

# 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

## Cholestatic

- 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
- 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 hypersensitiv.
  - 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

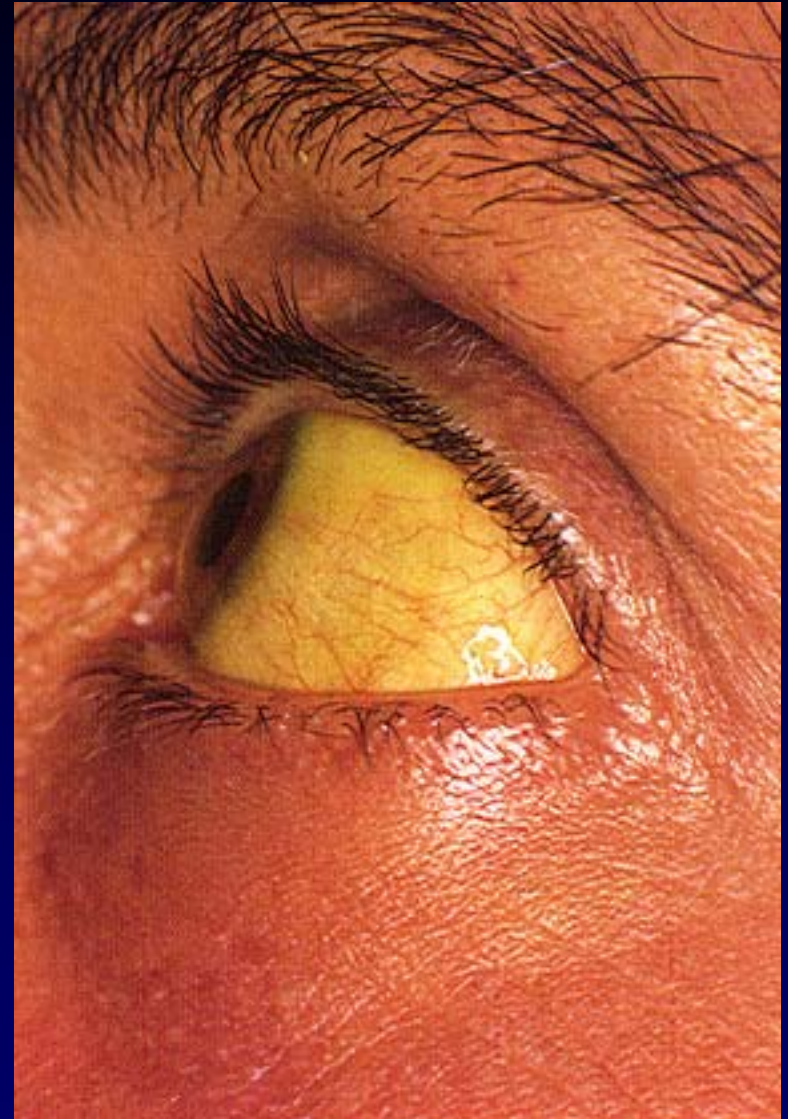


**urobilin**



# 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**

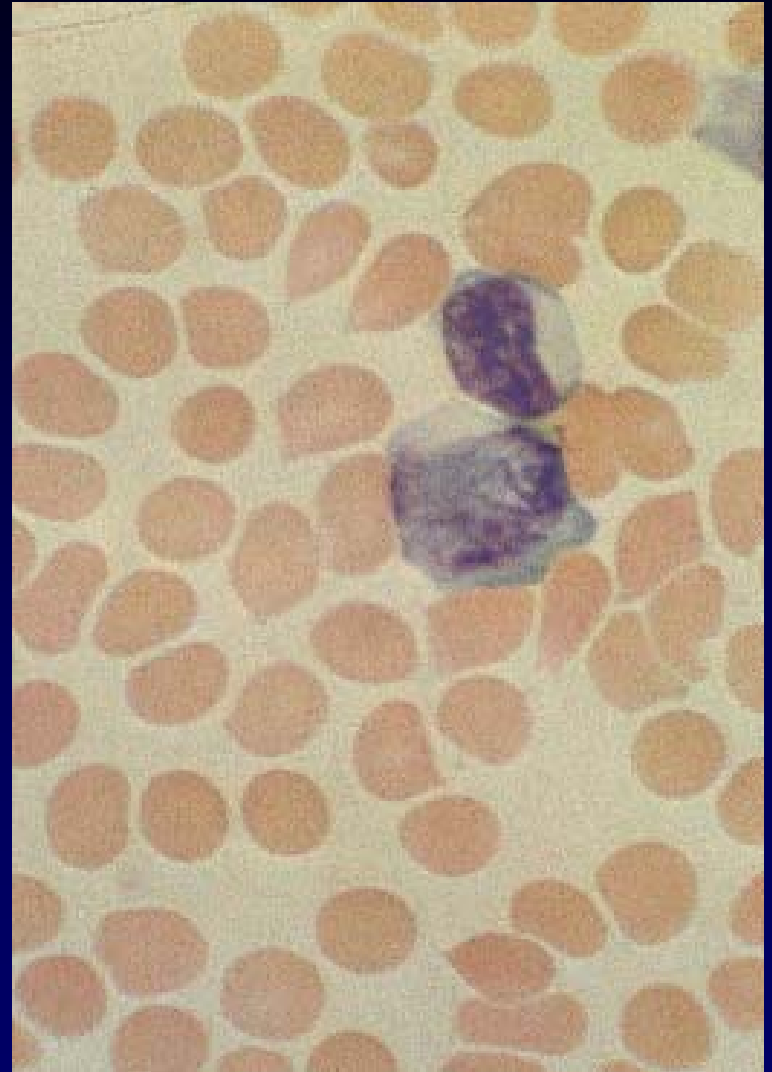
# Epstein-Barr Virus & Diseases

- Virus originally isolated from Burkitt's lymphoma--but IM was first recognized dis.
- Ubiquitous B lymphotropic 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



IM infl



Antibiotic induced rash in IM

# 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

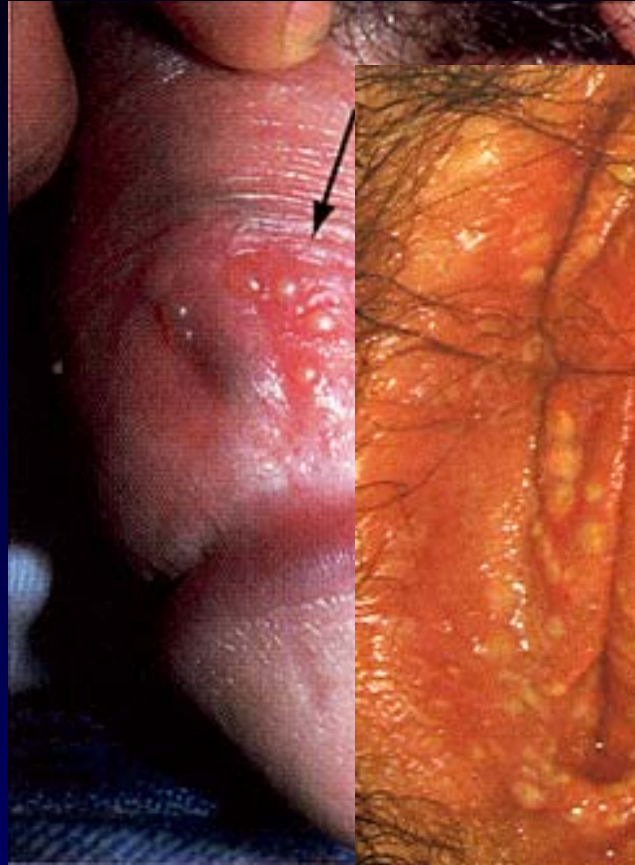


**Herpes labialis**

# 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 on



Herpes, vulva



# Herpes simplex-2, continued

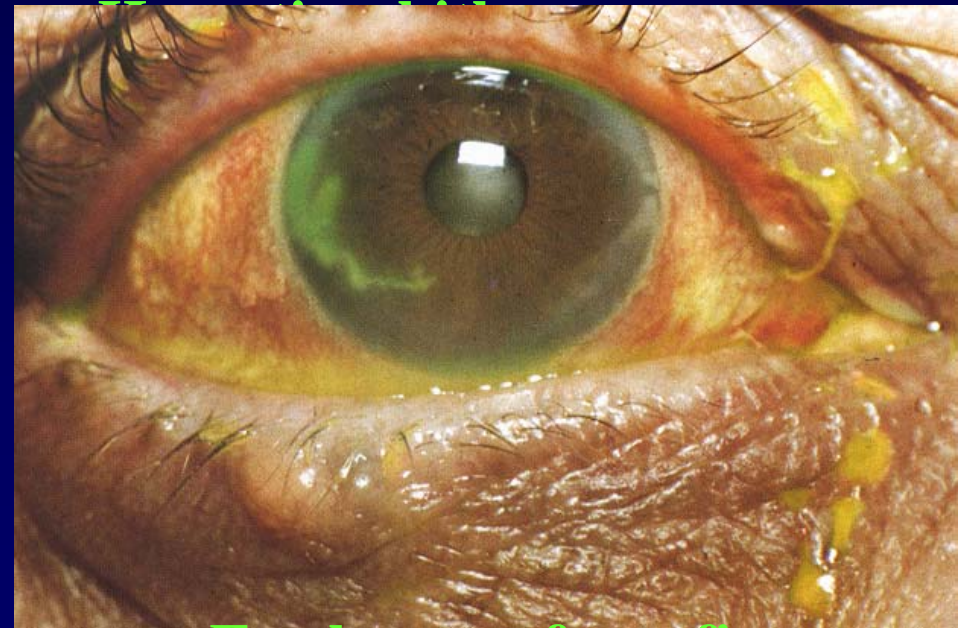
- Accelerates HIV to AIDS,
- Enhances transmission
- some implication in cervical cancers
  - cervical dysplasia\*
- Serious complications in congenital infections
  - blindness, meningitis, disseminated necrosis of skin,
  - potentially fatal
  - abortions & premature births
- C-section indicated during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



Eye herpes, from fingers

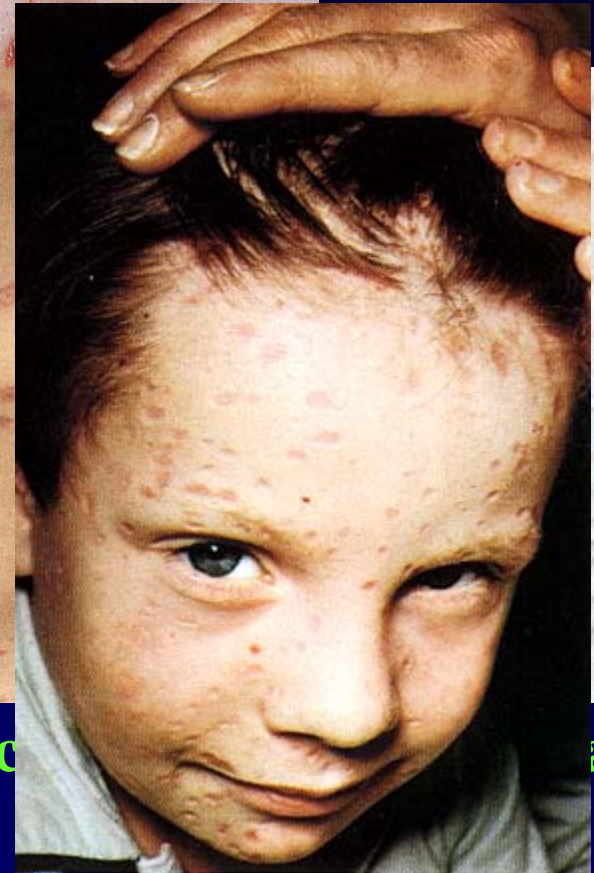
# Varicella/Zoster

- 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



Immunoc

a

Varicella scars

# 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 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!



**Trigeminal nerve**



**Disseminated from Breast cancer**