Viral pathogenesis and transmission

Viral pathogenesis is defined as the mechanism by which viruses causes disease. A simple view of viral pathogenesis is that viruses replicate and kill cells, thus causing disease. For example, death of liver cells (hepatocytes) causes hepatitis, death of enterocytes may cause diarrhea, death of respiratory epithelial cells may cause severe respiratory tract disease

Signs and symptoms of disease can also result from tissue damage caused by host immune responses. Inflammation, killing of virus-infected cells by the immune system, or deposition of immune complexes are examples.

The host cells must be **accessible** to the virus, and those cells must be **susceptible** to infection, meaning that the cells express the receptors to which the virus can bind. This affinity for susceptible tissues is known as **tropism**. The cells must also be **permissive** to infection, meaning that they contain the proteins and molecules within the cell that are necessary for replication to occur. There are also mechanical, chemical, and microbiological barriers to infection at every site within the body, and the host's immune system is quickly activated to eradicate the virus.

Transmission methods

Viral transmission is the process by which viruses spread between hosts. It includes spread to members of the same host species or spread to different species in the case of viruses that can cross species barriers

Contact transmission includes direct contact or indirect contact.

1.direct contact transmission.

Person-to-person transmission such as touching, kissing, sexual intercourse, or droplet sprays.

Direct contact can be categorized as vertical, horizontal, or droplet transmission.

A. Vertical direct contact transmission occurs when pathogens are transmitted from mother to child during pregnancy, birth, or breastfeeding. **B**. **horizontal direct contact transmission**. Often, contact between **mucous membranes** is required for entry of the pathogen into the new host, although skin-to-skin contact can lead to mucous membrane

contact if the new host subsequently touches a mucous membrane. Contact transmission may also be site-specific; for example, some diseases can be transmitted by sexual contact but not by other forms of contact , When an individual coughs or sneezes, small droplets of mucus that may contain pathogens are ejected.

2. Indirect contact transmission involves inanimate objects called **fomites** that become contaminated by pathogens from an infected individual or reservoir

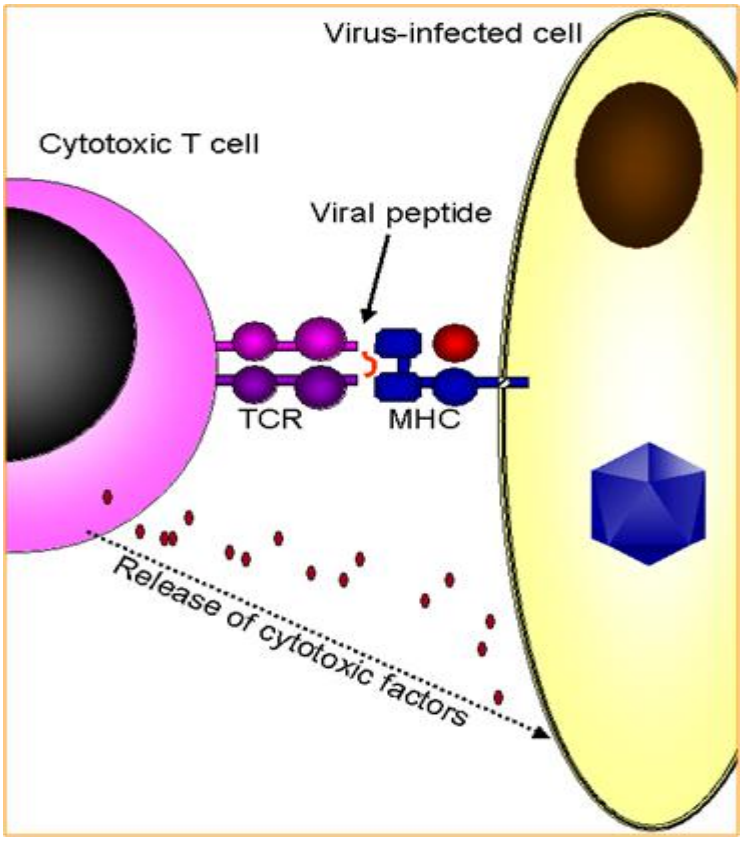
For example, an individual with the common cold may sneeze, causing droplets to land on a fomite such as a tablecloth or carpet, or the individual may wipe her nose and then transfer mucus to a fomite such as a doorknob or towel. Transmission occurs indirectly when a new susceptible host later touches the fomite and transfers the contaminated material to a susceptible portal of entry. Fomites can also include objects used in clinical settings that are not properly sterilized, such as syringes, needles, catheters, and surgical equipment. Pathogens transmitted indirectly via such **fomites** are a major cause of healthcare-associated infections .

Immunity response for viral infection

When a virus infects a person (host), it invades the cells of its host in order to survive and replicate. Once inside, the cells of the immune system cannot 'see' the virus and therefore do not know that the host cell is infected. To overcome this, cells employ a system that allows them to show other cells what is inside them – they use molecules called class I major histocompatibility complex proteins (or MHC class I, for short) to display pieces of protein from inside the cell upon the cell surface. If the cell is infected with a virus, these pieces of peptide will include fragments of proteins made by the virus.

A special cell of the immune system called a T cell circulates looking for infections. One type of T cell is called a cytotoxic T cell because it kills cells that are infected with viruses with toxic mediators. Cytotoxic T cells have specialised proteins on their surface that help them to recognise virally-infected cells. These proteins are called T cell receptors (TCRs). Each cytotoxic T cell has a TCR that can specifically recognise a particular antigenic peptide bound to an MHC molecule. If the T cell receptor detects a peptide from a virus, it warns its T cell of an infection.

The T cell releases cytotoxic factors to kill the infected cell and, therefore, prevent survival of the invading virus (Figure 1).

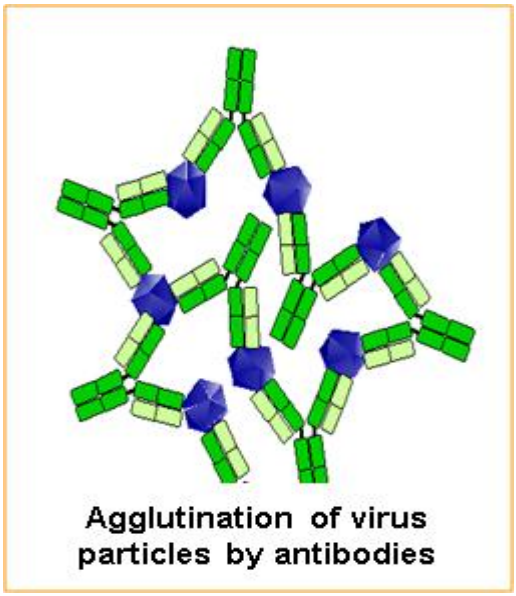


Viruses are highly adaptable, and have developed ways to avoid detection by T cells. Some viruses stop MHC molecules from getting to the cell surface to display viral peptides. If this happens, the T cell doesn't know there's a virus inside the infected cell.

However, another immune cell specialises in killing cells that have a reduced number of MHC class I molecules on their surface – this cell is a natural killer cell or NK cell for short. When the NK cell finds a cell displaying fewer than normal MHC molecules it releases toxic substances, in a similar way to cytotoxic T cells, which kill the **virally-infected cell.**

Virally infected cells produce and release small proteins called **interferons**, which play a role in immune protection against viruses. Interferons prevent replication of viruses, by directly interfering with their ability to replicate within an infected cell

Viruses can also be removed from the body by **antibodies** before they get the chance to infect a cell.



Labrotary diagnosis of viral infection

In the diagnostic laboratory virus infections can be confirmed by a multitude of methods. Diagnostic virology has changed rapidly due to the advent of molecular techniques and increased clinical sensitivity of serological assays

1. Nucleic acid based methods

Molecular techniques are the most specific and sensitive diagnostic tests. They are capable of detecting either the whole viral genome or parts of the viral genome.

A. Polymerase chain reaction(PCR)

Detection of viral RNA and DNA genomes can be performed using polymerase chain reaction. This technique makes many copies of the virus genome using virus-specific probes. Variations of PCR such as nested reverse transcriptase PCR and real time PCR can also be used to determine viral loads in patient serum. This is often used to monitor treatment success in HIV cases.

B. Sequencing

Sequencing is the only diagnostic method that will provide the full sequence of a virus genome. Hence, it provides the most information about very small differences between two viruses that would look the same using other diagnostic tests. Currently it is only used when this depth of information is required.

2. Microscopy based methods

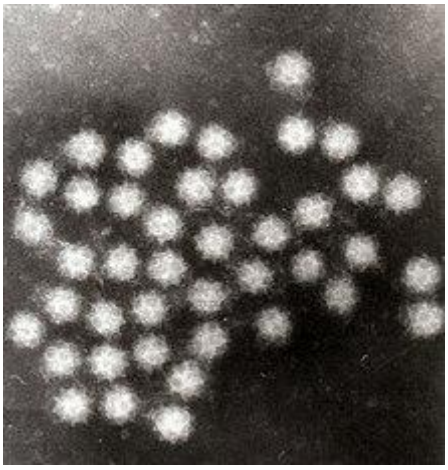
A. Immunofluorescence or immunoperoxidase

Immunofluorescence or immunoperoxidase assays are commonly used to detect whether a virus is present in a tissue sample. These tests are based on the principle that if the tissue is infected with a virus, an antibody specific to that virus will be able to bind to it. To do this, antibodies that are specific to different types of viruses are

mixed with the tissue sample. After the tissue is exposed to a specific wavelength of light or a chemical that allows the antibody to be visualized.

B. Electron microscopy

Electron microscopy is a method that can take a picture of a whole virus and can reveal its shape and structure. It is not typically used as a routine diagnostic test as it requires a highly specialized type of sample preparation, microscope and technical expertise



Electron microscopy of the Sappovirus

3. Host antibody detection

A person who has recently been infected by a virus will produce antibodies in their bloodstream that specifically recognize that virus. This is called humoral immunity. Two types of antibodies are important. The first called IgM is highly effective at neutralizing viruses but is only produced by the cells of the immune system for a few weeks. The second, called, IgG is produced indefinitely. Therefore, the presence of IgM in the blood of the host is used to test for acute infection, whereas IgG indicates an infection sometime in the past.Both types of antibodies are measured when tests for immunity are carried out.

Antibody testing has become widely available. It can be done for individual viruses (e.g. using an ELISA assay) but inautomated panels that can screen for many viruses at once are becoming increasingly common.

4. Hemaglutination assay

Some viruses attach to molecules present on the surface of red blood cells, for example, influenza virus . A consequence of this is that – at certain concentrations – a viral suspension may bind together (agglutinate) the red blood cells thus preventing them from settling out of suspension.