Pathogenic Viruses
DNA Viruses

• DNA viruses that cause human disease
• Classified based on
  – type of DNA they contain
  – presence or absence of an envelope
  – Size
  – host cells they attack
• Contain either double-stranded DNA (dsDNA) or single-stranded DNA (ssDNA) for their genome

Poxviridae

- Double-stranded DNA viruses
- Have complex capsids and envelopes
- Largest viruses
- Infect many mammals
- Most animal poxviruses are species specific
  - Unable to infect humans because they cannot attach to human cells
- Infection occurs primarily through the inhalation of viruses
  - Close contact is necessary for infection by poxviruses
• Smallpox and molluscum contagiosum are the two main poxvirus diseases of humans
• Some diseases of animals can be transmitted to humans (cowpox)
• All poxviruses produce lesions that progress through a series of stages
Smallpox

- In the genus Orthopoxvirus
- Commonly known as variola
- Exists in two forms
  - Variola major causes severe disease that can result in death
  - Variola minor causes a less severe disease with a much lower mortality rate
Smallpox

• Both forms infect internal organs and then move to the skin where they produce pox
• Scars result on the skin, especially on the face
• Smallpox is the first human disease to be eradicated
Smallpox

• There are a number of factors that allowed eradication of smallpox
  – Inexpensive, stable, and effective vaccine
    • Vaccinia virus – antigenically similar
  – No animal reservoirs
  – Obvious symptoms allow for quick diagnosis and quarantine
  – Lack of asymptomatic cases
  – Virus is only spread via close contact
Varicella-Zoster Virus Infections

• Herpes Virus
• Commonly referred to as VZV
• Causes two diseases
  – Varicella
    • Often called chicken pox
    • Typically occurs in children
  – Herpes zoster
    • Also called shingles
    • Usually occurs in adults
VZV Infections

• Chickenpox - highly infectious disease
• Viruses enter the skin through the respiratory tract and the eyes (Droplet transmission)
• Virus replicate at the site of infection then travel via the blood throughout the body
• Characteristic skin lesions appear 2-3 weeks after infection
• The disease is usually mild
• Chickenpox in adults is typically more severe than the childhood illness
Epidemiology and Pathogenesis of VZV Infections

- Latent virus can reactivate producing a rash known as shingles
- The rash is characteristic for its localization along a dermatome
Figure 24.10

Initial infection: viruses move up spinal nerve

Reactivation: viruses move down spinal nerve at a later time

Shingles

Spinal nerve dermatome

Spinal cord

Spinal dorsal root ganglion

Latent virus in nerve cell body

Nerve cell body
Figure 24.10, step 1

Initial infection: viruses move up spinal nerve

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Figure 24.10, step 2

- Spinal cord
- Spinal dorsal root ganglion
- Nerve cell body
- Latent virus in nerve cell body
Figure 24.10, step 3

Reactivation: viruses move down spinal nerve at a later time

Shingles

Spinal nerve dermatome

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Diagnosis, Treatment, and Prevention

• Diagnosis
  – Chickenpox - characteristic lesions
  – Shingles lesions more difficult to diagnose
    • localization along a dermatome is characteristic

• Treatment
  – Chickenpox is usually self-limiting
  – Shingles treatment involves management of the symptoms and bed rest

• Prevention
  – Difficult to prevent exposure to VZV because the viruses are shed from patients before obvious signs appear
  – Vaccine (killed) – shingles protection unknown
Papillomavirus Infections

- Causes papillomas, commonly known as warts
  - Benign growths of the epithelium of the skin or mucous membranes
- Papillomas form on many body surfaces
  - Often painful and unsightly
- Genital warts are associated with an increased risk of cancer
Seed Warts
(b) Plantar Warts

Figure 24.17b
Figure 24.17c

Flat Wart
Epidemiology and Pathogenesis

- Transmitted via direct contact and via fomites
- Can also be spread from between locations on a given person
- Viruses that cause genital warts invade the skin and mucous membranes during sexual intercourse
- Genital warts are the most common sexually transmitted disease
Diagnosis, Treatment, and Prevention

• Diagnosis
  – Usually based on observation of the papillomas
  – Diagnosis of cancers results from inspection of the genitalia and by a PAP smear in women

• Treatment
  – Some warts can be removed through various methods
  – Treatment of cancers involves radiation and chemical therapy
Diagnosis, Treatment, and Prevention

• Prevention
  – Prevention of most types of warts is difficult
  – Genital warts can be prevented by abstinence or mutual monogamy
  – Vaccine now available for Human Papilloma Virus (HPV)
    • Against 2 strains of HPV responsible for 70% of cancer cases
Hepadnaviridae

- Enveloped DNA viruses
- Icosahedral capsids
- Genome = both ssDNA & dsDNA
- Includes the hepatitis B virus (HBV)
Hepatitis B

- HBV replicates through an RNA intermediary, – a phenomenon unique among DNA viruses
- HBV invades and replicates in liver cells
- HBV is the only DNA virus that causes hepatitis
Hepatitis B Infections

• Causes inflammation of the liver known as hepatitis
• Can cause severe liver damage
• Symptoms can include
  – jaundice
  – enlargement of the liver
  – abdominal distress
  – and bleeding into the skin and internal organs
• Coinfection with hepatitis D virus can increase the risk of permanent liver damage
Epidemiology & Pathogenesis of HBV Infections

- Virions are shed into saliva, semen, and vaginal secretions

- **Transmission**
  - infected body fluids in contact with breaks in the skin or mucous membranes (particularly blood)
  - through infected needles, sexual intercourse, and passage to babies during childbirth

- Many are asymptomatic or produce mild symptoms

- HBV has been shown to be associated with liver cancer (why?)
Diagnosis, Treatment, and Prevention

• Diagnosis
  – Uses labeled antibodies to detect the presence of viral surface antigens released from HBV-infected cells

• Treatment
  – No universally effective treatment
  – The best treatment is prevention

• Prevention
  – Vaccination and safer sexual practices has helped reduce the number of cases of hepatitis B
RNA Viruses

- RNA viruses are the **only** infective agents that use RNA molecules to store their genetic information.

- RNA viruses are categorized by:
  - genomic structure
  - presence of an envelope
  - size and shape of their capsid
RNA Viruses

• 4 types of RNA viruses
  – Positive single-stranded RNA (+ssRNA) viruses
    • Picornaviridae, Caliciviridae, Astroviridae, Togaviridae, Flaviviridae, and Coronaviridae
  – Retroviruses (+ssRNA viruses that convert their genome to DNA inside a cell)
  – Negative single-stranded RNA (-ssRNA) viruses
    • Paramyxoviridae, Rhabdoviridae, Filoviridae, Orthomyxoviridae, Bunyaviridae, and Arenaviridae
  – Double-stranded RNA (dsRNA) viruses
    • Reoviridae
Influenza

- Enveloped, segmented, neg. strand RNA virus
- Orthomyxovirus
  - types A, B & C
- Infection - through inhalation of airborne viruses
Influenza
Influenza

- Influenza viruses causes death of the epithelial cells of lungs and throat
  - first line of defense
- More susceptible to secondary bacterial infections
- Symptoms include fever, malaise, headache, and myalgia
  - Induced by cytokines released as part of the immune response
The genome of flu viruses are highly variable (especially envelope components). The changing antigens guarantee that there will be susceptible people.
Antigenic drift

Antigenic Drift creates virus with slightly modified antigens.

Will the antibodies you made to last seasons flu neutralize this virus?
(b) Antigenic Shift

1. Influenza viruses 1 and 2 enter host cell
2. Genes and antigens from both viral types are incorporated into new virions
3. Influenza virus 3 very different from viruses 1 and 2

Occasional outbreaks of very severe influenza

Number of cases

Time (years)
Antigenic shift generates viruses with entirely unique antigens
# Known Flu Pandemics

<table>
<thead>
<tr>
<th>Name of Pandemic</th>
<th>Date</th>
<th>Deaths</th>
<th>Subtype involved</th>
<th>Pandemic severity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Russian Flu</strong></td>
<td>1889-1890</td>
<td>1 million possibly</td>
<td>H2N2?</td>
<td></td>
</tr>
<tr>
<td><strong>Spanish Flu</strong></td>
<td>1918–1920</td>
<td>40 to 100 million</td>
<td>H1N1</td>
<td>5</td>
</tr>
<tr>
<td><strong>Asian Flu</strong></td>
<td>1957-1958</td>
<td>1 to 1.5 million</td>
<td>H2N2</td>
<td>2</td>
</tr>
<tr>
<td><strong>Hong Kong Flu</strong></td>
<td>1968–1969</td>
<td>0.75 to 1 million</td>
<td>H3N2</td>
<td>2</td>
</tr>
</tbody>
</table>
1919 Spanish Flu
Bird Flu (Avian Flu)

- H5N1
THE NEXT PANDEMIC?
Although the H5N1 virus, known as the avian flu virus, does not usually infect humans, new mutated forms of this virus could represent a realistic risk of a flu pandemic, experts say.

**Shorebirds**
Are natural carriers of the avian flu virus in the wild.

**Domestic birds**
Intermediate hosts and easily infected by the virus through contact with nasal or fecal material. Contact with other domestic animals favors the spread of the disease.

**Mammals**
Intermediate hosts. Hogs can also be infected by human flu virus, which increases the risk of mutated human compatible viruses.

**Waterfowl**
Infected by shared water sources.

**Pandemic cycle**

**Humans**
Rarely infected by unaltered strains of the avian flu virus. Experts think that mutated viruses could spread from human to human.

**Major Flu Pandemics**
Number of deaths in the USA:

<table>
<thead>
<tr>
<th>Flu Type</th>
<th>Number of Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spanish Flu (1918)</td>
<td>500,000</td>
</tr>
<tr>
<td>Asian Flu (1957)</td>
<td>70,000</td>
</tr>
<tr>
<td>Hong Kong Flu (1968)</td>
<td>34,000</td>
</tr>
</tbody>
</table>

**Global Killer**: The [A(H1N1)] strain of the flu virus, commonly known as the "Spanish Influenza" killed more than 50 million people worldwide.

Sources: Centers for Disease Control, World Health Organization
Swine Flu

- H1N1

- Confirmed cases followed by death
- Confirmed cases
- Unconfirmed or suspected cases
## Mortality Rates

<table>
<thead>
<tr>
<th></th>
<th>H1N1</th>
<th>Seasonal Flu + Influenza A</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Death since April 2009</td>
<td>171</td>
<td>29</td>
</tr>
</tbody>
</table>
Diagnosis & Treatment

• Diagnosis
  – Manifestations of flu signs and symptoms during a community-wide outbreak of the flu is often sufficient

• Treatment
  – Drugs are available that prevent uncoating of the virus or block release of virions from infected cells
    • Must be administered early because they don’t prevent the later manifestations of the disease
Antiviral Drugs

- Neuraminidase Inhibitors
  - Oseltamivir (Tamiflu)
  - Zanamivir (Relenza)

- M2 Ion Channel Inhibitors
  - Amantadine
  - Rimantadine
Prevention

• Prevention
  – Immunization with multivalent vaccines
    • Contain several antigens within a single vaccine
    • Protective only against the strains included in the vaccine
  – Hand Washing & use of alcohol based sanitizers
  – Avoid large groups of people or public places
Rabies

- Attaches to skeletal muscle cells
  - Travels through neurons to the central nervous system
  - Salivary glands
- Central nervous system involvement =
  - Hyperactivity
  - Aggressive behavior
  - Hydrophobia
- Lethal disease (100% fatality)
  - Respiratory paralysis
Diagnosis & Treatment

• Diagnosis
  – Neurological symptoms of rabies are unique and usually sufficient
  – By the time symptoms and antibodies occur it is too late to intervene

• Treatment
  – Treatment of the site of infection
  – Injection of human rabies immunoglobulin (HRIG)
    • passive immunization
  – Attenuated vaccine
Prevention

• Prevention
  – Control
    • Vaccination of domestic dogs and cats
  – Little can be done to eliminate rabies in wild animals (skunks, bats, raccoons, wolves, etc.)
Retroviridae

• Studied more than any other group of viruses
• Polyhedral capsids with spiked envelopes
• Genomes - two identical molecules of positive ssRNA
• Don’t conform to the “central dogma”
• Retroviruses transcribe dsDNA from ssRNA using reverse transcriptase
• Two types of retroviruses
  – Viruses that are primarily oncogenic
  – Viruses that are primarily immunosuppressive
Oncogenic Retroviruses

• Infections are chronic and long-term prognosis of patients is poor
• Exact way oncogenic retroviruses cause cancer is unclear
Acquired Immunodeficiency Syndrome

– AIDS is not a disease but a syndrome
– AID Syndrome
  • Certain opportunistic or rare infections that occur in the presence of antibodies against HIV and a CD4 white blood cell count below 200 cells/microliter of blood
– HIV
  • Likely arose from mutation of simian immunodeficiency virus
  • Only replicates in humans
  • Destroys the human immune system
Acquired Immunodeficiency Syndrome

- Two major types of HIV
  - HIV-1 is prevalent in the United States and Europe
  - HIV-2 is prevalent in West Africa
- Surface proteins - glycoproteins gp120 and gp41 impede the immune clearance of HIV
  - antigenic variability (gp120)
  - ability to fuse with host cells (gp41)
- HIV replication cycle is similar to other animal retroviruses
Epidemiology of HIV

• AIDS - 1st recognized in young male homosexuals in US
• Found throughout the world as a heterosexual disease
• HIV is found in sufficient concentrations to cause infection
  – in blood, semen, saliva, vaginal secretions, and breast milk
• Blood and semen are more infective than other secretions
The global prevalence of HIV
Epidemiology of HIV

- Infected fluid must come in contact with a tear or lesion in the skin or mucous membranes or be injected into the body

- Transmitted
  - sexual contact
  - intravenous drug use
  - mother to baby across the placenta and in breast milk
Modes of HIV transmission in Americans during 2007

**Adult Males**
- Male homosexual contact: 71%
- Other: 1%
- High-risk heterosexual contact: 14%
- Use of injected drugs: 10%

**Adult Females**
- Male homosexual contact: 83%
- High-risk heterosexual contact: 8%
- Use of injected drugs: 16%
- Other: 1%

Figure 25.24
Acquired Immunodeficiency Syndrome

— Diagnosis

• Serological diagnosis involves detecting antibodies against HIV - ELISA
  — Positive test does not indicate presence of AIDS

• Signs and symptoms vary according to the diseases present

• Long-term nonprogressors appear not to develop AIDS
  — May be due to defective virions or lack of effective coreceptors for the virus
Acquired Immunodeficiency Syndrome

– Treatment
  • HAART currently used to reduce viral replication
    – Cocktail of antiviral drugs
    – Not a cure
  • Vaccine development has been difficult

– Prevention
  • Behavioral changes can slow progression of AIDS epidemics
    – Abstinence and safe sex
    – Use of clean needles
    – Screening of blood products
    – Administering AZT to infected pregnant women