Check for updates
CC BY

https://doi.org/10.29326/2304-196X-2024-13-1-11-19

Molecular epidemiology of foot-and-mouth disease (review)

Aleksey V. Scherbakov
Federal Centre for Animal Health, Yur'evets, Vladimir 600901, Russia

ABSTRACT

Molecular epidemiological studies are an important tool for regional and global surveillance of foot-and-mouth disease (FMD). These tests are based on constantly progressing technologies of nucleic acid sequencing and phylogenetic analysis. The use of these technologies made it possible to assess the genetic diversity of the FMD virus, to analyze the evolution of the virus in the enzootic regions, and track the pathways of FMD epizootic and panzootic spread. Molecular epidemiological studies have shown that within the long-known seven serotypes of the FMD virus, there are numerous topotypes (geographical types), genetic lineages and sublineages. Usually, the foot-and-mouth disease virus of a certain topotype and genetic lineage evolves within a certain area, periodically causing regional epizootics. However, over the past 30 years, two FMD panzootics have occurred, invloving several continents. The first panzootic occurred in the late 1990s – early 2000s and was caused by O/ME-SA/PanAsia FMD virus, and the second, caused by O/ME-SA/Ind-2001 virus, began in 2013 and continues to the present. The emergence of FMD panzootics is probably a consequence of the economic globalization. FMD is not enzootic in Russia, but sporadic outbreaks of this disease are periodically reported. Molecular epidemiological studies have shown that these outbreaks are caused by the infection introduction from neighboring Asian countries, mainly from China. The FMD virus, which has come to the Russian Federation from other countries, is characterized by great genetic diversity and belongs to three serotypes, five topotypes and eight genetic lineages: O/Cathay, O/ME-SA/PanAsia, O/SEA/Mya-98, O/ME-SA/Ind-2001, O/ME-SA/unnamed, A/Asia/Iran-05, A/Asia/Sea-97, Asia1/V. The results of molecular epidemiological studies are taken into account when vaccine strains are to be selected for preventive vaccination of livestock in FMD high-risk areas. The review is based on the analysis of 68 literature sources.

Keywords: review, foot-and-mouth disease virus, phylogenetic analysis

Acknowledgements: The study was funded by the Federal Centre for Animal Health within the research topic "Veterinary Welfare".

For citation: Scherbakov A. V. Molecular epidemiology of foot-and-mouth disease (review). *Veterinary Science Today*. 2024; 13 (1): 11–19. https://doi.org/10.29326/2304-196X-2024-13-1-11-19

Conflict of interests: The author declares no conflict of interests.

For correspondence: Aleksey V. Scherbakov, Cand. Sci. (Biology), Head of Reference Laboratory for Highly Dangerous Diseases, Federal Centre for Animal Health, Yur'evets, Vladimir 600901, Russia, *e-mail: ascherbakov@arriah.ru*

УДК 619:616.98:578.835.2:616-036.22:578.5:616-076

Молекулярная эпизоотология ящура (обзор)

А. В. Щербаков
ФГБУ «Федеральный центр охраны здоровья животных» (ФГБУ «ВНИИЗЖ»), мкр. Юрьевец, г. Владимир, 600901, Россия

РЕЗЮМЕ

Молекулярно-эпизоотологические исследования являются важным инструментом регионального и глобального надзора за ящуром. Эти исследования базируются на постоянно прогрессирующих технологиях секвенирования нуклеиновых кислот и филогенетического анализа. Применение данных технологий позволило оценить генетическое разнообразие возбудителя ящура, изучить эволюцию вируса в регионах, энзоотичных по заболеванию, и отслеживать пути распространения эпизоотий и панзоотий ящура. Молекулярно-эпизоотологические исследования показали, что в пределах давно известных семи серотипов вируса ящура существуют многочисленные топотипы (географические типы), генетические линии и сублинии. Обычно вирус ящура того или иного топотипа и генетической линии эволюционирует в пределах определенного ареала, периодически вызывая региональные эпизоотии. Однако за последние 30 лет случились две панзоотии ящура, охватившие несколько континентов. Первая панзоотия произошла в конце 1990-х – начале 2000-х гг. и была обусловлена вирусом ящура O/ME-SA/PanAsia, а вторая, вызванная вирусом O/ME-SA/Ind-2001, началась в 2013 г. и продолжается до настоящего времени. Возникновение панзоотий ящура, вероятно, является следствием глобализации мировой экономики. В России ящур не энзоотичен, однако периодически регистрируются спорадические вспышки этой болезни. Молекулярно-эпизоотологические исследования показали, что эти вспышки вызваны заносом инфекции из соседних азиатских стран, главным образом из Китая. Вирус ящура, проникавший на территорию Российской Федерации из других стран, характеризуется большим генетическим разнообразием и относится к трем серотипам, пяти топотипам и восьми генетическим линиям: O/Cathay, O/ME-SA/PanAsia, O/SEA/Mya-98, O/ME-SA/Ind-2001, O/ME-SA/unnamed, A/Asia/Iran-05, A/Asia/Sea-97, Asia1/V. Результаты молекулярно-эпизоотологических исследований учитываются при выборе вакцинных штаммов для профилактической вакцинации скота в зонах с высоким риском заноса ящура. Обзор составлен на основе анализа 68 источников.

© Scherbakov A. V., 2024
© Federal Centre for Animal Health, 2024

Ключевые слова: обзор, вирус ящура, филогенетический анализ

Благодарности: Работа выполнена за счет средств ФГБУ «ВНИИЗЖ» в рамках тематики научно-исследовательских работ «Ветеринарное благополучие».

Для цитирования: Щербаков А. В. Молекулярная эпизоотология ящура (обзор). *Ветеринария сегодня*. 2024; 13 (1): 11–19. https://doi.org/10.29326/2304-196X-2024-13-1-11-19

Конфликт интересов: Автор заявляет об отсутствии конфликта интересов.

Для корреспонденции: Щербаков Алексей Владимирович, канд. биол. наук, заведующий референтной лабораторией по особо опасным болезням ФГБУ «ВНИИЗЖ», мкр. Юрьевец, г. Владимир, 600901, Россия, *e-mail: ascherbakov@arriah.ru*

INTRODUCTION

Foot-and-mouth disease (FMD) is a highly contagious viral disease of cloven-hoofed animals, that may cause epizootics and inflict dramatic economic damage.

The causative agent of the disease is a non-enveloped RNA virus, which belongs to *Aphthovirus* genus of the *Picornaviridae* family. There are seven viral serotypes: O, A, C, Asia-1, SAT-1, SAT-2 and SAT-3.

Currently, the disease is widespread in Africa, Asia and some parts of South America, in which it causes huge economic losses to the agricultural sector. For the FMD-free countries there is still a danger of the disease introduction from the infected regions.

FMD is characterized by a very dynamic and complex epidemiology. The FMD virus (FMDV) is rapidly evolving, new genetic and antigenic variants of the virus are constantly emerging that can overcome the immunity of vaccinated animals and cause outbreaks of the disease. This significantly complicates the control of the disease and determines the need to constantly monitor the FMDV diversity in nature and to timely develop new vaccines adapted to emerging viral lineages.

Global FMD surveillance is performed by the FMD reference laboratory network of the World Organization for Animal Health and the Food and Agriculture Organization of the United Nations (WOAH/FAO) [1], with the main task to monitor the emergence of new FMDV variants with modified genetic and antigenic properties which render the available vaccines ineffective. An important surveillance tool is the molecular genetic analysis of the FMDV.

THE HISTORY OF THE DEVELOPMENT OF MOLECULAR EPIDEMIOLOGICAL TECHNIQUES

Molecular epidemiology as a scientific field is the combination of molecular biology, epidemiology and population genetics that has become a powerful tool to develop control strategies for infectious diseases [2].

Historically, the first attempts to use laboratory methods in epidemiological studies of FMD were associated with serological tests. More recently, biochemical methods such as FMDV SP polyacrylamide gel electrophoresis and T1 oligonucleotide fingerprinting of the viral genome began to be used [3, 4, 5, 6]. However, the resolution of these methods was low, and they were not widely used.

A revolutionary event in the molecular epidemiology of foot-and-mouth disease was the use of sequencing technologies and phylogenetic analysis of the viral genome sequences. In 1987 E. Beck and K. Strohmaier showed that sequencing and comparative analysis of the VP1 gene of FMDV field isolates from the outbreak reveal their origin [7]. In particular, they established that 14 out of 18 FMD outbreaks in Western European countries between 1964 and 1985 were caused by vaccine strains. In most cases they were induced by improperly inactivated FMD vaccines. Several more outbreaks could occur as a result of the virus escape from the vaccine production plants. The German scientists suggested that nucleotide sequence analysis should be used as a standard method of diagnosis, because when compared with other techniques it more clearly reveals the origin and course of epizootics and offers the possibility of preventing further outbreaks. Beck E. and Strohmaier K. also proposed to prohibit the use of formalin-inactivated FMD vaccines, since they are the main source of FMDV in Europe. After this proposal was implemented, no FMD cases have been reported in Europe.

Since the late 1980s and early 1990s, nucleotide sequence analysis has been widely used to characterize FMDV field isolates [8–28].

Initially, the so-called direct RNA sequencing method was used for these purposes [29]. It included such preparatory steps as FMDV propagation in cell culture, purification and concentration of the virus and viral RNA, and therefore the method was very laborious and time-consuming. In addition, it allowed the determination of only 130–150 nucleotide bases of the FMDV VP1 gene. Since the mid-1990s, polymerase chain reaction (PCR) has been used to amplify genetic material for sequencing [30, 31]. The PCR use has literally revolutionized the FMDV nucleotide analysis technology: the time needed for testing was reduced from 1–2 weeks to 1–2 days, it became possible to produce the full genome sequence of the VP1 gene and even of the FMDV. To sequence the FMDV full genome, E. M. Cottam et al. amplified 24 overlapping viral genome fragments using PCR [32]. Further progress in full genome sequencing was associated with the use of NGS (next-generation sequencing) technology [33].

STUDY OF THE FMDV GENETIC DIVERSITY

An impressive bank of nucleotide sequences of FMDV field isolate VP1 genes from different countries has been created at the World Reference Laboratory for Foot-and-Mouth Disease (Pirbright, UK) and the WOAH/FAO FMD regional reference laboratory network for FMD. The analysis of this database made it possible to evaluate the virus genetic diversity, to determine the viral evolution patterns in the endemic regions, and track the pathways of the FMD epizootic spread.

Molecular biological studies have shown that there are several levels of the FMDV genetic diversity: types, topotypes, genetic lineages and sublineages. The division of the virus into types fully corresponds to its classification into serotypes, that is, at the genetic level, as well as at the antigenic level, seven groups of the virus are distinguished, defined as types: A, O, C, Asia-1, SAT-1, SAT-2 and SAT-3. VP1 varies by 30–50% between the types [34].

Within each serotype, A. R. Samuel and N. J. Knowles [35] identified geographical types, which they called topotypes. VP1 nucleotide differences between the topotypes are up to 15–20%. It is obvious that the topotypes were formed as a result of the relatively independent FMDV evolution in certain geographical regions. The figure shows current FMDV pools. The FMDV division into topotypes generally corresponds to the division of the viral distribution into pools [36].

There are 11 topotypes within type O lineage: Cathay (China), SEA (Southeast Asia), ME-SA (Middle East and South Asia), Euro-SA (Europe and South America), WA (West Africa), EA-1 (East Africa-1), EA-2 (East Africa-2), EA-3 (East Africa-3), EA-4 (East Africa-4) and two extinct Indonesian topotypes ISA-1 and ISA-2 [37, 38, 39].

FMD type A virus is differentiated into 3 topotypes: Euro-SA (Europe and South America), Asia and Africa. Within each of these three topotypes, a very large genetic diversity of the virus has been revealed.

The emergence of the topotypes within serotypes A and O common for Europe and South America is explained by the fact that FMD of these two types was introduced to the American continent from Europe in the 19th century.

Antigenically FMD Asia-1 viruses are less diverse than other serotypes. All known Asia-1 isolates form the only topotype – Asia. Knowles N. J. and Samuel A. R. explain the relatively low genetic diversity of the the serotype by its more recent origin than the others, or a severe 'bottleneck' purification with only a single topotype surviving [34].

FMDV serotype C has not been detected since 2004 and is currently considered to be extinct. FMDV type C, like serotypes A and O, is presumed to have been introduced into South America from Europe. However, the results of molecular biological studies allowed the British scientists from the Pirbright Institute to assume that the serotype C was introduced to South America and evolved from type A in around 1870 [40]. Later, this serotype was introduced to Europe from South America, and from Europe it spread to Africa and Asia. The scientists assume that exactly the occurrence of serotype C viruses in South America is the reason for their lower suitability to the ecological conditions of the other continents, which prevented them from persistence in the Old World.

SAT-1, SAT-2 and SAT-3 viruses are clustered into 13 (from I to XIII), 14 (from I to XIV) and 5 (from I to V) topotypes, respectively [37, 38, 39].

The discovery of the viral topotypes and their distribution pattern formed the basis for global FMD control strategy, which suggests clustering of seven regional alliances (seven regional FMDV pools) of FMD infected countries and coordination of national roadmaps for FMD progressive control pathway [41].

The FMDV is continuously evolving within each topotype, generating new genetic lineages that force out previously existing ones. Some lineages extinct quite quickly after their emergence, while others are able to circulate in their pools for a long time. The viral divergence within such "long-lived" genetic lineages leads to the emergence of sublineages. For example, by 2021, 17 sublineages were distinguished within the genetic lineage A/Iran-05, and 8 sublineages within O/PanAsia-2 [42].

It was found that FMDV genetic lineages evolve at very similar rates, estimated at an average of 1.3×10^{-2} nucleotide substitutions/site/year (min-max range of $1.1 \times 10^{-2} - 1.4 \times 10^{-2}$). These results indicate that FMDV evolves under a strict molecular clock that is largely constant among the different serotypes [42].

STUDY OF FMD PANZOOTIC SPREAD

Usually, FMDV of a certain topotype and genetic lineage evolves within a certain area (pool), periodically causing regional epizootics. However, over the past 30 years, two FMD panzootics have occurred, invloving several continents.

Molecular epidemiological studies made it possible to trace in detail the movements of the most devastating FMD panzootic on record caused by O/ME-SA/PanAsia virus. The virus was first isolated from FMD outbreaks

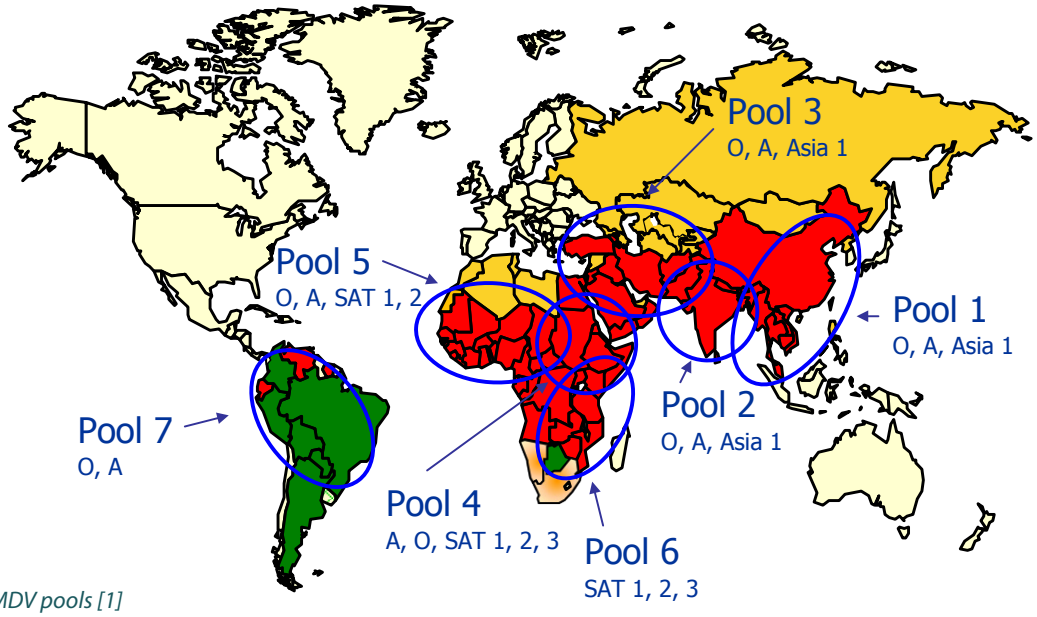

Fig. FMDV pools [1]

in northern India in 1990. From 1991 to 1997 the new lineage appeared to spread to other parts of India and in 1998 it spread to Bahrain, Iran, Jordan, Kuwait, Lebanon, Syria, Saudi Arabia, and Yemen. In 1999, the spread of the PanAsian virus in the Middle East continued (outbreaks in Israel, Turkey and the United Arab Emirates), and it started rapidly spreading eastward from Hindustan: in May 1999 China reported FMD outbreaks caused by this virus, and in June O/ME-SA/PanAsia virus was isolated in Taiwan. Towards the end of 1999, the PanAsia virus moved to Myanmar, Thailand, Vietnam, Laos and by April 2000 all mainland Southeast Asian countries had experienced outbreaks due to the new strain. In March 2000 FMDV type O appeared in South Korea and Japan, and in April in Mongolia and Primorsky Krai of the Russian Federation. It should be noted that these East Asian territories previously had been free from FMD for many decades [34, 43, 44].

FMD panzootic caused by O/ME-SA/PanAsia virus was not limited to Asia. In September 2000 FMD type O was first reported in the Republic of South Africa. The outbreak occurred near the port of Durban. The origin was traced to feeding pigs with uncooked swill from a ship arrived from Asia. In February 2001, PanAsia virus was introduced and caused devastation in the United Kingdom. To eradicate the outbreak 6.5 million animals were destroyed, and direct and indirect losses to the country amounted to about 8 billion pounds. From the UK FMD moved to Ireland, France and the Netherlands [45].

Another FMD epidemic, but less serious, started in 2013. It was caused by O/ME-SA/Ind-2001 genetic lineage and covered the entire Asian continent and North Africa. This virus was first isolated in India in 2001 [45]. By 2009 it had spread widely in the territory of Hindustan and diversified into five sublineages: a, b, c, d, and e. In 2009, the O/ME-SA/Ind-2001 virus moved beyond its original range for the first time and caused an outbreak in Iran. Since 2013, the virus became panzootic and caused extensive outbreaks in North Africa and the Middle East in 2013–2014 [46, 47, 48], in Southeast Asia in 2015 [49] and East Asia in 2016–2017 [50].

Using the nucleotide sequences of VP1 ($n = 424$) full genome ($n = 74$) of O/ME-SA/Ind-2001 isolates from different countries, K. Bachanek-Bankowska et al. [50] used phylodynamic and phylogeographic reconstructions to track the global spread of this virus. In particular, it was shown that FMD outbreaks in the Middle East and North Africa in 2013–2015 resulted from five independent introductions of O/Ind-2001d sublineage virus from Hindustan, and outbreaks in Saudi Arabia in 2016 were caused by two independent introductions of another sublineage – O/Ind-2001e.

In 2015, O/ME-SA/Ind-2001 virus started its spreading eastward from Hindustan: from Bangladesh to Vietnam, and then sublineage d was introduced to Laos, and sublineage e was introduced through Myanmar in 2016 to Thailand and Vietnam. After that O/Ind-2001e sublineage virus caused an FMD epizootic in East Asia, involving China, South Korea, Mongolia and the Zabaikalsky Krai of the Russian Federation.

In December 2021, O/ME-SA/Ind-2001 virus caused an outbreak in the Orenburg Oblast of the Russian Federation, and in January 2022 in the Republic of Kazakhstan [51].

This means that the panzootic caused by O/ME-SA/Ind-2001 virus had much in common with the previous one caused by O/ME-SA/PanAsia virus: both genetic lineages originated from the Indian subcontinent (Bangladesh, Bhutan, India and Nepal), in both cases the disease spread first to the west (to Central and Western Asia), and only then the virus was introduced into Southeast and East Asia. Both viruses demonstrated the ability to spread rapidly in regions where other type O genetic lines were enzootic, as well as to spread to normally FMD-free countries [50]. The emergence of FMD panzootics is probably a consequence of the economic globalization.

REGIONAL FMD EPIZOOTICS IN POOLS 1 AND 3

FMD panzootics, covering the entire Asia and even several continents, are a rather rare event. Most FMD epizootics never expand beyond their regional pools. Regional epizootics occur when antigenically modified FMDV variants appear that break through the existing population immunity [52].

The FMD situation in the Russian Federation is influenced by epizootic in Pools 1 (East and Southeast Asia) and 3 (West and Central Asia).

In Western and Central Asia (Pool 3), the largest regional epizootics were caused by A/Iran-05, O/PanAsia-2 and Asia1/Sindh-08 lineages.

The A/Iran-05 virus was first identified in Iran in 2003. In 2005 it spread widely in this country, and then caused an epizootic that covered Turkey, Afghanistan, Pakistan, Bahrain, Saudi Arabia, Jordan, and Iraq. Sporadic FMD outbreaks caused by this virus were reported in Israel, Lebanon, and Kuwait. A/Iran-05 has forced previously circulating A/Iran-96 and A/Iran-99 lineages out from the Middle East and is dominating in this region to the present. During this period, the virus diverged into many sublineages. Some sublineages (for example, Iran-05^{BAR-08}) became widespread, while others (for example, Iran-05^{ARD-07} and Iran-05^{EZM-07}) were reported only in one country (Turkey). Iran-05^{BAR-08} sublineage virus was introduced to Libya in 2009, and to Egypt in 2010 [53, 54, 55, 56, 57].

O/ME-SA/PanAsia-2 virus is derived from the O/ME-SA/PanAsia lineage, which became widespread in Western and Central Asia in the late 1990s. As an independent lineage, O/ME-SA/PanAsia-2 was first reported in Iran in 2006. In 2007, the virus of this lineage was introduced to Turkey, Afghanistan, Pakistan, Saudi Arabia, Israel, and then to other countries in the Middle East. In 2011, the virus from Turkey was introduced to Bulgaria. O/ME-SA/PanAsia-2 virus has been dominating in Pool 3 since 2007. During this time, it has diverged into several sublineages, among them sublineage PanAsia-2^{SIS-10} is the most widespread [55, 56, 57]. In 2010, the virus of this sublineage spread beyond Western Asia and caused FMD outbreaks in Libya and Bulgaria [56].

Another significant regional FMD epizootic in Western and Central Asia was caused by the Asia1/Sindh-08 virus. It was first identified in 2008 in Pakistan, from where it spread to Afghanistan, Iran, Iraq, Bahrain and Turkey. The Asia1/Sindh-08 virus has forced three other Asia-1 genetic lineages out from the pool and is dominating this region to the present [55, 56, 57].

In 2021, A. Di Nardo et al. [42] reconstructed the evolutionary history and spatial dynamics of FMD in Western and Central Asia (Pool 3) over the last 20 years. Having analyzed the history of A/Iran-05, O/PanAsia-2 and Asia1/Sindh-08 genetic lineages, they showed they highlighted the pivotal role played by virus circulation in Pakistan, Iran, and Afghanistan. These countries represent primary

conveyors of FMDV infection across the region and are important sites for generating genomic diversity in Western and Central Asia. Phylogeographic reconstructions further revealed three main patterns of transboundary movements of viruses in Pool 3: 1) the continuous virus interchange between Pakistan, Afghanistan, and Iran, likely constituting interconnected large metapopulations; 2) the key role of Iran as hub of virus diffusion to the west; and 3) the unidirectional migration of viruses from Iran toward Turkey. This spatial pattern of FMDV spread in the region is common to all its serotypes.

In the 20th century, the region of Western and Central Asia (Pool 3) had an enormous impact on the FMD situation in Russia, however, in the 21st century the main source of FMD for the Russian Federation was Pool 1, which includes East and Southeast Asia. This is explained by the drastic change in the FMD situation in this region. The FMD situation in most of the East Asia countries remained relatively favourable during the 20th century: Japan was free since 1908, Korea since 1934, the Far East of the Russian Federation since 1964, Mongolia since 1973 [43]. To a large extent, this favourable situation was achieved by the buffer role of China, which separated these countries from Southeast Asia, where FMD of types O and A is enzootic. In China itself, probably only the O/Cathay virus has historically been enzootic. This virus has a unique feature: it is capable of causing clinical disease only in pigs [58]. Probably, the absence in China of FMDV capable of infecting cattle ensured the disease freedom in Mongolia, Korea, Japan and the Russian Far East during the 20th century [59].

Globalization and the PRC economic development have changed the situation. In the late 1990s, FMD O/ME-SA/PanAsia virus was introduced and widespread in China, which probably moved from China to South Korea, Japan, Mongolia and the Primorsky Krai of the Russian Federation in 2000.

Numerous Asia-1 FMD outbreaks were reported first in China, and then in Russia (Amur Oblast, Primorsky and Khabarovsk Krais, Chita Oblast), Mongolia and North Korea in 2005–2006. The virus responsible for this epizootic had only 1.11–1.74% VP1 nucleotide difference from viruses from India collected in 1980–1981 and had no close relatives among the isolates circulating at that time [60, 61]. The most probable cause explaining the extremely close relationship of the isolates from 2005–2006 and 1980–1981 is the use of the Indian strain-based vaccine in China [61, 62].

In 2009–2010 East Asia was almost simultaneously covered by two epizootics caused by FMD A/Asia/Sea-97 and O/SEA/Mea-98 viruses. Both genetic lineages are enzootic in Southeast Asian countries. In 2009, the geographic range of A/Asia/Sea-97 expanded and caused outbreaks in six provinces of China, and in January 2010 in South Korea [63]. In 2013, the virus moved from the PRC territory to the RF Zabaikalsky Krai and Amur Oblast and Mongolia [64]. The O/SEA/Mea-98 virus was responsible for a larger epizootic in East Asia in 2010: FMD outbreaks caused by this strain were reported in China, Korea, Japan, Mongolia and the Zabaikalsky Krai of the Russian Federation [63, 65].

Since 2016, O/ME-SA/Ind-2001 virus has probably spread through China to Russia, Mongolia and South Korea [50].

This means, if 25 years ago only FMD O/Cathay virus was enzootic in China, currently four more genetic lineages are circulating in the country: O/ME-SA/PanAsia, O/SEA/Mea-98, O/ME-SA/Ind-2001 and A/Asia/Sea-97. This poses a high risk of FMD introduction from China to Russia.

MOLECULAR EPIDEMIOLOGICAL STUDIES OF FOOT-AND-MOUTH DISEASE IN THE RUSSIAN FEDERATION

In the Russian Federation, FMDV phylogenetic studies are conducted at the Federal Centre for Animal Health (Vladimir), which is the WOAH Regional Reference Laboratory for FMD for Eastern Europe, Transcaucasia and Central Asia and the FAO Reference Center for FMD. Since 2005 the Federal Centre for Animal Health has been involved into the network of WOAH/FAO reference laboratories for FMD responsible for the global FMD surveillance, with the main task to monitor the emergence of new FMDV variants with modified genetic and antigenic properties which render the available vaccines ineffective. The identification of FMDV genetic lineages and variants with modified antigenic properties makes it possible to promptly develop new vaccines against them. Within its international responsibilities the Federal Centre for Animal Health analyzes molecular genetic and antigenic properties of FMDV isolates responsible for the FMD outbreaks in the Russian Federation, Central Asia and Transcaucasia. FMDV isolates that caused outbreaks in Russia, CIS countries and in Mongolia were characterized by molecular genetic methods at the Federal Centre for Animal Health in the period from 1995 to 2022 [51, 59, 62, 64, 65, 66, 67, 68].

Studies showed that FMD outbreaks in post-Soviet Russia were caused by the introduction of the virus belonging to various serotypes, topotypes and genetic lineages from infected Asian countries (Table 1). For example, FMD O/Cathay, O/ME-SA/PanAsia, O/SEA/Mya-98, O/ME-SA/Ind-2001, Asia1, A/Asia/Sea-97 viruses were introduced from China to various regions of the Russian Federation.

Table 1
Characteristics of the virus responsible for FMD outbreaks in the Russian Federation in 1995–2021

Year	Region	Virus (type/topotype/genetic lineage)
1995	Moscow Oblast	O/Cathay
2000	Primorsky Krai	O/ME-SA/PanAsia
2004	Amur Oblast	O/ME-SA/PanAsia
2005–2006	Amur Oblast, Primorsky Krai, Khabarovsk Krai, Chita Oblast	Asia1/V
2010–2011	Zabaikalsky Krai	O/SEA/Mya-98
2012	Primorsky Krai	O/ME-SA/PanAsia
2013	Kabardino-Balkaria, Karachay-Cherkessia, Krasnodar Krai; Zabaikalsky Krai, Amur Oblast	A/Asia/Iran-05 A/Asia/Sea-97
2014	Primorsky Krai Zabaikalsky Krai	O/SEA/Mya-98 O/ME-SA/PanAsia, A/Asia/Sea-97
2016	Zabaikalsky Krai	O/ME-SA/Ind-2001
2017	Republic of Bashkortostan	O/ME-SA/unnamed
2018	Zabaikalsky Krai	O/ME-SA/PanAsia
2019	Primorsky Krai, Khabarovsk Krai; Zabaikalsky Krai	O/SEA/Mya-98 O/ME-SA/Ind-2001
2020	Zabaikalsky Krai	O/SEA/Mya-98
2021	Orenburg Oblast	O/ME-SA/Ind-2001

Table 2
Characteristics of the virus responsible for FMD outbreaks in the CIS countries and Mongolia in 1996–2022

Year	Country	Virus (type/topotype/ genetic lineage)
1996	Armenia	O/ME-SA/Iran-01
1997	Georgia	O/ME-SA/Iran-01
1998	Armenia	A/Asia/Iran-96
1999	Georgia	A/Asia/Iran-96
2000	Armenia, Georgia	Asia-1, O/ME-SA/PanAsia
2000–2002	Mongolia	O/ME-SA/PanAsia
2001	Georgia	Asia1/VI
2001	Kyrgyzstan, Tajikistan	O/ME-SA/PanAsia
2003	Tajikistan, Uzbekistan	Asia1/II
2004	Kyrgyzstan, Tajikistan	Asia1/II
2004	Mongolia	O/SEA/Mya-98
2005	Mongolia	Asia1/V
2006	Armenia	A/Asia/Iran-05
2007	Kyrgyzstan	A/Asia/Iran-05
2007	Kazakhstan, Kyrgyzstan	O/ME-SA/PanAsia-2
2008	Tadjikistan	O/ME-SA/PanAsia-2
2010	Tadjikistan	A/Asia/Iran-05
2010	Kazakhstan	O/ME-SA/PanAsia-2
2010	Mongolia	O/SEA/Mya-98
2011	Kazakhstan, Kyrgyzstan, Tajikistan	O/ME-SA/PanAsia-2
2011	Kyrgyzstan	A/Asia/Iran-05
2011	Tadjikistan	Asia1/Sindh-08
2011	Kazakhstan	O/ME-SA/PanAsia
2012	Kazakhstan	O/ME-SA/PanAsia
2013	Kazakhstan, Mongolia	A/Asia/Sea-97
2014	Tadjikistan	O/ME-SA/PanAsia-2
2014	Mongolia	O/ME-SA/PanAsia
2015	Tadjikistan	O/ME-SA/PanAsia-2
2015	Mongolia	O/SEA/Mya-98, O/PanAsia
2016	Armenia	A/Asia/G-VII
2016	Tadjikistan	O/ME-SA
2016	Mongolia	A/Asia/Sea-97
2017–2018	Mongolia	O/PanAsia, O/Ind-2001
2021	Mongolia	O/ME-SA/Ind-2001
2022	Kazakhstan	O/ME-SA/Ind-2001

FMD outbreaks in the North Caucasus in 2013 were caused by the introduction of A/Asia/Iran-05 virus from Transcaucasia, and the introduction of O/ME-SA virus of a rare non-classified group from Central Asia caused outbreaks in the Republic of Bashkortostan in 2017. In 2021 O/ME-SA/Ind-2001 virus was probably introduced to the territory of the Russian Federation from Kazakhstan. Thus, the results of the studies conducted by the Federal Centre for Animal Health suggest a large genetic diversity of FMDV introduced to the Russian Federation.

Phylogenetic analysis of the virus isolates responsible for FMD outbreaks in Transcaucasia (Armenia and Georgia) and Central Asia (Kazakhstan, Kyrgyzstan, Tajikistan, Uzbekistan) revealed that they belong to genetic lineages that dominated Pool 3 at different periods: O/ME-SA/Iran-01, A/Asia/Iran-96, O/ME-SA/PanAsia, Asia1/VI, Asia1/II, A/Asia/Iran-05, O/ME-SA/PanAsia-2, Asia1/Sindh-08, A/Asia/G-VII (Table 2). In 2011–2013, FMD outbreaks caused by O/ME-SA/PanAsia and A/Asia/Sea-97 viruses, introduced from China were reported in eastern regions of Kazakhstan. In 2022, O/ME-SA/Ind-2001 virus was introduced from China to Kazakhstan.

FMD outbreaks in Mongolia were caused by the virus responsible FMD epizootics in Pool 1: O/ME-SA/PanAsia, O/SEA/Mya-98, A/Asia/Sea-97, O/ME-SA/Ind-2001.

Within the network of the WOAH/FAO reference laboratories for FMD, the Federal Centre for Animal Health shares information on FMDV field isolates responsible for oubreaks in various regions of the world. The VP1 nucleotide sequences and full genomes of FMDV isolates responsible for the outbreaks in Russia, CIS countries and Mongolia produced by the Federal Centre for Animal Health were used to track the spread of global and regional epizootics caused by O/ME-SA/PanAsia, Asia1/II, Asia1/V, O/SEA/Mya-98, A/Asia/Sea-97, O/ME-SA/Ind-2001 viruses [42, 43, 47, 50, 60, 61].

The results of molecular epidemiological studies performed by the Federal Centre for Animal Health are taken into account for the strain selection to manufacture vaccines and vaccinate livestock in FMD risk areas.

CONCLUSION

Thirty-five years of experience in molecular epidemiology of foot-and-mouth disease proves that phylogenetic analysis of the viral genome nucleotide sequences is an effective tool to monitor FMD both on the regional and global levels. FMD surveillance, which makes it possible to track the emergence of new viral variants with modified genetic and antigenic properties, allows for the rapid development of new vaccines and thus for a significant improvement of FMD control performance.

The use of molecular biological methods has made it possible to progress significantly in understanding of FMD epidemiology, which is important for the development of effective control strategies. The discovery of FMDV topotypes and their distribution pattern formed the basis for global FMD control strategy, which suggests clustering of seven regional alliances (seven regional FMD pools) of infected countries and coordination of national roadmaps for FMD progressive control pathway.

REFERENCES

1. WOAH/FAO Reference Laboratory Network for Foot-and-Mouth Disease. https://www.foot-and-mouth.org

2. Klein J. Understanding the molecular epidemiology of foot-and-mouth-disease virus. *Infection, Genetics and Evolution.* 2009; 9 (2): 153–161. https://doi.org/10.1016/j.meegid.2008.11.005

3. Domingo E., Dávila M., Ortín J. Nucleotide sequence heterogeneity of the RNA from a natural population of foot-and-mouth-disease virus. *Gene*. 1980; 11 (3–4): 333–346. https://doi.org/10.1016/0378-1119(80)90073-6

4. King A. M. Q., Underwood B. O., McCahon D., Newman J. W. I., Brown F. Biochemical identification of viruses causing the 1981 outbreaks of foot and mouth

disease in the UK. *Nature*. 1981; 293: 479–480. https://doi.org/10.1038/293479a0

5. Anderson E. C., Underwood B. O., Brown F., Ngichabe C. K. Variation in foot-and-mouth disease virus isolates in Kenya: An examination of field isolates by T1 oligonucleotide fingerprinting. *Veterinary Microbiology*. 1985; 10 (5): 409–423. https://doi.org/10.1016/0378-1135(85)90023-9

6. Knowles N. J., Hedger R. S. A study of antigenic variants of foot-and-mouth disease virus by polyacrylamide gel electrophoresis of their structural polypeptides. *Veterinary Microbiology*. 1985; 10 (4): 347–357. https://doi.org/10.1016/0378-1135(85)90005-7

7. Beck E., Strohmaier K. Subtyping of European foot-and-mouth disease virus strains by nucleotide sequence determination. *Journal of Virology*. 1987; 61 (5): 1621–1629. https://doi.org/10.1128/JVI.61.5.1621-1629.1987

8. Dopazo J., Sobrino F., Palma E. L., Domingo E., Moya A. Gene encoding capsid protein VP1 of foot-and-mouth disease virus: a quasispecies model of molecular evolution. *Proceedings of the National Academy of Sciences*. 1988; 85 (18): 6811–6815. https://doi.org/10.1073/pnas.85.18.6811

9. Knowles N. J., Marquardt O., Samuel A. R. Antigenic and molecular characterization of virus isolates from recent outbreaks of foot-and-mouth disease in the Federal Republic of Germany. *Report of the Session of the Research Group of the Standing Technical Committee of the European Commission for the Control of Foot-and-Mouth Disease* (*Prague, Czechoslovakia, 20–23 September 1988*). Rome: FAO; 1988; Appendix 24: 149–155. https://www.fao.org/3/ca9409en/ca9409en.pdf

10. Knowles N. J., Samuel A. R. Molecular and antigenic analysis of foot-and-mouth disease type C viruses isolated from outbreaks in Italy during 1988 and 1989. *Report of the Session of the Research Group of the Standing Technical Committee of the European Commission for the Control of Foot-and-Mouth Disease* (*Lindholm, Denmark, 25–29 June 1990*). Rome: FAO; 1990; Appendix 22: 122–128. https://www.fao.org/3/ca9410en/ca9410en.pdf

11. Martinez M. A., Carrillo C., Plana J., Mascardla R., Bergada J., Palma E. L., et al. Genetic and immunogenic variations among closely related isolates of foot-and-mouth disease virus. *Gene*. 1988; 62 (1): 75–84. https://doi.org/10.1016/0378-1119(88)90581-1

12. Martinez M. A., Dopazo J., Hernández J., Mateu M. G., Sobrino F., Domingo E., Knowles N. J. Evolution of the capsid protein genes of foot-and-mouth disease virus: antigenic variation without accumulation of amino acid substitutions over six decades. *Journal of Virology*. 1992; 66 (6): 3557–3565. https://doi.org/10.1128/JVI.66.6.3557-3565.1992

13. Marquardt O., Adam K. H. Sequences of capsid protein VP1 of two type A foot-and-mouth disease viruses. *Virus Genes*. 1989; 2 (3): 283–291. https://doi.org/10.1007/BF00125344

14. Marquardt O., Adam K.-H. Foot-and-mouth disease virus subtyping by sequencing VP1 genes. *Veterinary Microbiology*. 1990; 23 (1–4): 175–183. https://doi.org/10.1016/0378-1135(90)90147-n

15. Marquardt O., Krebs O. Outbreaks of foot-and-mouth disease near Hannover in 1987 and 1989: evidence for two strains of virus. *Tierärztliche Umschau*. 1992; 47 (3): 137–140.

16. Piccone M. E., Kaplan G., Giavedoni L., Domingo E., Palma E. L. VP1 of serotype C foot-and-mouth disease viruses: long-term conservation of sequences. *Journal of Virology*. 1988; 62 (4): 1469–1473. https://doi.org/10.1128/JVI.62.4.1469-1473.1988

17. Sobrino F., Martinez M. A., Carrillo C., Beck E. Antigenic variation of foot-and-mouth disease virus of serotype C during propagation in the field is mainly restricted to only one structural protein (VP1). *Virus Research*. 1989; 14 (4): 273–280. https://doi.org/10.1016/0168-1702(89)90021-x

18. Carrillo C., Dopazo J., Moya A., Gonzalez M., Martinez M. A., Saiz J. C., Sobrino F. Comparison of vaccine strains and the virus causing the 1986 foot-and-mouth disease outbreak in Spain: epizootiological analysis. *Virus Research*. 1990; 15 (1): 45–55. https://doi.org/10.1016/0168-1702(90)90012-z

19. Samuel A. R., Knowles N. J., Kitching R. P. Preliminary molecular analysis of foot-and-mouth disease virus type O in the Middle East. *Report of the Session of the Research Group of the Standing Technical Committee of the European Commission for the Control of Foot-and-Mouth Disease (Lindholm, Denmark, 25–29 June 1990)*. Rome: FAO; 1990; Appendix 24: 133–138. https://www.fao.org/3/ca9410en/ca9410en.pdf

20. Samuel A. R., Ansell D. M., Rendle R. T., Armstrong R. M., Davidson F. L., Knowles N. J., Kitching R. P. Field and laboratory analysis of an outbreak of foot and mouth disease in Bulgaria in 1991. *Revue Scientifique et Technique*. 1993; 12 (3): 839–848. https://doi.org/10.20506/rst.12.3.718

21. Krebs O., Berger H. G., Marquardt O. The capsid protein-encoding sequence of foot-and-mouth disease virus O_2Brescia. *Archives of Virology*. 1991; 120 (1–2): 135–143. https://doi.org/10.1007/BF01310956

22. Armstrong R. M., Samuel A. R., Knowles N. J., Ulutürk S. Genetic studies on FMD viruses isolated from samples collected in Turkey. *Report of the Session of the Research Group of the Standing Technical Committee of the European Commission for the Control of Foot-and-Mouth Disease* (*Mittelhaüsern, Switzerland, 8–11 September 1992*). Rome: FAO; 1992; Appendix 11: 64–69. https://www.fao.org/3/ca9412en/ca9412en.pdf

23. Armstrong R. M., Samuel A. R., Carpenter W. C., Kant R., Knowles N. J. A comparative study of serological and biochemical methods for strain differentiation of foot-and-mouth disease type A viruses. *Veterinary Microbiology*. 1994; 39 (3–4): 285–298. https://doi.org/10.1016/0378-1135(94)90165-1

24. Vosloo W., Knowles N. J., Thomson G. R. Genetic relationships between southern African SAT-2 isolates of foot-and-mouth-disease virus. *Epidemiology and Infection*. 1992; 109 (3): 547–558. https://doi.org/10.1017/s0950268800050536

25. Saiz J. C., Sobrino F., Dopazo J. Molecular epidemiology of foot-and-mouth disease virus type O. *Journal of General Virology*. 1993; 74 (10): 2281–2285. https://doi.org/10.1099/0022-1317-74-10-2281

26. Ansell D. M., Samuel A. R., Carpenter W. C., Knowles N. J. Genetic relationships between foot-and-mouth disease type Asia 1 viruses. *Epidemiology and Infection*. 1994; 112 (1): 213–224. https://doi.org/10.1017/s0950268800057587

27. Woodbury E. L., Samuel A. R., Knowles N. J., Hafez S. M., Kitching R. P. Analysis of mixed foot-and-mouth disease virus infections in Saudi Arabia: prolonged circulation of an exotic serotype. *Epidemiology and*

Infection. 1994; 112 (1): 201–211. https://doi.org/10.1017/s0950268800057575

28. Stram Y., Chai D., Fawzy H. E.-D., Molad T., Meiri N., Van-Ham M., et al. Molecular epidemiology of foot-and-mouth disease (FMD) in Israel in 1994 and in other Middle-Eastern countries in the years 1992–1994. *Archives of Virology.* 1995; 140 (10): 1791–1797. https://doi.org/10.1007/BF01384342

29. Knowles N. J. A method for direct nucleotide sequencing of foot-and-mouth disease virus RNA for epidemiological studies. *Report of the Session of the Research Group of the Standing Technical Committee of the European Commission for the Control of Foot-and-Mouth Disease* (*Lindholm, Denmark, 25–29 June 1990*). Rome: FAO; 1990; Appendix 19: 106–112. https://www.fao.org/3/ca9410en/ca9410en.pdf

30. Drygin V. V., Gusev A. A., Perevozchikova N. A., Scherbakov A. V. Amplification and sequencing of genomic segments of foot-and-mouth disease virus (FMDV) using polymerase chain reaction (PCR). *Report of the Session of the Research Group of the Standing Technical Committee of the European Commission for the Control of Foot-and-Mouth Disease held jointly with the FMD Sub-group of the Scientific Veterinary Committee of the Commission of the European Community* (*Vienna, Austria*, *19–22 September, 1994*). Rome: FAO; 1994; Appendix 7: 40–44. https://www.fao.org/3/ca9413en/ca9413en.pdf

31. Knowles N. J., Samuel A. R. Polymerase chain reaction amplication and cycle sequencing of the 1D (VP1) gene of foot-and-mouth disease viruses. *Report of the Session of the Research Group of the Standing Technical Committee of the European Commission for the Control of Foot-and-Mouth Disease held jointly with the FMD Sub-group of the Scientific Veterinary Committee of the Commission of the European Community* (*Vienna, Austria*, *19–22 September, 1994*). Rome: FAO; 1995; Appendix 8: 45–53. https://www.fao.org/3/ca9413en/ca9413en.pdf

32. Cottam E. M., Wadsworth J., Shaw A. E., Rowlands R. J., Goatley L., Maan S., et al. Transmission pathways of foot-and-mouth disease virus in the United Kingdom in 2007. *PLoS Pathogens.* 2008; 4 (4):e1000050. https://doi.org/10.1371/journal.ppat.1000050

33. Logan G., Freimanis G. L., King D. J., Valdazo-Gonzalez B., Bachanek-Bankowska K., Sanderson N. D., et al. A universal protocol to generate consensus level genome sequences for foot-and-mouth disease virus and other positive-sense polyadenylated RNA viruses using the Illumina MiSeq. *BMC Genomics*. 2014; 15 (1):828. https://doi.org/10.1186/1471-2164-15-828

34. Knowles N. J., Samuel A. R. Molecular epidemiology of foot-and-mouth disease virus. *Virus Research*. 2003; 91 (1): 65–80. https://doi.org/10.1016/s0168-1702(02)00260-5

35. Samuel A. R., Knowles N. J. Foot-and-mouth disease type O viruses exhibit genetically and geographically distinct evolutionary lineages (topotypes). *Journal of General Virology*. 2001; 82 (3): 609–621. https://doi.org/10.1099/0022-1317-82-3-609

36. Sumption K., Domenech J., Ferrari G. Progressive control of FMD on a global scale. *Veterinary Record.* 2012; 170 (25): 637–639. https://doi.org/10.1136/vr.e4180

37. Knowles N. J., Wadsworth J., Hammond J. M., King D. P. Foot-and-mouth disease virus genotype definitions and nomenclature. *Report of the Open Session of the Standing Technical Committee of the European Commission for the Control of Foot-and-Mouth Disease (EuFMD)* (*Vienna, Austria, 29 September – 1 October 2010*). Rome: FAO; 2010; Appendix 43: 172–174. https://www.fao.org/3/bs516e/bs516e.pdf

38. Knowles N. J., Wadsworth J., Bachanek-Bankowska K., King D. P. VP1 sequencing protocol for foot and mouth disease virus molecular epidemiology. *Revue Scientifique et Technique* (*International Office of Epizootics*). 2016; 35 (3): 741–755. https://doi.org/10.20506/rst.35.3.2565.

39. World Reference Laboratory for Foot-and-Mouth Disease. FMD prototype strains. https://www.wrlfmd.org/fmdv-genome/fmd-prototype-strains#panel-3401

40. Paton D. J., Di Nardo A., Knowles N. J., Wadsworth J., Pituco E. M., Cosivi O., et al. The history of foot-and-mouth disease virus serotype C: the first known extinct serotype? *Virus Evolution.* 2021; 7 (1):veab009. https://doi.org/10.1093/ve/veab009

41. OIE/FAO. The global foot and mouth disease control strategy: Strengthening animal health systems through improved control of major diseases. 2012. http://www.fao.org/3/an390e/an390e.pdf

42. Di Nardo A., Ferretti L., Wadsworth J., Mioulet V., Gelman B., Karniely S., et al. Evolutionary and ecological drivers shape the emergence and extinction of foot-and-mouth disease virus lineages. *Molecular Biology and Evolution.* 2021; 38 (10): 4346–4361. https://doi.org/10.1093/molbev/msab172

43. Knowles N. J., Samuel A. R., Davies P. R., Kitching R. P., Venkataramanan R., Kanno T., et al. Emergence of a pandemic strain of foot-and-mouth disease virus serotype O. *Report of the Session of the Research Group of the Standing Technical Committee of the European Commission for the Control of Foot-and-Mouth Disease* (*Borovets, Bulgaria, 5–8 September 2000*). Rome: FAO; 2000; Appendix 1: 20–31. https://www.fao.org/3/ca9419en/ca9419en.pdf

44. Knowles N. J., Samuel A. R., Davies P. R., Midgley R. J., Valarcher J.-F. Pandemic strain of foot-and-mouth disease virus serotype O. *Emerging Infectious Diseases.* 2005; 11 (12): 1887–1893. https://doi.org/10.3201/eid1112.050908

45. Hemadri D., Tosh C., Sanyal A., Venkataramanan R. Emergence of a new strain of type O foot-and-mouth disease virus: its phylogenetic and evolutionary relationship with the PanAsia pandemic strain. *Virus Genes*. 2002; 25 (1): 23–34. https://doi.org/10.1023/a:1020165923805

46. Knowles N. J., Bachanek-Bankowska K., Wadsworth J., Mioulet V., Valdazo-González B., Eldaghayes I. M., et al. Outbreaks of foot-and-mouth disease in Libya and Saudi Arabia during 2013 due to an exotic O/ME-SA/Ind-2001 lineage virus. *Transboundary and Emerging Diseases*. 2016; 63 (5): e431–e435. https://doi.org/10.1111/tbed.12299

47. Valdazo-Gonzalez B., Knowles N. J., King D. P. Genome sequences of foot-and-mouth disease virus O/ME-SA/Ind-2001 lineage from outbreaks in Libya, Saudi Arabia, and Bhutan during 2013. *Genome Announcements*. 2014; 2 (2):e00242-14. https://doi.org/10.1128/genomeA.00242-14

48. Bachanek-Bankowska K., Wadsworth J., Gray A., Abouchoaib N., King D. P., Knowles N. J. Genome sequence of foot-and-mouth disease virus serotype O isolated from Morocco in 2015. *Genome Announcements*. 2016; 4 (2):e01746-15. https://doi.org/10.1128/genomeA.01746-15

49. Qiu Y., Abila R., Rodtian P., King D. P., Knowles N. J., Ngo L. T., et al. Emergence of an exotic strain of serotype O foot-and-mouth disease virus O/ME-SA/Ind-2001d

in South-East Asia in 2015. *Transboundary and Emerging Diseases*. 2018; 65 (1): e104–e112. https://doi.org/10.1111/tbed.12687

50. Bachanek-Bankowska K., Di Nardo A., Wadsworth J., Mioulet V., Pezzoni G., Grazioli S., et al. Reconstructing the evolutionary history of pandemic foot-and-mouth disease viruses: the impact of recombination within the emerging O/ME-SA/Ind-2001 lineage. *Scientific Reports.* 2018; 8 (1):14693. https://doi.org/10.1038/s41598-018-32693-8

51. Nikiforov V., Shcherbakov A., Chvala I., Kremenchugskaya S., Korennoy F., Mayorova T., et al. Insights into the molecular epidemiology of foot-and-mouth disease virus in Russia, Kazakhstan, and Mongolia in terms of O/ME-SA/Ind-2001e sublineage expansion. *Viruses.* 2023; 15 (3):598. https://doi.org/10.3390/v15030598

52. Sumption K., Pinto J., Lubroth J., Morzaria S., Murray T., De La Rocque S., Njeumi F. Foot-and-mouth disease: situation worldwide and major epidemiological events in 2005–2006. *FAO EMPRES. Focus on: Bulletin.* 2007; 1: 1–11. https://www.fao.org/3/ai339e/ai339e.pdf

53. Klein J., Hussain M., Ahmad M., Normann P., Afzal M., Alexandersen S. Genetic characterization of the recent foot-and-mouth disease virus subtype A/IRN/2005. *Virology Journal.* 2007; 4 (1):122. https://doi.org/10.1186/1743-422X-4-122

54. Knowles N. J., Nazem Shirazi M. H., Wadsworth J., Swabey K. G., Stirling J. M., Statham R. J., et al. Recent spread of a new strain (A-Iran-05) of foot-and-mouth disease virus type A in the Middle East. *Transboundary and Emerging Diseases*. 2009; 56 (5): 157–169. https://doi.org/10.1111/j.1865-1682.2009.01074.x

55. Jamal S. M., Ferrari G., Ahmed S., Normann P., Belsham G. J. Genetic diversity of foot-and-mouth disease virus serotype O in Pakistan and Afghanistan, 1997–2009. *Infection, Genetics and Evolution*. 2011; 11 (6): 1229–1238. https://doi.org/10.1016/j.meegid.2011.03.006

56. Brito B. P., Rodriguez L. L., Hammond J. M., Pinto J., Perez A. M. Review of the global distribution of foot-and-mouth disease virus from 2007 to 2014. *Transboundary and Emerging Diseases*. 2017; 64 (2): 316–332. https://doi.org/10.1111/tbed.12373

57. World Reference Laboratory for Foot-and-Mouth Disease. Country Reports. https://www.wrlfmd.org/country-reports

58. Mason P. W., Grubman M. J., Baxt B. Molecular basis of pathogenesis of FMDV. *Virus Research.* 2003; 91 (1): 9–32. https://doi.org/10.1016/s0168-1702(02)00257-5

59. Scherbakov A. V. FMD molecular epizootology in Russia (phylogenetic analysis of Russian FMDV isolates). *Veterinary Science Today.* 2015; (3): 30–36. EDN: UMSJWD (in Russ.)

60. Valarcher J. F., Knowles N. J., Ferris N. P., Paton D. J., Zakharov V., Sherbakov A., et al. Recent spread of FMD virus serotype Asia 1. *Veterinary Record.* 2005; 157 (1):30. https://doi.org/10.1136/vr.157.1.30

61. Valarcher J. F., Knowles N. J., Zakharov V., Scherbakov A., Zhang Z., Shang Y. J., et al. Multiple origins of foot-and-mouth virus serotype Asia 1 outbreaks, 2003–2007. *Emerging Infectious Diseases*. 2009; 15 (7): 1046–1051. https://doi.org/10.3201/eid1507.081621

62. Scherbakov A. V., Timina A. M., Yakovleva A. S., Drygin V. V., Zakharov V. M. Phylogenetic analysis of Russian FMDV isolates. *Proceedings of the Federal Centre for Animal Health*. 2006; 4: 12–15. EDN: MEHSNF (in Russ.)

63. Knowles N. J., He J., Shang Y., Wadsworth J., Valdazo-González B., Onosato H., et al. Southeast Asian foot-and-mouth disease viruses in Eastern Asia. *Emerging Infectious Diseases.* 2012; 18 (3): 499–501. https://doi.org/10.3201/eid1803.110908

64. Scherbakov A. V., Timina A. M., Zinyakov N. G. Phylogenetic study of foot-and-mouth disease virus isolates responsible for the outbreaks in Russia in 2013. *Veterinariya.* 2014; 7: 22–25. EDN: SKOKYX (in Russ.)

65. Scherbakov A. V., Timina A. M. Phylogenetic analysis of FMD virus isolates, which induced the disease outbreaks in Russia and Mongolia in 2010. *Proceedings of the Federal Centre for Animal Health*. 2011; 9: 5–11. EDN: OHSKVJ (in Russ.)

66. Shcherbakov A. V., Andreev V. G., Drygin V. V., Gusev A. A. Molecular epizootology of foot-and-mouth diseases. *Agrarian Russia*. 2002; 2: 8–11. https://doi.org/10.30906/1999-5636-2002-2-8-11 (in Russ.)

67. Lozovoy D. A., Scherbakov A. V., Zakharov V. M., Fomina S. N. Phylogenetic characteristics of the isolates of the virus type O, taked in Russian Federation. *Veterinariya*. 2018; 5: 3–8. https://doi.org/10.30896/0042-4846.2018.21.5.03-08 (in Russ.)

68. Scherbakov A., Timina A., Borisov V. Phylogenetic study of FMDV isolates collected in Russia, CIS-countries and Mongolia in 2000–2007. *Report of the Session of the Research Group of the Standing Technical Committee of the European Commission for the Control of Foot-and-Mouth Disease* (*Erice, Italy, 14–17 October 2008*). Rome: FAO; 2008; Appendix 9: 69–72. https://www.fao.org/3/k4881e/k4881e.pdf

Received 26.08.2023
Revised 01.09.2023
Accepted 22.09.2023

INFORMATION ABOUT THE AUTHOR / ИНФОРМАЦИЯ ОБ АВТОРЕ

Aleksey V. Scherbakov, Cand. Sci. (Biology), Head of Reference Laboratory for Highly Dangerous Diseases, Federal Centre for Animal Health, Vladimir, Russia;
https://orcid.org/0000-0001-8326-4201,
e-mail: ascherbakov@arriah.ru

Щербаков Алексей Владимирович, канд. биол. наук, заведующий референтной лабораторией по особо опасным болезням ФГБУ «ВНИИЗЖ», г. Владимир, Россия;
https://orcid.org/0000-0001-8326-4201,
e-mail: ascherbakov@arriah.ru

Contribution: review concept, exploration and analysis, tabulation for data visualization, article draft preparation and writing.

Вклад автора: концепция обзора, проведение поисково-аналитической работы, составление таблиц для визуализации данных, подготовка и написание статьи.