

Review

official reviewer for the dissertation work of Mingcheng Liu on the topic: «Experimental research on pathogenesis of *Streptococcus suis* infection», which was submitted for obtaining the scientific degree of Doctor of Philosophy in the field of knowledge 21 «Veterinary», specialty 211 «Veterinary Medicine»

1. Relevance of the dissertation topic.

Streptococcal infection of pigs is registered in pig farms of Ukraine, the People's Republic of China and other countries of the world, causing large economic losses to livestock farmers. Due to the growing problem of antibiotic resistance of bacteria, therapeutic measures for bacteriosis have low effectiveness. *Streptococcus suis* is an important zoonotic pathogen that can cause serious diseases such as meningitis, pneumonia, endocarditis, polyserositis, arthritis, septicemia and abortion in pigs. Pigs are also asymptomatic carriers of *Streptococcus suis* 2. This pathogen is also potentially dangerous for humans, which is a serious threat to the safety of public health. The incidence of streptococcal infection in various countries of the world tends to increase. Therefore, implementation of effective measures to prevent and combat this disease is an urgent task. The effectiveness of control measures is based on the study of the pathogenesis of streptococcal infection. The prerequisite for the pathogenetic development of meningitis is the penetration of *S. suis* into the central nervous system through the blood-brain barrier. This histohematic barrier is located in the central nervous system at the border between blood and nervous tissue and regulates the flow of substances circulating in the blood from the blood into the cerebrospinal fluid and nervous tissue. The complex physiological mechanism of the body provides protection of brain tissue from damage and maintenance of central nervous system homeostasis. Endothelial cells of the microvessels of the brain are the main components that interact with pathogens, after which the pathogens penetrate through the blood-brain barrier (BBB), causing infection of the brain. Antibacterial drugs used to treat bacterial infections cannot cross the blood-brain barrier to reach the therapeutic target site, which is a major factor in the control of bacterial meningitis caused by *S. suis*. Thus, the experimental study of the pathogenetic mechanisms of *S. suis* penetration through the blood-brain barrier into the central nervous system is an important aspect in the development of a strategy to control swine streptococcal infection.

2. Connection with scientific topics.

Dissertation studies were carried out in accordance with the priority direction «Life sciences, new technologies for the prevention and treatment of the most common diseases». The materials of the dissertation research are part of comprehensive scientific research of the Department of Epizootology and Parasitology, Faculty of Veterinary Medicine of the Sumy National Agrarian University according to the thematic plan of the research work «Optimization of the set of measures to prevent the occurrence and spread of infectious diseases of

animals in the farms of the North-Eastern region of Ukraine» (№ 0122U001254) . Experimental research on the topic of the dissertation was conducted in the period from 2019 to 2023 at the Department of Epizootology and Parasitology of the Sumy National Agrarian University. The dissertation is a fragment of the research programs of the National Natural Science Foundation of China «Project for the Development of Young Talents of Henan Province».

3. Scientific novelty and theoretical significance of the dissertation.

Acquaintance with the content of the dissertation, conclusions, recommendations and main scientific works made it possible to determine the scientific novelty of the obtained research results. The main scientific results of the research, which reflect the scientific novelty of the dissertation work, are an experimental study of the pathogenetic processes of the development of meningitis due to streptococcal infection of pigs. The following new scientific results were obtained in the dissertation: the pathogenesis of meningitis was investigated from the point of view of pyroptosis. The bacterial pathogen *S. suis* (serotype 2) previously isolated from pigs was used in the experiments, the identification of which was carried out at the Henan Institute of Technology (Henan Province, China). The paper presents the results of experimental studies of virulence factors of isolates, as well as genes associated with the development of pathogenetic processes of pyroptosis in cell culture. In *in vitro* experiments, the acquirer worked out various schemes for infecting the culture of endothelial cells of the brain microvessels of white mice (Bend3) with the bacterial pathogen *S. suis* 2.

In the experiment, the method of RNA indication of the genome of *S. suis* serotype 2 was improved, reverse transcription of the genome of this pathogen to stable DNA was obtained for the detection of related cytokines.

With the help of electron microscopy, the pathomorphological changes characteristic of pyroptosis in the culture of endothelial cells of microvessels of the brain of mice (b.End3) infected with *S. suis* 2 were proven. Thus, for the first time, the development of pyroptosis as the final link of the pathogenetic process of meningitis due to streptococcal infection of pigs caused by *S. suis* was experimentally proven (serotype 2).

4. The practical significance of the results of the dissertation.

On the basis of the obtained results of experimental studies, the pathogenesis of streptococcal infection of pigs was proven based on the *in vitro* study of the pathogenetic mechanism of the development of meningitis. Liu Mingcheng's dissertation presents the theoretical rationale for the prevention and treatment of this infection based on the use of targeted drugs and the development of new vaccines. The research results presented in the dissertation are well-founded and reliable.

The main provisions of the dissertation were included in the scientific and practical recommendations «Streptococcus suis infection (Etiology, Epidemiology, Laboratory diagnosis, Prevention and Treatment)», authors: Liu Mingcheng, Kasianenko Oksana (approved at the meeting of the Academic Council of the Sumy

National Agrarian University, protocol № 18 of 05.29.2023). The main results of the dissertation work were implemented in the educational process during the teaching of the disciplines: «Epizootology and infectious diseases», «Veterinary technologies for the prevention of infectious diseases of animals», «Anti-epizootic measures in animal husbandry» at the department of epizootology and parasitology in the training of specialists with the degree of higher education «Master» from specialty 211 «Veterinary Medicine» at Sumy National Agrarian University.

5. The main results obtained personally by the author.

The author, with the Scientific supervisor (consultant) - doctor of veterinary sciences, professor O. I. Kasianenko - determined the goal and task of the work, substantiated the scientific direction and research program, analyzed the obtained results. The ideas, hypotheses, and experimental data included in the dissertation research are not duplicated, planned, executed, and belong to the dissertation student. Independently developed scientific provisions, carried out laboratory research, analysis and interpretation of the obtained results, processing of literary sources of foreign authors, statistical processing of materials and formulated conclusions.

An analysis of the plagiarism check report for the presence of textual borrowings (Strike plagiarism program) was carried out. The reviewers came to the conclusion that the dissertation work of Liu Mingcheng (Mingcheng Liu) on the topic: «Experimental study of the pathogenesis of streptococcal infection in pigs» («Experimental research on pathogenesis of Streptococcus suis infection») is the result of independent research of the acquirer and does not contain elements of plagiarism and borrowing in accordance with the resolution of the CMU dated 12.01.2022 No. 44, paragraph 9. The used ideas, results and texts of other authors have a link to the corresponding source.

6. Number of scientific publications.

The main provisions of the dissertation research are covered in 13 scientific works, including 5 articles in specialized scientific publications, 7 publications of an approbation nature, 2 of which were published in publications of foreign countries; one scientific and practical recommendation.

7. Remarks and wishes for the content.

The dissertation submitted for review is written in English in accordance with the current requirements of the Ministry of Education and Science of Ukraine and includes all necessary sections. The main content of the dissertation consists of an abstract in English and Ukrainian, an introduction, a review of the literature, research materials and methods, the results of own research, their generalization and analysis, conclusions, proposals for production, a list of used literary sources, which includes 222 titles in Latin, as well as appendices, containing materials and acts of implementation of scientific and practical use of research results.

While giving a general high rating to Lui Mincheng's dissertation work, it is necessary to point out the identified individual shortcomings and inconsistencies,

namely stylistic exposition of the material. However, the above-mentioned remarks are not fundamental and do not reduce the overall positive assessment and scientific significance of Liu Mincheng's dissertation work.

8. Correspondence of the thesis to the specialty and profile of the council:

Dissertation work of Mingcheng Liu (Mingcheng Liu) on the topic: «Experimental study of the pathogenesis of streptococcal infection in pigs» («Experimental research on pathogenesis of Streptococcus suis infection»), which was submitted for defense to the specialized scientific council for obtaining the degree of Doctor of Philosophy in the field of knowledge 21 «Veterinary Medicine» in the specialty 211 «Veterinary Medicine» according to its relevance, scientific and theoretical level, the main results of validity, the main provisions and results published in professional publications, the novelty of the formulation and the practical significance meet the requirements of the order of the Ministry of Education and Culture of Ukraine № 40 of January 12, 2017 «On the approval of requirements for the preparation of a dissertation» and Resolution of the Cabinet of Ministers of Ukraine of January 12, 2022 № 44 «On the approval The procedure for awarding the degree of Doctor of Philosophy and annulment of the decision of the one-time specialized academic council of the institution of higher education, scientific institution on awarding the degree of Doctor of Philosophy» with changes made in accordance with Resolution of the Cabinet of Ministers № 341 dated 03.21.2022. The content of the dissertation corresponds to the passport of the specialty.

Reviewer
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