

## Diagnostic Significance of C-Reactive Protein in Acute and Chronic Pelvic Inflammation in Animals (Review)

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### Abstract

The purpose of this article is to review the research aimed at the study of C-reactive protein in the blood serum of animals, in particular cattle. The article considers the use of C-reactive protein (CRP) as an indicator and predictor of inflammation diagnosis in animals. CRP is referred to the "main" proteins of the acute phase (APP) of inflammation in humans and animals because its level increases very quickly (during the first 6-8 hours) and in large amounts (20-100 times). It has been established that the study of CRP in the blood serum of cattle for the diagnosis of inflammatory diseases of the pelvic organs (IDPO) is a promising direction in veterinary obstetrics and gynecology. There are few studies in this direction, the results of which are contradictory, which requires further study. In spite of the "fuzzy" limits of the norm of CRP in the blood of cattle, it has been established that a level of more than 60 µg/ml on the 3rd day after calving is a predictor of postpartum endometritis and requires therapeutic measures. But, when studying CRP in cows, it is necessary to take into account the living conditions, because they affect the indices of this protein.

**Keywords:** APP, CRP, endometritis, cervicitis, cows, diagnosis, infertility, predictors of inflammation, IDPO.

**Introduction.** IDPO is a serious problem for cattle breeding. Taking into account the absence of pre-pregnancy preparation of cows before artificial insemination, and understanding its importance and necessity, it is necessary to find a predictor of pelvic inflammation, which allows to indicate an inflammatory process in the body in a minimal time interval and with a high accuracy. The main part of pelvic inflammation in cows is represented by latent endometritis, which is asymptomatic and is not treated in time.

As a rule, latent endometritis develops into a chronic form and causes infertility and subsequent loss of the animal from the herd. Many diagnostic methods of hidden endometritis (bacteriology, histology, cytology, etc.) are time-consuming, labor-intensive, require veterinary specialists to master complex research techniques, which is a limiting factor of their application in the production process. The use of biochemical predictor of pelvic inflammation, in particular CRP, will help to avoid diagnostic difficulties and economic costs.

### Literature review

Dairy farming suffers huge economic losses due to diseases of the reproductive tract (mastitis, endometritis), which are a huge problem for veterinary obstetrics and gynecology, because it leads animals to pregnancy of different etiology and pathogenesis, which subsequently reduces and stops lactation [11]. Early diagnosis of pelvic inflammation is difficult, because they often occur in the form of erased forms, passing into the chronic form, which complicates the diagnosis of postpartum endometritis: there is no unified approach to the diagnosis of

postpartum endometritis and the definition of criteria for its differentiation. The study of APP content is reasonable for making a diagnosis in pelvic inflammation and differentiating latent forms of endometritis from clinical ones [1]. CRP has been used for more than a century. In the beginning, it was measured by a semi-quantitative method. Nowadays, high-precision studies are used [4]. The study of the concentration of CRP (the main in a number of APPs of inflammation) is the optimal method for diagnosing inflammation. APP concentrations in inflammation change in relation to the stage of the inflammatory process. Like all APPs, CRP is produced by hepatic cells under the influence of modulating interleukin, oncostatin and tumor necrosis factors. CRP refers to the major BOPBs because its concentration increases very rapidly (6-8 hours) and very significantly (20-100-fold, sometimes 1,000-fold). This change occurs due to an increase in the concentration of APP in the blood serum. The increase in  $\alpha$ -globulin fraction of proteins shows the strength of the inflammatory reaction, since  $\alpha$ -globulin fraction is represented by the APP of inflammation [2,3]. CRP is the most characteristic and most accurate qualitative and quantitative laboratory predictor of inflammation and tissue death. The amount of CRP changes rapidly in response to worsening inflammation or its decline. The shift in the levels of CRP has become an indicator of general and local inflammation, which shows with great accuracy the changes in the organism under the influence of various etiological factors, such as bacteria, viruses, as well as inflammation with spillover course (acute and chronic), metastasis of tumors in oncology, complications after surgical and gynecological interventions, etc. [5, 12, 18]. In humans, 10 to 30 mg/L of CRP has been found in: bacterial and viral infections, acute chronic inflammations, tissue damage; 40 to 100 mg/L (and sometimes up to 200 mg/L) of CRP in: metastatic tumors, chronic and systemic rheumatic diseases. Up to 300 mg/L and more SRB increases in: severe generalized infections, burns, sepsis. With effective therapy of bacterial infections, the level of CRP decreases the next day; if not, more effective antibacterial treatment is needed. Diagnosis of inflammation by SRB should be used to: determine the severity of inflammatory processes caused by bacterial and viral infections, monitor changes in the severity of such processes in order to correct their therapy, monitor the patient's condition after surgical intervention, monitor the rejection of a transplanted organ [3].

CRP began to be used in veterinary practice as a predictor of inflammation and also as an indicator informing the treating physician of positive changes in the patient's body, or of the absence of positive dynamics in the chosen treatment strategy [19]. When using CRP as a diagnosis of IDPO in cattle, it should be taken into account that lactation affects the production of CRP: there is a positive correlation between the increase of CRP in blood and increased lactation, especially in the period up to 1 to 4 months of pregnancy. Also, serum CRP level correlates with genetic predisposition of animals to high milk yields. The higher is the productivity of animals, the higher is the level of CRP in serum [14].

The average level of CRP in healthy cows is  $39.8 \pm 47.5$  mcg/ml [17]. According to another study, the amount of CRP in healthy cows was 22.4 ng/ml [21].

The determination of CRP is of particular interest in the early diagnosis of pyometra in females.

The results of the study show that the development of inflammation in the uterus in females is accompanied by a moderate increase in total protein. The content of CRP increases from the upper limit of the norm by 3.46 times. [2]. However, studies by other scientists have not confirmed a positive correlation between the increase in CRP in bitches with pyometra compared to the control group of animals [19].

Despite conflicting data, CRP remains one of the most common predictors of inflammation in the serum of various animals. Lee W. C. et al. (2003) found that cattle housing conditions correlated with serum CRP levels: the farm with good housing conditions and minimal stress factors had the lowest CRP levels. Animals, even healthy ones, kept on farms with poor living conditions contained elevated amounts of CRP in their blood. There is a hypothesis that zoohygienic parameters and stress can affect the levels of CRP in cattle [15]. The liver is responsible for the synthesis of CRP, which begins to release it actively into the bloodstream during illness or in the presence of increased stressors. It is released into the bloodstream to provide immediate protection against a stressor [20] and is an essential part of the natural active immunity that the animal receives at birth and serves as a major protective factor in the response to the introduction of a foreign substance [8]. CRP is found in diseases of dogs [7], unpaired ungulates (horses) [22], and pigs [6]. There is an opinion that in cows the amount of CRP is not able to change in an amount informative for disease diagnosis, as a result of which CRP is not considered a IDPO for cows [10]. However, some studies have shown that infections increase serum CRP levels in cows. Increased levels of CRP have been reported in the diagnosis of mastitis. Serum CRP levels are 3 times higher in cows with endometritis than in the control group ( $48.88 \pm 3.92$  mcg/ml), which is an informative indicator in the diagnosis of latent and clinical endometritis [9, 10, 16].

Diseases provoke the release of CRP by the liver into the circulatory system. In diseases, predominantly acute infections, huge amounts of CRP are produced than in the presence of stressors or in lactation. For example, mastitis in cows raised the serum CRP level to 100 mg/ml (healthy lactating animals have a level of  $34.5 \pm 3.7$ ). Fever and pneumonia increased the serum CRP level of cows up to 295 mcg/ml. The quantitative values of CRP in serum of cows with endometritis are  $122.34 \pm 12.72$  mcg/ml, in the control group -  $48.88 \pm 3.92$  mcg/ml [15, 16].

When diagnosing inflammatory diseases of reproductive organs, one should keep in mind that when diagnosing IDPO in the first day after delivery, the amount of CRP cannot provide an informative diagnostic result - its increased level represents an adaptive reaction of the body to stress during labor, possible surgical delivery, etc. Therefore, CRP cannot be used as an early diagnosis of postpartum endometritis. The threshold diagnostic values of CRP on the first day after delivery are 69 mg/ml and 60 mg/ml on the third day. On the third day after delivery, the CRP determination is moderately sensitizing (79%), highly species-specificity (93%), and predictive (93%). In addition, according to the results of statistical analysis, the determination of CRP level on the third day after delivery is sufficiently indicative to use this indicator as a predictor of inflammation development after delivery (endometritis) in women with an increased risk of suppurative-septic complications [13].

**Materials and research methods.** For conducting the study, the authors used a review of the literature data, in which CRP was considered as a predictor of the diagnosis of inflammatory diseases in animals, in particular in IDPO in cows.

**Study results.** Based on the results of the literature review, it was found that in healthy cows, the serum CRP is  $39.8 \pm 47.5$  mg/ml,  $48.88 \pm 3.92$  mcg/ml or 22.4 ng/ml according to different authors. Inflammation increases the CRP to  $122.34 \pm 12.72$  mcg/ml, and severe body conditions associated with fever and pneumonia increase the CRP to 295 mcg/ml (Table1).

Table 1. CRP content in cattle under different physiological and pathological conditions.

Animal Group	Indicator	Source of literature
Healthy animals	$39,8 \pm 47,5$ mgc/ml	[17]
	22,4 ng/ml	[21]
	$48,88 \pm 3,92$ mgc/ml	[14]
Lactation period	$34,5 \pm 3,7$ mgc/ml	[15]
Mastitis	Up to 100 mgc/ml	[14]
Fever and pneumonia	Up to 295 mgc/ml	[16]
Endometritis	$122,34 \pm 12,72$ mgc/ml	[14]

## Discussion

Literature data on the blood serum CRP content in cattle have scattered, unstructured data. There is no single standard for the blood serum CRP content in healthy animals. It is difficult to study these data and the fact that environmental factors (content) affect this indicator, so in further studies, to verify research, it is necessary to collect anamnes vitae, taking into account a large number of data (zoohygienic parameters, microbial load, staff treatment of animals, type of housing, type of milking machine, etc.). The conclusions of scientists, in relation to the same object of study are different. One group of researchers hold by an opinion that CRP is the optimal predictor of IDPO in cows and backs up their words with specific studies and numerical results of their work. At the same time, other scientists hold by an opinion that the examination of CRP in IDPO in cows is not a sensitive method. Such disagreement, together with the few studies in this direction, is a prerequisite for further research in this area.

At present, it is clear that IDPOs increase CRP to amounts 3 to 4 times higher than the norm. Therefore, it is reasonable to study the amount of CRP in the serum of cows at IDPO, taking into account the maintenance factors.

## Conclusion

The determination of CRP for diagnosis and prevention of IDPO is reasonable to begin on the third day after delivery. When examining CRP, it is necessary to take into account the conditions in which the animals are kept. An increase in the amount of CRP over 60 mg/ml is an informative indicator of postpartum inflammation (endometritis) with sensitization of 79% and high informative value of 93%.

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