Postpartum complications in cows: diagnosis, treatment, prevention

D. V. Chabanenko1, M. M. Zhelavskyi1, P. M. Skliarov2, B. V. Gutyj3, M. Wrzecińska4, F. A. Lone5, S. Rana6, O. V. Khmeleva2, R. V. Mylostyvyi2

1Vinnytsia National Agrarian University, Soniachna Str., 3, Vinnytsia, 21000, Ukraine
2Dnipro State Agrarian and Economic University, S. Efremov Str., 25, 49600, Dnipro, Ukraine
3Stepan Gzhytskyi National University of Veterinary Medicine and Biotechnologies Lviv, Pekarska Str., 50, Lviv, 79010, Ukraine
4West Pomeranian University of Technology, 71-270, Janickiego Str., 29, Szczecin, Poland
5Sher-e-Kashmir University of Agricultural Sciences and Technology of Kashmir, 190006, India

Abstract

This review contains an analysis of domestic and foreign researchers regarding the occurrence of postpartum complications in cows, which represents a significant veterinary problem. Diagnostic methods and treatment regimens for postpartum pathologies of various origins are presented. Difficulties and errors in diagnosing uterine inflammation lead to improper treatment, prolonged infertility, and significant economic losses. Based on an analysis of the literature, it has been proven that clinical forms of endometritis often develop into a subclinical course. The proportion of hidden endometritis can account for up to 80% of the total amount of endometrial inflammation. The problem with postpartum complications of the uterus is that the inflammatory processes spread to the ovaries, and this can lead to complete infertility in animals. Rectal examination of cows remains one of the primary methods for diagnosing endometritis. Treatment generally involves the use of a wide range of antibiotics. Data on the hormonal causes of postpartum pathologies of the reproductive system of cows are also presented. A big problem is follicular and luteal cysts, their timely diagnosis and appropriate treatment. The leading cause of cysts is a disruption of the hypothalamic-pituitary-gonadal axis. A practical method for diagnosing cysts is ultrasound, and the type of cyst can be determined by the level of progesterone in the blood. A practical method of treating cysts is the use of hormonal drugs. Data are also presented confirming the significant role of microflora in the occurrence of inflammatory changes in the reproductive organs of cows. The main types of causative agents of inflammatory processes in the genital organs of cows in the postpartum period are given. In cows with endometritis, an imbalance of the uterine microflora is detected, and the growth of bacteria of the genus Bacteroides and Tenericutes. Data are presented that rumen acidosis can cause inflammation of the uterus, and this is associated with the penetration of Fusobacterium necrophorum into the blood circulation. The effectiveness of intravaginal treatment of cows with a mixture of lactic acid bacteria (L. rhamnosus, P. acidilactici, and L. reuteri) has been shown.

Keywords: cows; inflammation; uterine diseases; endometritis; follicular and luteal cysts; microbiota of the genital tract.

1. Introduction

Declining fertility is a significant concern for dairy farming, as the associated extended calving intervals, decreased milk yields, and increased rates of herd culling result in substantial economic losses. Along with the use of modern technologies and the creation of highly productive herds, livestock breeders and veterinarians are faced with the problem of a significant deterioration in the health of cows. Most researchers in the field of cattle reproduction agree that increased milk production is the cause of the decreased reproductive performance of cows (Yáñiz et al., 2008; Pegolo & Cecchinato, 2022; Mylostyvyi et al., 2024). Data from literature sources (Vieira-Neto et al., 2017; Pajohande et al., 2023) indicate that impaired reproductive function and a decrease in milk productivity of cattle are closely related to the development of postpartum pathological conditions in cows (vestibulovaginitis, vaginitis, cervicitis, endometritis, and salpingitis). The increased incidence of disease in ani-
mals is associated with intensive lactation, during which a significant amount of essential substances is excreted from the body, which leads to its depletion. They believe that such cows have a high level of metabolism and a sensitive neurohumoral regulatory system, which react even to minor violations of housing and feeding conditions, primarily by reducing immune reactivity.

Disease of the reproductive organs in cows is a significant cause of decreased reproduction in dairy cattle breeding. Very often, after calving, acute postpartum endometritis occurs, reducing milk production and the nutritional value of milk, often leading to subfertility, premature culling, and even death of sick animals.

The most risky periods for developing various diseases are the dry and postpartum periods. Due to the disruption of involutional processes in cows, various pathologies of the postpartum period occur, but more often, subinvolution of the uterus and postpartum metritis occur. Placenta retention and metritis are clinical components of a single pathogenetic chain in the postpartum period. Their acute course, with timely detection and effective treatment, usually finishes with the recovery of cows by the end of the first month after calving. However, in most animals, uterine inflammation takes a chronic, predominantly subclinical form and remains undiagnosed for 2–3 months after birth.

Highly productive animals are characterized by hormonal imbalances. In cows with a high degree of productivity, anovulation and the absence of pronounced signs of estrus and general agitation are more often noted. The main reason for this is the low production of sex steroids or an imbalance in their ratio. In particular, anovulation is associated with low progesterone levels in the previous cycle and low estrogen concentrations (Sklarov et al., 2023).

One of the main reasons for the occurrence of postpartum complications is an increase in the virulence of opportunistic microflora and a decrease in the resistance of the animal body. In 80–90% of cases, the cause of the disease is the entry into the uterine cavity of opportunistic microorganisms (staphylococci, diplococci, streptococci, E. coli, saprophytes). Therefore, along with other diagnostic measures, the central and essential point in making a diagnosis is a microbiological examination of the contents of the uterus (Holubiev et al., 2023).

2. Postpartum pathology of the uterus

Involution of the genital organs is accompanied by significant functional and structural restructuring of the reproductive organs. At the same time, profound neurohumoral changes are observed in the body of highly productive livestock. In addition, in the body of animals, organs and systems involved in reproduction, which are characteristic of a non-pregnant state, are restored (Amin et al., 2023).

It should be noted that with a decrease in the size of the uterus and its structures, involution is not completed. In parallel, histological changes occur in the endometrium. At different times after calving, it was found that from the 1st to the fifth day, necrosis (death) of the surface layer of the endometrium and its peeling on the 6–7th day are noted. In parallel with the degeneration and peeling of the epithelium, its partial absorption and destruction by macrophages, the process of epithelial regeneration begins. During the 15–25 days, the endometrium acquires the same color and histological condition. However, complete restoration of the histostructure of the uterus and uterine glands is closely related to the hormonal profile, as well as the restoration of ovarian function, and is completed in 41–50 days.

A clear understanding of the ordinary course of postpartum involution of the uterus makes it easier for specialists to identify deviations from the norm, which allows them to make a timely diagnosis of the presence of an inflammatory process in the uterus and determine its form.

The most common complications in cows during the postpartum period are disorders caused by inflammatory processes in the uterus (subinvolution and endometritis). Subinvolution of the uterus poses a particular danger to the development of infertility. In the absence of ineffective treatment, in 50% of cases, acute postpartum endometritis develops against its background, predominantly of the catarrhal-purulent type. Catarrhal or purulent endometritis can become chronic or subclinical. In the first case, there is a violation of the reproductive cycles, but cows can become fertilized when ovulation occurs. Moreover, in most cases, hidden abortions are observed in such cows, after which the cows can again come into heat. In the second case, there is no disturbance in reproductive cycles; animals are inseminated many times without fertilization, which is the main sign of latent endometritis.

With the introduction of industrial milk production technology and the associated year-round keeping of cows indoors, the number of animals suffering from endometritis has increased. According to individual authors (Pascottini et al., 2017; Wagener et al., 2021), from 14 to 40% of calving cows are characterized by postpartum inflammation of the endometrium, which occurs in 21 or more days after calving (Sheldon et al., 2006). Other studies have found (Dubuc et al., 2010; Bradford et al., 2015; Osawa, 2021) that in some cases, postpartum endometritis occurs in 50 to 90% of cows.

Additionally, endometrial pathology increases in cows that develop subclinical mastitis on the first day after calving. Studies have shown that 37% of cows in the postpartum period are affected by both mastitis and endometritis (in 54% of cases, purulent-catarrhal form), which is directly related to pathogenic and opportunistic microflora (Makki et al., 2017; Okawa et al., 2017; Amin et al., 2023).

It should be noted that subclinical endometritis develops with late diagnosis or unqualified care, which is one of the most common causes of reproductive system disorders in livestock (Pascottini & Opsomer, 2016). This disease is the most common of all uterine diseases and affects up to 30% of lactating dairy cows in a herd (Kenide et al., 2014; Pajohande et al., 2023). Multiple and ineffective fertilizations manifest the course of subclinical endometritis.

Pathogenetic changes in endometritis in cows are primarily determined by the state of the body's natural resistance, and the level of local protection of any organ is inextricably linked with the level of its structural organization; however, this fact is not always taken into account in the pathogenesis of endometritis (Yániz et al., 2008; Pleticha & Heuwieser, 2009; Wagener et al., 2017).

The critical point in the pathogenesis of endometritis is microbial contamination of the uterus of cows during calving and the postpartum period. The main predisposing factors for the development of postpartum complications include inadequate conditions for keeping cows in the prenatal period, during and after calving, as well as high microbial contamination of the uterus and postpartum metritis (Holubiev et al., 2023).
contamination of premises due to the lack of disinfection (Ivankiv & Vlasenko, 2012).

According to individual observations (Ivankiv & Vlasenko, 2012), when the period of stay of cows in postpartum boxes is shortened, and there is no isolation, animals are more often diagnosed with inflammation of the reproductive organs. In cows with high milk production, postpartum diseases of the reproductive organs are more common and more severe. Up to 60–75 % of calving cows undergo uterine subinvolution; most of them are then diagnosed with acute postpartum endometritis 7–12th days after birth.

Numerous researchers argue that in addition to the clinical manifestations of diseases of the reproductive organs, cows are diagnosed with a subclinical or latent form of endometritis, which is associated with the widespread use of hormonal stimulation of oestrus and artificial insemination. They account for up to 75–80.0 % of nonspecific inflammation of the uterus (LeBlanc et al., 2011; Diaz-Lundahl et al., 2022; Pascottini et al., 2023).

Understanding the factors that delay uterine involution is important because completion of involution is associated with fertility. It is believed that it takes 3–4 weeks to completely restore the typical architecture of endometrial tissue and restore the sexual cyclicity of cows. Some experts indicate that not only does acute postpartum endometritis affect the manifestation of sexual cyclicity and pregnancy in cows after fertilization, but the inflammatory process often spreads to the oviducts, completely eliminating the possibility of fertilization of the female (Cheong et al., 2017; Magata et al., 2019).

Long-term inflammatory processes in the reproductive organs of cows lead to irreversible changes in the endometrium. This causes long-term infertility and subsequently leads to premature culling of animals. Both domestic (Basarab & Stefanyk, 2016; Masalovych et al., 2017) and foreign (Lince et al., 2007; Pascottini & Opsomer, 2016) researchers indicate a significant prevalence of subclinical endometritis among the causes of long-term infertility in cows. In some cases, with latent endometritis, cows ovulate, and fertilization occurs. However, the presence of adhesions and changes in the pH of the uterine contents interfere with the development of the fetus, which leads to early hidden abortions or abortions in the deep pregnancy period. Therefore, early diagnosis of chronic or latent endometritis and timely treatment can preserve the reproductive function of cows. Clinical diagnostic methods and laboratory tests suit this: cytological, physicochemical, biological, and hormonal.

Rectal examination reveals the decreased tone of the uterine horns in the premature phase of the sexual cycle when the corpus luteum undergoes regression. After the end of estrus, you can see the presence of purulent threads or flakes in the mucus. Several researchers indicate that 24–65 % of cows develop complications in latent endometritis after clinical recovery (Pascottini et al., 2017; Wagener et al., 2021). This may not be noticed when examining the animal. Therefore, in order to prevent the process from passing into a latent form, it is necessary to promptly detect acute postpartum endometritis both by clinical signs and by the dynamics of structural changes in the tissues of the uterus.

Intrauterine or parenteral antibiotics are most often used to treat uterine infections. Preference may be given to third-generation cephalosporins (for example, Ceftriaxone hydrochloride; Cephalixin Benzathine), which have proven themselves in the treatment of clinical and subclinical endometritis (LeBlanc, 2008).

3. Postpartum complications in cows are associated with hormonal disorders

The reproductive function of females is a complex system consisting of the cerebral cortex, pituitary gland, hypothalamus, and reproductive organs (uterus and ovaries). During the sexual cycle, the hypothalamus synthesizes gonadotropin-releasing hormone, which, in turn, triggers the formation of follicle-stimulating and luteinizing hormones in the pituitary gland. The action of these hormones activates the synthesis of estrogens, a sharp increase in the concentration of which leads to a peak of luteinizing hormone, the critical ovulation hormone. In place of the ovulating hormone, the corpus luteum is formed, the function of which is to produce progesterone until the next ovulation cycle (Vlasenko, 2011; Skliarov et al., 2022).

The sexual cycle of cows, which takes 18–21 days, has two, three, and less often four follicular waves. The number of follicular waves is controlled by follicle-stimulating hormones and estrogens. Accordingly, the level of estrogen and progesterone in the blood is important for the normal physiological course of the reproductive cycle in cows. The uterus of cows is most sensitive to estrogens in the estrus stage, while the sensitivity of the uterus to progesterone is observed 2–5 days after the end of estrus. Estrogens and progesterone regulate the growth and differentiation of the endometrium. Estrogens also contribute to the vascularization of the endometrium, increased secretory function in the cervix and oviducts, increased contractile function of the uterus, and effects on the immune system (Vlasenko, 2011; Gruntkovskii et al., 2014).

One of the common postpartum complications in cows is ovarian hypofunction. Ovarian follicular cysts are a serious reproductive problem in lactating dairy cows. Traditionally, ovarian follicular cysts have been defined as nonovulatory follicular structures more significant than 25 mm that persist for at least ten days without a functional corpus luteum (Lüttgenau et al., 2016). Today, follicular cysts are defined as follicular structures with a diameter of 17 to 22 mm that persist for 7 to 8 days (Cattaneo et al., 2014). Luteal cysts, as a rule, have one spherical cavity, the wall of which is formed by several layers of proliferating cells of the connective tissue membrane of the follicle. They are thick-walled and challenging to remove. Luteal cysts have luteal tissue from the inside, which synthesizes progesterone.

Individual researchers have reported that the incidence of ovarian cysts in dairy cattle can range from 3–15 % (Cattaneo et al., 2014) to 6–30 % (Yamamoto et al., 2020), with a peak incidence between 14 and 40 days after calving. According to some data, up to 70 % of ovarian cysts occur between 16 and 50 days after calving, with the highest incidence occurring between 30 and 40 days postpartum (Yimer et al., 2018).

In the period before the 16th and after the 50th day after calving, the lowest incidence of ovarian cysts is observed (Roth et al., 2012). Genetic correlations between ovarian cysts and milk production traits suggest that selection for milk yield will increase the incidence of ovarian cysts. In addition, the incidence of these diseases will increase with-
out changes in genetic selection methods (Berry et al., 2011).

The hypothesis explaining the formation of ovarian cysts is based on changes in the release of luteinizing hormone in the hypothalamic-pituitary-gonadal system, namely, disturbances in the estrogen feedback mechanism at the hypothalamic-pituitary level. Additionally, at the ovarian level, it may be cellular and molecular changes in growing follicles that promote anovulation and cyst formation (Vanholder et al., 2006). Some studies explain that altered expression of steroid and gonadotropin receptors may disrupt endocrine signaling pathways (Salvetti et al., 2012).

Regarding cellular changes, it is hypothesized that follicular cysts are a particular stage of follicular differentiation with a specific protein and gene expression profile in ovarian cells that differs from that found in atretic follicles or other categories of follicles (Matiller et al., 2014).

Metabolic changes correlated with hormonal imbalance may influence cyst formation (Xu et al., 2023). Delayed follicular regression after ovulation (change in proliferation/apoptosis balance) is a trigger for the pathogenesis of ovarian cysts, as preovulatory follicles that can neither ovulate nor become atretic impair ovarian function, creating a starting point (Ortega et al., 2015). The persistence of these structures allows them to continue to secrete altered levels of cytokines, growth factors, and hormones and, therefore, underlies the pathogenesis of ovarian cysts (Stassi et al., 2019). A separate study (Hatler et al., 2003) noted that 66 % of ovarian cysts in dairy cattle were associated with supraval levels of progesterone, which blocks preovulatory elevated luteinizing hormone levels but does not suppress pulsatility as it occurs with average luteal progesterone concentrations. That is, an anovulatory persistent follicle begins to develop with a larger diameter and longer duration of existence than usual, along with an increase in peripheral estradiol concentrations (López-Gatius, 2022).

Stress may be one of the reasons for the development of ovarian cysts in cattle (Ortega et al., 2015). First, adrenocorticotropic hormone stimulates the release of cortisol and progesterone. Increased progesterone secretion inhibits gonadotropin-releasing hormone extraction, whereas increased cortisol secretion decreases estradiol secretion and luteinizing hormone/choriogonadotropin receptor content in antral follicles. Subsequently, the feedback between estradiol and the hypothalamus and pituitary gland worsens, the secretion of luteinizing hormone is inhibited, ovulation does not occur, and the follicle becomes cystic (Marelli et al., 2014).

Follicular ovarian cysts are detected by the results of a rectal examination in the presence of one or more layer-like fluctuating formations with a diameter of more than 2 cm in one or both ovaries in the absence of the corpus luteum. The study is carried out 2–3 times with an interval of several days. The method of ultrasound diagnosis of ovarian cysts is also effective (autrop). Ultrasound scanning is performed several times, with an interval of 4–11 days. Ultrasound diagnostics significantly improves and accelerates the detection of cystic ovarian pathologies and allows for differential hormone therapy of cows with luteal and follicular ovarian cysts, which makes it possible to evaluate its effectiveness already 4–5 days from the start of treatment. Based on the level of progesterone in the blood, it is possible to differentiate follicular cysts from luteal cysts. Low progesterone and luteotropin levels in cows with ovarian cysts indicate impaired ovarian hormonal function due to insufficient gonadotropic stimulation (Yblonsky & Khomin, 2006).

Drug treatment of cows with follicular cysts includes a complex of 5 stages:

1. General stimulating therapy includes the use of subcutaneous injection of one of the tissue preparations (for example, a suspension of cattle liver, 0.5 % solution of sodium humate, 7 % solution of ichthyol or autologous blood) with the obligatory prescription of a multivitamin preparation;

2. Pathogenetic therapy is based on the use of novocaine solution (0.25 %) intra-aortically;

3. Use of a hormonal drug that stimulates the pituitary gland to release luteinizing hormone for luteinization of the cystic follicle (gonadotropin-releasing hormone or luteinizing hormone drugs). The effectiveness of this treatment can be monitored on days 10–12 when the corpus luteum forms in the ovary or the concentration of progesterone in the blood increases;

4. Administration of a luteolytic drug (on the 11th day from the start of treatment);

5. Stimulation of folliculogenesis with folliculotropic drugs (starting from the 14th day of treatment).

It is practical to carry out daily, for 7–8 days, intramuscular injection of 2–3 ml of a 2.5 % progesterone solution, with simultaneous oral administration of 50–100 mg of potassium iodide, and on the 10–11th day of treatment, add follicle-stimulating hormone and progaglandin analogue F2α. Potassium iodide can be used intramuscularly for five days in the form of a 5 % aqueous solution in increasing doses (60, 80, 100, 120, 140 ml). It stimulates the synthesis of luteinizing hormone through the thyroid gland, under the influence of which the cyst turns into the corpus luteum. Its degeneration is accelerated by progaglandin F2α, with simultaneous hormonal stimulation of folliculogenesis (Yblonsky & Khomin, 2006).

Today, among the wide range of hormonal drugs proposed for the treatment of ovarian cysts in cows, the most commonly used drugs are gonadotropin-releasing hormone, human chorionic gonadotropin (for the treatment of follicular cysts), and prostaglandin F2α (for the treatment of luteal cysts). In cases where the differential diagnosis of a cyst cannot be accurately established, it is recommended to combine the administration of human chorionic gonadotropin or gonadotropin-releasing hormone with a double injection of prostaglandin F2α every 10–12 days. During the first heat after this treatment, the cow can be inseminated (Diaz et al., 2015).

4. Impact of microbiota on the development of postpartum complications

One of the critical factors in maintaining the normal state of the endometrium is the microflora of the genital tract of cows. It includes not only bacteria but also other microorganisms such as fungi, archaea, viruses, and protozoa (Lacroix et al., 2020; Adnane & Chapwanya, 2022). The bovine reproductive tract microbiota performs physiological functions such as maintaining the integrity of the endometrial epithelium, protecting against pathogens, and regulating host immunity (Galvão et al., 2019; Sheldon et al., 2019).

The microbiome of the reproductive organs of cattle still needs to be sufficiently studied, especially in terms of the microbiome's specific taxonomic classification and functional aspect. This is useful for the development of diagnos-
tic methods such as microbial biomarkers and dysbiosis indices. The microflora of the genital organs of animals have protective functions against the primary pathogens.

Many factors influence the diversity of the cow's reproductive tract microbiome, some of which are specific, such as estrous cyclicity and pregnancy (Deng et al., 2019; Barba et al., 2020). Most bacteria of the genital tract are non-pathogenic and are present with enterocytes in a symbiotic relationship.

The load and diversity of microorganisms in the cow's vagina and uterus are highly dynamic and depend on factors such as the origin of contamination, mode of delivery, feeding, and postpartum complications (Adnane & Chapwanya, 2022). Thus, in cows with developing endometritis, the microflora contains predominantly Bacteroidetes, Fusobacteria, and a lower relative abundance of Proteobacteria and Tenericutes. At the same time, the same pathogens of endometritis (Bacteroides, Fusobacterium, and Porphyromonas) are part of the normal flora of the rumen and are excreted in feces. Thus, colonization of the uterus with relevant environmental bacteria may contribute to the development of endometritis (Machado et al., 2012; Lima et al., 2015). In addition, possible routes of infection of the uterus are Bacteroides, Fusobacterium, and Porphyromonas coming from the vagina (Bicalho et al., 2017; Basbas et al., 2023).

It should be noted that the uterus is characterized by a unique microbiome, especially during pregnancy when the contents of the cervix are isolated from the vagina due to the formation of a cervical mucus plug (Galvão et al., 2019). Although mixed bacterial infections usually cause uterine infections, the major microbial pathogens include Trueperella pyogenes (T. pyogenes), Fusobacterium necrophorum (F. necrophorum), Bacteroides spp. and Prevotella spp. (Santos et al., 2011). However, a fascinating fact is that Fusobacterium necrophorum enters the bloodstream, probably during ruminal acidosis, and causes cow liver abscesses. F. necrophorum is also commonly co-cultured with Trueperella (Arcanobacterium) pyogenes, another common uterine pathogen (Tadeponi et al., 2009).

Although genital tract microorganisms are thought to originate from the environment or various organs such as the rumen, skin, rectum, or feces, the vagina is considered the primary source of endometrial microfauna, especially during periods when the cervical lumen is enlarged: during estrus, mating or calving. Vaginal mucus is less viscous during these times, allowing colonization of the uterus by a variety of bacteria, fungi, viruses, and protozoa of vaginal origin (Vagios & Mitchell, 2021).

However, it should be considered that microorganisms can also enter the genital tract through the hematogenous route (Jeon et al., 2017). Blood is a standard component of lochia, so maternal blood naturally enters the uterine lumen after the fetus's birth due to severe swelling of the endometrium. This results from vascular changes, which lead to leakage of blood components into the lumen of the uterus (Pascottini et al., 2023).

During calving, microbes from the environment enter the cow's uterus. From an immunological point of view, these microorganisms are recognized by the host's immune defense system as pathogenic, thereby causing the elimination of the pathogen. Typically, in cattle, activation of the host defense system and clearance of bacteria occurs during endometrial involution during the first five weeks after calving (Lin et al., 2021).

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