



TEAM443
MICROBIOLOGY

Viral hepatitis A, E and others

Dr. Malak & Al Hetheel



Objectives



-The etiology of enteric viral hepatitis (HAV, HEV) from other viral hepatitis EBV, CMV, Yellow fever virus.



-The main characteristics of HAV, HEV, EBV, CMV, Yellow fever virus.



-The clinical manifestations of enteric viral hepatitis and other viruses causing hepatitis.



-The epidemiology and the mode of transmission of these viruses.



-The laboratory methods used to diagnose enteric hepatitis other viruses causing hepatitis.



-The treatments and the prevention measures available for these viral infections.

Any future corrections will be in the editing file, so please check it frequently

Color Index:

Main text

Important

Doctor Notes

Males slide

Females slide

Extra



Hepatitis A & E

What is the Definition of hepatitis

Hepatitis :Inflammation of the liver (1)

What are the Etiology Of hepatitis (2), (3)

Generalized infection

- CMV (Cytomegalovirus)
- Yellow fever virus
- EBV (Epstein-barr virus)

Primary infection

- Hepatitis B virus (HBV)
- **Hepatitis A virus (HAV)**
- 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) *has been reported in the literature but not confirmed*
- Hepatitis G virus (HGV)

How can we classify Hepatitis?

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

Blood borne hepatitis

Parenterally transmitted hepatitis

Includes hepatitis B, C, D & G viruses.

Water borne hepatitis
Faecal borne hepatitis


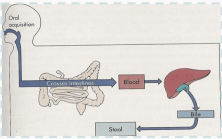
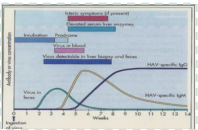
Enterically transmitted hepatitis

Includes hepatitis A and E viruses



Hepatitis A

Hepatitis A virus (Acute Hepatitis)

Family & Genus	Family: Picornaviridae	Genus :Hepatovirus	
Characteristics (similar to Hepatitis E)	Virion Non-enveloped and consist of : ○ Icosahedral capsid ○ Positive sense ss-RNA ○ One serotype		
Presentation (other names)	○ Short incubation hepatitis ○ Infectious hepatitis ○ Epidemic hepatitis		
Epidemiology	Distribution : ○ Worldwide endemic in tropical countries. Age : ○ In developing countries: children ○ In developed countries: young adults		
Transmission	○ Fecal-oral route (major route) E.g. contaminated food & water ○ Sexual contact (homosexual men) ○ Blood transfusion (very rarely) (4)		
Pathogenesis	 <p>The virus enters the body by ingestion of contaminated food → it Will stand in the harsh condition of the stomach and intestines → It replicates in the intestine (epithelium) Pathogenesis → effects the blood (transient viremia) → Spreads to the liver where it multiplies in the hepatocytes → damage the hepatocyte by CMI → lead to Increase ALT, AST & Bilirubin → Excreted in stool (5)</p>		
Manifestations	○ Asymptomatic & anicteric infection: is common ○ Symptomatic illness : increases with age (7) ○ Incubation period (IP): 2-6 weeks (short IP) Has two phases ○ Pre-icteric phase: fever, fatigue, nausea, vomiting, right upper quadrant pain ○ Icteric (jaundice) phase: dark urine , pale stool , jaundice		
Lab diagnosis (9)	Serology (by ELISA) : ○ Anti-HAV IgM: current infection ○ Anti-HAV IgG: previous infection or immunity		(6) 
Treatment	There's no specific antiviral therapy only Supportive therapy (self-limiting)		
Prevention (10)	○ Sanitation & hygiene measures		
	○ Human Ig (passive immunization): given before or within 2 weeks of exposure. - Indication: travelers, unvaccinated, exposed patients. ○ Vaccine (active immunization): inactivated (killed), given IM in two doses at 0.6-12 m , >1 year of age. - Indication: people at high risk of infection (travelers) and people at high risk of severe disease - Side effects: mild local reaction (11) - Combination of vaccine (HAV & HBV)		
Prognosis	○ Acute mild self-limited disease ○ Fulminant hepatitis (8): rare (mainly in patients with chronic liver disease) ○ Mortality rate ~ 0.1 - 0.3% ○ No chronicity or malignancy changes not cause hepatocellular carcinoma		

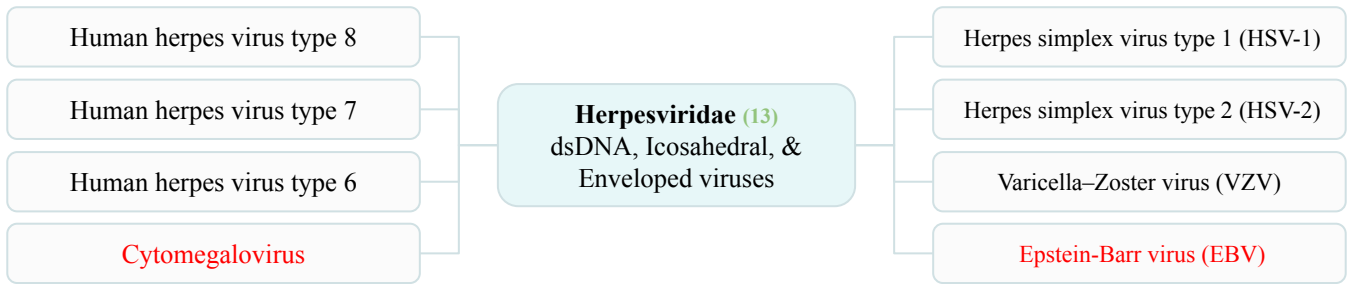


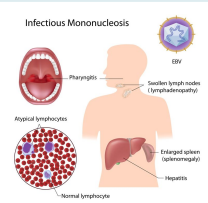
Hepatitis E

Hepatitis E virus	
Family	Hepeviridae
Characteristics	Non-enveloped virion consisting of : <ul style="list-style-type: none"> ○ Icosahedral capsid ○ Positive sense ss-RNA ○ One serotype
Clinical features	Similar to HAV infection with exceptions: <ul style="list-style-type: none"> ○ Longer IP (4-8 weeks) ○ Chronic hepatitis, cirrhosis, but not HCC (HepatoCellular Carcinoma) (12) ○ Fulminate disease “ the fulminant disease more than HAV but it is rare in both ” ○ Mortality rate 10 times higher than HAV ~1-3% (20% in pregnancy especially in 3ed trimester)
Epidemiology	Major cause of outbreak of water-borne hepatitis & sporadic cases of viral hepatitis Age: young adults
Transmission	4 routes of transmission; <ul style="list-style-type: none"> ○ Water-borne (most common) “When we see waterborne we think of HEV Then HAV” ○ Zoonotic (food-borne) undercooked meat of infected animals ○ Perinatal ○ Blood-borne
Lab diagnosis	Serology <ul style="list-style-type: none"> ○ Detection of anti-HEV IgM by ELISA
Treatment	Not specific
Prevention	<ul style="list-style-type: none"> ○ Sanitation & hygiene measures ○ No immunoglobulin ○ No vaccine



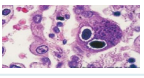
Herpesviridae



Virus	Epstein–Barr Virus (EBV)
Characteristics	<p>It is lymphotropic (14)</p> <p>It has oncogenic properties:</p> <ul style="list-style-type: none"> ○ Burkitt’s lymphoma ○ Nasopharyngeal carcinoma
Epidemiology	<p>Distribution: worldwide</p> <p>Age: depends on SE (Socio-Economic status)</p> <ul style="list-style-type: none"> - Low SE class: early childhood - High SE class: Adolescent
Transmission	<ul style="list-style-type: none"> ○ Saliva (kissing disease) ○ Blood [rarely]
Clinical features	<p>Immunocompetent host:</p> <ul style="list-style-type: none"> - Asymptomatic (especially in children) - Infectious mononucleosis (or glandular fever): ○ Mainly in teenagers & young adults ○ IP = 4-7 weeks ○ Fever, pharyngitis (15), malaise, hepatosplenomegaly, abnormal LFT & hepatitis ○ Complications (16) : acute airway obstruction (with pharyngitis), splenomegaly, CNS infection -Chronic EBV infection  <p>Immunocompromised host :</p> <ul style="list-style-type: none"> ○ Lymphoproliferative disease (LD) ○ Oral hairy leukoplakia (OHL)
Lab diagnosis	<p>Hematology: ↑ WBC: lymphocytosis (atypical lymphocytes) (17)</p> <p>Serology:</p> <ul style="list-style-type: none"> ○ Non-specific AB test (Paul-bunnell or monospot test): Heterophile antibodies +ve (18) ○ EBV-specific AB test : IgM Abs to EBV capsid antigen
Treatment	<p>Antiviral drug is not effective in infectious mononucleosis Cuz the symptoms and signs of IMN caused by hematological attack</p>
Prevention	<p>No vaccine</p>



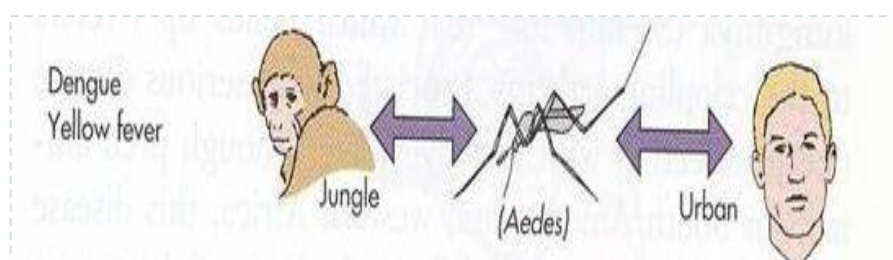
Herpesviridae

Virus	Cytomegalovirus CMV	
Special Features	<ul style="list-style-type: none"> ○ Infected cell enlarged with multinucleated [cyto = cell, megalo = big] ○ Resistant to acyclovir ○ Latent in monocyte, lymphocyte, & other cells. ○ It's replication cycle is longer 	
Epidemiology	Worldwide	
Transmission	<ul style="list-style-type: none"> ○ Early in life: Transplacental, Birth canal , Breast milk ○ In children: Saliva ○ Later in life: Sexual contact, blood transfusion, & organ transplant (19) 	
Clinical features (20)	<p>1- acquired infection</p> <ul style="list-style-type: none"> ○ Immunocompetent host : Asymptomatic Self-limited illness: -Hepatitis -Infectious mononucleosis like syndrome [heterophile AB is -ve] ○ Immunocompromised host : Systemic symptoms: Encephalitis, Retinitis, Pneumonia GIT symptoms: Hepatitis, Esophagitis, Colitis <p>2- Congenital Infections</p>	
Lab diagnosis (21) (22)	<p>Histology: large cell with intranuclear inclusion bodies (Owl's eye)</p>	
	<p>Culture</p> <ul style="list-style-type: none"> ○ In human fibroblast: CBE (cytopathic effects) after 1-4 wks ○ Shell vial assay after 1-3 days 	
	<p>Serology</p> <ul style="list-style-type: none"> ○ Ab → IgM: current infection, IgG: previous exposure (but not immunity) ○ Ag → CMV pp65 Ag (phosphoprotein 65) by IFA 	
	<p>PCR</p>	
Treatment (23)	<ul style="list-style-type: none"> ○ Ganciclovir is effective in the treatment of severe CMV infection ○ Foscarnet: the 2nd drug of choice 	
Prevention	<ul style="list-style-type: none"> ○ Screening: organ donors, organ recipients, blood donors. (24) ○ No vaccine ○ Prophylaxis: Ganciclovir, CMVIG ○ Use leukocyte-depleted blood (25) 	



Arthropod-borne Viruses (Arboviruses)

Virus	Yellow Fever virus
Family	Flaviviridae
Epidemiology	Tropical Africa & South America
Clinical features	Asymptomatic to Fever ± Jaundice (hepatitis) In Severe cases ± hemorrhage ± renal failure, shock
Types of fever	<p>1. Jungle Yellow Fever (26)</p> <ul style="list-style-type: none"> - Vector: mosquito - Reservoir: monkey - Accidental host: human - It is a disease of monkeys <hr/> <p>2. Urban Yellow Fever</p> <ul style="list-style-type: none"> - Vector: mosquito - Reservoir: human - It is a disease of humans
Lab diagnosis (27)	<p>Lab. Methods:</p> <ol style="list-style-type: none"> 1. Isolation (gold standard) 2. IgM-AB by ELISA or immunofluorescence (most used) 3. YFV-RNA (Arbovirus) by RT-PCR
Prevention (28)	<p>Vector Control (general methods):</p> <ul style="list-style-type: none"> ○ Elimination of vector breeding sites ○ Using insecticides ○ Avoidance contact with vectors (repellants, net) <p>Vaccine (specific methods)</p> <ul style="list-style-type: none"> ○ Yellow Fever vaccine; LAV (live attenuated vaccine); 1 dose / 10 yrs ○ It's recommended for travelers





1. What's the meaning of hepatitis? Inflammation of liver

What are the causes ? infectious causes like viruses (most common), bacteria, parasites
non infectious like alcohol, toxins, drugs, autoimmune diseases

2. What is the difference between primary and secondary hepatitis?

secondary hepatitis: that cause hepatitis as part of generalized infection

Primary hepatitis: effect only the liver

When we say viral hepatitis we mean that it effect liver primarily

3. **HAS, HEV**, they affect the liver primarily by fecal-oral route so they are non-enveloped

CMV, EBV, Arbovirus they cause hepatitis as part of systemic illness most common virus is B, they are enveloped

4. it can be transmitted by sexual contact but not considered as sexual disease, also it can be transmitted by blood but it is not the major route of transmission

5. the virus will appear in the stool 2 weeks before the symptoms and 1 week after the symptoms, once the symptoms appear, the concentration of virus will decline within one week

6. The immune system against hepatitis virus consists mainly by presence of Ig-M specific against virus A, followed 2-3 week by Ig-G.

Present of IgM occur in symptoms period

7. severity of the disease is increase with the age so children have asymptomatic illness

8. fulminant hepatitis :massive or severe necrosis with the liver failure some time it is associated with encephalopathy

9. present of IgG with absence of IgM indicates either previous exposure or immunity due to vaccination

10. there are general prevention and specific prevention

general prevention like :sanitation, hygiene

specific prevention :

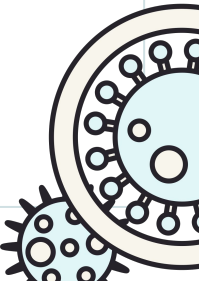
- Passive immunization like :HIg; it gives immediate immunity

- Active immunization like: vaccine it gives long live immunity

They both can be used pre exposure and post exposure

11. safe highly effective and has mild local reaction as ADR

12. usually cause acute hepatitis and it may cause chronic hepatitis and cirrhosis in immunocompromised pt but not malignancy





13. herpesviridae it cause mild self limited hepatitis in general however it may cause severe hepatitis in immunocompromised Pt
14. It is lymphotropic It infect and become latent in lymphoid cells mainly B lymphocytes
15. any sore throat with hepatitis = EBV and some without sore throat
- 16.-complications are rare, acute airway obstruction due to swelling of cervical with enlargement of lymph node and edema, splenic rupture due to splenomegaly , CNS infection like meningitis and encephalitis
- 17.-atypical lymphocytes that are cytotoxic T cells reactive against B cells infected by EBV
- 18.highly sensitive Specially in adults and less sensitive in the children so it may give false-negative results

- 19..it is important to know that CMV is transmitted by blood transfusion and organ transplant so it is important for prevention to screening the blood and the organ to detect Igg cuz the Igg is indicates latent infection

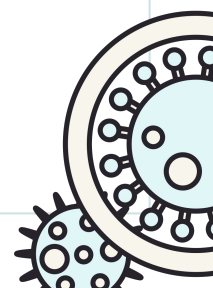
- 20.it is asymptomatic specially in young children it's may cause infection mononucleosis like syndrome like EBV But it's different in different way it's characterized by febrile illnesses with mild hepatitis and fever ,anorexia
not cause or less common to give pharyngitis or lymphadenopathy.
why is it Heterophile AB -ve ? Because CMV doesn't affect B cells

21. IgM for immunocompetent host.
Why is IgM not used for immunocompromised patients? because their immunity unable to produce IgM
22. so how do we diagnose the disease in immunocompromised patients? by histological examination in addition to antigen detection and PCR to detects genome of the virus
23. drug of choice Ganciclovir in the immunocompromised patients if there's is resistance we use foscarnet
24. screening is for detect IgG it should be negative donor to negative receiver
- 25.what's the meaning of leukocyte depleted blood ? Blood without leukocytes because CMV becomes latent in the Monocytes

26. jungle fever is a disease of monkey human infected accidentally when he is working in the jungle or visiting jungle while urban fever is a disease of human

27. most common route to diagnose yellow fever is serology by detection of IgM antibody agonist yellow fever virus

28. The vaccine is indicated for travelers in epidemic area ,only one dose each 10 years
contraindicated for pregnant women and infant less than one year





Summary

<p>Hepatitis A virus</p>	<ul style="list-style-type: none"> ○ Characteristics of the virus : Non-enveloped, ssRNA ○ Epidemiology: In developing countries especially children ○ Transmission by Fecal-oral route E.g. contaminated food & water ○ pathogenesis : damage the hepatocyte by CMI ○ HAV cause : Acute mild self-limited disease No chronicity or malignancy changes ○ Prevention <ul style="list-style-type: none"> Human Ig for prevention Vaccine : inactivated (killed) ○ Incubation period (IP): 2-6 weeks (short IP) ○ Lab diagnosis (Serology) <ul style="list-style-type: none"> Anti-HAV IgM: current infection Anti-HAV IgG: previous infection or immunity
<p>Hepatitis E virus</p>	<ul style="list-style-type: none"> ○ Characteristics of the virus : Non-enveloped, ssRNA ○ Epidemiology :Adult ○ Incubation period (IP)Longer IP (4-8 weeks) ○ HEV cause : usually acute, may cause Chronic hepatitis, cirrhosis, but not HCC ○ Transmission by Water-borne, Zoonotic (food-borne) undercooked meat ○ Lab diagnosis (Serology) :Detection of anti-HEV IgM by ELISA ○ Prevention no vaccine no Ig
<p>Epstein–Barr Virus (EBV)</p>	<ul style="list-style-type: none"> ○ Characteristics : It's lymphotropic, It has oncogenic properties ○ Transmission by kissing disease ○ Clinical Features: Infectious mononucleosis (or glandular fever): <ul style="list-style-type: none"> Fever, pharyngitis Complications : acute airway obstruction, splenomegaly, CNS infection ○ Chronic EBV infection (in immunocompetent host) ○ Lab diagnosis <ul style="list-style-type: none"> Hematology : lymphocytosis (atypical lymphocytes) Serology Heterophile antibodies +ve
<p>Cytomegalovirus CMV</p>	<ul style="list-style-type: none"> ○ Special Features : <ul style="list-style-type: none"> Enlarged Infected cell with multinucleated Latent in monocyte, lymphocyte, & other cells. ○ Transmitted mainly by blood transfusion, & organ transplant ○ Clinical Features: Infectious mononucleosis like syndrome ○ Lab diagnosis <ul style="list-style-type: none"> Serology : heterophile AB is -ve Histology : intranuclear inclusion bodies (Owl's eye) ○ Prevention: Screening for organ donors, organ recipients, blood donors.
<p>Yellow Fever virus</p>	<ul style="list-style-type: none"> ○ Types Of fever <ul style="list-style-type: none"> Jungle Yellow Fever “disease of monkeys” Vector: mosquito Reservoir: monkey Urban Yellow Fever “disease of humans” Vector: mosquito Reservoir: human ○ Prevention <ul style="list-style-type: none"> General method → Vector Control Special Method → vaccine : LAV (live attenuated vaccine)



MCQs

1- what is the kissing disease ?

- A) Yellow Fever virus B) CMV C) hepatitis A D) EBV

2- which of the following virus has -ve heterophile AB ?

- A) EBV B) Yellow Fever virus C) CMV D) hepatitis A

3- which of the following can be prevented by LAV ?

- A) Yellow Fever virus B) CMV C) EBV D) hepatitis A

4-Which of the following is the major transmission route for Hepatitis A virus?

- A) Fecal-Oral route B) Respiratory secretion C) Airborne route D) skin penetration

5- Which of the following is an indication of Hepatitis infection?

- A) decrease Bilirubin B) Decrease ALT C) Increase ALT D) Decrease AST

6- Which of the following viruses has an envelope?

- A) Norovirus B) HAV C) EBV D) HEV

0-9
0-5
A-4
A-3
C-2
D-1



Case 1

A 28-year-old pregnant woman is brought to the emergency by her husband for lethargy, nausea, and vomiting for 4 days. This morning she became drowsy. She returned from a business trip to Sudan 3 weeks ago. Her immunizations are up-to-date and she has never received blood products. Examination shows jaundice and mild asterixis. Lab tests reveal highly elevated ALT & AST. An ELISA for HIV is negative.

Q1: What is the most likely diagnosis? Fulminant hepatic failure due to hepatitis E infection

Q2: What is the predisposing factor? Pregnancy and travel to HEV-endemic country (Sudan)

Q3: What test is used to confirm the diagnosis? Anti-HEV IgM titer

Case 2

A 32-year-old woman comes to the emergency for a 1-week history of jaundice and nausea. She recalls eating seafood last weekend at a cookout. The liver is palpated 2-cm below the right costal margin and is tender.

Q1: What is the most likely diagnosis? Hepatitis A infection

Q2: What is the route of transmission? Fecal-oral (eating seafood)

Q3: What test is used to confirm the diagnosis? Hepatitis A IgM antibodies

Q4: She lives at home with her 8 months-old son who is unvaccinated. What is the most appropriate recommendation for him at this time? Administer hepatitis A immunoglobulin for post-exposure prophylaxis



TEAM 443
MICROBIOLOGY

Team leaders

Aishah Boureggah

Aroub Almahmoud

Maryam Alghannam

Nazmi M Alqutub

Team Members

Mohammd Alqutub

Raghad Almuslih

Khalid Alsobei

Afnan Alahmari

Lama Alotabi



Wajd Almutairi

Sultan Albaqami

Zahra Alhazmi



Nourah Alarifi

Moath Alhudaif

Almas Almutari

Sarah Alajaji

Aban Basfar

Reema Almotairi

Alhawraa Alawami



Mohammed Alarfaj

Reema Algarni

Shahad Alzaid

Faris Alzahrani

Farah Abukhalaf

Danah Almuhausen

Abdulrahman Almusallam

Remaz Almahmoud

Areej Alquraini

Zeyad Alotaibi

Aleen Alkulyah

Layan Al-Ruwaili

Luay Alhudaithy

Rafan Alhazzani

Haya Alzeer

Nazmi A Alqutub

Reuf Alahmari

Raseel Almutairi

Rahaf Alshowihi

Reena Alsadoni