Viral hepatitis

Dr. Abdulkarim Alhetheel and Dr. Malak Elhazmi

Assistant Professor

College of Medicine & KKUH

Objectives

The student should know:

1. The etiology of enteric viral hepatitis (HAV, HEV) from other viral hepatitis EBV, CMV, Yellow fever virus.
2. The main characteristics of HAV, HEV, EBV, CMV, Yellow fever virus.
3. The clinical manifestations of enteric viral hepatitis and other viruses causing hepatitis.
4. The epidemiology and the mode of transmission of these viruses.
5. The laboratory methods used to diagnose enteric hepatitis other viruses causing hepatitis.
6. The treatments and the prevention measures available for these viral infections.

Hepatitis

- Is inflammation of the liver.

Etiology

❑ Primary infection:

- ➢ Hepatitis A virus (HAV)
- ➢ Hepatitis B virus (HBV).
- ➢ Hepatitis C virus (HCV), was known as non-A non-B hepatitis,
- ➢ Hepatitis D virus (HDV) or delta virus.
- ➢ Hepatitis E virus (HEV).
- ➢ Hepatitis F virus (HFV).
- ➢ Hepatitis G virus (HGV).

❑ As part of generalized infection:

- ➢ (CMV, EBV, Yellow fever virus)

Continued ….

- Hepatitis F has been reported in the literature but not confirmed.
- Viral hepatitis is divided into two large groups, based on the mode of transmission:

1– Enterically transmitted hepatitis or water-borne hepatitis. This group includes hepatitis A and E viruses.

2– Parenterally transmitted hepatitis or blood-borne hepatitis. This group includes hepatitis B, C, D & G viruses.

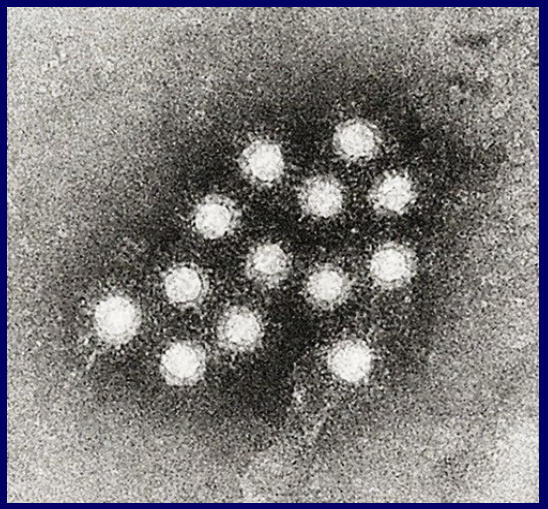
Characteristics of HAV

Family of *Picornaviridae.*

Genus: *Hepatovirus*.

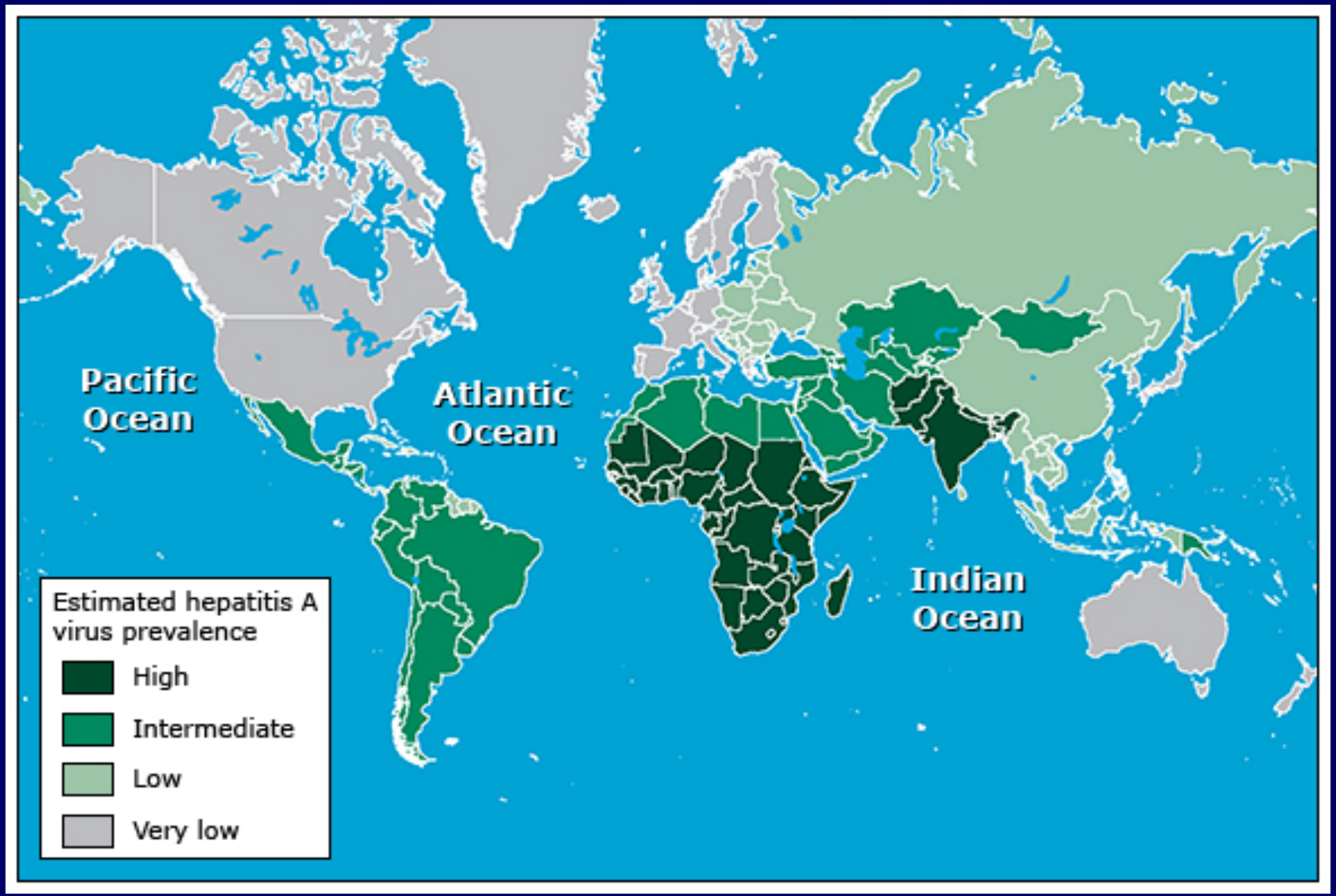
Virion non-enveloped and consist of:

- Icosahedral capsid.
- Positive sense ss-RNA.



- Short incubation hepatitis
- Infectious hepatitis
- Epidemic hepatitis

Geographic Distribution of HAV Infection



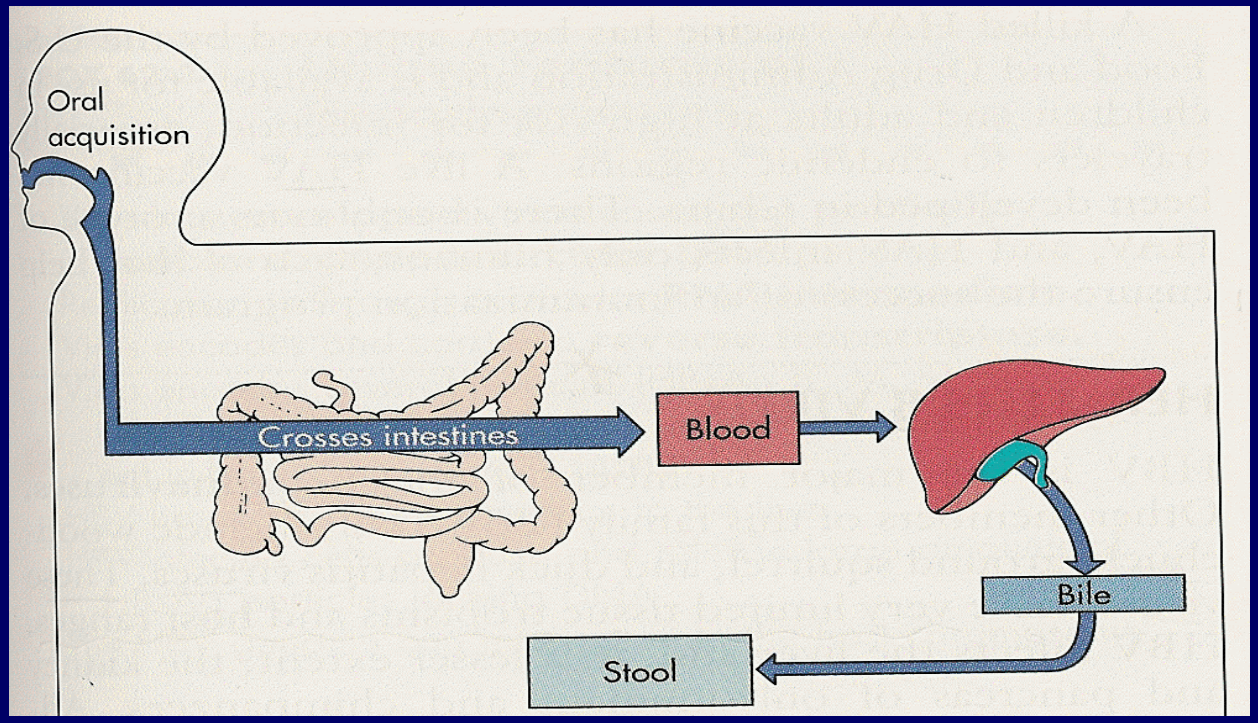
Epidemiology

HAV

- Distribution:
  - Worldwide, endemic in tropical countries
- Transmission:
  - Faecal-oral route [major route]
    Contaminated food &water
  - Sexual contact (homosexual men)
  - Blood transfusion (very rarely)
- Age:
  - In developing countries; children
  - In developed countries; young adults

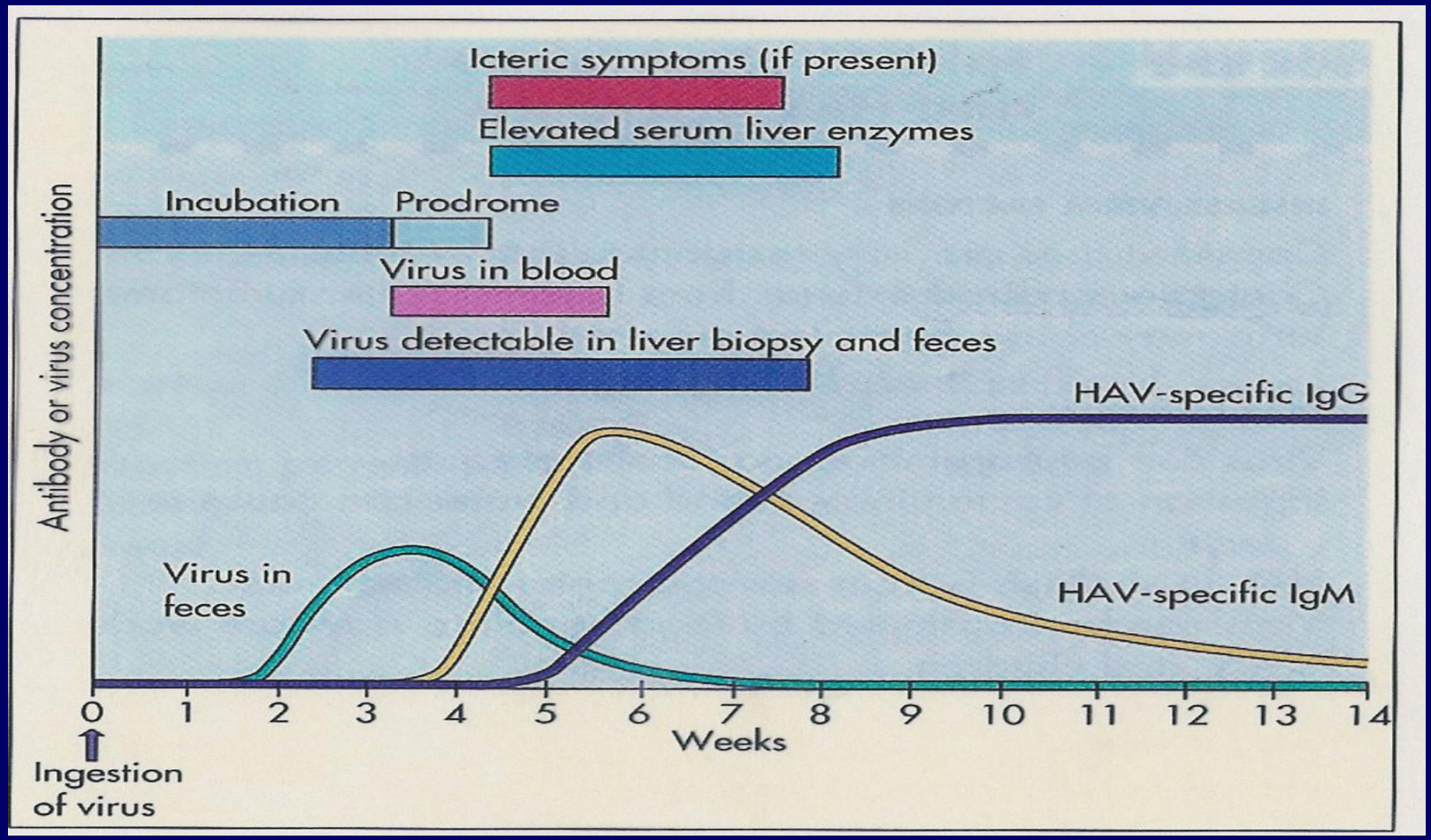
Pathogenesis

HAV



- The virus enters the body by ingestion of contaminated food. It replicates in the intestine, and then spread to the liver where it multiplies in hepatocytes.
- CMI ➡ Damage of virus-infected hepatocytes
  ➡ ⬆ ALT, AST & Bilirubin

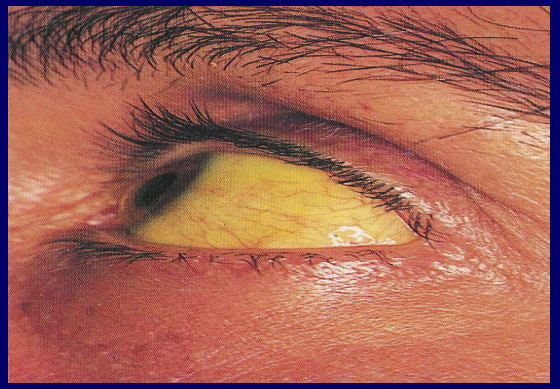
HAV


Icteric symptoms (if present)
Elevated serum liver enzymes
Incubation
Prodrome
Virus in blood
Virus detectable in liver biopsy and feces
HAV-specific IgG
Antibody or virus concentration
Virus in feces
HAV-specific IgM
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14
Weeks
Ingestion of virus

Manifestations

HAV

- Hepatitis
  - Asymptomatic & anicteric inf → common
  - Symptomatic illness → ↑ age
  - IP=2-6 Ws
  - Pre-icteric phase: fever, fatique, N, V, & RUQP (right upper quadrant pain)
  - Icteric phase: dark urine, pale stool, jaundice



Prognosis

HAV

- Self-limited disease
- Fulminant hepatitis → rare
- Mortality rate ~ 0.1 - 0.3%
- No chronicity or malignancy changes

HAV

Lab Diagnosis

- Serology:
  - Detection of anti-HAV IgM → Current infection
  - Detection of Anti-HAV IgG → Previous infection
    → Immunity

Management

HAV

- Treatment:
  - Supportive therapy
- Prevention:
  - Sanitation & hygiene measures
  - Hig: Given before or within 2 Ws of exposure
    - Indication: travellers, unvaccinated, exposed patients.
  - Vaccine: inactivated (killed)
    - Given IM in two doses
    - >1 Y of age
    - Indication: Patients at high risk of infection and severe disease

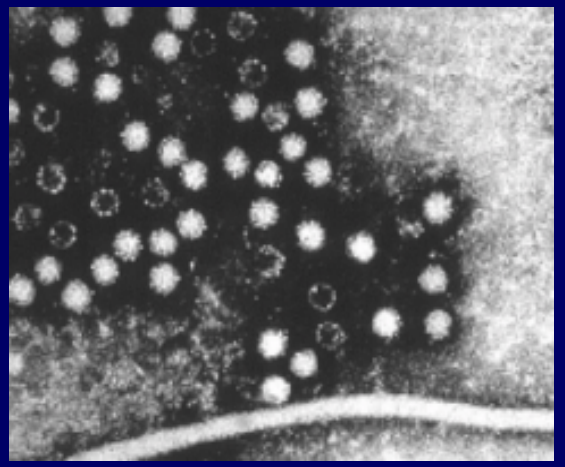
Characteristics of HEV

Family of *Hepeviridae*.

Genus: *Hepevirus*.

Virion non-enveloped and consist of:

- Icosahedral capsid.
- Positive sense ss-RNA.



HEPATITIS E VIRUS

- Epidemiology:
- Outbreak of water-borne & sporadic cases of VH
- Age; young adults
- 4 routes of transmission;
  - Water-borne
  - Zoonotic food-borne
  - Blood-borne
  - Perinatal

HEPATITIS E VIRUS

- Clinical features:
  - Similar to HAV infection with exceptions:
    - Longer IP =4-8 Ws
    - Chronic hepatitis, cirrhosis, but not HCC.
    - Fulminant disease
    - Mortality rate ~10 times > HAV

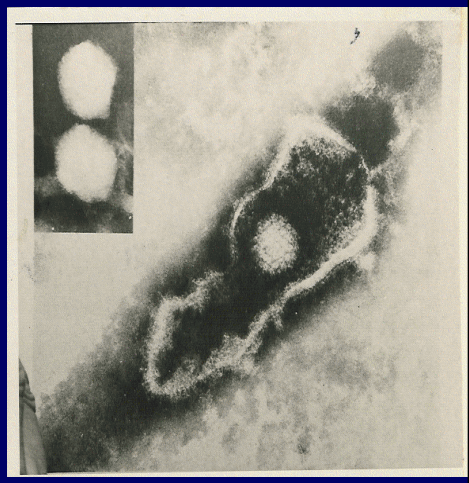
      ~ 1-3% [20% in pregnancy]

HEPATITIS E VIRUS

- Lab diagnosis:
  - ELISA → Anti-HE IgM
- Treatment:
  - Not specific
- Prevention:
  - Sanitation & hygiene measures
  - No Immunoglobulin
  - No vaccine

Herpesviridae

1- Herpes simplex virus type -1	HSV-1
2- Herpes simplex virus type -2	HSV-2
3- Varicella –Zoster virus	VZV
4- Epstein-Barr virus	EBV
5- Cytomegalovirus	CMV
6- Human herpes virus type-6	HHV-6
7- Human herpes virus type-7	HHV-7
8- Human herpes virus type-8	HHV-8



dsDNA , Icosahedral & Enveloped Virus

Epstein – Barr Virus EBV

EBV

- It is lymphotropic.
- It has oncogenic properties; Burkitt's lymphoma
  Nasopharyngeal carcinoma

Epidemiology

- Distribution: worldwide
- Transmission:
  - Saliva [kissing disease]
  - Blood [rarely]
- Age:

  Socio-economic status: SE
  - Low SE class → early childhood
  - High SE class → adolescence

Clinical Features:

EBV

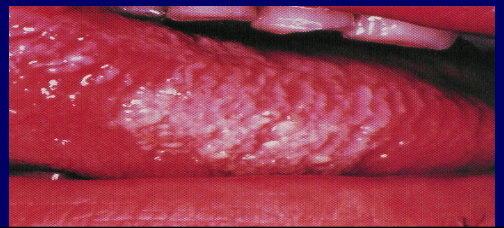
1-Immunocompetent host

- Asymptomatic
- Infectious mononucleosis [or glandular fever]
  - Mainly in teenagers & young adults
  - IP = 4-7 weeks
  - Fever, pharyngitis, malaise, hepatosplenomegaly & abnormal LFT, hepatitis.
  - Complications

    (acute air way obstruction, splenic rupture, CNS inf)
- Chronic EBV infection

2- Immunocompromised host

- Lymphoproliferative disease (LD)
- Oral hairy leukoplakia (OHL)



Diagnosis:

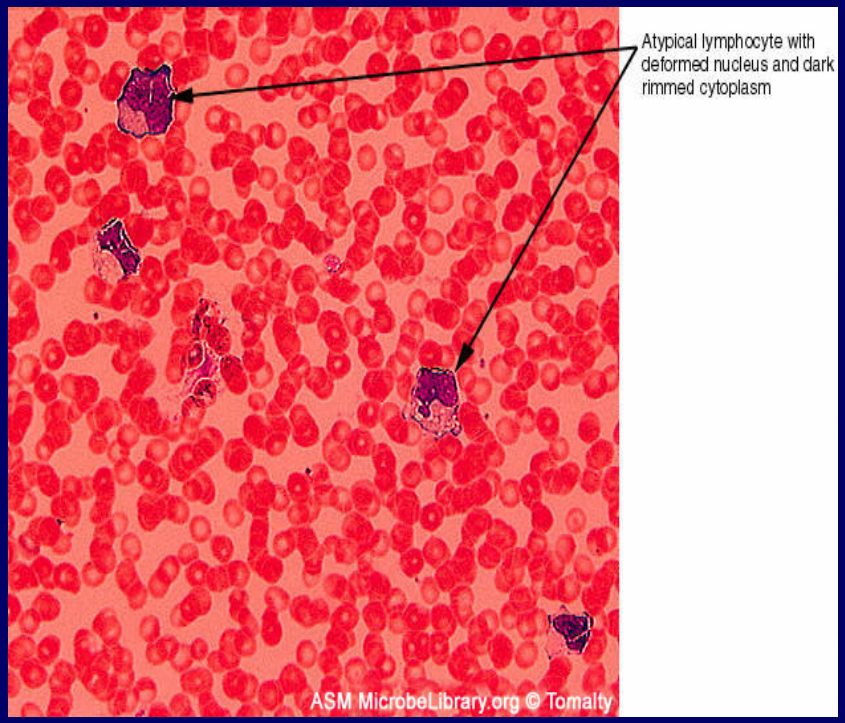
EBV

Hematology:

- ↑ WBC

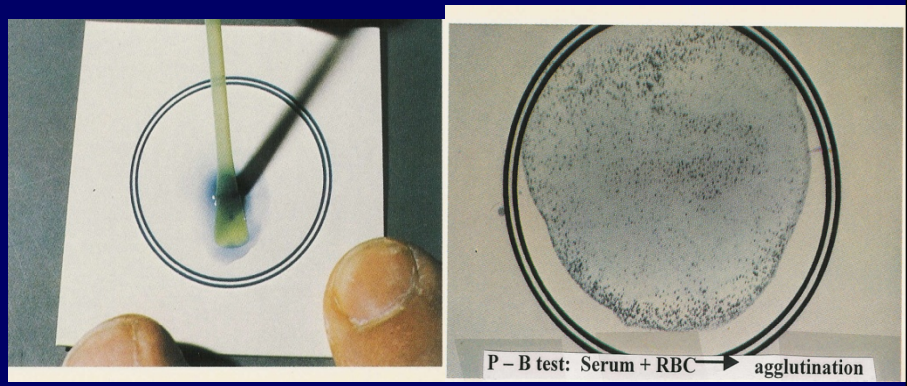
  lymphocytosis

  (Atypical lymphocytes)



Serology:

- Non-specific AB test ;
  - Heterophile Abs +ve
  - Paul-Bunnell or monospot test



- EBV-specific AB test:

  IgM Abs to EBV capsid antigen

Management:

- Treatment:
  - Antiviral drug is not effective in IMN
- Prevention:
  - No vaccine

Cytomegalovirus CMV

- Special features;
  - Its replication cycle is longer.
  - Infected cell enlarged with multinucleated.

    [cyto=cell, megalo=big]
  - Resistant to acyclovir.
  - Latent in monocyte, lymphocyte & other.

- Distribution: worldwide .
- Transmission;
  - Early in life:
    - Transplacental
    - Birth canal
    - Breast milk
  - Young children: saliva
  - Later in life: sexual contact, Blood transfusion & organ transplant.

Acquired Infection;

- Immunocompetent host
  - Asymptomatic
  - Self-limited illness
    - Hepatitis
    - Infectious mononucleosis like syndrome

[Heterophile AB is –ve]

- Immunocompromised host
  - Encephalitis , Retinitis , Pneumonia ,
  - Hepatitis, Esophagitis, Colitis.

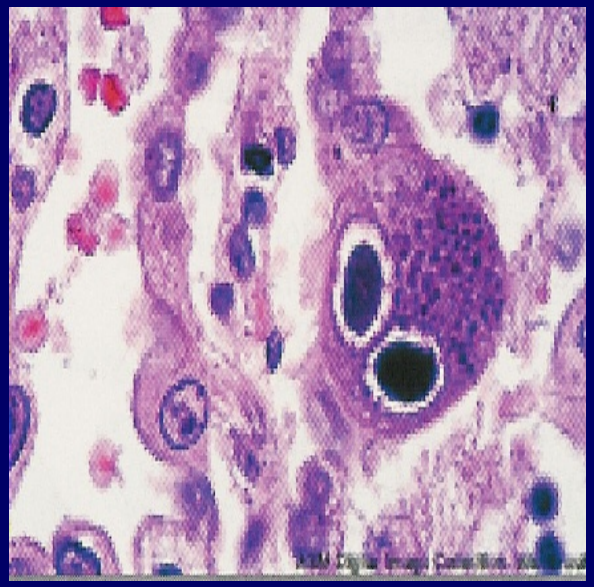
Congenital Infections

Lab Diagnosis

CMV

- Histology:

  Intranuclear inclusion bodies [Owl's eye]



- Culture:
  - In human fibroblast

    1-4 wks → CPE
  - Shell Vial Assay → 1-3 days

- Serology :
  - AB → IgM: current inf
    IgG: previous exposure
  - Ag → CMV pp65 Ag by IFA

- PCR

Treatment:

- ***Ganciclovir***

  is effective in the treatment of severe CMV inf.
- ***Foscarnet:*** the 2nd drug of choice .

Prevention:

- Screening;
  - Organ donors
  - Organ recipients
  - Blood donors
- Leukocyte-depleted blood.
- Prophylaxis: Ganciclovir, CMVIG.
- No vaccine.

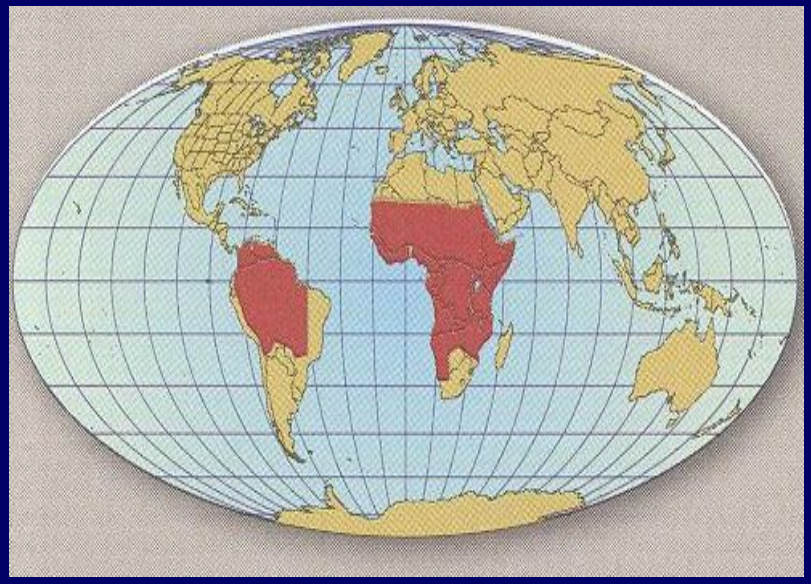
Arthropod –borne Viruses (Arboviruses)

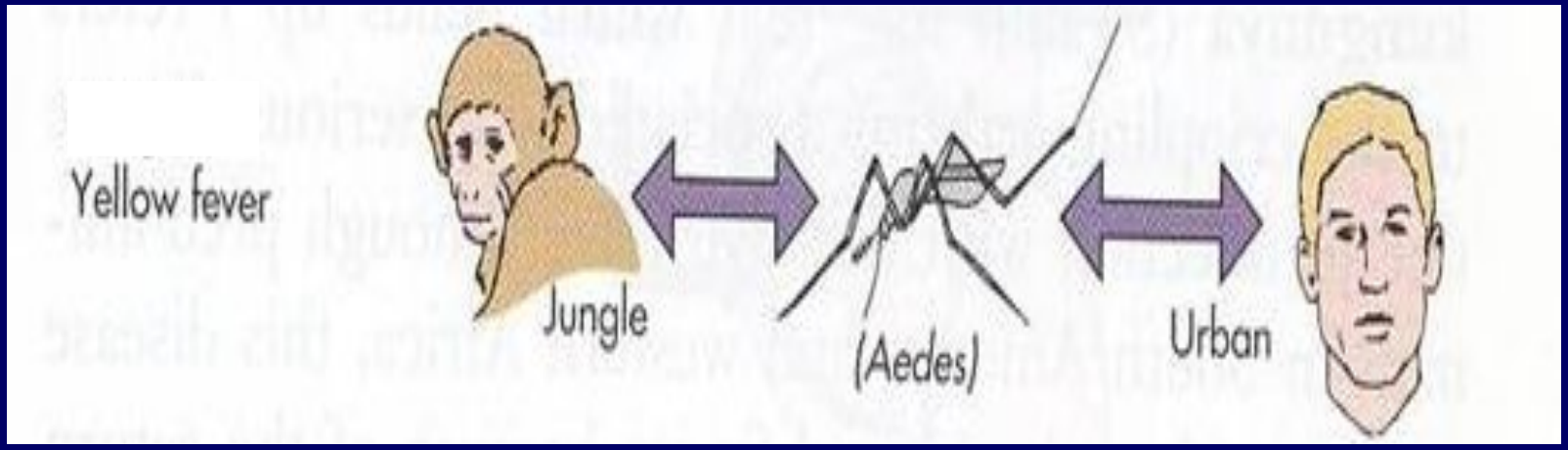
Yellow Fever virus

- Family: *Flaviviridae*
- Asymptomatic to Jaundice (hepatitis) + Fever ± hemorrhage ± renal failure
- Epidemiology

  Tropical Africa & South America

  1. Jungle Yellow Fever
  2. Urban Yellow Fever





Jungle Yellow Fever:

- Vector: mosquito
- Reservoir: monkeys
- Accidental host: humans
- It is a disease of monkeys

Urban Yellow Fever

- Vector: mosquito
- Reservoir: human
- It is a disease of humans

Diagnosis:

- Reference Lab
- Lab Methods:

A- Isolation (Gold standard)

B - IgM-Ab - ELISA, IF: (most used)

C - Arbovirus RNA by RT-PCR

Prevention:

1-Vector Control:

- Elimination of vector breading sites
- Using insecticides
- Avoidance contact with vectors

2-Vaccines:

Yellow Fever vaccine (LAV, one dose /10 yrs)

It is recommended for travelers.

Reference books

&the relevant page numbers

Medical Microbiology.

By: David Greenwood ,Richard Slack,
John Peutherer and Mike Barer.

17th Edition, 2007.

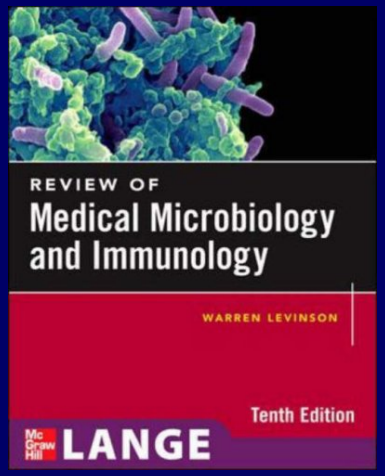
Pages; 428-435, 484-485, 507-523, 533-534.

Review of Medical Microbiology and Immunology.

By: Warren Levinson.

10th Edition, 2008.

Pages; 257-259, 292-294, 301, 305-306.



Thank you for your attention !