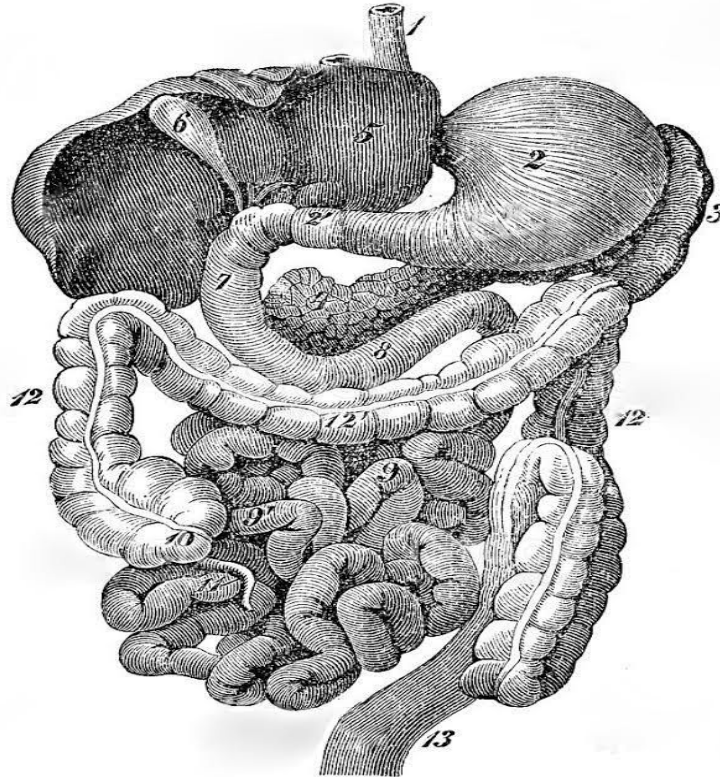


Microbiology

435's Teamwork
GastroIntestinal & Nutrition Block



- Kindly check our [Editing File](#) before studying the document.
- 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** | **Males**.
- **color code:** **Female's notes** | **Male's notes**.

Revised by

خولة العماري & هشام الغفيلي



Hepatitis B, C, D and G

Resources: Sherris Medical Microbiology, LIR Microbiology,...

Learning Objectives:

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

1. Characteristics
2. Mode of transmission
3. Markers
4. Serological profile
5. Stages
6. Lab diagnosis
7. Management & treatment

Of. Viral hepatitis

VIRAL HEPATITIS

Etiology:

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

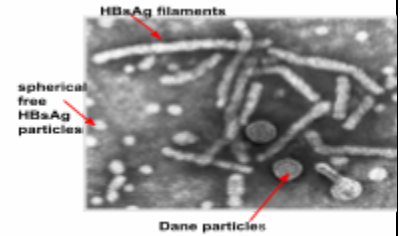
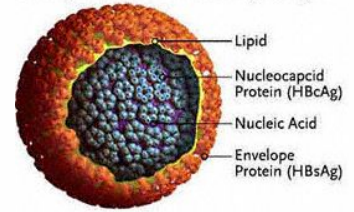
OR

- **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) | Non envelope | |
| Family: <i>hepadnaviridae</i> | Family: <i>Flaviviridae</i> , genus: <i>Hepacivirus</i> . | | | | |
| <i>Parenterally transmitted hepatitis or bloodborne hepatitis</i> | | | | <i>Enterically transmitted hepatitis or waterborne hepatitis (FECAL ORAL ROUTE)</i> | |
| <i>Acute and/or chronic infections</i> | | | | <i>ACUTE</i> | |
| <i>vaccine available</i> | <i>NO vaccine available</i> | | | <i>vaccine available</i> | <i>NO vaccine available</i> |

Hepatitis B

| | | | |
|----------------------------|---|---|--|
| Characteristics | <p>Virion¹ consists of:</p> <ul style="list-style-type: none"> Outer envelope containing hepatitis B surface antigen (HBsAg). Internal core (nucleocapsid) composed of hepatitis B core antigen (HBcAg). The viral genome which is small partially circular ds-DNA. The virus contains the enzymes reverse transcriptase². <p>There are 8 genotype (A-H), genotype D is dominant in Saudi Arabia. جدا مهم.</p> | | |
| | <p>The serum of infected individual contains 3 types of hepatitis B Particles :</p> <ul style="list-style-type: none"> Large number of small spherical free HBsAg Particles. جزء من غلاف الفايروس عائم لحاله. Some of these HBsAg particles are linked together to form filament. The complete HBV particles (Dane particles بعضه على الفايروس كله على بعضه). | | |
| Transmission | Parentally | <p>يعني عبر الدم فينتقل باي طريقه ممكن يحصل فيها اختلاط دم</p> <ul style="list-style-type: none"> - Direct exposure to infected blood or body fluids (e.g. receiving blood from infected donor). - Using contaminated or not adequately sterilized tools in surgical or cosmetic practice (dental, tattooing, body piercing). - Sharing contaminated needles, razors مثلا or tooth brushes. | |
| | Sexually (unprotected sex) | through close personal contact with body fluids of infected individuals. | |
| | Perinatally (from mother to baby) | <ul style="list-style-type: none"> • Infected mothers can transmit HBV to their babies mostly during delivery. • Breastfeeding is also way of perinatal transmission. | |
| Risk factors | <ul style="list-style-type: none"> • Intravenously drug users. • Hemodialysis patients. • Patients receiving clotting factors. لان الفايروس يحب الدم ومتعلق بالكلوتنق فاكثور وتصعب ازالته منها. • Individuals with multiple sexual partners. • Health care workers with frequent blood contact. • Individuals who exposed to tattooing, body piercing or cupping الحجامه. | | |
| The clinical outcome | About 90 % of infected adults will develop acute hepatitis B infection and recover completely . | less than 9 % of the infected adult, 90% of infected infants and 20% of infected children may progress to chronic hepatitis B . <i>(The majority of patients with chronic hepatitis B and C are asymptomatic or have mild fatigue only)</i> | < 1 % may develop fulminant hepatitis B , characterized by massive liver necrosis, liver failure and death . |
| Lab diagnosis ³ | <ul style="list-style-type: none"> - detection of HBsAg in the blood.. Positive results must be repeated in duplicate. Repeatedly reactive results must be confirmed by neutralization test (to distinguish acute from chronic infections) - Additional lab investigations: <ol style="list-style-type: none"> 1- Liver function tests (LFT). 2- Ultrasound of the liver. 3- Liver biopsy to determine the severity of the diseases. | | |
| Treatment | <ul style="list-style-type: none"> • Pegylated alpha interferon inhibits protein synthesis of the vs and the host cell • Lamivudine (antiviral drug: nucleoside analogue prevent viral replication in infected cells) • Adefovir (antiviral drug: nucleoside analogue) | | |



¹ infective form of a virus outside a host cell

² generates mutations in the genomes of replicating virus at a high rate

³ The purpose of diagnostic laboratory studies of patients with clinical hepatitis is to, first, determine which hepatitis virus is the cause of the illness and, second (for HBV), to distinguish acute from chronic infections.

| | |
|----------------|---|
| vaccine | <ul style="list-style-type: none"> It contains highly purified preparation of HBsAg particles, produced by genetic engineering in yeast (The current vaccine is a recombinant product derived from HBsAg grown in yeast. Excellent protection) It is a recombinant and subunit vaccine⁴. The vaccine is administered in three doses at 0,1, & 6 months. نعطيه اليوم وبعد شهر وبعد سنت اشهر. The vaccine is safe and protective |
|----------------|---|

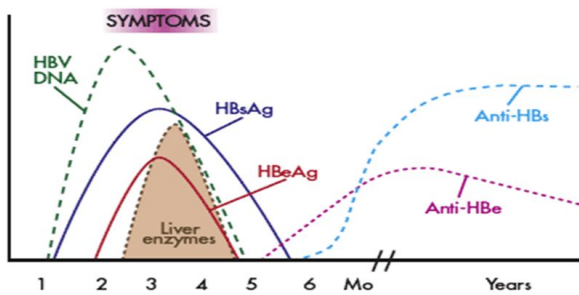
Acute hepatitis B infection الدكتور من يوم بدا المحاضرة يقول ابكم تعرفون الماركز

- Acute viral hepatitis usually lasts for several weeks or less than 6 months.
- Most acute hepatitis **B & C** are **asymptomatic** or **anicteric**.

| | | |
|--|---------------------------------|---|
| Clinical presentation لا تصيبون الاعراض بتصير نفسها في كل الاشخاص ترى في ناس مايمرون بمرحلة الصفار | 1) Anicteric ⁵ phase | Low grade fever, anorexia, malaise, nausea, vomiting and pain at the right upper quadrant of the abdomen , raised liver enzyme . |
| | 2) Icteric ⁶ phase | which is characterized by jaundice , dark urine and pale stool . |
| | 3) Convalescent phase. | متماثل للشفاء |

| Hepatitis B markers كلها جدا مهمه وينسالكم عنها | Types | Description | Serological Profile |
|--|--|--|---|
| | HBV DNA | Marker of infection | the 1st marker that appears in circulation , 3-4 week after infection. |
| | HBsAg | يعني اول ما شوفها بدم المريض اقول انه مصاب بالهبتايتس | is the 2nd marker that appears in the blood and persists up to 6 month then disappear . اذا قد اكثر من ست شهور نقول عن المرض انه مزمن. |
| | Hepatitis B e antigen (HBeAg) Viral protein | Marker of active virus replication, the patient is highly infectious , the virus is present in all body fluids هذي مصيبه اذا شفتها بتدل ان الفايروس قاعد يتكاثر بشكل رهيب بالكبد وانتشر لجميع اجزاء الجسم والشخص يكون جدا جدا معدي في هذي المرحلة | HBeAg is the 3rd marker that appears in circulation and disappears before the disappearance of HBsAg نعمة انه هذي المرحلة الي يكون فيها الشخص جدا معدي تخلص بسرعه : |
| | Antibody to hepatitis B core (Anti-HBc) | Marker of exposure to hepatitis B infection. مايقولي اذا هو معدي او لا او اكيوت او كرونك پس يقولي انه عنده هيبتايتس | Anti-HBc Ab is the 1st antibody that appears in the blood and usually persists for several years. |
| | Antibody to hepatitis B e antigen (Anti-HBe) | Marker of low infectivity The patient is less infection | Appears with the disappearance of HBeAg, anti-HBe appears and usually persists for several years. |
| Antibody to hepatitis B surface antigen (Anti-HBs) | Marker of immunity. NOT CONTIGUOUS. | Anti-HBsAg (Anti-HBs) is the last marker that appears in the blood, It appears few weeks after disappearance of HBsAg and persists for several years, It indicates immunity to hepatitis B infection. وترى هذي الي used as marker of past infection or vaccination | |

هالصورة تشرح نفس الكلام الي فوق: لاحظو انه اول ماتطلع الانتي بوديز يختفي الانتيجينز وكل الانتي بوديز تستمر لسنوات (وعشان يسهل عليكم الحفظ لاحظو ان الانتيجينات بالنسبه للاكيوت تظهر خلال 6شهور بعدها تختفي)
اول واحد يبني يطلع هو HBV DNA



⁴ These are the components of the pathogenic organisms. Subunit vaccines include proteins, peptides and DNA

⁵ Anicteric means no yellowish

⁶ Icteric means yellowish

Chronic hepatitis B infection

- **Chronic hepatitis B is defined by the presence of HBsAg or HBV-DNA in the blood for more than 6 months.** مهم جدا جدا
- HBsAg may persist in the blood for life⁷.
- Chronic infection associated with HBsAg persistence and **NO** development of anti-HBs.
- After disappearance of HBsAg, anti-HBs Ab appears and persists for several years. لكن في مرحله الكرونيستي مايكون الانتي بودي موجود.
- **Two types of chronic hepatitis can be distinguished:**

- In one, HBsAg is detected but not HBeAg; these patients usually show minimal evidence of liver dysfunction. *(The majority of patients with chronic hepatitis B and C are asymptomatic or have mild fatigue only)*

- In the other, both antigens (HBsAg & HBeAg) are found; the process is more active, with continued hepatic damage that may result in cirrhosis & hepatocellular carcinoma. زي ماقلنا فوق مصيبه اذا لقيت HBeAg نل ان الفايروس قاعد يتكاثر بشكل رهيب و الشخص جدا معدي.

complication⁸ of severe active hepatitis

u will study it in pathology with more details ,so u can skip it :)

| | |
|--|---|
| Cirrhosis | Is a chronic diffuse liver disease. |
| | Characterized by fibrosis and nodular formation. |
| | Results from liver cell necrosis and the collapse of hepatic lobules. |
| | Symptoms ascites, coagulopathy (bleeding disorder), portal hypertension, hepatic encephalopathy, vomiting blood , weakness, weight loss. |
| Hepatocellular carcinoma (HCC) | - One of the most common cancer in the world . Also, one of the most deadly cancer if not treated. |
| | - Hepatitis B and C viruses are the leading cause of chronic liver diseases. |
| | Symptoms abdominal pain, abdominal swelling, weight loss, anorexia, vomiting, jaundice . |
| | Physical examination hepatomegaly, splenomegaly and ascites. |
| | Prognosis without liver transplantation, the prognosis is poor and one year survival is rare. |
| | Diagnosis alpha-fetoprotein measurement with multiple CT-abdominal scan are the most sensitive method for diagnosis of HCC. |
| Treatment surgical resection and liver transplant. | |

EXTRA SKETCHES

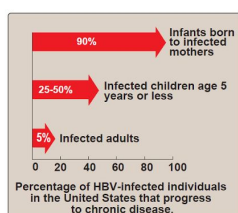


Figure 26.9
Effect of patient's age on the tendency of acute hepatitis B virus (HBV) infection to progress to chronic disease.

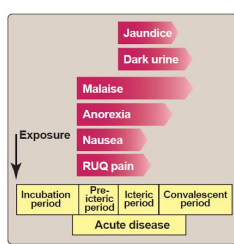


Figure 26.6
Symptoms of acute hepatitis B infection. RUQ = right upper quadrant.

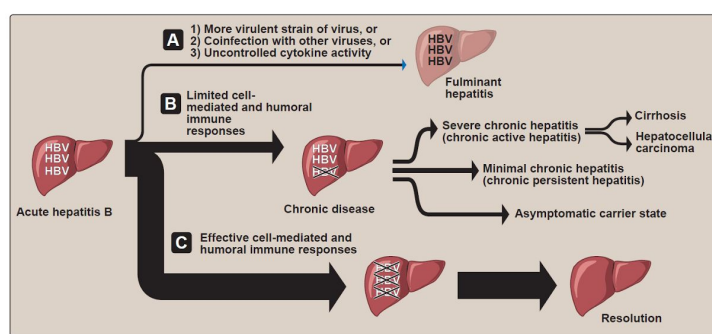


Figure 26.5
Clinical outcomes of acute hepatitis B virus (HBV) infection.

| SERUM MARKER | RESOLVED | CHRONIC ¹ | VACCINATED |
|--------------|----------|----------------------|------------|
| HBsAg | - | + | - |
| HBeAg | - | + | - |
| Anti-HBeAg | + | + | - |
| Anti-HBsAg | + | - | + |

The absence of anti-HBs is an indication that the infection has become chronic.

The currently used vaccine, containing recombinant hepatitis surface antigen, elicits only anti-HBsAg antibody, which is the neutralizing antibody.

¹One year after initial infection.

HEPATITIS B DISEASE

CLINICAL CAPSULE
Hepatitis B virus is the cause of what was formerly known as "serum hepatitis." This name was used to distinguish it from "infectious hepatitis" and reflected the association of this form of hepatitis with needle use or blood transfusion. Hepatitis B is usually an asymptomatic or limited illness with fever and jaundice for days to weeks. It becomes chronic in up to 10% of patients and may lead to cirrhosis or hepatocellular carcinoma.

⁷ في ناس تقعد عندهم سنه و في ناس طول حياته، انت وحظك متى ماراحت راح المرض

⁸ The major long term risk of chronic HBV infection are **cirrhosis with hepatic failure** and **hepatocellular carcinoma**, when HBV genome integrates into hepatocytes DNA.

Hepatitis C virus

Clinically the acute infection with HCV is milder than infection with HBV

| | | | |
|--|---|---|--|
| Classification & structure | <ul style="list-style-type: none"> Consists of an outer envelope icosahedral core and linear positive polarity ss-RNA genome. There are 6 major genotypes (1 – 6), genotype 4 is the dominant in Saudi patients. | | |
| Transmission | Similar to HBV: Parenterally - Sexually(at lesser extend) - From mother to child perinatally | | |
| The clinical outcome <i>عكس هيبتايتس بي</i> | About 80 % of the infected will progress to chronic hepatitis C(<i>The majority of patients with chronic hepatitis B and C are asymptomatic or have mild fatigue only</i>) | About 20 % of the infected individuals will develop self-limiting acute hepatitis C and recover completely. | < 1 % will develop fulminant hepatitis C, liver failure and death(same as HBV) |
| مهمه مهم مهمه markers | 1- Hepatitis C virus RNA : | Is the 1st marker that appears in circulation, it appears as early as 2-3 weeks after exposure. It is a marker of infection. | |
| | 2- hepatitis C core antigen. | The 2nd marker that appears in the blood, usually 3-4 weeks after exposure. Marker of infection. | |
| | 3- IgG Hepatitis C antibody | is the Last marker that appears in the blood, usually appear 50 days after exposure (long window period ⁹), does not give an accurate result could indicate that the pt is infectious or recovered | |
| Lab diagnosis | By detection of both:Antibody to HCV & HCV-RNA | | |
| vaccine | No vaccine available to hepatitis C. | | |
| Treatment | combined therapy using: Pegylated alpha interferon and ribavirin. | | |

EXTRA SKETCHES



HEPATITIS C DISEASE

CLINICAL CAPSULE

Hepatitis C is an insidious disease in that it does not usually cause a clinically evident acute illness. Instead, its first manifestation (in 25% of those infected) may be the presence of smoldering chronic hepatitis that may ultimately lead to liver failure. Its transmission is less well understood than for hepatitis A, B, and D. Hepatitis C was the major cause of posttransfusion hepatitis until a serologic test for screening blood donors was developed.

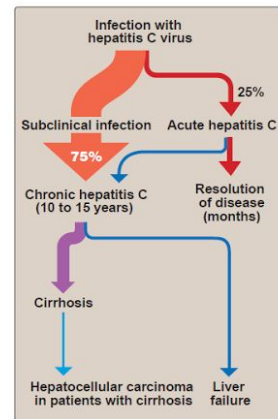
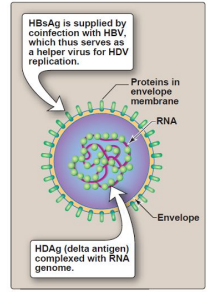


Figure 27.10
Natural history of infection with hepatitis C virus.

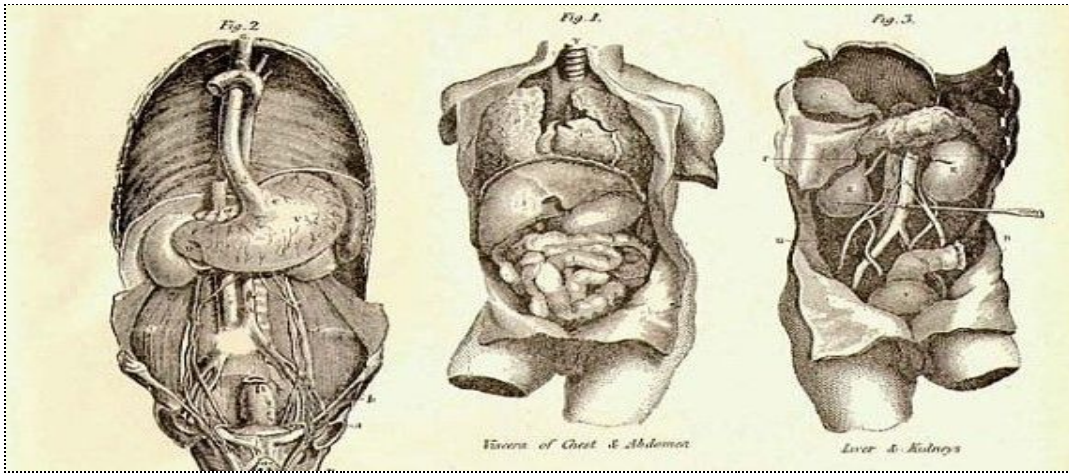
⁹ The window period is time between potential exposure to infection and the point when the test will give an accurate result.

Hepatitis D virus (delta virus)

| | | |
|-----------------------------|---|--|
| Structure & Characteristics | <ul style="list-style-type: none"> - It is a defective virus يعني اذا دخلني وانا ماعندي هيناتين بي مراح يقدر يعمل حاجه, that cannot replicate by its own. - It requires a helper virus is HBV (HBV provides the free HBsAg particles to be used as an envelope) - Composed of small ss-RNA genome, surrounded by delta antigen that form the nucleocapsid. | |
| Types of infection | <p>1- Co-infection: The patient is infected with HBV and HDV at the same time leading to severe acute hepatitis.</p> <p>- Prognosis: <u>recovery is usual</u>.</p> | <p>2- Super infection: In this case, delta virus infects those who are already have chronic hepatitis B leading to severe chronic hepatitis.</p> |



| <h3 style="text-align: center;">Hepatitis G virus هذا الفايروس ينتقل عبر الدم ولا انا ولا انتم نعرف عنه شي لانه مكتشف حديثا</h3> <p style="text-align: center;">Usually occurs as co-infection with HCV, HBV and HIV.</p> | |
|--|---|
| Structure & Characteristics | <ul style="list-style-type: none"> - Share about 80% sequence homology with HCV. - Enveloped, ss-RNA with positive polarity. |
| Transmission | same HCV Parenterally, sexual and from mother to child transmission have been reported. |
| Causes | mild acute and chronic hepatitis infection. |



إِنَّا كُلُّ شَيْءٍ خَلَقْتَهُ بِقَدْرِ ٤٩

Team Leaders

Rawan Aldhuwayhi & Ali Alzahrani

Heartful thanks to our phenomenal team members

Afnan Almalki
 Alanoud Alomair
 Asrar Batarfi
 Amjad Alduhaish
 Farrah Mendoza
 Ghadah Alqasimi
 Johara Almalki
 Lamees Altamimi
 Luluh Alzeghayer
 Morooj Alharbi
 Norah Alakeel
 Reham Alobaidan
 Raghad Alnafisah
 Reem Albahlal
 Reem Alageel
 Reneem Aldubaikhi
 Sara Alkhalifah

Abdulrahman Alanazi
 Abdulrahman alsayyari
 Fawzan Alotaibi
 Ibrahim Yousef
 Majed Alosaimi