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Cardiogenic and Non-Cardiogenic Pulmonary Oedema in a Domestic Cat: Pathological Mechanisms, Differential Diagnosis, and Treatment

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Abstract. The relevance of this study is conditioned upon the prevalence of pulmonary oedema in cats and special approaches to their therapy. In this regard, this paper is aimed at identifying aetiological factors, breed predisposition, clinical manifestations, haematological parameters, and radiological signs. Leading in the study of this issue is an integrated approach, which includes consideration of the aetiology, pathogenesis, diagnosis of cardiogenic and non-cardiogenic pulmonary oedema and treatment of cats. It was found that in the conditions of the "Vet House" Veterinary Centre (Vinnytsia), cats of the British Shorthair, Sphinx, Maine Coon breeds and their hybrids were most often registered with this pathology. 68 cats were diagnosed with cardiogenic pulmonary oedema due to hypertrophic, restrictive, and unclassified cardiomyopathy. 42 animals were found to have non-cardiogenic pulmonary oedema due to traumatic brain injury, toxic substance poisoning, anaphylactic reaction, airway obstruction, and electric shock. It was found that the most informative during the differential diagnosis of pulmonary oedema in cats are the results of echocardiography and X-ray examination. It was established that for the differential diagnosis of cardiogenic and non-cardiogenic pulmonary oedema, clinical indicators and results of haematological examination of animals are low in information. It was discovered that therapeutic measures for pulmonary oedema are effective in considering aetiological factors, although at the first stage, for both forms of pulmonary oedema, they are aimed at reducing and eliminating the manifestations of acute respiratory failure. The materials of this paper are of practical value for veterinary doctors of general practice and intensive care on differential diagnosis, prediction of the development of the disease and effective treatment of cats

Keywords: biochemical and morphological parameters of blood, shortness of breath, interstitial pattern, pathogenesis, radiography

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Introduction

Pulmonary oedema in a domestic cat develops quickly and threatens the animal's life. For cardiomyopathy complicated by pulmonary oedema, mortality among cats is 23%, regardless of the age of the animal at the time of diagnosis [1]. Different forms of the disease can have various clinical manifestations and course. In the first stages of the development of the disease, cats may not show any symptoms at all and appear absolutely healthy. Therefore, it is exceedingly difficult to detect and prevent this disease [2]. However, during a clinical examination, a veterinary doctor may detect some early symptoms of cardiovascular diseases. A range of factors can lead to acute pulmonary oedema, but the most common among them are cardiovascular diseases, electric shock, poisoning, asthma, injuries, sepsis, and shock. The physiological movement of fluid through the vascular membrane into the surrounding tissues depends on three factors – membrane permeability, oncotic pressure gradient, and hydrostatic pressure [3-5]. As an added factor, the state of the lymphatic drainage system counteracts extravascular fluid. Oedema develops if one of these factors is disturbed so much that it cannot be compensated. There are two main types of pulmonary oedema: cardiogenic and non-cardiogenic [3; 4]. Accurate differential diagnosis is based on data from clinical and radiological examinations.

Pulmonary oedema is the accumulation of extravascular fluid inside the pulmonary parenchyma or alveoli. The two main forms of the disease are high-pressure oedema (due to increased hydrostatic pressure in the capillaries of the lungs) and high-permeability oedema (due to damage to the microvascular barrier and alveolar epithelium in more severe cases). According to various scientific sources, for the development of pulmonary oedema, it is always necessary to increase intravascular hydrostatic pressure or disrupt vascular permeability [2-4].

Pulmonary oedema leads to a decrease in oxygenation, usually due to a mismatch between ventilation and perfusion; and therefore, 98% of animals have symptoms of respiratory failure. Some of these patients are extremely vulnerable to stress. Therefore, before even conducting a clinical examination, it is worth considering evaluating the risk-benefit ratio. Oxygen therapy should be given to all patients with respiratory failure. Initial diagnostic assessment should be aimed at identifying the severity of the respiratory disease and the underlying cause [5].

As with many critical conditions, the severity of the course of the disease is often inversely proportional to the duration of clinical symptoms. In animals with symptoms of pulmonary oedema, during auscultation of the lungs, "crackling" is not heard in all cases. However, 80% of patients will hear either loud lung sounds or "crackling" sounds. It is especially difficult to hear the sounds of "crackling" and "crunching" in the lungs in patients with rapid breathing and small respiratory volume. Careful auscultation can help localise abnormal lung sounds in one area, and it can help in diagnostics, for example, differentiate between traumatic brain injury and aspiration pneumonia [6].

Differentiation between cardiogenic and non-cardiogenic oedema is critical for patient survival, as the treatment of these conditions varies. It is even more important to determine the particular cause of non-cardiogenic oedema, not only from a therapeutic, but especially from a prognostic standpoint. Depending on the cause, the prognosis can range from unfavourable to favourable [7]. According to foreign scientists, pulmonary oedema causes life-threatening respiratory disorders in cats, which requires their artificial ventilation for 50-60% of animals [6; 8]. Therewith, cardiogenic pulmonary oedema is diagnosed in 68.5% of cats, non-cardiogenic – in 31.5% of animals and is a common pathology [5; 7; 8].

Finding the factors of occurrence of pulmonary oedema is the leading point affecting the success of treatment of an animal. In 45% of cats, the medical history of the disease is non-specific, and changes in clinical parameters are atypical. A critical situation for the animal is also severe shortness of breath, which can lead to threatening decompensation due to a stress reaction in response to conducting differential diagnostics. Heart failure can be suspected based on the animal's anamnesis data on the presence of previously diagnosed cardiomyopathy or cardiomyopathy of genetic origin. A history of coughing or wheezing in cats with heart failure is infrequent and, in 87% of cases, is a manifestation of respiratory tract pathology [9].

With cardiogenic pulmonary oedema, the life expectancy of an animal is affected by the degree of damage to their parenchyma, visualised by radiography, the presence of systolic dysfunction, and changes in the size of the left atrium during heart sonography. It was proved that spontaneous contrast and the size (thickness) of the left ventricular myocardium do not affect the patient's life expectancy at the beginning of hospitalisation [7; 10; 11].

Acute respiratory distress syndrome (ARDS) can provoke the development of non-cardiogenic pulmonary oedema [12; 13]. It is based on severe diffuse damage to the pulmonary parenchyma, which leads to a violation of the permeability of the endothelium and epithelium and the appearance of oedema with a high-protein content. This syndrome is often the result of primary lung damage, such as inhalation of toxic gases (smoke poisoning) and hyperbaric oxygen (oxygen poisoning), aspiration of stomach contents, and pneumonia. It can also occur as a complication of serious systemic diseases such as sepsis, burns, and acute pancreatitis. At the same time, the prognosis is unfavourable even in the case of overly complex maintenance therapy [5; 8]. The pathogenesis of ARDS is understudied.

Another important group of causes of non-cardiogenic pulmonary oedema is neurogenic oedema. Excessive sympathetic adrenergic activation leads to a redistribution of blood from the large to small circulatory system, an increase in hydrostatic pressure, and, finally, the development of oedema. Causes include head trauma, epileptic seizures, and electric shock [7; 14].

Thus, due to the low attention of Ukrainian scientists to the aetiology, mechanism of development, treatment, and prognosis of pulmonary oedema in a domestic cat, due to the lack of publications on the clinical practice of Ukrainian veterinary doctors, this issue requires research.

The purpose of this study was to determine the features of the aetiology, pathogenesis, diagnosis of cardiogenic and non-cardiogenic pulmonary oedema and treatment of cats in conditions of Ukrainian veterinary clinics.

To achieve this purpose, it was necessary to perform the following tasks: to identify the most common aetiological factors, breed predisposition, clinical symptoms of this pathology, radiological and haematological indicators, the mechanism of its development in a domestic cat, to investigate

and justify the protocol of differential diagnosis and treatment of cats, depending on the form of the disease.

Materials and Methods

The study was performed based on the Veterinary Centre "Vet House" (Vinnytsia) in 2018-2022, considering the requirements of the European Convention for the protection of vertebrates that are used for experimental and other purposes (Strasbourg, 1986), the European Convention for the protection of domestic animals (2013) and the Law of Ukraine "On the Protection of Animals from Ill-treatment" (2006) [15-17]. The registration forms of the electronic database of animal registration, the owners of which applied to the "Vet House" Veterinary Centre, were evaluated. For this study, cats with pulmonary oedema who were admitted to a veterinary centre were selected to stabilise their serious condition. The diagnosis was established based on data from a clinical examination of animals, the results of chest X-ray examination, echocardiography (EchoCG) and laboratory analysis of blood samples. During 2018-2022, 110 cats were examined with a diagnosis of "pulmonary oedema". The average body weight of the animals was 4.0±0.4 kg, and their average age was 7 years (from 2 to 12 years). Sick animals were divided into two experimental groups according to the form of pulmonary oedema. The first study group (cardiogenic oedema) included 68 cats, the second study group (non-cardiogenic oedema) – 42 animals. In cats of both groups, differential diagnosis was evaluated based on the results of clinical examination, echocardiography, radiography, and laboratory analysis of blood parameters. The control group included ten clinically healthy cats who underwent a preventive examination at the "Vet House" Veterinary Centre.

Special studies of the clinical condition of animals were carried out using an ultrasound machine (GE Logiq E9, USA) and an X-ray machine (MicroCC-20Plus, USA). During the ultrasound examination, basic measurements of the size of the heart were made. X-rays of the chest cavity were performed in direct and right lateral projections.

Laboratory blood tests were carried out based on the diagnostic laboratory of the veterinary centre using a semi-automatic biochemical analyser BS-3000M (SINNOWA, China) and reagents from the companies SpinLab (Ukraine) and High Technology Inc. (USA). Blood collection from cats was performed from the lateral or medial vein of the pelvic extremities (*v. safena*).

In blood serum, the concentration of total protein, glucose, albumin, total bilirubin, direct bilirubin, total calcium and inorganic phosphorus was determined by generally accepted colorimetric methods; activity of enzymes – alkaline phosphatase (ALP, EC 3.1.3.1), aspartate aminotransferase (AST, EC 2.6.1.1), alanine aminotransferase (ALT, EC 2.6.1.2) and gamma-glutamyl transferase (GGT, EC 2.3.2.2) – by kinetic methods.

The general clinical analysis of whole blood included counting erythrocytes and leukocytes in a chamber with a Goryaev grid using an Axioskop 40 microscope (ZEISS, Germany), determining the haemoglobin content according to the haemoglobin cyanide method with acetone cyanhydrin, deriving a leukogram according to the Schilling calculation method. Blood smears were stained with a set of paints "Leucodif 200" (LDF 200) (Erba Lachema s.r.o., Czech Republic). A puncture was performed, and blood was taken into test tubes with heparin. Potassium concentration was determined using a semi-automatic analyser Genrui GE-1, reagent – Pak GE500 (Genrui, China). The sample was measured using ion-selective electrodes for 1 min. 100 µL of blood was used to analyse the sample. The results were displayed and printed automatically.

For non-invasive monitoring, random verification, display, storage, and transmission of blood oxygen saturation information (SpO_2) the UT1OOV pulse oximeter (China) was used. The device works with particular sensors that provide SpO_2 measurements and the pulse rate in animals. The sensor was placed on an unpigmented area, usually the mucous membranes of the tongue and lips, as well as the prepuce, vulva, ear, or membranes between the fingers of the extremities.

A Pettrust automatic tonometer (BioCare, Taiwan), a battery-type device that measures blood pressure (systolic, diastolic, and mean) and heart rate in cats based on the principle of plethysmography, was used for non-invasive automated monitoring of blood pressure. The cuff of the device was applied to the pelvic limb or to the base of the animal's tail. The average value was calculated from 3-4 measurements of these indicators.

The resulting digital data was processed using Statistica 6.0 (StatSoft Inc., USA). The M±m format was used to represent the data in the table. Differences in $P<0.05$, $P<0.01$, and $P<0.001$ were considered statistically probable.

Results and Discussion

Among the cats with symptoms of pulmonary oedema under study, breed characteristics were established. These were cats of different breeds and mixed breeds, namely British Shorthair – 44 animals, Sphinx – 24, Maine Coon – 22, mixed breeds – 20 animals. 61.8% of cats with symptoms of pulmonary oedema were diagnosed with cardiomyopathy, among them: 47.0% were diagnosed with hypertrophic cardiomyopathy (HCMP), 26.5% – with restrictive cardiomyopathy (RCMP), 26.5% – with non-classified cardiomyopathy (NCMP) (Table 1). 38.2% of the animals were diagnosed with non-cardiogenic pulmonary oedema. The factors that caused non-cardiogenic pulmonary oedema included traumatic brain injury – in 35.7%, electric shock – in 23.8%, toxic substance poisoning – in 19.1%, anaphylactic reaction – in 11.9%, airway obstruction – in 9.5% of animals.

Table 1. Causes of pulmonary oedema in a domestic cat

Cardiogenic pulmonary oedema, n = 68		**Non-cardiogenic pulmonary oedema, n = 42**	
Hypertrophic cardiomyopathy	32	Traumatic brain injury	15
Restrictive cardiomyopathy	18	Electric shock	10
Non-classified cardiomyopathy	18	Poisoning with toxic substances	8
		Anaphylactic reaction	5
		Airway obstruction	4

In cats, cardiogenic pulmonary oedema was more likely to have an abrupt and severe course. The occurrence of symptoms in most cases was caused by corresponding stressful situations (visit to the clinic, fixation, ovariohysterectomy). The release of catecholamines into the blood causes vasoconstriction and increases blood volume during cardiac output, which leads to the sudden occurrence of clinical symptoms. As a result, the pressure in the cavity of the left ventricle, left atrium, and pulmonary veins increases (over 12 mm Hg and sometimes above 20, if the process is chronic). This causes an increase in hydrostatic pressure in the pulmonary veins and effusion of plasma into the interstitium of the lungs and pleural cavity [10; 18].

In 30 animals with symptoms of heart failure, tachypnoea (30-110 respiratory movements/min) and shortness of breath were observed, which develop due to pulmonary oedema and effusion of fluid into the pleural cavity. Paradoxical breathing was observed in 15 cats due to effusion into the pleural cavity. No changes (noise, gallop rhythm, or arrhythmia) were observed during cardiac auscultation in 13 animals. During the examination, 10 cats showed pallor of the visible mucous membranes (conjunctiva and gums), weak pulse, sometimes a decrease in body temperature (36.5-37.5°C), arrhythmia, noise, weak/filamentous pulse, and prolonged capillary filling time with blood.

Among all animals with symptoms of heart failure, changes in the lungs and pleural cavity were detected during X-ray examination. The most characteristic of them were visualisation of the interstitial pattern in the lung parenchyma of varying severity in 38 animals, free fluid in the chest cavity was visualised in 14 animals, and a more pronounced venous pattern of the lungs was noted in 16 animals.

The development of non-cardiogenic oedema occurs by various pathological mechanisms: a decrease in alveolar pressure (rapid removal of fluid or air from the pleural cavity, obstruction of the upper respiratory tract), an increase in vascular permeability, an increase in hydrostatic intravascular pressure, and a combination of these mechanisms [10; 11].

Pulmonary oedema due to obstruction of the cranial (upper) airway in cats is more often recorded than diagnosed. Many cases of post-obstructive oedema are misinterpreted as cardiogenic oedema, since shortness of breath and oedema occur due to physical exertion or a stressful situation, e.g., oedema due to laryngeal paralysis or oedema during or after anaesthesia, or because the animal has two pathologies at once [19].

Another important group of causes of non-cardiogenic pulmonary oedema is neurogenic oedema. Excessive sympathetic adrenergic activation leads to a redistribution of blood from the large to small circulatory system, an increase in hydrostatic pressure, and, finally, the development of oedema. Potential causes include head trauma, epileptic seizures, and electric shock [14; 20]. Acute respiratory distress syndrome (ARDS) is a substantial provoking factor in the development of non-cardiogenic pulmonary oedema. It is based on severe diffuse damage to the pulmonary parenchyma, which leads to a violation of the permeability of the endothelium and epithelium and the occurrence of oedema with a considerable protein content. Despite the insufficient study of the pathogenesis of ARDS, the main pathogenetic links of its development are as follows [21]:

1. The accumulation of numerous activated white blood cells and platelets, which excessively secrete biologically active substances (proteinases, lipid peroxidation products, leukotrienes, etc.) damages the epithelium of alveoli and blood vessels and changes the tone and reactivity of blood vessels. White blood cells enter the reactive process zone, and the lung parenchyma infiltrates.

2. Due to the altered vascular permeability, plasma, and red blood cells enter the alveoli and interstitium and develop pulmonary oedema and atelectasis.

3. With a considerable surfactant deficiency, hypoventilation of the alveoli occurs, the elasticity of their wall decreases, disc-shaped atelectasis, venous blood shunts into the arterial bed are formed, the process of ventilation-perfusion, oxygen and carbon dioxide diffusion is disrupted, hypoxia and hypercapnia develop.

4. In the absence of circulatory pathology, increased pressure in the pulmonary artery is a characteristic manifestation of pulmonary oedema.

Acute respiratory distress syndrome is often the result of primary lung damage, such as inhalation of toxic gases (smoke poisoning), aspiration of stomach contents, inhalation of hyperbaric oxygen (oxygen poisoning), and pneumonia. It can also occur as a complication of serious systemic diseases such as sepsis, burns, and acute pancreatitis. This syndrome is a known complication of the aforementioned diseases [14; 22], and the prognosis is unfavourable, even with very complex maintenance therapy.

A decrease in alveolar pressure develops after rapid removal of a pleural effusion, pneumothorax, or lung lobes, called re-dilation oedema. Mortality from this rare complication in humans is possible in 20%. In veterinary medicine, 2 cases were described among cats that died [5].

A decrease in alveolar pressure is also the result of obstruction of the cranial (upper) airways, called post-obstructive oedema, e.g., laryngeal paralysis, tracheal collapse, during intubation and bronchoscopy [19].

Oncotic pressure primarily depends on the concentration of albumin in the blood plasma and is one of the essential factors of fluid retention inside the vessels. The interstitial space of the lungs usually has a higher concentration of albumin than other interstitial tissue, and a small oncotic gradient, since the permeability of the pulmonary capillaries is higher than in other capillaries. When the plasma albumin content decreases, the concentration of albumin in the interstitium also decreases, and this substantially affects the oncotic gradient. Thus, it is unusual to detect pulmonary oedema when hypoalbuminemia is the only detected anomaly [18; 21].

Animals diagnosed with pulmonary oedema showed changes during auscultation of the lungs and heart (noise, gallop rhythm, arrhythmia). Cats in both groups were most likely to have tachypnoea or orthopnoea, respiratory distress, and cough. Patients with primary heart disease were diagnosed with arrhythmia, murmur, weak/filamentous pulse, and slow capillary refill rate (CRR). These changes were observed very unevenly in animals of both groups, and therefore it is impossible to diagnose pulmonary oedema only by symptoms in cats. Special research methods (chest X-ray, echocardiography) were used to confirm the diagnosis. Consequently, respiratory distress was the primary clinical sign for all examined animals with pulmonary oedema.

Radiologically, pulmonary oedema was described by a decrease in the transparency of the lung area and image instability (Figs. 1, 2). Radiographs of all the cats under study showed signs of a reticulated or granular interstitial pattern (Table 2). According to the features of changes in the pulmonary pattern for pulmonary oedema, radiographs were divided into groups: with diffuse/uneven pattern in 35 animals (31.8%); diffuse/uniform in 23 (20.9%); pronounced alveolar pattern in 52 (47.3%). Among the radiographs that visualised a pronounced alveolar pattern, there were air bronchograms in 66 animals (60%) and with an increased diameter of pulmonary vessels and a bronchial pattern in 44 animals (40%). According to the localisation of the process in the lungs, changes were visualised in the following areas: regionally in 37 animals (33.6%), ventrally in 33 animals (30%), caudally in 30 animals (27.3%), and in 10 animals (9.1%) – ventrally with subsequent spread. X-ray symmetry of lung structure damage, which was assessed by studying dorsoventral or ventrodorsal projections, could be determined for 33 animals (30%), in the remaining 77 animals (70%), X-ray lesions of the lung structure were asymmetrical in these projections. Areas of reduced lung transparency were bilaterally symmetrical in 42 animals (38.2%). In the remaining 52 (47.3%) of the animals under study, the lesion of the lung structure on radiographs was asymmetric, and in 16 (14.5%) of them – mainly right-sided.

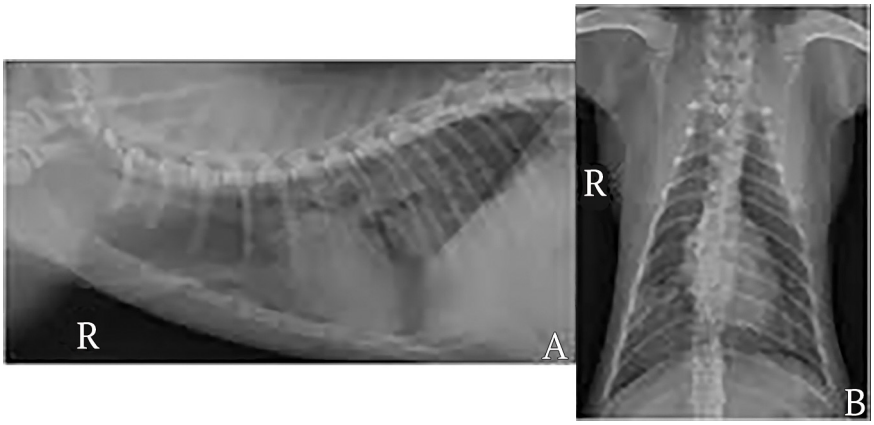

Figure 1. Mediolateral (A) and ventrodorsal (B) X-ray of the chest cavity of cats with signs of noncardiogenic pulmonary oedema; (R) right lung

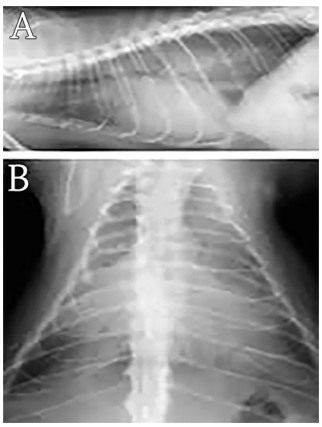

Figure 2. Mediolateral (A) and ventrodorsal (B) chest X-ray of cats with signs of cardiogenic oedema of lungs

Table 2. The most characteristic changes on radiographs of the chest cavity in cats with pulmonary oedema

Cardiogenic pulmonary oedema, n=68		**Non-cardiogenic pulmonary oedema, n=42**	
Description of pattern changes	**Quantity, (%)**	**Description of pattern changes**	**Quantity, (%)**
Pronounced mesh interstitial pattern with alveolar pattern and an increased diameter of pulmonary vessels	27 (39.7%)	Pronounced granular interstitial pattern with alveolar pattern and pronounced bronchial pattern	25 (59.5%)
Diffuse, inhomogeneous, asymmetrical interstitial pattern	22 (32.4%)	Diffuse, inhomogeneous, asymmetrical interstitial pattern	13 (31.0%)
Diffuse, uniform, symmetrical interstitial pattern	19 (27.9%)	Diffuse, uniform, symmetrical interstitial pattern	4 (9.5%)

Lateral radiographic projections mainly involved the caudodorsal quadrant of the pulmonary field. As a rule, animals with non-cardiogenic pulmonary oedema due to airway obstruction had the greatest degree of radiographic damage to the structure of the lungs. After them, the decrease was followed by animals with pulmonary oedema caused by craniocerebral trauma and electric shock.

To assess the severity of lung damage, the area of lesions was calculated on radiographs. Thus, local or diffuse lesions of the interstitial lung tissue that did not exceed 25% of the lung area on the radiograph were found in 30 animals; parenchymal lesions covering up to 50% of the lung area on the radiograph – in 45 animals; lung parenchymal lesions over 75% of the lung area on radiographs – in 35 animals.

Most of the values of the blood parameters of experimental cats for pulmonary oedema did not go beyond the physiological limits, and there was no statistically significant difference between them, depending on the form of oedema (Table 3).

Table 3. Haematological parameters in experimental cats, M±m, n=10

Indicator			Reference limits	Clinically healthy	Cardiogenic pulmonary oedema	Non-cardiogenic pulmonary oedema
Haemoglobin, g/L Lim $_{min-max}$			100-150	126.4 ± 2.8 115-142	139.7 ± 5.2* 122-159	139.2 ± 5.2* 112-167
Red blood cells, x10^{12}/L Lim $_{min-max}$			5.8-10.7	7.4 ± 0.4 5.9-9.3	8.2 ± 0.5 5.8-10.4	7.6 ± 0.5 5.9-10.0
White blood cells, x10^{9}/ L Lim $_{min-max}$			5-14	8.0 ± 0.8 5.4-14.0	15.8 ± 1.4*** 7.9-21	20.7 ± 2.5*** 12.4-34.4
Haematocrit value, % Lim $_{min-max}$			30-47	36.7 ± 0.9 32.6-41.8	41.9 ± 2.1* 32.6-51.0	39.3 ± 1.4 34.4-47.8
Platelets, x10^{9}/L Lim $_{min-max}$			200-600	373.3 ± 37.1 238-567	413.3 ± 55.8 212-634	428.4 ± 48.2 224-664
Thrombocrit, % Lim $_{min-max}$			0.1-0.5	0.32 ± 0.04 0.2-0.5	0.37 ± 0.05 0.2-0.6	0.37 ± 0.05 0.2-0.6
Leukogram, %	Basophils Lim $_{min-max}$		0-1	0.2 ± 0.1 0-1	0.7 ± 0.3 0-2	0.6 ± 0.3 0-2
	Eosinophils Lim $_{min-max}$		0-8	2.3 ± 0.7 0-6	5.9 ± 0.9** 1-10	5.1 ± 0.9* 1-10
	Neutrophils:	rod-shaped Lim $_{min-max}$	1-6	3.2 ± 0.4 1-6	5.2 ± 0.5** 2-8	5.5 ± 0.8* 1-9
		segmented Lim $_{min-max}$	40-68	52.3 ± 1.9 44.5-60.5	79.5 ± 3.2*** 69.4-93.5	75.2 ± 4.8*** 45.6-94.6
	Lymphocytes Lim $_{min-max}$		25-40	31.6 ± 1.8 25.0-37.7	43.2 ± 2.8** 39.5-55.0	39.0 ± 3.0* 26.4-58.5
	Monocytes Lim $_{min-max}$		0-5	1.7 ± 0.6 0-4	5.2 ± 0.7** 2-9	3.8 ± 0.5* 1-6
Total protein, g/L Lim $_{min-max}$			55-76	62.9 ± 2.4 56.1-75.4	63.7 ± 2.3 56.7-76.3	65.9 ± 2.2 56.3-75.6
Albumin, g/L Lim $_{min-max}$			25-40	32.4 ± 1.3 26.4-35.9	47.1 ± 3.4** 30.4-65.0	40.9 ± 3.4 26.9-65.4
Glucose, mmol/L Lim $_{min-max}$			1.6-6.5	5.2 ± 0.3 3.8-6.4	6.84 ± 0.50* 3.7-9.4	6.05 ± 0.72 3.0-9.3
Urea, mmol/L Lim $_{min-max}$			5.5-11.0	7.4 ± 0.6 5.5-10.6	15.9 ± 1.0*** 12.0-23.5	17.8 ± 2.7** 3.0-35.0
Creatinine, µmol/L Lim $_{min-max}$			50-140	83.4 ± 9.3 52.0-120.4	134.9 ± 15.2** 69.4-220.0	205.1 ± 35.1** 78.0-437.0
Total calcium, mmol/L Lim $_{min-max}$			2.0-2.7	2.36 ± 0.08 2.1-2.7	2.28 ± 0.08 2.0-2.5	2.31 ± 0.09 2.0-2.6

Table 3, Continued

Phosphorus inorg., mmol/L Lim $_{min-max}$	0.9-1.7	1.32 ± 0.09 0.9-1.7	1.86 ± 0.09** 1.1-2.2	1.96 ± 0.23* 0.9-3.2
Potassium, mmol/L Lim $_{min-max}$	3.5-5.3	4.49 ± 0.19 3.7-5.3	5.51 ± 0.21** 4.3-6.3	5.12 ± 0.41 3.2-6.5
Total bilirubin, μmol/L Lim $_{min-max}$	0.5-10.0	6.3 ± 0.8 2.7-3.5	6.0 ± 0.9 2.1-10.0	4.9 ± 0.7 2.4-9.5
Direct bilirubin, μmol/L Lim $_{min-max}$	0.5-8.0	5.4 ± 0.6 2.4-8.4	5.39 ± 0.45 3.0-7.4	4.96 ± 0.62 3.0-8.0
Alkaline phosphatase, U/L Lim $_{min-max}$	12.0-100.0	47.2 ± 7.3 11.5-68.5	96.4 ± 16.9* 12.0-165.4	93.3 ± 9.7** 54.6-156.0
Alanine aminotransferase, U/L Lim $_{min-max}$	5.0-75.0	42.7 ± 7.7 14.7-69	145.3 ± 9.4*** 98.6-189.0	109.2 ± 7.4*** 84.7-154.0
Aspartate aminotransferase, U/L Lim $_{min-max}$	5.0-50.0	40.9 ± 6.2 13.9-94.8	108.8 ± 11.6*** 65.3-176.9	89.5 ± 10.1$_{***}$ 45.6-134.0
Gamma-glutamyltransferase, U/L Lim $_{min-max}$	0-10.0	5.8 ± 0.9 1.0-8.5	8.7 ± 1.3 4.9-16.4	8.3 ± 0.7$_{*}$ 5.6-12.5

Note: * *P<0.05,* ** *P<0.01,* *** *P<0.001 relative to the indicators of clinically healthy cats*

At the same time, in the blood of animals with cardiogenic pulmonary oedema, a probable increase was found: the number of white blood cells by 2.0 times, neutrophils by 29%, lymphocytes by 11.6%, eosinophils by 3.6%, monocytes by 3.5%, haematocrit value by 5.2%; the content of haemoglobin by 9.5%, albumin by 1.3 times, glucose by 1.2 times, urea by 2.1 times, creatinine by 1.6 times, phosphorus inorganic by 1.3 times, potassium by 1.2 times; ALT activity by 3.4 times, AST by 2.7 times, and ALP by 2.0 times, compared to clinically healthy cats (Table 3). In the blood of cats with non-cardiogenic pulmonary oedema, a probable increase was found: the number of white blood cells by 2.6 times, neutrophils by 25.2%, lymphocytes by 7.4%, eosinophils by 2.8%, monocytes by 2.1%; haemoglobin content by 9.0%, urea by 2.4 times, creatinine by 2.5 times, inorganic phosphorus by 1.3 times; ALT activity by 2.6 times, AST by 2.2 times and GGT by 1.3 times compared with the indicators of clinically healthy cats (Table 3). However, the results of morphological and biochemical studies of pulmonary oedema in cats constitute an added diagnostic method and allow determining the severity of the disease.

In case of lung pathology complicated by the development of acute renal failure (ARF), an increased concentration of creatinine and urea was recorded in the blood serum of cats. Upon the occurrence of pulmonary oedema of non-cardiogenic origin, the manifestation of the clinical picture of the disease in patients was determined by changes caused by the underlying disease. With the simultaneous development of acute hepatic insufficiency syndrome in the blood serum of cats, the activity of aminotransferases and GGT increased.

Arterial blood sampling is invasive and requires high qualification for rapid execution. This does not always depend on the severity of the patient's shortness of breath. But if the patient's condition allows for this manipulation, it was an ideal method for determining the clinical condition of the animal. More information can be obtained by calculating the alveolar-arterial oxygen gradient (Aa gradient). Then the $AaDO_2$ gradient is a comparison of the concentration of oxygen in the alveoli with the concentration of arterial blood. Values over 20 mm Hg. Art. may indicate a ventilation/perfusion mismatch.

In case of failure to collect arterial blood from the patient to assess the concentration of oxygen-rich haemoglobin, pulse oximetry (SpO_2) was used. Pulse oximetry is fast, non-invasive, and easily tolerated by most patients. Normal SpO_2 values for a patient who breathes room air are 95-99%. Patients with SpO_2 under 93% are considered hypoxemic and require added oxygenation.

Pathogenetic treatment used in animals for pulmonary oedema differed in several features depending on aetiological factors. At the initial stage of development of the disease, treatment tactics were aimed at reducing the clinical manifestation of acute respiratory failure.

To stimulate respiratory function, patients were given an oxygen mask or placed in a special oxygen chamber. Liquid therapy was developed for each animal individually.

At the beginning of treatment, most sick animals were unable to eat food and drink water on their own. Isotonic crystalloids, namely Ringer's solution and Ringer's lactate, were administered to maintain proper hydration and replace body losses. However, a sharp increase in intravascular volume can provoke an increase in hydrostatic pressure in the lungs and lead to a deterioration in the patient's health. Therefore, colloidal therapy is recommended for patients who do not have haemodynamic stability. Hetastarch® and Vetstarch® are large molecular weight hydroxyethyl starches that help maintain colloidal oncotic pressure and maintain blood pressure. Administration of these solutions to patients was avoided if substantial damage to the pulmonary endothelium was suspected, since these large molecules seep into the alveolar spaces. This can lead to a sharp deterioration in the patient's clinical condition [8; 20].

There is some debate about whether furosemide can be effective in treating cats with non-cardiogenic pulmonary oedema. Furosemide is a loop diuretic that is used to promote the free elimination of water and salt by the kidneys and is extremely effective in treating cardiogenic pulmonary oedema. However, it is not useful for patients with non-cardiogenic pulmonary oedema due to alveolar epithelial disorders and exudative effusion. Some studies have shown that low-dose, constant-rate furosemide infusion can be beneficial for patients by reducing capillary pressure in the lungs and reducing the amount of fluid "filling" lung tissue in patients with changes in permeability [22].

β_2-Adrenoceptor agonists such as terbutaline and albuterol have also been used to treat patients with non-cardiogenic pulmonary oedema. Although the effectiveness of these drugs is unknown, it is believed that by triggering receptors lining the alveolar epithelium, it can increase lung fluid clearance.

β_2-Adrenoceptor agonists provide temporary relief to the patient by reducing bronchospasm caused by non-cardiogenic pulmonary oedema. β_2-adrenoceptor agonists were used with caution, as they also have a cardiogenic effect: they increase the heart rate and blood pressure. These effects increase the hydrostatic pressure of the lungs, which increases the patient's pulmonary oedema. More research is required to determine the urgent need for the use of these drugs because these drugs should be used as a last resort [9].

Nutrition maintenance was considered at the beginning of the patient's treatment, especially if the patient suffers from burns to the oral cavity caused by electric shock. These patients are more likely to be reluctant to consume food due to elevated levels of shortness of breath and/or discomfort. A nasoaesophageal or nasogastric feeding tube was placed quickly and without much stress for the animal. Patients were fed liquid diets to speed up their recovery. Oxygen therapy and rest were used (Fig. 3).

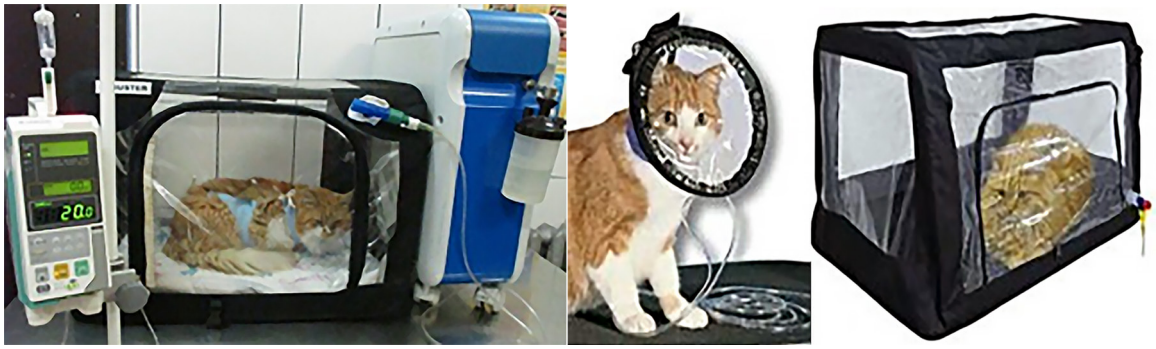

Figure 3. Oxygen therapy

Opioid painkillers (butorphanol 0.2-0.25 mg/kg) were used for sedation. In cardiogenic pulmonary oedema, the main therapeutic effect is to reduce the previous load due to aggressive diuresis with loop diuretics. Furosemide was used as a multiple bolus from 1 to 2 mg/kg or as an infusion at a constant rate of 0.66-1 mg/kg/h. Thoracocentesis was performed in the presence of pleural effusion. In cats with low cardiac output (bradycardia), treatment with pimobendane was considered. Patients, in the absence of an effect, were given dobutamine by infusion and at a constant rate (2.5-10.0 mcg/kg/min). Nitroglycerides and angiotensin-converting enzyme (ACE inhibitors) inhibitors were not indicated during the acute decompensation phase. Given the fact that diuresis does not affect the pathogenesis of non-cardiogenic oedema, fluid therapy is recommended for the supportive treatment of the underlying disease in various pathologies, rather than diuretics, as, e.g., in the case of sepsis or pancreatitis. However, in these cases, infusion therapy should be used with caution. Oxygenation is still the main means of maintaining the patient's respiratory function, and it is enough for the animal to be in a calm state in an environment saturated with oxygen. Furthermore, artificial ventilation may become necessary. The usefulness of corticosteroids is controversial [12].

Treatment of sick animals with corticosteroids and bronchodilators was not effective in patients with non-cardiogenic pulmonary oedema. Bronchodilators are prescribed for patients with diseases of the small respiratory tract, such as asthma, but do not work at the level of the alveoli. Corticosteroids may also be beneficial in patients with asthma but have not been shown to reduce or prevent lung endothelial damage [6; 11].

After the patient's condition stabilised, the focus was on maintenance treatment during the treatment of the underlying disease. To stop the progression of pulmonary oedema, aggressive therapy was used to eliminate the underlying disease. As a rule, maintenance therapy is required for 24-72 hours, until the symptoms of pulmonary oedema disappear.

The condition of cats with cardiogenic pulmonary oedema was stabilised depending on blood pressure indicators: for tonometry and detection of hypertension, angiotensin-converting enzyme (ACE) inhibitors (vasotop, enap, kapoten, hartil) were used; in case of hypotension, dobutamine 5 μg/kg/min, dopamine 3-5 μg/kg/min were administered. Nitroglycerides and ACE inhibitors were not used during the acute decompensation phase.

After stabilisation of the animal's clinical condition, it is recommended to transfer it to outpatient treatment as soon as possible. Repeated assessment of the condition is carried out 3-7 days after discharge (assessment of chronic heart failure, kidney function, and determination of the state of electrolyte metabolism). Owners should control the frequency of the cat's respiratory movements (during its sleep) at the rate of up to 30 breathing movements/min.

Among the examined 110 animals with symptoms of pulmonary oedema, 68 animals were transferred to outpatient treatment, 42 animals died.

Conclusions

Thus, according to the results of the study in the conditions of the "Vet House" Veterinary Centre, it was found that the differential diagnosis of pulmonary oedema in a domestic cat has an essential tactical and prognostic value. This involves the use of various therapeutic schemes. To confirm the diagnosis of this disease, it is necessary to comprehensively consider the indicators of the clinical examination of the animal, the results of X-ray examination of the chest cavity and laboratory analysis of blood parameters.

According to the results of the conducted research, the predisposition of certain breeds of cats and their hybrids was established: British Shorthair, Sphynx and Maine Coon. It was found that the most common aetiological factors for cardiogenic pulmonary oedema are hypertrophic, restrictive, and non-classified cardiomyopathies, and for non-cardiogenic oedema – traumatic brain injury, electric shock, toxic substance poisoning, anaphylactic reaction, and airway obstruction. Thus, cardiogenic and non-cardiogenic causes are responsible for the development of pulmonary oedema. Accurate determination of the underlying cause of this pathology is of paramount importance for therapy and prognosis.

The most probable indicators for differential diagnosis were X-rays of the chest cavity (the degree of lung damage and the degree of congestive phenomena), data on the size of the left atrium, and indicators of echocardiography to exclude or confirm cardiomyopathy. The least significant were the results of the clinical picture and haematological studies, which are not specific tests and reveal many common features for both forms of pulmonary oedema.

The main principle of animal therapy at the initial stage is to reduce the clinical manifestations of acute respiratory failure. Treatment of cats with pulmonary oedema has a pathogenetic justification and differs in several features depending on aetiological factors and the patient's condition. According to the results of treatment, 68 animals were transferred to outpatient treatment, 42 died.

It is promising to develop diagnostic algorithms and treatment protocols for pulmonary oedema in a domestic cat, depending on its form (cardiogenic or non-cardiogenic) and the results of blood pressure measurement.

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Кардіогенний та некардіогенний набряк легень у свійського кота: патологічні механізми, диференційна діагностика та лікування

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Анотація. Актуальність дослідження зумовлена поширеністю набряку легень у котів і особливими підходами до їх терапії. У зв'язку з цим, дана стаття спрямована на виявлення етіологічних факторів, породної схильності, клінічних проявів, гематологічних показників та рентгенологічних ознак. Провідним у дослідженні цієї проблеми є комплексний підхід, який включає розгляд етіології, патогенезу, діагностики кардіогенного і некардіогенного набряку легень та лікування котів. З'ясовано, що в умовах Ветеринарного центру «Vet House» (м. Вінниця) найчастіше за цієї патології реєстрували котів порід британська короткошерста, сфінкс, мейнкун і їх метисів. У 68 котів встановлено кардіогенний набряк легень за гіпертрофічної, рестриктивної і некласифікованої кардіоміопатії. В 42 тварин виявлено некардіогенний набряк легень за черепно-мозкової травми, отруєння токсичними речовинами, анафілактичної реакції, обструкції дихальних шляхів та ураження електричним струмом. З'ясовано, що найбільш інформативними під час диференційної діагностики набряку легень у котів є результати ехокардіографії та рентгенологічного дослідження. Встановлено, що для диференційної діагностики кардіогенного і некардіогенного набряку легень клінічні показники і результати гематологічного дослідження тварин мають низьку інформативність. Виявлено, що лікувальні заходи за набряку легень є ефективними за врахування етіологічних факторів, хоча на першому етапі за обох форм набряку легень спрямовані на зменшення і усунення проявів гострої дихальної недостатності. Матеріали статті становлять практичну цінність для лікарів ветеринарної медицини загальної практики та інтенсивної терапії з питань диференційної діагностики, прогнозування розвитку хвороби та ефективного лікування котів

Ключові слова: біохімічні і морфологічні показники крові, задишка, інтерстиціальний рисунок, патогенез, рентгенографія