

Pandemic Plan for the Church

Ministering to the Community in a Time of Crisis

Influenza Viruses and the Pathogenesis of Viral Diseases

Even a virus produced from a single cell
will include many variations of itself.
Viruses that carry RNA
mutate at much higher rates than those with DNA.

Introduction

Viruses are not considered to be living organisms due to the fact they do not have the capability to metabolize energy for respiration, growth, or reproduction. However, they are unique in their ability to mutate and adapt to outmaneuver their hosts.

Very little has been known about viruses until recently. They are the most abundant biological entities on planet Earth. They have had an enormous impact on humans and other organisms. All creatures of life are subject to a viral infection.

Viruses are the smallest infectious agent; they can range in size from about 20 to 400 nanometers. By comparison, a red blood cell is 6000 to 8000 nanometers (6-8 micrometers). They are hundred times smaller than a single bacteria cell which is ten times smaller than a human cell. Millions can fit inside one human cell.

They are the epitome of a parasite in that they are unable to replicate on their own and need to invade another organism to survive. In so doing their invasion can result in mild to severe illnesses in humans, animals, and plants. Some human diseases caused by viruses include the common cold, measles, chicken pox, hepatitis A and B, influenza, polio, rabies, HIV/AIDS, Ebola, COVID, SARS, herpes, mumps, dengue, and Respiratory Syncytial Virus.

Among several characteristic that separate them from living organisms are viruses:

- Do not have cell membranes - viruses have a protein shells
- Do not have organelles as other living cells
- Do not eat or burn energy
- Must invade living cells in order to reproduce

Virus Species

There are eighteen classifications grouped by their similar characteristics. These include the type of nucleic acid, the capsid symmetry, the presence or absence of an envelope, the hosts they infect, and the diseases they cause.

There are eighteen virus classifications grouped by their similar characteristics. They are classified by several qualities including the following:

- nucleic acid
- capsid symmetry
- presence or absence of an envelope
- hosts they infect
- diseases caused

For the purposes of this document, we will focus on the influenza virus.

Influenza Viruses

The influenza virus is a member of the Orthomyxoviridae family. As stated earlier, viruses are grouped by their similar characteristics and by the type of hosts they infect. Influenza viruses are RNA viruses that are further classified as A, B, or C. Influenza A is the most virulent (severe) of the three types and causes the most serious illness. It is the type A influenza that can cause deadly outbreaks and pandemics.

Influenza A viruses can cause influenza in birds and some mammals. All types of influenza A viruses have been found in wild birds, but it is rare that these produce illnesses in the birds. However, some variants of influenza A virus can cause severe sickness in domestic poultry and in humans. Occasionally, viruses are transmitted from wild birds to domestic poultry, causing sickness in them.

Type B influenza does not have the ability to infect a wide range of hosts. It also mutates much slower, so it does not pose as much danger as type A influenza. Seasonal influenza outbreaks are caused by types A or B influenza viruses, and both can cause epidemics. Influenza C is less common than types A and B and usually causes only mild illness.

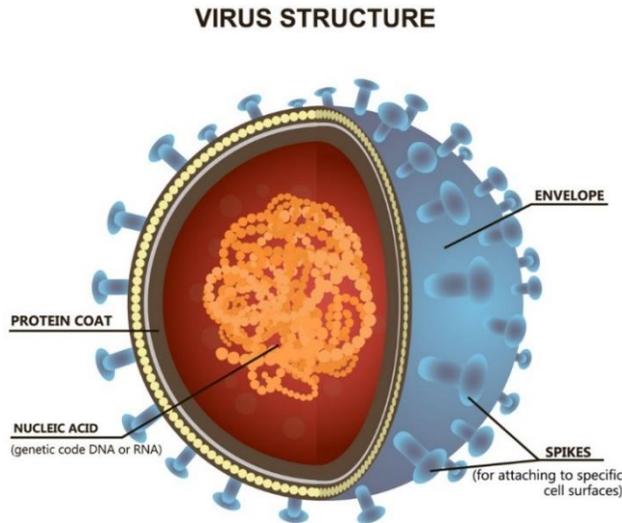
Structure of a Virus

A virion (virus particle) has three main parts:

- Nucleic acid – The substance within the core of the virus that holds the DNA or RNA (deoxyribonucleic acid and ribonucleic acid respectively). The DNA and RNA protein contain the genetic material.
- Coat (capsid) – The covering and protection of the nucleic acid.

- Lipid membrane (envelope) – The cover of the capsid. Some viruses may not have this membrane.

Viruses have proteins on the surface called *antigens*. It is by these antigens that viruses are able to attach to specific receptors on host cells. In addition, the immune system recognizes viruses by their various antigens, allowing the body to fight off the infection.

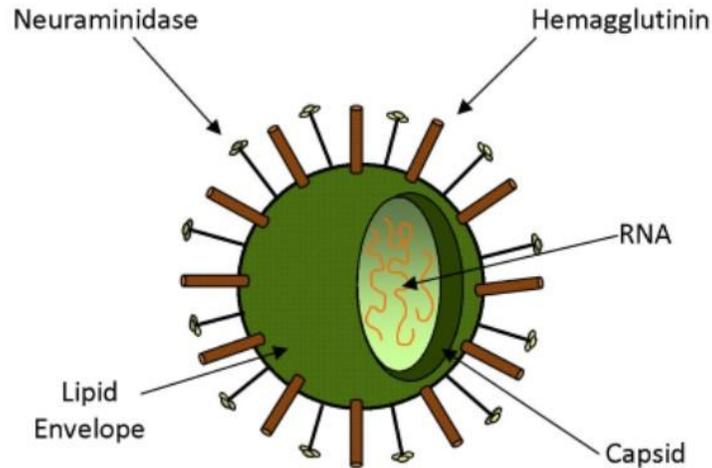


Structure of a Virus
SkyPics Studio/Shutterstock.comⁱ

Structure of an Influenza Virus

Influenza viruses A and B are of a spherical shape, although type C viruses can be both spherical and filamentous. The outer layer is a lipid envelope that covers the sphere. Just beneath the envelope is a protein shell that gives the virion its shape and rigidity. This protein shell, known as the capsid encapsulates the nucleic acid which consists of the genetic material DNA or RNA. The significance of DNA versus RNA will be discussed in the section “Viral Replication.” At this time, it is important to know that it is these proteins that enable a virus to mutate and cross the species barrier (avian to animal or human).

Coming from the capsid are the proteins called *hemagglutinin* (H or HA) and *neuraminidase* (N or NA) that enable a virus to attach and invade host cells. These proteins, also known as antigens, undergo mutation, or genetic variation. Mutation is the mechanism for the emergence of new strains. Type A in particular mutates frequently and can produce new strains to which few people are immune. This is how pandemics emerge.



Structure of an Influenza Virus

Influenza A viruses are categorized by the presence of these surface proteins, also known as antigens. It is the various combinations of the H's and the N's that determine the subtype strains, such as H5N1, H1N1. Three different subtypes of Influenza Type A have caused pandemics in the 20th century, H1N1, H2N2, and H3N2.

Currently there are eighteen hemagglutinin subtypes (H1-H18) and eleven different neuraminidase subtypes (N1-N11) that have been recognized to date.ⁱⁱ Many of the viruses are species specific, however some have crossed over and are able to infect other groups. To date, humans can be infected by H1, H2, H3, H5, H6, H7, H9, and H10. Birds can be carriers and become infected by all H subtypes except H17, and H18. The H5N1 subtype has been able to cross over to the most species of animals including birds, humans cattle, swine, cats, dogs, sheep, goats, alpacas, seals, and other mammals including ferrets, minks, mice, foxes, tigers, leopard, polar bears, among others.ⁱⁱⁱ

The H1N1 caused the "Swine Flu" pandemic in 2009. World health officials are watching the H5N1, and the H7N9 anticipating these may develop into serious threats if they become easily transmitted between people. Be reminded that the COVID-19 pandemic was caused by a corona virus (SARS-CoV-2)

Influenza (Flu)

Influenza, also known as the seasonal flu, is a highly contagious viral disease that tends to occur in epidemics during the colder and less humid months of the year. Symptoms are mainly fever, cough, sore throat, fatigue and body aches. Infection can easily spread in airborne droplets from coughs and sneezes. Some people may also experience symptoms of nausea, vomiting and diarrhea. Complications can lead to pneumonia and dehydration.

Infections from influenza occur mainly in the upper respiratory tract. This is due to the fact that the upper respiratory tract epithelium (cells that lines cavities and covers surfaces) tissue contains receptors to which these viruses target and bond.

Most people have some immunity to circulating strains of influenza virus and, as a result, the severity and effect of seasonal influenza is substantially less than during pandemics. Each year, health officials study the circulating strains and predict which three will be the most likely to cause the most illness for the coming flu season. A trivalent influenza vaccine is prepared in advance of the anticipated seasonal outbreak and it includes those strains (two type A and one type B).

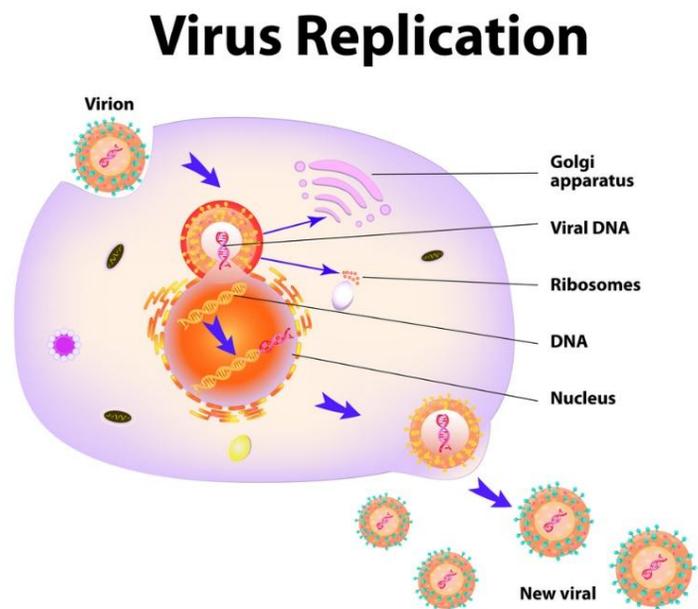
Pathogenesis of Viral Diseases

Pathogenesis is the process in which a disease develops. Understanding the lifecycle of a virus will shed light on the onset, progression, and maintenance of the clinical illness presenting in a person.

Life Cycle of a Basic Virus

Viruses are only capable of reproducing inside a living “host” cell that they have invaded. There are a few basic steps that all infecting viruses follow called the lytic cycle. These steps include:

1. Adsorption – A virus first attaches to a host cell by its receptor. Then the virus gains entry by either being engulfed or by fusing with the cell membrane.
2. Entry – The virus injects its DNA or RNA into the host cell.
3. Replication – The DNA or RNA of the virus then takes over the functions of the host cell in order to reproduce new viruses. This may also be known as assembly.
4. Release – The host cell then dies and ruptures releasing the new viruses to find new host cells.

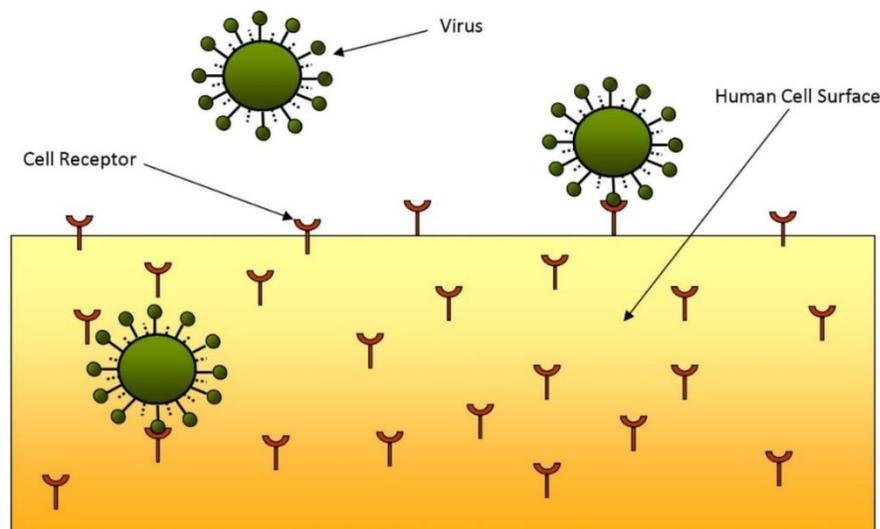


The first step in the infectious process is the entrance of the virus into a susceptible host in order to penetrate the host's cells. The influenza virus enters the body from the environment once it has been emitted from another infected individual (carrier). It spreads primarily through respiratory droplets when an infected person coughs, sneezes, or talks. Less commonly, the virus can be spread when a person touches a contaminated surface, then touches their own eyes, mouth, or nose.

Viruses do not have the reproductive means needed to multiply or replicate; therefore, they must use the mechanisms of host cells to replicate in order to survive. This is the sole purpose of a virus – to enter a host cell, replicate, breakout, and find another host cell to invade.

1. Adsorption and Receptors

Once the virus has entered a host, it now must gain entrance into the cells. Viruses are not simply taken into cells, they must first attach to a receptor on the surface of a host cell.



Viruses and Host Cell Receptors

Each virus has its own specific receptor, or a complementary structure on the surface of the host cell to which it can bind and attach itself. These specific receptors can be by cell, tissue, or organs.

The receptor molecules on host cells of a specific tissue type determine the preference of a specific virus. A influenza virus, for example, will target cells that line the respiratory (i.e. the lungs) or digestive (i.e. the stomach) tracts. The HIV (human immunodeficiency virus) that causes AIDS attacks the T-cells (a type of white blood cell that fights infection and disease) of the immune system. Although enteroviruses enter through the gastrointestinal tract, they can target other systems in the human body. Polio for example, targets the central nervous system. Ebola targets endothelial cells (cells that line the interior surface of blood and lymphatic vessels).

The cells with specific matching receptors for the virus are called host cells. It is the hemagglutinin protein that is responsible for the virus attaching itself with the receptors of *sialic acid* (a sugar molecule) that protrude from the surface of upper respiratory cells. When the hemagglutinin spike touches these they bind to the sialic acid receptor. Some call the hemagglutinin the “Key”.

2. Entry

Once these two shapes fit snugly together they bind allowing the virus to enter the cell. This is called *adsorption*, or adherence to the body of the target cell. Once inside the cell the virus injects its RNA.

3. Viral Replication

Since viruses lack the needed components to reproduce on their own, they hijack those inside a living host cell which they have invaded. Influenza viruses contain only RNA; unlike some other viruses whose genes consist of DNA. Once a virus has entered a host cell, the RNA takes over the functions of the cell in order to replicate new viruses. Even a virus produced from a single cell will include many variations of itself. Viruses that carry RNA mutate at much higher rates than those with DNA. This will be discussed in greater detail.

4. Release

The neuraminidase protein enables the virus to be released from the host cell. At the top of each neuraminidase, under an electron microscope, it appears that there are propellers similar to those of a helicopter. These blades allow the neuraminidase to break up the sialic acid remaining on the cell surface. This is significant in that the virus would be trapped by the sialic acid when the new viruses burst from the cell after replication. The blades on the head of each spike destroy the acid's ability to bind to the newly formed, escaping influenza viruses. This ensures the new viruses can break free to invade other host cells. Some call the neuraminidase the “scalpel”.

In addition to the aiding in the release of new viruses, neuraminidase may also help during the binding process. The helicopter like blades on these proteins destroys the sialic acid in the mucus, enabling the hemagglutinin to bind to the receptor on the cell surface.

The mechanics involved in a virus taking over the metabolic machinery of the host cell has considerable medical significance. Some antiviral medications target the reproductive process in order to constrain further replication. Neuraminidase inhibitors such as Oseltamivir (Tamiflu), and Zanamivir (Relenza) work by blocking the function of neuraminidase and causing the newly formed viruses to stick together when escaping the host cell. Although this class of antiviral drugs do not actually kill the virus, they slow the disease process to allow the immune system to wage a fair fight against the invading antigen. The development of other antiviral drugs that would further interfere with viral replication would also interfere with the functions of the host cell and hence are too toxic for clinical use.

Clinical Illness Due to Cell Destruction

The replication and release processes the virus follows eventually destroy the host cell. Clinical illness is due to the destruction of the virus-infected cells in the target tissue. During this cycle and the subsequent destruction of cells, the host becomes ill displaying signs and symptoms of the viral infection. An influenza virus that infects humans and attaches to receptors in the respiratory tract will cause a respiratory infection. Symptoms such as a sore throat, fever, chest congestion, nausea, vomiting and diarrhea are just some effects of a viral disease. Some tissue may regenerate easily after a viral attack without much damage, for example intestinal epithelium. Other tissues may not regenerate and may never return to normal functioning after the virus has destroyed its host cells, such as with nervous system tissue.

Signs and Symptoms of Influenza

Depending on the severity of a viral infection, or preexisting conditions, the level of illness can be mild to severe. At times, an influenza infection can lead to death. People can experience some or all of the following signs and symptoms of influenza:

- Sore throat
- Cough
- Muscle or body aches
- Headache
- Runny/stuffy nose/sinus congestion
- Fever
- Chills
- Fatigue
- Stomach upset
- Nausea/Vomiting
- Diarrhea

It may take a few days or even up to two weeks to recover; however, some people may develop complications resulting from their illness. Some of these complications include:

- Bronchitis
- Pneumonia
- Sinus and ear infections
- Inflammation of the heart, brain, or muscles
- Worsening of chronic health conditions
- Multi-organ failure and death

It is important to note that complications can arise with anyone no matter their health or their age. However, pregnant women, young children, the elderly, and people with preexisting medical conditions such as asthma, heart disease, cancer, or diabetes may be more at risk for developing complications.^v (Northwestern Medicine, 2024)

Depending on the severity of the circulating seasonal influenza, estimates of flu-associated deaths in the United States range from a low of 6,300 to 52,000.^{vi}

Recovery From Infection – Immune System

The immune system makes antibodies when there is an exposure to a new antigen. These antibodies bind to the proteins (Hs and Ns) of the virus, which prevents the virus from continuing its lifecycle. Depending on the health of the host and the robustness of their immune system, it will either kill or slow down the virus. This can make the difference between a fever and a cough, vs. pneumonia and death.

The immune system is in a constant battle to recognize, fight, and destroy disease and foreign antigens when they enter our bodies. This constant battle has been likened to “Red Queen” dynamics after the Red Queen in Lewis Carroll’s “The Looking Glass.”

“It takes all the running you can do, to keep in the same place.”

The host’s immune system is what eventually destroys the invading virus. This will include both antibodies recognizing and attacking the virus, and other cellular components of the immune system. The host will either succumb or recover.

Virus Shedding

Viral shedding is when the infected person releases viral particles into the environment. When shedding takes place, it allows the repopulation of the virus to ensure its survival. This usually occurs from the same site used for entry. For example, a cough or a sneeze will release an influenza virus back into the environment from the tissue it just invaded. During this period, an infected host is infectious and can spread the virus. The virus leaves the host by the way it entered through:

- Sneezes
- Coughs
- Feces
- Blood
- Other bodily fluids

Recovery of Target Cells

Some cells and tissue recover completely over time with cell division and regeneration. Depending on the virus and the target tissue, some may not recover.

Gastrointestinal tract - Intestinal epithelium (also known as stomach flu) Common culprits include the norovirus, rotavirus, and adenovirus.

- Rapidly regenerates after a viral attack
- Able to withstand extensive damage

Nervous System Tissue (the enterovirus and polio)

- Not able to regenerate
- Never resumes normal functioning
-

Respiratory Tissue

- Recovery process can vary depending on age, overall health and severity of the infection
- Damaged epithelial cells are replaced eventually with cell division
- Even after apparent recovery, the lungs may show persistent inflammation
- Some may experience long-term respiratory issues

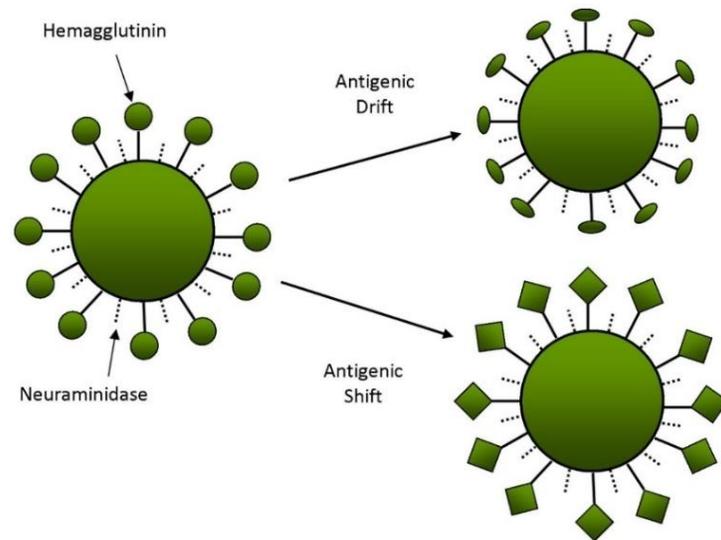
Influenza Virus Mutation – “Drift” and “Shift”

The protein antigens, hemagglutinin and neuraminidase, are also important structures for the spread of the virus. The immune system recognizes viruses by these antigens. When viruses reproduce, the antigens on the new viruses may become slightly different to prevent the immune system from recognizing the virus. This is called mutation and is a normal part of the virus' lifecycle. Slight changes are known as antigenic drift, and much larger, abrupt changes are called antigenic shift and can result in epidemics and pandemics. These mutations can result in influenza viruses jumping between species of animals and even its ability to be transmitted from animals to humans.

Antigenic Drift

Antigenic drift are small changes in the virus that happen continually over time. This type of mutation produces new virus strains that may not be recognized by the body's immune system. The progression of antigen drift is a person becomes infected with a particular flu virus strain. Their immune system then makes antibodies against that virus according to the antigens presented on the virus' surface. When that virus replicates, the mutations lead to changes to the antigens and a new virus is introduced. The immune system no longer recognizes the new virus and reinfection can occur. This is why people are able to get the flu more than once, even in the same season. In addition, these mutations are the reason that people need to be vaccinated against the seasonal flu each year

Health officials predict the influenza strain most likely to cause the current seasonal flu epidemic then the flu vaccine is updated. However, as in the flu season of 2014-2015, the match to the circulating flu strain and the vaccine may not always be a good one.



Antigenic Drift vs. Antigenic Shift

Antigenic Shift

The second type of change is called antigenic shift. This is a significant change in the influenza A virus resulting in new hemagglutinin and/or new hemagglutinin and neuraminidase proteins. Antigenic shift results in a whole new influenza A subtype. When shift happens, most people have little or no protection against the new virus.

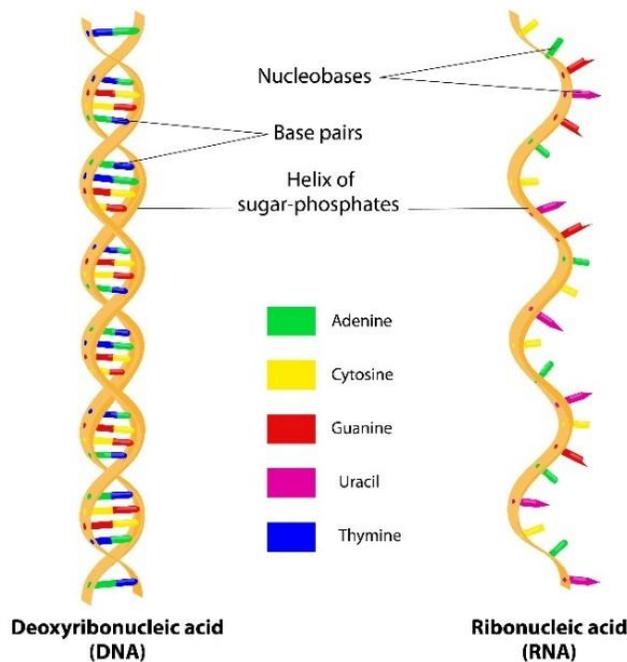
Antigenic shift occurred in the spring of 2009, when a new H1N1 virus with a new combination of genes emerged to infect people and quickly spread, causing a pandemic.

While influenza viruses are changing by antigenic drift all the time, antigenic shift happens only occasionally. Type A viruses undergo both shift and drift types of changes; however, influenza type B viruses only undergo the more gradual process of antigenic drift.

Significance of RNA vs. DNA

In most life forms, genes are made of DNA (deoxyribonucleic acid), which is a long filament type molecule. DNA usually exists as a double-stranded structure, with both strands coiled together to form its characteristic double-helix. Each single strand of DNA is a chain of four types of nucleotides having the bases: adenine, cytosine, guanine, and thymine (commonly noted as A, C, G, and T). DNA carries the information for making all of the cell's proteins. These proteins implement all of the functions of a living organism and determine the organism's characteristics.

Structure of DNA & RNA



DNA vs. RNA

Designua/Shutterstock.com ^{vii}

When a cell reproduces, it has to pass all of this information on to the offspring cells. Before a cell can reproduce, it must first replicate or make a copy of its DNA. DNA contains deoxyribose; “deoxy” means there are no hydroxyl (-OH) groups. The absence of hydroxyl groups means that the chemical bonds between the molecules are not easily broken down into water (H₂O).

RNA, conversely, consists of a single strand of nucleotides, that also contains ribose. The ribose contains a hydroxyl group that makes it more susceptible to hydrolysis. Hydrolysis means that the chemical bond between molecules can be easily broken into water. As a result, RNA is intrinsically fragile and its strands can be easily broken. Therefore, the presence of hydroxyl groups makes RNA less stable than DNA. Many viruses, including the influenza virus, encode their genes in RNA.

Whenever an organism reproduces, its genes contained in DNA or RNA attempt to make exact copies of themselves, but mistakes can happen. These mistakes are known as mutations. DNA has a kind of built in proofreading mechanism to prevent these alterations or mutations. During the replication process, DNA has an enzyme complex that moves along the new strand as it is being synthesized. This enzyme complex recognizes any errors and removes the nucleotide. It then returns to replace a correct nucleotide in its place.

RNA has no such proofreading mechanism, consequently, there is no protection against mutations. Even a virus produced from a single cell will include many variations of itself.

Viruses that carry RNA mutate much faster than a DNA virus. Up to one million times faster. The influenza virus, HIV, and the coronavirus (SARS) are all among those that contain RNA and all mutate the fastest in the world of viruses.

Genetic Reassortment

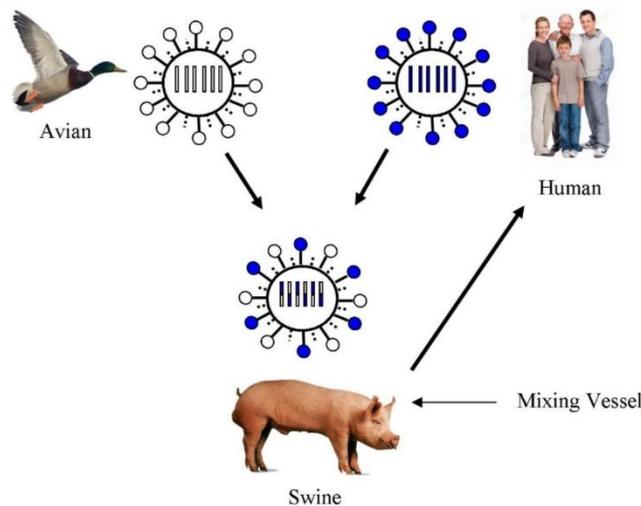
All categories of type A influenza viruses are constantly mutating, including those that regularly cause seasonal epidemics in humans. There are two consequences to this constant mutation. Antigenic drift, as stated above, allows the virus to genetically elude the host's immune system.

The second type of mutation, antigenic shift, as stated is of greater concern. Influenza viruses, including subtypes from different species, can swap or reassort genetic materials with the host and merge. This process is called *genetic reassortment*. Reassortment results in a new subtype different from both parent viruses.

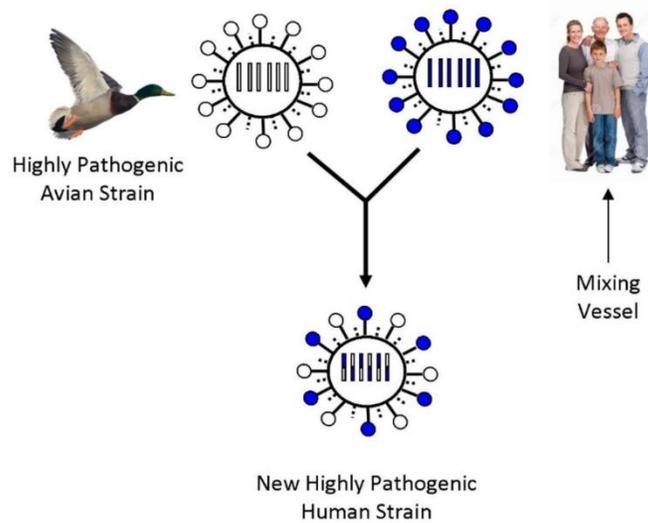
Pigs are susceptible to infection from both avian (bird) and mammalian (human) viruses, they can serve as a vessel for the mixing of genetic material from both type viruses. This can result in a new viral subtype. Due to the fact that humans live in close proximity to domestic pigs and poultry, it lends to favorable conditions for antigenic shift.

Evidence also shows that humans can also serve as a mixing vessel. This adds to the possibility of antigenic shift producing a deadly virus that can be transmissible from person-to-person.

The following are illustrations that demonstrate how both swine and humans can serve as "mixing vessels." By this exchange of genetic material of these animal and human species, new strains of influenza viruses are created.



Genetic Reassortment in Influenza Viruses with Swine as Mixing Vessels



Genetic Reassortment in Influenza Viruses with Humans as Mixing Vessels

The HPAI H5N1, is currently experiencing a concerning increase in its ability to jump between species, including mammals. This means the virus, which primarily affects birds, is now infecting a wider range of animals, including dairy cattle and even some humans. The virus's ability to evolve and spread to new hosts raises significant public health concerns.

ⁱ SkyPics Studio/Shutterstock.com, <http://www.shutterstock.com/pic-293747246.html>

ⁱⁱ About Influenza A in Animals, Overview, Centers for Diseases Control, June 3, 2025, <https://www.cdc.gov/flu-in-animals/about/index.html>, accessed August 7, 2025

ⁱⁱⁱ About Influenza A in Animals, Overview, Centers for Diseases Control, June 3, 2025, <https://www.cdc.gov/flu-in-animals/about/index.html>, accessed August 7, 2025

^{iv} Designua/Shutterstock.com, <http://www.shutterstock.com/pic-138350861.html>

^v Flu: Who is Most at Risk?, North Western Medicine, September 2024, <https://www.nm.org/healthbeat/healthy-tips/flu-who-is-most-at-risk>, accessed August 6, 2025

^{vi} Facts about Estimated Flu Burden, Centers for Disease Control, <https://www.cdc.gov/flu-burden/php/about/faq.html>, accessed August 6, 2025

^{vii} Designua/Shutterstock.com, <http://www.shutterstock.com/pic-124474282.html>