Learning Outcomes

- Define the term Virus and introduce virology
- Early development of virology
- Interpret the key characteristics of viruses
- Understand the structure
- Classification
- Biochemistry
- Reproduction of viruses
- Pathogens of clinical importance
- Current and emerging methods for the diagnosis of viral infections
- Specific applications of virology including viral vaccines and anti-viral drugs
INTRODUCTION TO VIROLOGY

- Virology is that branch of science in microbiology that deals with the detail study about viruses

- Virus in Latin means *poison*

- The existence of virus was first proved by Ivanowski in 1892

- Defined viruses as sub-microscopic, self reproducing particles capable of being introduced into living cells and reproducing inside such cells only”
IMPORTANT CHARACTERISTICS OF VIRUSES

- They are the simplest forms of life
- They are neither prokaryotes nor eukaryotes
- More than 600 viruses are known that infect humans and most of these have been identified in the last 50 years
- Viruses are too small to be seen under the light microscope
- Extremely small in size (0.01-0.4μm)—smaller than bacteria

http://static.newworldencyclopedia.org/thumb/2/24/Microscope-IMG_0518.jpg/300px-Microscope-IMG_0518.jpg
# IMPORTANT CHARACTERISTICS OF VIRUSES

- They can be observed using an electron microscope.
- Viruses cannot be cultured freely in the laboratory, except in living cells.
- Huge diversity.
- They live inside living cells.
- Cannot carry out any metabolic reactions on their own.
- They are potentially infectious.
Viral Structure

- The protein coat is known as a capsid.
- Capsid is composed of protein subunits called capsomeres.
- Capsids can have several shapes: polyhedral, rod or complex.
## Viral Structure

- Some viruses have an additional outer protective envelope.
- Viral enzymes are used in the infective process.
- Viral enzymes are not found in the host cell so are good targets for anti-viral therapy.
- They are unable to carry out any metabolic processes outside the host cell.
## Construction of an enveloped virus

- The envelope is the outer surface of the virus.
- Knowledge of the structure and properties of the outer surface of the virus are important in understanding the process of infection.
- In general, naked (envelope-free) viruses are resistant and survive well in the outside world.
- Enveloped viruses are more susceptible to environmental factors.
- These differences influence the ways in which these viruses can be transmitted.
Construction of an enveloped virus

- **nucleocapsid**
  - nucleic acid
  - capsid

- **envelope**
  - derived from host cell membranes (surface, internal, nuclear)
  - with inserted viral glycoproteins

- **glycoprotein**
- **matrix proteins**
TERMINOLOGY

- **Virions**: used to describe an entire mature virus particle consisting either of nucleic acid and capsid (naked virus) or nucleic acid, capsid and envelope (enveloped virus). Virions are found outside the host cell and are capable of transmission from one host to another.

- **Virus**: or viral particle, refers to the intracellular infectious particle consisting of nucleic acid and a protein coat.

- **Viroid’s**: infectious agents that lack a capsid and consist only of a closed circular RNA molecule. Usually plant pathogens.

- **Prions**: unusual infectious agents which appear to consist only of protein without any genetic material.
## Viruses - Classification

- Each virus has a distinct shape and structure.

- The type of genetic material found in a particular virus depends on the nature and function of the specific virus.

- The genetic material is covered by a protein coat.

- Two major divisions based on the genetic material they contain:
  - DNA viruses
  - RNA viruses
  - Single /double stranded

**INFECTION OF THE HOST CELL**

- **Viruses show host specificity.**
- **The initial basis of specificity is the ability of the virus particle to attach to the host cell.**
- **The process of attachment to, or adsorption by, a host cell depends on general intermolecular forces.**
- **In many cases, there is a specific interaction with a particular host molecule.**
INFECTION OF THE HOST CELL

- After fusion of viral and host membranes the virus particle is carried into the cytoplasm.
- The envelope and/or the capsid are shed and the viral nucleic acid released.
- The virus is now no longer infective: this 'eclipse phase' persists until new complete virus particles reform after replication.
- The way in which replication occurs is determined by the nature of the nucleic acid concerned.
Summary of the different stages involved in infection of the host cell & viral replication

<table>
<thead>
<tr>
<th>Stage</th>
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</thead>
<tbody>
<tr>
<td>Adsorption</td>
</tr>
<tr>
<td>Penetration</td>
</tr>
<tr>
<td>Un-coating</td>
</tr>
<tr>
<td>Synthesis</td>
</tr>
<tr>
<td>Assembly</td>
</tr>
<tr>
<td>Synthesised capsomeres are assembled in host cell</td>
</tr>
<tr>
<td>Release</td>
</tr>
</tbody>
</table>
Stages in the infection of a host’s cell and replication of a virus.

Several thousand virus particles may be formed from each cell.
REPLICATION

http://creationwiki.org/pool/images/0/0e/Nbt0104-31-F1.jpg
### MULTIPLICATION OF PAPOVAVIRUS – A DNA CONTAINING VIRUS

- The actual method of viral replication varies.
- The replication of dsDNA viruses essentially follows the usual pathways for nucleic acid and protein synthesis.
- The viral DNA directs the synthesis of viral messenger RNA and proteins and the assembly of the viral components into new viral particles.
MULTIPLICATION OF PAPOVAVIRUS – A DNA CONTAINING VIRUS

1. Virion attaches to host cell
2. Virion penetrates cell and its DNA is uncoated
3. Viral DNA enters nucleus, viral mRNA synthesised in nucleus
4. Viral DNA is replicated
5. Late translation; capsid proteins are synthesized
6. Assembly of new virions
7. Virions are released

Multiplication of a DNA-containing virus

From Microbiology and Infection Control for Health Professionals, (5th ed), by G. Lee & P Bishop. 2013. Frenchs Forest, NSW. Pearson Education,
### INFECTION AND REPLICATION BY VARIOUS RNA VIRUSES

- The details of replication of the different RNA viruses are quite complex.

- ssRNA viruses like retroviruses have a completely different pathway of synthesis.

- Replication initially involves a reverse process whereby viral DNA is first synthesized from the single-strand (ss) viral RNA, using a viral enzyme called reverse transcriptase.

- The viral DNA is then transcribed into viral messenger RNA, protein and new viral RNA.

The next slide illustrates the steps involved in the synthesis of a retrovirus.
INFECTION AND REPLICATION BY VARIOUS RNA VIRUSES
# TERMS – REPLICATION OF HIV

- **Reverse transcriptase** – an enzyme found in HIV that creates double stranded DNA using viral RNA as a template and host tRNA as primers

- **Integrase** – An enzyme found in retroviruses including HIV that permits the viral DNA to be integrated into the DNA of the infected cell

- **Genomic RNA** – the nucleic acid that contains all of the hereditary information of a virus, and is found in a mature virion

- **gp120** – an HIV glycoprotein having a molecular weight of 120 kilodaltons that protrudes from the outer surface of the virion. This glycoprotein binds to a CD4 receptor on a T cell to facilitate entry of viral nucleic acid and proteins into the cell

- **Protease** – an enzyme that hydrolyzes or cuts proteins and is important in the final steps of HIV maturation
The HIV replication cycle:

The virus enters the cell either by fusion with the cell membrane at the cell surface or via uptake into a vacuole and release within the cell.
INFECTION OF HOST CELLS

- Virus particles enter the body of the host in many ways

- The most common methods of transmission:
  - Inhaled droplets
  - Food or water
  - Direct transfer
  - Vector arthropods
Viral infections

- Health professionals need to understand:
  - The characteristics of viral infection in humans
  - The outcome for the human
  - The implications for transmission, treatment and prevention
  - The mechanisms of viral replication

- Understanding these factors and the course of viral diseases can aid in the development of suitable treatments or preventative methods
Types of Viral Infections

Acute lytic infection

Virus infects host cell, new viruses are created, host cell dies, virus spreads to neighbouring host cells
TYPES OF VIRAL INFECTIONS

Subclinical infection

- No recognisable symptoms.
- General malaise.
- Occasional serious side effects.
- Mild in adult but can cause congenital defects.
- EBV, Polio, Hepatitis B and C can also occur subclinically with consequences.
Types of Viral Infections

**Latent viral infections**

- Virus remains dormant in some of host cells and can be reactivated later
- Common in herpes family of viruses
- Initial disease symptoms followed by apparent recovery but not all viruses are cleared
- Examples include herpes simplex type I and 2, *Varicella zoster* (Chicken pox and Shingles)
TYPES OF VIRAL INFECTIONS

Chronic viral infections

- Virus remains in host and produces at low levels - the carrier state
- Can occur after an acute illness or subclinical infection
- Examples: Hepatitis B, HIV
# Viruses and Cancer: A Link

<table>
<thead>
<tr>
<th>Virus</th>
<th>Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epstein-Barr virus</td>
<td>♦ Burkitt's lymphoma</td>
</tr>
<tr>
<td></td>
<td>♦ Certain nose and throat cancers</td>
</tr>
<tr>
<td></td>
<td>♦ B-cell lymphomas in people with a weakened immune system (such as those with AIDS)</td>
</tr>
<tr>
<td>Hepatitis B and C viruses</td>
<td>Liver cancer</td>
</tr>
<tr>
<td>Herpesvirus 8</td>
<td>♦ Kaposi's sarcoma in people with AIDS</td>
</tr>
<tr>
<td></td>
<td>♦ Non-Hodgkin lymphoma in people with AIDS</td>
</tr>
<tr>
<td>Human papillomavirus</td>
<td>Cervical cancer</td>
</tr>
</tbody>
</table>
VIRUSES AND CANCER: A LINK – ONCOGENIC VIRUSES

Some viruses alter the DNA of their host cells in a way that helps cancer develop. As a result of the alteration the host cell loses control of replication.

Only a few viruses are known to cause cancer, but there may be others.

Burkitt’s Lymphoma Cancer
http://www.thachers.org/images/Noma.jpg

Kaposi’s Sarcoma
http://0.tqn.com/d/menshealth/1/0/h/blkaposi_photo2.jpg

Cervical Cancer
Viral Infections in Humans

- Some viral infections are asymptomatic
- Viruses have particular cells that they can infect
- Not all viruses are capable of attaching to all types of animal cells- there is a very defined host specificity
- The same apparent disease symptoms can be caused by more than one type of virus: e.g. the common cold is caused by Adenoviruses, Rhinoviruses, Parainfluenza viruses, Enteroviruses etc.
## Viruses of Medical Importance

- **Rhinoviruses, Adenoviruses**: common cold
- **Arbovirus, Herpes virus**: encephalitis
- **Rotavirus and Enterovirus**: gastroenteritis
- **EBV**: infectious mononucleosis (glandular fever)
- **Hepatitis A-E**: hepatitis
- **HIV**: AIDS
- **Varicella zoster**: chicken pox and shingles
- **Enteroviruses and Varicella**: meningitis
- **Rubella**: German measles
- **Papilloma**: warts
Examples - Viruses - Diseases

- Picornavirus
- Astrovirus
- Calcivirus
- Flavivirus
- Togavirus
- Coronavirus

- Retrovirus
- Reovirus
- Bunyavirus
- Orthomyxovirus
- Arenavirus

- Filovirus
- Rhabdovirus
- Paramyxovirus
- Hepadnavirus
- Papovavirus
PATHOGENESIS OF THE COMMON COLD

In the **first step**, viral particles start to attach to the nasal epithelium.

In the **second step**, viral particles get adsorbed on the cilia present on the nasal epithelium.

In the **third step**, viral particles start to replicate inside the host cell.
PATHOGENESIS OF THE COMMON COLD

Step 5
Host defence mechanisms then get activated

Step 4
- After virus starts to replicate
- Cells get damaged
- Infection spreads and Virus is shed
PATHOGENESIS OF THE COMMON COLD

Step 6
Host defence mechanisms then get activated

Step 7
- Recovery
- through interferon and antibody production
The pathogenesis of mumps

- silent entry into respiratory tract
  - spread to local lymph nodes
  - primary viremia
    - spread to salivary glands, testes, ovaries, pancreas, central nervous system
      - viremia
    - generalized spread to salivary and other glands, and to other body sites including the kidneys
      - viremia
Deaths due to avian flu.

- **Hong Kong, 1997-2003**
- **Thailand, 2004-2005**
Early spread of HIV infection (now worldwide). HIV-1 may have been present in central Africa for many years before increased migration and socioeconomic upheaval caused it to begin spreading in the late 1970s. Outside Africa, most infections occurred in men.
The clinical features and progression of untreated HIV infection
Contamination of shellfish by hepatitis A virus (HAV) can lead to human infection

Pathogenesis of cold sores and zoster

In both herpes simplex virus and varicella-zoster virus infections, the virus (in mucocutaneous nerve endings) travels up the axon to reach the sensory neurons, where it becomes latent.
Recurrences are due to reactivation of the virus within the neurone to become infectious followed by passage of virus down the axon to mucocutaneous site(s) and local spread and replication to form clinical lesion(s)
The pathogenesis of rubella. Rubella is generally a very mild, often subclinical infection, but it can cause arthritis and has a major impact when it infects the fetus.
Examples of Viral Infections

- Chicken pox
- Enlarged lymph nodes in Glandular Fever
- Tonsillitis in Glandular Fever


http://olddoc.tmu.edu.tw/pinging/teach/images/inf/lymphnode1.JPG

http://www.naturheilpraxis-hollmann.de/TonsillitisP.jpg
Influenza virus budding from the surface of an infected cell

Rhinovirus

Electron micrograph of an HIV particle
DIAGNOSIS

- Common viral infections may be diagnosed based on symptoms
- Infections that occur in epidemics can help identify the infection
- Blood tests and cultures may be done
- Blood may be tested for antibodies

Computer generated Virology Results

http://ari.ucsf.edu/images/features/zoila.jpg
DIAGNOSIS

- Polymerase chain reaction (PCR)
- Tests are sometimes done quickly for public safety
- A sample of blood or other tissues is sometimes examined with an electron microscope
### TREATMENT

- **Antiviral drugs**
  - Many antiviral drugs work by interfering with replication of viruses.
  - Antiviral drugs target some metabolic functions.
  - Antiviral drugs are much more difficult to develop than antibacterial drugs.
  - Antiviral drugs can be toxic to human cells.
  - Viruses can develop resistance to antiviral drugs.
TREATMENT

- Other antiviral drugs strengthen the immune response to the viral infection

- These drugs include several types of interferons, immunoglobulins, and vaccines
  - **Interferon** drugs are replicas of naturally occurring substances that slow or stop viral replication
  - **Immune globulin** is a sterilized solution of antibodies (also called immunoglobulins) collected from a group of people
  - **Vaccines** are materials that help prevent infection by stimulating the body's natural defense mechanisms
TREATMENT

- Many immune globulins and vaccines are given before exposure to a virus to prevent infection.

- Some immune globulins and some vaccines, such as those for rabies and hepatitis B, are also used after exposure to the virus to help prevent infection from developing or reduce the severity of infection.

- Immune globulins may also help treat some established infections and also prevent infection after future exposures to the virus.
ADMINISTRATION – TREATMENT OPTIONS

- Most antiviral drugs can be given by mouth. Some can also be given by injection into a vein (intravenously) or muscle (intramuscularly).

- Some are applied as ointments, creams, or eye drops or are inhaled as a powder.

- Antibiotics are not effective against viral infections, but if a person has a bacterial infection in addition to a viral infection, an antibiotic is often necessary.
## Important drugs - examples

<table>
<thead>
<tr>
<th>Drug</th>
<th>Condition</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acyclovir</td>
<td>♦ Genital herpes ♦ Herpes zoster (shingles) ♦ Chickenpox</td>
<td>Few serious side effects</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Nausea</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Vomiting</td>
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<tr>
<td></td>
<td></td>
<td>• Diarrhea</td>
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<td></td>
<td></td>
<td>• Headache</td>
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<tr>
<td></td>
<td></td>
<td>• Rashes</td>
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<tr>
<td></td>
<td></td>
<td>• Kidney damage (rare)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Confusion (rare)</td>
</tr>
<tr>
<td>Amantadine</td>
<td>♦ Influenza A</td>
<td>• Nausea or loss of appetite</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Nervousness</td>
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<tr>
<td></td>
<td></td>
<td>• Light-headedness</td>
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<tr>
<td></td>
<td></td>
<td>• Unsteadiness</td>
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<tr>
<td></td>
<td></td>
<td>• Sleeplessness</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Confusion</td>
</tr>
</tbody>
</table>
## IMPORTANT DRUGS - EXAMPLES

<table>
<thead>
<tr>
<th>Drug</th>
<th>Condition</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Famiclovir</td>
<td>• Genital herpes</td>
<td>Few serious side effects</td>
</tr>
<tr>
<td></td>
<td>• Herpes zoster (shingles)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Chickenpox</td>
<td></td>
</tr>
<tr>
<td>Interferon-alpha</td>
<td>• Hepatitis B and C</td>
<td>• Flu-like symptoms</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Depression</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Low white blood cell count</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Anemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Low platelet count</td>
</tr>
<tr>
<td>Penciclovir (cream)</td>
<td>• Cold sores</td>
<td>• Few side effects</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Headache</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Mild burning or stinging at the site of application</td>
</tr>
<tr>
<td>Trifluridine (eye drops)</td>
<td>• Herpes simplex infection of the cornea (keratitis)</td>
<td>• Stinging of the eyes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Swelling of the eyelids</td>
</tr>
</tbody>
</table>
### Viral diseases for which vaccines are available

<table>
<thead>
<tr>
<th>Disease</th>
<th>Recommended Schedule in Australia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chicken Pox</td>
<td>Recommended for health care workers and at risk individuals</td>
</tr>
<tr>
<td>Hep A</td>
<td>Three doses: Two I month apart, and a booster at any age</td>
</tr>
<tr>
<td>Hep B</td>
<td>Three doses: 1, 2 &amp; 6 mths apart, can be given at any age</td>
</tr>
<tr>
<td>Influenza</td>
<td>Different vaccine produced each year for prevalent strain. Recommended for elderly and ‘at risk’ patients</td>
</tr>
<tr>
<td>Measles</td>
<td>MMR: two doses, 12 months and 4 years</td>
</tr>
<tr>
<td>Mumps</td>
<td>MMR: two doses, 12 months and 4 years</td>
</tr>
<tr>
<td>Rubella</td>
<td>MMR: two doses, 12 months and 4 years. Booster may be required before becoming pregnant. Antibody titre should be checked</td>
</tr>
<tr>
<td>Polio</td>
<td>Sabin oral vaccine (OPV): 2, 4 &amp; 6 mths; booster at 18 mths, 5, 15 yrs</td>
</tr>
<tr>
<td>Rabies</td>
<td>Usually only after exposure to rabies virus, or bat lyssavirus</td>
</tr>
<tr>
<td>Yellow Fever</td>
<td>Recommended when travelling to endemic countries</td>
</tr>
</tbody>
</table>
### FUTURE DEVELOPMENTS

1. Improved adjuvants
2. Improved existing vaccines
3. Live vaccines for respiratory viruses
4. Antigens prepared by recombinant DNA technology
5. Viral vector vaccines
6. DNA vaccines
Readings and Resources

Resources:

- **Set Textbooks:**

- **Additional textbooks:**
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