Introduction to the Viruses of Medical Importance: The DNA Viruses

Chapter 24
viruses

- obligate parasites
- infect animals, plants, & other microbes
- All DNA viruses are double-stranded except for parvoviruses, which have ssDNA.
- All RNA viruses are single-stranded except for dsRNA reoviruses.
- Viruses are limited to a particular host or cell type.
viruses

- Most DNA viruses are budded off the nucleus.
- Most RNA viruses multiply in & are released from the cytoplasm.
- Viral infections range from very mild to life-threatening.
- Many viruses are strictly human in origin, others are zoonoses transmitted by vectors.
- Most DNA & a few RNA viruses can become permanent resident of the host cell.
- Several viruses can cross the placenta & cause developmental disturbances.
### TABLE 24.1

**DNA Virus Groups**

- **DNA Viruses**
  - **Enveloped**
    - Double-stranded genome
      - Poxviruses
      - Herpesviruses
      - Hepadnaviruses
  - Nonenveloped
    - Double-stranded genome
      - Adenoviruses
      - Papovaviruses
    - Single-stranded genome
      - Paroviruses
Poxviruses

- produce eruptive skin pustules called pocks or pox, that leave scars
- largest & most complex animal viruses
- have the largest genome of all viruses
- dsDNA
- multiply in cytoplasm in factory areas
  - Variola – cause of smallpox
  - Vaccinia – closely related virus used in vaccines
  - Monkeypox
  - Cowpox
Smallpox

- first disease to be eliminated by vaccination
- exposure through inhalation or skin contact
- infection associated with fever, malaise, prostration, & a rash
  - Variola major – highly virulent, caused toxemia, shock, & intravascular coagulation
  - Variola minor – less virulent
- routine vaccination ended in US in 1972
- vaccine reintroduced in 2002
Herpesviridae

- large enveloped icosahedra dsDNA
- replication within nucleus
- large family; 8 infect humans
  - HSV-1
  - HSV-2
  - VZV
  - CMV
  - EBV
  - HHV-6
  - HHV-7
  - HHV-8
Herpesviruses
Herpesviridae

- latency & recurrent infections
- complications of latency & recurrent infections become more severe with age, cancer chemotherapy, etc
- most common & serious opportunists among AIDS patients
Herpes Simplex Virus (HSV)

- **HSV-1** lesions on the oropharynx, cold sores, fever blisters
  - occurs in early childhood
- **HSV-2** lesions on the genitalia
  - occurs in ages 14-29
  - can be spread without visible lesions
- humans only reservoir
- treatment: acyclovir, famciclovir, valacyclovir
<table>
<thead>
<tr>
<th></th>
<th>HSV-1</th>
<th>HSV-2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Usual Etiologic</strong>&lt;br&gt;Agent of:</td>
<td>Herpes labialis&lt;br&gt;Ocular herpes&lt;br&gt;Gingivostomatitis&lt;br&gt;Pharyngitis</td>
<td>Herpes genitalis*</td>
</tr>
<tr>
<td><strong>Transmission</strong></td>
<td>Close contact, usually of face</td>
<td>Sexual or close contact</td>
</tr>
<tr>
<td><strong>Latency</strong></td>
<td>Occurs in trigeminal ganglion</td>
<td>Occurs primarily in sacral ganglia</td>
</tr>
<tr>
<td><strong>Skin Lesions</strong></td>
<td>On face, mouth</td>
<td>On internal, external genitalia, thighs, buttocks</td>
</tr>
<tr>
<td><strong>Complications</strong></td>
<td><strong>Whitlows</strong>&lt;br&gt;Among personnel working on oral cavity</td>
<td>Among obstetric, gynecological personnel</td>
</tr>
<tr>
<td></td>
<td>Neonatal encephalitis&lt;br&gt;Causes up to 30% of cases**</td>
<td>Causes most cases</td>
</tr>
</tbody>
</table>

*The other herpes simplex type can be involved in this infection, though not as commonly.
**Due to mothers infected genitally by HSV-1 or contamination of the neonate by oral lesions.
**Varicella-Zoster Virus (VZV)**

- causes chickenpox & shingles
- transmitted by respiratory droplets & contact
- primary infection – chickenpox – vesicles
- virus enters neurons & remains latent
- later, reactivation of the virus results in shingles with vesicles localized to distinctive areas, dermatomes
- treatment: acyclovir, famciclovir, interferon
- live attenuated vaccine
Cytomegalovirus (CMV)

- produce giant cells with nuclear & cytoplasmic inclusions
- transmitted in saliva, respiratory mucus, milk, urine, semen, cervical secretions & feces
- commonly latent in various tissues
- most infections are asymptomatic
- 3 groups develop a more virulent form of disease: fetuses, newborns, immunodeficient adults
Normal lung cell

Infected lung cell
**CMV**

- Newborns may exhibit enlarged liver & spleen, jaundice, capillary bleeding microcephaly, & ocular inflammation, may be fatal
  - Babies who survive develop neurological sequelae; hearing, visual disturbances & mental retardation
- Perinatal CMV infection – mostly asymptomatic, or pneumonitis, & a mononucleosis-like syndrome
- AIDS patients – CMV mononucleosis, disseminated CMV, retinitis,
- Transplant patients - pneumonitis, hepatitis, myocarditis, meningoencephalitis
- Treatment: ganciclovir, valycyclovir, foscarnet
Epstein-Barr Virus (EBV)

- infects lymphoid tissue & salivary glands
- transmission – direct oral contact & contamination with saliva
- by mid-life 90-95% of all people are infected
- causes **mononucleosis** – sore throat, high fever, cervical lymphadenopathy
- 30-50 day incubation
- most cases asymptomatic
- **Burkitt’s lymphoma** associated with chronic coninfections with malaria, etc
- **nasopharyngeal carcinoma** in Chinese & African men
Human Herpes Virus 6 (HHV-6)

- T-lymphotrophic virus
- transmitted by close contact
- very common – 95% prevalent
- causes roseola, an acute febrile disease in babies 2-12 months
- begins with fever, followed by a faint maculopapular rash
- usually self-limited
- adults may get mono-like symptoms, lymphadenopathy, hepatitis
- over 70% of MS patients show signs of infection
- can cause encephalitis, cancer
- **HHV-7** is closely related to HHV-6 causes similar diseases

- **Kaposi’s sarcoma**-associated virus or **HHV-8** is linked with common tumor of AIDS patients, also may be involved in multiple myeloma
Hepadnaviruses

- Enveloped DNA viruses
- Never been grown in tissue culture
- Unusual genome containing both double & single stranded DNA
- Tropism for liver
- **Hepatitis B** virus causes hepatitis & can be a factor in liver cancer
- Other members cause hepatitis in woodchucks, ground squirrels, & Peking ducks
Viral hepatitis

- hepatitis – an inflammatory disease of liver cells that may result from several viruses
- interferes with liver’s excretion of bile pigments, bilirubin accumulates in blood & tissues causing jaundice, a yellow tinge in skin & eyes
- caused by 3 principal viruses
<table>
<thead>
<tr>
<th>Property/Disease</th>
<th>HAV</th>
<th>HBV</th>
<th>HCV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Biology</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nucleic acid</td>
<td>RNA</td>
<td>DNA</td>
<td>RNA</td>
</tr>
<tr>
<td>Size</td>
<td>27 nm</td>
<td>42 nm</td>
<td>Various</td>
</tr>
<tr>
<td>Protein coat</td>
<td>–</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Cell culture</td>
<td>+</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Envelope</td>
<td>–</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><strong>Synonyms</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Infectious hepatitis, yellow jaundice</td>
<td>Serum hepatitis</td>
<td>Post-transfusional hepatitis</td>
</tr>
<tr>
<td><strong>Epidemiology</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reservoir</td>
<td>Endemic and epidemic</td>
<td>Endemic</td>
<td>Endemic</td>
</tr>
<tr>
<td>Transmission</td>
<td>Active infections</td>
<td>Chronic carrier</td>
<td>Chronic carrier</td>
</tr>
<tr>
<td></td>
<td>Oral-fecal; water- or food-borne</td>
<td>Overt inoculation from blood, serum; close contact</td>
<td>Inoculation from blood, serum; intimate contact</td>
</tr>
<tr>
<td><strong>Incubation Period</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2–7 weeks</td>
<td>1–6 months</td>
<td>2–8 weeks</td>
</tr>
<tr>
<td><strong>Symptoms</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fever, GI tract disorder</td>
<td>Fever, rash, arthritis</td>
<td>Similar to HBV</td>
</tr>
<tr>
<td><strong>Jaundice</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 in 10</td>
<td>Common</td>
<td>Common</td>
</tr>
<tr>
<td><strong>Onset/Duration</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Acute, short</td>
<td>Gradual, chronic</td>
<td>Acute to chronic</td>
</tr>
<tr>
<td><strong>Complications</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Uncommon</td>
<td>Chronic active hepatitis, hepatic cancer</td>
<td>Chronic inflammation, cirrhosis</td>
</tr>
<tr>
<td><strong>Availability of Vaccine</strong></td>
<td>+</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td><strong>Diagnostic Tests to Differentiate</strong></td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>
Hepatitis B virus

- multiplies exclusively in the liver, which continuously seeds blood with viruses
- $10^7$ virions/mL blood
- minute amounts of blood can transmit infection
- sexually transmitted
- high incidence among homosexuals & drug addicts
- can become a chronic infection
- increases risk of liver cancer
HBV

Filamentous form  Dane particle  Envelope
Hepatitis B virus

- chronic infection controlled with interferon
- HB immune globulin protects exposed people
- HBV vaccine – recombinant surface antigen made by yeast; given in 3 doses over 18 months
Papovaviruses

- Papillomavirus
- Polyomavirus
- Simian vacuolating virus
- 2 subtypes
  - Papillomavirus
  - Polyomavirus
- small nonenveloped icosahedra dsDNA
Papillomavirus

- papilloma – benign, squamous epithelial growth, wart
  - Neuraminidase (NA) – hydrolyzes mucus & assists viral budding & release
- caused by 40 different strains of HPV
- common seed warts – on fingers, etc
- plantar warts – on soles of feet
- genital warts – prevalent STD
- transmissible through direct contact or contaminated fomites
- Incubation – 2 weeks – more than a year
The Second World Wart.
Genital warts

- most common STD in US
- over 6 M new cases each year
- 30 M carriers of one of the 5 types of HPV associated with genital warts
- strong association with cervical & penile cancer – type 16 & 18
- podophyllin chemical treatment, cauterization, freezing, laser surgery, immunotherapy
Polyomaviruses

- induce tumors
- JC & BK viruses
- common throughout the world
- majority of infections are asymptomatic or mild
- not much is known
- BK infection in renal transplants causes complications in urinary function
- Progressive multifocal leukoencephalopathy (PML) is an uncommon fatal infection by JC
Virus Travel Agency

"Doorknob OK?"