Hepatitis and Herpes Viruses

These two virus groups are very diverse, but cause much human morbidity and mortality
Liver Functions

• Performs 3 major functions:
  
  – **Regulation**: of blood composition
    • glucose levels, pyruvate levels, protein & fat concentrations
  
  – **Metabolism**: processes nutrients adsorbed from intestine
    • converts them into useful components, stores Vitamins (especially A), and minerals, (especially iron), manufactures, serum albumin, cholesterol, clotting factors, etc.
  
  – **Detoxifies**: removing drugs, alcohol, & potentially harmful chemicals, excreting them in urine or feces
    • Removes **bilirubin**--jaundice and icterus
Hepatitis

- Any of 5 hepatotropic viruses

- **Acute**
  - abrupt, malaise, fatigue, elevated liver enzymes, dark urine, light stools, icterus

- **Anicteric**
  - mild, some enzyme elevation, no icterus

- **Fulminant**
  - severe hepatitis, liver failure, high serum enzymes, fatal without liver transplant

- **Cholestatic**
  - acute obstructive hepatitis, deep jaundice, pruritus, slow recovery

- **Chronic**
  - persistent hepatic injury, elevated serum enzymes, often asymptomatic

- **Cirrhosis**
  - end-stage liver disease, loss of liver function, fatal

- **Primary liver cancer**
  - due to chronic/cirrhosis
Hepatitis A

- Extremely infectious
  - highly stable virus
  - oral/fecal/fomite
    - food, minimal contamination needed
    - poor sanitation
- From GI to liver
  - virus in feces
  - also in blood
- liver necrosis
  - due to immune response
- Acute hepatitis
  - 70% jaundice
- Asymptomatic in children
- Serious hepatitis in adults
  - over 50 years may be fulminant
- World wide
  - American adults are immuno-naïve
  - Greatly at risk visiting underdeveloped countries
- New vaccine available
Hepatitis B

• Replication in liver
• Major antigen stored in cells—HBsAG
  – immune avoidance?
• Parental transmission
  – “serum hepatitis”
  – blood, I.V. drug use
  – needle sticks
• Virus in semen, vaginal secretions,
  – sexual transmission
  • especially homosexual
  – neonatal infections
• 10 weeks incubation
• pathology due to immune response
  – 70% mild disease
  – 30% acute disease
  – 10% no effective immunity—chronic
    • chronic is silent
    • >50% cirrhosis
    • final stage=cancer
• type III hypersensitivity.
  – glomerulonephritis
  – polyarthritis
• High in China, Africa
Hepatitis B, continued

- Liver infections seed blood @ $10^7$ viruses per mL!!
  - Infectious dose is very low—transmission is high
    - Razors, tooth brushes, tattoos, etc.

- Hepatocellular carcinoma
  - one of most common
    - 1 million deaths/annum
  - nearly always fatal
  - China, Africa, SE Asia,
  - Chronic > Cirrhosis > Cancer
  - Coinfection with HCV is greater risk

HBV from tattooing needle virus is highly infectious
Hepatitis C

- “Non A, Non B”
- rapid mutations impede immunity
- Parental exposure
  - sexual less important
- Anicteric hepatitis
  - rarely acute
  - fatigue & malaise
  - some autoimmune disorders
  - 20% lead to cirrhosis, cancer
    - Liver transplants common
  - >20% i.v. drug users

urobilin
Hepatitis D

• “Delta agent”
  – a defective virus
  – Needs HBV “helper”
  – RNA surrounded by delta protein and shell of HBsAG
  – Must be co-infected
    • high risk to fulminant
    • rapid progress to cirrhosis
    • no higher risk for cancer
  – Distribution not same as HBV
    • S. America, Middle East, Africa

Scleral icterus
Hepatitis E

- Unrelated to others
- Similar to HAV
- oral/fecal
  - See in developing countries
  - Strangely fatal in 15-25% pregnant women
  - Acute and epidemic

Jaundice
Herpes Viruses

Herpo means to “creep”, known since ancient times. Nearly all humans have at least one herpes infection.
Herpes Diseases

- All display latency
- DNA viruses, most form proviruses
- most often integrate in neural cells
- lytic state induced by stress, malnutrition, changes in immune status, etc.
- most infections are asymptomatic, but may cause serious diseases, even cancer.
Cytomegalovirus, CMV

- Large spectrum
  - asymptomatic to fatal
  - immunosuppressed
    - transplant patients
    - AIDS patients
- Enlarges cells
- Congenital, perinatal and post natal
  - 40% Europe, 100% Africa
  - 30% homosexual males have in semen
    - sexually transmitted especially in homosexuals

Fatal neonatal disseminated CMV
CMV continued

• Most asymptomatic
  – symptoms look like IM
  – Congenital are most serious
    • encephalitis, mental retardation, liver damage, chorioretinitis, may be fatal, depends on maternal immunity

– AIDS
  • fevers, pneumonitis, hepatitis, encephalitis
  • serious complication of AIDS

– Transplant patients
  • increasing problems

Congenital Cytomegalovirus infection with numerous birth defects
Epstein-Barr Virus & Diseases

- Virus originally isolated from Burkitt’s lymphoma--but IM was first recognized dis.
- Ubiquitous B lymphotrophic herpes virus
- World wide seroconversion = 80-90%
- As with others, both lytic and latent phases
- Latency in immortalized B-lymphocytes
- Numerous EBV neoplasms noted
  - Burkitt’s and other lymphomas, nasopharyngeal carcinoma, etc.
- Range of diseases not yet defined
Biology of Epstein-Barr Virus

- DNA virus, with adult seroconversion = 90%+
- Primary infection in children is asymptomatic, in adults it is IM
- Saliva transmission
- Mucosal cells introduce to blood, to B-cells
  - polyclonal stimulation
  - B-cell immortalization
  - heterophil antibodies
  - Neoplasms

Abnormal B-cells with EBV
Infectious Mononucleosis

• Incubation = 4-7 weeks
• Results in IM syndrome
  – fever, sore throat, lymphadenopathy, hepatosplenomegaly, hepatitis
  – fevers last 1-3 wks
  – 50% splenomegaly
  – rash occurs with antibiotic treatment (for mistaken Strept infection)
  – Major problem in AIDS
• Diagnosis:
  – lymphocytosis, atypical lymphocytes, heterophil antibody
Herpes Simplex 1 & 2

- Seemingly more cases in last 100 years
- HSV-I anciently noted, HSV-II since 1800s
- Similar viruses, but genetically distinct
- Biology is similar, lytic followed by neural latency
- HSV-1 is virus of ‘cold sores’
- HSV-2 venereal disease
  - but can cross infect
Herpes Simplex, Epidemiology

- World-wide prevalence
- Lesions highly infectious
  - From lips to hands to eyes common (leave cold sores alone!)
  - Antibodies will not prevent recurrence
- Pathogenesis:
  - Primary replication
  - Dorsal root ganglion
  - Recurrence from sensory neurons
  - May lead to viremia and systemic hemorrhagic necrosis

Gingivostomatitis, primary lesion
Herpes simplex clinical picture

- Primary lesion: HSV-1
  - children-asymptomatic
  - gingivostomatitis
    - drooling, fever, pain in mouth, edema, vesicles lymphadenopathy
  - Recurrences: Herpes labialis
    - cold sores, fever blisters
    - stress, UV-light, menses, trauma
    - edge of lip
    - usually in same place
    - vesicular fluid is highly infectious
    - ulceration & healing takes about 10 days
Herpes simplex-2

- Genital lesions
  - symptoms from notable to debilitating
  - modified by HSV-1
  - 2-7 days incubation
  - multiple painful lesions
    - penile or vaginal
    - fevers, malaise, lymphadenopathy,
    - recurrences, 5-8/yr
    - viral shedding between lesions! (importance?)
    - rectal & perianal becoming common*
    - Psychological scarring
      - nothing can be done
      - endangers partners
Herpes simplex-2, continued

- Accelerates HIV to AIDS,
- Enhances transmission
- some implication in cervical cancers
  - cervical dysplasia*
- Serious complications in congenital infections
  - blindness, meningitis, disseminated necrosis of skin,
  - potentially fatal
  - abortions & premature births
- C-section indicated during active infections

Eczema herpeticum, necrotic ulcers
Other Herpes Manifestations

- Herpetic whitlow
  - herpes fingers
    - occupational hazard of dental & medical
- CNS herpes
  - mortality=70%
- Eye herpes
  - usually from lips via hands
  - causes blindness
- Neonatal herpes
  - potentially fatal
  - C-section indicated in active genital herpes
- Immunocompromised***
Varicella/Zoster

- This herpes virus causes two distinct, but linked diseases: varicella (chickenpox) and herpes zoster (shingles)

- In USA over 90% infection rate

- Waiting for the other shoe to drop???
Epidemiology of varicella/zoster

• Global transmission
  – winter/spring more
  – aerosolization
  – vesicular fluid viral rich, crusty lesion viral poor
  – Infections may be fatal
    • immunocompromised
    • hemorrhagic varicella
  – in utero transmission
    • initial = shingles
  – Shingles all ages, but
    • by 85, 50% have had
    • alterations in CMI
Pathogenesis of varicella/zoster

- Respiratory > viremia > skin
- Vesicles initially clear, then cloudy as PMNs clear virus, then crusts over
- Virus retreats to basal ganglia = latency
- reduced CMI = recurrence
- virus travels along sensory nerves to form skin lesions
- Nerves show extensive inflammation, neural hemorrhagic necrosis
- Extremely painful
  - pain may last for months with nerve damage

Shingles along nerve tract
Shingles from facial nerve
Shingles and leukemia
Clinical Picture

- **Chickenpox**: lesions:
  - skin, mouth, vagina, rectum, conjunctiva
  - average 200
  - sore throat, fever, pruritus, anorexia

- **Neonatal**: in 1st trimester:
  - chorioretinitis, deafness, brain atrophy
  - if mother become infected within 5 days
    - 20% neonatal, of which 35% fatal

- **Shingles**: AIDS, bad!