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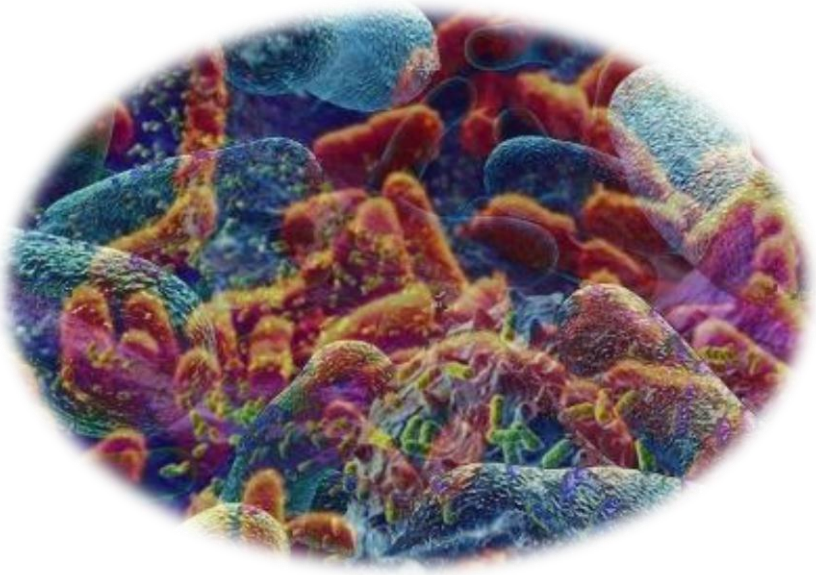
Microbiology Team

Hepatitis A & E

GIT & HAEMATOLOGY BLOCK



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Hepatitis A & E

As part of generalized infection (CMV, EBV, Yellow Fever virus) → to liver and other organs

Infect primarily the liver (viral hepatitis) ABCDE

1-Fecal- borne hepatitis → (A&E) **2-Blood-borne hepatitis (B, C, D,G)**

NOTE: all PATIENTs with HDV must have HBV but not vice versa .

FECAL-BORNE HEPATITIS

HAV	HEV
Hepatovirus, picornaviridae	**Hepevirus, hepeviridae**
Nonenveloped (resist harsh environment= acidity)	
Icosahedral	
ss, RNA + polarity	
One serotype	
Acute hepatitis	
Not associated with hepatocellular carcinoma	

HEPATITIS A VIRUS

- **Short incubation period → compared to the others**
- **Sometimes called infectious hepatitis → fecal-oral transmission**
- **Epidemic hepatitis .**

❖ Epidemiology

Distribution:

Worldwide, endemic in tropical countries

Transmission :

Fecal-oral (major)→ ex: infected food handler, contaminating food after poor washing, person ingesting fecally contaminated drinking water or close person to person contact (homosexual contact). (poor sanitation& hygiene)
Blood transfusion (very rare cases)

Age group:

- **In developing countries → children (poor hygiene)**
- **In developed countries → adults**

❖ Pathogenesis:

Enter through the mouth →reaches the gut →affect epithelial cells→invade to the blood causing viremia→disseminates to liver →multiply in hepatocytes →activation of immune system →producing cell mediated immunity (CMI) →Damage of virus-infected hepatocyte →causing an increase ↑in liver enzymes (ALT ,AST & Bilirubin).

NOTE: THE PATIENT IS infectious (virus appear in stool) about 2 weeks before the onset of symptoms and 1 week after onset of symptoms

Hepatitis A causes acute self limited hepatitis

❖ Manifestations:

- **Commonly Asymptomatic**
- **Symptoms increase with age**
- **Incubation period (IP): 2-6 Ws (viruses present in the feces 1-2 weeks before the symptoms appear)**
- **Pre-icteric [Pre-Jaundiced] phase: (prodrome or early symptoms): non-specific symptoms (fever, fatique, nausea, Vomiting & right upper quadrant pain (RUQP).**
- **Icteric phase: dark urine, pale stool, jaundice.**

• So patients with [Hepatitis A] are commonly present Asymptomatic or with anicteric infection (mild infection without jaundice) → common in children.
Or they could be Symptomatic (with jaundice, the risk will increase with age).

❖ Prognosis:

- **Self limited disease (patient recover spontaneously within few weeks)**
- **Fulminant hepatitis(severe deterioration in liver function) → rare (necrosis and liver failure)**
- **Mortality rate ~ 0.1- 0.3% increase with age.**
- **No chronicity or malignancy changes in contrast to HCV &HBV**

❖ Serology:

- **Anti-HAV IgM → marked for Current infection.**
- **Anti-HAV IgG → marked for immunity (either by vaccine or previous infection).**

❖ Management:

Treatment: Supportive therapy.

Prevention:

- **Sanitation & hygiene measures.**
- **HIg (human immunoglobulin) → passive immunization: Given before or within 2 Weeks of exposure.**

Indication:

1) travellers. 2) Unvaccinated, exposed patients.

Not given symptomatic patients → already producing their own antibodies.

Children less than 1 y/o

- **Vaccine: Inactivated (killed). Given IM at (6 -12 Months).**
- **>1 Y of age.**
- **Side effect: mild local reaction.**
- **Indication:**

1)Patients at high risk of infection. 2) Patients at high risk of severe disease.

A combination vaccine (HAV &HBV).

For children < 1 year → HIg is used.
For people from 1 -40 yrs → Vaccine is given
For old people > 40 yrs → both (vaccine & HIg) are given

HEPATITIS E VIRUS

Epidemiology :

- **(EPIDEMIC) Outbreaks of waterborne** & sporadic cases of VH
- **Age:** young adults
- **4 routes of transmission:** 1. **Waterborne (most common) fecally contaminated water 2.zoonotic foodborne HEV IS THE ONLY ZOONOTIC VIRAL HEPATITIS . 3.bloodborne 4.perinatal**

Clinical features:

Similar to HAV infection except:

- **Longer IP =4-8 Ws.**
- **Fulminant disease.**
- **Mortality rate is 10 times higher than HAV .**

~ 1-3% [20%in pregnancy]. (Because the immunity is decreased in pregnancy).

Lab Diagnosis: ELISA →Anti-HEV IgM.

Management:

Treatment: Not specific.

Prevention:

Sanitation & hygiene measures.

No HIg.

No vaccine.

Herpesviridae

These viruses cause hepatitis as part of the generalized infection (liver+ other organs)

Epstein- Barr virus (EBV).
Cytomegalovirus (CMV).
Description of both : dsDNA, Icosahedral & Enveloped Virus

EPSTEIN – BARR VIRUS (EBV)

It is lymphotropic→ growth of EBV in lymphocytes (B lymphocytes mainly) .
It has oncogenic properties: (progress into malignancies).

- **Burkitt's lymphoma**
- **Nasopharyngeal carcinoma**
-

Epidemiology:

Transmission:

- **Saliva [kissing disease]**
- **Blood [rarely]**

Age: Depending on Socio-economic status (SE):

- **Low SE class → early childhood (sharing items containing contaminated saliva).**
- **High SE c class → young adults (teenagers)**

Clinical presentation:

Depends on immune status and age of the host

Immunocompetent host:	*Immunocompromised host :*
• **Asymptomatic in children.** • **As part of Infectious mononucleosis [glandular fever].** ▪ **IP = 4-7 weeks** ▪ **Fever, pharyngitis, malaise, LAP, hepatosplenomegaly & abnormal LFT ± hepatitis. (Non specific symptoms).** o **Complications (rare):** ▪ **(acute air way obstruction n due to neck enlargement and edema, splenic rupture, CNS infection)** ▪ **Chronic EBV infection**	• **Sever Lymphoproliferative disease (LD).** • **Oral hairy leukoplakia (OHL) asymptomatic white lesion in the lateral border of tongue> mainly in HIV**

Diagnosis (Dx): MAINLY mononucleosis

Hematology	Serology
• : shows ↑ WBC (mainly lymphocytes) lymphocytosis, Atypical lymphocytes seen in blood smear • cytotoxic T cells against EBV infected B cells.	• Non-specific Antibody test →Heterophile antibody (antibody against EBV that cross reacts with and agglutinates sheep RBC) → however can be seen in serum sickness and HBV → not specific. findings: positive Heterophile Abs [they're –ve in CMV], OR Paul-Bunnell or Mono-spot test (rapid screening for mono). • EBV-specific AB test IgM Abs to EBV capsid antigen

Management:

- Treatment: Antiviral drug are *not effective* in *Infectious mononucleosis* [IMN] immunological mediated disease.
- Prevention: No vaccine.

CYTOMEGALOVIRUS(CMV)

Herpesviridae family

Special features:

- Its replication cycle is long .(2-3 weeks)
- Infected cell enlarged with multinucleated. [cyto=cell, megalo=big]
- Resistant to acyclovir (acyclovir used in treatment of herps type 1 &2).
- Latent in monocyte, lymphocyte & other.

Epidemiology:

- Distribution: worldwide.
- Transmission:
- Early in life: due to Transplacental transmission, Birth canal and Breast milk.
- Young children: saliva (most common).
- Later in life: sexual contact.
- Blood transfusion & organ transplant.

Clinical features:

ACQUIRED INFECTIONS:

- **Immunocompetent host:**
  - **Asymptomatic.**
  - **Self-limited illness:**
    - **Hepatitis.**
    - **Infectious mononucleosis like syndrome [Heterophile AB is –ve] → differ from EBV (heterophile +ve) (fever, malaise, spleenomegaly and hepatitis) pharygitis is not common**
- **Immunocompromised host:**
  - **Encephalitis, Retinitis, Pneumonia.**
  - **Hepatitis, Esophagitis, Colitis.**
    - **Congenital Infections: (if the infant got the infection during pregnancy).**

Lab Diagnosis:

- **Histology: Intranuclear inclusion bodies [Owl's eye].**
- **Culture: (most used)**
  - **grows in human fibroblast (very slow)**
  - **CPE (cytopathological effect).**
  - **Shell Vial Assay.**
- **Serology:**
  - **Antibody (AB) → (IgM: indicates current infection and IgG indicates immunity due to previous exposure only).**
  - **Antigen (Ag) →CMV pp65 Ag by IFA (best for immunocompromised patients)**
- **PCR.**

Management:

- **Treatment:**
  - ***Ganciclovir:* effective in treating severe CMV infection.**
  - ***Foscarnet:* the 2nd drug of choice. (if the virus is resistant to Ganciclovir)**
- **Prevention:**
  - **Screening:**
    - **Organ donors.**
    - **Organ recipients.**
    - **Blood donors.**
      - **Leukocyte-depleted blood. (Blood without leukocyte).**
      - **Prophylaxis: Ganciclovir, CMVIG (CMV immunoglobulin - passive immunization).**
      - **No vaccine.**

(Arboviruses)
Yellow Fever virus

Family: Flaviviridae

Asymptomatic to Jaundice + Fever ± hemorrhage ± renal failure

Epidemiology:

- **Tropical Africa & South America**
- **Jungle Yellow Fever affects monkeys.**
- **Urban Yellow Fever affects human.**
  The Vector is mosquito for both .

Lab Diagnosis:

- **Lab. Methods:**

- **Isolation (gold standard).**
- **IgM -AB* - EIISA, IF: (most used) for detection of yellow fever.**
- **Yellow Fever Virus - RNA by RT-PCR.**

❖ Management:

- **Prevention:**

- ***Vector Control:***
- **Elimination of vector breading sites.**
- **Using insecticides.**
- **Avoidance contact with vectors (repellants, net).**
- ***Vaccines:***
- **Yellow Fever vaccine (Life attenuated vaccine "LAV", one dose /10 yrs).**

Remember:

water borne hepatitis =HEV

Viruses that can be prevented by vaccine = HBV, HAV and yellow fever.

+ve heterophiles in EBV (infectious mononucleosis)

-ve heterophiles in CMV (mono like)

Summery

Viral hepatitis is generalized infection affect mainly the liver and it has two forms : 1-facal borne (A , E) 2- blood borne (B,C,D,G) .

HAV and HEV are non enveloped , SS RNA .

HAV

Short incubation period . produce cell mediated immunity **in the liver and cause increase in liver enzymes (ALT ,AST & Bilirubin).**

It is **Commonly Asymptomatic and Self limited disease .**

Anti-HAV IgM indicate Current infection while Anti-HAV IgG is marked for immunity (vaccine or previous exposure) .

Prevention:
Vaccine: Inactivated (killed) for 1) Patients with high risk of infection. 2) Patients at high risk of severe disease.
HIg for travellers. and Unvaccinated exposed patients.

HEV

cause **Outbreaks of waterborne** (**Waterborne** is the **most common** route of transmission)

HEV **Similar clinical features to HAV except Longe IP =4-8 Ws , Fulminant disease and the Mortality rate is 10 times higher than HAV .**
No vaccine and No HIg are available for HEV .

Herpesviridae (EBV and CMV) are (**ds DNA, Icosahedral & Enveloped Virus**)

EBV

has **lymphotropic oncogenic** properties . transmitted mainly by **Saliva [kissing disease]**

Asymptomatic in Immunocompetent host , **could be part of Infectious mononucleosis [glandular fever].**

Diagnosis : positive Heterophile Abs and high WBC count (mainly lymphocytes)

***Antiviral drugs are not effective and there is* No vaccine** available .

CMV

long replication cycle , common with **Blood transfusion & organ transplantation .**

Asymptomatic and Self-limited illness in Immunocompetent host . **Heterophile AB is negative**
The main Histological finding is Intranuclear inclusion bodies [Owl's eye].

Treated by *Ganciclovir* , No vaccine

(Arboviruses) Yellow Fever

virus has 2 types : Jungle Yellow Fever (monkeys) and Urban Yellow Fever (human).

Life attenuated vaccine

Questions:

1. the initial infection with human cytomegalovirus most commonly occurs
a. during early childhood, by exchange of body fluids.
b. in utero, by transplacental transmission from a latently infected pregnant woman.
c. by transfer of saliva between young adults
d. as result of blood trsansfusion or organ transplantation.

Answer is a.

2. The cellular response typical of infectious mononucleosis:
a. stimulation of B-cell proliferation by the EBV early proteins synthesized in the infected cells.
b. proliferation of cytotoxic T cells responding to EBV antigens expressed on the surface of infected B Cells
c. primary humoral immune response to the EBV infection.
d.macrophages responding to the death of EBV infection

answer is b.

3.A company held an elaborate holiday dinner party for its 42 employees. Within three to four weeks, may of the banquet attendees complained of experiencing fatigue, fever, nausea, and dark urine, and jaundiced. The group exhibited no bacterial infection in common. The employees who became ill had all eaten oysters at the party. The company doctor assayed a sample of the employees' blood for antiHBsAg IgM. THE causativr agent consistent with this history is most likely:
a.HAV
b.HBV
c.HCV
d.HDV
E. HEV

Answer is a. Fecal oral, acquired by eating contaminated food
HEV→ Enterically transmitted, water borne hepatitis in developing countries.
HBV→ negative test
HCV→ Transfusion, IV drug users, tattoos
HDV→ combination with B