

## VETERINARY RESEARCH

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**THE PATHOGENETIC ROLE OF GLYCOPROTEINS AND PROTEOGLYCANS IN DOG GLOMERULONEPHRITIS****Dmytro Morozenko, Yevheniia Vashchyk, Andriy Zakhariev, Seliukova Nataliia, Dmytro Berezhnyi, Kateryna Glibova**

**The aim:** to determine the main pathogenetic links of glomerulonephritis in dogs with the participation of connective tissue biopolymers.

**Materials and methods** The research was conducted by analyzing the sources of scientific literature (PubMed, Elsevier, electronic resources of the V. I. Vernadskyi National Library) and the clinical experience of the authors, thanks to which a scheme of the pathogenesis of glomerulonephritis in dogs with the participation of connective tissue biopolymers was developed.

**Results.** According to the results of our research, it was established, that chronic glomerulonephritis in dogs is accompanied by neutrophilia, lymphocytosis, as well as urinary and nephrotic syndromes, the progression of which causes a violation of the functional state of the kidneys and liver. Sick dogs develop a nephrotic symptom complex – persistent proteinuria, hypoalbuminemia, dysproteinemia, and hyperlipidemia. Clinically, edema was not observed, because it is known, that in dogs they are rarely detected with nephrotic syndrome. Inflammation in the kidneys is accompanied by an increase in the concentration of glycoproteins and sialic acids in the blood serum. After treatment, there was a decrease in the inflammatory process in the kidneys, which was manifested by a decrease in neutrophilia and lymphocytosis, as well as the content of glycoproteins and sialic acids in the blood serum. The content of total chondroitin sulfates and the fractional composition of glycosaminoglycans did not change, and the level of excretion of oxyproline and uronic acids decreased compared to the indicators before the start of treatment. This, in our opinion, is due to the slowing down of fibrotic processes in the kidneys. Thus, biochemical indicators of the state of connective tissue in the blood serum and urine of dogs with glomerulonephritis allowed us to evaluate the functional state of the kidneys for their inflammation (oxyproline and uronic acids), as well as to determine the violation of proteoglycan synthesis in nephrotic syndrome.

**Conclusions.** For glomerulonephritis in dogs on the background of depression, decreased appetite, polydipsia, pain during palpation in the lumbar region, periodic vomiting, neutrophilic leukocytosis, lymphocytosis, nephrotic syndrome (hypoalbuminemia, increase in  $\alpha$ - and  $\beta$ -globulins, cholesterol,  $\beta$ -lipoproteins), growth activity of ALT, AST, and alkaline phosphatase, a decrease in Veltman's test, hyperazotemia, hyperphosphatemia, proteinuria, microhematuria, and cylindruria, there is an increase in the content of glycoproteins, sialic acids, and chondroitin sulfates, as well as heparan sulfate in the blood serum of dogs. The increase in the blood serum of patients with canine glomerulonephritis, as a marker of connective tissue – glycoproteins, sialic acids, chondroitinsulfates, and urinary excretion of oxyproline and uronic acids is due to inflammatory and fibrotic changes in the basal membranes of the kidney glomeruli

**Keywords:** dogs, pathogenesis, glomerulonephritis, glycosaminoglycans, glycoproteins, oxyproline, uronic acids

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**1. Introduction**

Glomerulopathies are diseases of the kidneys, characterized by typical clinical manifestations, impaired glomerular filtration, tubular reabsorption and secretion, respectively, impaired urine production, caused exclusively by the localization of damage in the renal glomerulus. The most important glomerulopathies are glomerulonephritis and amyloidosis, their frequency increases with age. Glomerular diseases are more

common in dogs and less often in cats. These disorders often have an immunological substrate. Proteinuria is a marker for the diagnosis of glomerulopathies [1, 2].

An important issue of modern nephrology is the pathogenetic and structural role of one of the GAG (glycosaminoglycans) – heparansulfate in the basal membrane of the glomerular apparatus of the kidney. Recent studies have questioned the classic theory of the glomerular filtration mechanism based on the negative

charge theory. However, it remains likely that heparansulfate in the basal glomerular membrane plays a significant role in increasing the glomerular filtration barrier [3, 4]. The basement membrane of renal glomerular capillaries consists of a number of components, which include collagen IV and V types, fibronectin, laminin, as well as negatively charged heparan sulfate proteoglycans. All these components of the basement membrane form its corresponding electrostatic charge, the change of which is essential for the development of proteinuria [5, 6].

A study was conducted in rats to determine whether proteinuria is caused by degradation of GAG in the glomerular basement membrane. Rats of the first group were injected intravenously with heparinase to destroy the glomerular basement membrane. Urine samples were taken for research at certain time intervals, and at the end of the experiment, the animals underwent kidney extirpation. Heparinase injection ended with complete degradation of glomerular heparan sulfate, which was confirmed by immunofluorescence reaction with specific staining. However, proteinuria was not detected in any sample, and no morphological changes were detected in the kidneys. The rats of the second group were intravenously injected with neuraminidase, and urine samples were taken at certain time intervals for research. In this group of animals, massive proteinuria was observed, which was combined with an increase in the content of neuraminic acid in the urine. Specific lectin staining of renal glomeruli indicated a decrease in neuraminic acid [7]. Thus, degradation of heparan sulfate in the glomerular basement membrane is not

accompanied by proteinuria, whereas degradation of neuraminic acid causes massive proteinuria. It is also known about the important role of heparansulfate in the development of glomerular inflammation [8, 9].

**The aim of the research** to analyze clinical cases of diabetes mellitus in cats and to establish the effectiveness of clinical and laboratory research and treatment of animals with the help of insulin therapy.

**2. Materials and methods**

The research was conducted by analyzing the sources of scientific literature (PubMed, Elsevier, electronic resources of the V. I. Vernadskyi National Library) and the clinical experience of the authors, thanks to which a scheme of the pathogenesis of glomerulonephritis in dogs with the participation of connective tissue biopolymers was developed.

**3. Research results**

According to the results of our research, it was established, that chronic glomerulonephritis in dogs is accompanied by neutrophilia, lymphocytosis, as well as urinary and nephrotic syndromes, the progression of which causes a violation of the functional state of the kidneys and liver. Sick dogs develop a nephrotic symptom complex – persistent proteinuria, hypoalbuminemia, dysproteinemia, and hyperlipidemia. Clinically, edema was not observed, because it is known, that in dogs they are rarely detected with nephrotic syndrome. The development of the above disorders causes changes in the blood and urine of sick animals (Fig. 1)

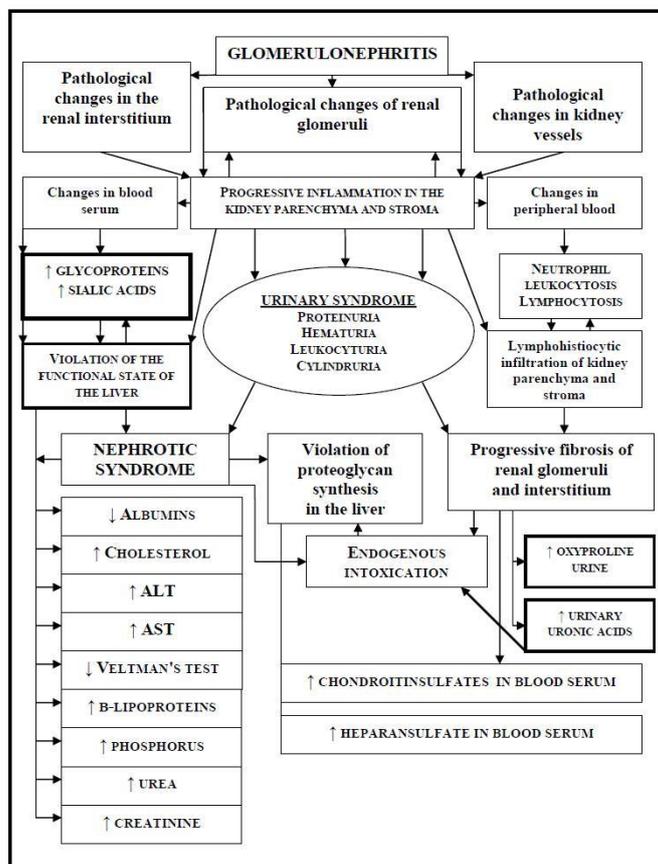


Fig. 1. Pathogenetic role of connective tissue metabolism disorders in canine glomerulonephritis: ↑ – growth of the indicator; ↓ – reduction of the indicator

It is known, that in nephrotic syndrome there is a violation of the synthesis of proteoglycans in the liver, during which the concentration of total chondroitinsulfates and heparansulfate increases in the blood serum [10]. In this case, the progressive inflammatory process in the glomerular apparatus of the kidneys causes the degradation of the glomerular basement membranes, as well as inflammatory-dystrophic changes in the tubules (hydropic and fatty dystrophy). The complex of pathological changes causes the progression of glomerular fibrosis and interstitium, which leads to a violation of the catabolism of collagen and GAG in the kidneys with an increase in the excretion of oxyproline and uronic acids. Inflammation in the kidneys is accompanied by an increase in the concentration of glycoproteins and sialic acids in the blood serum, as well as degradation of heparan sulfate [6, 11]. In the course of treatment, part of animals, suffering from glomerulonephritis, died. The cause of the death of the animals may have been the development and progression of mesangiosclerosing glomerulonephritis or amyloidosis of the kidneys, which in case of exacerbation are characterized by a rapid course and always an unfavorable prognosis. In the rest of the dogs, one of the possible factors in the development of chronic glomerulonephritis was the secondary microflora due to endometritis, which was transferred by the animals a few months before the diagnosis of glomerulonephritis and turned into a chronic form. In the rest of the experimental dogs, the root cause of the development of glomerulonephritis was not established. After treatment, there was a decrease in the inflammatory process in the kidneys, which was manifested by a decrease in neutrophilia and lymphocytosis, as well as the content of glycoproteins and sialic acids in the blood serum. The content of total chondroitin sulfates and the fractional composition of GAG did not change, and the level of excretion of oxyproline and uronic acids decreased compared to the indicators before the start of treatment. This, in our opinion, is due to the slowing down of fibrotic processes in the kidneys. Thus, biochemical

indicators of the state of connective tissue in the blood serum and urine of dogs with glomerulonephritis allowed us to evaluate the functional state of the kidneys for their inflammation (oxyproline and uronic acids), as well as to determine the violation of proteoglycan synthesis in nephrotic syndrome.

**Research limitations.** The research was analytical in nature and based on the modern literature and clinical experience of the authors in the diagnosis of glomerulonephritis in dogs.

**Prospects for further research.** A promising direction of research is the study of the biochemical methods of the diagnostic of glomerulonephritis in dogs.

#### 4. Conclusions

For glomerulonephritis in dogs on the background of depression, decreased appetite, polydipsia, pain during palpation in the lumbar region, periodic vomiting, neutrophilic leukocytosis, lymphocytosis, nephrotic syndrome (hypoalbuminemia, increase in  $\alpha_2$ - and  $\beta$ -globulins, cholesterol,  $\beta$ -lipoproteins), growth activity of ALT, AST, and alkaline phosphatase, a decrease in Veltman's test, hyperazotemia, hyperphosphatemia, proteinuria, microhematuria, and cylindruria, there is an increase in the content of glycoproteins, sialic acids, and chondroitin sulfates, as well as heparan sulfate in the blood serum of dogs. The increase in the blood serum of patients with canine glomerulonephritis, as a marker of connective tissue – glycoproteins, sialic acids, chondroitinsulfates, and urinary excretion of oxyproline and uronic acids is due to inflammatory and fibrotic changes in the basal membranes of the kidney glomeruli.

#### Conflict of interests

The authors declare that they have no conflict of interest in relation to this research, whether financial, personal, authorship or otherwise, that could affect the research and its results, presented in this article.

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