

FOOT-AND-MOUTH: ETIOLOGY, PATHOGENESIS, PREVENTION AND CONTROL MEASURES

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Annotation. The last outbreak of foot-and-mouth disease in the Republic of Kazakhstan was detected in the East Kazakhstan region in 2013. As part of the approved FMD control strategy, the country's territory is divided into 2 free FMD zones (with and without vaccination).

Specialists of the International Epizootic Bureau were invited to the republic, and the vaccines used were analyzed. And we must admit that this work has yielded certain results. Nine regions have been granted FMD-free status without vaccination. However, for the first time in many years, in January 2022, an outbreak of foot-and-mouth disease, a dangerous viral disease that can be transmitted to humans, was detected in the Karaganda region. Which crossed out almost all the work done on the way to well-being and zeroed out the chances for the development of export animal husbandry.

Foot-and-mouth disease is a cross-border disease, the source of which is domestic and wild ungulates. This disease is caused by a virus of the genus Aphthovirus of the Picornaviridae family, which affects artiodactyls, both wild and domestic. Transmission of FMD virus from sick animals to other susceptible animals can occur directly or indirectly. Treatment and control of foot-and-mouth disease among livestock or animals can be carried out through isolation and quarantine of sick animals, vaccination programs, biosafety measures in animal husbandry, monitoring of livestock movement and surveillance.

Key words: virus; etiology; pathogenesis; diagnosis; prevention.

Introduction

Foot-and-mouth disease is a well-known transboundary animal disease (TAD), recognized by the Steering Committee of the Global Framework for the Progressive Control of Transboundary Animal Diseases in Europe as a priority disease. Foot-and-mouth disease has a serious impact on livestock production, disrupting regional and international trade in animals and animal products. FMD can be transmitted to humans. The main way of infection of people is through raw milk of sick animals and products of its processing, less often through meat. In persons in direct contact with sick animals, direct transmission of infection is possible (during milking, care, treatment, slaughter), an airborne pathway of infection (when breathing, coughing animals), as well as through objects contaminated with their secretions. However, the infection is not transmitted from person to person. The disease circulates among 77% of the world's livestock: in Africa, the Middle East and Asia, as well as in a limited area in South America [1, 2]. Countries currently free of foot-and-mouth disease without vaccination remain under constant threat of this disease entering their territory. The rapid genetic evolution of viruses, the geopolitical situation, and the uncontrolled movement of livestock between regions or countries endemic to foot-and-mouth disease raise concerns about infection with a new genotype or serotype of foot-and-mouth disease.

The last outbreak of foot-and-mouth disease in the Republic of Kazakhstan was detected in the East Kazakhstan region in 2013. As part of the approved FMD control strategy, the country's territory is divided into 2 free FMD zones (with and without vaccination) (Figure 1).



Figure 1 - Zoning of the territory of Kazakhstan into FMD-free zones without vaccination (highlighted in blue) and with vaccination (highlighted in green)

The territory of the Republic of Kazakhstan was considered safe for foot-and-mouth disease. At the same time, in 2015, nine regions in the west, center and north were recognized as a FMD-free zone without vaccination. And in 2017, five more regions in the south and east received the status of FMD-free with vaccination [3].

However, for the first time in many years, on January 14, 2022, an outbreak of foot-and-mouth disease, a dangerous viral disease that can be transmitted to humans, was detected in the Karaganda region. Which crossed out almost all the work done on the way to well-being and zeroed out the chances for the development of export animal husbandry.

The disease is caused by a virus of the genus Aphthovirus of the Picornaviridae family [4]. The virus can spread through direct contact with infected livestock, semen, aerosols, parasites and food [5]. Infected livestock or animals exhibit clinical symptoms such as increased salivation, temperature above 40°C, anorexia, damage to cheeks, nostrils, muzzle, gums, inner surface of lips and hooves [6]. The incidence rate of this disease is 100%, and the mortality rate in the benign course is from 1 to 5%, and in the malignant course the mortality rate can reach from 20 to 80%. This disease rarely leads to death, with the exception of young cattle [7].

Foot-and-mouth disease is not a zoonotic disease, but even in this case it can lead to significant economic losses [4, 8]. Firman et al. [9] stated that the financial losses caused by foot-and-mouth disease consist in a decrease in milk production by 25% per year, a decrease in fertility, a decrease in the growth rate of beef cattle, culling chronically infected livestock, loss of labor, disruption of domestic trade, loss of opportunities for livestock exports, elimination costs and mortality. Because of these losses, foot-and-mouth disease must be controlled and prevented. This article discusses foot-and-mouth disease, in particular: causes (etiology), pathogenesis, prevention and control of this disease. Clinical symptoms, susceptible animals, and transmission of the virus to animals are also considered.

The purpose of the review. To summarize current scientific data on epizootology, pathogenesis, diagnosis and prevention of foot-and-mouth disease in order to assess the risk of introduction and spread of the disease to free territories.

Material and methods

The search for sources was carried out by screening the international scientific citation databases Web of Science, Scopus, Google Scholar and the Kazakh scientific citation database. After eliminating repetitive and unverified data and selecting publications that fully correspond to the purpose of the work, 29 sources were selected.

The main part. Etiology. The causative agent of foot-and-mouth disease is an RNA-containing

virus of the Picornaviridae family, genus Aphthovirus, characterized by significant antigenic variability [10]. The virus is a small, 26 nm in diameter, single-stranded RNA virus without a shell, with a genome consisting of about 8,500 bases, surrounded by four structural proteins that form an icosahedral capsid [7]. In addition, this virus also has a strong capsid, so it is resistant to disinfectants that dissolve fat [11]. However, some studies have shown that sodium hypochlorite solution is widely used to inactivate viruses, including foot-and-mouth disease. However, this solution must be stored in cool and dark conditions in order to preserve its viral effect [12]. The virus affects ruminants, both domestic and wild, such as cattle, goats, sheep, buffaloes, pigs, elephants, deer, camels and African buffaloes [13].

Aphthovirus is an RNA virus that has seven different serotypes, A, O, C, Asia-1, SAT-1, SAT-2, SAT-3 and more than 60 subtypes. The foot-and-mouth disease virus capsid contains 60 structural copies of proteins. These proteins are VP2, VP3, VP1, and there are 8 nonstructural proteins (3A, 3B, 3C, L, 2A, 2B, 2C, and 3D) [14]. Serotypes O and A are the most widespread because they infect livestock in Africa, Asia and South America. Types SAT-1, 2 and 3 are currently found only in Africa, and the Asia-1 serotype is found in Asia. All serotypes of the foot-and-mouth disease virus can penetrate into free areas, and periodically SAT spreads to the Middle East, and Asia-1 to Western and Eastern Eurasia. In India, most outbreaks of foot-and-mouth disease are caused by serotype O, followed by serotype A and Asia-1 [15]. All serotypes of FMD virus cause similar clinical symptoms 2-14 days after infection [12]. It is believed that great diversity is the result of high mutation rates, quasi-individual dynamics, and recombination. Genetic variations can occur as a result of mutation or homologous recombination between two different strains of the foot-and-mouth disease virus, which leads to the emergence of new variants of the foot-and-mouth disease virus. These new variants significantly influence the choice of the vaccine strain [7].

The method of transmission

Foot-and-mouth disease is a highly contagious disease that is highly transmitted from one animal to another. The virus that causes foot-and-mouth disease enters the body of livestock or animals by inhalation, ingestion and contact through wounds on the skin and mucous membranes. Vertical transmission of infection to the fetus has also been reported [16]. Transmission of the disease occurs through direct and indirect contact [17]. Direct transmission of the virus occurs when viral particles are inhaled from the respiratory tract of infected animals. Even the spread of the virus through the air can lead to the movement of the virus from one place to another for a considerable distance, even up to 2-5 kilometers, and in strong winds the virus can be transmitted up to 15 kilometers, and infection can occur after 14 days after infection [9]. The virus can persist in the air for a long time in temperate or subtropical regions, but in hot and dry climates the virus cannot persist for a long time [14]. Transmission of the virus through the air or through the respiratory system is a frequent occurrence and leads to rapid spread. Indirect transmission of the virus occurs due to environmental contamination by foot-and-mouth disease. In addition, transmission can also occur through contact with contaminated agricultural materials or tools, such as employees, vehicles, feed, drinkers, and agricultural products such as meat and milk [18]. The virus can persist in organs, bones, and milk [19]. The virus can also persist for a long time in favorable environmental conditions. The ideal conditions for the survival of the foot-and-mouth disease virus are temperatures below 50 °C, humidity above 55% and a neutral pH level [20].

Foot-and-mouth disease virus in sick animals is found in secretions and discharges such as air, milk, saliva, urine, feces, semen, fluid in the vesicles of the lesion, amniotic fluid and fetus as a result of miscarriage. The amount of virus released varies greatly and depends on the type of host and strain of the virus. Animals with foot-and-mouth disease can secrete the virus within 50 hours and transmit it to other pets. In pigs, the virus is released in the form of aerosols, and the animal can even remove 100-1000 times more virus than infected sheep or cattle [20]. Thus, keeping pigs near cattle poses a great threat in the spread of the foot-and-mouth disease virus, since this increases the risk of spreading the disease by airborne droplets. Cattle are more susceptible to aerosol viruses than other domestic animals.

At the same time, pigs are more resistant to airborne infection with foot-and-mouth disease. Infected animals can act as carriers of infection for 8-24 months. In addition to the method of transmission described above, foot-and-mouth disease can be transmitted sexually, mechanically (vomit) and by contact animals such as goats, cattle and sheep [15]. The large number of infected pets and the lack of strict biosafety measures, i.e. isolation, are factors in the transmission of the virus from one animal to another. In addition, potential factors for the spread of foot-and-mouth disease are the purchase of breeding animals and cattle outside the region, the concern of owners when selling sick cattle and veterinary specialists serving in several districts [6]. The high rate of spread of the disease from one region to another is usually associated with the movement of infected livestock, vector animals, infected animal products, and by air [21].

Pathogenesis and clinical symptoms

Initially, scientists believed that the path of penetration of foot-and-mouth disease viruses lies through the upper gastrointestinal tract. However, as early as 1952, the susceptibility of cattle to vaccinations through the respiratory tract was experimentally demonstrated [22]. The main route of infection with the foot-and-mouth disease virus is the respiratory system. After that, the virus multiplies in the pharyngeal membrane, enters the blood (viremia) and lymphatic vessels, and then spreads and develops in organs such as the oral cavity, mammary glands and feet, causing wounds or blisters [21]. The virus can be detected in cattle and sheep within 2 years after infection. The virus can also be found in many body fluids such as urine, semen, respiratory secretions, and milk. In the oral cavity of infected animals, the virus can persist for a long time [14]. In addition to inhalation, foot-and-mouth disease viruses can also enter the body of susceptible animals when swallowed, through wounds on the skin and mucous membranes of infected animals. After ingestion, the virus will multiply in the epithelial cells of the oral cavity, causing inflammation around the mouth [6].

Animals infected with FMD exhibit clinical symptoms such as the formation of bubbles or blisters in the mouth, gums, tongue, nipples and skin around the hooves, increased salivation (Figure 2), weight loss and productivity [23].

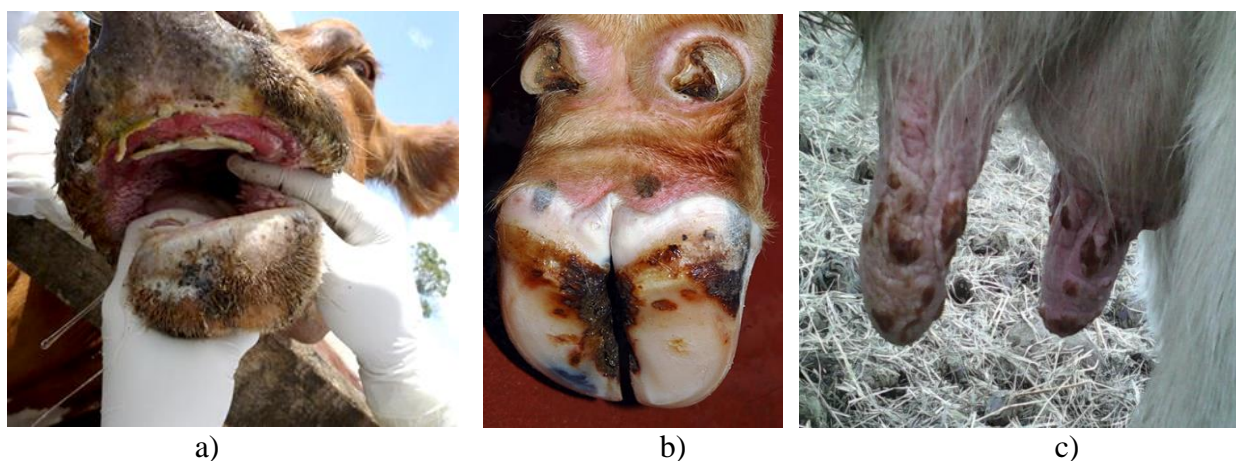


Figure 2 - Clinical picture of foot-and-mouth disease in cattle. Lesions of the oral cavity (a), hooves (b), udders (c).

Ismail et al. [16] analyzed the main clinical symptoms of foot-and-mouth disease in dairy cows that were infected with foot-and-mouth disease. The results showed that the clinical symptoms found were lameness (lesions on the legs) and increased salivation. Foot-and-mouth disease also causes abortion in pregnant cows and myocarditis in lactating cows. In addition to these symptoms, the disease causes other clinical signs such as fever up to 41 °C, anorexia and blisters in the mouth and legs; after 24 hours, the blisters burst and cause erosion. This follows from the results of a study conducted by Woolandani [6], which stated that meat cattle infected with foot-and-mouth disease have symptoms such as anorexia, blisters on the tongue, lips, gums, as well as increased salivation.

In sheep and goats, these lesions are less noticeable, but in young animals, lesions around the teeth and death are observed. In pigs, clinical symptoms appear in the form of blisters on the gums, tongue, cheeks, between teeth, palate, muzzle, lips, coronary ring, udder nipples. Lesions are also most noticeable on the hooves, where they form on the coronal traction, as well as on the calcaneal tubercle or in the interdigital fissure (Figure 3). Injuries in animals after death are found in the scar and myocardium, and some young animals are called "tiger heart" [24].

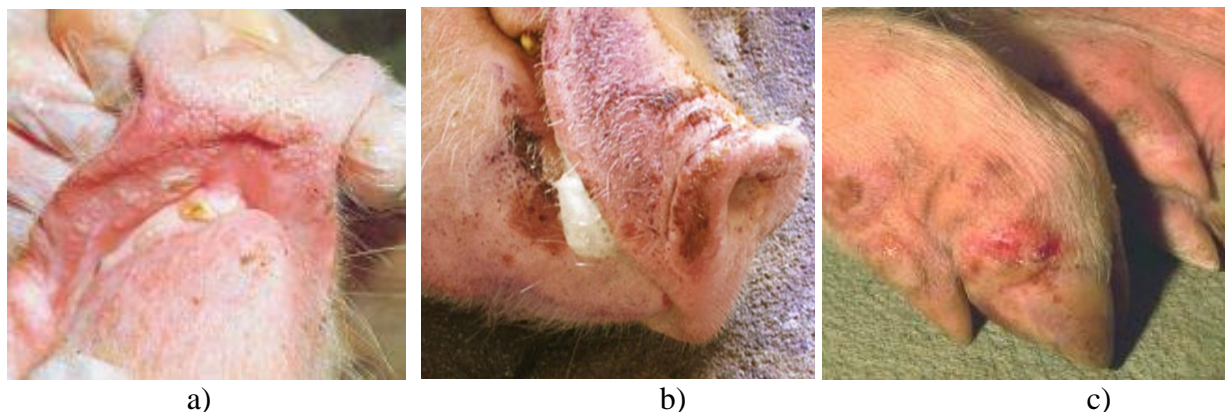


Figure 3 - The clinical picture of foot-and-mouth disease in pigs. Lesions in the oral cavity (a), on the patch (b), on the hooves (c).

Diagnostics

Accurate diagnosis of foot-and-mouth disease is important because it is linked to efforts to control and eradicate the disease in endemic areas and is an auxiliary step in the eradication of foot-and-mouth disease in the region. The diagnosis of foot-and-mouth disease is based on such clinical symptoms as high fever, increased salivation and the formation of bubbles on the mucous membrane of the mouth, nose and feet [6]. However, these clinical symptoms can be confused with other diseases such as vesicular stomatitis, so laboratory diagnosis is necessary. In addition, there is no cross-protection between serotypes, and the serotype of the virus that caused the outbreak cannot be determined based on clinical signs. Therefore, the serotype that caused the outbreak in the field should be determined in the laboratory to ensure proper animal protection. Various methods are used to diagnose the disease and confirm the serotype of the virus, such as the viral neutralization reaction (VN), which is the gold standard for detecting antibodies to structural proteins of the foot-and-mouth disease virus and is a mandatory test for certification of animals/animal products during import/export. Enzyme immunoassay (ELISA), virus isolation, reverse transcription polymerase chain reaction (RT-PCR), loop isothermal amplification of DNA and RNA (RT-LAMP), chromatographic test strips, differentiation between infected and vaccinated animals (DIVA) [25]. Longjem [26] stated that PCR makes diagnosis faster and more accurate. Multiplex PCR makes it possible to detect FMD in the largest number of samples (65.47%), followed by sandwich ELISA (53.57%) and virus isolation (42.85%). To detect the virus, samples of fluid from blisters, epithelial cells in blisters, or fluid from the oropharynx and blood are needed. If the animal dies, it is possible to take lymph nodes, thyroid, kidney, spleen and liver tissues. The samples to be tested must be stored properly so that laboratory tests correspond to the condition of the tested animal [13].

Prevention and control.

Foot-and-mouth disease is not a zoonotic disease, but even in this case it can lead to significant economic losses, so it is necessary to make great efforts to prevent and combat this disease. Some of the measures that can be taken to prevent and control foot-and-mouth disease include ensuring strict biosecurity, for example, protecting free zones by restricting the movement of livestock or animals, traffic control and supervision, banning the import of livestock from infected areas, slaughtering infected animals or those acting as vectors, disinfection premises where animals were and are kept, equipment (vehicles, clothing, cleaning equipment, etc.), destruction of carcasses and livestock products in infected areas, isolation and quarantine of livestock [27, 28, 13]. In addition, prevention and control of foot-and-mouth disease can also be carried out through

vaccination. However, this is difficult to do, since foot-and-mouth disease is caused by several serotypes of viruses, a variety of vectors and an extremely high transmission rate [17]. Meanwhile, according to [13], vaccination effectively eliminates foot-and-mouth disease in cattle. Vaccination against foot-and-mouth disease can only be carried out in healthy cattle and calves aged 2 weeks and older, the purpose of which is to develop immunity to foot-and-mouth disease [29].

Improving the methods and methods of FMD control requires a differentiated approach, taking into account regional peculiarities. In Kazakhstan and Central Asia, the need to strengthen border veterinary control is of particular importance, especially on the borders with China and the Kyrgyz Republic, where there is a high risk of infection [30], as well as the need to expand the use of modern vaccine preparations, the effectiveness of which has been confirmed against circulating strains of the virus [31, 32]. As for the countries of the Middle East and Africa, their primary tasks are the modernization of the material and technical base of diagnostic laboratories [25], the introduction of modern methods of molecular diagnostics [33] and strengthening cooperation with international organizations (OIE, FAO) in the field of epidemiological surveillance [31, 34]. At the same time, in Europe and North America, the main emphasis remains on maintaining the status of FMD-free territories, which is achieved through strict control of imported livestock products, improving the animal identification system and maintaining a high level of biological safety of enterprises [22, 32]. The identified regional features of the spread of foot-and-mouth disease emphasize the need to develop targeted preventive programs that take into account the local epidemiological situation, the genetic characteristics of circulating strains and the technical equipment of veterinary services [35], which together will optimize resources and increase the effectiveness of antiepidemic measures in each specific region.

Conclusion

Foot-and-mouth disease is caused by the foot-and-mouth disease virus, which belongs to the genus Aphthovirus and the family Picornaviridae. The disease affects four-legged or artiodactyl farm animals, both wild and domestic. The foot-and-mouth disease virus is very contagious, it enters the animal's body directly through the mouth or respiratory tract and multiplies on epithelial cells in the nasopharynx, then enters the bloodstream, where it multiplies on lymphoglandular glands and epithelial cells in the mouth and extremities, which leads to the formation of bubbles and blisters. Animals infected with FMD show clinical symptoms such as fever up to 41 ° C, the formation of bubbles or blisters in the mouth, gums, tongue, nipples and skin around the hooves, increased salivation, weight loss and decreased productivity of livestock. The fight against foot-and-mouth disease among livestock can be carried out by isolating and quarantining sick animals, vaccinating, disinfecting animal housing and inventory, monitoring livestock movement and conducting surveillance.

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АУСЫЛ: ЭТИОЛОГИЯСЫ, ПАТОГЕНЕЗІ, АЛДЫН-АЛУ ЖӘНЕ ОНЫМЕН КҮРЕСУ ШАРАЛАРЫ

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Аннотация. Қазақстан Республикасында аусылдың соңғы өршуі Шығыс Қазақстан облысында 2013 жылы анықталды. Аусылды бақылаудың бекітілген стратегиясы шеңберінде ел аумағы аусылсыз бос 2 аймаққа (вакцинациямен және вакцинациясыз) бөлінген. Республикаға халықаралық эпизоотиялық бюроның мамандары шақырылып, қолданылатын вакциналар талданды. Бұл жұмыс белгілі бір жеміс бергенін мойындау керек. Тоғыз аймақ вакцинациясыз аусылсыз деген мәртебеге ие болды. Кейінірек тағы бес аймаққа аусылсыз деген мәртебе берілді, бірақ вакцинациямен. Алайда, көптеген жылдардан кейін алғаш рет 2022 жылдың қаңтарында Қарағанды облысында аусыл ауруы – адамға жұғуы мүмкін қауіпті вирустық ауру анықталды. Ол осы ауру бойынша сәттілікке қол жеткізу жолында атқарылған барлық жұмыстарды сызып тастап, экспорттық мал шаруашылығын дамыту мүмкіндігін нөлге түсірді.

Аусыл-бұл трансшекаралық ауру, оның тарау көзі үй және жабайы тұяқтылар. Бұл ауруды *Picornaviridae* тұқымдасына жататын *Aphthovirus* тұқымдасының вирусы қоздырады, ол аша тұяқты жабайы да, үй жануарларына да жұғады. Аусыл вирусының ауру жануарлардан басқа қабылдағыш жануарларға берілуі тікелей немесе жанама түрде болуы мүмкін. Аусыл вирусы жануардың денесіне ауыз немесе мұрын арқылы тікелей еніп, мұрын-жұтқыншақ аймағындағы эпителий жасушаларында көбейіп, содан кейін қанға ену арқылы тез таралуы мүмкін (виремия), содан кейін лимфогландулярлы бездерде және аузындағы эпителий жасушаларында және табан жастықшаларында көбейіп, көпіршіктер мен күлбіреуге әкеледі. Үй жануарлары немесе жануарлар арасында аусыл ауруын емдеу және бақылау ауру жануарларды оқшаулау және карантин, вакцинация бағдарламалары, мал шаруашылығындағы биоқауіпсіздік шаралары, мал қозғалысын бақылау және қадағалау арқылы жүзеге асырылуы мүмкін.

Түйінді сөздер: вирус; этиология; патогенез; баламалау; алдын алу.

ЯЩУР: ЭТИОЛОГИЯ, ПАТОГЕНЕЗ, ПРОФИЛАКТИКА И МЕРЫ БОРЬБЫ С НИМ

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Аннотация. Последняя вспышка ящура в Республике Казахстан была выявлена в Восточно-Казахстанской области в 2013 году. В рамках утвержденной стратегии контроля ящура территория страны разделена на 2 свободные зоны ящура (с вакцинацией и без вакцинации).

В республику приглашались специалисты Международного эпизоотического бюро, анализировались используемые вакцины. И надо признать – эта работа дала определенные плоды. Девять регионов получили статус свободных от ящура без вакцинации. Позднее еще пяти областям также дали статус свободных, но с вакцинацией. Однако, впервые за много лет в январе 2022 года в Карагандинской области выявлена вспышка ящура – опасного вирусного заболевания, которое может передаваться человеку. Которая перечеркнула практически весь проделанный труд на пути к благополучию и обнулила шансы для развития экспортного животноводства.

Ящур – это трансграничная болезнь, источником которого являются домашние и дикие копытные животные. Это заболевание вызывается вирусом рода Aphthovirus семейства Picornaviridae, который поражает парнокопытных животных, как диких, так и домашних. Передача вируса ящура от больных животных другим восприимчивым животным может происходить прямо или косвенно. Вирус ящура может передаваться быстро, проникая в организм животного непосредственно через рот или нос и размножаясь в эпителиальных клетках в области носоглотки, затем попадая в кровь (виремия), затем размножаясь в лимфогландулярных железах и эпителиальных клетках во рту и подушечках лап, что приводит к образованию пузырьков и волдырей. Лечение и борьба с ящуром среди домашнего скота или животных могут осуществляться путем изоляции и карантина больных животных, программ вакцинации, мер биобезопасности в животноводстве, мониторинга движения скота и проведения эпиднадзора.

Ключевые слова: вирус; этиология; патогенез; диагностика; профилактика.