Viruses

Viruses are non-living chemical entities. They are parasites of living cells. They are can replicate only within living cells by using the cell’s enzyme systems. They have nucleic acid genomes, either DNA or RNA, but not both. Viruses have a narrow range of cells that they can infect but all or nearly all organisms can be infected by multiple kinds of viruses. There may be as many as $1 \times 10^{12}$ kinds of viruses.

The morphology of viruses is diverse but all have a nucleic acid core surrounded by a protein coat (capsid).

The capsid has either a helical or icosahedral shape or a combination of shapes.

Some viruses also have an envelope made of protein, glycoproteins and lipids. The lipids are usually derived from their host cell.
Viruses have a narrow **host range**.

Bacterial viruses (**bacteriophages**) only infect a limited number of bacteria.

Eukaryotic viruses often only infect a narrow range of closely related species but some can be transferred to distantly related species. (e.g. Bird flu, Swine flu, Ebola)

Infections in multicellular organisms often infect a narrow range of tissues (**tissue tropism**). (e.g. Hepatitis C)

Some viruses are benign and cause their host little or no harm. Others are highly virulent and quickly kill their hosts (Ebola).

Some viruses infect and then remain dormant, or **latent**, for long periods and can later be triggered to multiply. (e.g. Chicken pox and other herpes viruses).

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Viruses are small but vary greatly in size.

Viruses can’t be seen with light microscopes.
A virus particle outside a cell is called a **virion**.

Viruses infect cells through attachment and injection of the core or by traversing the cell membrane by endocytosis.

Encoded in the viral genome are the instructions for taking over the cell’s machinery and using the machinery for making new virus particles. The cell’s machinery for replication of nucleic acids, transcription, and translation of the viral genome are co-opted by the virus.

There is a series of genes expressed during infection. **Early genes, middle genes, and late genes** successively code for proteins that facilitate nucleic acid replication, capsid protein production, assembly, and proteins that result in release of new virions from the cell.

Viral genomes can be DNA or RNA.

RNA viruses are usually single-stranded and go through replication, transcription, and translation in the cell’s cytoplasm.

RNA replication is more error prone than DNA replication. High mutation rates make it difficult for host cells to develop defenses and make the development of vaccines and anti-viral drugs difficult.

**Retroviruses** have an RNA genome but use an enzyme encoded by their genome, *reverse transcriptase*, to make a complimentary DNA copy of their genome. The DNA code of many retroviruses can be incorporated into their host’s genome. (e.g. HIV).

DNA viruses are usually double-stranded and are replicated in the nucleus of eukaryotic hosts.
Bacteriophages are large viruses with a DNA genome. Many phages have two reproductive cycles - a **lytic** cycle and a **lysogenic** cycle. If they exhibit a lysogenic cycle they are called **temperate** phages.

The lytic cycle consists of attachment, penetration, synthesis, assembly, and release through lysis of the cell. Many phages only have a lytic cycle.

In the lysogenic cycle, after penetration, the viral genome becomes integrated into the host’s genome. The viral genome is then called a **prophage**.

A prophage gets replicated every time the host cell replicates and divides.

A prophage can be **induced** through cell stress to excise itself from the host’s genome and return to the lytic cycle.
Some of the genes of the prophage genome can be expressed and have effects on the phenotype of a host cell.

A host cell that exhibits an altered phenotype as a result of prophage gene expression exhibits **phage conversion**.

*Vibrio cholerae* is normally benign but after phage conversion expresses a phage gene for the cholera toxin.

**TABLE 37**

<table>
<thead>
<tr>
<th>Virus</th>
<th>Host</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dengue</td>
<td>Mosquito</td>
<td>Fever, rash, muscle pain</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>Rodent</td>
<td>Jaundice, fatigue</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Rodent</td>
<td>Liver damage</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>Rodent</td>
<td>Liver damage</td>
</tr>
<tr>
<td>Rabies</td>
<td>Bat</td>
<td>Paralysis, death</td>
</tr>
<tr>
<td>Toxoplasmosis</td>
<td>Cat</td>
<td>Neurological damage</td>
</tr>
</tbody>
</table>

Humans are infected by both DNA and RNA viruses.

Some human viruses are relatively benign but many can be fatal.
HIV (Human Immunodeficiency Virus) causes AIDS (Aquired Immunodeficiency Deficiency Syndrome).

HIV is similar to a common virus in monkeys, SIV (Simian Immunodeficiency Virus) and is most similar to a form of the virus found in chimpanzees. It appears to have entered the human population in the 1950s as the result of human contact with butchered chimpanzees.

The first report of HIV infection in the US was in 1981.

Human resistance to HIV varies. Many are very susceptible to infection and others are resistant. This may be the product of past infections of other viruses, like smallpox. Selection by smallpox for resistance in humans may have coincidentally caused resistance to HIV.

Once introduced into the human body through contact with blood or other fluids, HIV targets immune system cells - CD4+ cells and T-helper cells.

T-helper cells are involved in the immune response against foreign invaders.

HIV kills immune system cells until few are left. The host then becomes incapable of defending itself against many diseases and other organisms that are normally not infectious. Such infections are called opportunistic.

HIV normally integrates into the genome of CD4 cells and remains latent for 2 to 10 years.

HIV carriers have few or no symptoms and can transmit the virus to others during latency.

HIV testing involves detection of antibodies to HIV. Only individuals infected with HIV will produce antibodies to HIV.
A mutation in the virus or a failure of the immune system results in progression to AIDS.

AIDS treatments target multiple stages of the HIV reproductive cycle: viral entry, genome replication, integration of viral DNA, and maturation of HIV proteins.

A combination therapy can be very effective and has reduced mortality rates by 75% since it began in the 1990s. This regimen must be continued to control the virus.
Influenza virus causes flu. Flu has been a persistent cause of mortality in humans. The flu pandemic of 1918-19 killed up to 50 million people in 18 months.

Influenza virus is highly variable because of mutation and recombination.

Our immune system detects and attacks the viruses through cell surface proteins (antigens). The flu virus has two antigens - H and N. New H and N antigens arise through mutation and then different viruses infecting a single organism undergo recombination to produce new strains.

Type A influenza virus has 13 distinct H variants and 9 distinct N variants. Flu vaccines must match specific variants and thus must track changes in the virus.

Different flu pandemics have been caused by different combinations of H and N variants
- Spanish flu - A(H1N1) - 1918-19 - 20-50 million killed
- Asian flu - A(H2N2) - 1957 - 100,000 Americans killed
- Hong Kong flu - A(H3N2) - 1968 - infected 50 million Americans and killed 70,000

New influenza variants can come from other organisms when those organisms live in close contact with humans.

Hong Kong flu - A(H3N2) was the result of a recombination between A(H3N8) from ducks and A(H2N2) from humans.

Bird flu - A(H5N1) - can be transmitted from birds to humans has a mortality rate of 50% but to date has not been transmitted to a human from an infected human.
Some new human viruses originate in other host species. These are called **emerging viruses**.

Hantavirus from deer mice caused deaths in humans in the southwestern US in 1993.

Ebola virus infections have only been seen in central Africa. Its source is unknown. It has mortality rates of 90%. It is currently controlled by quarantining infected individuals.

SARS - Sudden Acute Respiratory Syndrome is caused by a corona virus that likely came from civets.

Some viruses cause cancer - as much as 15% of cancers worldwide.

Hepatitis B infections can progress to liver cancer.

HPV - Human Papillomavirus - infections can progress to cervical cancer.

Viral proteins may contribute to the development of cancer through interfering with regulation of oncogenes.
Subviral particles - Viroids and Prions

**Viroids** are small circular RNA molecules that cause many diseases in plants. The mechanism of transmission and expression is not understood.

Several diseases in humans and other animals have been associated with normal proteins that have undergone abnormal folding. These proteins are called **prions**.

TSE - Transmissible Spongiform Encephalopathy - results in spongy-looking brains as a result of massive death of nerve tissue.

Called “scapie” in sheep, “mad cow disease” in cattle, “chronic wasting disease” in deer and elk, and CJD or Creutzfeldt-Jakob disease in humans are all the result of abnormally folded proteins from a single gene (PrP). PrP<sup>c</sup> is the normal, and benign form of the protein. PrP<sup>sc</sup> causes the disease.

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**PrP<sup>sc</sup>** catalyzes the abnormal folding of PrP. Introduction of PrP<sup>sc</sup> can be passed through ingestion of infected tissue.

PrP<sup>sc</sup> is very resistant to degradation and can be contracted by consumption of well-done meat.

Mice lacking the gene for PrP can not be infected by consumption of brain tissue from infected mice.