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## Title: Rabies: historical information and world distribution area

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### Abstract

Rabies virus is neurotropic (collects in nerve cells) and mainly infects the central nervous system. In the body of sick animals, the virus is mainly located in the gray matter of the brain and multiplies there, accumulates during the disease and remains in the body for a long time (up to 3 months) after the animal dies, where it is not neutralized.

The most virulent virus is isolated from wolves and dogs, and the less virulent ones are isolated from horses, bulls, sheep and humans.

In addition to the nervous system, the virus is found in saliva and salivary glands, lacrimal glands, internal organs, urine, and in the early stages of the disease, in the blood. The development of the virus in the body also depends on the amount of the virus, the localization of the bite and its virulence. The incubation period of the disease is reduced, especially when the organs close to the brain are bitten - face, head, neck.

**Keywords:** Virus, rabies, area, wild animal, vaccine.

### Introduction

Rabies is a disease of neglect and poverty, as well as a social and economic problem. The majority of people who die from the disease are poor, do not seek medical attention, are far from adequate means of treatment, and at the same time have a poor attitude towards bites or contact cases [1,2]. The economic losses resulting from the occurrence of the disease among agricultural animals are also measured in the millions of US dollars.

Due to its biological properties, the rabies virus is a neurotropic virus (collected in nerve cells) and mainly affects the central nervous system. In the body of sick animals, the virus is mainly located in the gray matter of the brain, where it accumulates in large quantities during the period of the disease and remains in the body for up to 3 months after the death of the animal, remaining inactivated for a long

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time .

The highest virulence viruses are isolated from mammals and dogs , while the lowest virulence viruses - are isolated from horses , cattle , sheep , and humans .

In addition to the nervous system , the virus is found in saliva and salivary glands , lacrimal glands , - internal organs , urine , and in the blood in the early stages of the disease . The spread of the virus in the body also depends on the amount of virus , the localization of the bite , and its virulence . In particular , the duration of the disease is reduced when the head and neck are affected , especially when the head - and neck are affected [ 2,3 ] .

The disease is fatal in 100 % of cases . 99 % of cases in humans are transmitted by stray dogs . According to the World Health Organization ( WHO ) , an average of 60,000 people die from rabies every year . Although 5 million people and 10 million animals are vaccinated against rabies , thousands of people die from the disease every year . Every 10 minutes , a virus infects 1 person in the world . Despite the - achievements made and achieved , the existence of cancer in the wild is still a challenge , " One Health " *in the system* Its abolition is considered one of the most important tasks and problems facing specialists - and the public , as a priority [ 19 ] .

Although the world is making significant progress in the prevention of smallpox , combating the disease - remains a local and national problem , and its eradication is considered a global priority . The disease is endemic in more than 150 countries . The virus is also endemic in Azerbaijan , where it is considered - the most endemic country . The article reviews the history , prevalence , and epizootics of rabies - worldwide [ 15,20 ] .

## Methods and materials

During the study , scientific electronic portals, conference materials, international scientific journals, literature and archival materials, and materials from our own research were used.

## Research layers

The causative agent of rabies belongs to *the Rhabdoviridae* family of the *Monongavirus* family . *This* - family includes 18 genera and 12 *genotypes of the Lyssavirus genus* . The causative agent *of the* disease - in humans and animals is the RNA virus *of the Lyssavirus* genus ( Table 1 ) [ 3,4 ] .

Rabies has been known since ancient times , but this disease is widespread in dogs . The symptoms of - the disease , which were known 5,000 years ago, and the high mortality rate of the animal are still - preserved . In ancient times , the time when the sun 's rays were shining in the morning in the summer - was called the dog season , and it was believed that dogs were more susceptible to rabies during this - period . Therefore , the ancient people of Egypt , Greece and Rome believed that the occurrence of this disease was related to supernatural forces . Thus , normally quiet , talkative and gentle dogs suddenly - became aggressive for no reason . After a certain period of time , their condition changed , they - developed seizures , paralysis and eventually died [ 6,8 ] .

Democritus ( 500 BC ) and Aristotle ( 322 BC ) wrote about rabies in dogs and domestic animals . - Celsus ( 100 AD ) recognized that fear of water in humans was related to rabies in animals and - recommended the sealing of the teeth of dogs . Galen ( 200 AD ) considered it necessary to surgically - remove the rabies wound [ 8 ] .

**Table 1**

Rabies virus serotypes

<b>Serotypes</b>	<b>Geographical distribution area of the virus</b>	<b>Type of animal (including humans)</b>
1. Rabies (CVS)	Worldwide (except Australia, New Zealand, Scandinavian countries, British Isles, Japan, Hawaii)	Humans, wild carnivores, domestic animals, bats
2. Lagos State Bank (LBB)	Nigeria, Egypt, South Africa, North Africa, Zimbabwe, Guinea, Senegal, Ethiopia	Dogs, cats, bats
3. Mokola (MOKV)	Nigeria, Zimbabwe, Cameroon, CAR, Ethiopia	People, dogs, cats, rodents
4. Duvenhage (DUVV)	North Africa, Zimbabwe	Humans, wild carnivores, bats, rodents
5. EBL-1 (European Bat Lyssavirus)	European countries	People, bats
6. EBL-1 (European Bat Lyssavirus)	European countries	People, bats
7. ABL (Australian Bat Lyssavirus)	European countries	People, bats
8. Caravan (CARAV)	Central Asia	People, bats
9. Kivjan (KHHV)	Central Asia	People, bats
10. Irkut (Murina leucogaster)	Eastern Siberia (RF)	People, bats
11. West Caucasian bat virus (Miniopterus schreibersi)	Western Caucasus (RF)	People, bats
12. Shimon bat virus (SHIBV)	Africa (Kenya)	People, bats

According to archival data , until the 16th century , rabies was mainly transmitted by wild animals . The role of dogs in the spread of the disease and its preservation in nature was relatively small . Thus , rabies was known in Western Europe from 1271 and was mainly transmitted among wild animals in France . - The first written record of rabies transmission among domestic dogs was recorded in Italy in 1708 . In 1728 , an epizootic of the disease spread to many cities in Hungary , Germany , and France . Although rabies had been known in England since 1613 , no epizootic was observed among dogs until 1734 [ 12 ] .

There is no record of rabies being observed in North and South America until the colonization of Chile . There are written records of rabies cases in the archives of Virginia in 1753 and in the archives of - Carolina in 1762. By 1785 , rabies among dogs had spread throughout New England . Although rabies - was not observed in South America until 1803 , rabies was observed in Peru that same year , and in -

1806 among dogs brought to La Plata and Argentina by three British officers [ 16,17 ] .

The infectious nature of rabies was first proven by Sinque ( 1804 ) by inoculating the saliva of an infected dog with the virus . In 1813 , studies by Grüner and Salam - Reifers in Steydt led to this conclusion . The studies showed that the disease was infectious and that rabies could be eliminated by destroying infected dogs and quarantining them .

In the early 19th century , various opinions were expressed regarding the treatment of hydrophobia ( - fear of water ) . In the 1930s , a French physician , after collecting these opinions , concluded that the - symptoms were insignificant and that the fear of water was always fatal .

In 1879 , the French physician P.G. Du Bois , based on his observations and studies , noted that the - causative agent of rabies is localized in the brain of the animal . However , later , Pierre Victor Galtier - conducted extensive research in this area . For a long time , he headed the Department of Pathology of - Infectious Diseases at the Lyon Veterinary School , and the professor , after convincing experimental - results , prepared the first vaccine against rabies ( for laboratory animals ) . He proved the possibility of - rabies transmission from dogs to rabbits in 1879 , before L. Pasteur , and studied the high susceptibility - of rabbits to rabies . P. Galtier was the first to develop the concept of vaccine preparation and showed - that the disease could be treated with a vaccine during the incubation period of rabies . He also noted - the application of this method to other infectious diseases and the role of vaccines in treatment . This - also made it easier to study the experimental conditions of rabies .

In 1881 , P. Galtier reported to L. Pasteur the results of another study , which showed that by injecting - the saliva of a rabid animal into sheep and goats , they were resistant to rabies . However , this method - was effective for ruminant animals , but was not suitable for dogs .

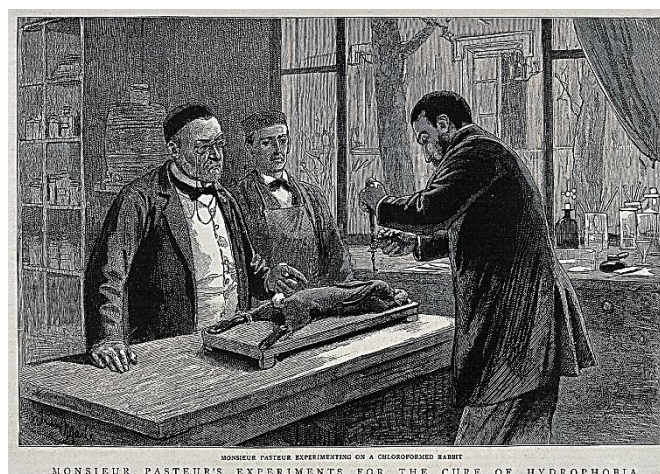
French biologist , chemist , pharmacist , and founder of modern microbiology and immunology , Louis - Pasteur , began systematic research on rabies in the late 1880s . There are two reasons for his research - on rabies : first , because the disease can be transmitted to humans as well as animals , and the disease ( - zoonosis ) is transmitted from veterinary medicine . Second , although this disease affects humans in - relatively small numbers , it is extremely dangerous for society .

L. Pasteur initially tried to find the causative agent of rabies microscopically by examining the saliva of - infected humans and animals , but he was unsuccessful . Because no one knew that the filtered rabies - virus was very small .

Later , L. Pasteur , through experiments in laboratory conditions , clearly established that the disease - never occurs spontaneously , but must have an agent . He noted the impossibility of obtaining a pure - culture even if the agent is in the saliva of a sick animal . Therefore , taking into account that there are - always many microorganisms in the saliva along with the agent , he decided to grow - the virus in living organisms .

the study was the disease's uncertainly long incubation period. So, to begin the study, it was necessary to find a way to safely transmit the pathogen from one laboratory animal to another, as well as to reduce the duration of the illness.

L. Pasteur 's comrade-in-arms, Pierre Paul Emile (Ru), knowing that the virus affects - the nervous system , decided to work - directly with the brain . For this , they - used the method of P. Galtier and - determined that the original causative agent of rabies could be obtained in a pure state from the brain of an animal that had died of the disease . The brains of sick animals were separated from the L. Pasteur ,



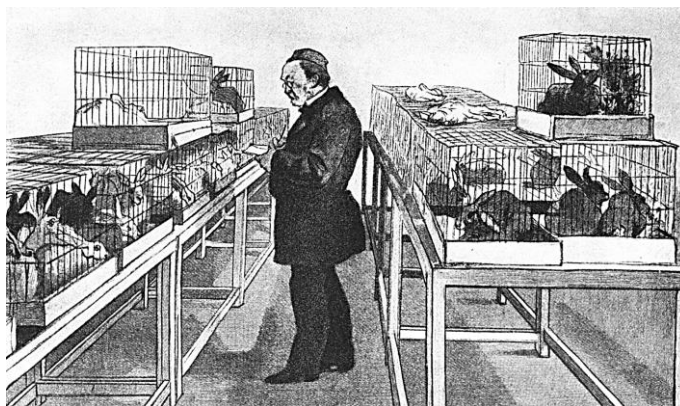
*the creator of rabies* , *called it a virus* (meaning "poison" in Latin) because it was impossible to accurately identify it with a microscope and *to cultivate it in ordinary food media* by trepanation of *a rabbit 's skull* .

In 1884 , after modifying the pathogen for its natural hosts by passing the rabies agent through the - intracerebral inoculation method from the body of another host , they attempted to obtain the same - infectious agent by passing the rabies agent into rabbits and other animals . Thus , with the resulting - culture , it would be possible to vaccinate susceptible animals against rabies . After each passage , the - virulence of the virus increased , the incubation period shortened , and the rabbits in the wild became - sick for a shorter period . After the 90th passage , the incubation period of the disease in the rabbits in - the wild stabilized at 7 days and did not change in subsequent passages .

L. Pasteur , E. Roux and S. Chamberlain were able to reduce the virulence of the identified virus by - growing it in the brains of monkeys and reducing its virulence for dogs . Thus , 5 years of laboratory - research aimed at preparing a vaccine against rabies came to an end . L. Pasteur successfully completed - the task he set and developed a method of prophylaxis against the disease [ 10 ] .

After the results of L. Pasteur 's experiments became known , a 9 -year-old boy named Joseph Meister , - who had been bitten in 14 places by a rabid dog , was brought to his grandmother 14 days after the - incident . He was the first to treat J. Meister with the vaccine he had prepared .

second person to be vaccinated against rabies was 14-year- old shepherd Jean-Baptiste Jupil . On October 16, 1885, while herding cattle , he saw a rabid dog attacking six children playing nearby and - tried to run away . The dog grabbed his hand , but the 14-year-old Jupil tied the dog 's mouth with a leash and killed it by hitting it on the head with a wooden shoe . The - young man , who had deep fang wounds on his hand , was brought to Pasteur six days - later . Because the courage of the young - shepherd pleased Pasteur and because he - received better results than the vaccination - he had given 6 or even 8 days after the - vaccination , which had not been done - before , the vaccination was successful . The Paris Academy awarded Jupiler 1000 francs - for his bravery in *the fight against rabies* , even though he had been fighting against the more serious - rabies of L. Pasteur 's laboratory animals .



L. Pasteur was later interested in the lives , education and behavior of J. Meister and J. Jupiler . When the Pasteur Institute was founded , at the request of L. Pasteur , a statue of Jupiler was erected in his - honor , and thus his heroic act was immortalized . The ape is also depicted as a man who has won an - unequal battle with a wild beast that has become wild . Today , the ape is also accepted as a symbol of - science and human sacrifice , as well as a symbol of L. Pasteur himself .

In Tsarist Russia , the disease was widespread among humans and animals , with animals being the main reservoirs of the disease . People who had been bitten by the plague came to Paris from the Smolensk , - Vladimir , Orlov , and St. Petersburg provinces of Russia to be treated at L. Pasteur 's laboratory . Thus , during the treatment , L. Pasteur observed that animals bite more dangerous organs than dogs - the head , neck and upper parts of the brain , and their teeth do not work as well . For the reasons indicated , the incubation period of rabies in people bitten by animals is much shorter than in dog bites , so delaying - vaccination can lead to unpleasant consequences , especially death . Therefore , L. Pasteur emphasized - the importance of vaccination against late bacteriological diseases . Not only victims of bacteriological - diseases , but also doctors and scientists from Russia came to L. Pasteur to learn his method .





The new University of Lisbon Faculty of Medicine building, 1906.

In the center, L. Pasteur, Robert Koch (left) and Emile Roux (right) address

Thus , in February 1886 , the Odessa Medical Society sent 27 - year - old Nikolai Fyodorovich Gamalei to Pasteur 's laboratory to study the methods of preparing and administering a rabies vaccine . Another - Russian physician who worked at Pasteur 's laboratory , N.M. Unkovsky , wrote in early April 1886 that - the scientist ( Pasteur ) was hiding nothing from us and considered it appropriate to establish a - vaccination institute in Moscow .

In early 1886 , NF Gamaleya , who had completed Pasteur 's studies , reported to the Odessa Society of Physicians that Pasteur had authorized the establishment of a rabies vaccination institute . I.I. - Mechnikov informed the physicians that this institute was his own " certificate and Pasteur gave him , and that three rabbits infected with the virus were sent from Paris to Odessa by Gamaleya .

On June 11 , 1886 , vaccination against the disease began at the Odessa rabies station . The first person - to be vaccinated was the 28 - year - old doctor Y.Y. Bardakh , the deputy director of the station , who - voluntarily underwent a dog bite . The aim was to determine how the vaccine virus behaved in the - human body .

On July 17 , 1886 , a month after the Odessa station was established , a Pasteur station was also - established in Moscow , headed by N.M. Kovskii . Within a year ( July 1886-1887 ) , 287 individuals - from 27 provinces of Russia who had been injured by rabid animals were vaccinated against rabies at this station .

The workers of the Pasteur Station established in St. Petersburg decided to obtain their own stable - viruses and prepare a vaccine . Kh.I. Gelman and N.A. Kruglevskiy made great contributions to the - establishment of this station . Pasteur maintained close ties with the St. Petersburg Station for many years ( from 1886 to 1892 ) .

In 1886 and 1887 , Pasteurization stations were established in many cities - Samara , Kiev , Kharkov , - Irkutsk . They were headed by people who had trained at Pasteur or the Odessa station . Later , - Pasteurization stations were transformed into research laboratories and institutes , where they were - engaged in the study of problems of microbiology and virology [ 9,10 ] .

In 1888, the first Pasteur Station was established in Tiflis to provide anti-rabies assistance to people in Zaqatli. Later, given the long-standing nature of the infection and the special role of anti-rabies assistance in preventive measures against rabies, it became necessary to establish such centers in the region. Thus, in 1924, the first Pasteur Station was established in the Republic of Azerbaijan, and its activities were expanded, and in 1951 its number was increased to 23 [5,14].

The achievements made in this area led to the elimination of rabies in some European countries (Sweden, Denmark, Norway, and some German provinces, such as Bavaria) by the end of the 19th century. In the 1930s, rabies epizootics were eliminated or even sharply reduced in western Europe, in Luxembourg, Austria, Hungary, France, and Belgium [13].

The new epizootics that arose in the 20th century were fundamentally different from the previous ones. Thus, it was determined that the main source of infection in nature was wolves in Europe and skunks in America. In East Prussia, rabies occurred and the virus spread rapidly in natural foci of the disease, especially among foxes, and partly in badgers. The area of new epizootics that arose as reservoirs of the disease began to expand. Despite the implementation of preventive measures, the virus spread to Western European countries at an average speed of 40 km/h. In 1950, the virus spread to the Elbe River, in 1954 to the Rhine River, in 1956 to Hungary, in 1964 to Denmark, in 1966 to Austria and Luxembourg, in 1967 to Switzerland, in 1968 to France, and in 1977 to Italy. The first case of the disease in foxes in Switzerland was recorded in 1967 on the border with Germany. Despite the mass vaccination of dogs and the implementation of measures aimed at the destruction of wild animals, it was not possible to limit the spread of the epizootic. In 6 months of 1977, 537 dogs and up to 85% of them were infected with foxes [13].

According to the International Bureau of Animal Health (IBAH), rabies was reported in 90,127 wild animals and 6,492 dogs between 1977 and 1981, including 17,123 foxes and 4,661 domestic animals - were recorded [18].

The situation with rabies in the former Soviet Union was similar to that in Europe. After the Second World War, the largest rabies epizootic was recorded in the USSR for the last 26 years, reaching its highest level in 1951. Although the source of the disease was previously in animals, it was later determined that foxes were the main reservoirs. The first case of rabies among foxes was recorded in the late 40s of the 20th century in the Tula and Voronezh regions, and then spread to other territories of the European part of the USSR.

In the second half of the 1980s, the most widespread transmission of rabies among wild animals was observed in Russia, Ukraine, and Belarus, and later in the Central Asian and Transcaucasian republics, with foxes being the main source [8,9].

Despite the increasing role of foxes in the epizootics of rabies, wild animals continue to play a major role in the spread of rabies. If in the 40s - 60s of the 20th century the extinction of wild animal foci was observed, then in the 70s - 80s there was a resurgence. Wild animals were the main cause of the spread of the virus in Kazakhstan, the northeastern coast of the Caspian Sea, the central regions of the RSFSR, Belarus, and Ukraine. In 1976-1980, the total percentage of human infections by animals with hydroxychloroquine in the USSR was 3.5% [7].

Thus, in Europe, the former part of Europe and North America, unlike in previous years, rabies has now emerged as a natural reservoir of rabies among wild animals. The measures taken to eliminate these reservoirs - capturing wild animals, shooting them and even digging up their nests to destroy their young, and vaccinating them with briquettes of vaccine mixed with food and creating immunity in them - are not yet fully effective.

For the first time, in 1927, at the International Conference on Rabies, it was decided that specific prophylactic vaccination of domestic animals was desirable.

In Azerbaijan, every year, in accordance with the plan of measures against epizootics, preventive vaccination against rabies is carried out in domestic animals (dogs, cats). In endemic areas, when -

infected farm animals come into contact with wild animals, they are also vaccinated in accordance with the instructions. In order to prevent the disease, educational activities have been carried out among the population in recent years, and in endemic areas, rabies vaccination has been carried out.

## WHAT IS IT ?

- As a preventive measure against rabies, the rules specified in the law on keeping pets, especially dogs, must be strictly followed;
- Dog owners should take their animals to veterinary services and vaccinate them against rabies on a regular basis;
- It is not allowed to travel without a bag or a mask;
- People should seek medical attention immediately if they are exposed to any bites, scratches, or saliva from animals (even those that appear healthy).
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