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Etiology and epizootology of bovine mastitis (analytical review)

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ABSTRACT

Mastitis is one of the most common global diseases of dairy cattle, it is detected in 5–36% animals in a herd undergoing a single examination, and the incidence reaches 68% within a year, given that some cows get reinfected more than once. The disease causes significant economic losses to dairy industry both in the Russian Federation and globally. Mastitis is an inflammation of the mammary gland that develops in response to the effects of various factors of the external and internal environment, which are classified as mechanical, physical, biological, etc. Based on the clinical symptoms, the disease has two forms: clinical and subclinical. Both the animal and its milk shall be subjected to a thorough examination for the diagnosis establishment. The final stage of the mastitis diagnosis in cows is laboratory testing. In this case, the most informative is the bacteriological method, which helps to isolate a pathogen's pure culture, identify it and determine sensitivity to antimicrobial drugs. The latter plays a specific role in indicating the direction of further therapeutic measures, since the obtained data facilitate selection of effective antibiotics against certain pathogens. Incorrect treatment, incompliances with the prescribed therapy, as well as unnecessary use of antimicrobials can lead to the generation of multi-resistant bacteria. Due to the widespread spread of antibiotic-resistant microorganism strains, despite the large number of drugs currently used, their effectiveness is constantly decreasing. The prospects for the further use of antibiotics as therapeutics are questioned by many researchers and international organizations due to antibiotic resistance rapidly developing in many agents. Vaccination plays a significant role in infectious disease control. The use of vaccines not only reduces mastitis occurrence in cows, but also significantly improves the quality of dairy products.

Keywords: review, bovine mastitis, etiology, epizootology, treatment, prevention, vaccination

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Этиология и эпизоотология мастита коров (аналитический обзор)

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РЕЗЮМЕ

Мастит является одним из самых распространенных заболеваний молочного скота во всем мире, при разовом обследовании стада выявляется у 5–36% животных, а в течение года заболеваемость достигает 68%, при условии что некоторые коровы переболевают два раза и более. В Российской Федерации, как и во всем мире, болезнь наносит значительный экономический ущерб молочному животноводству. Мастит – это воспаление молочной железы, которое развивается в ответ на воздействие различных факторов внешней и внутренней среды, которые классифицируют как механические, физические, биологические и другие. На основании клинических симптомов заболевание можно разделить на две формы: клиническую и субклиническую. Для установления диагноза необходимо проведение всестороннего обследования как животного, так и молока. Завершающим этапом при диагностике мастита коров является выполнение лабораторных исследований, в данном случае преимущество по информативности отдается бактериологическому методу, с помощью которого удается выделить чистую культуру возбудителя, провести его идентификацию и определить чувствительность к антимикробным препаратам. Последнее играет особую роль для определения вектора дальнейших лечебных мероприятий, поскольку полученная

информация позволяет подобрать эффективный антибиотик против конкретного возбудителя. Неправильный выбор, несоблюдение предписанного курса лечения, а также нецелесообразное применение противомикробных средств может привести к генерации мультирезистентных бактерий. Вследствие широкого распространения антибиотикорезистентных штаммов микроорганизмов, несмотря на большое количество используемых в настоящее время препаратов, их эффективность постоянно снижается. Перспективы дальнейшего использования антибиотиков в качестве лекарственных средств многие исследователи и международные организации ставят под сомнение из-за быстро развивающейся к ним резистентности у многих возбудителей. Вакцинопрофилактика занимает значительное место в борьбе с инфекционными болезнями. Применение вакцин позволяет не только снизить количество маститов у коров, но и значительно улучшает качество получаемой молочной продукции.

Ключевые слова: обзор, мастит коров, этиология, эпизоотология, лечение, профилактика, вакцинация

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INTRODUCTION

Mastitis is one of the most common global diseases of dairy cattle, it is detected in 5–36% of the herd population undergoing a single examination. Within a year the incidence reaches 68%, provided that some cows get diseased twice or more [1].

Mastitis is an inflammation of the mammary gland that develops in response to the effects of various factors of the external and internal environment when animal's body resistance decreases and infection becomes complicated. The disease is caused by various microorganism species that penetrate the mammary gland and, as a result of intensive reproduction, induce the infection. The main factors of mastitis are classified into mechanical, physical and biological. Concomitant factors are: animal's resistance and immune status, failures in pre-milking and post-milking udder hygiene procedure, incompliant disinfection of milking devices, etc. Based on the clinical symptoms, mastitis can be of two types: clinical and subclinical. Clinical mastitis is often diagnosed directly by visual assessment of udder inflammation or changes in the organoleptic properties of milk, whereas subclinical mastitis is a latent form of the disease characterized by absence of clinical signs and 3–4-fold rise in milk somatic cells count [2, 3, 4].

Mastitis causes significant economic losses consisting in reduced milk yields and deteriorated milk quality (66%), rejection of products with decreased nutritional and technological properties (6%), premature culling of high-yielding cows due to dysfunction of udder quarters (22%), burden of treatment costs (5%) and increased costs on veterinary staff labour (1%). Drinking colostrum from mastitis-infected cows to calves results in indirect, but significant losses, it generally leads to mass gastrointestinal diseases and is one of the causes for mortality in the early postnatal period. Mastitis is one of the most economically significant cow diseases worldwide. Thus, for example, the damage caused by this disease to the dairy industry in Russia annually amounts to about RUB 1 billion, in England losses reach up to GBP 50 million, and in the United States the annual estimated losses range from USD 3 to 403 per cow [1, 5]. In view of the above, the issues of cow mastitis etiology and epizootology are relevant for veterinary medicine and the developing dairy industry.

The novelty of this study consists in the systematization and detailed review of current data on the factors impacting mastitis occurrence, spread, treatment and prevention methods.

The aim of the review was to analyze and systematize data from current research publications on the etiology and basic patterns of development, spread, treatment and prevention of cow mastitis.

Mastitis is a multi-factorial disease that develops under the influence of mechanical, physical, biological and other factors.

Mechanical factors belong to the most numerous group of negative effects causing injuries to the udder and nipples (microtrauma, bruises, cracks and wounds). The injuries are often the result of incompliances with the milking rules and technology, the most common causes are: excessive vacuum or its fluctuations, high pulsation frequency, use of non-standard teat rubber, unsatisfactory pre-milking udder hygiene, as well as poor-quality preparation of milking equipment.

Physical factors predisposing to the occurrence of mammary gland pathology include non-compliance with the temperature conditions of reared animals. Inflammation can develop under exposure to high and low temperatures, resulting in tissue burns or frostbites which can subsequently lead to an inflammatory process [6, 7].

The biological factors of the disease include different microorganism species. The development of an inflammatory process in the udder often begins with the entry of the pathogen into the animal's body from the environment through the nipple canal. Almost any opportunistic microorganism can cause both clinical and subclinical mastitis when penetrating the mammary gland [8, 9]. The etiopathogenetic study shows that cow mastitis is a polyethiological disease, the most common pathogens are: *Streptococcus* spp. (*S. agalactiae*, *S. dysgalactiae*, *S. uberis*, etc.), *Staphylococcus* spp. (*S. aureus*, *S. hyicus*, *S. xylosus*, *S. epidermidis*, etc.), *Escherichia coli*, *Candida* spp. (*C. krusei*, *C. glabrata*, C. *rugosa*), *Mycoplasma* spp. (*M. bovis*, *M. dispar*, etc.), *Trueperella pyogenes* [10, 11, 12, 13, 14, 15, 16, 17, 18]. Watts J. L. came to the conclusion that 137 microbial species and subspecies may cause inflammation of cow's mammary glands, some of them are part of the normal microflora and, with rare exceptions, do not cause pathological changes in udder tissues [19]. The researcher considers *S. hyicus*, *S. epidermidis*, *Corynebacterium bovis* to be conditionally pathogenic bacterial species. A number of authors studying the problem of cow mastitis indicate that the most severe forms of clinical mastitis in dairy cattle were associated with group B hemolytic streptococcus infection (*S. agalactiae*) [20, 21, 22], *Staphylococcus aureus* (*S. aureus*) [23, 24] and pathogenic *E. coli* [25, 26, 27]. Analyzing the research papers of domestic and foreign authors, it can be concluded that the diversity of microorganisms capable of causing mastitis is very large, in addition, certain statistics on the prevailing pathogens in different countries around the world can be found in the literature [28, 29]. Thus, in the Russian Federation, *Staphylococcus aureus* with detectability ranging from 42.8 to 87.3%, *Streptococcus agalactiae* (9.5–52.0%) and a group of enterobacteria are of predominant importance in the development of mammary gland inflammation (9.6–16.7%) [27]. It should be noted that the mastitis agent detected in biological sample tests can be isolated both in monoculture and in various associations [30, 31].

A number of researchers (S. A. Sheveleva [32], P. N. Gonzalez et al. [33]) have the opposite opinion. They believe that incompliances with the veterinary and zootechnical rules for feeding, keeping and milking cows, injuries and postpartum complications play a major role in the etiology of mastitis. Moreover, the emphasis is made on feeding, and microorganisms are of secondary importance. If an enhanced control over milking, keeping, udder condition maintenance and other preventive measures is carried out in a dairy farm, the udder diseases are detected much less frequently.

The literature data indicate that the season of the year also affects the epizootic process of cow mastitis. Rodin N. V. et al. [34] note in their study that there is a tendency for an increase in cow mastitis cases in the autumn and spring periods, a decrease, in turn, occurs in the winter and summer months. Thus, 14.8% of mastitis cases occur in summer, while 26.9% occur in winter. The percentage of mastitis cases recorded in the autumn-spring period ranges from 19.4 to 40.0%. The largest number of diseased cows is registered in areas where the stall period is the longest [35].

Such factors as gas contamination of premises, the condition and type of flooring material in livestock holdings are also responsible for increased number of cow mastitis cases. According to M. V. Oskolkova and E. V. Kuzmina [36], the incidence of mastitis in winter decreases up to 16.9% when animals are kept in wooden premises with wooden flooring.

Mastitis can occur during lactation, late gestation period, dry period, or immediately after parturition. The transformation of mammary gland tissues during late gestation period, dry-off and before calving results in reduction in its resistance and, in case of infectious onset or a latent inflammatory process, triggers the development of clinical mastitis. Mastitis often occurs after calving due to intoxication as a result of udder edema and other post-parturient diseases [37, 38, 39, 40].

According to the literature, the same infectious agent, depending on its quantity and virulence, as well as local and general resistance of the animal's body, can induce both clinical and subclinical forms of mastitis [1, 2, 3].

Clinical mastitis is characterized by the presence of pronounced signs of udder inflammation and changes in milk properties and composition. A physical examination of the affected mammary gland reveals local symptoms such as hyperemia, redness and pain during palpation, swelling and lumpiness. The disease manifestations can also include such general symptoms as behavioral changes, fever, anorexia, depression, lethargy, inappetence and hyperthermia. Clots and flakes of precipitated casein, transparent or bloody inclusions, as well as pus are found in milk [3, 22, 39].

Subclinical mastitis, occurring without obvious signs of local inflammation or systemic damage, rarely poses an immediate life threat and occurs 15–40 times more frequently than clinical mastitis. But sometimes there are cases of short-term changes in milk composition [3, 23]. Due to the asymptomatic course, farmers often miss the onset of the inflammatory process, are unaware of the deterioration in milk quality and the existing risk of spreading mastitis pathogens to other cows in the herd. The disease becomes chronic if no treatment is administered for more than two months. Depending on the biological properties of the pathogen, the infection can persist throughout lactation or cow's life span [9].

Mastitis became widely known at the end of the nineteenth century. The data accumulated since that time made it possible to describe and classify the types of inflammatory processes occurring in the udder when the clinical form of the disease is manifested. The classification by A. P. Studentsov which identifies 5 main subgroups of clinical mastitis based on the nature of inflammation is most frequently used in practice.

The most common is *serous* mastitis (early stage of the disease) characterized by swelling as the main sign. The affected parts of the udder are hard, enlarged, with pronounced hyperthermia. The general condition of the animals is regarded as normal, without deviations. No abnormalities are found in milk during visual examination at the initial stage of the disease; casein flakes are found and milk becomes more liquid as the inflammatory process progresses [28].

Catarrhal mastitis occurs mainly when inflammation is localized in the teat cistern or in large ducts. In this case, casein flakes are observed only at the beginning of milking; in case of inflammation of the udder alveoli, the milk is heterogeneous and contains flakes throughout milking process. Catarrhal mastitis is typically characterized by gray-colored secretions, as well as a significant decrease in milk fat content due to the formation of protein clots [4].

Hemorrhagic mastitis often develops as a result of serous or catarrhal inflammation. With this type of cow mastitis, all udder quarters are affected. Animals demonstrate intense breathing, inappetence, body temperature can reach 40.0–41.0 °C, pronounced purple spots are found on the surface of the skin. The ejected milk is of pink-red color and has inclusions of casein flakes [41].

Fibrous mastitis is the most painful and one of the most dangerous types of cow mastitis. This form is characterized by a sharp decrease in milk productivity, animal's depression, a painful reaction and a typical sound of crepitation when the affected part of the udder is palpated. Most of the time, the cow lies down, gets up with difficulty, lameness of both hind limbs is frequently observed [4].

When *purulent* mastitis is developed, the general condition of the cow significantly deteriorates. This type is characterized by the formation of dense hard lumps, animals' body temperature increases by 1.0–2.0 °C. Milk contains pus. Abscess may develop in the udder as inflammation progresses. The prognosis is unfavourable in case of abscess or phlegmon. The mammary gland acquires pustules that spread to larger areas and, as a result, merge together. Eventually a part of the gland loses its ability to function. Milk obtained from the infected lobe (lobes) has a gray color and contains multiple clots [3].

When any form of mastitis occurs (clinical or subclinical), there is a deterioration in milk quality with regard to sensory parameters, bacterial count and somatic cell count. In case of mastitis, an increase in somatic cell and bacterial count in raw milk means increased activity of proteolytic and lipolytic enzymes. Plasmin, for example, is a caseinolytic enzyme synthesized from plasminogen, which develops in blood and most likely enters milk due to the destruction of mammary gland epithelium. Casein degradation will generate foul-smelling metabolites that will replace the pleasant odour associated with fresh milk [40, 42].

The regulatory document specifying the requirements imposed on milk and dairy products was substituted in the Russian Federation since January 1, 2016; the Customs Union's Technical Regulation "On safety of milk and dairy products" (CU TR 033/2013) was enforced instead of the Technical Regulation of Russia. The most significant changes related to the quality and safety of milk were the abolishment of milk grading and introduction of stricter standards for antibiotic content. To date, common milk standards have been approved, according to which milk can be placed on the market, or in case of non-compliance, it can be rejected without the possibility of further processing and sale at reduced prices. According to this document, the number of mesophilic aerobic and facultative anaerobic microorganisms shall not exceed 5×10^5 CFU/cm^3; number of pathogenic microorganisms shall be < 25 microbial cells, number of somatic cells shall be $< 7.5 \times 10^5$ in 1.0 cm^3 of the product.

Along with that, the content of antimicrobial drugs (AMDs) shall not exceed: 0.01 mg for levomycetin, 0.01 mg for tetracyclines, 0.2 mg for streptomycin, 0.004 mg for penicillin in 1 kg (litre) of the product. The AMDs admissible levels practically correspond to the analytical limits of methods used for detection of antibacterial drugs, and in general they can be classified as AMDs inadmissible levels.

The above information confirms the relevance of mastitis control issues and the need to prevent financial losses caused by this disease. Preventing the transition of the subclinical form of mastitis into a clinical one is one of the most important links in the complex of measures aimed at preserving udder health. This is possible in case of timely and regular diagnosis (at least once a month) [6].

To establish the diagnosis, it is necessary to examine the animal, measure its body temperature, pulse and respiratory rate. Particular attention should be paid to the inguinal lymph nodes and mammary glands during the examination. Udder examination includes visual examination, palpation and trial milking. Visual examination should be focused on skin integrity, color and udder symmetry. Signs of mastitis during palpation include fever in the udder, pain when pressed and typical lumps in mammary gland tissue. During trial milking the attention is paid to the effort required for milking, amount and sensory parameters of the ejected secretion [43, 44].

Latent (subclinical) mastitis is diagnosed using one of the rapid diagnostic tests (RDTs): dimastin, mastidine, mastotest, etc. The effect of RDTs is based on the detection of exceeding leukocyte levels and pH changes. Milk control plates divided into 4 round sections (one for each udder quarter) are used for testing. Both cisteral and parenchymal milk samples should be used to obtain reliable results [37].

The final stage in the diagnosis of cow mastitis is laboratory testing. In this case, the bacteriological method is preferable as it is the most informative [45], it helps to isolate a pure culture of the pathogen, identify it, perform a comprehensive study if necessary (describe its growth, proteomic and pathogenic properties) and determine susceptibility to antimicrobial drugs. Determination of antimicrobial drug susceptibility plays a specific role in determining further therapeutic measures due to the fact that in this case the data obtained helps to find an effective antibiotic against a specific pathogen. Incorrect treatment, incompliances with the prescription, as well as unnecessary use of antimicrobials can lead to the generation of multidrug-resistant bacteria [46].

Antibiotic therapy is used for all types of mastitis caused by bacterial microflora, or in cases where there is a secondary bacterial infection. The therapy has a number of positive aspects, such as rapid improvement in the animal's clinical condition, a low culling rate in a herd, predictable losses in milk yield, as well as negative ones: rejection of milk within the antibiotic withdrawal period during and after treatment. The presence of residual

amounts of antibiotics in milk is dangerous for human health and reduces the quality of dairy products, most drugs have a long withdrawal period; besides, the cost of AMDs is quite high [47, 48].

Due to the wide spread of antibiotic-resistant microorganism strains, despite the large number of drugs currently used, their effectiveness is constantly decreasing. The prospects for the further use of antibiotics as therapeutics are questioned by many researchers and international organizations due to the rapidly developing resistance to them in many agents. In recent decades, the antimicrobial resistance has become a global problem not only in public health, but also in veterinary medicine [49, 50, 51].

Irrational use of antibiotics, improper selection of therapeutics and non-compliance with the recommendations specified in the instructions, namely dosage, frequency, and duration of treatment, contribute to antibiotic resistance in bacterial populations. The AMR growth has caused serious concerns around the world both from the point of view of public health and food safety, and therefore use of antimicrobials in animal husbandry has been under constant control for many years [2].

It's worth noting that antibiotic therapy should be used only in extreme cases, mainly when the pathological process becomes life-threatening for the animal. In all other cases, it is best to treat animals with mastitis without using etiotropic therapy, and if this is not possible, it is recommended to use synthetic antimicrobials. The most common ones include sulfonamides and nitrofurans [52]. These AMDs have a number of advantages: a wide range of action, low toxicity, and relatively low cost. But there is also a significant drawback – inefficiency in the treatment of purulent mastitis [48].

The pathogenetic, along with etiotropic, therapy has become widespread, it includes methods that affect the nervous system and indirectly the entire body, contributes to an active influence on the course of the pathological process. The most common is novocaine blockade of udder nerves. Its application contributes to the healing of animals with mastitis, not only when used in combination with medicinal products, but also independently. The main novocaine blockades that are recommended for the treatment of cow mastitis are: short novocaine blockade of udder nerves according to D. D. Logvinov, blockade of the external sacral nerve according to B. A. Bashkirov, method of intra-aortic administration of novocaine according to D. D. Logvinov. Pathogenetic therapy is highly effective for acute mastitis before destructive tissue changes have occurred, particularly in case of serous, catarrhal, purulent-catarrhal mastitis [37, 44, 50].

Mastitis infection in cows often has consequences, even if the drug therapy is selected properly. Literature data, mainly foreign publications show evidence on the effectiveness of preventive vaccination of cows with mastitis. Staphylococcal toxoids, bacterintoxoids and their combinations with various adjuvants were used as immunizing agents in different countries [47, 53, 54, 55].

Vaccination plays a significant role in the infectious disease control. The use of vaccines allows not only reducing the number of cows with mastitis, but also significantly improving the quality of dairy products [2, 56, 57].

Vaccination of animals is a recognized way to reduce the cost of veterinary services. Thanks to the development of drugs for the prevention of mastitis, it has become possible to successfully control one of the most common diseases in dairy farming (the effectiveness of drug therapy ranges from 70 to 98%) [55, 56, 58, 59].

Several imported vaccines against cow mastitis are currently available on the global pharmaceutical market: two vaccines manufactured in Spain and one vaccine manufactured in France. However, due to the current global political situation, introduction of expanded sanctions and restrictions on the drugs that are not compliant with the Good Manufacturing Practice (GMP) standards, these vaccines are hardly accessible for the Russian livestock breeders.

This circumstance has become the key aspect for conducting research in order to develop new tools for the specific prevention of cow mastitis.

CONCLUSION

Modern scientific data confirm that mastitis is the main problem of dairy farming in all countries around the world, and its subclinical form (unlike clinical mastitis) is the most common. In addition, the literature data suggest that mastitis is a polyethiological disease. On the one hand, it is caused by infectious agents (bacteria, mycoplasmas, fungi), and on the other hand it is effected by environmental factors that reduce the resistance of the animal's body. Predisposing and concomitant factors have a great influence on the development of this disease. The former factors include animal's resistance and immune status, the latter factors include incompliance with zootechnical, preventive and therapeutic measures, non-performance of pre-milking and post-milking hygiene of the udder, lack of control over the serviceability of milking machines, as well as unsatisfactory disinfection of milking systems. Due to the fact that mastitis remains one of the most common global diseases, it can be assumed that farms engaged in breeding dairy cattle do not fully comply with the required zootechnological, preventive and therapeutic measures. With increased control over the implementation of a set of measures, it becomes possible to reduce the number of cases of clinical and subclinical cow mastitis. Specific prevention is the most effective way to control mastitis, however, a strong and stable immunity can be achieved only with strict observance of specific zoohygienic and technological requirements.

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