Dr. Hala Al Daghistani
Viruses

Non-living agents that infect all life forms (plants, phages, and animal viruses)

Viral cultivation differs from bacterial cultivation

Only EM allowed for visualization of viruses

Viruses have one major characteristic in common:

(they are obligate intracellular parasites).

No virus is able to produce its own energy (ATP) to drive macromolecular synthesis.
General Characteristics of Viruses

• Contain DNA or RNA

• Contain a protein coat = Capsid that made up of Capsomeres (NA + capsid → nucleocapsid).

• Some are enclosed by an Envelope (Naked, Enveloped)

• Some viruses have Spikes (COH/protein)

• Most viruses are tissue specific

• Host range is determined by specific host attachment sites and cellular factors
Morphology of an enveloped helical virus

(a) An enveloped helical virus

(b) Influenzavirus
<table>
<thead>
<tr>
<th>RECEPTOR</th>
<th>VIRUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICAM-1 (intracellular adhesion molecule 1 present on WBC, endothelium)</td>
<td>Polio</td>
</tr>
<tr>
<td>CD4</td>
<td>HIV</td>
</tr>
<tr>
<td>Acetylcholine (neural impulse transduction)</td>
<td>Rabies</td>
</tr>
<tr>
<td>EGF (epidermal growth factor)</td>
<td>Vaccinia</td>
</tr>
<tr>
<td>CR2/CD21 (complement receptors)</td>
<td>Epstein-Barr</td>
</tr>
<tr>
<td>HVEM (herpesvirus entry mediator)</td>
<td>Herpes</td>
</tr>
<tr>
<td>Sialic acid (common component of extracellular glycosylated proteins, surface cells)</td>
<td>Influenza, corona</td>
</tr>
</tbody>
</table>
Host Range and Specificity

Virus and host cell interaction usually very specific (narrow host range)

**Specific Tissue tropism** is the cells and tissues of a **host** which support growth of a particular **virus**.

- Some bacteria and viruses have a **Broad tissue tropism** and can infect many types of cells and tissues.

For example **rabies** virus affects primarily **neuronal** tissue.
Virus Shapes and Sizes

Human red blood cell
10,000 nm in diameter

Adenovirus
90 nm

Bacteriophage T4
225 nm

Rabies virus
170 × 70 nm

Bacteriophage M13
800 × 10 nm

Chlamydia elementary body
300 nm

Tobacco mosaic virus
250 × 18 nm

Ebola virus
970 nm

Viroid
300 × 10 nm

Poliovirus
30 nm

Prion
200 × 20 nm

Rhinovirus
30 nm

E. coli
(a bacterium)
3000 × 1000 nm

Plasma membrane
of red blood cell
10 nm thick

Vaccinia virus
300 × 200 × 100 nm
Structural Classes

• Icosahedral symmetry
• Helical symmetry
• Non enveloped (“naked”)
• Enveloped
Icosahedral capsids

a) Crystallographic structure of a simple icosahedral virus.

b) The axes of symmetry
In 1955, Fraenkel, Conrat, and Williams demonstrated that 
**tobacco mosaic virus** (TMV) spontaneously formed when mixtures of purified coat protein and its genomic RNA were incubated together.

Helical symmetry

**tobacco mosaic virus** (TMV), a filamentous virus
**Satellite virus**
- Contain nucleic acid
- Depend on co-infection (simultaneously) with a helper virus or superinfection (carrier, chronic)
- Mostly in plants, can be human e.g. Hepatitis delta virus (HDV), cannot propagate without HBV

**Viroids**
- Unencapsidated, small circular ssRNA molecules that replicate autonomously
- Only in plants, e.g. potato spindle tuber viroid

**Prions**
- No nucleic acid
- Infectious protein e.g. BSE (bovine spongiform encephalopathy or mad cow disease)

**Virons (viruse)**
- A complete viral particle, consisting of RNA or DNA surrounded by a protein shell and constituting the infective form of a virus.
Principle of viral infections

• All viruses package their genomes inside a particle that mediates transmission of the viral genome from host to host

• The viral genome contains the informations for initiating and completing an infectious cycle within a susceptible, permissive cell.

• An infectious cycle includes attachment, and entry of the particle, uncoating, transcription and or translation of viral genome, replication, and assembly and release of particles containing the genome
Typical infectious cycle

1. Attachment
2. Penetration
3. Uncoating
4. Transcription and/or Translation
5. Genome Replication
6. Assembly
7. Release
Attachment (Adsorption)

- Virus encounters susceptible host cells
- Adsorbs specifically to receptor sites on the cell membrane
- Because of the exact fit required, viruses have a limited host range
Penetration

• Flexible cell membrane of the host is penetrated by the whole virus or its nucleic acid
• Endocytosis: entire virus engulfed by the cell and enclosed in a vacuole or vesicle
• The viral envelope can also directly fuse with the host cell membrane

Uncoating

• Enzymes in the vacuole dissolve the envelope and capsid
• The virus is now uncoated
Synthesis

- Free viral nucleic acid exerts control over the host’s synthetic and metabolic machinery
- DNA viruses- enter host cell’s nucleus where they are replicated and assembled
  - DNA enters the nucleus and is transcribed into RNA
  - The RNA becomes a message for synthesizing viral proteins (translation)
  - New DNA is synthesized using host nucleotides
- RNA viruses- replicated and assembled in the cytoplasm

Assembly

Mature virus particles are constructed from the growing pool of parts
Release

- Nonenveloped and complex viruses are released when the cell lyses or ruptures.
- Enveloped viruses are liberated by budding or exocytosis.
- Anywhere from 3,000 to 100,000 virions may be released, depending on the virus.
- Entire length of cycle- anywhere from 8 to 36 hours.
Attachment, Penetration, and Uncoating

(a) Attachment
(b) Endocytosis
(c) Penetration
(d) Uncoating
Viral Replication

• Obligate intracellular parasites using host cell machinery

• Very limited number of genes encode proteins for
  – Capsid formation
  – Viral nucleic acid replication
  – Movement of virus into and out of cell

• Kill or live in harmony within the host cell

• Outside the cell, viruses are inert
How are viruses named?

• Based on:
  1- the disease they cause
      poliovirus, rabies virus
  2- the type of disease
      murine leukemia virus
  3- geographic locations
      Sendai virus, Coxsackie virus
  4- their discovers
      Epstein-Barr virus
  5- how they were originally thought to be contracted
      dengue virus ("evil spirit of Babylonia") cramp-like seizure, influenza virus (the "influence" of bad air)
  6- combinations of the above
      Rous Sarcoma virus
Taxonomy of Viruses

- No evidence for common viral ancestor.
- Taxonomy from Order downward (3 orders now recognized)
- Classification based on type of NA, strategy for replication, and morphology.
  - Family names end in -viridae
  - Many families have subfamilies. Ends in -virinae.
  - Genus and species names end in -virus.
- Viral species: A group of viruses sharing the same genetic information and ecological niche (host). Common names are used for species. Subspecies are designated by a number.
Taxonomy of Viruses

- Herpesviralis (order)
- Herpesviridae (family)
- *Herpesvirus* (genus)
- Human herpes virus (species)
- HHV-1, HHV-2, HHV-3
- (subspecies)

- Retroviralis (order)
- Retroviridae (family)
- *Lentivirus* (genus)
- Human immunodeficiency virus (species)
- HIV-1, HIV-2 (subspecies)
<table>
<thead>
<tr>
<th>Order</th>
<th>Family</th>
<th>Genus</th>
<th>Species</th>
<th>Host</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caudovirales</td>
<td>Poxviridae</td>
<td>Orthopoxivirus</td>
<td>Vaccinia virus</td>
<td>Animal</td>
</tr>
<tr>
<td></td>
<td>Herpesviridae</td>
<td>Cytomegalovirus</td>
<td>Human herpesvirus 5</td>
<td>Animal</td>
</tr>
<tr>
<td></td>
<td>Myoviridae</td>
<td>SPO1-like virus</td>
<td>Bacillus phage</td>
<td>Bacterium</td>
</tr>
<tr>
<td>Mononegavirales</td>
<td>Paramyxoviridae</td>
<td>Morbillivirus</td>
<td>Measles virus</td>
<td>Animal</td>
</tr>
<tr>
<td></td>
<td>Filoviridae</td>
<td>Ebola virus</td>
<td>Ebola virus</td>
<td>Animal</td>
</tr>
<tr>
<td></td>
<td>Sequiviridae</td>
<td>Sequivirus</td>
<td>Parsnip yellow fleck virus</td>
<td>Plant</td>
</tr>
<tr>
<td>Nidovirales</td>
<td>Togaviridae</td>
<td>Rubivirus</td>
<td>Rubella virus</td>
<td>Animal</td>
</tr>
<tr>
<td></td>
<td>Luteoviridae</td>
<td>Tobamovirus</td>
<td>Tobacco mosaic virus</td>
<td>Plant</td>
</tr>
</tbody>
</table>

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".

All viruses must produce mRNA, or (+) sense RNA
The Baltimore classification has + RNA as its central point
<table>
<thead>
<tr>
<th>Viral Nucleic Acid</th>
<th>Virus Family</th>
<th>Special Features of Biosynthesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>DNA, single-stranded</td>
<td>Paroviridae</td>
<td>Cellular enzyme transcribes viral DNA in nucleus</td>
</tr>
<tr>
<td>DNA, double-stranded</td>
<td>Herpesviridae, Papovaviridae, Poxviridae</td>
<td>Cellular enzyme transcribes viral DNA in nucleus</td>
</tr>
<tr>
<td>DNA, reverse transcriptase</td>
<td>Hepadnaviridae</td>
<td>Viral enzyme transcribes viral DNA in virion, in cytoplasm</td>
</tr>
<tr>
<td>RNA, + strand</td>
<td>Picornaviridae, Togaviridae</td>
<td>Cellular enzyme transcribes viral DNA in nucleus; reverse transcriptase copies mRNA to make viral DNA</td>
</tr>
<tr>
<td>RNA, − strand</td>
<td>Rhabdoviridae</td>
<td>Viral RNA functions as a template for synthesis of RNA polymerase which copies − strand RNA to make mRNA in cytoplasm</td>
</tr>
<tr>
<td>RNA, double-stranded</td>
<td>Reoviridae</td>
<td>Viral enzyme copies − strand RNA to make mRNA in cytoplasm</td>
</tr>
<tr>
<td>RNA, reverse transcriptase</td>
<td>Retroviridae</td>
<td>Viral enzyme copies viral RNA to make DNA in cytoplasm; DNA moves to nucleus</td>
</tr>
</tbody>
</table>
- Most genomes are non-segmented (the genome is all on one piece of RNA or DNA).

- Some genomes are segmented, meaning there are several fragments of genetic material that make a complete virus genome.

- Also, some genomes are linear, meaning that there is a beginning and end to the genome, while other genomes are circular (no beginning and no end).
Isolation, Cultivation, and Identification

- Viruses must be grown in living cells
  - **Bacteriophages** form plaques on a lawn of bacteria
  - **Animal viruses** may be grown in cell culture, embryonated eggs, or living animals
(a) Inoculation of embryo

(b) Inoculation of amniotic cavity

Inoculation of chorioallantoic membrane

Air sac

Amnion

Shell

Allantoic cavity

Albumin

Inoculation of yolk sac

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Using Cell (Tissue) Culture Techniques

• Most viruses are propagated in some sort of cell culture
• The cultures must be developed and maintained
• Animal cell cultures are grown in sterile chambers with special media
• Cultured cells grow in the form of a monolayer
• Primary or continuous
Virus Identification

• Cytopathic effects

• Serological tests
  – **Identify antibodies** against viruses in a patient
  – Use antibodies to **identify viruses** in neutralization tests, viral hemagglutination

• Nucleic acids
  – PCR
Anti-Viral Drugs

- **Attachment antagonists**
  - Block attachment molecule
    - Arildone

- **Inhibit Uncoating**
  - Neutralize acid environment
    - Amantadine
    - Rimantadine

- **Inhibit DNA/RNA synthesis**
  - Activation by phosphorylation of drug by viral kinases
    - Acyclovir
    - Gancyclovir
Bacteriophage: The Lytic Cycle

1. **Attachment** to cell surface receptors - no active movement

2. **Penetration** – only genome enters

3. **Biosynthesis** – Production of phage DNA and proteins

4. **Maturation** – assembly to form intact phage

5. **Release** due to phage induced lysozyme production

See Fig 13.11
Lytic Cycle of Bacteriophage

1. Attachment: Phage attaches to host cell.
2. Penetration: Phage penetrates host cell and injects its DNA.
3. Biosynthesis: Phage DNA directs synthesis of viral components by the host cell.

Fig 13.11
Lytic Cycle of a T-Even Bacteriophage

4 Maturation: Viral components are assembled into virions.

5 Release: Host cell lyses, and new virions are released.
Results of Multiplication of Bacteriophages

• **Lytic cycle**
  – Lytic or virulent phage
  – Phage causes lysis and death of host cell

• **Lysogenic cycle**
  – Lysogenic or temperate phage
  – Phage DNA incorporated in host DNA $\Rightarrow$ Prophage
  – Phage conversion
**Lytic and Lysogenic Cycles**

1. Phage attaches to host cell and injects DNA.
2. Phage DNA circularizes and enters lytic cycle or lysogenic cycle.
3. Phage DNA integrates within the bacterial chromosome by recombination, becoming a prophage.
5. Occasionally, the prophage may excise from the bacterial chromosome by another recombination event, initiating a lytic cycle.

**Lytic cycle**

- Many cell divisions

**Lysogenic cycle**

- Prophage

Fig 13.12
Viral Pathogenesis:
Elements of Virus-Host Interaction

- Viral strain
- Inoculum size
- Route of exposure
- Susceptibility of host
  - Is there pre-existent immunity from past exposure or vaccination?
  - Host genetic factors
- Immune status and age of host
Pathogenetic Steps in Human Viral Infection

- Virus may enter through skin, mucous membranes, respiratory tract, GI tract, via transfusion, needle-stick, or maternal-fetal transmission
- Local replication at site of inoculation
- Neurotropic agents may travel along nerve routes or reach CNS by viremic spread
Pathogenetic Steps in Human Viral Infection

• For many agents, there is replication in regional lymph nodes with subsequent viremia and spread to target organs
  – Some travel free in plasma (e.g., picornaviruses); some are cell associated (e.g., cytomegalovirus)

• Replication in target organs may lead to local damage and further viremia

• Non-specific and virus-specific host immune responses come into play to downregulate viral replication
Immune Response to Viral Infections

• Non-specific immunity
  – Phagocytic cells (neutrophils and monocyte-macrophages)
  – Cytokines (e.g., interferons)
  – Natural killer cells
  – Other ‘antiviral’ factors

• Specific immunity
  – Antigen specific B and T cell responses
    • Antibodies
    • Cytotoxic T cells
    • ADCC
Immune Response
VIRAL TAXONOMY

18 GROUPS (6 are DNA VIRUSES, 11 are RNA VIRUSES and 1 UNCLASSIFIED)

DNA VIRUSES

1. **Poxvirus**
   - (1) the largest viruses
   - (2) **enveloped** double stranded DNA viruses
   - (3) intracytoplasmic inclusion bodies
   - (4) skin is a primary target
   - (5) eg. smallpox, cowpox

2. **Herpesvirus**
   - (1) medium size
   - (2) **enveloped** Double-stranded DNA viruses
   - (3) intranuclear inclusion bodies
   - (4) skin is the major target.
   - (5) eg. Epstein Bar viruses
3. Adenoviurs
   (1) medium size
   (2) Double stranded DNA viruses
   (3) non-enveloped, intranuclear inclusion bodies
   (4) target: human lymphoid tissue.
   (5) eg. tumors in animals

4. Papovavirus
   (1) small size
   (2) non-enveloped double stranded DNA
   (3) tumor producing viruses
   (4) eg. papilloma virus of human, polyoma viruses of mice.
5. Parvovirus
   (1) ultra small in size
   (2) single stranded DNA viruses
   (3) among the most resistant viruses known.
   (4) eg. human parvovirus B19 or fifth disease

6. Hepadnavirus
   (1) enveloped DNA virus, Double stranded DNA
   (2) replication in liver cell
   (3) eg. hepatitis B
RNA VIRUSES

7. Myxovirus (Orthomyxoviruses)
   (1) medium size
   (2) enveloped single stranded RNA virus with helical symmetry
   (3) many can agglutinate red blood cells
   (4) eg. influenza viruses cause flu

8. Paramyxovirus
   (1) medium size
   (2) enveloped single stranded RNA viruses helical symmetry
   (3) both intracytoplasmic and intranuclear inclusion bodies
   (4) eg. measles, mumps
**9. Rhabdovirus**
- (1) medium size
- (2) single stranded RNA viruses, helical symmetry
- (3) bullet shaped envelop
- (4) intracytoplasmic inclusions
- (5) transmitted by animal or animal bites
- (6) eg. vesicular stomatitis, rabies

**10. Flavivirus**
- (1) small size
- (2) enveloped single stranded RNA viruses
- (3) transmitted by mosquitoes or ticks
- (4) eg. yellow fever, Dengue viruses, Japanese Encephalitis
11. **Togaviruses**
   (1) small size
   (2) **enveloped** single stranded RNA viruses
   (3) complex life cycle involving biting insects
   (4) eg. Dengue like fever.

12. **Arenavirus**
   (1) medium size
   (2) **enveloped** single stranded RNA viruses
   (3) transmitted by animal or animal bites
   (4) eg. South American hemorrhagic fever

13. **Bunyavirus**
   (1) medium size
   (2) **enveloped** single stranded RNA viruses
   (3) arthropod-borne viruses, transmitted by mosquitoes or ticks
   (4) eg. California encephalitis
14. **Reovirus**
   (1) medium size
   (2) Double stranded RNA viruses
   (3) transmitted by mosquitoes or ticks
   (4) in respiratory tract, enteric canal.
   (5) eg. infantile gastroenteritis

15. **Picornavirus**
   (1) smallest viruses
   (2) single stranded RNA viruses
   (3) enteric and related virus
   (4) eg. poliomyelitis, common cold.

16. **Coronavirus**
   (1) medium size
   (2) single stranded **enveloped virus** (helical symmetry)
   (3) eg. Avian infectious bronchitis
17. **Retrovirus**
   (1) small size
   (2) *enveloped* single stranded RNA tumor virus
   (3) has reverse transcriptase
   (4) *eg.* leukemia or sarcoma in mice, AIDS

18. **Other viruses**
   (1) unclassified
   (2) *eg.* some slow neurologic disorders.
The Effect of Virus Infection on the Host Cell

1. Cytopathic Effects

2. Inhibition of Host Macromolecular Biosynthesis

3. Changes in the Regulation of Gene Expression

4. Appearance of New Antigenic Determinants on the Cell Surface (If it is enveloped virus, the new determinants are likely to be viral envelope proteins. It can also be non-enveloped virus. The presence of these determinants serves to alert the immune mechanism).

5. Cell Fusion (the formation of giant syncytia, mass of cytoplasm bounded by one membrane that contain hundreds and even thousands of nuclei.)
6. **Abortive Infection** (viral infection that infects a cell without reproducing into more infectious viruses. This occur when a virus infects a cell, but cannot complete the full replication cycle

7. **Persistent Infection with Latency** (Persistent infection with no viral progeny. Latency is the phase that occur after initial infection and proliferation of virus. However, the viral genome is not fully eradicated. The result of this is that the virus can reactivate and begin producing large amounts of viral progeny without the host being infected by new outside virus.
RNA Viruses
<table>
<thead>
<tr>
<th>DNA Viruses</th>
<th>Genus of Virus</th>
<th>Common Name of Genus Members</th>
<th>Name of Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poxviridae</td>
<td>Orthopoxivirus</td>
<td>Variola and vaccinia, Herpes simplex (HSV) 1 virus, Herpes simplex (HSV) 2 virus,</td>
<td>Smallpox, cowpox, Fever blister, cold sores,</td>
</tr>
<tr>
<td>Herpesviridae</td>
<td>Simplexivirus</td>
<td>Varicella zoster virus (VZV)</td>
<td>Genital herpes, Chickenpox, shingles,</td>
</tr>
<tr>
<td>Cytomegalovirida</td>
<td></td>
<td>Human cytomegalovirus (CMV)</td>
<td>CMV infections, Adenovirus infection,</td>
</tr>
<tr>
<td>Adenoviridae</td>
<td>Mastadenovirus</td>
<td>Human adenoviruses</td>
<td>Several types of warts, Progressive multifocal</td>
</tr>
<tr>
<td>Papovaviridae</td>
<td>Papillomavirus</td>
<td>Human papillomavirus (HPV)</td>
<td>leukoencephalopathy (PML), Serum hepatitis,</td>
</tr>
<tr>
<td></td>
<td>Polyomavirus</td>
<td>JC virus (JCV)</td>
<td>Erythema infectiosum</td>
</tr>
<tr>
<td>Hepadnaviridae</td>
<td>Hepadnavirus</td>
<td>Hepatitis B virus (HBV) or Dane particle</td>
<td></td>
</tr>
<tr>
<td>Paroviridae</td>
<td>Erythrovirus</td>
<td>Parvovirus B19</td>
<td></td>
</tr>
<tr>
<td>RNA Viruses</td>
<td>Enterovirus</td>
<td>Poliovirus</td>
<td>Poliomyelitis, Hand-foot-mouth disease, Short-term</td>
</tr>
<tr>
<td>Picornaviridae</td>
<td></td>
<td>Hepatitis A virus (HAV)</td>
<td>hepatitis, Common cold, bronchitis, Viral diarrhea,</td>
</tr>
<tr>
<td>Calcivirus</td>
<td></td>
<td>Human rhinovirus</td>
<td>Norwalk virus syndrome, Eastern equine encephalitis</td>
</tr>
<tr>
<td>Caliciviridae</td>
<td>Calicivirus</td>
<td>Norwalk virus</td>
<td>(EEE), Eastern equine encephalitis (EEE)</td>
</tr>
<tr>
<td>Togaviridae</td>
<td>Alphavirus</td>
<td>Eastern equine encephalitis virus, Western equine encephalitis virus</td>
<td></td>
</tr>
<tr>
<td>Flaviviridae</td>
<td>Rubivirus</td>
<td>Yellow fever virus, St. Louis encephalitis virus, Rubella virus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Flavivirus</td>
<td>Dengue fever virus, West Nile fever virus, Bunyamwera viruses, Sin Nombre virus</td>
<td></td>
</tr>
<tr>
<td>Bunyaviridae</td>
<td>Bunyavirus</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bunaviruses</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Filoviridae</td>
<td>Filovirus</td>
<td>Filovirus, Ebolavirus, Marburg virus</td>
<td>Ebola fever, Crimean–Congo hemorrhagic fever virus,</td>
</tr>
<tr>
<td>Reoviridae</td>
<td>Reovirus</td>
<td>Colorado tick virus, Human rotavirus</td>
<td>Ebola fever, Crimean–Congo hemorrhagic fever virus,</td>
</tr>
<tr>
<td>Orthomyxoviridae</td>
<td>Influenza virus</td>
<td>Influenza virus, type A (Asian, Hong Kong, and swine influenza viruses)</td>
<td>Influenza or “flu”</td>
</tr>
<tr>
<td>Paramyxoviridae</td>
<td>Parainfluenza</td>
<td>Parainfluenza virus, types 1–5, Mumps virus, Measles virus</td>
<td></td>
</tr>
<tr>
<td>Rhabdoviridae</td>
<td>Morbillivirus</td>
<td>respiratory syncytial virus (RSV)</td>
<td></td>
</tr>
<tr>
<td>Retroviridae</td>
<td>Pneumavirus</td>
<td>Rabies virus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lyssavirus</td>
<td>Human T-cell leukemia virus (HTLV)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Oncornavirus</td>
<td>HIV (human immunodeficiency viruses 1 and 2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lentivirus</td>
<td>Lassa virus</td>
<td></td>
</tr>
<tr>
<td>Arenaviridae</td>
<td>Arenaviruses</td>
<td>Infectious bronchitis virus (IBV), Enteric corona virus</td>
<td></td>
</tr>
<tr>
<td>Coronavirus</td>
<td>Coronavirus</td>
<td>SARS virus</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
TABLE 25.1
RNA Viruses with Examples of Diseases

RNA Viruses
- Enveloped
  - Single-stranded genome
    - Segmented genome
      - Orthomyxoviruses
        - Influenza
    - Non-segmented genome
      - Paramyxoviruses
        - Measles
      - Rhabdoviruses
        - Rabies
  - Single-stranded genome encodes reverse transcriptase
    - Retroviruses
      - AIDS
      - Picornaviruses
        - Polio
        - Hepatitis A
      - Togaviruses
        - Rubella
      - Flaviviruses
        - Dengue fever
      - Calciviruses
        - Norwalk enteritis
      - Coronavirus
        - SARS
- Nonenveloped
  - Single-stranded genome
    - Reoviruses
      - Rotavirus
      - Diarrhea
  - Double-stranded genome
    - Arenaviruses
      - California encephalitis
Orthomyxoviruses: Influenza

- ssRNA, segmented, consists of 10 genes encoded on 8 separate RNA segments.
- 3 distinct influenza virus types: A, B, C; Type A causes most infections.
- Influenza A viruses are further classified, based on the viral surface proteins hemagglutinin (HA or H) and neuraminidase (NA or N).
- Key to influenza virus are
  - Influenza virus A infects humans, other mammals, birds, and causes all flu pandemics (H1N1, H1N2, H2N2, H3N1, H5N1, ....)
  - Influenza virus B infects humans and seals
  - Influenza virus C infects humans, pigs, and dogs.
- Virus attaches to, and multiplies in, the cells of the respiratory tract, assembled and budded off.
hemagglutinin (H) – 16 different subtypes; most important virulence factor; binds to host cells
neuraminidase (N) – 9 subtypes – hydrolyzes mucus and assists viral budding and release

• Both glycoproteins frequently undergo genetic changes decreasing the effectiveness of the host immune response.

Influenza B: Not known to undergo antigenic shift

Influenza C: Known to cause only minor respiratory disease; probably not involved in epidemics
Influenza A

- Acute, highly contagious respiratory illness
- Respiratory transmission
- Binds to ciliated cells of respiratory mucosa
- Fever, headache, myalgia, pharyngeal pain, shortness of breath, coughing
- Weakened host defenses predispose patients to secondary bacterial infections, especially pneumonia.
Diagnosis, Treatment, Prevention

- Rapid immunofluorescence tests to detect antigens in a pharyngeal specimen.
- Treatment: control symptoms; amantadine, rimantadine, zanamivir (Relenza) and oseltamivir (Tamiflu)
- Flu virus has developed high rate of resistance to amantadine and rimantadine.
- Annual trivalent vaccine recommended
Paramyxoviruses

Including the following viruses

1. Parainfluenza
2. Mumps virus
3. Morbillivirus (measles virus)
4. Pnuemonovirus (respiratory syncytia virus)

• Respiratory transmission
• Envelope has HN and specialized F spikes that initiate cell-to-cell fusion.
• Fusion with neighboring cells – syncytium or multinucleate giant cells form
Insert figure 25.5

Effects of paramyxoviruses
Parainfluenza

- Widespread as influenza but more benign
- Respiratory transmission
- Seen mostly in children
- Minor cold, bronchitis, bronchopneumonia, croup
- No specific treatment available; supportive therapy
Mumps

- Epidemic parotitis; self-limited, associated with painful swelling of parotid salivary glands
- Humans are the only reservoir.
- 40% of infections are subclinical; long-term immunity.
- Incubation 2-3 weeks fever, muscle pain and malaise, classic swelling of one or both cheeks
- Usually uncomplicated invasion of other organs; in 20-30% of infected adult males, epididymis and testes become infected; sterility is suspected
- Live attenuated vaccine **MMR**
Measles

- Caused by Morbillivirus
- Also known as red measles and rubeola
- Different from German measles
- Very contagious; transmitted by respiratory aerosols
- Humans are the only reservoir.
- Sore throat, dry cough, headache, conjunctivitis, lymphadenitis, fever, Koplik spots – oral lesions
- Exanthem
- Most serious complication is subacute sclerosing panencephalitis (SSPE), a progressive neurological degeneration of the cerebral cortex, white matter and brain stem.
- Attenuated viral vaccine **MMR**
pathognomonic of measles!

Typically involve the buccal and labial mucosa. Irregular, patchy erythema with tiny central white specks → 'grains of salt' appearance.
Rhabdovirus: Rabies

- Rabies virus
- Enveloped, bullet-shaped virions
- Slow, progressive zoonotic disease
- Primary reservoirs are wild mammals; it can be spread by both wild and domestic mammals by bites, scratches, and inhalation of droplets.
- Virus enters through bite, grows at trauma site and multiplies, then enters nerve endings and advances toward the ganglia, spinal cord and brain.

Clinical phases of rabies:
- **Prodromal phase** – fever, nausea, vomiting, headache, fatigue; some experience pain, burning, tingling sensations at site of wound
- **Furious phase** – agitation, disorientation, seizures, hydrophobia
- **Dumb phase** – paralyzed, disoriented, progress to coma phase, death
1. Virus enters tissue from saliva of biting animal.
2. Virus replicates in muscle near bite.
3. Virus moves up peripheral nervous system to CNS.
4. Virus ascends spinal cord.
5. Virus reaches brain and causes fatal encephalitis.
6. Virus enters salivary glands and other organs of victim.
- Often diagnosed at autopsy – intracellular inclusions (Negri bodies) in nervous tissue
- Preventive therapy initiated if signs of rabies appear
- Treatment – infuse the wound with human rabies immune globulin (HRIG); vaccination with an inactivated vaccine given in 6 doses.
- Control - vaccination of domestic animals, elimination of strays, and strict quarantine practices
Coronaviruses

- Relatively large RNA viruses
- Distinctively spaced spikes on their envelopes
- Common in domesticated animals
- **Coronaviruses** are species in the genera belonging to one of two subfamilies: **Coronavirinae** and **Torovirinae**.
- Coronaviruses primarily infect the URT and GIT of mammals and birds.
- Six different strains of coronaviruses infect humans.
- The most important human coronavirus, **SARS-CoV** which causes **SARS (Severe Acute Respiratory Syndrome)** associated with both URT and LRT infections. It is a serious form of pneumonia
- SARS is an airborne disease with 10% fatality.
- The virus is extremely contagious. It is able to survive several hours outside human body which increase the probability of someone becoming infected through a common object.
Rubellavirus (Togaviruses)

- **Rubella**
  - Caused by a Togavirus, ssRNA
  - Causative agent of **German measles**
  - Most cases reported are adolescents and young adults.
  - Transmitted through contact with respiratory secretions.
  - A rash may start around two weeks after exposure and last for three days. It usually starts on the face and spreads to the rest of the body. The rash is not as bright as that of **measles** and is sometimes **itchy**. **Swollen lymph nodes** are common and may last a few weeks. A fever, sore throat, and fatigue may also occur. In adults **joint pain** is common. Complications may include bleeding problems, **testicular swelling**, and **inflammation of nerves**.

- **Congenital rubella** – infection during 1\textsuperscript{st} trimester most likely to induce **miscarriage** or **multiple defects** such as cardiac abnormalities, ocular lesions, deafness, mental and physical retardation.
Rubella - German Measles

Typically mild (macular rash, fever), often unrecognized

**Teratogenic** during early pregnancy (*congenital rubella syndrome*)

*Attenuated viral vaccine MMR*
**Flavivirus (Flaviviridae)**

- Hepatitis C Virus (HCV), non-A non-B virus
- Acquired through **blood contact** – **blood transfusions, needle sharing by drug abusers**
- Possible to have severe symptoms without permanent liver damage; more common to have chronic liver disease
- Cancer may also result from chronic HCV infection.
- Treatment with interferon and ribavirin to lessen liver damage
- No vaccine
Retroviruses

HIV Infections and AIDS

• Human immunodeficiency virus or AIDS, First emerged in 1980s
• HIV-1 may have originated from a chimpanzee virus.
• Encode reverse transcriptase enzyme which makes a double stranded DNA from the single-stranded RNA genome
• Viral genes permanently integrated into host DNA
• HIV can only infect host cells that have the required CD4 marker plus a coreceptor.
• Transmission occurs by direct and specific routes: mainly through sexual intercourse and transfer of blood or blood products; babies can be infected before or during birth, and from breast feeding.
• HIV does not survive long outside of the body.
• Men account for 70% of new infections.
• In 2006, the number of infected individuals worldwide is estimated to be 45 million with ~1 million in the U.S.
HIV general structure

(a) GP-120
GP-41
Protease molecule
RNA strands
Capsid
Integrase molecules
Reverse transcriptase molecules

(b) Antireceptor spikes
HIV
CD4 receptor on white blood cell
Co-receptor on white blood cell
Pathogenesis and Virulence Factors of HIV

- HIV enters through mucous membrane or skin and travels to dendritic phagocytes beneath the epithelium, multiplies and is shed.
- Virus is taken up and amplified by macrophages in the skin, lymph organs, bone marrow, and blood.
- HIV attaches to CD4 and coreceptor; HIV fuses with cell membrane.
- Reverse transcriptase makes a DNA copy of RNA.
- Viral DNA is integrated into host chromosome (provirus).
- Can produce a lytic infection or remain latent
The virus is adsorbed and endocytosed, and the twin RNAs are uncoated. Reverse transcriptase catalyzes the synthesis of a single complementary strand of DNA (ssDNA). This single strand serves as a template for synthesis of a double strand (ds) of DNA. In latency, dsDNA is inserted into the host chromosome as a provirus.

After a latent period, various immune activators stimulate the infected cell, causing reactivation of the provirus genes and production of viral mRNA.

HIV mRNA is translated by the cell's synthetic machinery into virus components (capsid, reverse transcriptase, spikes), and the viruses are assembled. Budding of mature viruses lyses the infected cell.
Primary effects of HIV infection:

– extreme leukopenia – lymphocytes in particular
– formation of giant T cells and other syncytia allowing the virus to spread directly from cell to cell
– Infected macrophages release the virus in central nervous system.

Secondary effects of HIV:

– Destruction on CD4 lymphocytes allows for opportunistic infections and malignancies.
Signs and Symptoms of HIV Infections and AIDS

• Symptoms of HIV are directly related to viral blood level and level of T cells.
• Asymptomatic phase 2-15 years (avg. 10)
• Antibodies are detectable 8-16 weeks after infection.
• HIV destroys the immune system.
• When T4 cell levels fall below 200/μL AIDS symptoms appear including fever, swollen lymph nodes, diarrhea, weight loss, neurological symptoms, opportunistic infections and cancers.
Diagnosis of AIDS is made when a person meets the criteria:

1. Positive for the virus
2. They fulfill one of the additional criteria:
   - They have a CD4 count of fewer than 200 cells/ml of blood.
   - Their CD4 cells account for fewer than 14% of all lymphocytes.
   - They experience one or more of a CDC-provided list of AIDS-defining illnesses.
Preventing and Treating HIV

• No vaccine available
• No cure; therapies slow down the progress of the disease or diminish the symptoms
  – inhibit viral enzymes: reverse transcriptase, protease, integrase
  – inhibit fusion
  – inhibit viral translation
Nonenveloped Nonsegmented ssRNA Viruses

PICORNAVIRUSES
Picornaviruses represent a very large virus family with respect to the number but one of the smallest in terms of virion size and genetic complexity. They include two major groups of human pathogens:
1. Enteroviruses (POLIO VIRUS)
2. Rhinoviruses.

* Enteroviruses are transient inhabitants of the human alimentary tract and may be isolated from the throat or lower intestine.
* Rhinoviruses are isolated chiefly from the nose and throat.

Human rhinoviruses can be divided into major and minor receptor groups. Viruses of the major group use intercellular adhesion molecule-1 (ICAM-1) as receptor, expressed on endothelial cells and cells of the immune system and those of the minor group bind members of the low-density lipoprotein receptor (LDLR) family, found in the plasma membrane of cells involved in receptor-mediated endocytosis.
Poliomyelitis (polio) – acute enteroviral infection of the spinal cord that can cause neuromuscular paralysis

- Poliovirus – naked capsid; resistant to acid, bile, and detergents; can survive stomach acids when ingested
- Worldwide vaccination programs have reduced the number of cases; eradication is expected.
Transmitted by fecal-oral route

- Polioviruses adhere to receptors of **mucosal cells in oropharynx and intestine**, multiply in number and shed in throat and feces, some leak into blood.
- Most infections are short-term, mild viremia.
- Most infections are subclinical; only about 1% of infections result in clinical illness.
- The incubation period is usually 7–14 days, but it may range from 3 to 35 days.
- Polio virus destroys the motor neurons in the gray matter of the spinal cord or the brain
- Invasion of motor neurons causes paralysis.
The disease could be either:

A. **Mild disease**
This is the most common form of disease. Patient has only a minor illness, characterized by fever, malaise, drowsiness, headache, nausea, vomiting, constipation, and sore throat in various combinations. Recovery occurs in a few days.

B. **Nonparalytic poliomyelitis (aseptic meningitis)**
Patient with the nonparalytic form has stiffness and pain in the back and neck. Recovery is rapid and complete. Poliovirus is one of many viruses that produce aseptic meningitis.

C. **Paralytic poliomyelitis**
The predominating complaint is flaccid paralysis resulting from lower motor neuron damage.

D. **Progressive postpoliomyelitis muscle atrophy**
A recrudescence of paralysis and muscle wasting. Although progressive postpoliomyelitis muscle atrophy is rare.
Treatment and Prevention

• Treatment is largely supportive for pain and suffering; respiratory failure may require artificial ventilation; physical therapy may be needed.
• Prevention by vaccination.
  • Injected Inactivated (killed) polio vaccine (IPV) **Salk vaccine**
  • Oral live attenuated polio vaccine (OPV) **Sabin vaccine**
  • Worldwide eradication anticipated by 2008
Hepatitis A Virus and Infectious Hepatitis

• Cubical picornavirus relatively resistant to heat and acid
• Not carried chronically, principal reservoirs are asymptomatic, short-term carriers or people with clinical disease
• Fecal-oral transmission; multiplies in small intestine and enters the blood and is carried to the liver
• Most infections subclinical, flu-like symptoms occur; jaundice is present
• Only one serotype is known. No antigenic cross-reactivity with HBV or with the other hepatitis viruses.
• No specific treatment once the symptoms begin
• Inactivated and attenuated viral vaccine
• Pooled immune serum globulin for those entering into endemic areas
Hepatitis A virus

Capsid

RNA

VPG
Signs and Symptoms of Hepatitis?

- The acute phase of hepatitis

  - Diarrhea
  - Fatigue
  - Loss of appetite
  - Mild fever
  - Muscle or joint aches
  - Nausea
  - Slight abdominal pain
  - Vomiting
  - Weight loss
  - The acute phase is not usually dangerous,
Segmented, ds RNA genome, Nonenveloped
Reoviruses, Rotaviruses, and Caliciviruses

Unusual double-stranded RNA genome include the following:

- **Rotavirus** – oral-fecal transmission; primary viral cause of mortality and morbidity resulting from diarrhea in infants and children. treatment with rehydration and electrolyte replacement

- **Reovirus** – cold-like URT infection, enteritis

- **Caliciviruses** are small viruses. The family contains noroviruses, the major cause of nonbacterial epidemic gastroenteritis worldwide.
TABLE 6.2  Medi cally Relevant DNA Virus Groups

DNA Viruses

Enveloped

Double-stranded genome

- Poxviruses
- Herpesviruses

Nonenveloped

Double-stranded genome

- Adenoviruses (linear dsDNA)
- Papovaviruses (circular dsDNA)

Single-stranded genome

- Paroviruses

Source: Adapted from: Poxviridae from Buller et al., National Institute of Allergy & Infectious Disease, Department of Health & Human Services.
<table>
<thead>
<tr>
<th>FAMILY</th>
<th>ENVELOPE</th>
<th>SYMMETRY</th>
<th>DNA STRUCTURE</th>
<th>IMPORTANT VIRUSES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parvovirus</td>
<td>-</td>
<td>Icosahedral</td>
<td>SS, linear</td>
<td>B19 virus</td>
</tr>
<tr>
<td>Papovavirus</td>
<td>-</td>
<td>Icosahedral</td>
<td>DS, circular</td>
<td>HPV, Polyoma</td>
</tr>
<tr>
<td>Adenovirus</td>
<td>-</td>
<td>Icosahedral</td>
<td>DS, linear</td>
<td>Adenoviruses</td>
</tr>
<tr>
<td>Hepadnavirus</td>
<td>+</td>
<td>Icosahedral</td>
<td>DS, incomplete circular</td>
<td>Hepatitis B virus</td>
</tr>
<tr>
<td>Herpesviruses</td>
<td>+</td>
<td>Icosahedral</td>
<td>DS, linear</td>
<td>HSV, VZV, CMV, EBV, HHV6</td>
</tr>
<tr>
<td>Poxviruses</td>
<td>+</td>
<td>Complex</td>
<td>DS, linear</td>
<td>Vaccinia, Variola, Molluscum contagiosum</td>
</tr>
</tbody>
</table>
Double-stranded DNA, nonenveloped viruses

- All of the human adenoviruses are classified in the *Mastadenovirus genus*. Human adenoviruses are divided into six groups (A–F) on the basis of their genetic, physical, chemical, and biologic properties. Adenoviruses are cytopathic for human cell cultures, particularly kidney and epithelial cells.
- The cytopathic effect usually consists of marked rounding, enlargement, and aggregation of affected cells into grapelike clusters.

**Mastadenovirus**
- Respiratory infections in humans
- Tumors in animals
Double-stranded DNA, nonenveloped viruses

Papovaviridae

- Papillomavirus (human wart virus)
- Polyomavirus (Cause tumors)

Papillomaviruses cause skin cell proliferation \(\Rightarrow\) benign growth named **wart** or papilloma. Spread by direct contact. May regress spontaneously or be removed chemically or physically.
Double-stranded DNA, enveloped Poxviruses

**Poxvirus** are the largest and most complex viruses infecting humans.

- Smallpox, Molluscum Contagiosum, Cowpox
  - Smallpox virus (Orthopoxvirus). Two types: **variola major** (> 20% mortality); **variola minor** (< 1% mortality)
  - Respiratory transmission.
  - Virus moved to skin via bloodstream.
  - Human is the only host
  - The incubation period of variola (smallpox) was 10–14 days.
  - The onset was usually sudden. One to 5 days of fever and malaise appearance of the exanthems, which began as macules, then papules, then vesicles, and finally pustules ..........Pitted scars
Ds DNA, Enveloped, Herpesvirus

- The herpesviruses that commonly infect humans include:
- Herpes simplex virus types 1 and 2 (HSV-1, HSV-2).
- HSV-1 infections involved Oropharyngeal and may occur in the eye, producing severe keratoconjunctivitis, Encephalitis.
- Genital disease is usually caused by HSV-2, although HSV-1 can also cause clinical episodes of genital herpes
- Varicellazoster virus (HHV 3)
- Epstein-Barr virus (EBV, HHV 4). It is best known as the cause of infectious mononucleosis (glandular fever). Infection occurs by the oral transfer with saliva and genital secretions.
- Cytomegalovirus (CMV, HHV 5)
- Herpesviruses 6 and 7. HHV-6 infects T lymphocytes. It is typically acquired in early infancy and causes exanthem subitum (roseola infantum).
- HHV-7, also a T-lymphotropic virus, has not yet been linked to any specific disease.
- Herpesvirus 8 (Kaposi sarcoma-associated herpesvirus (KSHV, HHV 8).
- There are nearly 100 viruses of the herpes group that infect many different animal species
Important properties of herpesviruses

- Shape: icosahedral
- Genome: double-stranded DNA, linear, envelope: contains viral glycoproteins, Fc receptors
- Replication: nucleus, bud from nuclear membrane
- Establish latent infections
- Persist indefinitely in infected hosts
- Frequently reactivated in immunosuppressed hosts
- Some cause cancer

**HSV-1** can remain latent in trigeminal nerve ganglia
**HHV-2** can remain latent in sacral nerve ganglia.
HSV-1 in the Trigeminal Nerve Ganglion

- Trigeminal nerve
- Ganglion
- Site of viral latency
- Site of active lesion
Chickenpox (VZV or HHV-3)

Varicella–zoster or human herpes virus 3 of *Hepesviridae* family

Respiratory transmission $\Rightarrow$ to blood $\Rightarrow$ to skin ($\Rightarrow$ to sensory neuron)

**Macule** to **papule** to **vesicle** to **pustule** in 24 h

Pruritic (itchy) lesions – scratching may lead to serious 2° infections (*S. pyogenes* and *S. aureus*)

Complications: encephalitis and Reye’s syndrome.

After chickenpox, virus can remain latent in nerve cells. Reactivation later $\Rightarrow$ **shingles** = **Herpes zoster** (characteristic vesicular rash along affected cutaneous sensory nerves.)
Virus may remain latent in dorsal root ganglia

Occurrence of shingles when cell mediated immunity weak.

After healing may result in chronic pain → Post-herpetic neuralgia (may last for years)

(b) Recurrence of infection: shingles (herpes zoster)
Shingles or Herpes Zoster

About 20% of people who have had chicken pox will get zoster at some time during their lives. Most people will get zoster only once.
Hepadnaviridae

- Double-stranded DNA, enveloped viruses
- Hepadnavirus (Hepatitis B virus)
- Use reverse transcriptase to produce DNA from mRNA
Table 2 — Some viral causes of hepatitis in humans. Adapted from Cliver, 1997.

<table>
<thead>
<tr>
<th>Type</th>
<th>Former name</th>
<th>Transmission Mode</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Infectious hepatitis</td>
<td>Fecal-oral</td>
</tr>
<tr>
<td>B</td>
<td>Serum hepatitis</td>
<td>Parenteral</td>
</tr>
<tr>
<td>C</td>
<td>Non-A, non-B</td>
<td>Parenteral</td>
</tr>
<tr>
<td>D</td>
<td>Delta agent</td>
<td>Parenteral</td>
</tr>
<tr>
<td>E</td>
<td>Non-A, non-B</td>
<td>Fecal-oral</td>
</tr>
<tr>
<td>Name of Virus</td>
<td>Hepatitis A Virus (HAV)</td>
<td>Hepatitis B Virus (HBV)</td>
</tr>
<tr>
<td>--------------------</td>
<td>-------------------------</td>
<td>-------------------------</td>
</tr>
<tr>
<td>Classification</td>
<td>Picornavirus</td>
<td>Hepadnavirus</td>
</tr>
<tr>
<td>Viral genome</td>
<td>ssRNA</td>
<td>dsDNA</td>
</tr>
<tr>
<td>Transmission</td>
<td>Enteric</td>
<td>Parental</td>
</tr>
<tr>
<td>Incubation period</td>
<td>15-45 days</td>
<td>45-160 days</td>
</tr>
<tr>
<td>Chronic Hepatitis</td>
<td>No.</td>
<td>Yes. 10% chance</td>
</tr>
<tr>
<td>Cure?</td>
<td>No cure. Treatments usually tackle the symptoms.</td>
<td>No cure. Treatments usually tackle the symptoms.</td>
</tr>
</tbody>
</table>
Herpetic Whitlow

- Occupational hazard for health care professionals.
- Intense painful infection of the hand involving 1 or more fingers, typically terminal phalanx
- (60% HSV-1; 40% HSV-2)
Parvoviruses: simplest DNA animal viruses.
- Because of the small coding capacity of their genome, viral replication is dependent on functions supplied by replicating host cells or by coinfecting helper viruses.
- Parvovirus B19 is pathogenic for humans and has a tropism for erythroid progenitor cells.
- It is the cause of erythema infectiosum, (“fifth disease”), a common childhood exanthem.
- Polyarthralgia-arthritis syndrome in normal adults.
- Chronic anemia in immunocompromised individuals, Fetal death.
Parvovirus B19

- Family: *Parvoviridae*
  - Latin *parvus* means small
- ~20 nm in diameter
  - (0.02 μm)
- Single-stranded DNA virus
- Icosahedral capsid
- No envelope
- Only known human parvovirus
**ERYTHEMA INFECTIOSUM (Fifth disease)**

| Causative Agent          | Human Parvovirus B19  
<table>
<thead>
<tr>
<th></th>
<th>Spreads by Respiratory Secretions</th>
</tr>
</thead>
</table>
| Host and Environment     | Children 3 to 12 years of age  
|                         | Occurs in Winter and Spring    |
| Rash                     | Classic Bright-red facial rash ("slapped cheek") and progresses to lacy reticular rash; may wax and wane for 6 to 8 weeks |
| Clinical Features        | Mild Fever  
|                         | Arthritis in Adults  
|                         | Rash after fever resolves    |
| Diagnosis                | Serology – B19V IgM Antibodies Detection |
| Treatment                | Supportive                      |
Oncogenic DNA Viruses and RNA Viruses

- Papilloma virus (HPV) → cervical cancer
- Epstein-Barr virus (EBV) → Burkitt’s lymphoma
- HV8 → Kaposi’s sarcoma
- Hepatitis B virus (HBV) → liver cancer
- Hepatitis C virus (HCV) → liver cancer
- human T-cell leukemia virus (HTLV-1)