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EFFECTIVENESS COMPARISON OF TREATMENT OF FELINE ASSOCIATED BORDETELLA BRONCHISEPTICA INFECTION WITH THE IMMUNOSTIMULANTS

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Abstract. *There is a significant spread of infectious respiratory diseases among pets, which often lead to their death. Herpesviruses and caliciviruses are the main viral pathogens that cause respiratory pathology in cats, they are of etiological importance, as they have an expressed tropism for the mucous membranes of the respiratory tract. These viral pathogens can cause both mono infections and mixed or associative infections, which may include Chlamydia, Mycoplasma, and Bordetella. Infections associated with the Bordetella virus are accompanied by the development of catarrhal inflammation of the mucous membranes of the upper respiratory tract, oral cavity, and conjunctiva. The problem of treating Bordetella virus-associated infections in cats remains an urgent issue. The study of the elaboration of diagnostic kits, ways of treatment, and specific prevention of infectious diseases in cats is of paramount importance. Drugs that inhibit pathogenic microorganisms are available on the veterinary market, but direct support of the immune response is of particular importance in the treatment of associated viral respiratory infections. Such drugs exert a suppressive effect on the humoral and cellular immune response and have a strong immunomodulatory and interferon effect. As an interferon inducer, they block the transfer of viral proteins, thereby activating the body's immune response. Thus, the study of the peculiarities of the spread of feline-associated respiratory infections, as well as the improvement of their treatment plans, is an urgent issue and is important for solving the problem of this pathology.*

Keywords: cats, infectious respiratory diseases, immunostimulants, immune correction, treatment

Introduction. Feline *Bordetella* and viral respiratory associated diseases have recently become particularly widespread in places of mass concentration of susceptible animals – catteries, shelters, and stray cat populations (Helps et al., 2005; Severyn et al., 2023). This feature is associated with high contagiousness and low immune response to the pathogens in the environment. Crowding of susceptible animals is an important factor in the spread of diseases (Binns et al., 2000; Radford et al., 2009). *Herpesviruses* and *Caliciviruses* are the main pathogens that cause respiratory diseases in cats (Dmytryshyn et al., 2019). In nature, only felines of all ages and breeds, regardless of sex, are susceptible to viruses, with younger cats and cats with reduced immune responses being the most susceptible (Egberink et al., 2009; Tabatabaei et al., 2022). In the respiratory pathology of cats caused by viruses associations, *Bordetella bronchiseptica* plays a significant role. *Bordetella bronchiseptica* is a pathogenic microorganism of the genus *Bordetella*, belonging to the *Brucellaceae* family (Egberink et al., 2009; Molyneux et al., 2000; Register et al., 2012). The danger of such associated respiratory infections is the inability to remove completely pathogens from the body. For example, the herpes virus reproduces and persists in the trigeminal nerve ganglia, which leads to the lifelong

carriage with a constant threat of recurrence (Maggs 2005; Ruban et al., 2022; Thiry 2017).

The infection with *Bordetella bronchiseptica* is more likely to occur through direct contact, as well as through saliva secretions from infected objects, eyes, and nasal passages. The clinical course of the disease is the development of catarrhal lesions of the mucous membranes of the upper respiratory tract, oropharynx, and conjunctiva. Mortality is usually low, but in kittens, it can be up to 30%. (Di Francesco et al., 2006; Radford et al., 2009). The main danger is posed by vectors that release the virus into the environment.

The following associated diseases are difficult to treat (Gaskell et al., 2007; Kopečný et al., 2020; Molyneux et al., 2000). In the context of constant competition between pharmaceutical companies on the veterinary market of supportive drugs many immunostimulants have appeared, the use of them should be carried out in combination with antiviral and antibacterial drugs only, and this is not always considered when treating an animal.

The purpose of study was to test the efficacy of the treatment plan with the immunomodulator Ketferon in feline *Bordetella* and viral associated respiratory infection.

Methods and materials. The material for the study was the records of registration of sick animals, as well as sick cats with signs of upper respiratory tract diseases that were made in the veterinary clinic "Eskulap" in Apostolove, Dnipropetrovsk oblast in 2022-2024.

Two groups of animals were formed for the study based on the principle of balanced groups. The diagnosis was based on epizootic analysis, clinical examination, and laboratory test results. Laboratory tests were conducted at the Oblast State Laboratory of Veterinary Medicine, Kryvyi Rih. To verify the laboratory *Bordetella* isolation, the main methods for detecting the pathogen were the bacteriological and the polymerase chain reaction (PCR). The test samples were oropharyngeal swabs and, in some cases, transnasal washings. To isolate *B. bronchiseptica* the Regan-Lowe transport medium (charcoal-blood agar) was mainly used. Cephalixin was used as an inhibitor, which inhibited the growth of the associated microflora of the respiratory tract. To verify the laboratory feline infectious viral diseases diagnosis, rapid immunochromatographic tests (FHV Ag) manufactured by ASAN PHARM/ZRbio (China) were used. The tests provided 95% accuracy and specificity. For the specific antibody detection, the method of serological (retrospective) testing of enzyme-linked immunosorbent test was used with the ImmunoComb Feline VacciCheck test kit from Biogal, Israel.

We also evaluated the effectiveness of the Ketferon immunostimulant in the treatment of cats of different sexes and breeds from 2.5 months to 12 years old, which had associated respiratory infections. Clinical signs ranged from catarrhal respiratory syndrome to severe bronchopneumonia and ocular lesions (in kittens from 2 to 5 months old), including purulent conjunctivitis, keratoconjunctivitis and symblepharon, and osteolytic lesions of the nasal conchae. Cats with associated viral respiratory disease were treated with two treatment plans. 2 groups of cats (n=6) aged 2-12 months were formed on the analogue principle. Cats of the first group (A) were treated with the common treatment plan, and cats of the second group (B) were treated with the alternative updated plan. After the diagnosis, a treatment plan was elaborated using the veterinary drug Ketferon, which had an immunomodulatory antiviral effect.

Results and discussion.

The generalization of the results allowed us to find out that the occurrence of respiratory infections in cats for three years in Apostolove has had a rising trend: from 28.5% cases in 2022 to 38.0% cases in 2024. The following associated pathogens have been registered lately: infectious rhinotracheitis + *Bordetella*; calicivirus + *Bordetella*; panleukopenia + *Bordetella*; *Chlamydia* + *Bordetella* and other associations (Table 1).

Table 1

Nosological profile of feline-associated respiratory infections

No	Associated pathogens	Quantity (%)
1	<i>Bordetella</i>	16.5
1	Infectious rhinotracheitis + <i>Bordetella</i>	22.5
2	<i>Calicivirus</i> + <i>Bordetella</i>	19.5
3	<i>Panleukopenia virus</i> + <i>Bordetella</i>	9.5
4	<i>Chlamydia</i> + <i>Bordetella</i>	7.5
5	Other associated pathogens	24.0
6	Total	100

Table 1 demonstrates, that *Bordetella* was most often reported in association with infectious rhinotracheitis and calicivirus infections (22.5% and 19.5%, respectively). *Bordetella* also associated with panleukopenia (9.5%) and chlamydia (7.5%). Other associated infections totaled 24.0% of all cases of infectious diseases. *Bordetella* as a mono-infection was verified in 16.5%, which complies with the average statistical data reported by other researchers (Maggs D.J., 2005; Register K.B., 2016; Thiry E., 2017).

Cats with signs of respiratory infection were divided into age groups. Cats from 2 months to 2 years old were in the first group, cats from 2 to 7 years old – in the second. Cats aged from 7 to 12 years old were in the third group. Clinical signs of feline respiratory infections ranged from catarrhal respiratory syndrome to the development of severe bronchopulmonary pneumonia and eye lesions (in kittens 2-5 months old), purulent conjunctivitis, keratoconjunctivitis and phalanx of the thymus gland, as well as osteolytic lesions of the nasal concha in secondary bacterial infections in older cats (Table 2).

Table 2

Number of infected cats with different clinical signs

Clinical signs	Age groups of infected cats		
	First	Second	Third
Catarrhal and respiratory	31	12	12
Oropharyngeal infections	20	5	6
Eyes inflammations	21	3	8
Lesions of the nasal conchae	7	3	1
Infections of the gastrointestinal tract	42	1	5
Pregnancy pathology	2	1	0

Feline respiratory infections are highly contagious, widespread in the world in the cat populations, and in 10-50% of cases are etiological causes of upper respiratory tract disease. According to the academic literature, viral pathogens have a high mutation rate, which leads to numerous combinations with a wide range of virulence, antigenic, and immunogenic characteristics. Mutational variability is characteristic of infections, which explains the clinical diversity of the form of diseases: from subclinical with asymptomatic course with lesions of the mucous membranes of the mouth and eyes, upper respiratory organs with various severity degrees, to systemic infection with up to 20% mortality rate.

The choice of a treatment plan always requires careful clinical decision-making, compliance with the patient's needs, and consideration of the financial viability of the owner. Treatment alternatives include the use of broad categories of supportive care, antiviral, and supportive therapy. In most cases, practice shows that pet owners visit veterinary clinics, as a rule, somewhat late, when clinical signs of infectious diseases are

manifested. To maximize the effectiveness of treatment and ensure that the sick pet has all possibilities to recover, early and timely disease detection and provision of evidence-based treatment of feline respiratory infections remain important issues, so rapid and evidence-based therapy is the key to effective treatment and recovery.

Cats with associated Bordetella virus respiratory disease had two treatment options. 2 groups of cats (n=6) 6-12 months old were formed on the analogue principle. Cats of the first group (A) were treated with the common treatment plan, and cats of the second group (B) were treated with the alternative updated plan. The groups were formed on a rolling basis in the veterinary clinic "Eskulap" in Apostolove, and the treatment plan was provided according to the analogue principle. The main strategy for the treatment of feline infectious respiratory diseases was to maintain the organism's strength; alleviate the severity of signs; prevent secondary bacterial infecting the patient weakened by the virus; and enhance the immune response. When selecting an effective treatment plan, the main criterion was its capacity and versatility, considering all mechanisms of disease development. The main components of the feline infectious respiratory disease treatment plans are shown in Table 3.

Table 3

**Comparative table of feline infectious respiratory diseases treatment plans
(based on the data of the veterinary clinic "Eskulap", Apostolove)**

Groups of cats	
Group A (clinic's common plan)	Group B (elaborated plan)
Specific serum "CAT-PROTECT-4" subcutaneously 1 cm ³ three times in 12-24 hours	
-	Immunostimulant "Ketferon" intramuscularly 200,000 IU for 5-7 days
Sinulox antibiotic intramuscularly or subcutaneously, 8.75 mg per 1 kg of cat's weight, which is equivalent to 1 ml of the drug per 20 kg of weight, once a day for 3 to 5 days.	
Trifusol – Neo subcutaneously 1 cm ³ once a day for 7 days	
Cyanophor subcutaneously 2 cm ³ once a day for 7 days	
"Divopride" nose and mouth drops 2-3 drops into the conjunctival sac and nostrils 4-6 times a day for 14-20 days	

Cats were treated comprehensively, including rehydration infusion, antibacterial, symptomatic, and immunotherapy, in which all groups (except cats in group A) depending on the severity of the disease, received daily intravenously or subcutaneously 200,000 IU of Ketferon for 5-7 days.

To assess the efficacy of the treatment plans the dynamics of feline respiratory infections clinical signs were monitored and the periods of disappearance of clinical signs were recorded. During the treatment and clinical examination of the cats, it was noted that the cats of group B recovered faster, their body temperature normalized within 2-3 days, while the body temperature of the cats of group A remained high for 4-5 days. The lacrimation and rhinitis stopped on days 5-6 in the cats of group B, and on days 6-7 due to the combination of the herpesvirus infection and calicivirus healing of ulcers in the oral cavity was observed. In cats of group A, ulcers healed on the 8-9 day of the disease, and rhinitis with conjunctivitis lasted the same. In total, clinic treatment of cats of the group B lasted 9-10 days, provided that recovered cats had no bronchopneumonia complications. Then, the cats were discharged but their monitoring continued. The treatment of cats in group A was 2-3 weeks longer, as they had cough and pneumonia complications. Thus,

the selection of such treatment plans ensured faster recovery, the treatment lasted 9-10 days, while the common treatment plan of the clinic, the treatment was for 2-3 weeks. Almost in all cases of Ketferon use in a combined treatment plan, the recovery was rapid. In contrast, cats that did not receive Ketferon were treated on average for 10-14 days. The medication was most effective in kittens 2-5 months old. It should also be noted that cats treated with Ketferon did not subsequently become infected after contact with sick cats.

Thus, when using the immunostimulant Ketferon in the comprehensive treatment of feline Bordetella virus infection, an early improvement in the clinical state and a faster recovery was observed. No signs of allergic, local, or other side effects were observed in treated cats. Thus, immunostimulants as part of the comprehensive treatment of feline-associated Bordetella virus infections in cats of all ages and breeds increase the effectiveness of treatment and reduce the time of recovery.

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ПОРІВНЯННЯ ЕФЕКТИВНОСТІ ЛІКУВАННЯ АСОЦІЙОВАНОГО БОРДЕТЕЛІОЗУ КОТІВ ІЗ ЗАСТОСУВАННЯМ ІМУНОСТИМУЛЯТОРІВ

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Резюме. Серед домашніх тварин відзначається значне поширення інфекційних респіраторних захворювань, які нерідко призводять до їх загибелі. Основні вірусні патогени, які спричиняють респіраторну патологію у котів, такі як герпесвіруси та каліцивіруси, мають провідне етіологічне значення, так як володіють вираженим тропізмом до слизових оболонок респіраторного тракту. Зазначені вірусні патогени можуть викликати як моноінфекції, так і змішані або асоціативні, до складу яких підключаються хламідії, мікоплазми, бордетели. Вірус-бордетеліозні асоціативні інфекції супроводжуються розвитком катарального запалення слизових оболонок верхніх дихальних шляхів, ротової порожнини та кон'юнктиви. Проблема лікування вірус-бордетеліозних асоціативних інфекцій у котів за нинішніх умов залишається актуальним питанням. Провідне значення мають дослідження з розробки діагностичних наборів, засобів лікування та специфічної профілактики інфекційних захворювань у котів. Препарати, що пригнічують патогенні мікроорганізми, у великій кількості представлені на ринку ветеринарних препаратів, але при лікуванні асоційованих вірусних респіраторних інфекцій особливе значення має пряма імуностимуляція організму. Такі препарати стимулюють розвиток гуморального і клітинного імунітету, мають виражену імуномодулюючу та

інтерферонову дію. Будучи індуктором інтерферону, вони блокують трансляцію вірусних білків, тим самим активізуючи природну опірність організму. Отже, дослідження особливостей поширення асоційованих респіраторних інфекцій у котів, а також удосконалення схеми їх лікування, є актуальним питанням та має важливе значення для вирішення проблеми зазначеної патології.

Ключові слова: коти, інфекційні респіраторні захворювання, імуномодулятори, імунокорекція, лікування

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