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Emerging viral diseases

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Abstract

Emerging viral diseases encompass two types, those of new appearance in the population and those that we previously knew about or re-emerging, but that at a certain moment present an exponential increase in incidence or geographic distribution in the form of epidemics or outbreaks.

These emerging and re-emerging viruses share a series of characteristics that establish the emerging virus model, such as having an RNA genome, being zoonotic, transmitted by vectors and transmissible to humans, that the virus is able to recognize and provoke a response in receptors. Conserved in several species and inhabiting ecosystems that undergo ecological, demographic or social changes that favor the spread of the virus.

There are different factors that contribute to facilitating the emergence of viral infections, although this is made up of three fundamental aspects such as the susceptible population, the virus itself and the environment where both can interact.

Keywords: Emerging viral diseases; SARS-CoV-2; MERS-CoV; SRAG; Chikungunya virus; Zika virus

1. Introduction

When we talk about emerging viral diseases, we must take into account that they encompass two types, those of new appearance in the population and those that we previously knew (re-emerging) but that at a certain moment present an exponential increase in the incidence or in the geographical distribution in form of epidemics or outbreaks.

The mechanisms that facilitate the high incidence and expansion of these viruses can be classified into three groups. First, through the appearance of an unknown virus thanks to the evolution of a new variant. An interspecies jump can also take place, introducing a new host into the life cycle of the virus. Lastly, the geographic spread of a virus traditionally limited to an ecological niche, in which it emerged, may occur.

These emerging and re-emerging viruses share a series of characteristics that establish the emerging virus model, such as having an RNA genome, being zoonotic, transmitted by vectors and transmissible to humans, that the virus is able to recognize and provoke a response in receptors. conserved in various species and inhabiting ecosystems that undergo ecological, demographic or social changes that favor the spread of the virus.

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Emerging viral diseases (EVD) are in full swing since the new SARS-CoV-2 pandemic jumped worldwide in December 2019, the outbreak of which began in Wuham (China) (Figure 1). And currently on the new outbreaks after the confinement produced worldwide [1-5].

2. Factors contributing to its re-emergency

It is indisputable that there are various factors that contribute to facilitating the emergence of viral infections, although this is made up of three fundamental aspects such as the susceptible population, the virus itself and the environment where both can interact.

The current trend of migration to urban centers involves major demographic changes, to which we can add the migration caused by armed conflicts that displaces millions of people. The WHO estimates that by the year 2025 65% of the world's population will live in cities.

Global climate change affects strongly since it sometimes causes the migration of animal species, potential vectors, in search of a favorable environment in which the availability of water also influences.

With global warming, settlement is favored in areas where the vector did not previously inhabit. A key factor that favors the spread of these and other pathogenic viruses and microorganisms is poverty. Social inequalities favor overcrowding and poor sanitary conditions in the most disadvantaged population groups, which considerably increases the probability of transmission between humans and between species.

Throughout history, travel has often led to the spread of infectious diseases such as smallpox or those associated with rodents. Although there are currently great advances in communications and health alerts, there is also a greater flow of travelers around the world, which can cause a vector with the virus or a sick person to travel very far, introducing the virus into a new habitat [6-8].

The virus itself can adapt to the environment, even more so when its genome is made up of RNA. In RNA replication, the polymerase assumes a high rate of errors that can facilitate changes that contribute to adaptation, such as the modification of antigenic sites that provoke an immune response different from that generated against other strains. A clear example of this is the annual influenza epidemics produced by small genomic changes hitherto unknown by the immune system [9-11].

3. Emerging viral agents

3.1. New human viruses

In addition to the current SARS-CoV-2 there are and will be many others such as:

3.2. SARS coronavirus

In 2002, the WHO issued a global alert for a severe atypical pneumonia in humans that appeared in China and spread rapidly called Severe Acute Respiratory Syndrome (SARS).

Thanks to the cooperation of different WHO laboratories, the causative agent was identified and in a short time the complete sequence of the virus genome had been analyzed by PCR and classified as a new group of Coronaviruses. Its reservoir is animal and it is believed that the consumption of infected animals facilitated interspecific jumping.

In 2003, 8098 cases had been reported, 774 were fatal. Few cases of SARS have been reported since that year, but the existence of asymptomatic carriers of the virus has been demonstrated, although it is unknown whether the viral load is sufficient to cause infections.

3.3. Influenza A virus

Throughout history there are several flu pandemics. Those of 1957 and 1968 were due to hybrid human and avian strains. There are two families of proteins, hemagglutinins and neuraminidases, responsible for the different strains of Influenza A virus since they combine in different ways, causing new strains against which the human body has no previous protection. Migratory and domestic birds, pigs and humans are part of the virus cycle.

In 1997 the transmission from chickens to humans was detected in Hong Kong of the H5N1 strain, the so-called avian flu. In the Netherlands in 2003 the H7N7 strain was found.

In 2009, the H1N1 strain or swine flu caused a pandemic, decreeing the WHO an alert level 6. This strain presents genetic material from an avian strain, two swine strains and one human (WHO: Swine flu has pandemic potential. RFI April 25, 2009). This strain of influenza A virus caused deaths around the world. From 2013 to 2015, the epidemic-causing strain H7N9 has been detected in China (Human Infection with Influenza A (H7N9) Virus during 3 Major Epidemic Waves, China, 2013–2015).

3.4. Nipah and Hendra virus

These two viruses belong to the genus Henipavirus of the family Paramyxoviridae, it is thought that bats of the genus Pteropus could be their reservoir. In 1994 the Hendra virus caused 2 deaths in Australia out of 3 detected cases. The symptoms are similar to the flu, although it can evolve into encephalitis. In 1998 it was the Nipah virus that produced an outbreak of encephalitis with 276 infected and 105 deaths. In 2004, there was an outbreak in Bangladesh caused by a virus similar to Nipah, resulting in 14 deaths out of at least 42 confirmed cases.

3.5. Human metapneumovirus

Human metapneumovirus (hMPV) was described in 2001 as a new causative agent of acute respiratory disease, after its discovery in children with respiratory tract infection.

The discovery of this virus is a clear consequence of the fact that technological evolution in diagnostic methods has facilitated the detection of this difficult-to-grow virus in cell cultures. It seems to have been present since at least 1958, and although it was initially described in the Netherlands, it has also been found in other countries such as Australia, Canada, Finland, the United States, France and the United Kingdom. Also in Spain it has been found among other new countries.

3.6. MERS-CoV coronavirus causing Middle East Respiratory Syndrome Coronavirus

He was first identified in 2012 in Saudi Arabia. Infection by the virus causes severe acute respiratory disease that causes fever, cough, pneumonia, respiratory distress, kidney involvement, and high mortality, close to 36%. The bat appears to be its reservoir and is transmitted through camel saliva, almost all patients have been infected in the Arabian Peninsula and surroundings [9]. On May 29, 2013, the WHO warned that the MERS-CoV virus is a global threat, in November of that year 127 cases had been detected in Saudi Arabia, according to the press.

4. Expanding human viruses

4.1. West Nile virus (West Nile virus)

West Nile virus is a mosquito-borne flavivirus, with more than 25 species, that inhabits birds, but can affect other species, particularly humans and horses. It causes fever and can trigger encephalitis, although 80% of people are asymptomatic [10]. It was discovered in 1937 in Uganda, although it was not until the 1990s that it gained health importance due to important outbreaks in the Czech Republic, Russia and Israel, among others. In 1999 it appeared in New York, spreading to all of North and Central America. More than 8,000 cases have been detected in the US alone, resulting in more than 370 deaths.

4.2. Japanese Encephalitis Virus

It is a flavivirus closely related to the West Nile virus (West Nile virus), also recently updated, which is also transmitted by mosquitoes, its reservoir is aquatic birds and is amplified by domestic pigs. The transmitting mosquito inhabits rice crops in Asia, causing encephalitis, leaving neurological sequelae in 25% of patients. It was isolated in 1935, it produces around 40,000 cases a year, of which between 10% and 35% are fatal. In 1978 it appeared in Nepal, becoming a public health problem in the 1990s. There is an inactivated and an attenuated vaccine and they are used in some areas for their control.

4.3. Hantavirus

The genus Hantavirus has as a reservoir rodents in which it inhabits asymptotically. Through urine or feces of contaminated animals it can be transmitted to humans, although some person-person cases have been described. They produce two different pathologies: Hemorrhagic Fever with Renal Syndrome (FHSR), with a mortality of less than 10%

(Old World Hantavirus) and Hantavirus Pulmonary Syndrome (HPS), with a lethality of 40% in all America. The first is caused by the Hantan virus, discovered in the 70s, but the HPS-producing Sin Nombre Virus was discovered in the 90s.

4.4. Dengue virus

Dengue is an infection caused by a virus belonging to the flaviviridae family. It is transmitted by mosquitoes and only man and mosquito belong to its (urban) life cycle. It causes fever although it can complicate into hemorrhagic fever. According to the WHO, about half of the world's population is at risk of contracting the disease. WHO, in the last decades the incidence of this infection in the world has increased strongly. There is no specific treatment but early detection causes mortality to be below 1%.

4.5. Yellow fever virus

The virus that causes yellow fever is also a flavivirus whose vector is *Aedes aegypti*, and it has its monkey cycle, although when it is introduced into urban areas it can infect man. The first case described dates from 1768. In Senegal. It causes hemorrhagic fever and has a high mortality rate. The vaccine and the campaigns to eliminate the mosquito managed to reduce the number of affected cases, but currently its annual incidence has increased to 200,000 new cases, causing 30,000 deaths.

4.6. Rift Valley fever virus

We are talking about a phlebovirus that inhabits the sub-Saharan strip, isolated in Kenya in 1930. It affects cattle, although its reservoir is unknown, and is transmitted to humans, in which it produces a febrile syndrome, which can lead to encephalitis, eye damage or Hemorrhagic fever, has a mortality rate of less than 1%. Epizootics usually coincide with the increase in rainfall in several geographical areas simultaneously, which suggests that mosquitoes could be their own reservoir, transmitting transovarially.

There is a vaccine for veterinary use to control this disease in cattle, although in 2000 two outbreaks appeared within the Arabian Peninsula.

4.7. Ebola virus

It is a Filovirus wrapped with a chain of RNA, which has four species: Zaire, Sudan, Reston, TaiForest and Bundibugyo. It is believed to be transmitted by direct contact through mucosa, skin wounds, or parenteral introduction. Viral load has been detected in body fluids, genital secretions, and on the skin of infected people. Initially, it produces a clinic that is difficult to differentiate from a common flu syndrome, but later it evolves with systemic involvement, digestive, respiratory, vascular and neurological symptoms. Laboratory tests are less characteristic, highlighting marked leukopenia (< 1000 cels/uL), hypertransaminasemia (AST $>$ ALT), hyperproteinemia, and proteinuria. It usually presents with increased prothrombin and partial thromboplastin times and fibrin degradation products, indicating disseminated intravascular coagulopathy.

Virulence is variable, with Zaire (60-90%) and Sudan (40-60%) having the highest mortality rates.

Despite not knowing well its life cycle, its natural reservoir, and its pathogenic spectrum, there are experimental vaccines, some of them in advanced experimental development.

In 2014 the WHO reports several thousand infections, half of which die in Guinea, Liberia and Sierra Leone.

4.8. Chikungunya virus

This virus is an alphavirus arbovirus, the vector of which is mainly *Aedes aegypti*. During the last year there has been a great epidemic on the island of Reunion, importing some cases to our environment. The clinic presents with high fever, headache and great joint pain and rarely causes death. It has been described in Africa, Southeast Asia, southern India and Pakistan, with outbreaks coinciding with the rainy season that favors the mosquito's life cycle.

4.9. Zika virus

Zika virus is a member of the Flaviviridae family transmitted mainly by different species of *Aedes*, and there is evidence of vertical, sexual and blood transmission. It was identified in Uganda in 1947 in macaques and in 1952 in humans. In 2013 there was an outbreak in French Polynesia and at the end of 2014 the virus spread rapidly through Latin America and the Caribbean, coinciding with an increase in neurological pathologies and neonatal malformations in that area [11].

Patients with Zika virus disease may present symptoms such as: mild fever, rash, conjunctivitis, muscle and joint pain, malaise or headaches, according to the WHO.

4.10. New coronavirus SARS-CoV-2

We are witnessing with alarm the large number of contagions and recent outbreaks that are taking place around the world by the new SARS-CoV-2, whose outbreak began in Wuhan (China) last December [4,12,13]. And currently witnessing numerous outbreaks or a second wave of infections that are increasing very quickly throughout the world.

The emergence of this unknown virus means that the first measures enforced were based on the existing scientific knowledge and the precautionary principle. The evolution in the number of infections produced by the virus is rapidly increasing and the joint effort of the world scientific community, is generating a large amount of knowledge that is constantly updated with new discoveries.

A rapid diagnosis of all cases of infection is essential to quickly identify, isolate and treat patients infected with SARS-CoV-2, in order to prevent the transmission of the virus and to be able to decongest hospitals, mainly intensive care units and hospital emergency services.

One of the main measures needed is to have rapid tests, with high sensitivity, available to all clinical laboratories in hospitals. These tests are, necessary to carry out the screening of all professionals who have been in contact with patients. [8]. The structure of the SARS-CoV-2 virus is shown in Figure 1.

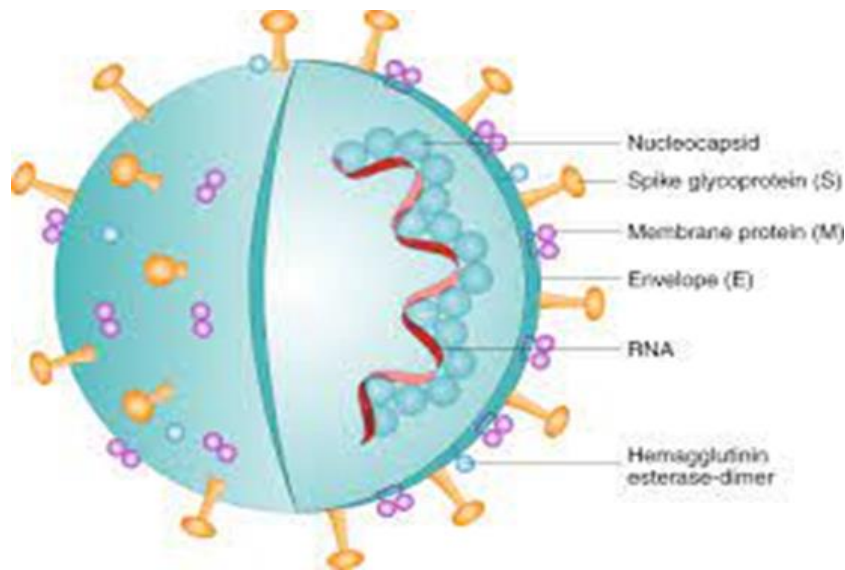


Figure 1 Structure of the new SARS-CoV-2 coronavirus (Source: 24)

The laboratory tests most currently used are tests based either on the detection of nucleic acids or on the antigen-antibody reaction (Ag-Ac), that detects antigens or antibodies (IgM and IgG) [14-16]. It now appears that the new coronavirus could have been in circulation for some time among humans without being detected, thus counteracting the theory that some argued about SARS-CoV-2 been created in a laboratory. A parent of the new virus may have jumped into humans after one of its mutations, before the pathogen was as contagious as in the current pandemic.

Since it is very possible that SARS-CoV-2 was between us more time than we thought, it could have been adapting until reaching the genomic characteristics of the new coronavirus. These adaptations, once acquired, could unleash the current aggressive potential of this virus [17], when direct contact with infected animals, or their secretions occurs.

In different studies with animal models with other coronaviruses, a tropism has been seen for the cells of different organs and systems, thus producing respiratory and gastrointestinal symptoms, which would indicate that the transmission from the animal to humans may be through respiratory secretions or by material from the digestive system [18].

Figure 2 shows the evolution of the different serological markers and the tests used [14-17].

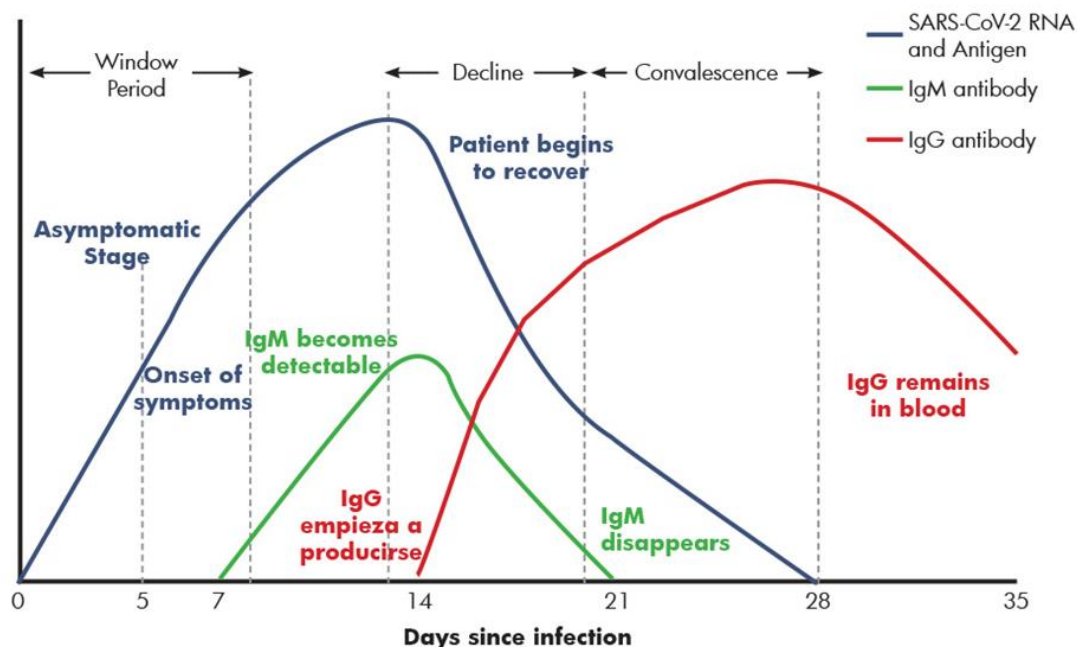


Figure 2 Evolution of the different SARS-CoV-2 serological markers and the different tests used according to the stage of the disease (X-axis, days since infection and Y-axis, exposure markers)

Currently, the coronavirus genome has already been sequenced by different researchers around the world [1,19]. In Spain, several autonomous communities have sequenced the complete genome of different strains of the SARS-CoV-2 virus from patients. This will allow comparing the sequences between different populations and countries to see how the virus has changed in the new variant of the Spanish coronavirus that is among us. The sequences are already accessible in the GISAID database, which is a public consortium dedicated to the study of influenza (<https://www.gisaid.org/>); the Nextstrain platform allows the spatial and temporal progression of the pandemic to be viewed from more than 500 genomes inserted by many countries (<https://nextstrain.org/>); also available in the Genbank database of genetic sequences from the NIH (National Institutes of Health of the United States) (<https://www.ncbi.nlm.nih.gov/genbank>).

The study of these genome analysis allows us to know the ways in which the virus has entered society and how it is currently transmitted, which will help control the spread of the virus in our country. This sequencing also allows us to know the mutations that the virus has suffered since the beginning of the epidemic. After studying the analysis carried out, no mutation associated with greater virulence or lethality or other factors with more clinical relevance, were found.

The available genomic information of the SARS-CoV-2 virus has been analyzed using bioinformatic applications, and it has been observed that the protein receptor binding domain of the virus (RBD), which is the protein that allows the virus to penetrate human cells, is so effective that its origin had to be a consequence of natural selection. In addition, mutations in protein S and the molecular structure of the virus, rules out that it could have been created in a laboratory.

These genomic characteristics of the virus have also been found to differ from those of other known coronaviruses, they are mostly similar to those found in bats and pangolins. Based on this theory, scientists claim that the natural selection of the coronavirus occurred in an animal host before it passed to humans, since the coronaviruses found in animals have a genome very similar to the one that infects humans.

Another theory is that natural selection occurred in humans, after the virus was transmitted between humans, after jumping from an animal host. Due to evolutionary changes over the years, it achieved ability to spread between people, and even cause serious illness [19-21].

5. Laboratory tests of SARS-CoV-2 Coronavirus

Detection of the presence, in patients, of nucleic acids from the virus by Polymerase Chain Reaction (PCR) is the most appropriate technique to use in diagnosis and, therefore, it should be considered as the reference technique because it allows the study of a large number of patients. Procedures can be automated and are much more sensitive and specific

than the rest of the available techniques. Also the presence of the virus is detected in nasopharyngeal samples from the beginning of the infection, in addition to other samples such as endotracheal aspirate, broncho aspirate and bronchoalveolar lavage [14-16].

Different kits of rapid PCR systems have also been commercialized, which allows for the rapid and correct diagnosis of patients in a very short time. Some kits already have the approval of the American FDA [14,15]. Studies show that the viral load in the nasal passages is higher than in the oropharynx and at the beginning of the infection the viral load varies between 104-108 copies of RNA/ml. This leads to think that the detection of SARS-CoV-2 antigens in this type of samples could have a good sensitivity if you have a strong antibody.

In the national and international market there are also kits or tests to detect IgM and IgG antibodies in serum, plasma or blood in the same test, using the immunochromatography technique. In a study by Li et al, they state that they present a sensitivity of 88.6% and a specificity of 90.6% [22]. Among the advantages these kits have is that serum, plasma and blood, from the puncture capillary, can be used. It could also complement the PCR studies when these are negative in patients with suggestive symptoms, or who no longer have a viral load, or when samples from the upper respiratory tract or, from the lower respiratory tract, cannot be obtained; In addition, immunochromatography assays usually produce results in just a few minutes. Among the disadvantages are the difficulty of using PCR or antigen detection tests that have a low sensitivity and specificity as a screening technique. A variable, or uncertain, dynamics of the IgM and IgG response throughout the infection causing a negative IgM and IgG result does not exclude for the patient to be infected, especially among patients who are immunosuppressed.

We are intensively working in different clinical trials with new pharmacological therapies, trying to apply different drugs used in other diseases and to get a vaccine [23].

6. Conclusion

We can say that most emerging viruses have the characteristic of presenting the RNA genome, in addition to being transmitted by vectors and affecting humans. Regarding its expansion, most of the processes that favor it have anthropogenic influence, which together with global warming with the increase in temperatures benefit the expansion of the vectors of these viruses.

In addition to human impact, many of these viruses infect livestock, causing significant monetary losses, which, added to the public health measures to be taken, negatively affect the economy of a country. For this reason, an effort should be made to integrate research in the human and veterinary health field.

Early detection and accurate identification of the infectious agent is important, since in an epidemic time is a key factor, which is why faster and more sensitive diagnostic tests are needed.

In relation to prevention, there should be an integration of epidemiological surveillance data that would help to act quickly and accurately. One of the main preventive actions to follow is vector control, for example using sentinel animals. Action plans in the event of the appearance of certain vectors should be established in advance, in order to avoid warning situations.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare that does not exist an interest conflict.

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