General Virology

- History
- Viruses
- Virion
- Size and Shape
- Structure
- Replication
- Viral Variation
- Classification
Viruses – Early History

- 18 Century – smallpox, Edward Jenner
- 1840 Jacob Henel, plant viruses
- 1892 TMV – Ivanowski
- 1898 Foot and Mouth disease – Loeffler & Frosch
- 1901 yellow fever, Walter Reed
- 1917 Bacteriophages F.W.Twort
Viral Properties

• Viruses are inert (nucleoprotein) filterable Agents
• Viruses are obligate intracellular parasites
• Viruses cannot make energy or proteins independent of a host cell
• Viral genome are RNA or DNA but not both.
• Viruses have a naked capsid or envelope with attached proteins
• Viruses do not have the genetic capability to multiply by division.
• Viruses are non-living entities
Virion

- Envelope
- Capsid
- Viral core
Cross Section of Enveloped Virus
Comparison of Naked and Enveloped Virus Particles

Naked virus
- Capsid (composed of capsomers)
- Nucleic acid

Enveloped virus
- Capsid
- Nucleic acid
- Envelope

Figure 10.3
Virus Structure

Types of Symmetry of Virus Particles

• Icosahedral symmetry (Cubic Symmetry)
• Helical symmetry

Complex Structures (Complex Virion)
Complex Symmetry: Poxvirus
Icosahedral Viruses
Icosahedral Symmetry: Adenovirus Virion
Cubic or icosahedral symmetry
Icosahedral capsids

a) Crystallographic structure of a simple icosahedral virus.

b) The axes of symmetry
Helical symmetry
Helical Symmetry: Parainfluenzavirus
Enveloped helical virus  Enveloped icosahedral virus
Chemical Composition of Viruses

- Viral Nucleic Acid
- Viral Protein
- Viral Lipid Envelopes
- Viral Glycoproteins
Reaction to Physical & Chemical Agents

Heat & Cold
There is great variability in the heat stability of different viruses. Icosahedral viruses tend to be stable, losing little infectivity after several hours at 37 °C. Enveloped viruses are much more heat-labile, rapidly dropping in titer at 37 °C. Viral infectivity is generally destroyed by heating at 50–60 °C for 30 minutes, though there are some notable exceptions (e.g., hepatitis B virus, polyomaviruses).

Stabilization of Viruses by Salts
Many viruses can be stabilized by salts in concentrations of 1 mol/L; i.e., the viruses are not inactivated even by heating at 50 °C for 1 hour. The mechanism by which the salts stabilize viral preparations is not known. Viruses are preferentially stabilized by certain salts. MgCl\(_2\), 1 mol/L, stabilizes picornaviruses and reoviruses; MgSO\(_4\), 1 mol/L, stabilizes orthomyxoviruses and paramyxoviruses; and Na\(_2\)SO\(_4\), 1 mol/L, stabilizes herpesviruses.
pH
Viruses are usually stable between pH values of 5.0 and 9.0.

Radiation
Ultraviolet, x-ray, and high-energy particles inactivate viruses. The dose varies for different viruses.

Photodynamic Inactivation
Viruses are penetrable to a varying degree by vital dyes such as toluidine blue, neutral red, and proflavine. These dyes bind to the viral nucleic acid, and the virus then becomes susceptible to inactivation by visible light.

Ether Susceptibility
Ether susceptibility can be used to distinguish viruses that possess an envelope from those that do not.
Detergents
Nonionic detergents—eg, NP40 and Triton X-100—solubilize lipid constituents of viral membranes. The viral proteins in the envelope are released (undenatured). Anionic detergents, eg, sodium dodecyl sulfate, also solubilize viral envelopes; in addition, they disrupt capsids into separated polypeptides.

Formaldehyde
Formaldehyde destroys viral infectivity by reacting with nucleic acid. Formaldehyde has minimal adverse effects on the antigenicity of proteins and therefore has been used frequently in the production of inactivated viral vaccines.
Virus Replication
The Lytic Replication Cycle

- Attachment
- Penetration
- Uncoating
- Macromolecular Synthesis
- Maturation (Assembly)
- Release
### Examples of Viral Receptors on Host Cells

<table>
<thead>
<tr>
<th>Receptor</th>
<th>Virus</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICAM-1</td>
<td>Rhinovirus</td>
</tr>
<tr>
<td>CD4</td>
<td>HIV</td>
</tr>
<tr>
<td>acetylcholine</td>
<td>rabies</td>
</tr>
<tr>
<td>EGF</td>
<td>vaccinia</td>
</tr>
<tr>
<td>CR2/CD21</td>
<td>Epstein-Barr</td>
</tr>
<tr>
<td>Heparan sulfate</td>
<td>Herpes simplex</td>
</tr>
<tr>
<td>Sialic acid</td>
<td>Influenza</td>
</tr>
</tbody>
</table>
Enveloped Virus

PEPLOMER
Specificity of Attachment
Ionic Binding Attachment
Proteolysis Prevents Attachment
Penetration

• Penetration - The process by which a virus penetrates the cell’s membrane barriers and gains access to the cytoplasm.

• Two basic processes:
  – *Direct penetration* of the plasma membrane
  – *Endocytosis* and subsequent penetration of the endocytic vesicle membrane

• For enveloped viruses, penetration usually involves a membrane *fusion* step.

• Penetration by nonenveloped viruses is less well understood.

• *Coreceptors* may be involved in penetration.
Methods of Viral Penetration

1. Virus Particle
2. Coated Pit
3. Lysosome
4. Fusion of Viral and Lysosomal Membrane
5. Ejection of Nucleo Capsid
Receptor-mediated endocytosis of poliovirus
Uncoating

- Uncoating is the process by which the viral genome is released from the nucleocapsid into the cytoplasm.
- This allows the genome to begin to function either in the cytoplasm or in the nucleus of the infected cell.
- Closely linked to Penetration.
Macromolecular Synthesis

• Viral gene expression
  – **Pre-early or immediate early genes** (complex DNA viruses): Cell cycle disruption, activation of other viral genes.
  – **Early genes**: genome replication and other functions.
  – **Late genes**: viral structural proteins

• Viral genome replication
  – Various replication mechanisms are used, depending on genome type (RNA or DNA), replication location (nucleus or cytoplasm) and type of virus.

• **Host macromolecular synthesis** is inhibited by most, but not all viruses.
Replication of RNA viruses

RNA-directed RNA transcription
1. Binding of virus to cell
2. Cell engulfs virus via endocytosis
3. Membrane of virus fuses with endosome; RNA released into cell
4. Viral polymerase produces mRNA from viral RNA
5. Protein, new RNA produced
6. Self-assembly produces virions
7. Virions bud off cell membrane
Morphogenesis (Assembly)

• The process of assembling new virions from virion subunits.
• Occurs in **nucleus or cytoplasm**, depending on virus type.
• Enveloped viruses usually acquire membranes by **budding through a cellular membrane**.
• “**Self-assembly**” - Components of many smaller viruses will spontaneously assemble into virions. Assembly of large or complex virions requires energy (ATP) and/or assembly proteins.
Maturation

• Self Assembly
  – Capsid protein
    Aggregation into stable state around nucleic acid
Assembly

Assembly of phage P22 capsid (procapsid)

Capsid maturation by insertion of the viral DNA
Release

• Release - Process by which progeny virions are released from the host cell.
• Viruses budding from the plasma membrane - these are released as part of the assembly process.
• Viruses assembled intracellularly - may utilize cellular secretory pathways (e.g., herpesviruses) or may depend on cell disruption (lysis) for release.
• Mechanisms responsible for lysis are not well understood.
Maturation and Budding of Enveloped Virion
• **Release**
  – Newly formed viruses are released to the outside environment upon lysis (*lytic viruses*)
  – Latent eukaryotic viruses
  – Why don’t viruses get stuck on the cellular receptors as they are released from the host cell?
    • Neuraminidase

*Measles virus released by budding*
Viral Cell Infections

- Lytic Infection (cytocidal Infection)
- Persistent Infection
- Latent Infection
- Transforming Infection
- Abortive Infection
Possible Effects that Animal Viruses May Have on Cells

Figure 10.22
Virus Replication at the Organism Level

- Virus Entry
- Virus Spread
- Cell Injury
- Host Response
- Virus Shedding
Manifestations of Viral Infections

- Asymptomatic
- Acute viral syndrome (influenza, rhinovirus, etc)
- Persistent viral syndrome (EBV)
- Chronic infection
  - Reactivating (HSV-1/2, VZV (chicken pox/shingles))
  - Progressive (HBV, HCV, HIV)
- Cancer (EBV, HPV-16, HBV, HCV, KSHV)
- Death (HIV, et al)
- Acute death (smallpox, Ebola, SARS)
Virus Entry and Primary Replication

• **Portal of Entry** - site where virus enters the body
  - Skin
  - Respiratory Tract
  - Gastrointestinal tract
  - Genital tract
  - Conjunctiva (eyes)
  - Crossing the placenta

• **Primary replication** - local replication near the portal of entry. Some infections remain local, others spread to various target organs.
Routes of Virus Transmission
# Common Routes of Viral Infection in Humans

<table>
<thead>
<tr>
<th>Route of Entry</th>
<th>Virus Group</th>
<th>Produce Local Symptoms at Portal of Entry</th>
<th>Produce Generalized Infection Plus Specific Organ Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild trauma</td>
<td>Papillomavirus</td>
<td>Most types</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Herpesvirus</td>
<td>Herpes simplex virus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Poxvirus</td>
<td>Molluscum contagiosum virus, orf virus</td>
<td></td>
</tr>
<tr>
<td>Injection</td>
<td>Hepadnavirus</td>
<td>Hepatitis B</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Herpesvirus</td>
<td>Epstein-Barr virus, cytomegalovirus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Retrovirus</td>
<td>Human immunodeficiency virus</td>
<td></td>
</tr>
<tr>
<td>Bites</td>
<td>Togavirus</td>
<td>Many species, including eastern equine encephalitis virus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Flavivirus</td>
<td>Many species, including yellow fever virus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rhabdovirus</td>
<td>Rabies virus</td>
<td></td>
</tr>
</tbody>
</table>
Portals of Entry for Pathogens

• Skin
  – Impenetrable (for the most part)
    » Not true if skin is broken
  – Hair follicles and sweat gland ducts (many of which have antimicrobial oils associated with them)
  – Parenteral route: When there is a break in the skin, the skin can be penetrated
  – Vaccinations
  – Insect bites
  – Animal bites
<table>
<thead>
<tr>
<th>Route of Entry</th>
<th>Virus Group</th>
<th>Produce Local Symptoms at Portal of Entry</th>
<th>Produce Generalized Infection Plus Specific Organ Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory tract</td>
<td>Parvovirus</td>
<td></td>
<td>B19</td>
</tr>
<tr>
<td></td>
<td>Adenovirus</td>
<td>Most types</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Herpesvirus</td>
<td>Epstein-Barr virus, herpes simplex virus</td>
<td>Varicella virus</td>
</tr>
<tr>
<td></td>
<td>Poxvirus</td>
<td></td>
<td>Smallpox virus</td>
</tr>
<tr>
<td></td>
<td>Picornavirus</td>
<td>Rhinoviruses</td>
<td>Some enteroviruses</td>
</tr>
<tr>
<td></td>
<td>Togavirus</td>
<td></td>
<td>Rubella virus</td>
</tr>
<tr>
<td></td>
<td>Coronavirus</td>
<td>Most types</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Orthomyxovirus</td>
<td>Influenza virus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Paramyxovirus</td>
<td>Parainfluenza viruses, respiratory syncytial virus</td>
<td>Mumps virus, measles virus</td>
</tr>
<tr>
<td>Mouth, intestinal tract</td>
<td>Adenovirus</td>
<td>Some types</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Herpesvirus</td>
<td>Epstein-Barr virus, herpes simplex virus</td>
<td>Cytomegalovirus</td>
</tr>
<tr>
<td></td>
<td>Picornavirus</td>
<td></td>
<td>Some enteroviruses, including poliovirus and hepatitis A virus</td>
</tr>
<tr>
<td></td>
<td>Reovirus</td>
<td>Rotaviruses</td>
<td></td>
</tr>
</tbody>
</table>
Portals of Entry

- Genitourinary tract
  - For STDs
  - Broken (parenteral route) or unbroken membranes (depends on the microbe)
  - Ex. HIV, Genital warts, Herpes

<table>
<thead>
<tr>
<th>TABLE 6-5</th>
<th>Examples of STDs Caused by Viruses</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Virus</strong></td>
<td><strong>Symptoms/Disease</strong></td>
</tr>
<tr>
<td>HIV-1 and HIV-2</td>
<td>AIDS</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Liver damage, possibly cancer</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>Liver damage, possibly cancer</td>
</tr>
<tr>
<td>Herpes simplex-2</td>
<td>Herpetic lesions of cervix and urethra</td>
</tr>
<tr>
<td>Papillomavirus</td>
<td>Genital warts, possibly cancer</td>
</tr>
</tbody>
</table>
Portals of Entry

• Conjunctiva
  – Epithelium covering the inner surface of the eyelid and the outer surface of the eye
  – Rare route
  – Injury to eyes
Viral Infections of the Eyes

Figure 6.5a: The conjunctiva of the eye.

Figure 6.5b: The pseudomembrane that can develop with EKC.
Virus Spread

• Systemic spread occurs by two major routes:
  – **Viremia** - Spread of virus through the blood
    • Cell-associated virus
    • Free virions
    • Many target organs possible
  – **Nervous system**
    • Target organs are usually the PNS or CNS
Mechanisms of Viral Spread of Pathogenesis

- Replication and infections within the host
  - Localized infections
  - Primary viremia
  - Systemic infections—lymph vessels

**TABLE 6-9**  Viruses That Cause Localized Infections

<table>
<thead>
<tr>
<th>Virus</th>
<th>Primary Replication Site</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhinovirus</td>
<td>Upper-respiratory tract</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>Intestinal epithelium</td>
</tr>
<tr>
<td>Papillomavirus (warts)</td>
<td>Epidermis</td>
</tr>
</tbody>
</table>

**TABLE 6-10**  Viruses That Cause Systemic Infections

<table>
<thead>
<tr>
<th>Virus</th>
<th>1º Replication</th>
<th>2º Replication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterovirus</td>
<td>Intestinal epithelium</td>
<td>Lymphoid tissues, CNS</td>
</tr>
<tr>
<td>HSV-2</td>
<td>Urogenital tract</td>
<td>Lymphoid cells, CNS</td>
</tr>
<tr>
<td>HSV-1</td>
<td>Oropharynx (the throat, including the tonsils)</td>
<td>Lymphoid cells, CNS</td>
</tr>
</tbody>
</table>
## Important Features of Acute Viral Diseases

<table>
<thead>
<tr>
<th></th>
<th>Local Infections</th>
<th>Systemic Infections</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Specific disease example</strong></td>
<td>Respiratory (rhinovirus)</td>
<td>Measles</td>
</tr>
<tr>
<td><strong>Site of pathology</strong></td>
<td>Portal of entry</td>
<td>Distant site</td>
</tr>
<tr>
<td><strong>Incubation period</strong></td>
<td>Relatively short</td>
<td>Relatively long</td>
</tr>
<tr>
<td><strong>Viremia</strong></td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td><strong>Duration of immunity</strong></td>
<td>Variable—may be short</td>
<td>Usually lifelong</td>
</tr>
<tr>
<td><strong>Role of secretory antibody (IgA) in resistance</strong></td>
<td>Usually important</td>
<td>Usually not important</td>
</tr>
</tbody>
</table>
Figure 6.12: Pathogenesis of Varicella zoster virus (causes chickenpox)

General patterns of infection

- Acute infection
  - Rhinovirus
  - Rotavirus
  - Influenza virus

- Persistent infection
  - Lymphocytic choriomeningitis virus

- Latent, reactivating infection
  - Herpes simplex virus

- Slow virus infection
  - Measles SSPE
  - Human immunodeficiency virus

Clinical latency
Virus Exit *Shedding*

• How do viruses get from one host to another?
• Viruses usually shed through routes of entry
  – Mucus
  – Saliva
  – Semen
  – Feces
  – Skin abrasions
  – Breast milk
  – Cervical secretions
  – Urine
  – Viremia—blood
Viral Immunology

- Non-Specific Immunity (Innate Immunity)
  - NK Cells
  - Type I interferons

- Specific Immunity
  - Humoral immunity
  - Cell mediated immunity
NK Cells

- Develop in the bone marrow from the common lymphoid progenitor cell and circulate in the blood
- **Antiviral Functions of NK cells**
  - Cytotoxicity activated by:
    - Arenaviruses (lymphocytic choriomeningitis virus),
    - Herpesviruses (herpes simplex virus)
    - Orthomyxoviruses (influenza virus)
    - Picornaviruses (coxsackie virus)
    - Protozoan parasite *Leishmania*
    - Bacterium *Listeria monocytogenes*
NK Cell Activity

Develop in the bone marrow from the common lymphoid progenitor

Have cytoplasmic granules

Can kill certain tumor cell lines in vitro

Mechanism of killing same as that used by cytotoxic T cells
Interaction of NK cell with uninfected healthy cell

NK cell

lytic granules

inhibitory receptor

activating receptor

MHC class I

ligand

Healthy cell

No killing of healthy cell

Interaction of NK cell with target cell in which MHC class I expression is lost

NK cell

Virus-infected cell (no MHC class I)

Killing of virus-infected cell in which MHC class I expression is inhibited

Figure 8-32 The Immune System, 2/e (© Garland Science 2005)
Interferons are small proteins released by macrophages, lymphocytes, and tissue cells infected with a virus. When a tissue cell is infected by a virus, it releases interferon. Interferon will diffuse to the surrounding cells. When it binds to receptors on the surface of those adjacent cells, they begin the production of a protein that prevents the synthesis of viral proteins. This prevents the spread of the virus throughout the body.

- Three types of interferons: IFN-α, IFN-β, IFN-γ
## Properties of Human Interferon

<table>
<thead>
<tr>
<th>Property</th>
<th>Alpha</th>
<th>Beta</th>
<th>Gamma</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Current nomenclature</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Former designation</strong></td>
<td>Leukocyte</td>
<td>Fibroblast</td>
<td>Immune interferon</td>
</tr>
<tr>
<td><strong>Type designation</strong></td>
<td>Type I</td>
<td>Type I</td>
<td>Type II</td>
</tr>
<tr>
<td><strong>Number of genes that code for family</strong></td>
<td>20</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>Principal cell source</strong></td>
<td>Most cell types</td>
<td>Most cell types</td>
<td>Lymphocytes</td>
</tr>
<tr>
<td><strong>Inducing agent</strong></td>
<td>Viruses; dsRNA</td>
<td>Viruses; dsRNA</td>
<td>Mitogens</td>
</tr>
<tr>
<td><strong>Stability at pH 2.0</strong></td>
<td>Stable</td>
<td>Stable</td>
<td>Labile</td>
</tr>
<tr>
<td><strong>Glycosylated</strong></td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Introns in genes</strong></td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Chromosomal location of genes</strong></td>
<td>9</td>
<td>9</td>
<td>12</td>
</tr>
<tr>
<td><strong>Size of secreted protein (number of amino acids)</strong></td>
<td>165</td>
<td>166</td>
<td>143</td>
</tr>
<tr>
<td><strong>IFN receptor</strong></td>
<td>IFNAR</td>
<td>IFNAR</td>
<td>IFNGR</td>
</tr>
<tr>
<td><strong>Chromosomal location of IFN receptor genes</strong></td>
<td>21</td>
<td>21</td>
<td>6</td>
</tr>
</tbody>
</table>
Mechanism of action of interferon

Interferon induced
Latent enzymes +
Product of
Virus infection →
Active enzymes

<table>
<thead>
<tr>
<th>Protein kinase PKR (inactive)</th>
<th>2',5' oligoadenylate synthetase (inactive)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phosphorylated PKR (active)</td>
<td>2',5' oligoadenylate synthetase (active)</td>
</tr>
<tr>
<td>Initiation factor elf - 2α</td>
<td>ATP</td>
</tr>
<tr>
<td>Phosphorylated elf - 2α</td>
<td>2',5' oligo adenylates → AMP</td>
</tr>
<tr>
<td>Phosphatase</td>
<td>Ribonuclease L (inactive)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Inhibition of initiation of translation</th>
<th>Inhibits initiation of translation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Degrades mRNA and rRNA</td>
<td>RNase L (active)</td>
</tr>
</tbody>
</table>

Inhibition of Protein synthesis
Humoral immunity

- Antibody: antigen-binding immunoglobulin (protein), produced by B cells; functions as the effector in an immune response.
B cell/Helper T cell/Plasma cell

- B-cell receptor (BCR)
- B cell
- Helper T cell
- Plasma cell
- Mitosis and Differentiation
- Lymphokines
- Antibodies
- Secretion
Types of cells: B Cells

- **B cells (B lymphocytes):** the humoral immune system and in the bone marrow until maturation.
Antigen /Antibody Connection

- Foreign molecules, or antigens, carry distinctive markers, characteristic shapes called epitopes that protrude from their surfaces.

- Our Immune system has the ability to recognize many millions of distinctive non-self molecules, and to respond by producing molecules, or antibodies - also cells - that can match and counter each one of the non-self molecules.
Complement System

- These complement proteins help the antibodies destroy bacteria.
- The diagram shows the C1 encountering an antibody bound to an antigen.
  The end product punctures the cell membrane of the target cell.
cell mediated Immunity

T cell-mediated response to viruses

Principal mediator is the CTL or the activated CD8\(^+\) T cell

TCR/CD3 + CD8

IFN-\(\gamma\) and TNF-\(\alpha\)

MHC-peptide

Viral infected Epithelial cell
Lethal Hit

Granule exocytosis a perforin-mediated lysis

Perforin creates osmotic defects

Lysis of targets

Ca^{2+} + H_{2}O

CD8+ CTL
Granzyme-mediated killing

Granule exocytosis
entry of granzymes
activation of caspases
apoptosis of target

Granzymes enter
through perforin
holes
activation of caspases

Apoptosis and
osmotic lysis of
cell

CD8+ CTL
Role of T\textsubscript{H} cells in viral clearance

CD\textsuperscript{4}+ helper T cell

CD\textsuperscript{8}+ T cell

cytokines

MHC Class II

MHC Class I

CD40L

CD40
Antibody-dependent cell mediated cytotoxicity (ADCC)

- Antibody-dependent cell mediated cytotoxicity (ADCC)
- NK cell
- FcγRIII (CD16)
- Activation and Expression of IFN-γ
- Viral protein
Types of Viral Vaccines

1. **Attenuated Vaccine**: Live, weakened form of the virus particles

2. **Inactivated Vaccine**: Virus particles are grown then killed by either heat or formaldehyde

3. **Recombinant Vaccine**: Only given antigen of virus
## Comparison of Characteristics of Killed and Live Viral Vaccines

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Killed Vaccine</th>
<th>Live Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of doses</td>
<td>Multiple</td>
<td>Single</td>
</tr>
<tr>
<td>Need for adjuvant</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Duration of immunity</td>
<td>Shorter</td>
<td>Longer</td>
</tr>
<tr>
<td>Effectiveness of protection (more closely mimics natural infection)</td>
<td>Lower</td>
<td>Greater</td>
</tr>
<tr>
<td>Immunoglobulins produced</td>
<td>IgG</td>
<td>IgA and IgG</td>
</tr>
<tr>
<td>Mucosal immunity produced</td>
<td>Poor</td>
<td>Yes</td>
</tr>
<tr>
<td>Cell-mediated immunity produced</td>
<td>Poor</td>
<td>Yes</td>
</tr>
<tr>
<td>Residual virulent virus in vaccine</td>
<td>Possible</td>
<td>No</td>
</tr>
<tr>
<td>Reversion to virulence</td>
<td>No</td>
<td>Possible</td>
</tr>
<tr>
<td>Excretion of vaccine virus and transmission to nonimmune contacts</td>
<td>No</td>
<td>Possible</td>
</tr>
<tr>
<td>Interference by other viruses in host</td>
<td>No</td>
<td>Possible</td>
</tr>
<tr>
<td>Stability at room temperature</td>
<td>High</td>
<td>Low</td>
</tr>
</tbody>
</table>
A flu virus contains eight gene segments. The goal is to combine the desired HA and NA genes from flu strain 1 with the six other genes from flu strain 2, which grows well in eggs and is harmless in humans.

1. After removing the dangerous part of the HA gene, scientists splice the HA and NA genes from flu strain 1 into circular pieces of DNA called plasmids.

2. Additional plasmids are created using the remaining six genes found in flu strain 2.

3. Scientists insert the HA and NA plasmids from flu strain 1 and the six plasmids carrying genes from flu strain 2 into animal cells growing in the laboratory.

4. The genes in the plasmids instruct the animal cells to make the desired new flu strain.
Targets for Antiviral Drugs

• Any of the 6 stages of the virus life cycle can be targeted for antiviral intervention:
  – 1. Attachment
  – 2. Penetration
  – 3. Uncoating
  – 4. Synthesis
  – 5. Assembly
  – 6. Release
Attachment

immune globulin

- HAV
- HBV
- VZV
- Rabies
- CMV
Penetration & Uncoating

Amantadine

Rimantadine

- Interfere with the function of the transmembrane domain of the M2 protein of influenza A viruses
- Decrease the release of influenza A viral particles into the host cell
Synthesis

- Interferon
- Nucleoside Analogs
  - ACYCLOVIR
  - Gancyclovir
  - Ribavirin
  - Idoxuridine
  - Trifluorothymididine
  - Vidarabine
  - Foscarnet
HIV treatment

- Nucleoside reverse transcriptase inhibitors
- Non-nucleoside reverse transcriptase inhibitors
- Protease inhibitors
Nucleoside reverse transcriptase inhibitors

Since reverse transcriptase is specific to the HIV virus, it serves as a good target.

- Azidothymidine (Zidovudin)
- Didanosine
- Zalcitabine
- Lamivudine
- Stavudine
Non-nucleoside reverse transcriptase inhibitors

- Nevirapine

Protease inhibitors

- Indinavir
- Ritonavir
- Saquinavir
Virus Classification

- Nucleic acid type
- Size and morphology
- Susceptibility to chemical and physical agents
- Viral enzymes
- Immunological properties
- Mode of replication
- Mode of transmission, cell tropisms, pathogenesis and symptomatology
How are viruses named?

• Based on:
  - the disease they cause
    rabies virus
  - the type of disease
    murine leukemia virus
  - geographic locations
    Ebola virus
  - their discovers
    Epstein-Barr virus
  - combinations of the above
    Rous Sarcoma virus
Virus Classification

Taxonomy from Order downward (three orders now recognized)

- Family often the highest classification. Ends in -viridae.
- Many families have subfamilies. Ends in -virinae.
- Many families have genera. Ends in –virus
- Many genera have types. Ends in –Number

Examples

family **Herpesviridae**
subfamily **Alphaherpesvirinae**
genus **Herpes Simplex Virus**
type species **Herpes Simplex Virus-1**
The Baltimore classification system

Based on genetic contents and replication strategies of viruses. According to the Baltimore classification, viruses are divided into the following seven classes:

1. dsDNA viruses
2. ssDNA viruses
3. dsRNA viruses
4. (+) sense ssRNA viruses (codes directly for protein)
5. (-) sense ssRNA viruses
6. RNA reverse transcribing viruses
7. DNA reverse transcribing viruses

where "ds" represents "double strand" and "ss" denotes "single strand".
<table>
<thead>
<tr>
<th>DNA</th>
<th>RNA</th>
</tr>
</thead>
<tbody>
<tr>
<td>double-stranded</td>
<td>single-stranded</td>
</tr>
<tr>
<td></td>
<td>double-stranded</td>
</tr>
<tr>
<td>circular linear</td>
<td>linear linear (circular)*</td>
</tr>
<tr>
<td>single single</td>
<td>(-)sense</td>
</tr>
<tr>
<td>multiple multiple</td>
<td>(+)sense</td>
</tr>
</tbody>
</table>

* For RNA, linear (circular) refers to molecules that have a circular structure with a linear backbone, often used in certain viral RNA segments.
## Virus Classification

### DNA viruses

**Double stranded DNA viruses**

<table>
<thead>
<tr>
<th>Family name</th>
<th>Symmetry of capsid</th>
<th>Envelope</th>
<th>Nucleic Acid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herpesviridae</td>
<td>Icosahedral</td>
<td>+</td>
<td>Linear</td>
</tr>
<tr>
<td>Adenoviridae</td>
<td>Icosahedral</td>
<td>-</td>
<td>Linear</td>
</tr>
<tr>
<td>Papillomaviridae</td>
<td>Icosahedral</td>
<td>-</td>
<td>Circular</td>
</tr>
<tr>
<td>Polyomaviridae</td>
<td>Icosahedral</td>
<td>-</td>
<td>Circular</td>
</tr>
<tr>
<td>Poxviridae</td>
<td>Complex</td>
<td>+ (complex)</td>
<td>Linear</td>
</tr>
</tbody>
</table>
## DNA viruses

### Single stranded DNA viruses

<table>
<thead>
<tr>
<th>Family name</th>
<th>Symmetry of capsid</th>
<th>Envelope</th>
<th>Nucleic Acid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parvoviridae</td>
<td>Icosahedral</td>
<td>-</td>
<td>Linear</td>
</tr>
<tr>
<td>Circoviridae</td>
<td>Icosahedral</td>
<td>-</td>
<td>Circular</td>
</tr>
</tbody>
</table>
## RNA viruses

### Double stranded RNA viruses

<table>
<thead>
<tr>
<th>Family name</th>
<th>Symmetry of capsid</th>
<th>Envelope</th>
<th>Nucleic Acid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reoviridae</td>
<td>Icosahedral</td>
<td>-</td>
<td>Segmented (10-12) Linear</td>
</tr>
<tr>
<td>Birnaviridae</td>
<td>Icosahedral</td>
<td>-</td>
<td>Segmented (2-3) Linear</td>
</tr>
</tbody>
</table>
## Single stranded RNA viruses (Positive Sense)

<table>
<thead>
<tr>
<th>Family name</th>
<th>Symmetry of capsid</th>
<th>Envelope</th>
<th>Nucleic Acid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Picornaviridae</td>
<td>Icosahedral</td>
<td>-</td>
<td>Linear</td>
</tr>
<tr>
<td>Caliciviridae</td>
<td>Icosahedral</td>
<td>-</td>
<td>Linear</td>
</tr>
<tr>
<td>Astroviridae</td>
<td>Icosahedral</td>
<td>-</td>
<td>Linear</td>
</tr>
<tr>
<td>Coronaviridae</td>
<td>Helical</td>
<td>+</td>
<td>Linear</td>
</tr>
<tr>
<td>Togaviridae</td>
<td>Icosahedral</td>
<td>+</td>
<td>Linear</td>
</tr>
<tr>
<td>Flaviviridae</td>
<td>Icosahedral</td>
<td>+</td>
<td>Linear</td>
</tr>
</tbody>
</table>
## Single stranded RNA viruses (Negative Sense)

<table>
<thead>
<tr>
<th>Family name</th>
<th>Symmetry of capsid</th>
<th>Envelope</th>
<th>Nucleic Acid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orthomyxoviridae</td>
<td>Helical</td>
<td>+</td>
<td>Segmented (7-8) Linear</td>
</tr>
<tr>
<td>Paramyxoviridae</td>
<td>Helical</td>
<td>+</td>
<td>Linear</td>
</tr>
<tr>
<td>Rhabdoviridae</td>
<td>Helical</td>
<td>+</td>
<td>Linear</td>
</tr>
<tr>
<td>Bunyaviridae</td>
<td>Helical</td>
<td>+</td>
<td>Segmented (3 segments) Circular</td>
</tr>
<tr>
<td>Arenaviridae</td>
<td>Helical</td>
<td>+</td>
<td>Segmented (2 segments) Circular</td>
</tr>
<tr>
<td>Filoviridae</td>
<td>Helical</td>
<td>+</td>
<td>Linear</td>
</tr>
</tbody>
</table>
DNA reverse transcribing viruses & RNA reverse transcribing viruses

<table>
<thead>
<tr>
<th>Family name</th>
<th>Symmetry of capsid</th>
<th>Envelope</th>
<th>Nucleic Acid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepadnaviridae</td>
<td>Icosahedral</td>
<td>+</td>
<td>Circular</td>
</tr>
<tr>
<td>Retroviridae</td>
<td>Icosahedral</td>
<td>+</td>
<td>Diploid (2 identical RNA)</td>
</tr>
</tbody>
</table>
## DNA Viruses

A diagram illustrating the classification of DNA viruses based on their genomic structure and morphology.

### Genomic Structure
- **Icosahedral**
  - Naked: ss linear (+) or (−)
  - Enveloped: ds linear
  - Naked/Env. (cytoplasmic): ds linear
- **Helical**
  - Naked/Env. (cytoplasmic): ds circular
- **Complex**
  - Enveloped (cytoplasmic): ds linear (x linked)

### Morphology
- **Parvo**
  - (−)
  - 18–26
  - 5
- **Papova**
  - (−)
  - 45–55
  - 5–8
- **Adeno**
  - (−)
  - 70–90
  - 36–38
- **Hepadna**
  - (+)
  - 42
  - 3.2
- **Herpes**
  - (−)
  - 150–200
  - 120–200
- **Irido**
  - (−)
  - 125–300
  - 150–350
- **Baculo**
  - (−)
  - 60 × 300
  - 100
- **Pox**
  - (+)
  - 170–200
  - 130–280
DNA Viruses

Adenovirus

Herpes Simplex Virus

Papillomavirus

Hepatitis B Virus
# RNA viruses

## Classification criteria

<table>
<thead>
<tr>
<th>Nucleic acid</th>
<th>Symmetry of capsid</th>
<th>Naked or enveloped</th>
<th>Genome architecture</th>
<th>Baltimore class</th>
</tr>
</thead>
<tbody>
<tr>
<td>RNA</td>
<td></td>
<td></td>
<td>ds 10–18 seg.</td>
<td>III</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ss 2 seg.</td>
<td>III</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(+) ss cont.</td>
<td>IV</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(-) ss cont.</td>
<td>IV</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(-) ss cont. 2 copies</td>
<td>IV</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(+) ss cont.</td>
<td>IV</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(-) ss cont. 3 seg.</td>
<td>IV</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(-) ss 8 seg.</td>
<td>IV</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(-) ss cont. 2 seg.</td>
<td>IV</td>
</tr>
</tbody>
</table>

## Family name

<table>
<thead>
<tr>
<th>Family name</th>
<th>Reo</th>
<th>Birna</th>
<th>Calici</th>
<th>Picorna</th>
<th>Flavi</th>
<th>Toga</th>
<th>Retro</th>
<th>Corona</th>
<th>Filo</th>
<th>Rhabdo</th>
<th>Bunya</th>
<th>Orthomyxo</th>
<th>Para-myxo</th>
<th>Arena</th>
</tr>
</thead>
<tbody>
<tr>
<td>Virion polymerase</td>
<td>(+)</td>
<td>(+)</td>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
<td>(+)</td>
<td>(-)</td>
<td>(-)</td>
<td>(+)</td>
<td>(+)</td>
<td>(+)</td>
<td>(+)</td>
<td>(+)</td>
<td>(+)</td>
</tr>
<tr>
<td>Virion diameter (nm)</td>
<td>60–80</td>
<td>60</td>
<td>35–40</td>
<td>28–30</td>
<td>40–50</td>
<td>60–70</td>
<td>80–130</td>
<td>80–160</td>
<td>80 X 790–1,400</td>
<td>70–85 X 130–380</td>
<td>90–120</td>
<td>90–120</td>
<td>150–300</td>
<td>50–300</td>
</tr>
<tr>
<td>Genome size (total in kb)</td>
<td>22–27</td>
<td>7</td>
<td>8</td>
<td>7.2–8.4</td>
<td>10</td>
<td>12</td>
<td>3.5–9</td>
<td>16–21</td>
<td>12.7</td>
<td>13–16</td>
<td>13.5–21</td>
<td>13.6</td>
<td>16–20</td>
<td>10–14</td>
</tr>
</tbody>
</table>
RNA Virus

- **Enterovirus**
- **Influenzavirus**
- **Paramyxovirus**
- **Rotavirus**
- **Rift Valley Fever Virus**