Transmission & Portal of Entry of viruses

Viruses are transmitted to the individual by many different routes, and their portals of entry are varied. For example, person-to-person spread occurs by transfer of respiratory secretions, saliva, blood, or semen and by fecal contamination of water or food. The transfer of blood, either by transfusion or by sharing needles during intravenous drug use, can transmit various viruses (and bacteria). The screening of donated blood for human immunodeficiency virus, human T-cell lymphotropic virus, hepatitis B virus, hepatitis C virus, and West Nile virus (as well as *Treponema pallidum*) has greatly reduced the risk of infection by these pathogens. Transmission can occur also between mother and offspring in utero across the placenta, at the time of delivery, or during breast feeding. (Transmission between mother and offspring is called **vertical transmission.** Person-to-person transmission that is not from mother to offspring is called **horizontal transmission.**) Animal-to-human transmission can take place either directly from the bite of a reservoir host as in rabies or indirectly through the bite of an insect vector, such as a mosquito, which transfers the virus from an animal reservoir to the person. In addition, activation of a latent, nonreplicating virus to form an active, replicating virus can occur within the individual, with no transmission from an external source.

Pathogenesis

Pathogenesis in the infected patient involves (1) transmission of the virus and its entry into the host; (2) replication of the virus and damage to cells; (3) spread of the virus to other cells and organs; (4) the immune response, both as a host defense and as a contributing cause of certain diseases; and (5) persistence of the virus in some instances. Most viral infections are either **localized** to the portal of entry or spread **systemically (generalized)** through the body. Some viral infections spread systemically, not via the bloodstream, but rather by retrograde axonal flow within neurons.

The steps for the infectious process involving viruses usually include the following:

1. Maintain a reservoir: A reservoir is a place to live and multiply before and after causing an infection, they must gain access to a susceptible host so that they can replicate. Thus the most common **reservoirs** of human viruses are

humans and other animals. Most often, viruses are transmitted from reservoir (a human host) to host (another human) to cause noticeable infection in a relatively short time frame. Because viruses require viable host cells in which to replicate, the source or reservoir may harbor large numbers of viral particles that can infect equally large numbers of new hosts upon their release.

2. Enter a host.

3. Contact and enter susceptible cells.

4. Replicate within the cells.

The first step in the infectious process is the attachment and entrance of the virus into a susceptible host and the host's cells. Entrance may be accomplished through one of the body surfaces: skin, respiratory system, gastrointestinal system, urogenital system, or the conjunctiva of the eye. Other viruses enter the host by sexual contact, needle sticks, blood transfusions and organ transplants, or insect **vectors** —organisms that transmit the pathogen from one host to another.

Regardless of the method of entry into the host organism, viral infection begins when the viral particle penetrates a host cell to gain access to the cell's replicative machinery. This process is called **adsorption ,** or the attachment to the cell surface. Recall that adsorption occurs because viruses produce specific protein ligands that bind to host cell receptors embedded within their plasma membranes. Host specificity for the virus is a function of viral gene expression; the virus must express the ligand so as to dock with a specific host cell. Protein ligands are usually positioned on the virus to maximize contact with the cell. Enveloped viruses use spikes—viral proteins that protrude from their membrane. The ligands of naked viruses are part of their capsid proteins.

Each viral ligand binds only to a complementary receptor on the host cell surface. Binding of a virus to its receptor typically results in penetration of the cell or the delivery of viral nucleic acid to the cytoplasm of the cell. In the case of human viruses, the viral genome enters the host cell by (1) endocytosis and the release of the genome from the capsid (uncoating), as with *Poliovirus* and the poxviruses; or (2) fusion of the viral envelope with the cell membrane and subsequent uncoating, as with influenza virus

Some viruses remain localized, replicating only in cells that constitute one tissue or organ (e.g., respiratory or gastrointestinal infections). Others spread to sites distant from the point of entry and replicate at these sites. For example, the *Poliovirus* enters through the gastrointestinal tract but produces disease in the central nervous system.

5. Release from host cells (immediately or delayed).

6. Evade the host's immune response.

The evasion of viral host defenses begins when the virus first infects the host. However, for the virus to cause a successful infection (from the viral point of view), it must be able to avoid host immunity so it can spread to a sufficient number of host cells to amplify the number of virions; this is when disease ensues. We thus discuss the evasion of host immunity as a prerequisite to viral spread. Viruses have evolved a variety of ways to suppress or evade the host's immune response. For instance, some viruses mutate and change antigenic sites (antigenic drift) on the virion capsids (e.g., the influenza virus) or may downregulate the level of expression of viral cell surface proteins (e.g., the herpesvirus). Other viruses (HIV) infect cells (T cells) of the immune system and diminish their function. HIV as well as the *Measles virus* and cytomegalovirus cause fusion of host cells. This allows these viruses to move from an infected cell to an uninfected cell without exposure to the antibody-containing fluids of the host.

The herpesvirus infects neurons that express little or no major histocompatibility complex molecules. The adenovirus produces proteins that inhibit major histocompatibility complex function. Finally, *Hepatitis B* virus-infected cells produce large amounts of antigens not associated with the complete virus. These antigens serve as decoys, binding available neutralizing antibody so that there is insufficient free antibody to bind with the complete virion. These are just a few examples of the ways in which viruses evade host defenses; our understanding of these and other mechanisms is advancing through genomics and the analysis of specific gene products.

7. Spread to adjacent cells (**Cell Tropism):** Mechanisms of viral spread vary, but the most common routes are the bloodstream and the lymphatic system. The presence of viruses in the blood is called **viremia .** In some instances, spread is by way of nerves (e.g., rabies, herpes simplex, and varicellazoster viruses).

Viruses exhibit cell, tissue, and organ specificities. These specificities are called **tropisms** (Greek *trope,* turning). A tropism by a specific virus usually reflects the presence of specific cell surface receptors on the eucaryotic host cell for that virus.

8. Be either cleared from the body of the host, establish a persistent infection, or kill the host(.**Virus-Host Interactions)**

Possible consequences of viral infection for the host cell:

— Cytocidal infection (necrosis): viral replication results directly in cell destruction (cytopathology, so-called "cytopathic effect" in cell cultures).

— Apoptosis: the virus initiates a cascade of cellular events leading to cell death ("suicide"), in most cases interrupting the viral replication cycle.

— Noncytocidal infection: viral replication per se does not destroy the host cell, although it may be destroyed by secondary immunological reactions.

— Latent infection: the viral genome is inside the cell, resulting in neither viral replication nor cell destruction.

— **Tumor transformation**: the viral infection transforms the host cell into a cancer cell, whereby viral replication may or may not take place depending on the virus and/or cell type involved.

9. Be shed back into the environment.

The last step in the infectious process is shedding of the virus back into the environment. This is necessary to maintain a source of viruses in a population of hosts. Shedding often occurs from the same body surface used for entry. During this period, an infected host is infectious (contagious) and can spread the virus. In some viral infections, such as a rabies infection, the infected human is the final host because virus shedding does not occur.

The success by which a virus accomplishes each of these steps contributes to its overall pathogenicity.

Persistent Viral Infections

• **Carrier state**: refers to people who produce virus for long periods of time and can serve as a source of infection for others. The carrier state that is frequently associated with hepatitis C virus infection is a medically important example.

• **Latent infections:** are those infections that are not producing virus at the present time but can be reactivated at a subsequent time. The latent infections that are frequently associated with herpes simplex virus infection are a medically important example.

• **Slow virus infections:** refer to those diseases with a long incubation period, often measured in years. Some, such as progressive multifocal leukoencephalopathy, are caused by viruses, whereas others, such as Creutzfeldt-Jakob disease, are caused by prions. The brain is often the main site of these diseases.