ANNOTATION
of the dissertation work by Aleshina Yuliya Yevgenyevna
on the topic "Viral infections of dogs complicated by associations of opportunistic microorganisms in the conditions of Kostanay city"
submitted for the degree of Doctor of Philosophy (PhD) in the specialty 8D09101 – Veterinary Medicine

1. Relevance of the research topic. Infectious diseases of dogs occupy one of the central places in contemporary veterinary medicine, determining the high level of morbidity and mortality of small domestic animals worldwide. The global population of domestic dogs numbers approximately 700 million individuals, of which about 75% belong to the category of free-roaming or stray animals. The high density of such populations, low vaccination coverage and limited access to veterinary care form sustained epidemiological conditions for the continuous circulation of viral pathogens, among which canine parvovirus type 2 (CPV-2) and canine adenovirus (CAV) are widespread. Dogs in close contact with humans and urban environmental objects serve as a significant reservoir of zoonotic and zooanthroponotic infections, while the growing phenomenon of antimicrobial resistance (AMR) gives the problem of viral-bacterial co-infections in these animals a distinct character of threat within the framework of the "One Health" concept.

Canine parvoviral enteritis type 2 (CPV-2) is one of the most pathogenic and epidemiologically significant infections of carnivores. First identified in the late 1970s, it spread rapidly to all regions of the world and to this day remains a leading cause of acute hemorrhagic diarrhea, dehydration and death in puppies. The pathogenesis of parvovirus is determined by its tropism for mitotically active cells, which results in viral replication in lymphoid tissue and intestinal crypts, the development of leukopenia, destruction of the intestinal barrier and, consequently, microflora translocation with the risk of bacteremia, sepsis and multiple organ failure. It is precisely because of these mechanisms that canine parvoviral enteritis is regarded in modern literature as a prognostic model of sepsis in small domestic animals.

Canine adenovirus also occupies an important place in the structure of infectious pathology of this species. CAV-1, the causative agent of infectious canine hepatitis (ICH), exhibits a pronounced tropism for endothelial cells, hepatocytes and cells of the renal epithelium. CAV-2, by contrast, predominantly affects the respiratory tract: it causes necrotizing bronchitis and bronchiolitis with the development of interstitial pneumonia, which proceeds substantially more severely in the presence of concomitant bacterial infection.

The phenomenon of mixed viral infections in gastroenteritis and respiratory diseases of dogs is attracting increasing attention from researchers. The degree of clinical aggravation in combined infections is largely determined by the severity of virus-induced immunosuppression, which opens the "entry gates" for opportunistic microflora.

It is precisely the problem of bacterial complications of viral infections that acquires particular significance against the background of growing antibiotic

resistance. Literature data show that in the analysis of bacteria isolated from dogs with CPV infection, signs of phenotypic resistance have been detected in all strains studied; the majority of Gram-negative isolates (*E. coli, Klebsiella pneumoniae*) carried genes for extended-spectrum β-lactamases, and some strains exhibited resistance to antibacterial drugs critically important for human medicine. Domestic animals living with humans act as a significant reservoir and source of dissemination of resistant strains, including producers of ESBL, MRSA and carbapenemase-producing Enterobacteriaceae; documented cases of zoonotic and anthroponotic transmission of AMR determinants indicate the bidirectional nature of their flow between animals and humans. In this regard, the World Health Organization and leading professional veterinary organizations insist on the integration of AMR monitoring in domestic animals into the global surveillance system within the framework of One Health.

The situation in the Republic of Kazakhstan reflects global trends and is at the same time characterized by a substantial shortage of scientific data. Under conditions of rapid urbanization, the number of stray and unsupervised dogs in the country's major cities continues to grow, while the absence of systematic veterinary control, the crowding of animals and unauthorized landfills create persistent foci of infections and parasitoses; serological and molecular studies conducted in Uralsk (Western Kazakhstan) have confirmed the role of stray dogs as an active reservoir of bacterial and parasitic zoonoses. In 2023–2024, the circulation of influenza viruses with potential zoonotic significance was documented for the first time in dogs in Kazakhstan, which testifies to the limitations of the existing systems of epizootological surveillance. Equally indicative is the lethal outbreak of acute gastroenteritis among service dogs in Almaty Region in 2023, in which molecular-genetic analysis confirmed co-infection of CPV-2 and canine circovirus, which contributed to enhanced replication of CPV-2 and to an increase in the severity of clinical manifestations. This case became the first description of such co-infection in the country and exposed a serious shortage of comprehensive epizootological data for the northern and central regions of Kazakhstan.

Thus, the combination of factors – the high morbidity and mortality in CPV-2 and CAV infections of dogs, their ability to form an immunosuppressive background creating conditions for the activation of opportunistic microflora with a growing level of AMR, the significant proportion of stray animals in the urban environment of Kazakhstan and the acute shortage of epizootological data for the region – determines the high relevance of a comprehensive study of viral infections of dogs complicated by opportunistic diseases in the city of Kostanay, Republic of Kazakhstan.

2. Aim of the dissertation research: to study the epizootological and pathogenetic features of viral infections of dogs (parvoviral enteritis and adenoviral infection) associated with opportunistic microorganisms and, on this basis, to substantiate effective therapeutic regimens in the conditions of the city of Kostanay.

3. Object of the research: the clinical status of dogs with parvoviral enteritis and adenoviral infection, and opportunistic microorganisms isolated from dogs with viral infections.

4. Subject of the research: epizootological features, clinical-hematological and biochemical parameters, species composition, phenotypic and genotypic antibiotic resistance of opportunistic microorganisms, as well as the effectiveness of therapeutic regimens for viral infections of dogs complicated by bacterial associations.

5. Objectives of the research:

–to carry out an analysis of the epizootic situation regarding viral diseases of dogs in the territory of the city of Kostanay for the period 2020–2024;

–to study the clinical-pathogenetic features of the course of parvoviral enteritis and adenoviral infection of dogs complicated by associations of opportunistic microorganisms;

–to study the species composition of opportunistic microorganisms isolated from dogs with viral infections;

–to determine the susceptibility of the isolated bacterial strains to antimicrobial agents and to identify the genetic determinants (genes) of their resistance;

–to develop and experimentally substantiate effective therapeutic regimens for viral diseases of dogs complicated by associations of opportunistic bacteria, taking their antibiotic resistance into account.

6. Scientific novelty:

1. For the first time, a comprehensive epizootological analysis has been carried out of viral infections of dogs (parvovirus CPV-2 and adenovirus CAV-2) in the territory of the city of Kostanay for the period 2020–2024. Regional features of distribution, seasonal dynamics, and age- and breed-related susceptibility of dogs to these diseases have been established.

2. For the first time, for the conditions of Kostanay, the species composition of associations of opportunistic microorganisms (*E. coli, Klebsiella spp., Citrobacter spp., Enterobacter spp., Proteus spp., S. aureus, Streptococcus spp.*) isolated in viral infections of dogs has been determined.

3. The level of phenotypic antibiotic resistance of the isolated strains of opportunistic bacteria has been studied. For the first time, genetic determinants of resistance to antibacterial drugs of six pharmacological groups have been identified.

4. The effectiveness of the use of antibacterial therapy in the treatment of viral diseases of dogs complicated by bacterial infection, based on the results of the antibiogram, has been scientifically substantiated and experimentally confirmed.

7. Provisions submitted for defense:

1. Regional features of the epizootic process of viral diseases of dogs (parvoviral enteritis and adenoviral infection) in the territory of the city of Kostanay in 2020–2024, including seasonal dynamics, age- and breed-related susceptibility.

2. The species composition of opportunistic microorganisms (*E. coli, Klebsiella spp., Citrobacter spp., Enterobacter spp., Proteus spp., S. aureus, Streptococcus spp.*) isolated from dogs with viral diseases.

3. The level of phenotypic resistance and the spectrum of genes encoding resistance to antibacterial drugs of six pharmacological groups in strains of opportunistic microorganisms.

4. A scientifically substantiated therapeutic regimen for viral diseases of dogs complicated by associations of opportunistic bacteria, based on the results of the antibiotic resistance of the accompanying microflora.

8. Practical significance of the obtained results.

On the basis of the studies carried out, the following have been developed and proposed:

–scientifically substantiated regimens of comprehensive therapy of canine parvoviral enteritis and adenoviral infection complicated by associations of opportunistic microorganisms, using antibacterial drugs prescribed in accordance with the results of the antibiogram;

–practical recommendations "Diagnosis and Therapy of Viral Diseases of Dogs Complicated by Associations of Opportunistic Bacteria" for practicing veterinary specialists working in clinics and diagnostic centers, lecturers, students, master's and doctoral students of veterinary specialties;

–Patent of the Republic of Kazakhstan for utility model No. 10722 "A Set of Species-Specific Nucleotide Sequences of Primers and Probes for the Identification of Canine Parvovirus (CPV-2) and Canine Adenovirus (CAV-1)";

–improved regimens of comprehensive therapy aimed at reducing the severity of the clinical course, preventing bacterial complications and increasing the survival of animals with viral diseases.

The results of the dissertation work have been introduced into the practical activities of the veterinary clinics of the city of Kostanay: "VET ZABOTA", "Dogma", and "Aibolit".

9. Personal contribution of the doctoral candidate. A significant part of the research was carried out independently: the collection and analysis of the epizootic situation regarding viral diseases of dogs (parvoviral enteritis and adenoviral infection) in the city of Kostanay were performed. The clinical-hematological and biochemical parameters of dogs with viral infections complicated by associations of opportunistic microorganisms were studied. The isolation, identification and analysis of the species composition of the opportunistic microflora were carried out. The author participated in molecular-genetic studies on the detection of viral DNA (CPV-2, CAV-2), as well as of antibiotic resistance genes in the isolated strains of microorganisms. The susceptibility of microorganisms to antibacterial drugs was studied; treatment protocols for dogs with viral diseases were developed and tested taking antibiotic susceptibility into account, and recommendations for the prevention of complications were proposed. The analysis, generalization and interpretation of the obtained results were carried out, and the manuscript of the dissertation was prepared.

10. Approbation of the results of the dissertation.

The main provisions of the dissertation have been reported and discussed at international scientific and practical conferences:

–at the IV International Scientific and Practical Conference "Contemporary Problems of Animal Husbandry," dedicated to the memory of Doctor of Agricultural Sciences, Professor Bakytzhan Muslimovich Muslimov, Kostanay: A. Baitursynov KRU, 2021. – pp. 134–138;

–at the International Scientific and Practical Conference “Contemporary Challenges for Biotechnology, Veterinary Medicine and Medicine during the COVID-19 Pandemic,” 2021. – pp. 113–120;

–at the International Scientific and Practical Conference dedicated to the memory of Doctor of Biological Sciences, Professor Vitaly Ilyich Ilyashchenko, Kostanay: A. Baitursynov KRU, 2022. – pp. 158–166;

–at the International Scientific and Practical Conference “Baitursynov Readings.” – Kostanay, 2023. – pp. 14–18;

–at the First International Conference of Veterinary Students, Kaunas, 2025. – p. 12.

11. Publications:

The results of the dissertation research and the main provisions submitted for defense have been published in 14 scientific works, including:

–3 articles in journals included in the international Scopus database (with percentiles – 94, 52, 26);

–5 articles in publications recommended by the CQASHE MSHE RK;

–5 articles in the proceedings of international conferences;

–1 article in a journal indexed in the RSCI.

A Patent of the Republic of Kazakhstan for utility model No. 10722 has been obtained. Practical and methodological recommendations have been issued.

12. Volume and structure of the dissertation.

The dissertation work is presented on 135 pages of computer-typed text and includes: an introduction, a literature review, the author’s own studies, a generalization of the results, a conclusion and a list of 200 references used. The text of the work contains 23 figures, 28 tables and 8 appendices.