EDITORIAL CONCEPT

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To the 55th Anniversary of the Department of Virus Ecology with the Scientific and Practical Center for the Ecology and Epidemiology of Influenza (D.I. Ivanovsky Institute of Virology of the N.F. Gamaleya National Research Center for Epidemiology and Epidemiology of the Ministry of Health of Russian Federation)

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Abstract
The article presents historical aspects and key achievements of the Department of Virus Ecology (DVE) with the Scientific and Practical Center for Influenza Ecology and Epidemiology, which was established in 1969 at the D.I. Ivanovsky Institute of Virology of Academy of Medical Sciences of the USSR. For over 50 years, the DVE has been devoted to addressing fundamental issues in virus ecology, including the formation of viral populations in nature, and conducting comprehensive large-scale studies in the interest of the state's biosecurity. The department's primary focus is on particularly dangerous (arboviral) and socially significant (influenza and other acute respiratory viral infections, parenteral hepatitis) viral infections. As a result of this extensive work in the Northern Eurasia region, over 2,000 strains of zoonotic viruses (17 genera, 8 families), ecologically linked to various arthropod vectors and vertebrate hosts, have been isolated. Many of them have been registered in international catalogs as new species. The role of these isolated viruses in human pathology has been studied, new viral infections have been described, and diagnostic preparations have been developed. The scientific results obtained by the department are of high priority and internationally recognized.

Keywords: *ecology of viruses; emerging and reemerging infections; influenza; tick-borne encephalitis; ARVI; arboviruses; parenteral hepatitis; coronaviruses*

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РЕДАКЦИОННАЯ КОНЦЕПЦИЯ

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55 лет отделу экологии вирусов с научно-практическим центром по экологии и эпидемиологии гриппа (Институт вирусологии им. Д.И. Ивановского ФГБУ «НИЦЭМ им. Н.Ф. Гамалеи» Минздрава России)

Львов Д.К.✉, Альховский С.В.

Институт вирусологии имени Д.И. Ивановского ФГБУ «Национальный исследовательский центр эпидемиологии и микробиологии имени почетного академика Н.Ф. Гамалеи» Минздрава России, 123098, г. Москва, Россия

Резюме

В статье приведены исторические аспекты и основные результаты работы отдела экологии вирусов (ОЭВ) с научно-практическим центром по экологии и эпидемиологии гриппа, который был организован в 1969 г. на базе Института вирусологии им. Д.И. Ивановского АМН СССР. Деятельность ОЭВ на протяжении более 50 лет была направлена на разработку фундаментальных проблем экологии вирусов, включая вопросы формирования популяционных генофондов вирусов в природе, и проведение комплексных крупномасштабных исследований в интересах биобезопасности государства. Основное внимание в работе отдела посвящено проблемам особо опасных (арбовирусных) и социально значимых (грипп и другие ОРВИ, парентеральные гепатиты) вирусных инфекций. В результате этой крупномасштабной работы на территории Северной Евразии были изолированы более 2 тыс. штаммов зоонозных вирусов (17 родов, 8 семейств), экологически связанных с различными видами членистоногих переносчиков и позвоночных хозяев. Многие из них были зарегистрированы в международных каталогах в качестве новых видов. Изучена роль выделенных вирусов в патологии человека, описаны новые вирусные инфекции, разработаны диагностические препараты. Полученные в отделе научные результаты имеют высокий приоритет и признаны на мировом уровне.

Ключевые слова: *экология вирусов; новые и возвращающиеся инфекции; грипп; клещевой энцефалит; ОРВИ; арбовирусы; парентеральные гепатиты; коронавирусы*

Для цитирования: Львов Д.К., Альховский С.В. 55 лет отделу экологии вирусов с Научно-практическим центром по экологии и эпидемиологии гриппа (Институт вирусологии им. Д.И. Ивановского ФГБУ «НИЦЭМ им. Н.Ф. Гамалеи» Минздрава России). *Вопросы вирусологии.* 2024; 69(1): 7–21. DOI: https://doi.org/10.36233/0507-4088-217 EDN: https://elibrary.ru/xdikxk

Финансирование. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.
Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

The article is devoted to the following anniversary events: 300th anniversary of the Russian Academy of Sciences, 225th anniversary of the Military Medical Academy, 80th anniversary of the D.I. Ivanovsky Institute of Virology and 110th anniversary of the birth of the Soviet virologist V.M. Zhdanov. A solid foundation of the medical and biological area of viral infection study in the interests of biological security of the state was created by our great predecessors, the most prominent being academicians and virologists M.P. Chumakov, A.A. Smorodintsev, V.M. Zhdanov and the creator of the doctrine of natural foci of infectious diseases E.N. Pavlovsky **(Figure 1)**. Superior intellect, broad outlook, indomitable energy and organizational talent ensured the formation of domestic scientific schools that were internationally recognized. The next generations of researchers, working in the harsh conditions of expeditions, often involving serious risks, and in laboratories, continued to develop a broad front of research on natural focal infections, both known and previously unknown that are potentially dangerous, posing a threat to biosafety.

The leading role in the development of Russian virology belongs to the D.I. Ivanovsky Institute of Virology (IV), established by the Decree of the Council of People's Commissars of June 30, 1944 No. 797 on the organization of the USSR Academy of Medical Sciences (USSR AMS). The USSR AMS included the Institute of Virology, founded at the Department of Virology of the Institute of Experimental Medicine (IEM). The name of the founder of virology D.I. Ivanovsky was given to the Institute by the Decree of the USSR Council of Ministers No. 4344 of December 19, 1950. The directors of the Institute were major health care organizers and world-famous scientists: A.T. Kravchenko (1944–1950), A.A. Smorodintsev (1950), M.P. Chumakov (1950–1955), P.N. Kosyakov (1956–1961), V.M. Zhdanov (1961–1986) and D.K. Lvov (1987–2016). V.M. Zhdanov turned the Institute into a modern, world-renowned scientific center. Six WHO Centers functioned at the Institute and a system of scientific training was organized on a national scale and abroad [1].

In the 1960s, the level of research on emerging and re-emerging infections increased significantly in the world, especially in the USSR and the USA [2–4]. In the interests of biological security of the state, a consensus

Fig. 1. E.N. Pavlovsky in the circle of teachers and students of the VI course of the General Biology and Parasitology Department of the S.M. Kirov Military Medical Academy, 1955.

Top row: Yu.V. Chicherin, A.A. Gorovenko, D.K. Lvov, K.F. Dobrovolsky, A.A. Karyakin; middle row: B.N. Nikolaev, G.G. Smirnov, E.N. Pavlovsky, A.V. Gutsevich; bottom row: V.N. Motorin, V.S. Nedelko, N.M. Ushakov, V.I. Shut.

Рис. 1. Е.Н. Павловский в кругу преподавателей и слушателей VI курса возглавляемой им кафедры общей биологии и паразитологии Военно-медицинской ордена Ленина академии им. С.М. Кирова, 1955 г.

Верхний ряд: Ю.В. Чичерин, А.А. Горовенко, Д.К. Львов, К.Ф. Добровольский, А.А. Карякин; средний ряд: Б.Н. Николаев, Г.Г. Смирнов, Е.Н. Павловский, А.В. Гуцевич; нижний ряд: В.Н. Моторин, В.С. Неделько, Н.М. Ушаков, В.И. Шут.

was formed in academic (USSR AMS, USSR Academy of Sciences) and administrative (USSR Ministry of Health, State Committee on Science and Technology – SCST) circles on the necessity to organize a system for the comprehensive study of the problem regarding out-of-state epidemic situations. The study of biological (like radiation) background on the territory of the country and neighboring countries was considered of great importance. For this purpose, the All-Union Center for Virus Ecology and Anti-Epidemic Protection of Population and Troops was established at the Virus Ecology Department (VED) of the D.I. Ivanovsky Institute of Virology [1]. The most important vertebrate animals which are natural reservoirs for zoonotic viruses are birds (*Aves*), rodents (*Rodentia*), and bats (*Chiroptera*). More than 200 known arboviruses are ecologically related to birds. In certain cases, birds are the main vertebrate host, taking an active part in the formation of the viral population gene pool, while in other cases, they serve as an effective amplifier for the virus. The role of birds in the circulation of arboviruses is determined by several factors, the most significant ones being: high abundance and population density in nesting (for water birds), resting and wintering areas, seasonal migrations with transcontinental transfer of viruses and vectors (ticks), nesting in burrows. For in-depth study of zoonotic viruses associated with birds, taking into account their role in the spread of viruses, the All-Union Ornithological Committee with the Coordinating Council on Bird Migration and Medical Ornithology was organized. This committee was formed at the Institute of Biology of the Biological Department of the USSR Academy of Sciences (headed by Ilyichev V.D.) and the D.I. Ivanovsky Institute of Virology of the USSR AMS (headed by Lvov D.K.). The VED had a wide network of reference bases in all regions of the USSR. A joint research program was developed and conferences were held twice a year to discuss the plans and results obtained.

The territorial support bases, located practically in all regions of the USSR, were headed by energetic professionals who in a short time formed scientific teams of specialists: virologists, zoologists, arachno-entomologists, capable of conducting complex field and laboratory studies. Almost all of the supervisors defended their doctoral theses, and the rest of the specialists – their PhD theses: I. Vinograd (Lvov, Ukraine), I. Voinov (Minsk, Belarus), P. Skofertsa (Kishinev, Moldova), F. Karas (Bishkek, Kyrgyzstan), T. Pak, M. Kostyukov (Dushanbe, Tajikistan), S. Karimov (Alma-Ata, Kazakhstan), M. Kostyukov (Dushanbe, Tajikistan), and M. Kostyukov (Dushanbe, Uzbekistan), S. Karimov (Alma-Ata, Kazakhstan), N. Mirzoeva (Baku, Azerbaijan), V. Zakaryan (Yerevan, Armenia), M. Kurbanov (Ashgabat, Turkmenistan), A. Meliev (Tashkent, Uzbekistan), V. Zlobin (Irkutsk), F. Busygin (Omsk), G. Leonova (Vladivostok), A. Timofeeva (Yuzhno-Sakhalinsk), and others.

Thus, in the USSR, research was conducted to identify, much like radiation, the biological background. These were permanent maneuvers to predict and reduce the consequences of emergency epidemic situations of natural and anthropological origin.

The VED with the Influenza Ecology and Epidemiology Center was organized in 1969 as part of the implementation of the State Research Program of the established All-Russian Center for Ecology of Viruses and Particularly Dangerous and Poorly Studied Infections at the D.I. Ivanovsky Institute of Virology of the USSR AMS. The

Fig. 2. Founder and Head of the Virus Ecology Department (1969–2023), Dr. Dmitry Konstantinovich Lvov, Professor, Academician of the Russian Academy of Sciences. Director of the D.I. Ivanovsky Research Institute of Virology (1987–2014). Honorary Doctor of the Military Medical Academy of the Order of Lenin named after S.M. Kirov (2004).

Рис. 2. Дмитрий Константинович Львов, д-р мед. наук, профессор, академик РАН, создатель и руководитель отдела экологии вирусов (1969–2023), директор НИИ вирусологии им. Д.И. Ивановского (1987–2014), почетный доктор Военно-медицинской ордена Ленина академии им. С.М. Кирова (2004).

Fig. 3. E.I. Burtseva, Dr. Sc. (Med.), Head of the Virus Ecology Department since 2023, Head of the Influenza Etiology and Epidemiology Laboratory.

Рис. 3. Е.И. Бурцева, д-р мед наук, руководитель отдела экологии вирусов с 2023 г., руководитель лаборатории этиологии и эпидемиологии гриппа.

founder and permanent head of the Department for more than 50 years was D.K. Lvov, Member of the Russian Academy of Sciences, Professor, Doctor of Medical Sciences **(Figures 1, 2)**. The main goal of the Department was to study the biodiversity and distribution of zoonotic viruses and to identify the threats they pose to the biosecurity of the country as pathogens of emerging and reemerging infections. The main areas of research included a comprehensive study of ecological, later and genetic, factors in the formation of population gene pools of pathogenic viruses in nature, analysis of mechanisms for viruses to overcome the interspecies taxonomic barrier, study of the causes of emergence and spread of emerging and reemerging viral infections. A great deal of attention in the work of the department was also given to the surveillance of the circulation of seasonal viruses with respiratory transmission (ARVI).

The VED consisted of first-class medical and biological specialists: virologists and biologists with vast experience in laboratory, zoological and arachno-entomological field studies in natural foci of infections. The staff of the related laboratories of the IV departments: Clinical Virology, State Collection of Viruses, Applied Virology and Immunology, Arboviruses and Molecular Virology actively participated in the complex research. In the course of its work, the Division cooperated closely with the N.F. Gamaleya Institute of Epidemiology and Microbiology of the Russian AMS, M.M. Shemyakin and Yu.A. Ovchinnikov Bioorganic Chemistry of the RAS, M.R. Kovalenko All-Russian Research Institute of Experimental Veterinary Science of the RAS. Furthermore, a number of studies were carried out at the Russian Antiplague Scientific Research Institute Microbe of Rospotrebnadzor, the V.A. Engelberg Molecular Biology Institute of the RAS, the M.M. Shemyakin and Yu.A. Ovchinnikov Russian Research Institute of Experimental Veterinary Medicine, V.A. Engelhardt Molecular Biology Institute of the RAS, the Central Research Institute of Epidemiology of Rospotrebnadzor, the A.N. Severtsev Problems of Ecology and Evolution of the RAS and other institutions of both sanitary-epidemiological and veterinary services of the Soviet Union and the Russian Federation.

In 2016, the Institute ceased to exist as an independent institution and became part of the N.F. Gamaleya National Research Center of Epidemiology and Microbiology of the Ministry of Health of the Russian Federation. Currently, the Department includes: Influenza Etiology and Epidemiology Laboratory (headed by E.I. Burtseva, Dr. Sc. (Med.) (from 2023 – head of the VED, **Figure 3**)), Biotechnology Laboratory (headed by S.V. Alkhovsky, Dr. Sc. (Biol.), corresponding member of the RAS) **(Figure 4)**. Virus Ecology Laboratory (Headed by I.T. Fedyakina, PhD) **(Figure 5)**.

The activity of the VED is related to the creation and development of a new scientific area in virology which is the ecology (molecular) of viruses. During our research, we took an ecological approach and used mathematical methods of multifactor analysis to create a new scientific concept regarding the patterns of virus circulation in different landscape and climatic zones of Northern Eurasia. For

this purpose, a unique method of ecological and virological probing of the Northern Eurasia territory and forecasting of epidemic (epizootic) situations in different landscape-climatic zones in the Soviet Union and neighboring countries was developed and used **(Figure 6)** [5–16].

As a result of this large-scale work, more than 2,000 virus strains of 8 families, 17 genera, ecologically related to various species of arthropod vectors and vertebrate hosts were isolated. Many of them were registered in international catalogs as new to science. The role of isolated viruses in human pathology was studied, new zoonotic infections were described, and diagnostic preparations were developed. The ubiquity of mosquito-borne viruses in the landscape zones of tundra, taiga and deciduous forests was shown, including viruses of the California encephalitis group (*California encephalitis orthobunyavirus* species) and the Bataille virus group (*Bunyamwera orthobunyavirus* species) of the *Orthobunyavirus* genus, *Peribunyaviridae* family **(Figure 7)**. The circulation and significance in human and animal pathology in the USSR, Finland (Pogost's disease) and Sweden (Okelbo's disease) of Sindbis virus – the pathogen of Karelian fever and Getah virus of the *Alphavirus* genus, *Togaviridae* family were shown and studied for the first time **(Figures 8, 9)**.

New viruses were discovered during surveillance in Central Asia and Transcaucasia. Issyk-Kul fever virus (Nairoviridae: *Orhonairoviruses*) associated with bats and their argas ticks was described for the first time **(Figure 10)**. New viruses of Tamda and Burana fevers (Nairoviridae: *Orthonairovirus*), Syrdarya fever (Picor-

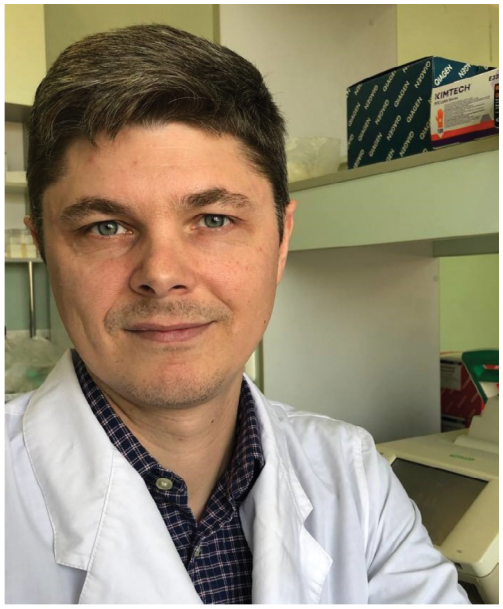


Fig. 4. S.V. Alkhovsky, Dr. Sc. (Biol.), corresponding member of the Russian Academy of Sciences, head of the Biotechnology Laboratory of the Virus Ecology Department.

Рис. 4. С.В. Альховский, д-р биол. наук, чл.-корр. РАН, руководитель лаборатории биотехнологии отдела экологии вирусов.

Fig. 5. I.T. Fedyakina, Ph.D., Head of the Virus Ecology Laboratory of the Virus Ecology Department.

Рис. 5. И.Т. Федякина, канд. биол. наук, руководитель лаборатории экологии вирусов отдела экологии вирусов.

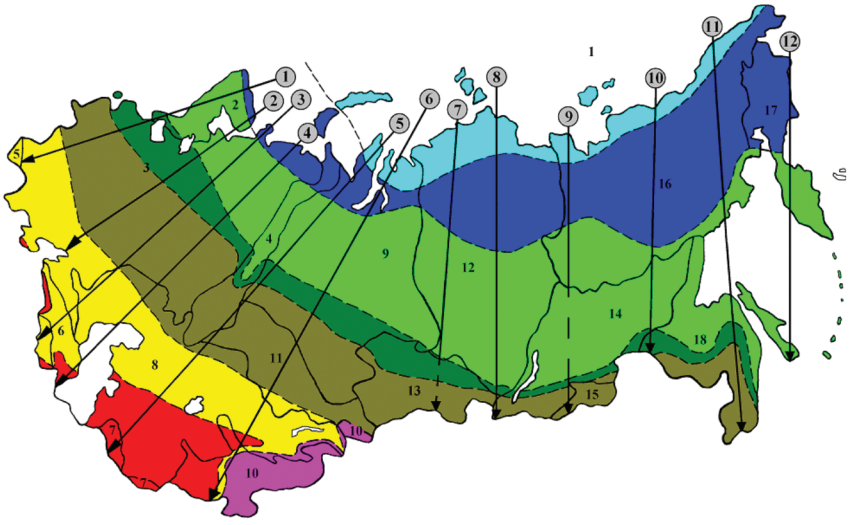


Fig. 6. Meridional sounding of the USSR territory – studies on identification of biological viral background similar to radiation and landscape-climatic zoning.

Рис. 6. Меридиональное зондирование территории СССР – исследования по выявлению биологического вирусного фона аналогично радиационному и ландшафтно-климатическому районированию.

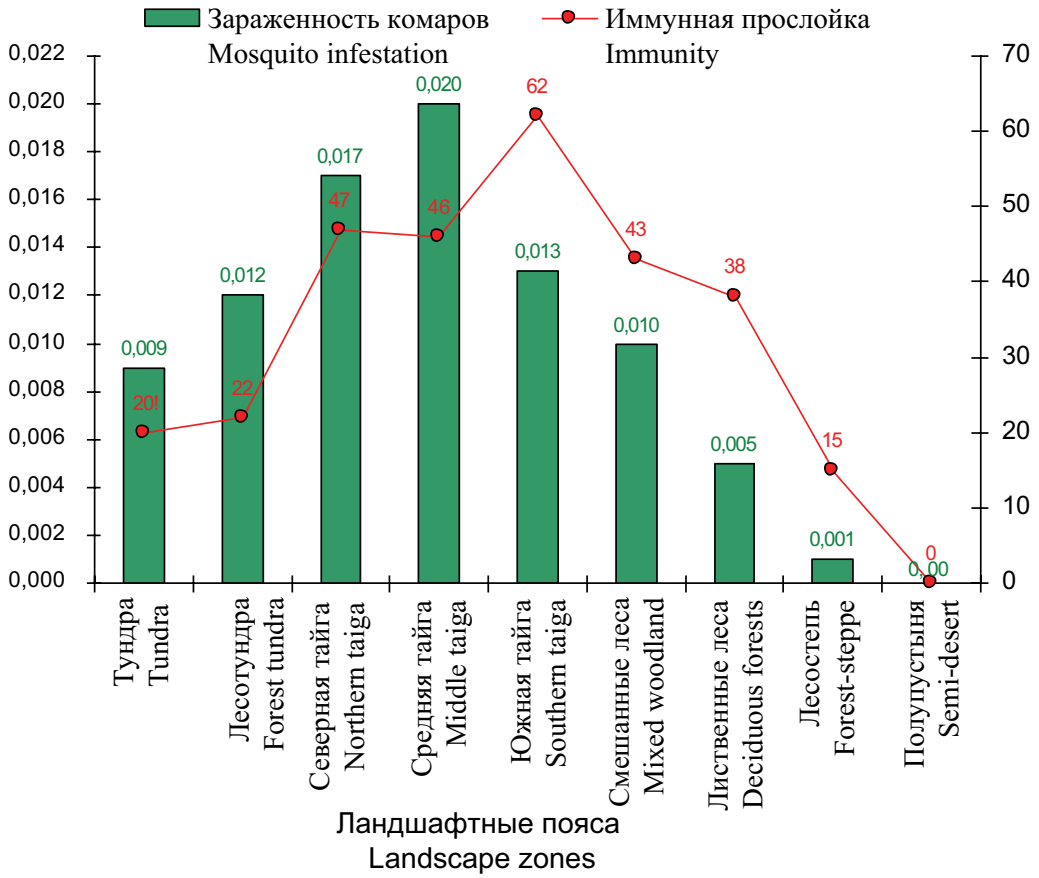


Fig. 7. Mosquito infestation and immunity in the population to California encephalitis serogroup viruses.
Рис. 7. Зараженность комаров и иммунная прослойка среди населения относительно вирусов серогруппы Калифорнийского энцефалита.

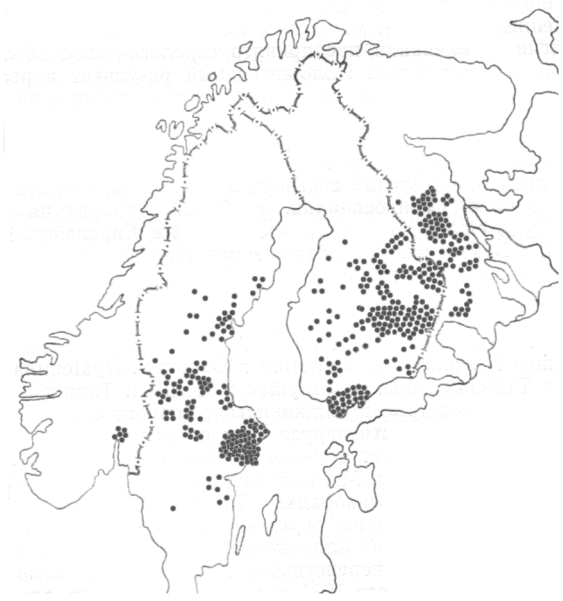


Fig. 8. Distribution of Sindbis virus, the Karelian fever pathogen (Okelbo fever, Pogost's disease) (Togaviridae: *Alphavirus*) in Fenoscandia.
Рис. 8. Распространение вируса Синдбис – возбудителя Карельской лихорадки (лихорадка Окельбо, болезнь Погоста) (Togaviridae: *Alphavirus*) в Феноскандии.

naviridae: *Cardiovirus*) were isolated from ixodal ticks collected from goats and cows in desert biocenoses. Several new viruses (Artashat, Chim, Geranium) were isolated for the first time from argas ticks collected from rodent burrows. The above viruses were classified as different species of the *Orthonairovirus* genus of the *Nairoviridae* family. Karshi virus (Flaviviridae: *Flavivirus*), related to Royal Farm virus (Afghanistan), isolated for the first time from argas ticks, belongs to the TBE (tick-borne encephalitis) complex and causes sporadic cases of febrile illness in humans. A new flavivirus, Sokuluk, ecologically related to bats and related to Entebbe bat virus from Africa, was isolated for the first time in Central Asia. In Kyrgyzstan, a new Tyulek virus, later assigned to the *Qaranjavirus* genus of the *Orthomyxoviridae* family, was isolated from argas ticks collected in nesting burrows of birds.

As part of a separate subprogram, ecological and virological studies of the «*Ixodes (Ceratixodes) uriae* ticks – colonial seabird» system were conducted in the Polar Region. In 1969–1974, hundreds of strains were isolated from *Ix. uriae* ticks collected from seabird colonies on the coasts of the Okhotsk, Bering and Barents Seas. Up to 7,000 ticks (all phases of metamorphosis – larvae, nymphs, adults) were collected from 1 square meter of nesting surface, from which up to 100 strains of various viruses were isolated, including genetically related viruses of tick-borne encephalitis and CCHF **(Figures 11, 12)**.

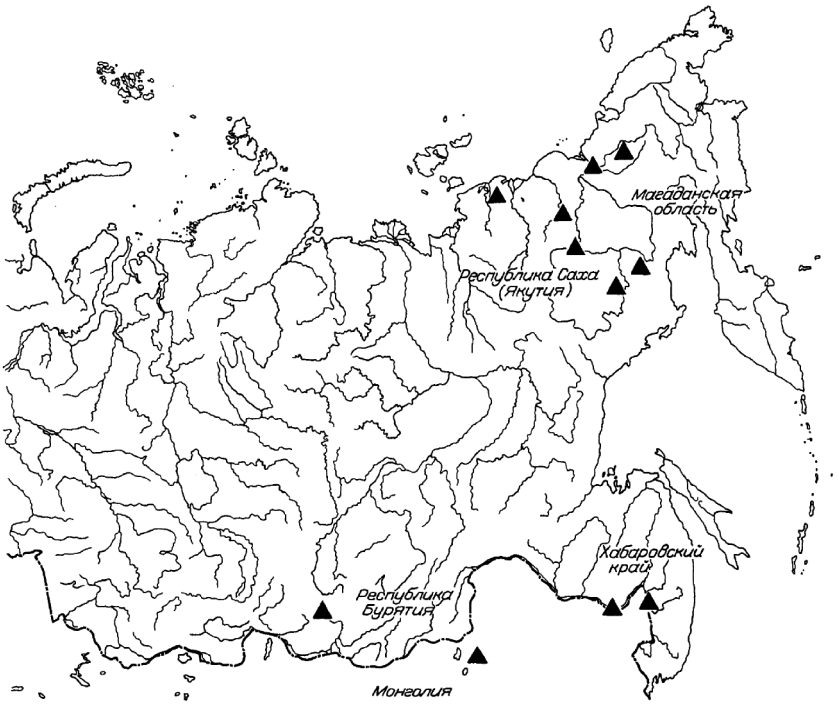


Fig. 9. Locations of Getah virus (Togaviridae: *Alphavirus*) isolation in Eastern Siberia, the Far East, and Mongolia.

Рис. 9. Места изоляции вируса Гета (Togaviridae: *Alphavirus*) в Восточной Сибири, на Дальнем Востоке, Монголии.

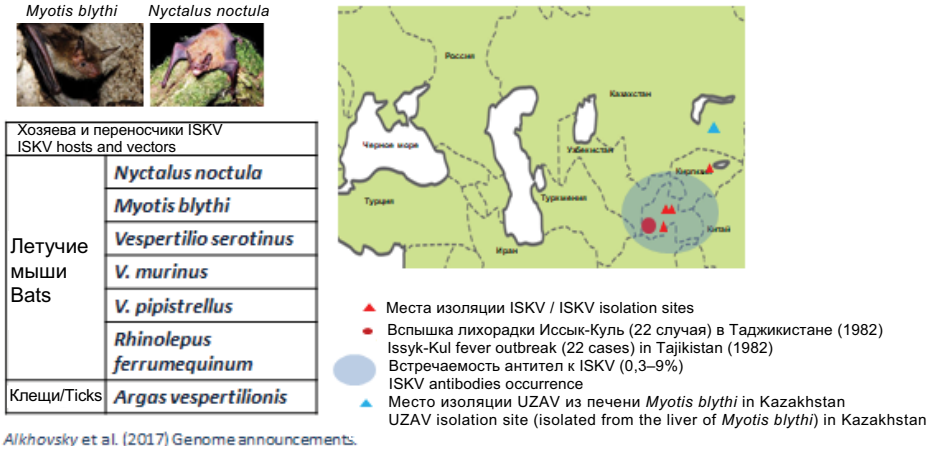


Fig. 10. New Nairoviruses (Nairovirus) associated with bats Issyk-Kul (ISKV) and Uzun-Agach (UZAV) viruses.

Рис. 10. Новые наировирусы (*Nairovirus*), ассоциированные с летучими мышами: вирусы Иссык-Куль (ISKV) и Узун-Агач (UZAV).

The circumpolar distribution of natural foci in the Northern and Southern hemispheres was established. The isolated strains were mainly classified as bunyaviruses, flaviviruses, and orbiviruses new to science, often only on the basis of virion morphology, as their antigenic relationships with other viruses had not been identified at that time. These included the first discovered Sakhalin and Paramushir bunyaviruses, which later formed the species *Sakhalin orthonairovirus* of the *Orthonairovirus* genus, *Nairoviridae* family. Several new viruses (Terpeniya Bay, Komandory, Rukutama) were described and later assigned to the *Uukuniemi phlebovirus* species of the *Phlebovirus* genus, *Phenuiviridae* family.

The new Tyulenii flavivirus and the closely related Kama virus from Tatarstan were first isolated and later became type representatives of the group of tick-borne seabird flaviviruses (Flaviviridae: *Flavivirus*). The distribution and ecological features of Okhotsk and Aniva viruses, two first described viruses of the Great Island virus species (Reoviridae: *Orbivirus*), have been studied in detail [17–21].

Genetic studies of newly isolated strains of Crimean-Congo hemorrhagic fever viruses (Nairoviridae: *Orthonairovirus*) and West Nile fever (WNF) viruses (Flaviviridae: *Flavivirus*), which caused extensive epidemic outbreaks with high mortality in 1999–2002 in southern Russia, were performed. The identity of WNF viruses during this period in Russia and the USA is shown. Year-round population relationships of WNF virus with vectors (mosquitoes, ticks) and vertebrates in the Volga River del-

Fig. 11. *Ixodes uriae* ticks (Tyulenii Island in the Sea of Okhotsk).
Рис. 11. Клещи *Ixodes uriae* (о. Тюлений в Охотском море).

Fig. 12. Nesting colonies of Thin-billed Buzzards (*Uria aalge*) on the Commander Islands.
Рис. 12. Гнездовые колонии тонкоклювых кайр (*Uria aalge*) на Командорских островах.

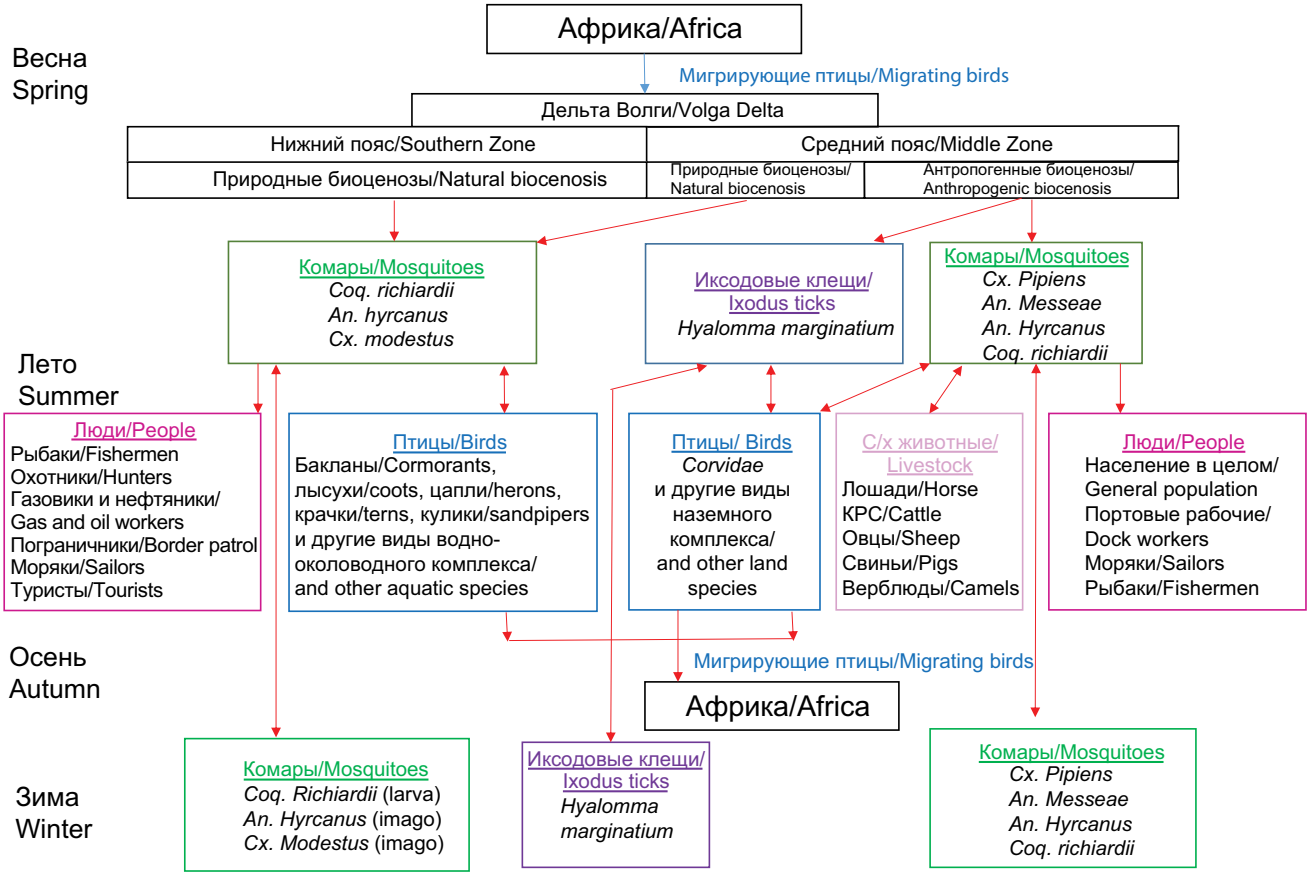


Fig. 13. Population interactions of WNF virus with arthropod vectors and vertebrate hosts.
Рис. 13. Популяционные взаимодействия вируса Западного Нила с членистоногими переносчиками и позвоночными хозяевами.

ta have been established **(Fig. 13)** [22–24]. This is a short list of the most notable new viruses discovered as a result of the research program; the main results are summarized in the Atlas of the Spread of Natural Focal Infections in the Russian Federation published in 2001 and a number of other books. For these achievements, the staff of the VED and collaborating organizations were awarded the State Prize of the Russian Federation in the field of science and technology in 1999, and the head of the project, Academician D.K. Lvov, was awarded the highest award of the Soviet Union – the Order of Lenin (the last in history) **(Figure 14)** [25].

- А.М. Бутенко – диагностика и идентификация вирусов
  A.M. Butenko – virus diagnostics and identification
- С.Я. Гайдамович – новые методы изучения биологических свойств вирусов
  S.Ya. Gaidamovich – new methods for studying the biological properties of viruses
- В.Л. Громашевский – изоляция вирусов и их идентификация
  V.L. Gromashevsky – virus isolation and identification
- П.Г. Дерябин – формирование коллекции вирусов
  P.G. Deryabin – creating a collection of viruses
- С.М. Клименко – электронная микроскопия
  S.M. Klimenko – electron microscopy
- Л.В. Колобухина – изучение клиники инфекций
  L.V. Kolobukhina – study of infection clinic
- С.Д. Львов – исследование вирусов в высоких широтах
  S.L. Lvov – study of viruses in high latitudes
- Д.К. Львов – руководитель программы
  D.K. Lvov – head of the program

Fig. 14. Winners of the State Prize for Science and Technology (1999).

Рис. 14. Лауреаты Государственной премии по науке и технике (1999).

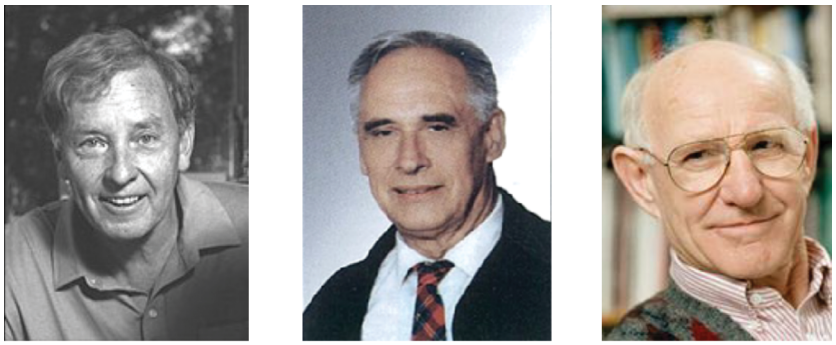


Fig. 15. Founders of the concept of natural foci of influenza A virus (Orthomyxoviridae, *Influenza A virus*).
From left to right Graham Laver (Australia), Dmitry Lvov (USSR), Robert Webster (USA).
Рис. 15. Основоположники концепции природной очаговости вирусов гриппа А (Orthomyxoviridae: *Influenza A virus*).
Слева направо Грэм Лавер (Австралия), Дмитрий Львов (СССР), Роберт Вебстер (США).

The final stage of these studies, led by Dr. S.V. Alkhovsky, corresponding member of the Russian Academy of Sciences, consisted of determining the genetic characteristics and taxonomy of isolated viruses using modern methods of genome analysis based on new generation sequencing (NGS). As a result of the introduction of these modern methods, about 200 previously unclassified strains have been genetically characterized on the basis of the biotechnology laboratory included in the department since 2012, of which more than 20 strains were described as virus species new to science and 2 new genera were formed. In total, more than 80 species of zoonotic viruses belonging to 12 different families circulating in Northern Eurasia have been identified. The population gene pool of potentially biosecurity-threatening zoonotic viruses with respiratory transmission (poxoviruses, orthomyxoviruses, coronaviruses, etc.) was forecasted. The data are taken into account in the latest international edition of the Virus Taxonomy.

Research on socially significant infections, in particular on parenteral hepatitis, was intensively carried out in the VED. In 1990–2000, large-scale epidemiologic and molecular genetic studies of the tender killer – the viral hepatitis C pathogen (Flaviviridae: *Hepacivirus*) were conducted. As a result of monitoring the distribution of its various genotypes in Russia, the ubiquitous dominance of the most pathogenic genotype 1b for the period of observation was established and a new genotype 2k was described. Recommendations on examination and treatment of patients were given. The reasons for the high incidence of viral hepatitis A (Picornaviridae: *Hepatovirus*), B (Hepadnaviridae: *Orthohepadnavirus*), and E (Hepeviridae: *Hepevirus*) in Central Asia have been studied [26–30].

Much attention was paid to the study of various aspects of the ecology and epidemiology of influenza. Based on the results of these studies, the leading role of birds in the evolution of influenza A viruses were revealed, which allows us to consider influenza A as a reverse zoonosis **(Figures 15, 16)**. Active circulation of 15 of 18 subtypes of influenza A virus (Orthomyxoviridae: *Alphainfluenzavirus*) known in the world

in natural biocenoses of Northern Eurasia, including genetic variants that are considered as possible precursors of new pandemic viruses **(Figure 17)** [31–34], has been established. The causes and consequences of the avian influenza H5N1 entry into Northern Eurasia and the global consequences of this process were studied **(Figure 18)**. One of the isolated strains was used for the production of avian influenza vaccine (FLU PROTECT H5) [35–39].

The Influenza Ecology and Epidemiology Center and the National Influenza Center (NIC), cooperating with WHO (Head – Academician of the Russian Academy of Sciences Lvov D.K., Deputy Head – Dr. Burtseva E.I.) operate at the VED. The Influenza Ecology and Epidemiology Center supervises 10 cooperating reference bases of the Centers of Hygiene and Epidemiology of Rospotrebnadzor in European Russia (Veliky Novgorod, Lipetsk, Vladimir, Yaroslavl, Penza, Cheboksary), in the Urals (Orenburg), in Siberia (Tomsk), and in the Far East (Vladivostok, Birobidzhan). The established system monitors the circulation of RNA- and DNA-containing viruses causing ARVI **(Fig. 19)**. Weekly reports of the Influenza Ecology and Epidemiology Center containing information on epidemiological, virological, antigenic and biological properties of pathogens are sent to the Ministry of Health of the Russian Federation, Rospotrebnadzor and WHO. As part of this work, the department is responsible for year-round monitoring for influenza virus circulation as part of the Influenza Ecology and Epidemiology Center and WHO NTF tasks. The first Russian strain of pandemic influenza virus A(H1N1)pdm09 was isolated and studied by the department in May 2009. The study of the entry and spread of influenza A(H1N1)pdm09 virus on the territory of our country was carried out. For the first time in Russia, molecular genetic factors in the development of primary viral pneumonia with high lethality have been identified – mutations in the binding site of the hemagglutinin HA1 receptor with a substitution of asparagic acid (D) for glycine (G) or asparagine (N) at position 222. These substitutions lead to a change in the receptor specificity of the virus with an increase in its ability to infect epithelial cells of the lower respiratory tract with a 70% mortality rate. Vaccination and early use of etiotropic drugs (neuraminidase inhibitors) prevent the formation of highly dangerous mutants [40–42].

After the emergence of the COVID-19 pandemic, active research on diagnostics and monitoring for SARS-CoV-2 (Coronaviridae: *Betacoronavirus*) morbidity in Russia was initiated in the laboratories of the Center. Together with other departments of the Center, studies of

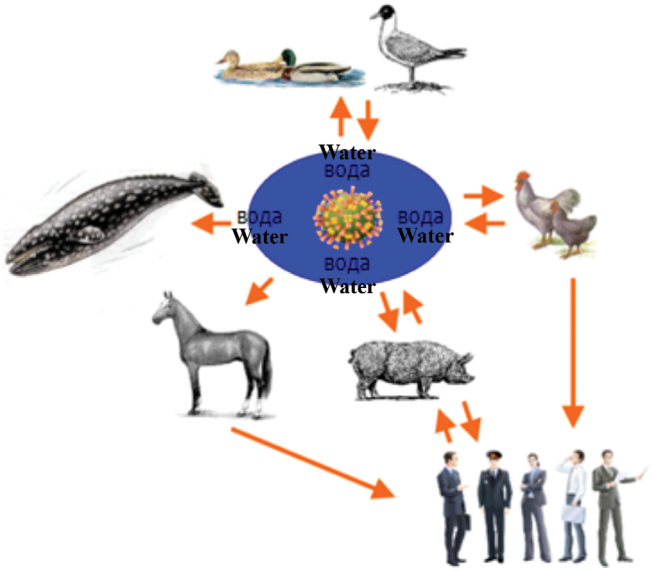


Fig. 16. Influenza A viruses in the biosphere.
Рис. 16. Вирусы гриппа А в биосфере.

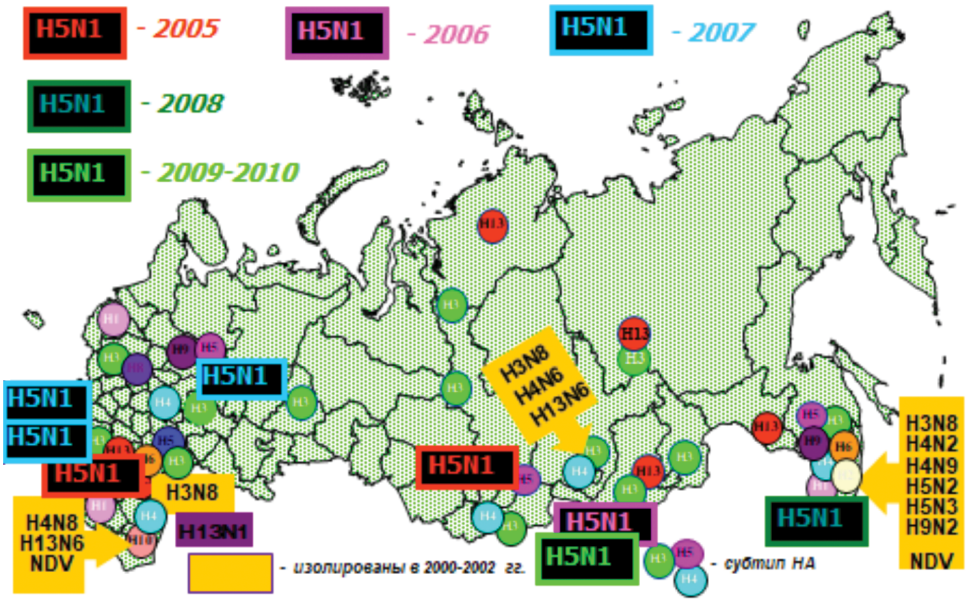
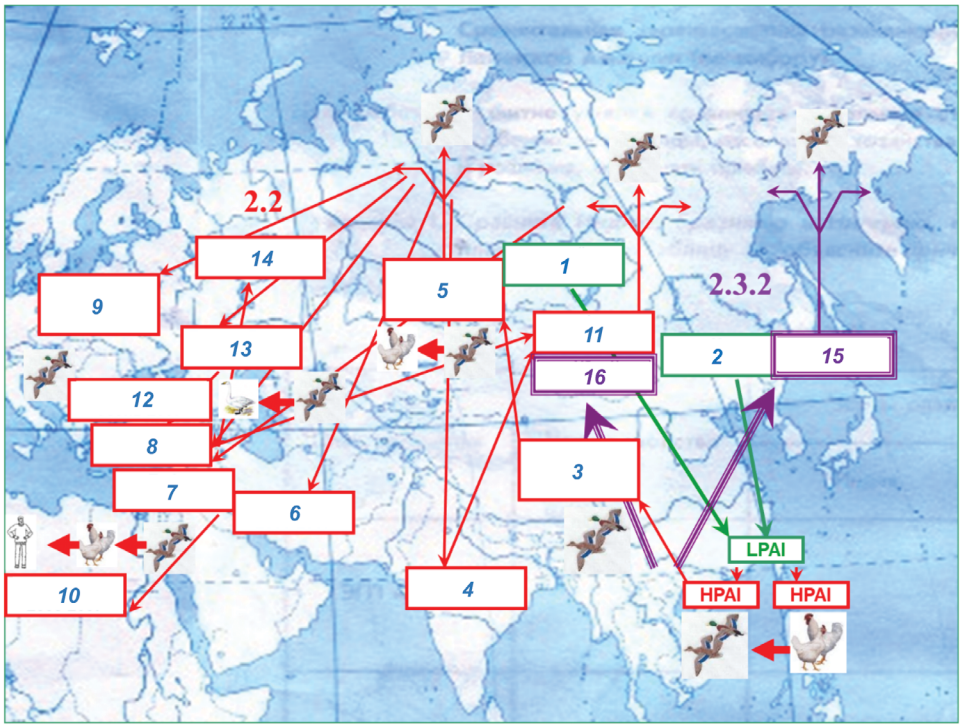


Fig. 17. Isolation of influenza A virus strains in natural foci of Northern Eurasia (1962–2011).
Рис. 17. Изоляция штаммов вируса гриппа А в природных очагах в Северной Евразии (1962–2011).



1 – Алтай, осень 1991
Altai, autumn 1991
2 – Оз. Ханка, осень 2001
L. Khanka, autumn 2001
3 – Оз. Кукунор, пров. Цинхай, весна 2005
L. Qinghai, spring 2005
4 – Индостан 2005–2007
Hindustan 2005–2007
5 – Западная Сибирь 2005–2007
West Siberia 2005–2007
6 – Иран 2005–2007
Iran 2005–2007
7 – Турция 2005–2007
Turkey 2005–2007
8 – Краснодар 2005–2007
Krasnodar 2005–2007
9 – Западная Европа 2005–2007
Western Europe 2005–2007
10 – Африка 2005–2007
Africa 2005–2007
11 – Оз. Убсу-Нур 2006–2007
Uvs Lake 2006–2007
12 – Ростор-на-Дону, осень 2007
Rostov-on-Don, autumn 2007
13 – Дельта Волги, осень 2007
Volga Delta, autumn 2007
14 – Подмосковье, зима 2007
Moscow Region, winter 2007
15 – Оз. Ханка, весна 2008
L. Khanka, spring 2008
16 – Оз. Убсу-Нур, весна 2009
Uvs Lake, spring 2009

Fig. 18. Causes and consequences of HPAI / H5N1 spread into Northern Eurasia (fall 2005).
Рис. 18. Причины и последствия проникновения HPAI/H5N1 в Северную Евразию (осень 2005 г.).

Семейство/Family	**Род/Genus**	**Типы и группы/Type and group**
Ortomyxoviridae, РНК/RNA	Influenza virus A, B, C	Вирусы гриппа А (вирусы гриппа человека и птиц), В и С Influenza virus A (human and avian influenza virus), B and C
Paramyxoviridae, РНК/RNA	Rubulavirus/ Respirovirus	Вирусы парагриппа типов 1, 2, 3, 4А и 4В(HPIV) Parainfluenza types 1, 2, 3, 4A and 4B (HPIV)
	Pneumovirus	Респираторно-синтициальный вирус, 2 группы –А и В (HRsV) Respiratory syncytial virus, 2 groups – A and B (HRsV)
	Metapneumovirus	Метапневмовирус, 2 группы – А и В (HMpV) Metapneumovirus, 2 groups – A and B (HMpV)
Picornoviridae, РНК/RNA	Enterovirus	Риновирусы, 3 вида (A, B, C) – 170 серотипов (HRV) Rhinovirus, 3 types (A, B, C) – 170 serotypes (HRV)
Coronoviridae, РНК/RNA	Alphacoronavirus Betacoronavirus	Коронавирусы сезонные Seasonal coronavirus SARS-CoV 2
Parvoviridae, ДНК/DNA	Bocavirus	Бокавирус, 4 типа (HBoV 1-4) Bocavirus, 4 types (HBoV 1-4)
Adenoviridae, ДНК/DNA	Mastadenovirus	Аденовирусы – (AdV), 7 типов/88 серотипов: A(3), B(10), C(5), D(50), E(1), F(2), G(1) Adenovirus – (AdV), 7 types/88 serotypes: A(3), B(10), C(5), D(50), E(1), F(2), G(1)

Fig. 19. Characterization of seasonal acute respiratory viral infection (ARVI) pathogens.
Рис. 19. Характеристика возбудителей сезонных острых респираторных вирусных инфекций (ОРВИ).

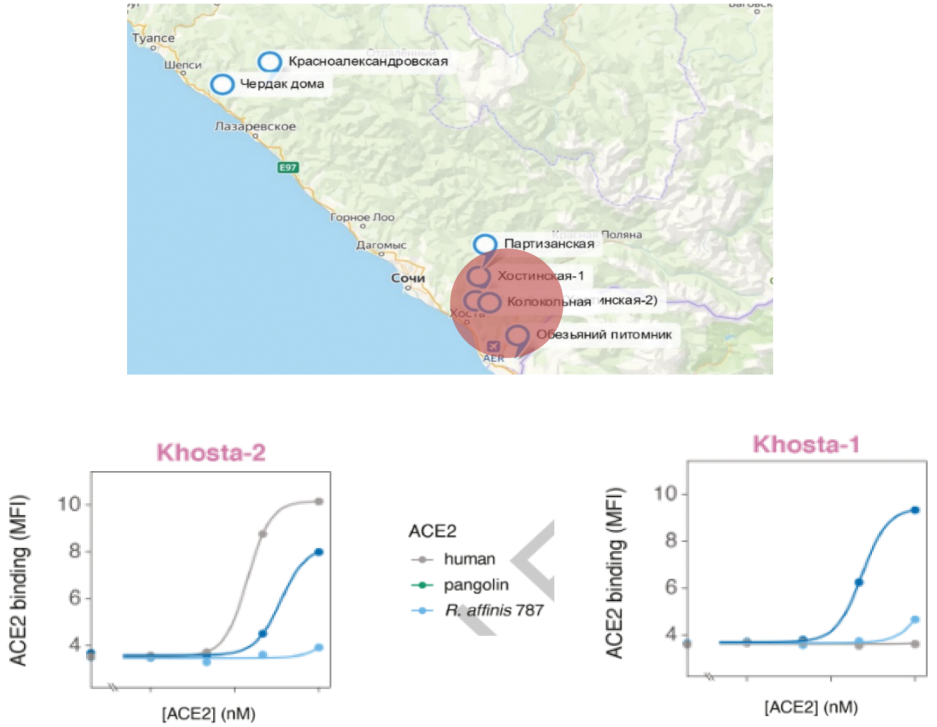


Fig. 20. Detection of circulating bat coronaviruses (Hosta-1 and Hosta-2) related to SARS-CoV-2 in southern Russia (northern coast of the Black Sea) in 2020.

The identified viruses are able to bind the ACE2 receptor of bats, Hosta-2 virus also effectively binds to the human ACE2 receptor and is capable of using it to infect the cell.

Рис. 20. Обнаружение циркуляции коронавирусов летучих мышей (Хоста-1 и Хоста-2), родственных вирусу SARS-CoV-2, на юге России (северное побережье Черного моря) в 2020 г.

Выявленные вирусы способны связывать рецептор ACE2 летучих мышей, вирус Хоста-2 также эффективно связывается с рецептором ACE2 человека и может использовать его для инфицирования клетки.

genetic variability of circulating variants of SARS-CoV-2 are being conducted. Another area of work is related to the study of mechanisms of emergence of new coronaviruses pathogenic for humans in nature. The territory of Russia and neighboring countries is being surveyed for the presence of zoonotic coronaviruses circulating in natural reservoirs. Their biological properties and pathogenic potential are being studied as well. In 2020, bat coronaviruses of the *Rhinolophus* genus (Hosta-1 and Hosta-2 viruses) related to the SARS-CoV-2 virus were identified and characterized for the first time in Russia **(Figure 20)** [43–45].

The identified viruses are able to bind the ACE2 receptor of bats, Hosta-2 virus also effectively binds to the human ACE2 receptor and is capable of using it to infect the cell.

Since 2023, Dr. E.I. Burtseva has been in charge of the VED. The Department continues active research of ecological, biological and genetic properties of viruses circulating in Russia and posing a threat as pathogens of new and reemerging infections. Much attention is paid to meeting the needs of practical healthcare in the field of diagnostics, prevention and treatment of viral infections (mainly ARVI). Circulation of influenza, SARS-CoV-2 and other acute respiratory viruses is constantly monitored, registration tests of new diagnostic test systems are conducted, state standard samples of respiratory virus strains are developed, and antiviral therapeutic and prophylactic drugs are tested *in vitro* and *in vivo*. Virus collections stored in the laboratories of the Department include hundreds of characterized strains.

The VED staff did a great deal of scientific and coordination work in training personnel for scientific institutions located throughout the USSR and later the Russian Federation. International relations of the VED were realized at regional meetings, symposia on arboviruses, influenza and viral hepatitis, and the 100th Anniversary of Virology. For more than 50 years, the activities of the VED were aimed at developing fundamental issues of formation of population gene pools of viruses in nature, conducting complex large-scale research in the interests of biosecurity of the state on the problems of especially dangerous (arboviral) and socially significant (influenza and other ARVI, parainternal hepatitis) infections with the priority of results at the world level. The world recognition of the Department's merits was expressed in the election of Academician D.K. Lvov as an international advisor to the American National Committee on Arboviruses, a member of the International Committee for the Study of Viruses in High Latitudes, a member of the Taxonomic Group on Bunyaviruses and Togaviruses of the International Committee on Taxonomy of Viruses, curator of influenza research within the framework of Russian-American cooperation on influenza problems, head of the WHO National Influenza Center, chairman of the Committee on Medical Sciences and Public Health of the World Health Organization (WHO), and a member of the International Committee for the Study of Viruses in High Latitudes.

The achievements of the VED are adequately reflected in a number of publications, including the 2-volume international monograph «History of Arbovirology: Memories from the fields» (Springer Nature Switzerland AG, 2023), which includes a chapter on the study of arboviruses in Northern Eurasia (Lvov D.K. and Alkhovsky S.V. as the authors) [46].

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