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Development of Veterinary and Sanitary Measures for the Prevention of Pasteurellosis Infection in Cattle: The Case of the Republic of Kazakhstan

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ABSTRACT

Cattle pasteurellosis is a dangerous infectious disease that leads to the death of farm animals just within a few days. This disease also spreads to many other wild animals, birds, and humans. Therefore, it is extremely important to understand the main manifestations of this disease and take timely measures to eliminate it. The study aimed to determine the strategy of veterinary and sanitary measures in the Republic of Kazakhstan for the prevention of pasteurellosis infection, based on the determination of zones by cattle pasteurellosis spread and the compilation of visualization maps using the results of the 2013-2021 monitoring. A clinical examination of cattle was carried out in the context of epizootological units within Kazakh economic entities and biomaterial for laboratory tests for pasteurellosis was selected. *Pasteurella multocida* isolates and strains were used in the experiments, and their cultural and morphological properties were studied. The obtained data from studies of the properties of isolated cultures in comparison with the characteristics of the reference strains gave grounds to attribute them to the Pasteurella genus. Based on the conducted study, epizootic visualization maps for cattle pasteurellosis for 2021 were developed.

Key words: Pasteurellosis, Epizootic situation, Distribution, Isolate, *Pasteurella multocida*, Visualization map.

INTRODUCTION

Animal husbandry is a strategic branch of agriculture that ensures a country's food independence regarding dairy and meat products (Haji Hajikolaei et al. 2010). For the stable development of animal husbandry, it is necessary to ensure the safety and growth of livestock, including its protection from infectious diseases (Ivanov et al. 2021; Boranbayeva et al. 2023).

The issue of infectious disease pathogens circulating in nature and asymptomatic bacterial carriers is relevant (Harper et al. 2015). Among all infectious diseases, pasteurellosis occupies a special place (Dzhupina 2016; Kapustin and Laishevtcev 2016). According to modern information about this disease, its pathogens are two different types of microorganisms (*Pasteurella multocida* and *Mannheimia haemolytica*) (Cassirer et al. 2001; Khaneev 2015; Umer and Mezgebu 2023). *P. multocida* is polymorphic, often short gram-negative, fixed ellipsoid rods, located in isolation, and found in pairs or less often in chains. They do not form spores and can be aerobes and facultative anaerobes (Garcia-Alvarez et al. 2017).

Pasteurellosis or hemorrhagic septicemia is an infectious disease affecting many types of domesticated and wild animals, characterized in the acute form by signs of septicemia, lobar pneumonia, pleurisy, and edema in various parts of the body and in the subacute and chronic forms – by purulent pneumonia, arthritis, and sometimes enteritis (Fett et al. 2009; Alarawi and Saeed 2021). Pasteurellosis is a serious and highly contagious bacterial infection affecting cattle and causing symptoms such as pneumonia, fever, and septicemia. The disease is caused by the gram-negative bacteria *P. multocida* found in the nasal passages and gastrointestinal tract of healthy animals (Chung et al. 2015).

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Outbreaks of the disease can lead to significant economic losses due to the death of sick animals, forced slaughter, reduced weight gain of animals, treatment costs,and general and special prevention and elimination of the disease (Raheel et al. 2021). To effectively manage the disease, it is extremely important to apply prevention and to prevent pasteurellosis, it is necessary to ensure the protection of non-infected farms from the introduction of the pathogen through sick animals, Pasteurella carriers, control measures, such as advanced management methods and vaccination, to minimize the spread of the disease and reduce the impact of outbreaks on livestock (Peng et al. 2019; Ryan and Feder 2019).feed, etc. Particular attention is paid to the observance of general veterinary and sanitary rules and the provision of animals with normal zoo-hygienic conditions and rational feeding (Martin et al. 2018).

The problem of pasteurellosis control is complicated by the fact that the pathogenic Pasteurella create a kind of stationary epizootic focus, persisting for a long time in the body not only of convalescent animals and those who have contacted them but also in the body of synanthropic rodents and birds (Vesza et al. 2017). In the Republic of Kazakhstan, pasteurellosis has become a serious problem for animal husbandry due to its high prevalence and significant economic impact.

The study aimed to determine the strategy of veterinary and sanitary measures in Kazakhstan for the prevention of pasteurellosis, based on the allocation of pasteurellosis spread zones in cattle and the compilation of visualization maps of the results of the 2013-2021 monitoring.

MATERIALS AND METHODS

Ethical Permission

The experiments and the methods used for researching laboratory animals comply with the requirements of biological safety and ethical principles of experimentation on animals set out in the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes. The research protocol was discussed and approved at the meeting of the local ethical committee of the Kazakh Scientific Research Veterinary Institute (KSRVI) of the Committee of Science of the Ministry of Education and Science of the Republic of Kazakhstan on April 6, 2020.

Period and Place of the Study

The studies were conducted in Kazakhstan from February to December 2021. From February to December 2021, we visited Epizootoological units (EUs) of economic entities in 12 regions of Kazakhstan (Almaty, East Kazakhstan, Kyzylorda, Pavlodar, Turkestan, Zhambyl, Aktobe, West Kazakhstan, Akmola, Karaganda, North Kazakhstan, and Kostanay) with various epizootological status to collect biomaterial (blood serum, nasal discharge) for research in the laboratory of the KSRVI and assessment of the epizootic state of these economic entities regarding cattle pasteurellosis.

Design of the Study

The study of the epizootic situation regarding pasteurellosis in mongrel cattle was carried out at the first stage by analyzing veterinary reporting data and conducting research. In the second stage, a clinical examination of cattle in their places of keeping was carried out, as well as serological and bacteriological studies of biomaterial taken from animals with clinical signs of pasteurellosis. In the first stage, we used official data from veterinary reports of the Committee for Veterinary Control and Supervision (CVCS) of the Ministry of Agriculture of the Republic of Kazakhstan, the Republican Anti-Epizootic Group, the Republican Veterinary Laboratory, the National Reference Center for Veterinary Medicine, and the National Research Institute for 2013-2020. For monitoring, a total of 4,305 samples were taken, of which 1,435 were blood serum samples for serological studies and 2,870 were swipes from the nasal mucosa (from both nostrils) for bacteriological research.

Analysis of Veterinary Reports

Based on epizootic focus (EF) data, the regions were divided into zones to determine the status of a subpopulation of animals regarding the contagious disease in Kazakhstan. The status of the regions was determined by the presence of the pathogen, by the use of vaccination, and by the risk level associated with the disease (its pathogen). By the presence of the pathogen, the regions were divided into safe regions, unsafe regions, and regions with unspecified status. Through the use of vaccination, the regions were divided into regions without vaccination and regions with vaccination. By the risk level of the disease (its pathogen), the regions were divided into high-risk regions, regions of uncertain risk, low-risk regions, and negligible-risk regions. Depending on the spread (occurrence) of cattle pasteurellosis and the veterinary measures carried out, the following types of zones were distinguished: safe zones, observation zones, buffer (protective) zones, dysfunctional zones, and other zones defined following international treaties ratified by Kazakhstan.

The division of the territory into zones in case of the spread (occurrence) of pasteurellosis was carried out based on epizootological examination of the focus (the level of morbidity, the presence of sources of infection, transmission factors, susceptible animals, examination of the boundaries of the focus, the degree of spread and course of the disease, the risk of spreading the infection pathogen, the accumulation of animals or herds with different disease status near the zones), geographical features (vegetation, landscape and other geographical features), and other factors (density of settlements, livestock facilities, animals, infrastructure development, presence of local and national highways, railways, ports, airports, trade routes, presence of processing enterprises, and other factors).

Laboratory Research Methods

For the study of cattle pasteurellosis, we took blood serum samples and swipes from the nasal passages of cattle, with the following symptoms: an increase in body temperature to 41°C, swelling of the tongue and neck, difficult coarse breathing, the presence of viscous saliva and nasal foamy discharge, visible cyanotic mucous membranes with multiple hemorrhages.

Samples from the nasal passages were taken with a sterile swab with a plastic handle in a 12x150 mm transport

tube with a transport medium (Amies medium) in individual packaging. Afterward, the test tube was marked with the application of the identification data of the animal. To obtain serum, blood for serological studies was sampled in the morning, before feeding the animals, in the amount of 10mm of blood from the jugular vein in the upper third of the neck of cattle in compliance with the aseptic rules. The selected samples were immediately immersed in a thermo-case with a refrigerant for further delivery to the laboratory.

Serological diagnostics was performed using an indirect hemagglutination test (IHT) based on the detection of an antigen-antibody complex (Chuzhebaeva 2017). We used a macro method for IHT, with the "Dry pasteurellosis erythrocyte antigenic Diagnosticum" diagnostic kit manufactured at the M. Aikimbayev National Scientific Center for Especially Dangerous Infections, Ministry of Health of the Republic of Kazakhstan (series 010422 B/K No.210, valid until 04/20/2024). The diagnostic kit includes Tween-80 in 1:100,000 dilution, serum under study, pasteurellosis agglutinating liquid serum 1:10 (positive control), and dry pasteurellosis erythrocyte antigenic Diagnosticum 2.5%.

The technique of setting the IHT for the detection and determination of the antibody titer is as follows. Equal doses of erythrocytes sensitized with antigen were added to successive 2-fold dilutions of the serum under study. The resulting mixture was left for 16-18 hours at 4°C. Then, a Tween-80 solution was introduced into the wells of the polystyrene plate in a dilution of 1:100,000 (0.5mL in each). 0.5mL of the serum under study was added to the first well of each row at a dilution of 1:10, consecutive double dilutions were made up to the 11th well. The 12th well serves to control the preparation. Then 0.05mL of dry pasteurellosis erythrocyte antigenic Diagnosticum with a 2.5% concentration was added to all wells. The plate was gently shaken and left at room temperature 22±4°C for 2-3 hours, after which the result was recorded. IHT results were checked visually and evaluated in crosses. IHT was accompanied by controls with negative and positive serum.

Bacteriological studies of biomaterial from the nasal passages have also been carried out to detect Pasteurella carriers in animals. *P. multocida* biovar bovis strains (collection number /B-0229/) were used as the control. Samples of biomaterial from cattle were seeded into test tubes with meat-peptone agar (MPA) (manufactured by Microgen Research and Development Center, Russia, date of manufacture 01.2021) and meat-peptone broth (manufactured by Microgen Research and Development Center, Russia, date of manufacture 03.2020). The composition of the MPA: pancreatic sprat hydrolysate: 17.9g/L; dry enzymatic peptone: 17.5g/L; microbiological agar: 11.2g/L; sodium chloride: 7.7g/L. Method of preparation of the MPA: 38g of the finished mixture was stirred in 1L of distilled water, boiled for 2min until the agar melted completely, filtered through a cotton-gauze filter, sterilized at a temperature of 121°C for 15min, after cooling the medium to 45°C, poured into sterile Petri dishes with a layer of 3-4mm. After solidification of the medium, observing the rules of asepsis, the dishes were dried in a thermostat at a temperature of 37°C for 60min.

The composition of the meat-peptone broth: meat extract: 10g/L, dry enzymatic peptone: 10g/L, sodium chloride: 5g/L, distilled water. Method of preparation: 15g of the finished mixture was stirred in 1L of distilled water, boiled for 2min, filtered through a paper filter, poured 10mL into sterile test tubes, and sterilized at a temperature of 121°C for 15min.

To study the biological properties of isolated Pasteurella cultures, smears were made from the samples, Gram stained (Microorganism Gram staining reagent kit, manufactured by GEMSTANDART-GRF, Russia, batch number 010221, date of manufacture 01.02.2021), and then viewed at 100 magnifications on a Leica DM1000 microscope (Germany). The bacteria Gram staining technique was used. The isolated cultures were identified by their enzymatic properties. Proteolytic activity was determined by the dilution of gelatin. For this purpose, a 0.5% gelatin solution was prepared, the medium was sterilized and 5% of cattle blood serum was added before seeding. The seeding in a gelatin stab was done with a deep injection. The cultures were incubated at room temperature (20-22°C) and the result was taken into account daily for seven days. If the microbe under study does not dilute gelatin, then the medium retains a dense consistency as in the control without cultures, and in the presence of gelatinase, the medium is liquefied.

To determine the hemolytic properties, the material was seeded on Hottinger agar consisting of enzymatic peptone (15g/L); sodium chloride (6.5g/L); yeast extract (0.5g/L); tryptophan (0.0015g/L), with the addition of 5-6% defibrinated blood of goats and sheep. The resulting cultures were recorded after 12-24 hours of incubation at 37°C, transferring the colonies typical for Pasteurella to fresh nutrient media to account for hemolysis on blood agar.

The biochemical properties of the isolated cultures were studied by determining their glycolytic activity by seeding on Gissa media (Russia) using mannitol, glucose, sucrose, dextrose, and maltose, followed by incubation at 37°C for 24 hours. The fermentation of carbohydrates was determined by the change in the color of the medium.

To detect indole, immediately after seeding, a strip of indicator (filter) paper soaked with a saturated solution of oxalic acid was inserted into the test tube so that the indicator paper did not touch the nutrient medium, for which the upper third of the strip was pressed with a cork against the wall of the test tube. The cultures were incubated for 1-2 days at a temperature of 37°C. Indole formation was determined by staining the lower end of the indicator paper in a pale pink color, clearly visible in the transmitted light. The catalase activity test was performed by applying a 0.3cm^3 pipette of freshly prepared 3% hydrogen peroxide to Pasteurella colonies grown on MPA for 18-24 hours. Foam formation was regarded as a positive test for catalase activity.

Investigation of the Properties of Isolated Cultures and the Reference Strain

Received samples of 2,870 swipes from the nasal mucosa (from both nostrils) of cattle were seeded in Petri dishes with the MPA. After 24 hours of cultivation in a thermostat at 37°C, the growth of microbial cultures was noted in all Petri dishes. When evaluating the results of

seeding, convex transparent colonies most characteristic of *P. multocida* were visually selected for their further identification. Cell morphology was determined by microscopy. In the Gram-stained smears, when magnified by 100, the following picture was visually visible: small, gram-negative microorganisms. For comparison, similar studies were conducted in parallel with the reference strain *P. multocida* bovis No. B-0229 and the biomaterial under study (Fig. 1 and 2). In Fig. 1 and 2, gram-negative, short, thick bacteria with rounded edges are observed. Gram-negative, polymorphic, short up to cocci, thick bacteria with rounded edges, located singly, in pairs, or in the form of short chains, were observed in the smears.

Data Analysis

When creating interactive visualization maps of the epizootic process, the QGIS 3.30.1-'s-Hertogenbosch platform was used to graphically display the database.

RESULTS

Zoning of Kazakhstan by the Degree of Spread of Pasteurellosis Infection in Cattle for 2013-2020

Monitoring of cattle pasteurellosis in Kazakhstan shows that one of the main causes of the spread of the disease is latent pasteurellosis, i.e., the asymptomatic course of the disease in animals. The movement of infected animals across the regions of Kazakhstan without appropriate anti-epizootic measures has led to the widespread incidence of the disease and an increase in the number of unsafe economic entities.

As can be seen from Table 1, during the study period in Kazakhstan, the disease was registered annually, mainly in the spring and summer periods. During the analyzed period, 100 EF of the disease were registered in 13 regions of Kazakhstan. The East and West Kazakhstan regions are the most unsafe ones in terms of cattle pasteurellosis incidence.

As can be seen from the presented data, the disease has been registered in Kazakhstan for many years. The range of cattle pasteurellosis covers 13 regions of Kazakhstan, but the degree of problems varies widely. The most unsafe regions for the incidence of cattle pasteurellosis are West Kazakhstan, East Kazakhstan, and Aktobe regions, where the indicators exceed similar indicators for the rest of the regions of Kazakhstan by a factor of 2 or more.

The most unfavorable years for the entire period of the study were 2016 when 16 pasteurellosis EF was established in Kazakhstan, 2017 with 14 EF, and 2018 with 11 EF.

Zoning and regionalization of Kazakhstan by the degree of intensity of the epizootic situation for cattle pasteurellosis are shown in Fig. 3.

From Fig. 3, it can be seen that the entire territory of Kazakhstan was conditionally divided into four zones, depending on the amount of cattle pasteurellosis EF in the region. Thus, an area with the number of 15 EF or more was assigned to a zone with a high degree of cattle pasteurellosis spread (East Kazakhstan and West Kazakhstan regions), from 6 to 15 EF to a zone with an average degree of spread (Atyrau, Aktobe, Kostanay, Karaganda, Almaty, Zhambyl regions), and from 1 to 5 EF to the zone with a low degree of spread (Kyzylorda, Akmola, and Pavlodar regions). Mangystau, North Kazakhstan, and Turkestan regions are considered safe from this infection.

Results of Study on the Biological Properties of Isolated Cultures

The main biological properties of 17 isolated cultures and the reference strain *P. multocida* bovis No. B-0229 are shown in Table 2.

The data in Table 2 indicate that the main biological properties of the isolated cultures correspond to the reference strain *P. multocida* bovis No. B-0229. As a result, in the Hiss medium, the culture under study had a fermenting effect on mannitol, sucrose, glucose, dextrose, and maltose; it did not have a fermenting effect on gelatin, formed indole, and did not have hemolytic properties. The species *P. multocida* bovis included bacteria with the properties described above.

Zoning of Kazakhstan by the Degree of Cattle Pasteurellosis Spread in 2021

Serological studies conducted using the IHT showed that antibodies to the pasteurellosis pathogen were detected in most samples of delivered serum. The results of serological and bacteriological studies of biomaterials from various regions of Kazakhstan are presented in Table 3.

As the data in Table 3 show, in 192 cases the diagnostic titer was higher than 1:100 in IHT from 1,435 samples examined (13.4%), which may be due to routine vaccination. Epizootic outbreaks of cattle pasteurellosis are caused by the virulence of pasteurellosis, as well as the state of natural resistance of animals. The disease occurs as a result of the suppression of immune mechanisms in animals due to adverse factors. Against the background of a sharp decrease in the resistance of the animal's body, pasteurellosis can manifest itself as a second infection and proceed in the form of an epizootic disease.

The largest number of positively reacting animals was detected in Kyzylorda (27; 22.8%), Karaganda (24; 20.1%), West Kazakhstan (22; 18.9%), Turkestan (22; 18.3%), Pavlodar (19; 15.8%), Akmola (15; 12.5%), Aktobe (10; 12.5%), East Kazakhstan (12; 10.0%), Zhambyl (10; 9.8%), Almaty (13; 8.9%), North Kazakhstan (8; 6.8%), and Kostanay (5; 4.2%) regions. As a result, a visualization map for 2021 was compiled based on the results of our study (Fig. 4).

DISCUSSION

In Kazakhstan, according to veterinary reports and our research, a prevalence of cattle pasteurellosis can be observed. Based on the results of bacteriological studies, the isolated cultures of the disease pathogen are identical in their biological, biochemical, and immunological properties to the reference strains. A study of the biological properties of 17 isolates was carried out. All the studied isolates have been assigned to the *P. multocida* species. The most unsafe years for the entire period of the study were 2016 when 25 pasteurellosis EF were established in Kazakhstan, 2013 and 2015 with 15 EF, and 2017 with 14 EF.

The practical conclusions based on the results of our study include the created classification based on the allocation of 4 zones in Kazakhstan, depending on the number of cattle pasteurellosis EF in each of the zones.

Table 1: Number of unsafe points regarding cattle pasteurellosis according to CVCS data for the last 8 years

Region name	2013	2014	2015	2016	2017	2018	2019	2020	Total
	Number of unsafe points								
Akmola	1								1
Almaty	2	1	5	1	3				12
Atyrau		1	1	7	2	2			13
Aktobe	1			5	1	2	1	1	11
East Kazakhstan	3	3	1	8	2	3	1	3	24
Zhambyl	2	1							3
West Kazakhstan	4	3	2	2	3	2	2	3	21
Karaganda	1		2	2	2	2			9
Kostanay	1		2						3
Kyzylorda			2						2
North Kazakhstan									-
Pavlodar					1				1
South Kazakhstan									-
Total:	15	9	15	25	14	11	4	7	100

Table 2: Basic biological properties of isolated cultures and the reference strain *P. multocida* bovis No. B-0229

Properties	Cultures under study																Reference culture
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	
Hemolysis on blood agar	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Gelatine liquefaction	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Mannitol fermentation	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sucrose fermentation	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Glucose fermentation	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Dextrose fermentation	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Maltose fermentation	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Catalase activity	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Indole formation	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

Note: "+": positive; "-": negative.

Table 3: Results of the study of biomaterial on cattle pasteurellosis for 2021

Region name	No. of samples examined serology/bacteriology	No. of animals studied	Reacted positively to IHT		Bacteriology results	
			abs	%	abs	%
Turkestan region	120/240	120	22	18.3	0	0.0
Zhambyl region	102/204	102	10	9.8	1	0.5
North Kazakhstan region	116/232	116	8	6.9	1	0.4
Kostanay region	118/236	118	5	4.2	0	0.0
Kyzylorda region	118/236	118	27	22.9	3	1.3
East Kazakhstan region	120/240	120	12	10.0	2	0.8
Pavlodar region	120/240	120	19	15.8	2	0.8
Almaty region	146/296	146	13	8.9	2	0.7
Aktobe region	120/240	120	15	12.5	2	0.8
West Kazakhstan region	116/232	116	22	19.0	2	0.9
Akmola region	120/240	120	15	12.5	0	0.0
Karaganda region	119/238	119	24	20.2	2	0.8
TOTAL	4,305	1,435	192	13.4	17	0.6

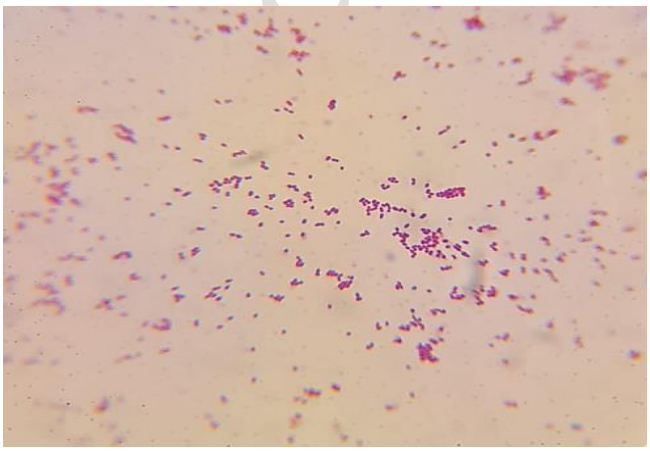

Fig. 1: The result of a Gram-stained reference strain of *P. multocida* bovis No. B-0229.

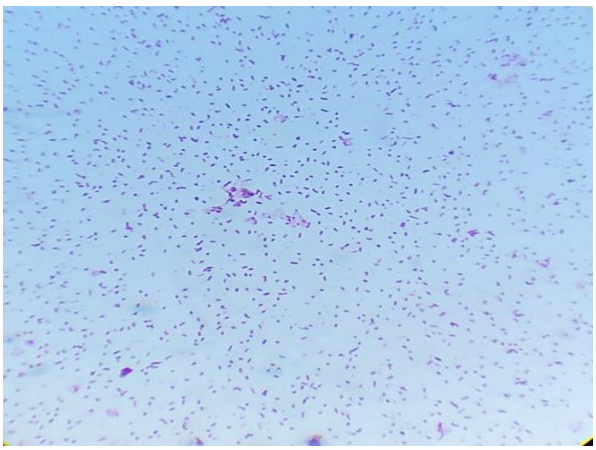

Fig. 2: The result of Gram-stained biomaterial under study.

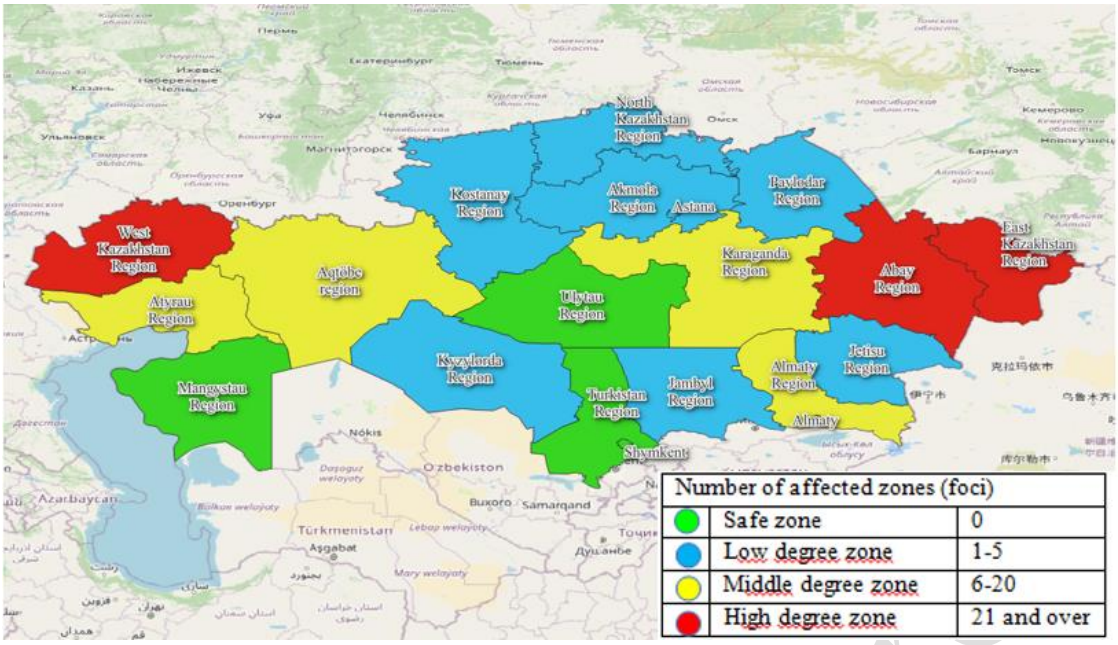

Fig. 3: Zoning of Kazakhstan by the degree of cattle pasteurellosis spread for 2013-2020.

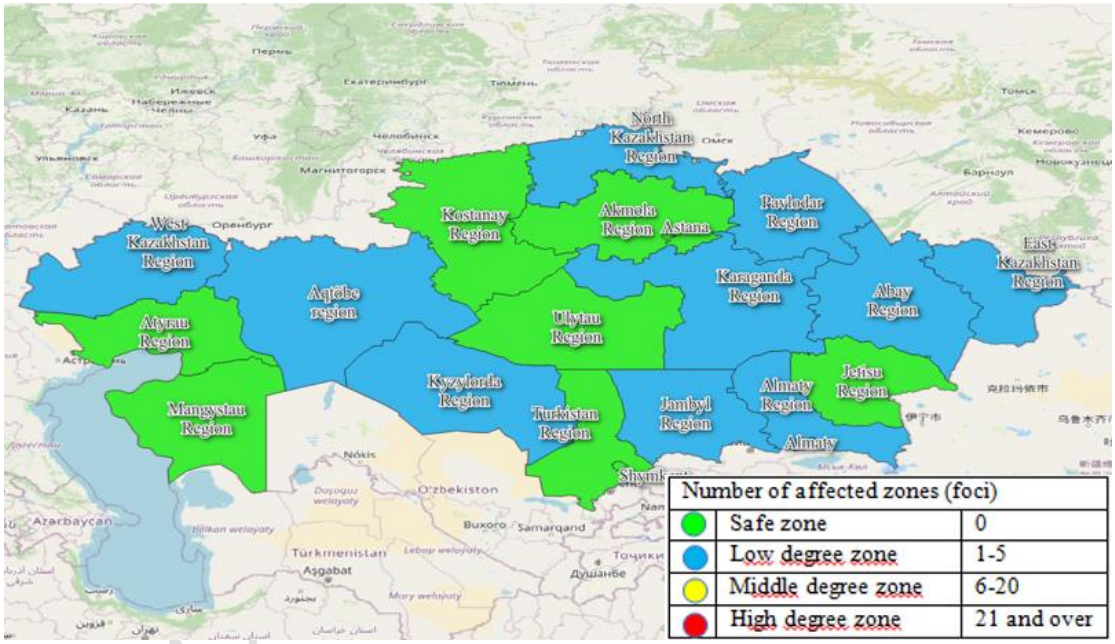

Fig. 4: Zoning of Kazakhstan according to the degree of spread of cattle pasteurellosis in 2021 based on our study.

Based on the visualization map created by us for the last eight years 2013-2020 according to the CVCS of the Ministry of Agriculture of the Republic of Kazakhstan and for 2021 based on the results of our study, we can make a forecast about a decrease in the incidence of cattle pasteurellosis throughout Kazakhstan. This forecast includes both a zone of stable safety and a zone of moderate risk, characterized by relative safety with periodic registration of isolated cases of the disease that do not spread.

Monitoring of cattle pasteurellosis in Kazakhstan shows that one of the main reasons for the appearance of the disease is the large range of susceptible animals and the exceptional adaptability of the pathogen to inhabit the body of various species of living beings to a large extent. The disease is accompanied by a decrease in productivity, and long-term carrying of pathogenic forms of the microbe, and in addition, animals carrying Pasteurella can cause the emergence of new EF.

Based on the purpose of our study, we did not include the determination of the exact causes of the spread of pasteurellosis among the foci we identified. However, our conclusions do not contradict previous studies, according to which factors contributing to the spread of pasteurellosis can be feed, water, air, bedding, care items infected with the secretions of sick animals, slaughter products, leather, wool, and other raw materials obtained from sick animals, slaughtered out of necessity or having died from pasteurellosis (Ujvári et al. 2019; Tkalich 2020; D'Amico et al. 2022). Besides, we believe that the disease is characterized by seasonality (summer period) and stationarity.

The intensity of the epizootic situation for pasteurellosis can be reduced by the developed strategy and

some special measures (both one-time and recurrent). Vaccination plays a crucial role in the prevention of cattle pasteurellosis. The introduction of appropriate vaccines can provide immunity against *P. multocida* and significantly reduce the risk of infection. Research results show that for effective vaccination, it is necessary to determine the most effective vaccine and develop and follow the vaccination schedule (El-Jakee et al. 2020; Mostaan et al. 2020; Zhao et al. 2022). Currently, in Kazakhstan, vaccines against pasteurellosis have shown mixed results, but none of them provided full protection (Kirkimbaeva et al. 2014). For vaccines that are used for cattle vaccination in Kazakhstan, there are problems with compliance with the schedule of their use. The logistics of delivering vaccines to remote rural areas are often difficult, resulting in insufficient vaccination coverage in these regions. The lack of an automated information system for recording and compliance with the vaccination schedule may lead to cattle not being vaccinated on time. Some farms refuse to use vaccines due to a lack of funds for the keeping of animals. Further research is needed to develop more effective vaccines that can more consistently prevent pasteurellosis. As climate change affects weather patterns, it also changes disease patterns. Therefore, when using and developing vaccines, it is necessary to take into account the seasonality factor. For Kazakhstan, the dangerous season is the summer period.

In addition to vaccination, it is necessary to constantly observe special measures that will help prevent cattle pasteurellosis. The introduction of strict biosafety measures is vital to prevent the introduction and spread of pasteurellosis (Callan and Garry 2002). This includes controlling the movement of animals, limiting contact with infected animals or carrier animals, and observing hygiene rules, such as proper disinfection of equipment, vehicles, and premises (Faradzhov and Alieva 2018; Tkalich 2020).

Besides, when introducing new animals into the herd, it is important to require the farm to quarantine new animals for a certain period (Karabassova et al. 2022) and conduct appropriate tests to identify any carriers of *P. multocida* (Alarawi and Saeed 2021). This step helps prevent bacteria from entering the herd and allows timely treatment or drafts of infected animals.

Another important element of the strategy aimed at reducing the intensity of the epizootic situation in Kazakhstan is to ensure optimal nutrition and a well-balanced diet for animals. Farms need to better monitor the consumption of essential nutrients and vitamins by animals, which helps to maintain the overall health of the herd, reducing susceptibility to pasteurellosis.

We believe that it is necessary to develop and implement a strategy with the mandatory support of relevant government agencies and the allocation of financial resources, which would include conducting additional research to develop more effective vaccines, improving logistics and supply chains to ensure the availability of vaccines in all regions of Kazakhstan, promoting professional training of farm workers regarding the benefits of vaccination and effective methods for pasteurellosis introduction prevention, implementation of more advanced data management systems for tracking vaccinations, and regulation of the use of antimicrobial medications. Preserving the health of cattle in Kazakhstan is crucial not only for the country's food supply but also for the economic safety of farms (Kaliyev et al. 2019).

Conclusion

Based on the results of the conducted study, we have developed visualization maps with qualitative and quantitative indicators of the epizootic process in various regions of Kazakhstan regarding cattle pasteurellosis for 2013-2021. The maps show detailed epizootological data characterizing the degree of infection spread in the context of regions, districts, rural districts, and EUs, and the level of pasteurellosis cattle. Based on the data obtained, a forecast was made about a decrease in the incidence of cattle pasteurellosis throughout Kazakhstan. This forecast includes both a zone of stable safety and a zone of moderate risk, characterized by relative safety with periodic registration of isolated cases of the disease that do not spread.

In our study, we did not determine the exact causes of the spread of pasteurellosis among the foci of infection identified by us. Further research should be aimed at studying the factors contributing to the spread of pasteurellosis in each area where a focus of infection is detected.

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Authors' Contribution

Z.K. Buienbayeva: conception and design, acquisition of data. Z.A. Latypova: analysis and interpretation of data, revising it critically. B.Zh. Issakulova: conception and design, acquisition of data, drafting the article. F.A. Bakiyeva: acquisition of data, drafting the article, final approval. A.M. Namet: analysis and interpretation of data, revising it critically. Anda Valdovska: drafting the article, final approval.

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