Review Report

Anovular conditions impacting fertility in dairy cattle and considerations for clinical management

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Abstract

Reproductive performance is a primary driver of herd profitability and reproductive failure or infertility is one of the main causes of culling in USA dairy herds. Nearly ⅓ of dairy cows in USA experience anovulation in early lactation leading to increases in days open and reductions in first service conception rates. Anestrus and anovulation in dairy cows can be attributed to many causes including parity, postpartum uterine or systemic diseases, nutritional deficiencies, body condition loss, and stress. Identification and management of anovular cows, including strategies to reduce the incidence of anovulation, are critical to the overall reproductive performance of the herd. The aim of this review is to highlight causes, recent research on anovulatory conditions, and clinical approaches to management to improve dairy herd reproductive outcomes.

Keywords: Anovulation, anestrus, dairy cattle, infertility

Introduction

Optimizing profitability is a primary focus of producers and veterinarians in the USA dairy industry. One of the drivers of maintaining profitability within a dairy herd is the ability to achieve optimal reproductive performance and minimize the number of days open after calving. Many factors influence the number of days open or the calving to conception interval including, but not limited to, herd management, nutrition, metabolic disease during early lactation, uterine health, and ovarian function. Failure of cyclicity in early lactation or anovulation has been a focus of researchers and clinical veterinarians for decades.

In cattle, anovulation is broadly defined as lack of ovulation during the normal 21-day estrous cycle. The term anovulation is often used interchangeably with anestrus; however, it is important to distinguish anovulation from anestrus as it is not uncommon for cows in the postpartum period to have a silent estrus at first postpartum ovulation. Four types of anovulation have been described in cattle. Type I involves follicle growth only to emergence, Type II is characterized by follicle growth to deviation with failure to reach ovulatory size, Type III is follicle growth to ovulatory size or larger and may be referred to as persistent or cystic follicles, and Type IV is anovulation as a result of a prolonged luteal phase[1,2] In dairy production, postpartum anovulation of any type can delay cows' ability to conceive and result in economic losses due to increases in the number of days open or culling due to subfertility.

Incidence of anovulation in the USA varies by region, farm, and parity; analysis of data across 4 geographical regions identified 28.5% anovulation rate (8.1-49.6% among farms).[3] The ranges emphasized the variability of the condition across various management systems. In addition, there is also opportunity for veterinarians to influence herds' reproductive health and performance by focusing on diagnostics and interventions to reduce the economic impact of anovular conditions.

Postpartum anovulation

Uneventful calving followed by normal uterine involution and return to cyclicity are critical milestones in the postpartum period of dairy cows. Although this appears simple, in theory, the return to cyclicity depends upon an intricate series of events involving an array of molecular and cellular signaling, with the production and release of hormones throughout the hypothalamic-pituitary-ovarian axis. The modern dairy cow experiences many stressors in the postpartum transition period that can disrupt the delicate balance of this complex

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biological phenomenon. On average, the first postpartum ovulation occurs around 30 days in milk (DIM); however, this can be impacted by nutritional status, uterine health, and presence or absence of concurrent diseases.[4-7] During the postpartum period, it is common to observe a voluntary waiting period (VWP) during which, despite cows exhibiting estrous signs, producers elect to delay insemination to allow uterine involution completion to ensure uterine environment readiness for subsequent pregnancy. Length of VWP varies depending on farm management but is typically 60-80 days postpartum. As many as 20-30% of cows may be anovular at the end of the VWP, which can decrease conception rates after first artificial insemination (AI) and increase days open.[8]

Postpartum diseases have substantial impact on ovular status of dairy cows. Among anovular cows, 63.8% were diagnosed with at least 1 postpartum health problem.[7] Prevalence of retained fetal membranes, metritis, ketosis, and digestive disease (e.g. displaced abomasum) and lameness were significantly higher among anovular compared to cyclic cows. Additionally, cows experiencing 1 health event had 2-fold increase in risk of anovulation whereas cows with 2 or more health events were 3 times more likely to be anovular compared to cows that remained healthy in the postpartum period.[7]

Nutritional status also has an important role in return to cyclicity in the postpartum period. The transition from the dry period to early lactation involves a major shift in energy requirements as milk production commences whereas dry matter intake does not increase as rapidly to keep up with the demand for increased energy. Consequently, dairy cows in early lactation experience a state of negative energy balance (NEB) that can result in diversion of nutritional resources away from the reproductive tract.[2] The mechanism by which NEB delays onset of first postpartum ovulation has been attributed to low blood concentrations of glucose, insulin and insulin-like growth factor-I, and inhibition of LH pulse frequency.[4] In addition, increases in circulating non-esterified fatty acids (NEFA) and ketone bodies that are often associated with NEB in cows can have negative effects on oocytes and granulosa cells[9] and high NEFA concentrations have been associated with higher risk of anovulation around 63 DIM.[6] A study evaluating blood metabolites and activity data in cows ovulating early or late in the postpartum period, defined as before or after 33 DIM, implied that earlier ovulating cows had lower serum concentrations of free fatty acids, beta-hydroxybutyrate, and haptoglobin and spent more time eating and less time resting in the first 3 weeks after calving compared to cows that ovulated later. Additionally, early ovulating cows lost less body condition in the first 9 weeks postpartum.[5] In a study evaluating 942 Holstein primiparous and multiparous cows, those with a lower body condition score (BCS) at 35 DIM were more likely to be anovular compared to those with higher BCS.[7] The interconnectedness of nutrition, postpartum health, and reproductive performance underscores the importance of focusing on the postpartum period when working up cases of poor reproductive performance in dairy herds.

Diagnosis of postpartum anovulation is via transrectal palpation or ultrasonographic examination or measurement of serum or milk progesterone concentrations. The most practical and commonly implemented methods in commercial dairies are transrectal ultrasonography or palpation. Absence of corpus luteum at either of 2 ultrasonographic examinations performed at a 14-day interval has been used as criteria for determining an anovular state.[7] Anovular cows diagnosed with small ovaries via transrectal palpation alone may be referred to as static; however, even in the case of small ovaries, there may still be follicular activity and growth beyond emergence of the deviation stage of development, making ultrasonography a more reliable means to assess the ovarian activity of anovular cows.[1] Despite the apparent lack of ovarian activity in cows with small ovaries on transrectal palpation or ultrasonography, follicles that have reached the deviation stage may be capable of responding to exogenous gonadotropin releasing hormone (GnRH) and presynchronization protocols using timed injections of GnRH and prostaglandin have been successful in reducing the prevalence of anovular cows in early lactation.[1,10-12]

Resolution of anovular conditions can be achieved using progesterone exposure to reinitiate the hypothalamic responsiveness to estradiol to stimulate an LH surge from the anterior pituitary. In anovular cows, a minimum of 3 days of progesterone exposure improved ovulation.[13] From a practical standpoint when designing protocols to be implemented on farm, 7 days of progesterone exposure is more commonly used to reduce labor associated with additional handling of synchronized cows. Although exogenous progesterone sources are available for use in lactating dairy cows, a more widely adopted strategy to increase circulating progesterone involves a presynchronization protocol that induces ovulation with subsequent formation of a CL and increase in endogenously produced progesterone. Presynch-Ovsynch and Double Ovsynch are presynchronization protocols used in many dairy herds. Multiple studies have implied that GnRH and prostaglandin (PGF)-based presynchronization like Double Ovsynch is more effective for inducing ovulation and decreasing the number of anovular cows prior to the breeding Ovsynch portion of the protocol as compared to a PGF-based presynchronization like Presynch-Ovsynch.[14] Cows with progesterone concentrations < 1 ng/ml at the final PGF injection of Ovsynch are more likely to experience a short luteal phase and significantly lower pregnancy rate per AI (P/AI) than cows with serum progesterone > 1 ng/ml.[8] Therefore, an important component in management of anovular cows in the postpartum period should be implementation of presynchronization protocols capable of achieving higher serum progesterone concentrations at final PGF injection of the protocol.

Uterine health and anovulation

Uterine involution and clearance of uterine contamination in the postpartum period is another critical factor in return to cyclicity. Reproductive challenges of cows experiencing retained fetal membranes, puerperal metritis, and delayed involution have been well documented.[3,15-19] Effects of postpartum uterine diseases on fertility and cyclicity have been attributed to bacterial uterine contamination leading to systemic inflammation and endotoxins in follicular fluid and systemically. The inflammatory process may lead to a decrease in LH secretion, slower follicular growth and reduced size of the dominant follicle, and reduced steroidogenesis within the follicle, all of which negatively impact return to cyclicity.[3]

The intimate association of the uterine vein and ovarian artery that allow for countercurrent exchange of prostaglandin from the uterus to the ovary also has the potential to transport endotoxins and other proinflammatory cytokines from an infected postpartum uterus to the ovary. Endotoxins reach follicular fluid causing inflammation, oxidative stress, and ultimately, delayed oocyte development and ovulation.[20] Anovular cows had higher concentrations of endotoxin in follicular fluid and a greater degree of systemic inflammation as measured by serum haptoglobin compared to ovular cows in the early postpartum period.[21] However, it is important to note that a robust local inflammatory response within the uterus on the day of calving is positively correlated with return to cyclicity.[21] The reported benefits of inflammation on the day of calving are consistent with other research indicating that dysregulation of the inflammatory process in the immediate postpartum period contributed to retained fetal membranes.[22] Consequently, some degree of inflammation is beneficial to postpartum uterine health whereas increased inflammation associated with increased bacterial contamination of the uterus is detrimental to fertility.

Clinical endometritis or subclinical endometritis, identified clinically as cows with purulent vaginal discharge (PVD) or abnormal endometrial cytology after 21 days postpartum, respectively, also result in negative effects on postpartum fertility and cyclicity.[3,23] Cytological endometritis (CE) is often used as a proxy for subclinical endometritis. Cows with subclinical endometritis may go undiagnosed by farm personnel due to lack of visible clinical signs. In contrast, cows with PVD, or clinical endometritis, are easily identified and may be managed more aggressively to address uterine inflammation. Clinically, these conditions are often considered less severe compared to puerperal metritis but any postpartum condition that results in prolonged inflammation has the potential to reduce first service conception rates, increase days open and reduce fertility, thereby contributing to increased risk of culling and decrease in productive life of dairy cows.

Cows diagnosed with CE experience significantly prolonged postpartum anovulation (OR = 1.52) compared to cows that are not diagnosed with CE.[6] Combined with anovulation, effects of CE are even more substantial. Individual and combined effects of anovulation and cytological endometritis in 1,569 cows across 3 states were evaluated.[23] Cyclicity was determined via serial transrectal ultrasonographic examinations at 35 and 49 DIM. Cows without a corpus luteum at both time points were diagnosed as anovular. Cows that were anovular and were diagnosed with CE had a first service pregnancy per AI (P/AI) of 21.3% compared to healthy cyclic cows that achieved P/AI of 46.7% whereas cows that were healthy but anovular had a P/AI of 37.9%.[23] In addition, cows that were anovular, with or without CE, had more days open compared to healthy cows with or without CE. Although this study demonstrated that uterine disease combined with anovulation has an additive negative effect on reproductive performance, the reduction in P/AI for healthy, anovular cows in this study reinforced the importance of return to cyclicity and its impact on fertility.

In another study, the combined effect of anovulation and purulent vaginal discharge (PVD) in 10,995 cows in 16 herds across USA were evaluated.[3] Diagnosis of PVD was made at 28 DIM and anovulation was diagnosed via transrectal ultrasonographic examinations at 40 and 54 DIM. The mean prevalence of anovulation and PVD was 28.5 and 25.7%, respectively.[3] Cows diagnosed with both PVD and anovulation had decreased first service conception rates and increased days open compared to healthy cows or cows with either PVD or anovulation alone.

Cows that are pregnant at 130 DIM are more likely to maintain or gain body condition in the first 30 days of the next lactation, leading to a greater chance of pregnancy and reduced pregnancy losses after insemination.[24] This concept, referred to as the high fertility cycle, relies on prompt insemination of cows in early lactation with the goal of maintaining health and fertility in each subsequent lactation. Anovulation and uterine disease in the postpartum period have the potential to make this goal unattainable, leading to farm reproductive losses. Therefore, management practices should be aimed at optimizing postpartum uterine health and reducing the herd prevalence of metritis and endometritis, as the effects of these conditions combined with anovulation are detrimental to herd reproductive performance.

Large ovary syndrome and anovulation

Large ovary syndrome (LOS) is a collection of conditions that may cause anovulation in the cow and includes ovarian cysts, abscesses, hematomas, and neoplasia. Among LOS cases referred to a veterinary teaching hospital, 60% were granulosa theca cell tumors (GTCT).[25] Although rare, GTCT is the most common ovarian neoplasm reported in cattle and leads to anovulation via production of anti-Müllerian hormone (AMH), inhibin, and estradiol that arrest follicular development on the contralateral ovary through negative feedback to the hypothalamus and pituitary.[26] The predominance of GTCT cases in referral centers is most likely related to the fact that other causes of LOS, particularly ovarian cysts, are managed on farm by the clinician and not referred. In a commercial dairy, it is unlikely that GTCT cases would be treated as it is more economical to cull these animals from the herd. However, in animals of high value or genetic merit, the clinician may be requested to investigate or treat an animal with suspected GTCT. The diagnosis of GTCT can be presumptively made via transrectal ultrasonography and confirmed via hormonal assays or histopathology; AMH and inhibin may be used to confirm GTCT diagnosis versus other causes of LOS.[26,27] Unilateral ovariectomy to remove the affected ovary can lead to favorable outcomes including return to fertility in the majority of cases; however, other reproductive comorbidities such as pneumovagina or urovagina may contribute to culling.[25] Therefore, it is important to consider all factors, including economics and genetic value of the animal, prior to investing in GTCT treatment to resolve anovulation in these cases.

Cystic ovarian disease

Cystic ovarian disease (COD), another condition broadly classified within LOS, represents a significant challenge in dairy cattle management, impacting reproductive efficiency and economic sustainability within the industry. This section aims to elucidate the complexities of COD, from its etiology to its diagnosis and management strategies.

Cystic ovarian disease is defined as the presence of anovulatory follicles > 17 mm in diameter in the ovaries that interfere with cyclicity and persist for more than 6 days, with low to intermediate concentrations of progesterone indicative of the absence of a corpus luteum.[28,29] The fluid-filled structures in the ovaries are classified as follicular or luteal cysts based on steroid production. The disease etiology and progression are not entirely understood; however, environmental and hereditary factors are speculated that affect clinical outcomes. The most consistent hypothesis for occurrence of COD is a dysfunction of the neuroendocrine system, specifically in the hypothalamic-pituitary axis. Cystic ovarian disease is caused by a disturbance of the estrogen positive feedback on the hypothalamus that leads to failure of preovulatory LH surge and consequently leads to anovulation.[1] The disturbance is associated with an unresponsiveness of the hypothalamus, caused by either decreased estradiol or abnormal progesterone concentrations. Another factor that can predispose cows to develop ovarian cysts is increased milk production and associated stress, through the adrenocorticotropic hormone (ACTH) and cortisol secretion. The secretion of both ACTH and cortisol suppresses the preovulatory LH surge and increased ACTH can downregulate the expression of LH receptor mRNA in the ovarian follicle.[30] Additionally, delayed uterine involution, retained fetal membranes, and peripartum hypocalcemia can have a role in the development of cysts.[31] The heritability of this disease is speculated to be low but breeds and certain bloodlines selected for higher milk production had increased incidence of ovarian cysts.[32,33]

Prevalence of COD varies; follicular cysts occurred in 6 to 19% of lactating dairy cows[1] and was 4.6% in abattoir sourced tracts.[34] Ovarian cysts develop more commonly in dairy cattle, specifically during the early postpartum period and before the first ovulation. Presence and development of these fluid-filled structures affect fertility by increasing the calving intervals, delaying the first postpartum ovulation and estrus, and subsequently increasing the days to first AI.[35,36]

Although through the years transrectal palpation has been the most common method of diagnosing COD, the diagnostic accuracy of palpation alone, as well as the ability to differentiate follicular versus luteal cysts, is relatively poor.[37] As a way of improving diagnosis and management of cystic cows, other tests can be performed to better assess ovarian cysts. Ultrasonography is the most reliable tool in diagnosing COD since native anatomical ovarian structures can be differentiated from true cysts. These cysts are distinguished via ultrasonography by their wall thickness. Follicular cysts have a wall thickness of ≤ 3 mm whereas luteal cysts are ≥ 3 mm thick.[38] To further differentiate cystic ovarian structures, color doppler ultrasonography (CDU) was used to measure ovarian vascular function; follicular cysts had notably lower blood flow values than luteal cysts and the diagnostic accuracy of CDU was superior to B-mode ultrasonography.[39] The combination of wall thickness measurement and blood flow area measurements increased the sensitivity to differentiate a follicular from a luteal cyst. The evaluation of progesterone concentrations in combination with the ultrasonography analysis may also aid in differentiation of the type of cyst, as progesterone concentration thresholds for follicular and luteal cysts are < 1 ng/ml and ≥ 1 ng/ml, respectively.[39]

Some behavioral abnormalities that might be observed in cattle with COD are related mostly to the neuroendocrine imbalance. One abnormality the cow may present with is nymphomania, a frequent, irregular, and prolonged estrus. Other clinical signs at evaluation include elevation of tail-head, relaxation of pelvic ligaments, and even masculine phenotype in chronic cases.[38] Although all of these are possible clinical signs of the disease, prolonged anestrus due to failure of ovulation is the most commonly observed manifestation of COD in dairy cattle. It is recommended to perform transrectal palpation or transrectal ultrasonography for evaluation of the cyst wall thickness and plasma progesterone concentrations to have a more accurate diagnosis of COD.

For many years, the treatment of COD was manual rupture of the cysts via transrectal palpation. However, this treatment is no longer recommended due to the potential negative effects including ovarian trauma, hemorrhage, and an increased risk of ovariobursal adhesions.[31] Fortunately, many studies have reported that approximately 60% of cystic cows undergo spontaneous recovery and cyst regression by the first postpartum ovulation.[31] The mechanism by which the cysts regress spontaneously is still unknown. Nowadays the most common treatment for COD involves the use of gonadotropin releasing hormone (GnRH) to stimulate an LH surge from the anterior pituitary, resulting in luteinization of the cyst.[40] The efficacy of these treatments varies across studies and the significance, or lack thereof, of reported rates of resolution is likely attributed to small numbers of cows in each study. Human chorionic gonadotropin hormone (hCG) has also been used in the treatment of COD as it has LH-like activity and luteinizes the cysts, leading to increased progesterone concentrations;[31,41] the resulting luteal cysts are then treated with prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) that cause the structure to regress, resulting in expression of estrus within 2-5 days.

Treatment with GnRH and $PGF_{2\alpha}$ in combination is beneficial for luteal and follicular cyst regression and early return to estrus.[31] The use of exogenous progesterone with or without the Ovsynch protocol are other options for the treatment of COD in cows. Exogenous progesterone treatment can reestablish the hypothalamic response to the estrogen positive feedback mechanism and return the animal to normal cyclicity. Single controlled internal drug release device (CIDR) for 14 days in cows with endocrinologically active cysts (determined via circulating estradiol concentrations) initiated emergence of a new follicular wave within 3 days after CIDR insertion.[42] However, this treatment was ineffective for cysts that were not estrogen producing. The Ovsynch artificial insemination protocol has also been used successfully on cows with cystic ovaries. In a study comparing Ovsynch to an exogenous progesterone source for 7 days followed by an injection of $PGF_{2\alpha}$ (with estrus detection as an option) for treatment of cystic cows, the use of the Ovsynch protocol increased the percentage of cows inseminated, but the conception rates and pregnancy rates did not differ across groups.[35] Using the findings of this study, an economic analysis was conducted showing that treatment of COD with a timed AI protocol had an $11.39 advantage over a CIDR-based protocol.[43] Ultimately, the decision on which protocol to implement for management of COD depends on the farm's ability to achieve protocol compliance, value of the cow, stage of lactation at diagnosis, and the cost benefit ratio of each treatment option.

Cystic ovarian disease remains as a substantial concern in dairy cattle management, demanding ongoing research efforts and collaborative initiatives. Preventing COD necessitates a multifaceted approach encompassing genetic selection, nutritional management, prioritization of animal welfare, and evidence-based reproductive protocols. By enhancing our understanding of its etiology, refining diagnostic techniques, and implementing effective management strategies, clinicians can work with dairy clients to minimize the economic burden of COD and optimize reproductive outcomes.

Technology for identification of anovular cows

The availability and affordability of agricultural technologies has been increasing over the past decade. The use of automated activity monitors (AAM) on dairy farms has enabled producers to gather more data on health and reproductive parameters than ever before. Automated activity monitor systems use sensor technology incorporated into ear tags, neck collars, leg bands, or boluses allowing dairy producers to monitor cow activity and rumination. The associated software determines baseline data for each cow and monitors daily movement facilitating detection of changes in activity patterns that are associated with behavioral estrus. The challenge with increasing amounts of data is determining how to best use the available data to make management decisions to improve production at the herd level. With respect to anovulation, the use of AAM in the postpartum period may enable farmers to identify anovular cows and act more promptly to improve reproductive outcomes.

Anovular cows in the postpartum period were identified via AAM; 35.9% were in the first 30 DIM,[44] 20.8% at 60 DIM,[45] and 17% at 80 DIM.[46] Although the rates decreased as DIM increased, these studies were consistent with previous data indicating that, on average, > 20% of cows remain anestrus at the end of VWP. Lack of estrus expression before 60 DIM is negatively associated with reproductive performance with cows that did not express estrus had prolonged interval to first AI, reduced estrus duration and intensity, longer days to pregnancy, and reduced first service pregnancy per AI (P/AI) compared to cows that were detected in estrus.[45,47] Furthermore, cows that had 2 or more estrus events prior to the end of VWP were more likely to be inseminated by 100 DIM with a higher first service P/AI, and increased likelihood of pregnancy by 200 DIM compared to cows with 0 or 1 estrus event in the same period.[45]

Lack of estrus expression may not always coincide with lack of ovulation. From a clinical perspective, at the herd level, methods to assess the true ovarian status of individual cows are rarely practical. Blood progesterone measurements are expensive, require additional labor, and samples must be submitted to an outside laboratory. In-line milk progesterone monitoring is not widely available, and serial ultrasonography of ovarian structures requires additional time, labor, and veterinary cost. However, the use of confirmatory tests is crucial in understanding the validity of the on-farm AAM systems that many producers use to identify anovular or anestrous cows.

Based on blood progesterone to assess resumption of cyclicity, 9% of cows were truly anovular despite 17% diagnosed as anestrus.[46] In an assessment of sensitivity and specificity of AAM to detect resumption of cyclicity compared to serum progesterone, AAM had a sensitivity and specificity of 34.1 and 84.0%, respectively.[44] The authors attributed the low sensitivity for identification of cyclic cows to the silent estrus often observed in early postpartum cows. However, the higher specificity indicated that the AAM system was able to correctly identify a majority of the anovular cows. Although this means that some cows diagnosed as anovular may be cyclic and could be enrolled into a synchronization protocol aimed at managing anovular cows, there is little risk in doing so. Enrollment in a synchronization protocol in early lactation improves P/AI to first service, reduces days open, and improves overall reproductive performance, regardless of ovular status.[48] It is noteworthy to consider a presynchronization protocol such as Double Ovsynch over a basic Ovsynch protocol for synchronization of anovular cows as a management strategy. Although anovular cows ovulated in response to GnRH injections, conception rates were lower for anovular cows compared to ovular cows whether they are inseminated after detected estrus or Ovsynch.[48] A combination strategy of AAM to detect anovular cows and enrollment in an appropriate synchronization protocol is likely most beneficial in improving reproductive performance and the greatest return on investment of these technologies.

Targeted reproductive management programs aim to make the best use of AAM along with customizing management protocols for groups of cows within a herd, particularly those that are anestrus and anovular. These programs typically involve allocation of cows to various management strategies for first service insemination based on estrus expression identified by automated activity alerts during the VWP and the use of these data as a proxy for cyclicity. The feasibility of implementing these programs is still a subject of research. For example, prioritization of AI after estrus detection based on estrus expression prior to the end of VWP resulted in similar proportion of cows pregnant around 150 DIM despite a lower first service P/AI compared to a Double Ovsynch protocol.[49] Targeted reproductive management using AAM may provide additional options to improve or at least maintain reproductive performance in herds whose goal is to reduce the cost and labor associated with enrolling all cows in a timed AI protocol for first service.

Future directions

Until now, research on anovular conditions focused on the underlying mechanisms, contribution of postpartum diseases, and the use of commercially available formulations of various reproductive hormones to initiate resumption of ovarian activity. There are opportunities to explore hormones for management of anovular conditions that target the hypothalamic-pituitary-ovarian axis via different mechanisms than current commercially available reproductive hormones. Synthetic kisspeptin, a peptide hormone, has a role in facilitation of the GnRH surge, and can stimulate ovulation in postpartum cows.[50] A single injection of kisspeptin was capable of inducing ovulation in postpartum anovular cows with a dominant follicle > 10 mm in diameter, followed by a normal length estrous cycle. Cows receiving kisspeptin had significant increases in FSH and LH compared to controls but the ability of the kisspeptin-induced LH surge to cause ovulation was dependent on follicular size. Although this study only enrolled a limited number of cows, there is a potential for an alternate clinical tool in the management of anovulatory cows. Future studies need to examine the effects of kisspeptin treatment on days open, first service P/AI, and pregnancy losses to determine if this management tool has positive impact on fertility in anovular postpartum cows. An additional hurdle for kisspeptin use on a larger scale is that there is currently no commercially available product in the USA; however, the importance of reproductive performance to the USA dairy industry and high prevalence of anovulation in postpartum cows could make development of such a product a viable option for future application.

Conclusion

Regardless of cause, anovulation has substantial negative effects on reproductive performance and occurs at a relatively high rate in USA dairy cattle. Management practices to reduce within-herd rates of anovulation should be focused on maintaining nutritional status and minimizing body condition loss in the postpartum period, reducing risks for uterine and nonuterine diseases by supporting immune function and overall health, and reducing stress in the postpartum period. Early identification of anovular cows using activity monitoring systems, ultrasonographic examinations during routine herd health visits, or milk progesterone monitoring may allow for enrollment in targeted reproductive management programs to improve reproductive outcomes in this subgroup of cows. Clinical knowledge of the benefits and shortcomings of each management strategy will enable the reproductive practitioner to better assist dairy herd clients achieving their herd reproductive goals.

Conflict of interest

Jennifer Roberts is employed by Boehringer Ingelheim Animal Health; authors have no other conflicts of interest to declare.

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