

THE STRUCTURE OF VIRUSES AND VIRUS TYPES THAT AFFECT HUMANS

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Abstract: From the Latin, the word virus means poison and "infectious disease agent", before Dmitri Ivanovsky discovered viruses in 1892, was first recorded in 1728. The debate on whether viruses are alive or not is still running and since viruses are found wherever life exists, it is thought that viruses have been present ever since living cells first developed. Viruses can exist as virions and independent viral particles in the infected cell or in the process of infection. Virion, a single virus particle that contains all the structures of a virus, consists of two or three parts; a viral genome, which may be either DNA or RNA and large molecules carrying genetic material, a protein layer called capsid that surrounds and protects genetic material and a lipid envelope surrounding the protein layer. In this study, the sections that compose the structures of viruses were generally examined and types of viruses that derive from different sources, have different genetic structure and affect people were discussed.

Keywords: Disease, pandemic, epidemic, DNA virus, RNA virus, virion

Introduction

Almost every ecosystem in the world contains viruses. Viruses exist in a form called virion (represents a whole virus particle with a nucleic acid (RNA or DNA) inside its core structure that has a protein shell). It is roughly one hundredth the size of a bacteria and consists of two or three parts.

The parts that make up a virus are briefly explained below.

***Genetic material (DNA or RNA);** This is the nucleic acid (RNA or DNA), the most important part of the virus. Nucleic acid, acting as a preservative, cooperates with one or more viral polypeptides that are in the form of a protective sheath (shell) to form a helical nucleoprotein complex or that are in close communication with the nucleic acid (NA). Nucleic acid/protein or protein/protein interactions play an important role in the morphology (origin and development of structural characteristics) of viruses. These interactions determine whether the nucleoprotein complex structure, an arrangement of nucleosomes or an icosahedral shell.

***Protein protecting genetic material, capsid;** This is the outermost protein sheath surrounding the nucleic acid or nucleoprotein complex. Capsids generally have a cubic symmetry (mostly icosahedral) however, there are also ones with cylindrical form. Morphological units, in other words building blocks, that form the capsid, are called **capsomeres**. These capsomers are arranged in different ways in different viruses, and these sequences form the symmetrical structures of viruses. The shape of the virus depends on this structure. **Nucleocapsid (NC);** this is a nucleic acid containing a protective protein shell complex, which can be of icosahedral, helical or complex symmetry.

***In some viruses, there are enveloped lipids,** on the protein on the outer surface of the virus. They usually occur by budding from the host cell membrane. Some viruses bud through special parts of the plasma membrane of the host cell, e.g. The Ebola virus is associated with sphingomyelin, cholesterol and glycoprotein-rich lipid stack. The Pox virus is a rare virus budding with a mechanism different from the mechanism used by other viruses (Crosta, 2020).

***Envelope or virus membrane** are lipid bilayer with glycoprotein projections (spikes, knobs, etc.) called **peplomer**. The membrane (envelope) of some viruses such as *Coronaviridae* also contain an extra protein (Nermut, 1987). Enveloped viruses are able to bud outside without having to kill the host cell, which is why they can cause

permanent infection. If the enveloped virus is not corrupted it can easily be transmitted (due to the viral envelope of the host cell receptor recognizing the protein fragment) (Hunt, 2003).

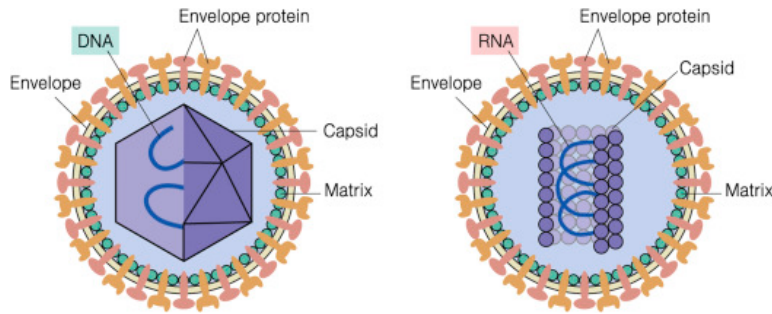


Figure 1. The parts of a virion, which is a whole virus particle (Ryu, 2017).

If viruses are similar to pavoviruses as diameter, it can vary from 20 nanometers to hundreds of nanometers (in case of filovirus) (Hunt, 2003).

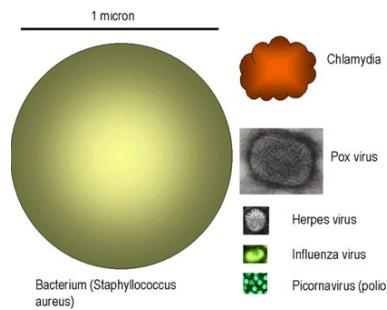


Figure 2. *Staphylococcus aureus* bacteria and relative sizes of some viruses (Hunt, 2003).

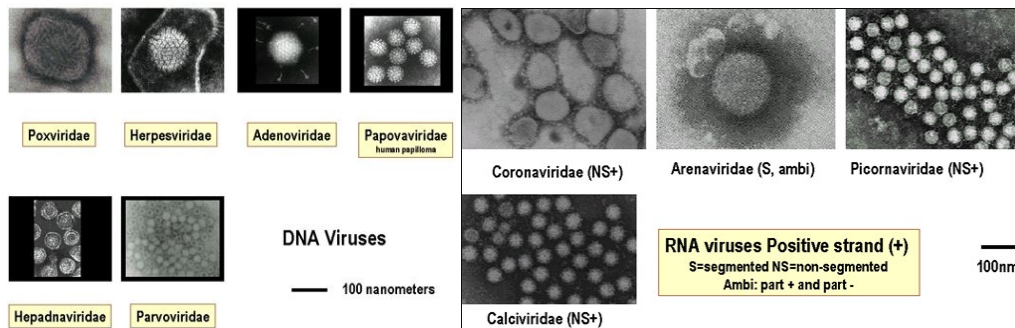


Figure 3. Relative sizes of some DNA viruses (left), relative sizes of some RNA viruses (right) (Hunt, 2003).

Viruses do not possess ribosome. Thus, they do not produce protein. This makes them completely dependent on the host cell. In other words, they are the only microorganisms that cannot reproduce without the host cell. After they get into contact with the host cell, the virus sends its genetic material into this host cell, through which it seizes the functions of the cell and takes over its management. After capturing the cell, the virus starts copying itself and starts producing more viral protein genetic material (Crosta, 2020).

Classification of Viruses according to the Symmetric Structure created by Capsids

Viruses can be of different sizes and shapes. They can be classified according to nucleic acid type, size and morphology, additional structures such as envelopes and tail and type of cell it infects (animal, plant, human) According to the symmetrical structure of their capsids, viruses are categorized as follows.

- Icosahedral symmetry viruses
- Helical symmetry viruses
- Complex symmetry viruses

Icosahedral symmetry viruses

They are also called viruses with cubic symmetry. The icosahedral symmetry structure has 12 corners and 30 edges, which is formed by the combination of capsomers arranged in 20 equilateral triangles. An icosahedron has two, three and five rotational symmetrical axes passing through the edges, surfaces and corners of the icosahedron, respectively (Burrell et al., 2017).

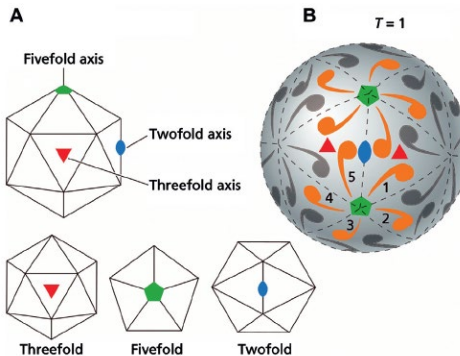


Figure 4. Schematic view of the icosahedral symmetry structure (Burrell et al., 2017).

Helical symmetry viruses

The nucleocapsid of most RNA viruses is in a cylindrical structure, in which the protein structures are arranged in a helix, hence they are called viruses with helical symmetries. The plurality of identical protein-protein interfaces on structural units supports the symmetrical structure of the helix. In a helical symmetrical nucleocapsid, the RNA genome forms a helix together with the nucleocapsid. Most of plant viruses with helical nucleocapsid are rod-shaped and do not have an envelope. The helical structure of tobacco mosaic virus is among the first viral structure determined by electron microscopy. Later, its detailed structure was revealed by X-ray crystallography. In addition, in all vertebrate viruses with helical symmetry, the nucleocapsid is wrapped in a secondary coil and wrapped with a lipoprotein envelope. Examples for this are rhabdoviridae and paramyxoviruses (Burrell et al., 2017).

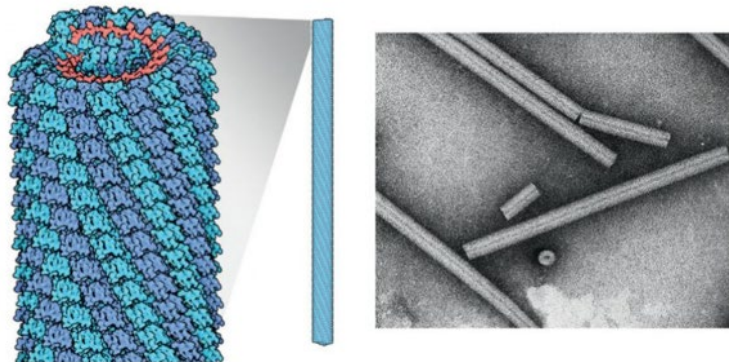


Figure 5. Tobacco mosaic virus model with helical symmetry (left), electron microscope image of tobacco mosaic virus particle (right) (Burrell et al., 2017).

Complex symmetry viruses

Some viruses do not have a specific symmetry structure. These have more complex and different capsid structures. Tubular elements are found on the surfaces of such viruses. For example, in poxviruses the viral genome with DNA character is located in the middle and shows a biconcave localization. In addition, lateral bodies are found in the central parts (orthopoxviruses). Parapoxviruses have diagonal structures on their surface. A lipid-rich envelope surrounds the poxviruses (Arda, 2020).

Some diseases caused by viruses in humans are smallpox, the common cold and the flu, measles, rubella, mumps, zoster, hepatitis, herpes, polio (infantile paralysis), rabies, ebola and hemorrhagic fever, AIDS and SARS.

Some Types of Viruses Deriving from Various Sources and Affecting Humans

Some types of viruses deriving from various sources and affecting humans are explained below.

Influenza (Flu) Virus

Influenza viruses are characterized by segmented negative chain RNA genomes that require an RNA polymerase bound to viral origin RNA for replication. There are 4 types of influenza viruses; A, B, C and D. Human influenza viruses (A and B) cause seasonal diseases every year. The influenza A viruses is the only known flu virus to cause global outbreaks of flu disease. When a new and different influenza A virus emerges, it will not only be able to infect people but also spread among people causing a pandemic. Influenza C viruses generally cause mild diseases and it is thought that they do not cause flu epidemics. Influenza D viruses mostly affect cattle and it is not known to infect or cause disease in humans (Centers for Disease Control and Prevention, 2020a).

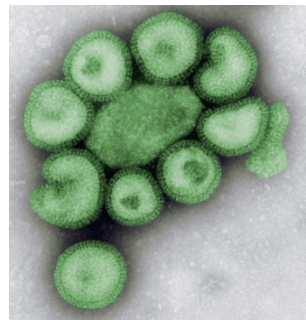


Figure 6. Microscopic image of influenza A virus (Burrell et al., 2017).

Variola virus (Smallpox virus)

The origin of smallpox, one of humanity's biggest threats, is not known, which creates a concern for the scientific community. Smallpox is caused by the variola virus (VARV) of the genus orthopoxvirus. In the last century it had been declared that humanity had overcome smallpox and that this disease is in fact beatable. However, the structure of the mechanisms responsible for the emergence of dangerous pathogens has not been fully resolved. Evolutionary analysis of molecular genomic data of various orthopoxviruses containing a wide range of epidemiological and historical information about smallpox, had made it possible to date the emergence of VARV. Comparison of the VARV genome with genomes of the most closely related orthopoxviruses showed that VARV emerged 3000 to 4000 years ago in the East of the African continent. Camels' entry into Africa and simultaneous changes in climate are possible main factors for triggering different evolutions of an ancestor virus and thus the emergence of VARV (Babkina and Babkin, 2015).

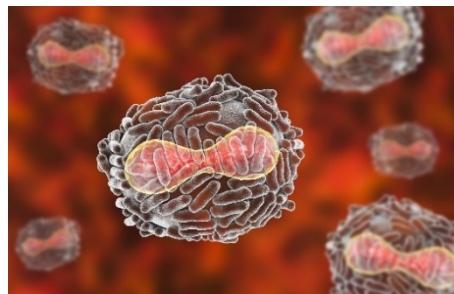


Figure 7. Variola (smallpox) virus (Bryner, 2020).

HIV (Human Immunodeficiency Virus)

The first AIDS (Acquired Immune Deficiency Syndrome) cases were reported in the spring of 1981 in the United States of America. The virus was first isolated in 1983 and in 1984 it was found to be linked to AIDS. The second HIV virus emerged in West Africa. Therefore, the viruses were named HIV-1 and HIV-2, respectively. The HIV-1

and HIV-2 viruses belong to the *Retroviridae* family and the *Orthoretrovirinae* subfamily. *Retroviridae* are enveloped RNA viruses. They copy their genomes from RNA to DNA with enzyme reverse transcriptase, which is then integrated into the host cell genome with an integrase enzyme. Thus, they become part of the cellular DNA and they start replicating themselves. HIV-1 and HIV-2 are two known human retroviruses belonging to the Lentivirus genome (IARC Working Group on the Evaluation of Carcinogenic Risk to Humans, 2012).

HIV is a virus that spreads through certain body fluids and attacks the body's immune system, especially the CD4 cells called T cells. HIV destroys most of these cells, which makes the body incapable to fight against infections and diseases. These special T cells help the immune system fight against infections. If not treated, HIV will reduce the number of CD4 (T cells) in the body. This damage to the immune system makes it difficult for the body to fight against infections and some other diseases. Infections or cancers take advantage of this situation and benefit from the weak immune system, leading to the person getting AIDS (Acquired Immune Deficiency Syndrome). Unlike some other viruses, humans cannot fully recover from HIV, even when treated. In other words, HIV will last a lifetime once infected (Centers for Disease Control and Prevention, 2020b).

Hepatitis Viruses

Viral hepatitis has emerged as a major public health problem throughout the world affecting several hundreds of millions of people. Viral hepatitis is a cause of considerable morbidity and mortality in the human population, both from acute infection and chronic sequelae which include, in the case of hepatitis B, C and D, chronic active hepatitis and cirrhosis. Hepatocellular carcinoma which is one of the ten most common cancers worldwide, is closely associated with hepatitis B, and at least in some regions of the world with hepatitis C virus.

Hepatitis A (HAV); The Hepatitis A virus (HAV), classified as Hepatovirus, is a small, unenveloped, symmetrical RNA virus with many features of the picornavirus family, caused by an orally transmitted infection or epidemic. Humans generally get infected by Hepatitis A virus from eating or drinking something contaminated with the virus.

Hepatitis B (HBV); Hepatitis B virus, a member of the Hepadnavirus family, is a double chain DNA virus that reproduces by reverse transcription. Hepatitis B virus is endemic in the human population and hyperendemic in many parts of the world. It is known that this virus has several variants. Natural hepadnavirus infections are also seen in other mammals, wood beetles, beech squirrels and also ducks. It spreads through body fluids of an infected person.

Hepatitis C (HCV); Although it is not transmitted by arthropod vectors, it is a coiled single chain RNA virus that is remotely related to flaviviruses. The infection of this virus is very common in many countries. Hepatitis C virus is related to chronic liver disease and primary liver cancer in some countries. The Hepatitis C virus does only spread through contact with blood.

Hepatitis D (HDV); This is a rarely seen, single-stranded round RNA virus. This virus needs the auxiliary functions of the hepadnavirus to reproduce in hepatocytes and is an important cause of acute and severe chronic liver damage in many parts of the world (Zuckerman, 1993).

Swine Flu Virus

H1N1 influenza virus is an orthomyxovirus and a enveloped virion with a diameter of 80 to 120 with a 13.5 kb RNA genome.

H1N1 swine flu is a subtype of influenza A virus (an infectious viral disease) and causes upper and lower respiratory tract infections in the infected host with symptoms such as runny nose, chills, fever and decreased appetite. H1N1 swine flu is a common infection in pigs worldwide, which is why it is known as swine flu. H1N1 swine flu causes respiratory diseases that can potentially infect the pig's respiratory tract. Sometimes people who closely work with pigs or are near them can get infected with swine flu and swine flu viruses can potentially cause infections in humans.

In 1918 the deadly flu epidemic caused by H1N1 influenza virus, also known as Spanish flu, infected 500 million people worldwide and caused the death of approximately 50 to 100 million people (3% 5% of the world's population). It has gone down in history as one of the deadliest disease outbreaks in human history worldwide. In 2009 a new type of H1N1 swine flu rapidly spread amongst humans and the World Health Organization (WHO) classified this as an epidemic (Jilani et al., 2018).

In the spring of 2009 scientists reported that there is a flu virus called H1N1. This virus is actually a combination of viruses coming from pigs, birds and humans. During the flu season of 2009-2010, H1N1 caused respiratory infection, commonly referred to as swine flu, in humans. Since most of the people got sick that year, the World Health Organization declared the flu caused by H1N1 as a global epidemic (Mayo Clinic, 2020).

As of August 2010, 73 cases of symptomatic human SIV infections have been documented in the medical literature (except 2009 pandemic H1N1 influenza virus case) and 10% of these cases resulted in death. While contact with pigs is generally considered a risk factor for human SIV infections, it was reported that 37 (51%) of the 73 cases did not have any known contact to pigs. As a result, it is thought that SIV is likely to be transmitted to people through transmission routes that are not yet known (Krueger and Gray, 2013).

In 2010 scientists started to change the names of the viruses. H1N1 virus is now known as H1N1v. The letter V represents the variant of the virus and shows that it normally occurs in animals but has also been detected in humans. Since 2011, H3N2v has been circulating in humans, causing flu (Mayo Clinic, 2020).

Avian Influenza Virus

Avian influenza refers to the infection of birds with avian influenza type A viruses. These viruses are naturally found worldwide amongst wild aquatic birds and can affect domestic poultry and other bird and animal species. Wild aquatic birds can be infected with avian influenza A viruses in their intestines and respiratory tract, but usually do not get sick. However, avian influenza A viruses are very contagious among birds and some of these viruses can sicken and even kill certain domesticated bird species including chickens, ducks, and turkeys. Avian influenza viruses can be found in the saliva, nasal secretions and feces of infected birds. Some susceptible birds get infected when they get in contact with other infected birds. They can also get infected by getting into contact with virus-contaminated surfaces. Avian influenza A viruses are classified in two categories: low pathogenic avian influenza (LPAI) A viruses and highly pathogenic avian influenza (HPAI) A viruses. These categories refer to the molecular properties of the virus and the virus's ability to cause disease and death in chickens in a laboratory setting. The infection of poultry with LPAI viruses causes almost no disease or only mild diseases (such as a decrease in egg production). The infection of birds with HPAI viruses can cause serious diseases with high mortality rates. Both HPAI and LPAI viruses can rapidly spread amongst poultry. However, it can also be transmitted to ducks without any signs of disease (Centers for Disease Control and Prevention, 2020c).

Even though avian influenza A viruses generally do not affect humans, there are some rare cases of infection. Infected birds spread the disease through saliva, mucosa and feces. Avian influenza viruses can infect people when it gets into the person's eyes, nose or mouth or when it is inhaled. This can happen when the virus is in the air (droplets or possibly dust) and when a person inhales it or touches their mouth, eyes, or nose after getting into contact with a virus-infected surface. The incidence of avian influenza A viruses spreading from one patient to another has rarely been reported. However, due to the avian influenza viruses gaining the ability to easily spread among people, monitoring human infection and person-to-person transmission has become extremely important for public health (Centers for Disease Control and Prevention, 2020c).

MERS-CoV

Middle East Respiratory Syndrome Coronavirus (MERS-CoV) derived from a 60-year-old Saudi patient who applied to a private hospital in the western part of the Kingdom of Saudi Arabia in 2012. Later, MERS-CoV caused many cases, multiple domestic contamination and major outbreaks in healthcare settings. Of all the cases reported within the Kingdom of Saudi Arabia, 38% of the cases were primary, 45% were healthcare-associated infection, and 14% were household infections. The clinical spectrum of MERS-CoV infection consists of asymptomatic infections, mild or moderate symptomatic cases, serious diseases requiring intensive care and fatal cases (Al-Tawfiq and Memish, 2016).

MERS-CoV was transmitted from desert camels to humans and from there from human to human. Current epidemiological evidence shows that direct contact with live camels or people with symptomatic MERS plays a huge role in the transmission of the virus (Killerby et al., 2020).

MERS-CoV is a coronavirus originally called HCoV-EMC. The virus was later renamed to MERS-CoV with global unanimous vote. Coronaviruses are common viruses amongst humans causing mild or moderate upper respiratory tract diseases. Human coronaviruses are enveloped RNA viruses and were first defined in the mid-1960s. There are

four virus clusters in the *Coronavirinae* subfamily. These are: alpha coronavirus, beta coronavirus and gamma coronavirus. The fourth cluster, delta coronavirus, is a temporarily assigned new group. All known human coronaviruses belong to the alpha coronavirus (HCoV-229E and HCoV-NL63) and beta coronavirus (HCoV-OC43, HCoV-HKU1 and SARS-CoV) type (Killerby et al., 2020).

SARS-CoV-2

This virus emerged in December 2019 in the province Wuhan of China. This virus (2019-nCoV), officially called “Severe Acute Respiratory Syndrome” (SARS) causes Covid - 19 disease with the associated Coronavirus 2 (SARS-CoV-2). Amongst people it is known as Coronavirus. The name Coronavirus comes from the Latin word meaning crown or halo and is related to the characteristic view of virions (infective form of the virus) under the electron microscope (Pal et al., 2020).

Coronaviruses are enveloped, 120- to 160- nm particles that contain an unsegmented genome of single-stranded positive-sense RNA (27–32 kb), the largest genome among RNA viruses. They are the biggest amongst RNA viruses. RNAs are infectious. The spiral nucleocapsid (the nucleus of the virus, consisting of nucleic acid surrounded by a protein envelope) is 9-11 inches in diameter. The envelope has widely spaced 20 nm long petal-shaped protrusions on the outer surface. The viral structural proteins include a 50–60 kDa phosphorylated **nucleocapsid (N) protein**, a 20–35 kDa **membrane (M) glycoprotein** that serves as a matrix protein embedded in the envelope lipid bilayer and interacting with the nucleocapsid, and the spike (S; 180–220 kDa) glycoprotein that makes up the petal-shaped peplomers. Spike glycoprotein is the virus’s receptor. It is the part that binds to any cell and is referred to as angiotensin-converting enzyme 2 (ACE2) in the literature. It is also known as the receptor of the SARS-nCoV virus (Riedel et al., 2016).

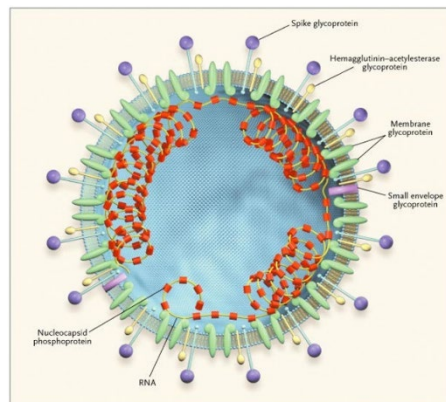


Figure 8. Structure of SARS-CoV-2 virus (İstanbul Üniversitesi, 2020)

More simply, it is a membrane-surrounded particle containing pointed proteins, in addition to the genetic material (RNA). Its structure resembles a crown, hence the name. There are different types of coronavirus according to the affected region (respiratory or digestive system). They can cause mild symptoms, such as the common cold. However, some types of coronaviruses can cause diseases that cause severe symptoms such as SARS-CoV emerging in China in 2003 or MERS-CoV emerging in the Middle East (Saudi Arabia) in 2012. The coronavirus that caused lung inflammation in China in 2019 was named (SARS-CoV-2). It is known that many coronaviruses are present in many animal species. In some cases, these viruses can spread from animals to humans (İnal, 2016).

The Journey of the Coronavirus in the Body

The main reason for the spreading of the coronavirus is coughing or contact with body fluids that occurs when the person touches his or her face after touching a contaminated surface. The journey of the virus begins here and continues deep into the body (Prompetchara et al., 2020).

The target is the lungs, the spleen and the intestines, where it creates the most severe effect. The lungs are surrounded by billions of epithelial cells. These cells are boundary cells that align organs and mucosa in the body. Thus, these are infected first. The coronavirus binds to a specific receptor in these cells to inject its genetic material (RNA).

The virus will then continuously copy itself without the cell knowing it. It continues to fill the cell with copies of the original virus until it reaches the critical point. After reaching said critical point it will destroy itself. The cell melts and releases the new coronaviruses, which are ready to attack more cells. Thus, the number of infected cells increases. After approximately 10 days millions of body cells become infected and billions of viruses will spread around the lungs. Immune system cells will come to the lungs to fight against the virus but the coronavirus will infect some of these cells, creating chaos. (Cells communicate with the help of small communication proteins called cytokines.) The coronavirus causes the immune cells that it infected to overreact and cause them to kill whatever comes their way. In this case the immune system sends more cells than needed to fight the virus, causing it to waste resources and ensuring environmental damage. There are two cells causing the chaos. Neutrophils and T cells (Li et al., 2020).

Neutrophils kill everything, including our cells. The neutrophil cells, which are sent into the turmoil, start secreting lethal enzymes. T cells however, tell other cells to commit suicide in a controlled manner. Cells receiving this order tell healthy cells to also kill themselves. So, the more immune cells come in, the more damage they can cause and the healthier lung cells get killed. This may lead to permanent, irreversible damages. In some cases, the immune system takes control over the situation by killing the infected cells, preventing the virus from infecting other cells and cleaning the battlefield. After this the healing process begins. However, most cases progress and reach critical points. Although the exact percentage is not known, it can be said that there are more cases than the flu. In severe cases billions of epithelial cells die and the protective layer of the lungs disappears. In this case the alveoli, which take part in our breathing, can be occupied by bacteria. Patients get pneumonia and breathing becomes harder and may even stop. The immune system that has produced millions of antiviral weapons that have worked at full power until now has become tired and becomes more and more unable to fight against the rapid proliferation of bacteria. The bacteria then enter the bloodstream and envelop the whole body. As a result, death occurs (Prompetchara et al., 2020).

Coronavirus is not only much more dangerous than the influenza but also more infectious and more rapid in spreading.

The most important actions to be taken to be protected from coronavirus is to wash hands. The coronavirus is embraced by a simple oil sheath and soap prevents infection by breaking that sheath (Prompetchara et al., 2020).

According to a study published in the New England Journal of Medicine, SARS-COV-2 viruses are able to survive up to a few days in different environments. SARS-COV-2 viruses can survive up to 72 hours on plastic surfaces, up to 48 hours on stainless steel surfaces, up to 24 hours on carton, up to 4 hours on copper surfaces and up to 3 hours in the air (Valkin, 2020).

Conclusion

Since viruses do not contain ribosome and are unable to create protein, they are completely dependent on the host cell. Thus, they transfer their genetic material to the host cell, seize the functions of the cell and take over its management. Therefore, they can cause serious damage to the species it enters and even cause death in some situations. This study examined the structure of viruses and explained how different types of viruses' effect humans. Although the debate about whether viruses are alive or not continues, it is known that viruses are everywhere where life exists. Although their size is so small that they are invisible to the eye, it has been observed that its effects on people can have very serious consequences.

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