Chapters 19-24: Selected Viral Pathogens

1. DNA Viral Pathogens

2. RNA Viral Pathogens
1. DNA Viral Pathogens
Smallpox

Caused by *variola* virus (dsDNA, enveloped):

- portal of entry is the respiratory tract
- infects internal organs and skin resulting in characteristic skin pustules ~10 days post infection
- mortality rate up to 20% if untreated

- has been effectively eradicated due to vaccination (which are no longer given!)
- only real risk these days is bioterrorism

Figure 21.9
Family *Herpesviridae*

Enveloped, ds DNA viruses, several of which are common pathogens:

**Human Herpes Virus-1 & 2 (HHV-1 & HHV2)**
- aka “Herpes Simplex Viruses”
- responsible for fever blisters, genital herpes

**Human Herpes Virus-3 (HHV-3)**
- aka “Herpesvirus Varicella Zoster”
- responsible for chicken pox, shingles

**Human Herpes Virus-4 (HHV-4)**
- aka Epstein-Barr virus (EBV)
Herpes Simplex

Caused by HHV-1 and HHV-2:

HHV-1

• very common & typically benign infection found in ~90% of the U.S. population

• responsible for cold sores & fever blisters

• transmission through respiratory or oral routes

HHV-2

• responsible for genital herpes from sexual contact
Outbreak of facial/oral lesions due to HHV-1:

- due to latent infection (provirus) of trigeminal ganglion nerves

- lesions triggered typically by stress or UV exposure
Genital Herpes

The STD “genital herpes” is primarily caused by Human Herpesvirus 2 (HHV-2):

- oral-genital transmission of HHV-1 can also cause genital lesions
- transmission due to sexual contact is followed by a ~1 wk incubation period and then:
  - burning sensation followed by the appearance of painful blister-like vesicles that eventually heal
- like all herpes viruses, HHV-2 infection results in latent provirus, periodic reactivation
- antiviral drugs can manage, but not cure the disease
Chicken Pox & Shingles

Chicken pox is caused by Herpesvirus varicella-zoster (HHV-3):

- due to symptoms of initial infection
- respiratory portal of entry
- skin cells then infected to cause “pox”
- becomes latent infection in spinal cord

(a) Initial infection: chickenpox (varicella)
Shingles is due to the activation of latent HHV-3:

- only occurs in people who have had chicken pox
- appears in people who are immunologically weakened due to stress or age
Epstein-Barr Virus

The Epstein-Barr virus (EBV) or human herpesvirus 4 (HHV-4) is responsible for:

**MONONUCLEOSIS**

- transmitted via saliva
- virus infects B cells
- sore throat, swollen lymph nodes, extreme fatigue

**Burkitt’s & other LYMPHOMAS**

- malignant lymphocyte cancers
- chromosomal translocations
Human Papillomavirus

HPV is a dsDNA, nonenveloped virus that is the cause of papillomas (aka verrucae or “warts”):

- generally benign tumors of the skin epithelium

- transmitted via direct contact or fomites (towels or other objects)

- genital warts are spread by sexual contact
  - some strains (e.g., HPV-16) can cause cervical or penile cancer
  - new vaccine Gardasil provides complete protection fr. select strains
2. RNA Viral Pathogens
Poliomyelitis

Caused by *Poliovirus* (RNA+, nonenveloped):

**TRANSMISSION:** ingestion of water contaminated with fecal material (vehicle transmission)

**SYMPTOMS:** sore throat & nausea initially, potential CNS infection leading to paralysis, respiratory failure

**DIAGNOSIS:** virus in feces or throat material

- nearly eradicated due to vaccination
Influenza (flu)
Caused by various strains in the genus \textit{Influenzavirus} (RNA-, enveloped):

- H spike (hemagglutinin) mediates attachment
  - 15 known types, determines host range

- N spike (neuraminidase) aids in detachment from host during release
  - 9 known types

- H & N combinations distinguish different strains (e.g. H5N1)
Influenzavirus Genera

Influenzavirus A:
- natural hosts include aquatic birds, pigs
- new strains can occasionally “jump” from animal hosts to humans
- source of most dangerous outbreaks in humans

Influenzavirus B:
- limited almost exclusively to humans
- not as dangerous

Influenzavirus C:
- generally limited to humans, less common
Generation of New Strains

Antigen *Drift*:

- changes in viral genome due to natural mutation
  - viral RNA-synthesizing enzymes are relatively error-prone, lack “proofreading” capability of most DNA polymerases
  - change is gradual, not usual source of pandemics

Antigen *Shift*:

- new variants due to simultaneous infection of same cell with *different* strains (usu. in bird or pig)
  - can produce new H:N combos via “shuffling” of RNA frags.
  - limited primarily to type A, source of most pandemics
Antigenic Shift in Influenza

(A) H1N1 influenza virus
Bird-to-human transmission of H1N1 virus
N spike
H spike
All 8 genetic segments thought to have originated from avian influenza virus

(B) H2N2 influenza virus
Reassortment human H2N2
Three new genetic segments from avian influenza virus introduced, including H and N; containing 5 RNA segments from 1918

(C) H3N2 influenza virus
Reassortment human H3N2
Two new genetic segments from avian influenza virus introduced, including H; containing 5 RNA segments from 1918

(D) Next pandemic virus?
avian virus, or...
Avian virus
H3N2 human virus
All eight genes new or further derivative of 1918 virus

Relative number of influenza cases (not to scale)

Year
1900
1918–1919
1932
1947
1957
1968
1977
1983

“Spanish” influenza
First virus isolation from humans
“Asian” influenza
“Hong Kong” influenza
Reappearance of H1N1

Antigenic Shift in Influenza
TRANSMISSION: contact, airborne, highly contagious, (some Type A strains can “jump” from animal to human)

DIAGNOSIS: symptoms & signs, PCR

TREATMENT: Oseltamivir, Zanamivir (neuraminidase inhibitors), antibiotics to protect from secondary infection

<table>
<thead>
<tr>
<th>TABLE 24.2</th>
<th>Human Influenza Viruses*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
<td>Antigenic Subtype</td>
</tr>
<tr>
<td>A</td>
<td>H3N2 (the first “modern” pandemic; originated in southern China)</td>
</tr>
<tr>
<td></td>
<td>H1N1 (Spanish)</td>
</tr>
<tr>
<td></td>
<td>H2N2 (Asian)</td>
</tr>
<tr>
<td></td>
<td>H3N2 (Hong Kong)</td>
</tr>
<tr>
<td></td>
<td>H1N1 (Russian)†</td>
</tr>
<tr>
<td>B</td>
<td>None</td>
</tr>
<tr>
<td>C</td>
<td>None</td>
</tr>
</tbody>
</table>

*The conventional wisdom is that H1, H2, and H3 are human-infecting strains; H4, H5, H6, and H7 primarily infect animals, especially swine and poultry. (Avian influenza strains H5N1 and H7N7 have caused human fatalities.)

†Probably escaped from a laboratory. At this time persons over age 20 were mostly immune from similar viruses circulating in the 1950s and earlier in the century.

Rhinovirus

A non-enveloped RNA+ virus that is the most common cause of “common colds”:

• >100 strains of *Rhinovirus* are known to cause the common cold

  • strains of *Coronavirus, Adenovirus* and others also cause common colds

TRANSMISSION:
direct contact or airborne droplets, fomites

TREATMENT:
none other than medications to treat symptoms
Rabies

- rabies virus is a _Lyssavirus_ (enveloped, RNA-)
- transmitted via bite of infected animal (dogs, bats)
- incubation can be weeks to years, prodromal period unremarkable
- ultimate infection of CNS which is fatal
Viral Hepatitis

Hepatitis is the inflammation of the liver which in most cases is due to one of several viruses and can be life-altering, even lethal:

• symptoms include fever, malaise, jaundice (yellow tint to eyes & skin, dark urine due to excess bilirubin)

• incubation periods are usually several weeks but can be months or years

Hepatitis A (hepatitis A virus, HAV: RNA+, non-enveloped)

• ingested via contaminated food (typically seafood), water, or contact with fecal matter from infected person
Hepatitis B (hepatitis B virus, HBV: dsDNA, enveloped)

- transmitted parenterally, sexually
- ~1% of infections are lethal, 10% become chronic
- has also been known to cause liver cirrhosis, cancer

Hepatitis C (hepatitis C virus, HCV: RNA+, enveloped)

- transmitted parenterally (blood transfusion, injected drugs)
- incubation period can be up to 20 years!
- ~85% of infections become chronic
- cirrhosis, liver cancer, even death are common outcomes
**Hepatitis D** (hepatitis D virus, HDV: RNA-, non-enveloped)

- by itself is NOT infectious
- infectious **only** when it acquires an HBV envelope and thus requires coinfection with HBV or superinfection of someone already infected with HBV
- this HBV, HDV combination has the highest hepatitis mortality rate of 20%!

**Hepatitis E** (hepatitis E virus, HEV: RNA+, non-enveloped)

- fecal-oral transmission
- endemic in areas with poor sanitation (rare in U.S.)
- afflicts young adults mainly, is especially dangerous for pregnant women (20% mortality)
Viral Gastroenteritis

The leading cause of childhood diarrhea worldwide is infection with rotavirus:

• dsRNA virus, non-enveloped (Reoviridae)

• infects and kills intestinal epithelial cells

• kills over 600,000 children/year throughout the world

  • mostly in the developing world

  • largely due to dehydration

• no successful vaccine has yet been produced
Human Immunodeficiency Virus (HIV) & AIDS

A type of *Lentivirus* (in the family Retroviridae)

- genetic material is RNA
- contains reverse transcriptase which copies viral RNA into DNA
- infects human $T_H$ cells, macrophages, dendritic cells & smooth muscle cells
HIV Transmission

Infection occurs via body fluids of an infected individual:

- blood contains the greatest density of HIV virions
- semen also contains significant numbers
- other fluids (e.g., saliva) generally don’t contain a sufficient density of HIV virions to transmit infection

Transmission typically occurs through:

- sexual contact
- blood transfusions
- puncture with contaminated needles
Attachment & Penetration

- gp120 “spikes” bind “viral receptor” on target cells
  - CD4 in association with CCR5 or CXCR4 (T<sub>H</sub> cells)
  - OR
  - CD4 in association with CCR5

- entry via fusion

(b) HIV infecting a CD4 T cell. The gp120 spike of HIV attaches to a CD4 receptor with CCR5 or CXCR4 coreceptors. The HIV capsid then enters the cell by fusion, leaving its envelope behind.
Biosynthesis vs Latency

- DNA is inserted into host cell chromosome (provirus)
- can remain latent for years, or express viral genes
  - virions can be latent too!
Key Terms for Viral Pathogens
(Chapters 19-24)

- papilloma
- jaundice
- hemagglutinin
- neuraminidase
- antigenic shift, antigenic drift