cysts have lost the ability to respond to the positive feedback effect of estradiol. Exposure to progesterone appears to restore the ability of the hypothalamus and pituitary to generate a LH surge in response to estradiol. Progesterone induces regression of the cyst, allows normal follicular turnover and ovulation following termination of progesterone treatment. The treatment protocol requires daily injection for 10-14 days or insertion of one or two intravaginal progesterone devices for 9-14 days. Estrus will occur 3 or 4 days following device removal.

The initial treatment for cysts was manual rupture. Although rupture of the cyst remains a common practice, its use is controversial. This method cannot be recommended due to the possibility of excessive trauma and hemorrhage, possibly resulting in parovarian adhesions. Very thin-walled cysts may rupture with minor ovarian manipulation. This cannot be prevented and is likely not detrimental, however use of excessive force to rupture the cyst should be avoided.

Drainage of cysts with a needle placed through the vaginal wall or ultrasound guided transvaginal aspiration has been used to remove fluid from the cyst. However, with either drainage or rupture, the underlying endocrine disturbance is not corrected and the cyst is likely to reoccur.

The cystic condition in cattle is characterised by the dynamic nature of the condition. The fate of the follicular cyst has several possibilities. It may persist for a prolong period as a dominant structure that interferes with normal follicular growth and turnover, it may lose dominance and be replaced by a new cyst from a new follicular wave as cyst turnover, or it may lose dominance and regress, allowing new follicular wave emergence and ovulation. It is impossible to determine which event will occur without serial monitoring.

There may be a mixture of dominant cysts, young cysts and non-dominant cysts, each with different hormonal profiles. The intrafollicular concentration of estradiol and progesterone may change over time. The dominant cysts remain estrogenic for prolong periods when exposed to intermediate progesterone levels and high baseline LH. Dominant cysts have increased expression of LH receptors compared to dominant follicles and higher basal LH may be responsible for prolonged growth and increased steroidogenesis of cysts compared to follicles. Loss of dominance is associated with atresia of granulosa cells, loss of LH receptors and decreased steroidogenesis. Many of the non-dominant cysts may undergo atresia or luteinization and be replaced.

Some cysts persist for a prolonged period of time, but appear to be inactive and do not inhibit normal cyclicity. During routine examination of the ovaries, the cyst is identified because of the dominant size of the structure, however, ultrasonographic examination is necessary to identify the presence of a CL. Administration of $PGF2\alpha$ to these cows may result in luteolysis followed by estrus and ovulation, and pregnancy following insemination. The cyst may remain for a prolong time during pregnancy.

Ambrose et al (2004) published a seminal paper on cystic ovarian disease. They identified 26 cows with ovarian cysts and treated them with Ovsynch or Ovsynch plus CIDR. Ovarian dynamics were monitored by ultrasonography and hormone levels were determined. The cows were classified as Follicular Cyst (FC): cows with cysts, no CL and low progesterone; Luteal Cyst (LC): cows with cyst, luteinization, no CL and high progesterone; and Persistent Cyst (PC), cows with a cyst, a CL and high progesterone. The results are shown in table 1.

Table 1: Observations of ovarian responses and pregnancy results following treatment of ovarian cysts

Observation	Cows with FC	Cows with LC	Cows with PC	All Cows
Number of cows	15	1	10	26
Ovulation of cyst after 1st GnRH	0	0	0	0
Ovulation of an existing follicle after 1st GnRH	8/15(53%)	0/1(0%)	5/10(50%)	13/26(50%)
Cows that developed new follicle after 1st GnRH	15/15(100%)	1/1(100%)	10/10(100%)	26/26(100%)
Cows that ovulated the new follicle:				
- after 2nd GnRH	8/10(80%)		7/8(88%)	15/18(83%)
- after CIDR removal	5/5(100%)	0/1(0%)	2/2(100%)	7/8(88%)
Cows that developed new CL	13/13(100%)	0/1(0%)	9/9(100%)	22/23(96%)
Cows pregnant at 32d	5/9(56%)		2/8(25%)	7/17(41%)
Cyst detectable at 32d	6/9(67%)		5/8(63%)	11/17(65%)

In the cows treated with Ovsynch plus CIDR, estrogen levels declined rapidly and cyst size decreased following treatment. Progesterone had a negative feedback on LH, thereby removing maintenance for cyst growth.

This paper contains very valuable information. It documented the dynamic nature of the condition. The first GnRH injection resulted in initiation of a new follicular wave in 100% of the cows, regardless of type of cyst. Following the second GnRH, 83% ovulated, and 88% ovulated spontaneously following CIDR removal. Following ovulation, 96% of cows developed a new CL. The conception rate was 41% following timed insemination.

The paper emphasized the necessity of ultrasonography for classification of ovarian cysts. It is common for cows to have a CL in addition to a cyst, as did 38% of animals in this trial. Identification of the CL by per-rectal palpation may be difficult. Cows with CLs are cycling normally. This information calls into question all the previous papers that classified cysts as luteal cysts based on serum progesterone levels. It is common for the cyst to remain following ovulation of a new follicle, as occurred in 65% of cows in this trial, with apparently no negative effect on pregnancy. This is in agreement with numerous previous reports.

It is important to note that none of the existing cysts ovulated following the first GnRH, as is commonly believed. Only two cysts luteinized after first GnRH.

This trial concluded that COD cows can be successfully treated with the Ovsynch program, with or without exogenous progesterone, and that the physical presence of the cyst did not interfere with new follicular growth or pregnancy.

Bartolome et al (2000) reported on a project comparing conception rate and pregnancy rate in normal and cystic cows following Ovsynch with insemination either following estrus or by timed AI. The results are in table 2.

Table 2: Conception and pregnancy rates of cows with ovarian cysts treated with the Ovsynch program

	Normal cows (timed AI)	Cystic cows (timed AI)	Cystic cows (AI after estrus, no 2nd GnRH)
Conception rate	31.5% (n=209)	23.6% (n=76)	51.7% (n=29)
Pregnancy rate	31.5% (n=209)	23.6% (n=76)	18.0% (n=83)*

* the heat detection rate was 35%

These results support the use of Ovsynch as a treatment for ovarian cysts.

Stevenson (2006) argues that infertility due to cystic ovarian disease is overrated. He reported on 51 cows with ovarian cysts. Of these cows 19 (37%) had a CL and were likely cycling normally. The other 32 cows had no CL but 12 of these cows ovulated a normal follicle following GnRH treatment. Stevenson suggests these 12 cows are normal as they had a normal response to treatment. Of the 20 remaining cows, 14 had luteal cysts that should respond to prostaglandin. Stevenson suggested that only 6 cows (12%) in this group had a functional, pathological cyst that might interfere with fertility.

These results support the use of the Ovsynch program, possibly including a CIDR or PRID, for treatment of the COD condition in dairy cattle. The COD condition is a multifactorial, dynamic entity which possibly has been incriminated too harshly as a cause of infertility. Interestingly, while some of the old treatments were correct, the rationale for their use was completely erroneous due to poor experimental design and equipment limitations. The use of ultrasonography to monitor ovarian dynamics has provided important new information to improve understanding of COD.

Intensive health management programs will reduce the number of anovulatory cows and identify the true problem cows so further treatments can be applied to these animals (Rhodes et al., 2003). Cows may be monitored for cyclicity using ultrasonographic evaluation of the ovaries or milk progesterone tests during the Presynch-Ovsynch protocol. All cows should have a CL at the time of first GnRH treatment in the Ovsynch program. If there is no CL, the cows are considered to be anovular. The use of supplemental progesterone in an Ovsynch plus CIDR will benefit some of these anovular cows (Wiltbank et al., 2004).

Several managerial policies may improve reproductive efficiency.

- Separate first lactation heifers from older cows
- Avoid overcrowding and provide adequate bunk space
- Minimize movement between groups to avoid disrupting the social order
- Detect and treat sick cows
- Delaying time to first insemination will decrease the impact of anovulation, but will not eliminate it.

Conclusions

The pathophysiology of anovulation prior to deviation is not well investigated. Anovulatory conditions following deviation is characterised by greater negative feedback effect of estradiol on GnRH/LH pulses than in normal cows. Ovulation failure of large dominant follicles is characterised by failure of the hypothalamus to respond to the positive feedback effects of estradiol. Treatments with exogenous progesterone may reset hypothalamic responsiveness to the positive feedback effects of estradiol resulting in increased GnRH and LH production, follicular maturation and ovulation. The Presynch-Ovsynch program, possibly including a CIDR or PRID, will treat or prevent many of the anovulatory conditions of postpartum dairy cows.

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