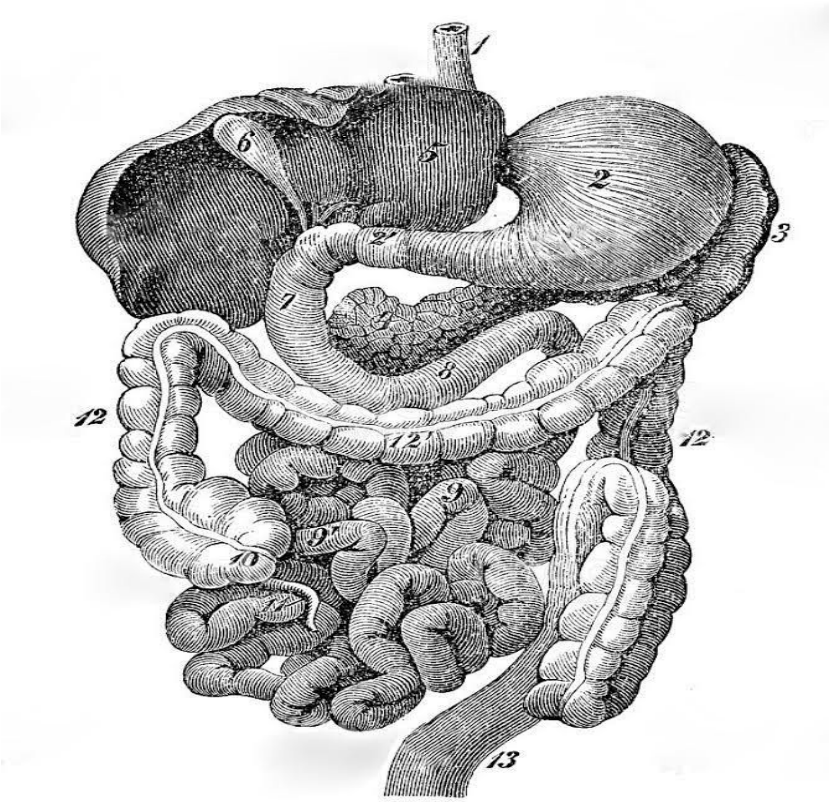
Microbiology

435's Teamwork
GastroIntestinal & Nutrition Block



- Please contact the team leaders for any suggestion, question or correction.
- Pay attention to the statements highlighted in red.
- Extra explanations are added for your understanding in grey.
- **Footnotes color code:** General | Females | Male

Revised by

خولة العماري & هشام الغفيلي

DONE BY:Rawan ALdhuwayhi,Morooj Alharbi,Raghad Alnafisah &Johara Almalki

Viral hepatitis A ,E & others

Resources: male & female slides,...

Learning Objectives:

By the end of this lecture, you should know the…

1. Know the classification of viruses causing hepatitis.
2. Viruses causing entericaly transmitted hepatitis:HAV,HEV.
3. Viruses that are causing hepatitis during their course of infection: Cytomegalovirus (CMV) ,Epstein-Barr virus (EBV),Arbovirus (yellow fever virus)

Recall from the previous lecture:

VIRAL HEPATITIS

Etiology:

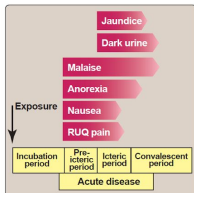
- **As part of generalized infection:**(Cytomegalovirus, Epstein–Barr virus, Yellow fever virus)

OR

- **Primary infection:** hepatitis **A**,**B**,**C***(was known as non A non B hepatitis)*,**D**,**E** & **F***(in the literature but not confirmed)*

B	C	G	D	A	E
ds-DNA	ss-RNA with positive polarity				
Envelope			Defective v (use HBV as envelope)	Nonenveloped [1] (have One serotype)	
Family:*hepadnaviridae* .	Family: *Flaviviridae*, genus: *Hepacivirus.*			Family:picornaviridea	Family:Hepeviridae
Parenterally transmitted hepatitis or bloodborne hepatitis				*Enterically transmitted hepatitis or waterborne hepatitis OR fecal borne (FECAL ORAL ROUTE)*	
Acute and/or chronic infections				*ACUTE*	
vaccine available	*NO vaccine available*			*vaccine available*	*NO vaccine available*

[1] None enveloped viruses so they have capsid and remain for long peroid in the body

	Hepatitis A Virus **Other names (Short incubation hepatitis, Infectious hepatitis** called infectious cuz it's easily transmitted **, Epidemic hepatitis)**	Hepatitis E Virus more severe compared to HA
Epidemiology	A worldwide, endemic in tropical countries most common in developing countries with poor sanitation(+outbreak of waterborne HEV)	
Transmission	• Faecal-oral route **(major route)**:Contaminated food & water مهمه	
	• Sexual contact (homosexual men) • Blood transfusion (v.rarely) لانه اكيوت فتظهر عليه الاعراض بسرعه فيعرفون ان عنده عدوى فمايأخذون منه دم فلهذا السبب ماينتقل بكثرة عن طريق الدم	• Zoonotic foodborne unlike other vs it can be transmitted from animal to human احسها بتجي سؤال مدري ليش • Bloodborne • Perinatal from mother to infant
Age	• In developing countries: Children • In developed countries: Young adults	Young adults different than HAV which can affect children
Pathogenesis	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 → the immune system (cellular mediated immunity) starts to attack the hepatocyte infected by the virus causing Damage of virus-infected hepatocytes leads to ↑ ALT, ↑AST & ↑Bilirubin (((HAV&HEVdon't cause cytopathic effect but the immune system cause damage to hepatocyte احسها موضع اسئله مدري ليش)))	
Manifestation	incubation period of 2-6 weeks (short IP and cause epidemic hepatitis) Usually followed by the onset of fever, fatigue, nausea, vomiting & pain in the right upper abdominal quadrant(Pre-icteric phase or anicteric phase) and, within several days, jaundice. Dark urine and pale stools **may be** noticed not commonly seen (Icteric phase) **TO SUM UP:** • Asymptomatic & anicteric infection (common) • The severity of the Symptoms increase with age. 	**Similar to HAV infection & exceptions:** -Longer IP=4-8 weeks -Fulminant disease more common (it is massive necrosis with hepatocellular failure) -Mortality rate 10 times higher than HAV, high mortality rate especially in pregnancy (20% of cases)
Prognosis	The prognosis is generally favorable(self limiting), and the development of fulminant hepatitis and chronic hepatitis is **RARE**.	
Lab diagnosis	• ***Serology:***Early antibody responses are predominantly **IgM**(indicates current infection) → During recovery antibody**IgG**predominates(indicates previous infection OR immunity)when we talk about AB'S against certain antigen mostly we r using ELISA	Anti-HE IgM can be detected by ELISA
Treatment	Supportive therapy ,Not specific	
Prevention	• **Sanitation & hygiene measures** • **HIg[2](human immunoglobulin) passive immunization:** protective if given before or during the IP of the disease Given before or within 2 weeks of exposureHig اذا جاك شخص قالك انا خالطت مصاب بهيتايتس أي من قبل اكثر من اسبوعين أقوله خلاص فات الفوت ماينفع اعطيك ***Indication***:travelers Persons from areas of low endemicity traveling to areas with high infection rates may receive HIg before departure , who recently exposed to Hepatitis A patients and has not been	• **Sanitation & hygiene measures** • **No HIg** • **No vaccine**

[2] human immunonglbuilin antibodies given to person living with one diagnosed with hepatits A or the infected person his infection within 2 wks (in early stage) we may give him HIg
لو واحد ساكن مع شخص مشخص بـhepatitis A نعطيه HIg مانعطيه فاكسين ليه ؟ لأن الفاكسين ياخذ وقت اطول فالاميونون قلوبيلن اسرع واحد

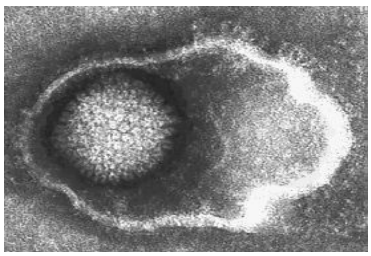
	vaccinated against Hepatitis A • **Vaccine:** -Vaccines prepared from whole virus inactivated -recommended for children less than 1 year ,should given to patients at high risk of infection or severe diseases. -A combination vaccine(called Twinrix) is available to protect against both HAV&HBV -should Given IM ,*Side effect:* mild local infection	

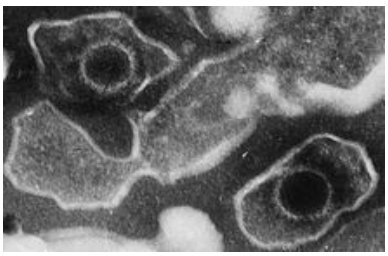
Herpesviridae

(dsDNA, Icosahedral & Enveloped virus transmitted by blood)

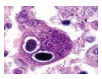
Herpes viruses are well known that they stay in the body as latent viruses , so EBV & CMV they stay latent inside the WBC .mainly b-lymphcyte

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)





Virus	**Epstein-Barr virus (EBV)**	**Cytomegalovirus (CMV)***(cyto=cell, megalo=big)*
Characteristic	• It is lymphotropic mainly B lymphocyte • It has oncogenic properties:Burkitt's lymphoma ,Nasopharyngeal carcinoma	• Infected cell enlarged with multinucleated causes enlargement of infected cell • Resistant to acyclovir • Latent in monocyte, lymphocyte & other تتوزا داخلها وتقعد ساكنه
Epidemiology	• **Distribution:** worldwide • **Transmission: saliva (kissing disease)** • **Age:** Based on socio-economic status 'SE': (High SE=adolescence) (Low SE=early childhood) In more highly developed countries and in individuals of higher socioeconomic status EBV infection tends to be acquired later in life than in individuals from developing countries of lower socioeconomic status	• **Distribution:** worldwide • **Transmission:** can infect the person at any age of his life هي تحب تقعد في سوائل و افرازت الجسم زي اللعاب والحليب والمني فتنتقل عند الاختلاط بافرازات المصاب ❑ *Early in life:* transplacental, birth canal, breast milk ❑ *Young children:* saliva ❑ *Later in life:* sexual contact,Blood transfusion & organ transplant

Clinical features	**-Immunocompetent host** • Children are asymptomatic • adolescents and young adults show the typical symptoms of ***Infectious mononucleosis*** (glandular fever):IP=4-7 weeks ❑ *symptoms:*Fever, pharyngitis, malaise, hepatosplenomegaly & abnormal LFT ± hepatitis ❑ *Complications* rare but serious:acute air way abstruction , splenic rupture, CNS infection • If the symptoms last more than 6 months Chronic EBV. **-Immunocompromised host:** Lymphoproliferative diseases ,Oral hairy leukoplakia white patches appear in the tongue	1. **Acquired infections** • **Immunocompetent host:** -the majority of cases r Asymptomatic [3] -Some pts develop Self-limited illness{such as mild Hepatitis & Infectious mononucleosis like syndrome (Heterophile AB is -ve)[4] } • represents a serious threat to**Immunocompromised host:**infect all organs of the body:Encephalitis, Retinitis, Pneumonia ,**Hepatitis**, Esophagitis, Colitis 2. **Congenital infections** CMV is the most common cause of intrauterine infections and congenital abnormalities
Investigation	• **Hematology:**Increase WBC=lymphocytosis (Atypical lymphocytes) • **Serology:** *-Non-specific AB test:*Paul-Bunnell or mono-spot test: looking for Heterophile Abs[5] →+ve in EBV *-specific AB test:* **IgM** Abs to EBV capsid antigen (definitive diagnosis)	• **Histology:**Intranuclear inclusion bodies ***(Owl's-eye)***  • **Culture:**CMV is slow growing so we don't depend on culture -culture Of human fibroblast for 1-4 weeks looking for any Cytopathic effect. -OR by using modified cell culture called Shell vial assay provide result within 1-3 days • **Serology:**by looking for: ❑ AB=Early antibody responses are predominantly **IgM**(indicates current infection) →During recovery antibody of **IgG** predominates(indicates previous infection, DOES NOT MEAN immunity) ❑ antigen=CMV pp65 Ag by IFA(Indirect fluorescent antibody) it's better to look for Ag not antibodies cuz AB don't usually indicate infection but antigen will give direct diagnosis • **PCR :**for detection viral DNA
Treatment	Antiviral drug is not effective in IMN	• **Ganciclovir:** is effective in the treatment of severe CMV infection • **Foscarnet:** the second drug of choice active against resistant strain
Prevention	No vaccine	• Screening:Organ donors,Organ recipients&Blood donors • Leukocyte-depleted blood cuz virus is latent in Leukocytes فنحاول نفصل اللوكوسايت من الدم • Prophylaxis: Ganciclovir&CMVIG (CMV immunogloblin) • No vaccine

[3] EBV and CMV usually appear and cause the disease when the immune system drop but in immunocompetent even if person is infected the symptoms will appear for short time or he may become asymptomatic .

[4] The major distinguishing feature of CMV infectious mononucleosis the absence of the heterophile antibodies that characterize infectious mononucleosis caused by EBV

[5] is nonspecific elevation of Abs produces during polyclonal stimulation of B cells by EBV infectionAB's produced by none specific b-cells

<table>
<tr><th colspan="3">Yellow Fever Virus</th></tr>
<tr><td>morphology</td><td colspan="2">Family: Flaviviridae (ssRNA)</td></tr>
<tr><td>Clinical presentation</td><td colspan="2">The majority of cases r Asymptomatic or present with mild nonspecific illness such jaundice &fever , however few cases may present with hemorrhage ± renal failure</td></tr>
<tr><td>Epidemiology</td><td colspan="2">Considers as Arthropod-borne Viruses (Arboviruses) common in Tropical Africa & South America</td></tr>
<tr><td rowspan="2">Classified according to the epidemiological pattern into</td><td>Jungle Yellow Fever
بالغابات</td><td>• Vector : mosquito
• Reservoir: Monkey,It is a disease of Monkeys
• Accidental host: human مايجيك هالمرض الا اذا خالطت القرد</td></tr>
<tr><td>Urban Yellow Fever بالمدن</td><td>• Vector: mosquito
• Reservoir: human ,It is a disease of humans</td></tr>
<tr><td>Diagnosis</td><td colspan="2">Lab.Methods:
• Detection of IgM by ELISA, IF: (most used)
• In some cases, virus isolation or demonstration of specific viral antigens is also suitable.
• Yellow Fever V- RNA by RT-PCR</td></tr>
<tr><td>Prevention</td><td colspan="2">1. Vector Control:
• Elimination of vector breeding sites
• Using insecticides
• Avoidance contact with vectors (repellants  , net )
2. Yellow Fever vaccine:Live Attenuated Vaccine, one dose provides immunity for10 years</td></tr>
</table>

SUMMARY

Done by: JOHARA H. ALMALKI

Remember those things and you're good to go! =)

HAV (Picornaviridae) ssRNA	**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 inf. And IgG previous exposure **(and immunity)**. **Prevented by HIg and vaccine (inactivated)**
HEV (Hepeviridae) ssRNA	**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 (Herpesviridae) dsDNA**	**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 (Herpesviridae) dsDNA	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 (Flaviridae)	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.