Microbiology
437

MED437
KING SAUD UNIVERSITY

VIRAL HEPATITIS A&E

VIRAL INFECTION OF GIT

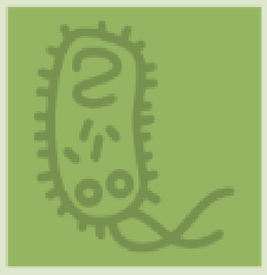
Hepatitis

- Is inflammation of the liver.

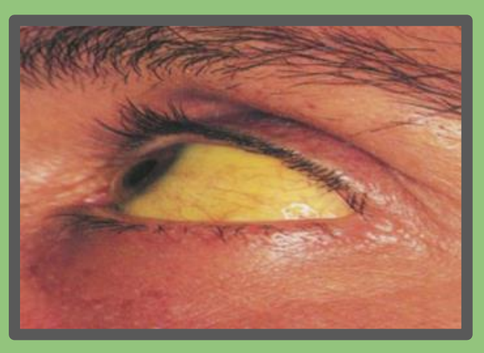
Primary infection	As part of generalized infection
Hepatits A virus (HAV) Hepatits B virus (HBV). Hepatitis C virus (HCV), was known as non-A non-B hepatitis, Hepatitis D virus (HDV) or delta virus. Hepatitis E virus (HEV). Hepatitis F virus (HFV).Hepatitis F has been reported in the literature but not confirmed. Hepatitis G virus (HGV).	(CMV, EBV, Yellow fever virus)

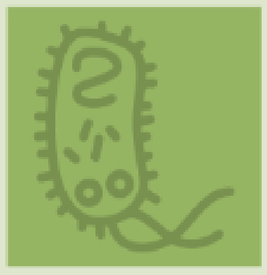
Viral hepatitis is divided into two large groups, based on the mode of transmission

Enterically Transmitted Hepatitis or water-borne hepatitis	Parenterally Transmitted Hepatitis or blood-borne hepatitis
This group includes hepatitis A and E viruses.	This group includes hepatitis B, C, D & G viruses.

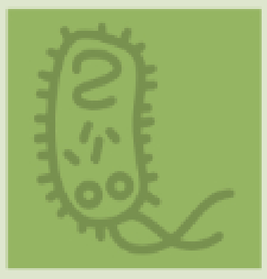



Hepatitis A Virus

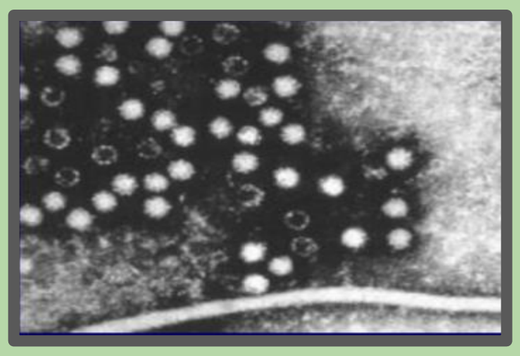
Characteristics 	**- Family** : Picornaviridae. Other names for hepatitis a virus: **- Genus**: Hepatovirus. - Short incubation hepatitis (Hepatitis E virus is longer) - Infectious hepatitis - Epidemic hepatitis - Virion non-enveloped and **consist of:** 1. Icosahedral capsid. 2. Positive sense ss-RNA.
Epidemiology	
Distribution	Worldwide, endemic in tropical countries due to poor hygiene
Transmission	- Faecal-oral route [major route] : - Contaminated food & water - Sexual contact [homosexual men] (unlike Hepatitis E) - Blood transfusion (very rarely so we don't screen for it)
Age	In developing countries; children(many kids sharing the same toys which contains their saliva ^^) In developed countries; young adults
Pathogenesis	- The virus enters the body by ingestion of contaminated food. It replicates in the intestine (epithelium), and then spread to the liver where it multiplies in hepatocytes. - Cell mediated immunity → Damage of virus-infected hepatocytes and increase ALT, AST & Bilirubin
Manifestations 	Hepatitis: (causes acute benign self-limiting infection) • Asymptomatic & anicteric infection is common • Symptomatic illness increases with age • Incubation period= 2-6 Weeks. (in Hepatitis E it's 4-8) • **Two Phases:** **1- Pre-icteric phase**: fever, fatigue ,nausea, vomiting, & RUQP (right upper quadrant pain) **2- Icteric phase**: dark urine, pale stool, jaundice

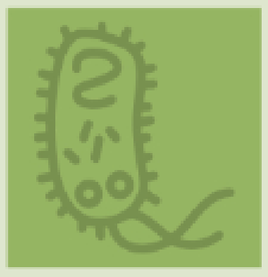



Management	
Treatment	Supportive therapy (self-limiting)
Prevention	Sanitation & hygiene measures HIG (human immunoglobulin): Given before or within 2 Weeks of exposure (**shorter** immunity) - Indication: travellers, unvaccinated, exposed patients.
	Vaccine - Inactivated (killed) (**longer** immunity), Given IM in two doses >1 Y of age Indication: - Patients at high risk of infection and severe diseas (active immunity for infants, and antibodies/passive immunity for travellers)
Lab Diagnosis	Serology: • Detection of anti-HAV IgM → Current infection • Detection of Anti-HAV IgG → Previous infection OR Immunity
Prognosis	• Self-limited disease • Fulminant hepatitis rare (severe necrotic infection of liver lead to liver failure) • Mortality rate ~ 0.1 - 0.3% • No chronicity or malignancy changes

Hepatitis E Virus

Characteristics 	- Family of Hepeviridae - Virion non-enveloped and consist of: - Genus: Hepevirus. - Icosahedral capsid. - Positive sense ss-RNA.
Epidemiology	
Distribution	Outbreak of water-borne & sporadic cases of viral hepatitis (+associated with pork consumption)
Transmission	1. Water-borne The main route 2. Zoonotic (from animals) food borne 3. Blood-borne Rare 4. Perinatal From pregnant mother to her baby - (not sexually)
Age	Age; young adults
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]
Lab diagnosis	ELISA → Anti-HEV IgM (igM like hepatitis A)
Treatment	Not specific
Prevention	•Sanitation & hygiene measures • No Immunoglobulin • No vaccine

Herpesviridae

dsDNA , Icosahedral & Enveloped Virus

1- Herpes simplex virus type-1 → HSV-1

2- Herpes simplex virus type-2 → HSV-2

3- Varicella –Zoster virus → VZV HSV-3

4- Epstein-Barr virus → EBV HSV-4

5- Cytomegalovirus → CMV HSV-5

6- Human herpes virus type-6 → HHV-6

7- Human herpes virus type-7 → HHV-7

8- Human herpes virus type-8 → HHV-8

Extra from the doctor:

Herpes is classified into three categories:

α:HSV 1-2-3: mild diseases - easy to treat

β :HSV 5-6-7:mild disease - hard to treat

γ: HSV 4-8 :carcinogenic - no treatment

Epstein-Barr Virus (EBV)

Characteristics	-It's lymphotropic. Likes lymphoid organs	- It has oncogenic properties; (Burkitt's lymphoma, Nasopharyngeal carcinoma)
Epidemiology		
Distribution	worldwide	
Transmission	1-saliva (kissing disease)	2-blood(rare)
Age	Socio-economic state (SE): 1. Low SE : early childhood (developing countries) 2. High SE : adolescence (developed countries)	

Clinical features

Immunocompetent host:

1. Asymptomatic (usually)
2. Infectious mononucleosis (or glandular fever)
   a. Mainly in teenagers & young adults
   b. IP= 4-7 weeks
   c. Fever, pharyngitis, malaise, lymphadenopathy hepatosplenomegaly & abnormal LFT, hepatitis.
   d. Complications are rare but serious:
      I. acute airway obstruction, splenic rupture, CNS infection
   a. Chronic EBV infection

Immunocompromised host:

(HIV)

Lymphoproliferative disease (LD)

Oral hairy leukoplakia (OHL) pic:

Lab diagnosis	**Hematology:** - Increased WBC - Lymphocytosis (atypical lymphocytes)	**Serology:** 1. Non-specific AB test: good for adults i. Heterophile Abs +ve (CMV will be-ve) ii. Paul-Bunnell or monospot test 2. EBV-specific AB test: good for kids IgM Abs to EBV capsid antigen
Treatment	Antiviral drug is not effective in IMN	
Prevention	No vaccine	

Cytomegalovirus (CMV) (compare it with EPV)

Special Feature

- Its replication cycle is longer.
- Infected cell enlarged with multinucleated. [cyto=cell,megalo=big] (change in cell)
- Resistant to acyclovir.
- Latent in monocyte, lymphocyte & other

Distribution

Worldwide

Transmission

Early in life: Transplacental From pregnant mother to her baby causing a congenital infection- Birth canal - Breast milk
Young children: saliva
Later in life: sexual contact, Blood transfusion & organ transplant.

1. Acquired Infection:

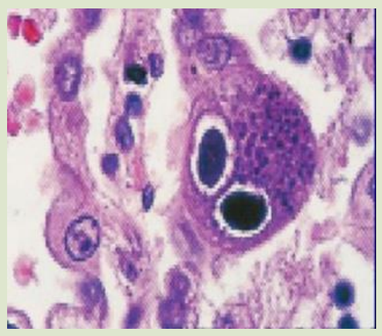
a. Immunocompetent host:
   i. Asymptomatic (in kids)
   ii. Self-limited illness
   - Hepatitis
   - Infectious mononucleosis like syndrome [Heterophile AB is –ve]

a. Immunocompromised host :
   i. Encephalitis , Retinitis , Pneumonia, Hepatitis & Esophagitis, Colitis.

1. Congenital Infections

Lab Diagnosis

Histology:
Intranuclear inclusion bodies [Owl's –eye] pic



Culture:
In human fibroblast 1-4 wks → CPE (very slow growing disease)

Shell Vial Assay → 1-3 days

Serology :
1. AB:
   a. IgM: current infection
   b. IgG: previous exposure
2. Ag: CMV pp65 Ag by IFA

In neonates & immunocompromised the AB test can be false -ve so for them we will use Ag & molecular test

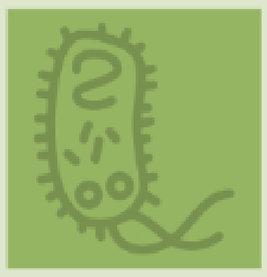
PCR
Not routinely

Treatment:

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

Prevention

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

Arthropod -borne Viruses (Arboviruses)
Yellow Fever virus (because of jaundice)

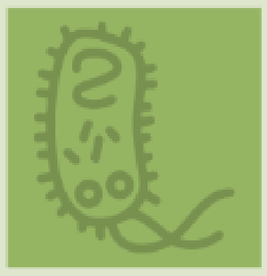
Family: **Flaviviridae**

Asymptomatic to Jaundice + Fever ± hemorrhage ± renal failure

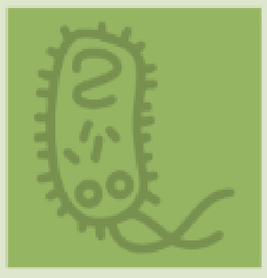
Epidemiology	**Jungle Yellow Fever**	**Urban Yellow Fever**
(Tropical Africa & South America)	Vector: mosquito Reservoir: monkeys Accidental host: humans It is a disease of monkeys	Vector: mosquito Reservoir: human It is a disease of humans
Diagnosis	- Reference Lab - Lab Methods: A. Isolation (Gold standard) B. IgM-Ab - ELISA, IF: (most used) C. Arbovirus RNA by RT-PCR	
Prevention	**1. Vector Control:** a. Elimination of vector breeding sites b. Using insecticides c. Avoidance contact with vectors **2. Vaccines:** **a. Yellow Fever vaccine** (LAV, one dose /10 yrs) is recommended for travelers	

Hepatitis Summary:

B	C	G	D	A	E
ds-DNA	ss-RNA with positive polarity				
Enveloped			Defective virus (use HBV as envelope)	Non-enveloped	
Family: hepadnaviridae	Family: Flaviviridae Genus: Hepacivirus			Family: Picornaviridae	Family: Hepeviridae
Parenterally transmitted hepatitis or bloodborne hepatitis				Enterically transmitted hepatitis or waterborne hepatitis OR fecal borne *(FECAL ORAL ROUTE)*	
Acute and/or Chronic				Acute	
Vaccine available	NO vaccine available			Vaccine available	No vaccine available

HAV	• **Short incubation hepatitis**, Infectious hepatitis, Epidemic hepatitis. • Major rout of transmission is fecal oral rout. • Has pre-icteric and icteric phases. • Self-limited. • No chronicity or malignancy changes. • In serology IgM indicates current infection And IgG previous exposure (and immunity). • Prevented by HIg and vaccine (inactivated).
HEV	• outbreak of waterborne. • You should remember it can be zoonotic foodborne. • It's similar to HAV but has longer duration of action, and can be more serious. • In ELISA we detect Anti-HE IgM. • No vaccine, No Ig.
Epstein Barr Virus (EBV) 	• **Kissing disease (Transmitted by Saliva)** • Lymphotropic • **Oncogenic: causes Burkitt's lymphoma and nasopharyngeal carcinoma.** • In **immunocompetent** it can be asymptomatic or causes Infectious mononucleosis or chronic EBV. • In **immunocompromised** causes Lymphoproliferative disease • Serology can be non-specific (Paul-Bunnell or mono-spot test) which is **+ve for Heterophile** • **Abs** , or specific and we will have IgM Abs to EBV capsid antigen. • No vaccine.
Cytomegalovirus (CMV)	• Infected cell **enlarged** and multinucleated. • **Resistant to Acyclovir** . • Latent in monocytes and lymphocytes. • It can be acquired and congenital infections. • In immunocompetent could be Asymptomatic or **causes Infectious mononucleosis like syndrome** . • In immunocompromised causes hepatitis esophagitis and colitis. • In Histology (the gold standard) we see intranuclear inclusion bodies (**OWL'S EYE**). • In serology IgM abs for current infection, IgG for previous exposure (**But not immunity**) and Ag: CMV pp65 ag by IFA. • Rx: ***Ganciclovir*** and Foscarnet (2nd), • Prevention: there is CMV Ig but no vaccine
Yellow fever virus	• Asymptomatic to Jaundice + Fever ± hemorrhage ± renal failure. • *Tropical Africa and south America*. • 2 types: **Jungle and Urban** , in both of them the vector is **mosquito** . • **Jungle** yellow fever is a **disease of monkeys** (reservoir is monkey) but human is an accidental host . • **Urban** yellow fever is **a disease of humans** (reservoir is human). • The gold standard test is ELISA, IF (IgM abs). • Prevented by yellow fever vaccine which is live attenuated vaccine.

MCQs:

1- which of the following is carcinogenic?
A-Epstein-barr virus(EBV).
B-hepatitis A.
C-Hepatitis E.
D-Cytomegalovirus (CMV).

2-which of the following is transmitted via saliva?
A-Epstein-barr virus(EPV).
B-hepatitis A.
C-Hepatitis E.
D-hepatitis B.

3-which one of the following is heterophile Ab+ve?
A-Epstein-barr virus(EPV).
B-yellow fever virus.
C-Hepatitis C.
D-Cytomegalovirus (CMV).

4-which of the following is transmitted sexually ?
A-Epstein-barr virus(EPV).
B-hepatitis A.
C-Cytomegalovirus (CMV).
D- B&C

5-which of the following has a severe increase in the mortality rate if the patient is pregnant?
A-Epstein-barr virus(EPV).
B-hepatitis A.
C-Hepatitis E.
D-ALL

6-which of the following is <u>false</u>?
A-hepA. has a vaccine while HepE. doesn't
B-jaundice is a part of the icteric phase.
C- IgM against EBV capsid is a specific test.
D-CMV prophylaxis : ganciclovir or vaccine.

SAQ:

1-A 4-D
2-A 5-C
3-A 6-D

A 30-year-old male presents at his primary care physician's office with jaundice and upper quadrant pain. Preceding onset of these symptoms, the patient had suffered from fever, nausea, myalgia, and headache. The patient had recently returned from an extensive trip throughout Southeast Asia, and he had not been vaccinated against endemic infections prior to travel. The physician confirms her suspicions by conducting liver enzyme and serum IgM tests. AST and ALT levels were elevated; IgM specific for the virus shown was detectable. The physician informs the patient that vaccination would have prevented this food-borne infection, but that the prognosis for his recovery was good.

1-What is the most likely etiology and infection?
2-If the virus shown is a picornavirus, what type of capsid does it have?
3-Mention two routes of transmission?

1-Hepatitis by Hepatitis A
2-Icosahedral capsid
3--fecal-oral 2-sexual

THANK YOU!

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