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Virus and its Identification in Modern Era

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ABSTRACT

While discoveries about viruses, which carry the largest genetic information code in nature, have continued unabated for more than a century, viruses are constantly affecting the global biological balance. The main characteristics that make viruses important in this balance include epidemics and mass deaths, the risks of being used as biological weapons, and the continued lack of an effective vaccine or specific treatment for many viruses. However, viruses also offer incredible opportunities for the scientific world, due to biotechnological innovations that have gained momentum in recent years. The detection of viruses is of urgent importance for the early detection of pandemics and epidemics. In this chapter, we discuss the classification of viruses, the effects of viruses on biological balance of our planet, the importance of detecting viruses that have the potential to be used as biological weapons or that carry epidemic or pandemic risks, and the characteristics of such viruses.

KEYWORDS: *virus, biotechnology, epidemic*

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INTRODUCTION

Viruses are non-living micro-organisms that are only able to replicate in living cells. However, a given virus cannot replicate or cause disease in all living organisms, because the replication of viruses is restricted by host and tissue tropism. Different types of virus infect different cellular organisms. Some viruses are able to infect fungi, plants, archaea, and bacteria, but these viruses do not cause infection or disease in humans. According to Current Taxonomy Release 2019, produced by the International Committee on Taxonomy of Viruses (ICTV), more than 6500 viruses have been identified at the species level. More than 300 of these viruses are associated with human infection, but not all viral infections result in disease. Viruses that cause disease are defined as pathogenic species, and the number of virus species that causes disease in humans is over 200. Pathogenic viruses that spread among humans and animals can cause serious mortality and morbidity, as well as significant economic burdens.

Viruses are important to humanity for a variety of reasons. Smallpox virus, Nipah virus, Lassa fever virus, Rift Valley fever virus, Crimean Congo hemorrhagic fever virus, Ebola virus, and Marburgvirus are important as biological warfare agents, while some viruses are critical, as they have pandemic potential (influenza viruses, coronaviruses).Congenital infections (such as cytomegalovirus, rubella, and parvovirus), childhood diarrheal diseases (rotavirus), recurrent or reactivated infections in cases of immunodeficiency (human cytomegalovirus, JC virus, BK virus, and Epstein-Barr virus), chronic diseases (the hepatitis B and C viruses, HIV), and viruses that lead to economic damage to agriculture and veterinary medicine (rabies virus, foot and mouth disease virus, influenza virus, and Newcastle disease virus) are further examples. Viruses are classified into two main groups, DNA and RNA viruses, based on their genetic structures [1]. RNA viruses usually cause transient infections and are cleared by the immune system, however, there are exceptions to this. Hepatitis C virus is an RNA virus that can be completely cleared from the body, but if left untreated, it can become permanent, because it can escape from the control of the immune system.

In the last 30 years, there have been significant changes in the epidemiology of viruses associated with human infections. While many viruses (such as the West Nile virus) have spread to regions where they had never been detected before, others have caused global concern after a long period of silence, such as the Zika virus. Apart from this, new viruses have emerged and caused regional and global epidemics, such as theMiddle East respiratory syndrome-related coronavirus (MERS-CoV) and severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2). Moreover, due to developments in molecular biology and genetics, it is also important to monitor the natural viruses and modified viruses that can be manipulated more easily and which have the potential to be used as biological warfare agents.

Viruses are mainly transmitted to humans through the respiratory tract, food and drink, skin, and blood. Some viruses are transmitted to humans by insects, such as mosquitoes and ticks, and mammals, such as cats, dogs, mice, bats, and birds. Since viruses are host-dependent micro-organisms, their distribution in geographic regions is directly related to their host distribution. Humans are the only hosts of some viruses in nature; such viruses, which do not have an animal reservoir, continue their existence by spreading among people. Cultural habits, nutritional and sanitation conditions, the frequency of risky behaviors, drug addiction, the proportion of the immune deficient population in a society, access to health services, vaccination programs, and other health policies are some of the social characteristics that define the boundaries of the epidemiology of these viruses. On the other hand, in the distribution of animal viruses associated with human infections (zoonotic viruses), the possibility of contact between humans and animals (for example, the intersection of the habitats of humans and reservoir animals) plays an important role in viral epidemiology. The effects of climate change on the circulation of migratory birds and arthropods such as mosquitoes, human movements that have accelerated with the increase in transportation facilities, and forced migration are other factors that determine the distribution boundaries of viral diversity in human populations.

Importance of virus detection:
Typical (pathognomonic) symptoms with diagnostic value can be seen in some viral infections. However, in most viral infections, the clinical findings are similar to those for multiple viruses, and sometimes infections can take place without any symptoms (asymptomatic). Therefore, precise diagnoses of viral infections are carried out using laboratory tests (figure 1.1). Viral infections can be diagnosed directly by methods such as the visualization of viruses, the detection of viral antigens, the isolation of a virus by replicating it in a cell culture medium, and by the observation of viral nucleic acids. Viral infections can also be identified indirectly by different methods, such as the detection of virus-specific antibodies, the examination of changes (such as inclusion bodies) in infected cells using light microscopy, and the indirect examination of growths in cell cultures. Laboratory tests are also used for different clinical purposes, such as monitoring the patient in some infections, investigating the presence of antiviral resistance, and distinguishing between primary and reactivated infections. The detection of viruses is also critically important in epidemic outbreak surveillance and other epidemiological and environmental analyses, phylogenetic studies, the screening of blood and blood products, veterinary studies, and tests for biosecurity breaches (due to the risk that a virus may be used as a biological weapon).

Figure: virus Detection

Nowadays, new molecular techniques that allow the detection of unknown microorganisms, specific cell lines, and chimeric cultures, animal models that increase the probability of isolation of viruses, and metagenomic-metaviromic studies have increased the number of known viruses and made it possible to monitor genomic variations and epidemiological changes in these viruses. The fast detection of pathogens, using methods that offer specific, sensitive, fast, and reproducible results, plays an important role in preventing the spread of viral infections and decreasing the pathologies (mortality and morbidity) associated with infection. Rapid identification of the presence of a virus in contaminated food or water, surfaces, or patient samples is a prerequisite for effectively preventing viral outbreaks, epidemics, and bioterrorism. As we have experienced in the SARS-CoV-2 pandemic, it is far from realistic for developed countries to isolate themselves from the rest of the world due to intense and rapid human movement. For these reasons, the development of easy-to-use, low-cost detection methods that require fewer complex devices and equipment in epidemic management and isolation-based public health policies is critical in the management of global epidemics.

Coronavirus:

Coronavirus The name coronavirus is derived from the Latin word 'corona,' meaning halo, which expresses the similarity of the characteristic appearance of the surface protrusions of the virus to the halo (solar corona) around the Sun. There are 46 virus species in five genera in the Coronaviridae family. Six of these species were known to be associated with human infection. In the last days of 2019, a new coronavirus identified as a pneumonia agent, which first appeared in Wuhan, China, spread rapidly among people, and the number of coronavirus species associated with human infection was updated to seven. Among these viruses, HCoV-229E (mid-1960), HCoV-OC43 (mid-1960), NL63 (in 2004), and HCoV-HKU1 (in 2005) are known to be seasonal coronaviruses that are common worldwide and which cause respiratory infections that are generally associated with mild symptoms in humans.

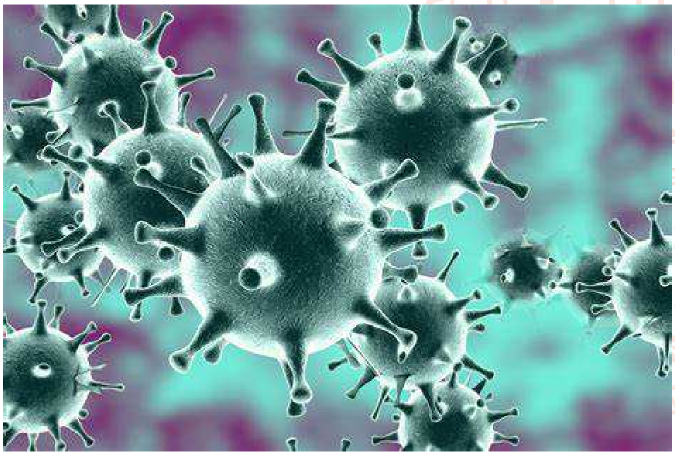

Figure: Corona- virus

The major transmission route of coronaviruses in humans, which is similar to those of other respiratory viruses, is through the inhalation of droplets containing infective viral particles produced when an infected person speaks, coughs, or sneezes. Although it is not a predominant transmission mode, touching the mouth, nose, or eyes (autoinoculation) after contact with virus-contaminated surfaces or fomites is also considered to be one of the possible transmission routes. The most effective way to prevent coronavirus infections, which exhibit similar transmission characteristics to those of other respiratory infections, includes standard measures taken to prevent droplet and aerosol transmission. Inactivated full-virus vaccines, messenger RNA (ribonucleic acid) vaccines, and vector-based vaccines developed within about a year of the onset of the SARS-CoV-2 epidemic have been administered to millions of people worldwide. Even if these vaccines do not prevent the transmission of infection, they are expected to prevent serious illnesses requiring hospitalization and SARS-CoV-2 related deaths and slow the spread of the epidemic. The protection period and protective effectiveness of vaccines in different populations are expected to be revealed in upcoming studies. Laboratory diagnosis of coronavirus infections is based on tests that aim to detect viral RNA using a PCR (polymerase chain reaction) and viral antigens or specific antibodies against the virus. Virus isolation is time-consuming; it is not used in routine diagnosis and also requires a biosafety level 3 (BSL-3) laboratory using BSL-3 practices. During the COVID-19 pandemic, it has been of great importance for the rapid and correct diagnosis of cases, for the detection and isolation of people with asymptomatic infections who can spread the infection, and to keep the pandemic under control. For this purpose, many biosensor-based methods have also been developed.

Human immunodeficiency virus:

There are ten different viruses in the Lentivirus genus of the Retroviridae family, and two of these viruses, human immunodeficiency virus 1 (HIV-1) and HIV-2, are associated with human infection.The disease known as acquired immunodeficiency syndrome (AIDS) was first reported in 1981 in the United States of America (USA) in a group of homosexual men with Pneumocystis jirovecii pneumonia and Kaposi's sarcoma. In 1982, some researchers from the CDC (Centers for Disease Control and Prevention) described similar cases in injected-drug users, sex workers, and people using blood and blood products. As a result of subsequent studies, the HIV-1 and HIV-2 viruses were found to be infectious agents for AIDS in 1983 and 1986, respectively. HIV-1 accounts for the vast majority of human lentivirus-originated disease worldwide. HIV-2, whose genetic composition and disease symptoms are very similar to HIV-1, is endemic in West Africa and is seen in the USA, albeit at low rates. Within days or weeks following exposure to HIV, a disease picture that is defined as primary HIV infection (acute viral syndrome) and which usually presents acute flu-like symptoms occurs in most infected individuals. AIDS patients typically show signs of a selective decrease in the CD4+ helper-T lymphocytes in their peripheral blood samples and immune system failure, which is due to this decrease. After acute infection, due to the establishment of a balance between viral replication and host immune response, a latency period begins, during which clinical symptoms are not seen for many years in most infected individuals. However, the phrase 'latency period' can be misleading, given the very high rate of virus replication and the high daily production–destruction rate of CD4+ T-cells. Because this process causes a gradual decrease in CD4+ T-cells, albeit slowly, when the CD4+ T-cell ratio falls below 200 μL−1, many AIDS defining diseases, including various opportunistic infections and some cancers, are seen, and the process results in death in untreated cases.

Although an effective treatment exists today, these high mortality rates seem to be related to the inability to control the infection in regions where the majority of infected individuals have limited access to treatment. All these data highlight that HIV is one of the most important viral infections that has affected humanity in the last 40 years. HIV infection is transmitted mainly by unprotected sexual intercourse with an infected partner, the injection or transfusion of contaminated blood or blood products, infertility treatment practices, skin grafting, organ transplantation, the sharing of non-sterile injection equipment previously used by an infected person, and mother-to-baby transmission (during pregnancy, birth, and breastfeeding).

A preventive vaccine has not yet been developed for HIV infection. To reduce the effects of infection and to control or eliminate HIV-1 reservoirs, there is increasing interest in the use of agents that activate the latent virus, therapeutic vaccines, widely neutralizing monoclonal antibodies, gene therapy, and a variety of other pharmacological and immunological approaches.

Many different tests can be used to diagnose acute HIV-1 infection. Laboratory diagnosis of HIV infection is based on the detection of virus and virus components including viral deoxyribonucleic acid (DNA), RNA, and antigens, as well as antibodies against the viral antigens in the blood. The diagnosis of acute infection is based on the detection of HIV-1 replication by molecular methods in the absence of HIV-1 antibodies (as they are not yet present in the early stages of infection).

Hepatitis:

During many viral infections, liver tissue can be directly or indirectly affected, and hepatitis may develop. However, the definition of hepatitis viruses is used to refer to viruses that show tropism directly to the liver: the hepatitis A virus (Hepatovirus A), the hepatitis B virus, the hepatitis C virus (Hepacivirus C), the hepatitis D virus (of the hepatitis genus Deltavirus), and the hepatitis E virus (Orthohepevirus A). Each of these viruses is classified as belonging to a different family, and they are RNA viruses except for the hepatitis B virus, whose genome structure is DNA. Among these viruses, hepatitis B and C viruses can cause chronic infection, liver disease, cirrhosis, and even hepatocellular carcinoma (HCC) in the long term. Chronic hepatitis B and C infections are the most important causes of HCC, and these two viruses constitute the majority of cases (80%) worldwide.

Although hepatitis A, B, C, D, and E viruses all cause liver disease, they differ in important ways, such as their transmission patterns, the severity of the disease, geographic distribution, and prevention. While hepatitis A and hepatitis E viruses are common in countries with poor sanitation conditions in the world, hepatitis B and C are seen all over the world, being more common in some parts of Africa, Asia, and South America. It is estimated that 325 million people worldwide are living with hepatitis B and/or C, and that most are without access to diagnosis and treatment. Hepatitis A and E viruses are mainly transmitted by the fecal–oral route, while the hepatitis B, C, and D viruses are mainly transmitted by the parenteral route. For the hepatitis B virus, perinatal transmission and horizontal transmission (exposure to infected blood) are important transmission routes, while needle stick injury, exposure to infected blood and body fluids, and sexual transmission are other transmission routes. The hepatitis C virus, on the other hand, spreads via blood and injected-drug use through the sharing of injection equipment. While there is a preventive vaccine for hepatitis A, B, and E (the hepatitis E vaccine is used in China), a preventive vaccine has not yet been developed for the hepatitis C virus. Although powerful treatment protocols have been developed and are in use for the hepatitis B and C viruses, which are associated with chronic diseases, access to treatment is easier in developed countries, but a large proportion of infected people is deprived of access to treatment.

Ebola:

There are six genera and 11 species in the Filoviridae family; one species in the Marburgvirus genus in this family (Marburg marburgvirus) and four species in the Ebolavirus genus are associated with human infection. The Ebolavirus species isolated on the African continent, namely, the Bundibugyo Ebola virus, the Sudan Ebola virus, and the Zaire Ebola virus cause outbreaks with high mortality in humans, but Taï Forest Ebola virus infections are rare. Although there are serological data on human infections for Reston Ebola virus, another species first isolated in macaques in the Philippines, human–human transmission has not been demonstrated. Ebola virus disease (EVD) is an acute severe illness with a high mortality rate caused by pathogenic Ebola virus strains. The mortality rate has ranged from 25% to 90% in various outbreaks of the disease over 40 years. The Ebola virus was first identified in 1976 in Zaire (now the Democratic Republic of the Congo (DRC)) and South Sudan during two concurrent outbreaks. In these epidemics, a total of 602 people were infected with Ebola virus and the mortality rate was found to be 71.59%. On March 23, 2014, the West African epidemic broke out, which represented the first global threat posed by Ebola virus. A few months later, the World Health Organization (WHO) stated that this epidemic was an international 'public health emergency.' In the biggest Ebola virus outbreak, 28603 EVD cases were reported with a mortality rate of 39.5%. Although Ebola virus infections are only common in West Africa, the virus is classified as a category A pathogen that could be abused as a bioterrorism agent due to its potential to spread globally. Ebola virus infections can be transmitted in the following ways: via the contact of infected organisms with tissue, blood, and other body fluids, via contaminated materials or medical devices, and during unhygienic practices (such as cutting up a chimpanzee for food or traditional burial practices). The Ebola virus is classified at level 4 in the biosafety risk group; when working with it in the laboratory, facilities and equipment that provide the highest level of biosecurity are required. The laboratory diagnosis of Ebola virus can be accomplished by examining blood, body fluids, and other clinical specimens from animals and humans. Enzyme-linked immunosorbent (ELISA) tests, antigen detection tests, serum neutralization tests, and reverse-transcription PCR can be used to examine these samples. IgM and IgG antibodies can be measured using immunofluorescence antibody (IFA), or immunoassay-based tests.

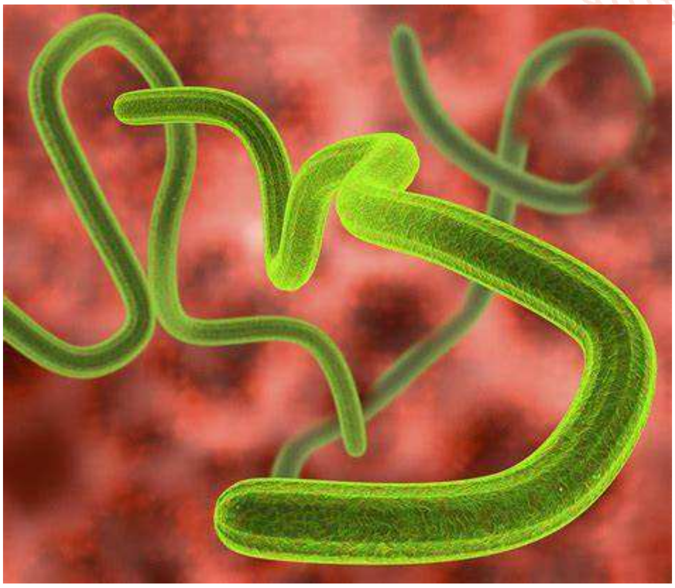

Figure: E-bola virus

Zika

Zika virus is one of the 53 different species of the Flaviviridae family in the Flavivirusgenus. It was first discovered in the Zika forest (Kampala, Uganda) in 1947.The majority of Zika virus infections have a subclinical course, but some patients may experience clinical symptoms similar to those of other arboviral infections. Eighty percent of infected people are asymptomatic. The disease symptoms are usually mild and are characterized by the acute onset of mild fever, maculopapularrash, arthralgia, and non-purulent conjunctivitis. Until 2015, no deaths were attributed to Zika virus infections. Three deaths attributed to the Zika virus were first reported in Brazil, including the death of a newborn with microcephaly, on 28November 2015. Also, various neurological (Guillain Barré syndrome, meningoencephalitis) and autoimmune (thrombocytopenic purpura, leukopenia) complications have been reported in Zika-virus-infected people. While the Zika virushas attracted great attention in recent years due to the epidemics it causes and it spossible relationship with serious autoimmune–neurological diseases, it was identified as an urgent public health problem of international importance by the WHO in February 2016.

Norovirus

Norwalk virus, the only species in the Norovirus genus, is a non-enveloped, positive sense RNA virus classified as being in the Caliciviridae family. Another species associated with human infection in the Caliciviridae family is the Sapporo virus, theonly species in the Sapovirus genus. Both viruses generally induce self-limiting gastroenteritis. Long-term illness is seen in immunocom promised individuals. Vomiting is a consistent and remarkable symptom; other symptoms may include nausea, diarrhea, abdominal cramping, fever, and malaise. Norwalk virus causes a brief but unpleasant illness, also known as stomach flu, viral gastroenteritis, and winter vomiting.

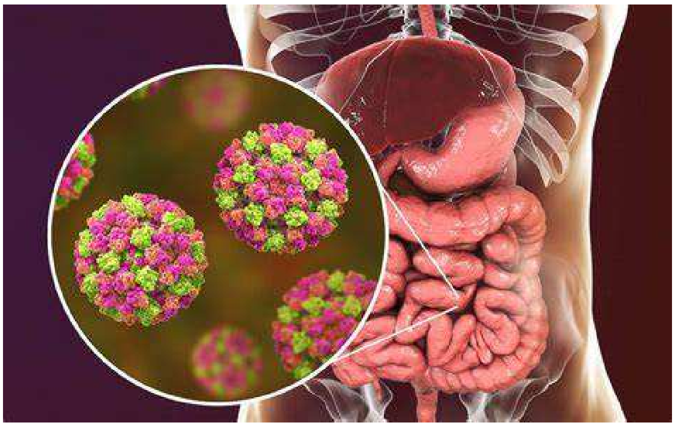

Figure: E-bola virus

Influenza

Viruses in the Orthomyxoviridae family are enveloped and have single-stranded segmented RNA genomes. This family includes viruses that can be transmitted by respiration, direct contact, water, or ticks. Orthomyxoviruses can cause infection in humans, birds, many mammal species, and fish. The most medically important viruses in this family are the influenza virus species. These viruses (influenza viruses A, B, and C) are associated with respiratory tract infections that can lead to serious clinical consequences in humans. Influenza viruses canlead to seasonal epidemics and sometimes pandemics (influenza A). Throughout history, influenza A pandemics have been blamed for the deaths of tens of millions of people. Birds are the main reservoir of influenza A viruses, and humans and many animal species (such as pigs, horses, seals, whales, and mink) are affected by the virus. Very virulent or pandemic reassortant strains may arise when influenza A viruses that cause infections in different species cross the species barrier. Seasonal influenza is an acute respiratory infection caused by influenza viruses circulating around the world. There are four types of seasonal influenza virus: influenza viruses A, B, C, and D. Influenza A and B viruses circulate around the world and are associated with seasonal epidemic diseases. Some influenza A viruses can cause a pandemic, usually at intervals of 20–30 years. An influenza virus pandemic occurs when a new strain circulates among humans, since most people are not immune to this new virus.

Discussion:

The early and rapid identification of viruses that are emerging, have epidemic potential, cause permanent damage, or pose a biosecurity risk is critical. These risks are increasing day by day. It is estimated that 60%–80% of newly emerging or re-emerging viruses are zoonotic (animal-borne) viruses. Any event that increases the likelihood of zoonotic viruses being transmitted to humans plays a role in the spread of these infections. The coexistence of different animal species in wet markets and the increase in the frequency of contact with them, the establishment of settlements in the habitats of animals, the increase in the frequency of working with different animal species in laboratories (by which we do not mean biological warfare studies but strictly normal scientific studies), climate change (mosquito movements) and the large increase in the international mobility of people (transport by plane, tourism, international sports events, commercial activities, and educational travel) are the most important reasons. However, viruses can also be useful tools.

Conclusion:

Viruses can be used as vectors for therapeutic purposes and in vaccine studies, to combat other viruses or bacterial infections resistant to antibiotics, such as bacteriophages. Viruses can function like a small hand with which we can touch cells at the electron-microscope scale if used for good purposes; conversely, they have been used maliciously in the past by people who want to destroy humanity and are likely to be so used in the future. In the future, viral engineering studies may need to be subjected to worldwide inspection for reasons of of national and global security.

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