Viruses

- Obligate parasites
- Infect animals, plants, & other microbes
- DNA viruses are usually double-stranded except for paroviruses, which have ssDNA
- Viruses are limited to a specific host or cell type

Viruses - Continued

- Most DNA viruses are budded off the nucleus
- 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 residents of the host cell

Clinical Considerations

- Course of viral disease: invasion at portal of entry and primary infection; some viruses replicate locally, others enter the circulation and infect other tissues
- Common manifestations: rashes, fever, muscle aches, respiratory involvement, swollen lymph nodes
- Body defenses: combined action of interferon, antibodies and cytotoxic T cells; frequently results in lifelong immunity

Survey of DNA Viruses

- Animal viruses are categorized according to nucleic acid, capsid, and presence or absence of envelope
- 7 DNA viral families
- DNA viruses causing human disease:
  - enveloped DNA viruses
  - nonenveloped DNA viruses
  - nonenveloped ssDNA viruses

Poxviruses

- Produce eruptive skin pustules called pox 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, causes toxemia, shock, & intravascular coagulation
  - Variola minor - less virulent
- Routine vaccination ended in US in 1972
- Has been used historically as bioweapon
- Vaccine reintroduced in 2002

The Herpesviridae: Common, Persistent Human Viruses

- All members show latency and cause recurrent infection; viral DNA forms episome
- Clinical complications of latency and recurrent infections become more severe with advancing age, cancer chemotherapy, or other conditions that compromise the immune defenses
- Common and serious opportunists among AIDS patients
- Large enveloped icosahedral dsDNA
- Replicates within nucleus

Herpesviridae

- Large enveloped icosahedral dsDNA
- Large family; 8 “species” infect humans
  - HSV-1
  - HSV-2
  - VZV
  - CMV
  - EBV
  - HHV-6
  - HHV-7
  - HHV-8

Pathology of Herpes Viruses

- Transmission by direct exposure to secretions containing the virus; active lesions most significant source; genital herpes can be transmitted in the absence of lesions
- HSV multiplies in sensory neurons, moves to ganglia
  - HSV-1 enters 5th cranial nerve
  - HSV-2 enters lumbosacral spinal nerve trunk ganglia
- Recurrent infection is triggered by various stimuli
  - Fever, UV radiation, stress, mechanical injury
- Newly formed viruses migrate to body surface, producing a local skin or membrane lesion
Herpes Simplex Viruses

- HSV-1: lesions on the oropharynx, cold sores, fever blisters
  - occurs in early childhood
- HSV-2: lesions on the genitalia
  - occurs primarily in ages 14-29
  - can be spread without visible lesions
- Humans only reservoir
- Treatment: acyclovir, famciclovir, valacyclovir

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

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
CMV - Continued

- AIDS patients – CMV mononucleosis, disseminated CMV, retinitis
- Transplant patients - pneumonitis, hepatitis, myocarditis, meningoencephalitis
- Treatment: ganciclovir, valacyclovir, 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 co-Infections
- Nasopharyngeal carcinoma in Chinese & African men

Hepadnaviruses

- Enveloped DNA viruses
- Never grown in tissue culture
- Unusual genome containing both double & single stranded DNA
- Specificity for the 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 principle viruses; hepatitis B is only DNA virus

Hepatitis B virus

- Multiples exclusively in the liver, which continuously seeds blood with virus
- $10^7$ 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

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

Adenoviruses
- Non-enveloped, ds DNA
- 30 types associated with human disease
- Infect lymphoid tissue, respiratory & intestinal epithelia & conjunctiva
- Oncogenic in animals, not in humans
- Spread by respiratory & ocular secretions
- Causes colds, pharyngitis, conjunctivitis, keratoconjunctivitis, acute hemorrhagic cystitis
- Inactivated polyvalent vaccine

Papovaviruses
- Papillomavirus
- Polyomavirus
- Small nonenveloped icosahedral dsDNA

Papillomavirus
- Papilloma – benign, squamous epithelial growth (wart)
- Caused by 40 different strains of HPV
- Common seed warts – on fingers, etc
- Plantar warts – on soles of feet
- Genital warts – prevalent STI
- Transmissible through direct contact or contaminated fomites
- Incubation – 2 weeks – more than a year
Genital warts

- Very common STI in US
- Over 6 M new cases each year
- 30 M carriers of one of the 5 types of HPV associated with genital warts
- Nine HPV types increase risk for developing reproductive cancer; 2 account for 70% of metastatic cervical tumors
- Vaccine (Gardasil) is advised to reduce risk of cervical cancer
- Podophyllin chemical treatment, cautery, freezing, laser surgery, immunotherapy

Polyomaviruses

- Induce tumors
- JC & BK viruses
- Common throughout the world
- Majority of infections are asymptomatic or mild
- BK infection in renal transplants causes complications in urinary function
- Progressive multifocal leukoencephalopathy (PML) is an uncommon fatal infection by JC virus

Parvoviruses

- Non-enveloped icosahedra, ssDNA
- Small diameter & genome size
- Causes distemper in cats, enteric disease in dogs, fatal cardiac infection in puppies
- B19 is cause of "fifth disease", erythema infectiosum rash of childhood
  - Child may have fever & rash on cheeks
  - Severe anemia can result if pregnant woman transmits virus to fetus