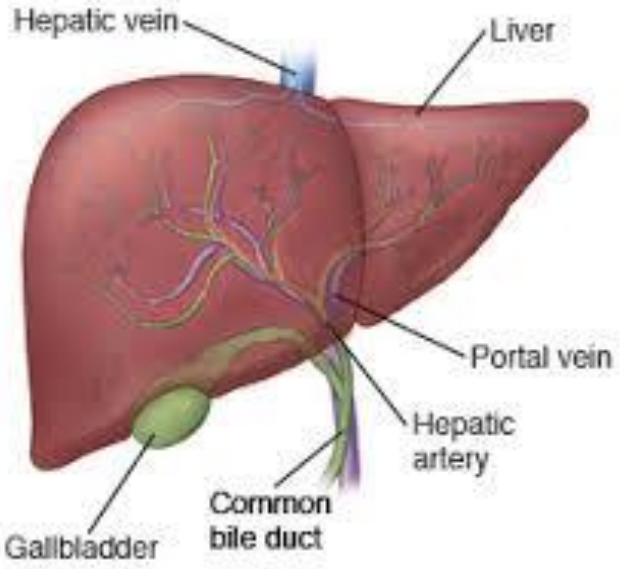
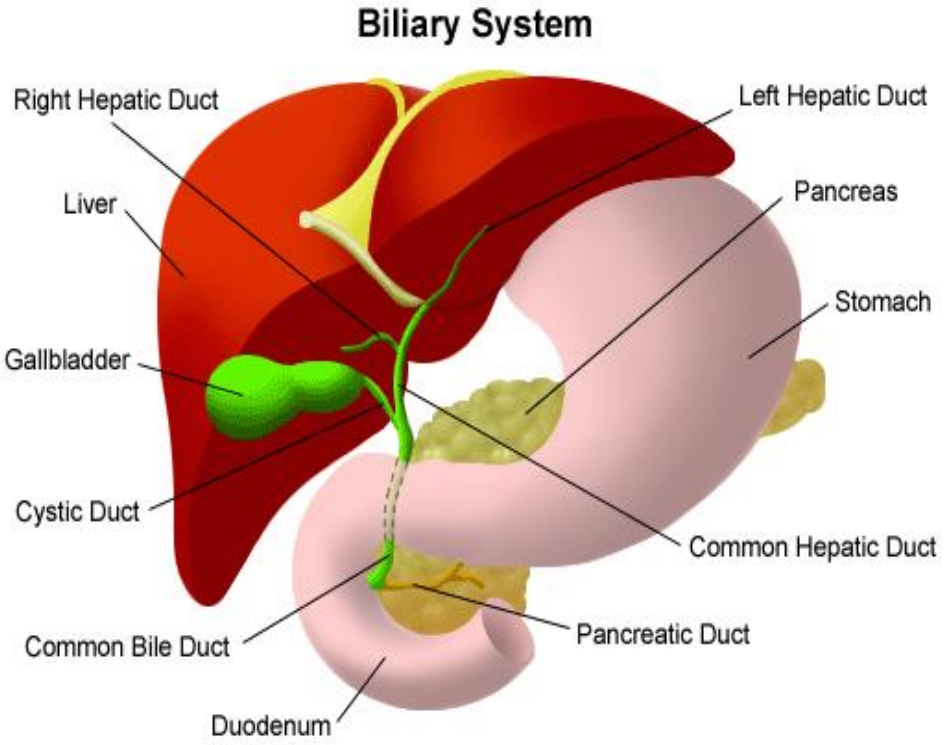
- *Clinical syndromes in liver diseases*
- *Syndrome of portal hypertension, ascites, jaundice, liver failure*
- *Chronic hepatitis and liver cirrhosis*
- *Cholelithiasis. Biliary colic. Clinical and instrumental diagnosis. Medical emergency*

Rodica Bugai, dr. șt. med., conf. univ.


Hepatic vein
Liver
Portal vein
Hepatic artery
Common bile duct
Gallbladder


Biliary System
Right Hepatic Duct
Left Hepatic Duct
Liver
Pancreas
Stomach
Gallbladder
Cystic Duct
Common Hepatic Duct
Common Bile Duct
Pancreatic Duct
Duodenum

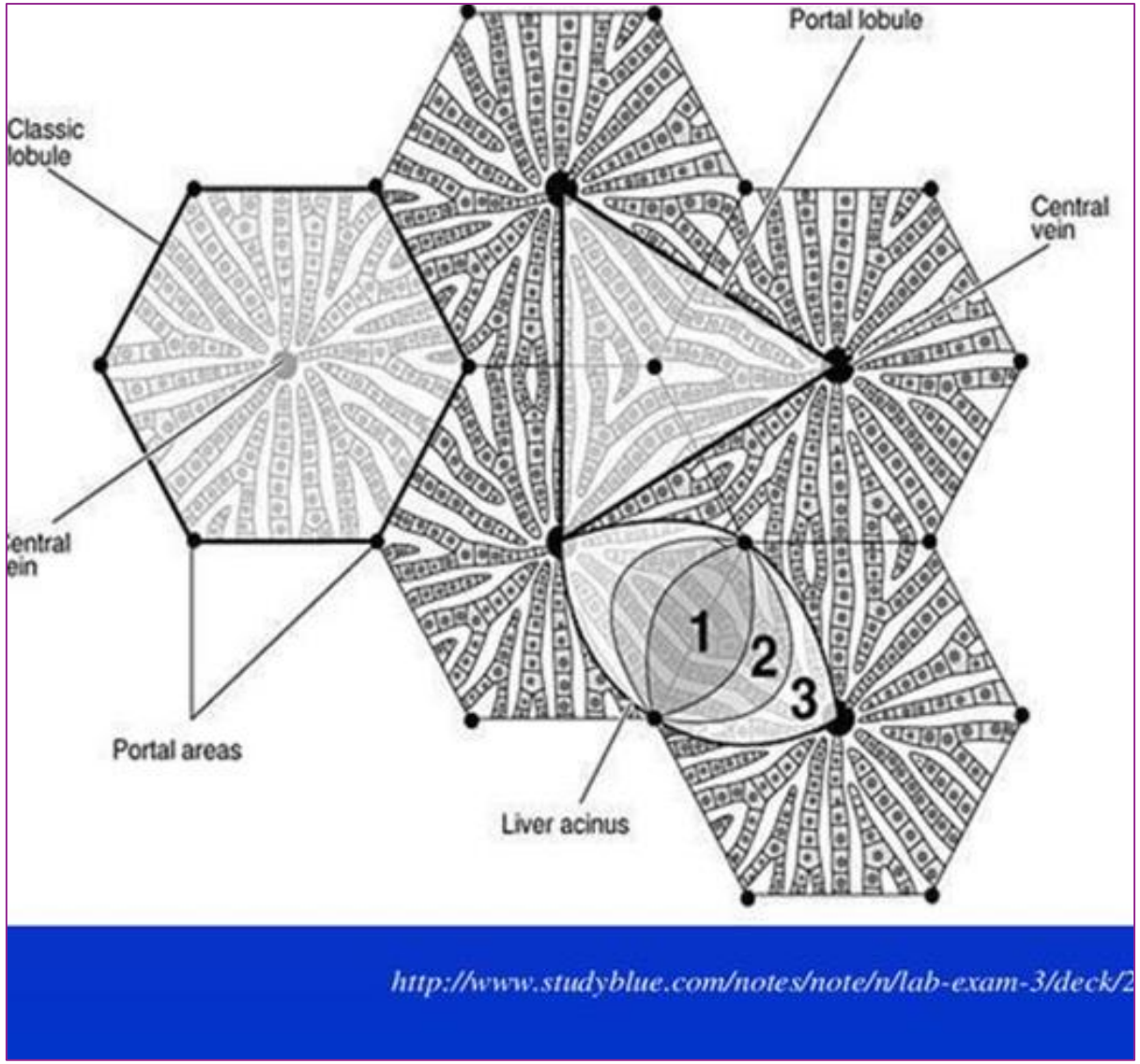
Liver-anatomical data

Due to its volume and weight, the liver is the largest secretory gland in the body..

- It is an organ with a porous, fine, dark red texture, and its intensity varies depending on the amount of blood contained. In a healthy adult, the liver weighs, on average, about 1.5 kg and measures approx. 15 cm. The size of the liver varies according to its functional state - in the secretory phase, during the day, the liver is smaller and increases in size at night, in the assimilation phase, when it can add up to 500 gr in weight and much more. It explains the nocturnal predilection of pain in some liver diseases.

- Part of the digestive tract, the liver is located on the right side of the abdomen, below the diaphragm, being made up of two unequal lobes, the right lobe and the left lobe. The right lobe of the liver is about 6 times larger than the left.In turn, the two main lobes are made up of smaller lobes, known as lobules.

- The liver can have up to 100,000 lobes. Each liver lobe consists of hepatocytes (liver cells), sinusoidal capillaries and bile ducts (into which the bile flows).


Portal lobule
Classic lobule
Central vein
Central vein
Portal areas
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1
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Liver-anatomical data

- The classical hepatic lobe has a polygonal shape (hexagon, pentagon), being composed of cords of **Remak hepatocytes**, tributary to a central vein (centrolobular vein).The Kiernan port space (interlobular space) is located at the intersection of several lobes, having a triangular shape.
- Among the liver cells are **hepatocytes and non-hepatocyte cells, non-parenchymal,** they are: **Kupffer cells, endothelial cells, lipophagous cells.**
- Hepatocytes have a cuboidal shape, being placed in the form of cords in the capillary network. Each hepatocyte has two poles, one vascular, where it comes in contact with the sinusoidal capillaries and one biliary, where it pours its external secretion product (bile).
- Hepatocytes (liver cells) make up about 60% of the liver and have the role of absorbing nutrients, detoxifying and removing harmful substances from the blood.
- A hepatocyte has an average lifespan of 150 days.

Liver-anatomical data

- Unlike many organs that have a single blood supply, the liver receives blood from 2 sources: the **hepatic artery** - which provides O2-rich blood from the heart - thus replenishing 25% of the blood in the liver; **The portal vein**, which transports blood through the digestive tract where it collects nutrients as food is digested, transports them to the liver for processing or eventual storage, is the source of 75% of the O2-rich blood supply of the liver.

- The small blood vessels of the hepatic artery and portal vein are found around each hepatic lobe. This network of blood vessels is responsible for the vast flow of blood through the liver: 1.4 liters / min. Blood comes out of the liver through the hepatic vein.

Liver functions

Biliary function: -bile secretion results from the activity of Kupffer cells and liver cells.

- Bile salts are the most important component of bile. **Their functions:**

-participates in the emulsification of fats in the intestine and in the establishment of these emulsions; this greatly increases the surface area of fatty particles, intensifying the enzymatic attack.

-the activity of pancreatic lipase itself is activated by bile salts

-have an important role in the absorption of Vit. fat-soluble (A, D, E, K), absorption of iron and calcium calcium-stimulates bile secretion ,

- an important role in stimulating intestinal peristalsis and

-a role in maintaining intestinal microbism

Liver functions

- **Glycogenetics -** synthesizes glycogen from glucose, cleaves glycogen and glucose, forms glycogen from fats and amino acids
- **Adipogenetics-**fat is stored in the liver. It trains the body's reserve fats in case of starvation. It synthesizes fats from fatty acids, converts excess carbohydrates into fats and vice versa.
- Contributes to the **esterification of cholesterol.**
- **Hemostasis control -** synthesizes *fibrinogen*, *prothrombin*, *proconvertin*, *Stuart-Prower factor and partially proaccelerin*.
- The **synthesis of creatine** in the liver is followed by its deposition mostly in the muscles and less in the nerve tissue.

Liver functions

- The function of **protein formation**-consists in the synthesis of albumin, globulins, helping to maintain the balance of proteins in the blood; synthesizes fibrinogen and prothrombin with a role in coagulation. Every day, the liver synthesizes approximately 18g of albumin, through processes involving the endoplasmic reticulum, ribosomes and mRNA produced in the nucleus. The synthesis and transport of an albumin molecule takes an average of 20 minutes, and certain amino acids and hormones can influence this.
- The liver also produces **globin** - one of the two components that make up hemoglobin
- **Ureogenic** function - consists in manufacturing urea from excess amino acids, used or not used in synthesis;
- It intervenes in the metabolism of **minerals**: Cl, Na, K, Cu, Fe (it is an iron deposit)
- Role in **water metabolism**, regulating diuresis by neutralizing hormones (adrenal, estrogen, antidiuretics)

Liver functions

- Synthesizes **ferments -** arginase, urease, which intervene in urogenic processes in the liver; tributirase, which participates in the burning of fatty acids: phosphatases and phosphorylases with a role in phosphorylating fats and carbohydrates; transaminase, which promotes the reactions between methionine and choline
- The **hematopoietic**-liver function forms red blood cells in the intrauterine period of the fetus, being at the same time a place of destruction of aged red blood cells.
- The liver has a role in regulating **the acid-base balance** by intervening in the transformation of lactic acid into glucose, the formation of ammonia from amino acids.
- **Antitoxic function -** neutralization of endogenous and exogenous toxic substances
- The **thermoregulatory-liver** function generates heat at rest

Liver functions

- It is a **storehouse of fat-soluble and water-soluble vitamins**. The liver is the richest store of Vit. A from the body, about 95%:Water-soluble vitamins can also be stored or used in the liver. Thiamine, Riboflavin, Niacin, Pyrodoxin, Pantothenic Acid, Biotin, Folic Acid Vitamin B12, Ascorbic Acid

- **Ketogenesis** is specific to the liver and represents the physiological pathway of fatty acid metabolism.

- **Plasma purification** function

-The liver is responsible for 80-90% of the functional capacity of the **reticuloendothelial system**, which includes tissue and circulating macrophages with the role of phagocytizing and destroying various colloidal substrates or particles foreign to the body or their own become "nonself", due to distortion by various agents . The macrophage system makes up 35% of all liver cells and is represented by sinusoidal cells, including Kupffer and endothelial cells.

-The **purification of antigenic substances of intestinal origin** is strictly necessary, in the absence of its performance, for example in the case of intra- or extrahepatic anastomoses, inducing an intense immune response. Also, in the liver, the **purification of bacterial endotoxins of digestive** origin takes place, the presence of these endotoxins in the systemic circulation representing an index of the disturbance of the hepatic activity.

Liver

- The liver **performs more than 500 different functions**, each of which is essential to life.
- The liver is unique among the organs of the human body due to its ability to regenerate, replenish cells that have been destroyed by a disease or short-term injury.
- But, if the liver suffers repeated, long-term damage (chronic diseases), the changes become irreversible, interfering with its function.
- The liver is a "**silent organ**", does not hurt and has no obvious symptoms of a disease. Because of this, many patients find that they suffer from liver disease accidentally, often in an advanced stage of development.

Chronic hepatitis (CH)

- Chronic hepatitis is defined as an inflammatory liver disease with persistence of clinical manifestations and biochemical changes lasting at least 6 months.

Etiology

1. Viral:

-viruses with obligatory hepatotropism: hepatitic v. A, B, C, D, E, F, G

- facultative hepatotropic viruses: v. Ebstein-Barr, v. cytomegalovirus, v. herpes simplex, v. varicella, rubella, v. ECHO;

2. Bacterial: syphilis, leptospirosis, Burnetti coxiella, salmonella ...

3. Toxic: alcohol, drugs (isoniazid, oral contraceptives, chlorpromazine, salicylates, hydralazine, halothane, iron, erythromycin ...), industrial chemicals, household ...

4. Autoimmune CH

5. Chronic parasitic infestations: Schistosomiasis, E. Histolitica

6. Hereditary metabolic causes: α- 1 antitrypsin deficiency, B. Wilson, congenital galactosemia, hereditary fructose intolerance

7. Other causes: terminal ileitis, ulcerative colitis, prolonged biliary obstruction: cystic fibrosis, choledochal cyst, primary biliary cirrhosis, primary sclerosing cholangitis ...

Etiological classification of chronic hepatitis (1994, Los Angeles, USA):

-Chronic viral hepatitis B.
-Chronic hepatitis B with chronic D.
-Chronic viral hepatitis C.
-Chronic mixed viral hepatitis (B + C, B + C + D).
-Autoimmune hepatitis.
-Chronic hepatitis not classified as viral or autoimmune.
-Drug or toxic hepatitis.
-Wilson's disease.
-A1-antitrypsin deficiency.
-Primitive biliary cirrhosis.
-Primary sclerosing cholangitis.

Anatomopathological classification of chronic hepatitis

-Persistent chronic hepatitis
-Chronic active hepatitis, mild and severe forms
-Chronic lobular hepatitis
-Chronic septal hepatitis

International Classification of Chronic Hepatitis, Revision X (ICD 10)

-B18 Chronic viral hepatitis

-B18.0 Chronic viral hepatitis B with Delta antigen

-B18.1 Chronic viral hepatitis B without Delta antigen

-B18.2 Chronic viral hepatitis

-CB18.8 Chronic viral hepatitis of another genesis

-B18.9 Chronic viral hepatitis, of unspecified genesis

-K70.1 Alcoholic hepatitis (acute and chronic)

Chronic hepatitis-pathogenesis

- **The evolution** from the stage of acute hepatitis - to chronic hepatitis and cirrhosis depends on the **individual reactivity** and in particular, on **the immune response** and can be:

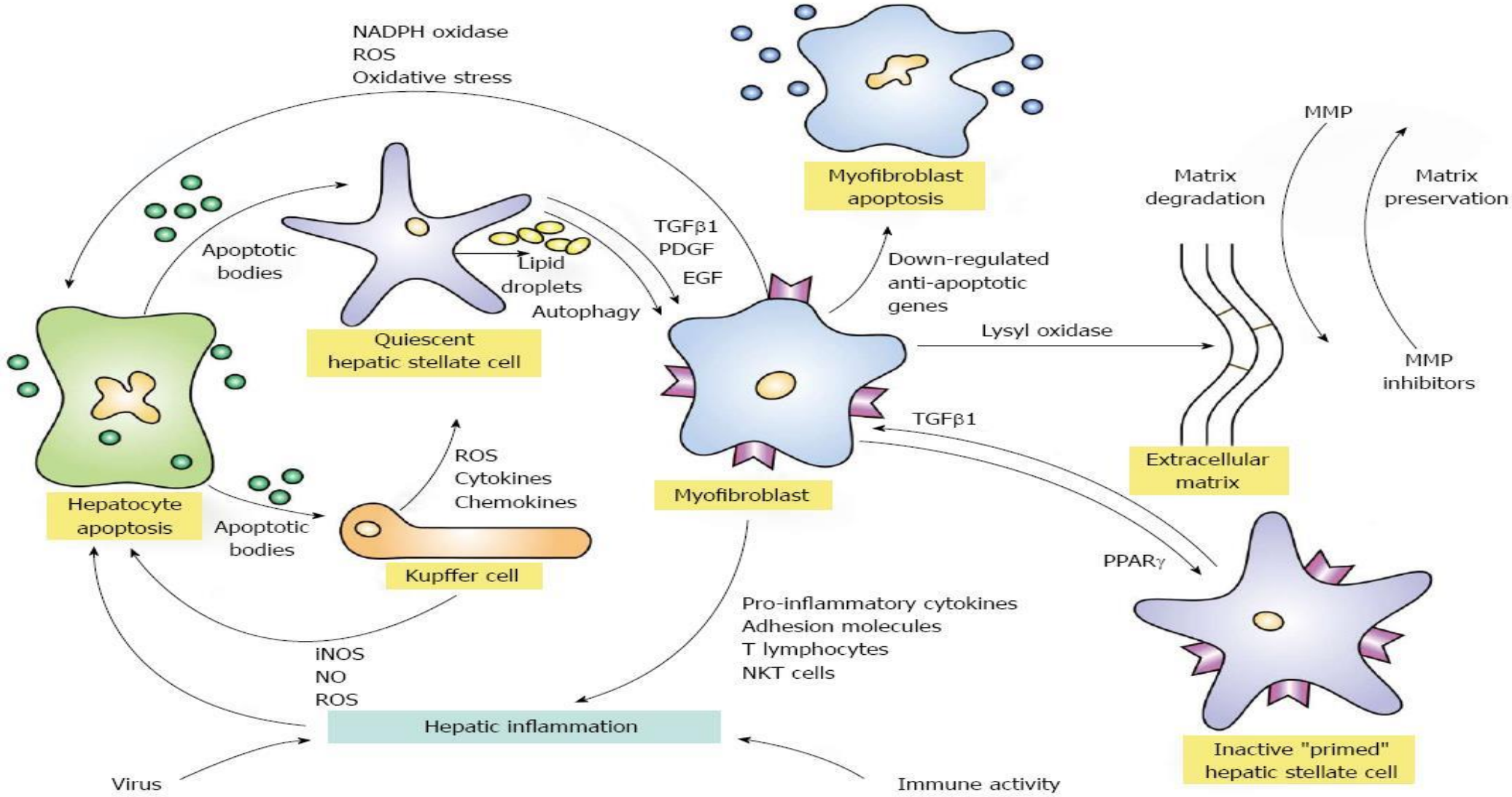
• fast

• slow-undulating

• or after a long period of latency (unidentified chronic hepatitis)

- The pathogenesis of HC can be interpreted in terms of the relationships between etiological factors  and the individual reactivity of the person

Chronic hepatitis-pathogenesis



Diagnosis of Chronic Hepatitis

1. Clinical criteria:

-*change in general condition*: low-grade fever, asthenia, fatigue, postprandial drowsiness.
-*change in nutritional balance*: weight loss.
-*digestive signs*: anorexia, nausea, vomiting, postprandial bloating, abdominal pain (diffuse /right hypochondrium, accentuated by exertion or postprandial)

- jaundice: persistent / recurrent- hyperchromic urine and discolored stool
- hepato and / or splenomegaly, ascites, edema

2. Biochemical criteria

a. **Mesenchymal inflammation tests**: quantitative changes in plasma proteins:
-increase in α-globulins
-increase in serum immunoglobulins.

b. **hepatic cytolysis tests:**

- marker enzymes of hepatic cytolysis:*-ALAT / TGP*
  -ASAT / TGO

Diagnosis of Chronic Hepatitis

c. tests to explore the exreto-biliary function

- ↑ Total bilirubin with predominantly conjugated bilirubin
-determination of serum activity of hepatocyte enzymes related to excretory function:↑FA, GGTP, cholesterol, total lipids, phospholipids and LDL fraction of serum lipoproteins

d. tests that show impairment of metabolic and liver detoxification functions (hepatopriv syndrome):
-tests for exploring the capacity of protein synthesis: serum albumin ↓
- highlighting the low synthesis of coagulation factors ↓fibrinogen, factors II, VII, IX, X, XI)
- expression of disturbance of hepato-cellular synthesis and metabolic functions is: ↓- esterified cholesterol, pseudocholinesterase, serum ceruloplasmin, serum lipoproteins

Diagnosis of Chronic Hepatitis

3. Histological criteria:

Liver biopsy (rarely performed) may show:

- general preservation of hepatic architecture
- the presence of histological changes characteristic of HC: inflammation of the gate spaces and proliferation of the structures of the gate spaces peripheral parcel necrosis (piecemeal necrosis) formation of port-portal bridges; porto-central fibrosis process with onset in the portal spaces and peri- and / or intralobular extension rosette phenomena

4. **Serological tests.**

Hepatitis A

- Viral hepatitis A is generally a mild disease, without extrahepatic changes, anicteric in 90% of cases and asymptomatic, rarely severe.
- Incubation period - 15-45 days and occurs acutely.
- The route of transmission is fecal-oral (parenteral only exceptionally): through direct contact or through food and water, through oral-anal sex
- After a short incubation period, the virus is excreted in the faeces, with the preicteric and jaundiced phases appearing in about two weeks. Anti-HAV IgM usually appears from the beginning of these phases and transaminases increase. Elevated levels of anti-HAV IgM are present only in the acute phase and disappear in about 10 weeks. From this moment on, anti-HAV IgGs appear which confer protection.
- Chronic portage- abs
- Mortality - 0.1-0.2% (in fulminant forms).
- Receptivity to disease - general.
- Prophylaxis is achieved by isolating patients and contact control, health education, protection of water and food, hygiene control. There is also specific prophylaxis, in individual cases, with Vaccine and Gamaglobulin.

https://www.who.int/news-room/fact-sheets/detail/hepatitis-a 9 July 2019

Hepatitis A-**Symptoms**

- The incubation period of hepatitis A is usually 14–28 days.
- Symptoms of hepatitis A range from mild to severe, and can include fever, malaise, loss of appetite, diarrhea, nausea, abdominal discomfort, dark-coloured urine and jaundice (a yellowing of the skin and whites of the eyes). Not everyone who is infected will have all of the symptoms.
- Adults have signs and symptoms of illness more often than children. The severity of disease and fatal outcomes are higher in older age groups. Infected children under 6 years of age do not usually experience noticeable symptoms, and only 10% develop jaundice. Among older children and adults, infection usually causes more severe symptoms, with jaundice occurring in more than 70% of cases. Hepatitis A sometimes relapses. The person who just recovered falls sick again with another acute episode. This is, however, followed by recovery.

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Hepatitis A- **Who is at risk?**

- Anyone who has not been vaccinated or previously infected can get infected with hepatitis A virus. In areas where the virus is widespread (high endemicity), most hepatitis A infections occur during early childhood.

Risk factors include:

- poor sanitation;
- lack of safe water;
- living in a household with an infected person;
- being a sexual partner of someone with acute hepatitis A infection;
- use of recreational drugs;
- sex between men;
- travelling to areas of high endemicity without being immunized.

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Hepatitis A-**Diagnosis**

- Cases of hepatitis A are not clinically distinguishable from other types of acute viral hepatitis.
- Specific diagnosis is made by the detection of HAV-specific Immunoglobulin G (IgM) antibodies in the blood.
- Additional tests include reverse transcriptase polymerase chain reaction (RT-PCR) to detect the hepatitis A virus RNA, and may require specialized laboratory facilities.

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Hepatitis A-**Treatment**

There is no specific treatment for hepatitis A.

- Recovery from symptoms following infection may be slow and may take several weeks or months.
- Most important is the avoidance of unnecessary medications. Acetaminophen / Paracetamol and medication against vomiting should not be given.
- Hospitalization is unnecessary in the absence of acute liver failure.
- Therapy is aimed at maintaining comfort and adequate nutritional balance, including replacement of fluids that are lost from vomiting and diarrhea.

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Hepatitis A-**Prevention**

- Improved sanitation, food safety and immunization are the most effective ways to combat hepatitis A.

The spread of hepatitis A can be reduced by:

-adequate supplies of safe drinking water;

-proper disposal of sewage within communities;

-personal hygiene practices such as regular hand-washing before meals and after going to the bathroom

-vaccination

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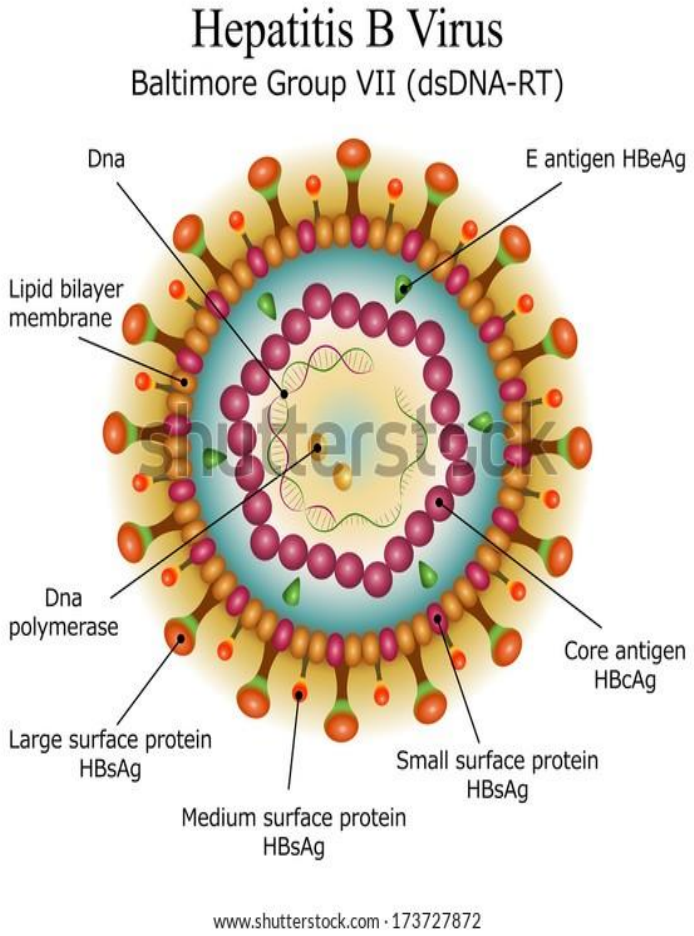
Viral hepatitis B

- The viral hepatitis B virus (HBV) belongs to the Hepadnaviridae family and was discovered in 1971 by Dane.
- It consists of a lipoprotein envelope containing the HBs antigen and a central nucleocapsid (core) containing circular DNA and DNA polymerase.
- The capsid forms the central antigen (HBc) to which the HBe antigen is associated (in masked form). The latter can be found in the circulating blood in free or associated form.
- It should be noted that the HBs antigen has many subtypes



Hepatitis B

The virus is most commonly transmitted from mother to child during birth and perinatal, as well as through contact with blood or other body fluids.

The most important ways to get the B virus are:

- Sex with an infected person
- Sex with more than one partner
- Unprotected casual sex
- Living with people who have the B-household virus
- Occupation that allows contact with human blood, secretions or tissues (healthcare workers)
- Injecting drug use
- Piercingtattoo
- Manicure, pedicure, shaving or hairdresser used by someone else who has the virus
- Receiving blood transfusions (very low risk due to testing)
- Surgical and dental instruments

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Hepatitis B

HBV infection ranges from inapparent, unrecognized forms to fatal, fulminant forms

- Many cases are asymptomatic and categorized as influenza
- Therefore, many patients who have not had a history of hepatitis have serological markers that suggest a history of HBV exposure (as in the case of HAV infection).
- Incubation is 30-120 days.
- The disease occurs insidiously and is accompanied in 10% of cases of jaundice. Sometimes, a few weeks before the disease is recognized as acute hepatitis, arthralgia, rash, or hives can occur. The acute phase usually lasts a few weeks.
- The clinical signs and symptoms of viral hepatitis A are almost identical to those seen in acute HBV infection.
- !!! HBV is much more contagious than HIV, primarily due to its resistance to external factors and the body., Survives in the external environment min. 7 days. Chronic portage is noted in 5-10% of cases of infection and mortality is estimated at 0.5-2%. 5-40% of medical staff, with variations depending on the category, have markers of HBV infection.

https://www.who.int/news-room/fact-sheets/detail/hepatitis-b JULY 18, 2019

Hepatitis B-**Symptoms**

Most people do not experience any symptoms when newly infected.

- However, some people have acute illness with symptoms that last several weeks, including **yellowing of the skin and eyes (jaundice), dark urine, extreme fatigue, nausea, vomiting and abdominal pain.**
- A small subset of persons with acute hepatitis can develop acute **liver failure**, which can lead to death.
- In some people, the hepatitis B virus can also cause a chronic liver infection that can later develop into **cirrhosis** (a scarring of the liver) or **liver cancer.**

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Hepatitis B-**Who is at risk of chronic disease?**

The likelihood that infection becomes chronic depends on the age at which a person becomes infected.

Children less than 6 years of age who become infected with the hepatitis B virus are the most likely to develop chronic infections.

- In infants and children:
- 80–90% of infants infected during the first year of life develop chronic infections; and
- 30–50% of children infected before the age of 6 years develop chronic infections.

In adults:

- less than 5% of otherwise healthy persons who are infected as adults will develop chronic infections; and
- 20–30% of adults who are chronically infected will develop cirrhosis and/or liver cancer.

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Hepatitis B- **Diagnosis**

It is not possible, on clinical grounds, to differentiate hepatitis B from hepatitis caused by other viral agents, hence, laboratory confirmation of the diagnosis is essential.

- A number of blood tests are available to diagnose and monitor people with hepatitis B. They can be used to distinguish acute and chronic infections.
- Laboratory diagnosis of hepatitis B infection focuses on the detection of the hepatitis B surface antigen HBsAg. WHO recommends that all blood donations be tested for hepatitis B to ensure blood safety and avoid accidental transmission to people who receive blood products.
- Acute HBV infection is characterized by the presence of HBsAg and immunoglobulin M (IgM) antibody to the core antigen, HBcAg. During the initial phase of infection, patients are also seropositive for hepatitis B e antigen (HBeAg). HBeAg is usually a marker of high levels of replication of the virus. The presence of HBeAg indicates that the blood and body fluids of the infected individual are highly infectious.
- Chronic infection is characterized by the persistence of HBsAg for at least 6 months (with or without concurrent HBeAg). Persistence of HBsAg is the principal marker of risk for developing chronic liver disease and liver cancer (hepatocellular carcinoma) later in life.

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Hepatitis B -treatment

There is no specific treatment for *acute* hepatitis B.

- Therefore, care is aimed at maintaining comfort and adequate nutritional balance, including replacement of fluids lost from vomiting and diarrhoea.
- !!! Most important is the avoidance of unnecessary medications. Acetaminophen/Paracetamol and medication against vomiting should not be given.
- *Chronic* hepatitis B infection can be treated with medicines, Treatment can slow the progression of cirrhosis, reduce the incidence of liver cancer and improve long-term survival.
- Only a part (10% - 40% depending on the eligibility criteria) of people with chronic hepatitis B infection will need treatment.
- The WHO recommends the use of oral treatments - tenofovir or entecavir.

In most people, however, the treatment does not cure hepatitis B infection, but only suppresses the replication of the virus. Therefore, most people who start hepatitis B treatment must continue it for life.

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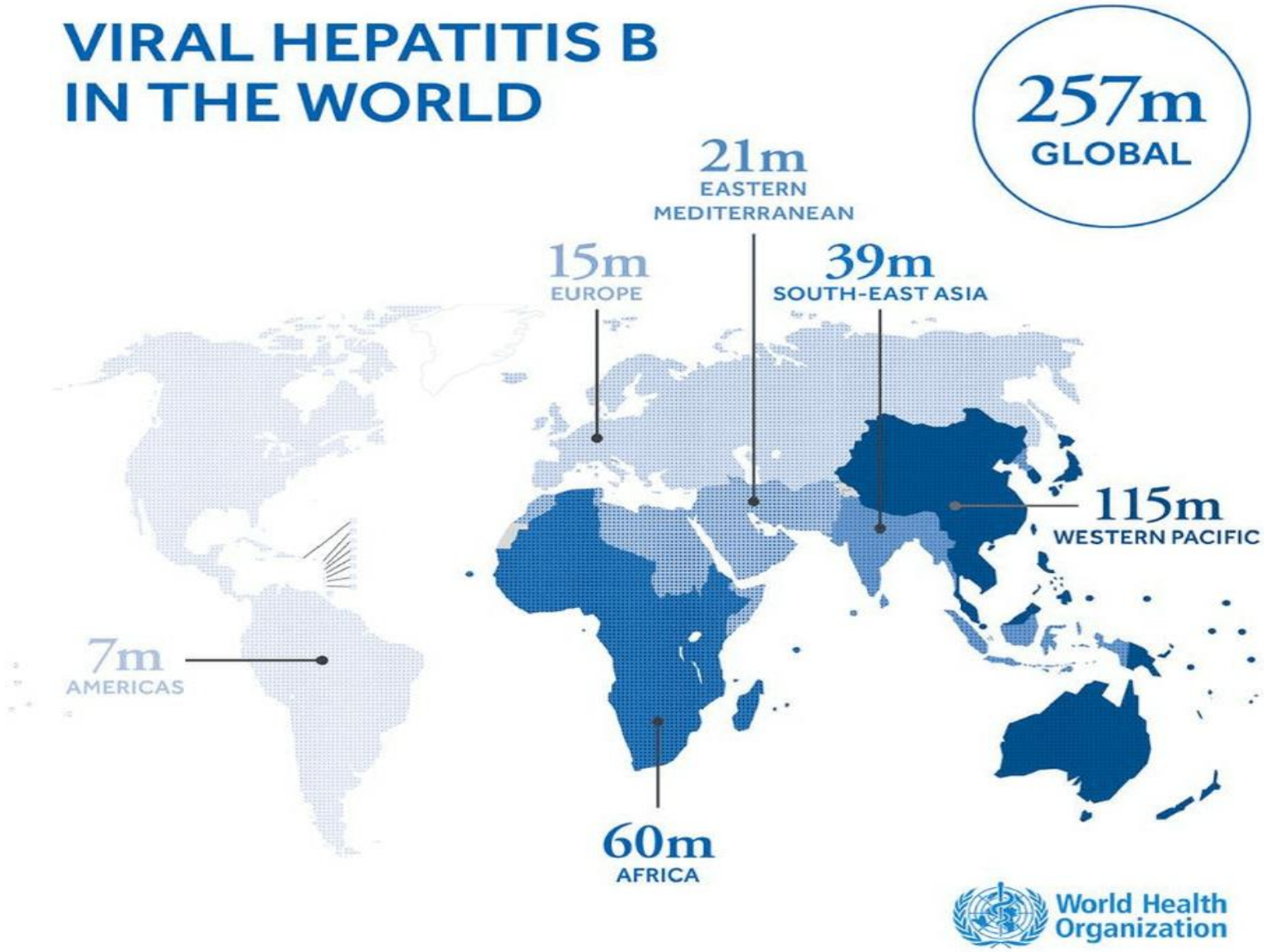
Hepatitis B- **Prevention**

The hepatitis B vaccine is the mainstay of hepatitis B prevention.

- WHO recommends that all infants receive the hepatitis B vaccine as soon as possible after birth, preferably within 24 hours.
- a 3-dose schedule of hepatitis B vaccine, with the first dose (monovalent) given at birth and the second and third doses (monovalent or combined vaccine) given at the same time as the first and third doses of diphtheria, pertussis (whooping cough), and tetanus – (DTP vaccine); or
- a 4-dose schedule, where a monovalent birth dose is followed by 3 monovalent or combined vaccine doses, usually given with other routine infant vaccines.
- The complete vaccine series induces protective antibody levels in more than 95% of infants, children and young adults.
- Protection lasts at least 20 years and is probably lifelong.
- Thus, WHO does not recommend booster vaccinations for persons who have completed the 3 dose vaccination schedule.

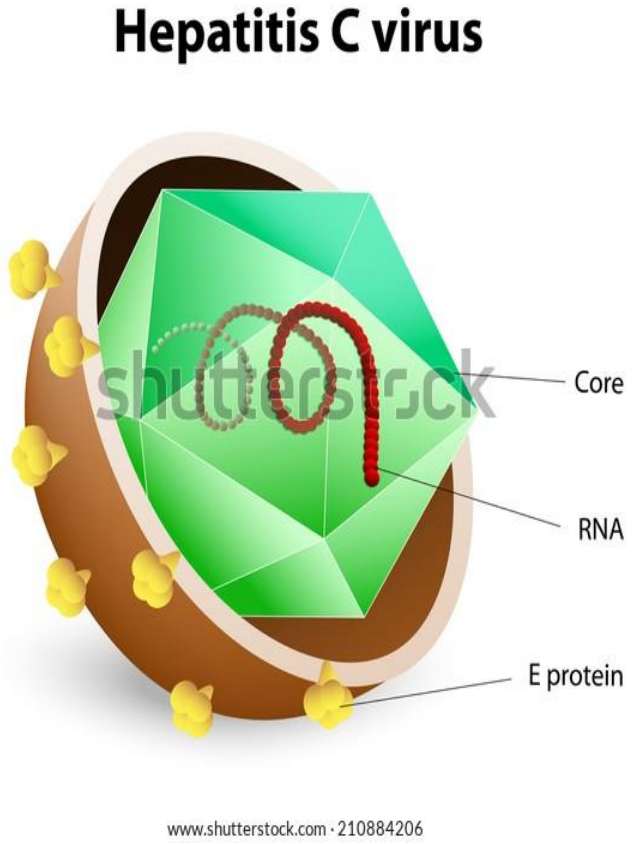
- https://www.who.int/news-room/fact-sheets/detail/hepatitis-b 18 JULY 2019

VIRAL HEPATITIS B IN THE WORLD



Hepatitis C

- Viral hepatitis C virus (HCV) is also called non-A-B, like-B hepatitis virus or post-transfusion virus.
- It belongs to the Flaviviridae family and comes in the form of a particle with a diameter of 50-60 nm that contains a lipid envelope with transmembrane proteins and single-stranded RNA.



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Hepatitis C

- The route of transmission is usually parenteral. But there is also the possibility of sexual transmission.
- The incubation period is 3-150 days (most often 8 weeks).HCV causes acute and chronic infections.
- !!! New HCV infections are usually asymptomatic.
- About 30% (15–45%) of infected people spontaneously eliminate the virus within 6 months of infection without treatment.
- The remaining 70% (55-85%) of people will develop chronic HCV infection.
- Among those with chronic HCV infection, the risk of cirrhosis is 15-30% within 20 years.
- The onset of the acute form is nonspecific and in 25% of cases is followed by jaundice.
- The disease cannot be differentiated from hepatitis B by clinical examination alone.

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Hepatitis C

- Hepatitis C virus causes both acute and chronic infection.
- New HCV infections are usually asymptomatic. Some persons get acute hepatitis which does not lead to a life-threatening disease.
- Around 30% (15–45%) of infected persons spontaneously clear the virus within 6 months of infection without any treatment.
- The remaining 70% (55–85%) of persons will develop chronic HCV infection. Of those with chronic HCV infection, the risk of cirrhosis ranges between 15% and 30% within 20 years.

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Hepatitis C-**Transmission**

The hepatitis C virus is a bloodborne virus.

It is most commonly transmitted through:

- injecting drug use through the sharing of injection equipment;
- the reuse or inadequate sterilization of medical equipment, especially syringes and needles in healthcare settings;
- the transfusion of unscreened blood and blood products;
- sexual practices that lead to exposure to blood (for example, among men who have sex with men, particularly those with HIV infection or those taking pre-exposure prophylaxis against HIV infection).
- HCV can also be transmitted sexually and can be passed from an infected mother to her baby; however, these modes of transmission are less common.
- Hepatitis C is not spread through breast milk, food, water or casual contact such as hugging, kissing and sharing food or drinks with an infected person.
- https://www.who.int/news-room/fact-sheets/detail/hepatitis-c 9 JULY 2019

Hepatitis C-symptoms

- The incubation period for hepatitis C ranges from 2 weeks to 6 months.
- Following initial infection, approximately 80% of people do not exhibit any symptoms.
- Those who are acutely symptomatic may exhibit fever, fatigue, decreased appetite, nausea, vomiting, abdominal pain, dark urine, grey-coloured faeces, joint pain and jaundice (yellowing of skin and the whites of the eyes).

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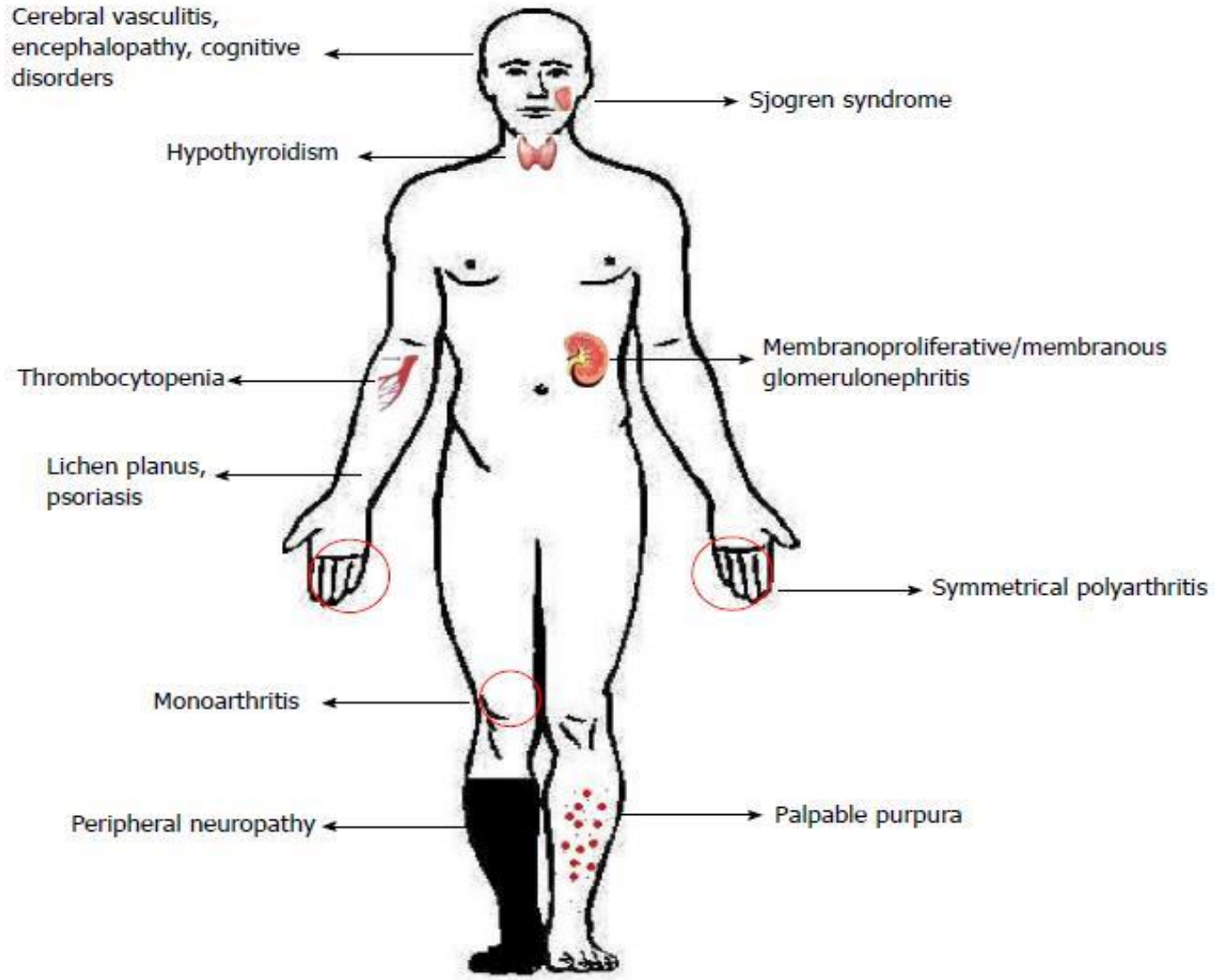
Hepatitis C- extrahepatic symptoms



Hepatitis C- **Testing and diagnosis**

- about 30% of people infected with HCV spontaneously clear the infection by a strong immune response without the need for treatment. Although no longer infected, they will still test positive for anti-HCV antibodies.

- After a person has been diagnosed with chronic HCV infection, they should have an assessment of the degree of liver damage (fibrosis and cirrhosis). This can be done by liver biopsy or through a variety of non-invasive tests. Because new HCV infections are usually asymptomatic, few people are diagnosed when the infection is recent. In those people who go on to develop chronic HCV infection, the infection is also often undiagnosed because it remains asymptomatic until decades after infection when symptoms develop secondary to serious liver damage.

- *HCV infection is diagnosed in 2 steps:*

-Testing for anti-HCV antibodies with a serological test identifies people who have been infected with the virus.

-If the test is positive for anti-HCV antibodies, a nucleic acid test for HCV ribonucleic acid (RNA) is needed to confirm chronic infection because

- https://www.who.int/news-room/fact-sheets/detail/hepatitis-c 9 JULY 2019

Hepatitis C

- Early diagnosis can prevent health problems that may result from infection and prevent transmission of the virus. WHO recommends testing people who may be at increased risk of infection.
- Populations at increased risk of HCV infection include:
- people who inject drugs;
- people in prisons and other closed settings;
- people who use drugs through other routes of administration (non-injecting);
- people who use intranasal drugs;
- recipients of infected blood products or invasive procedures in health-care facilities with inadequate infection control practices ;
- children born to mothers infected with HCV ;
- people with sexual partners who are HCV-infected;
- people with HIV infection;
- prisoners or previously incarcerated persons; and
- people who have had tattoos or piercings.

https://www.who.int/news-room/fact-sheets/detail/hepatitis-c 9 JULY 2019

Hepatitis C-**Treatment**

- A new infection with HCV does not always require treatment, as the immune response in some people will clear the infection. However, when HCV infection becomes chronic, treatment is necessary. The goal of hepatitis C treatment is cure.

- WHO's updated 2018 guidelines recommend therapy with pan-genotypic direct-acting antivirals (DAAs). DAAs can cure most persons with HCV infection, and treatment duration is short (usually 12 to 24 weeks), depending on the absence or presence of cirrhosis.

- WHO recommends treating all persons with chronic HCV infection over the age of 12. Pan-genotypic DAAs remain expensive in many high- and upper-middle-income countries. However, prices have dropped dramatically in many countries (primarily low-income and lower middle-income countries), due to the introduction of generic versions of these medicines.

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Hepatitis C-**Primary prevention**

There is no effective vaccine against hepatitis C, therefore prevention of HCV infection depends upon reducing the risk of exposure to the virus in health-care settings and in higher risk populations, for example, people who inject drugs and men who have sex with men, particularly those infected with HIV or those who are taking pre-exposure prophylaxis against HIV.

The following list provides a limited example of primary prevention interventions recommended by WHO:

- safe and appropriate use of health care injections;
- safe handling and disposal of sharps and waste;
- provision of comprehensive harm-reduction services to people who inject drugs including sterile injecting equipment and effective treatment of dependence;
- testing of donated blood for HBV and HCV (as well as HIV and syphilis);
- training of health personnel;
- prevention of exposure to blood during sex;
- hand hygiene, including surgical hand preparation, hand washing and use of gloves; and
- promotion of correct and consistent use of condoms.

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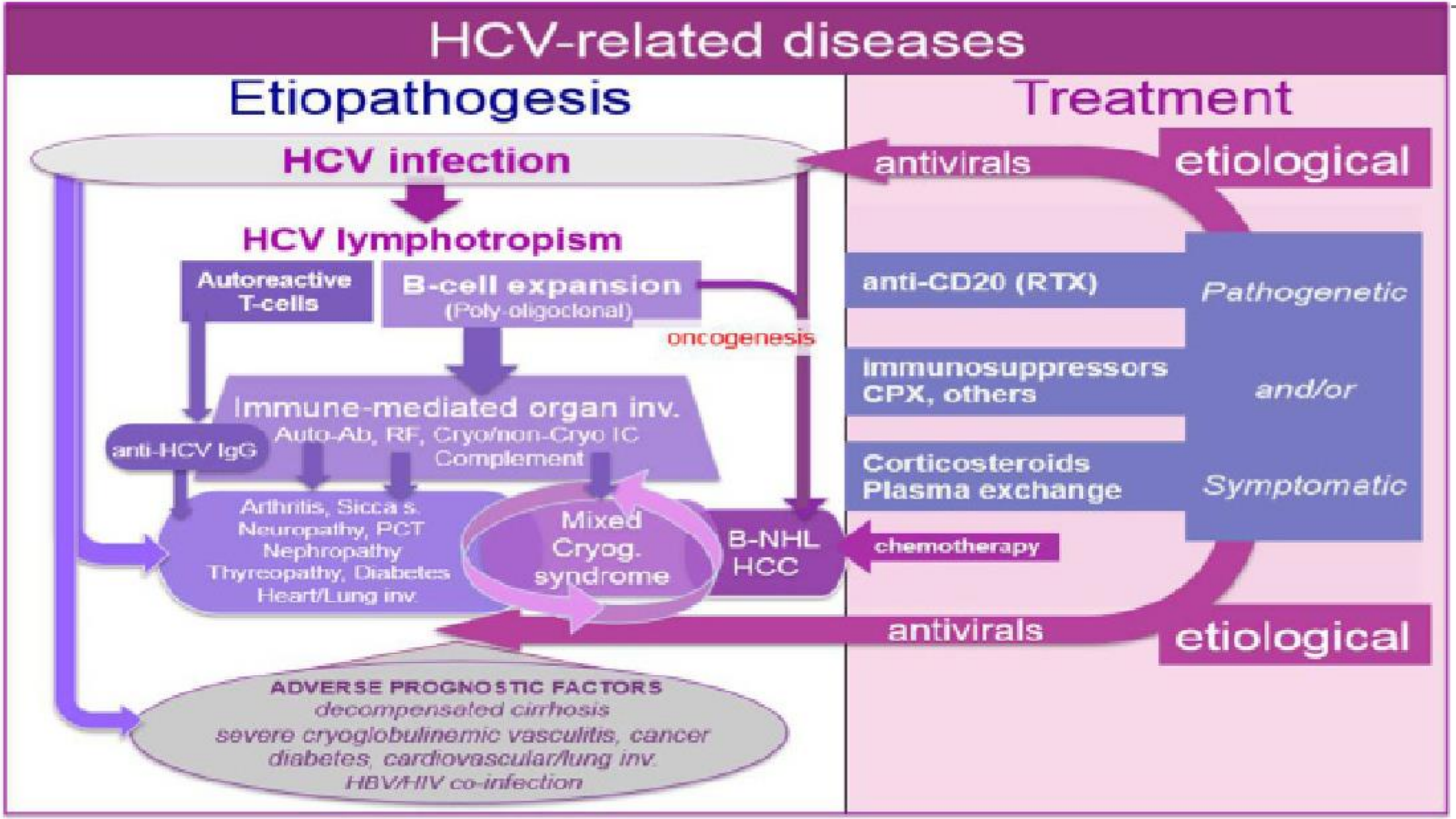
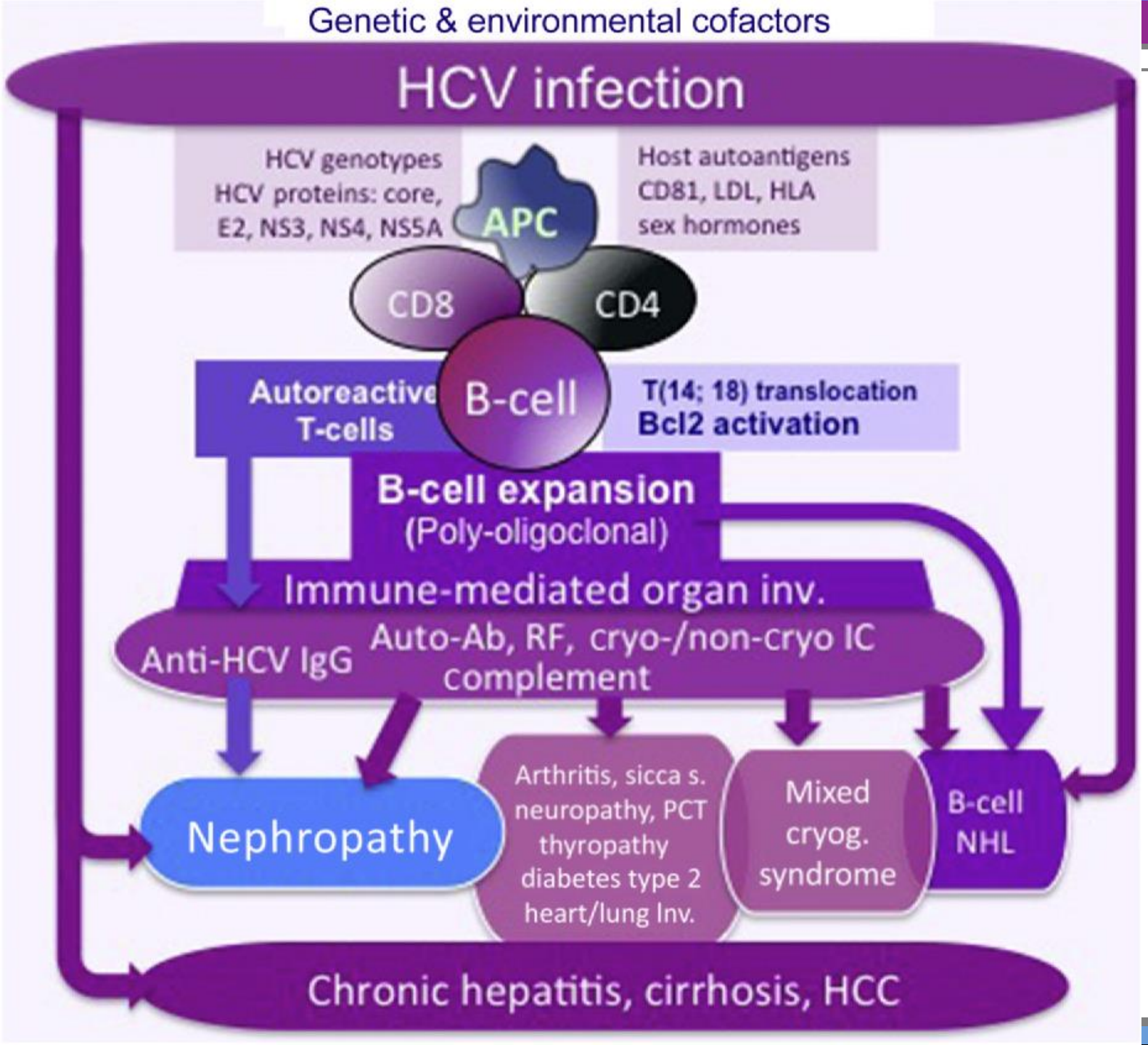
Hepatitis C- **Secondary prevention**

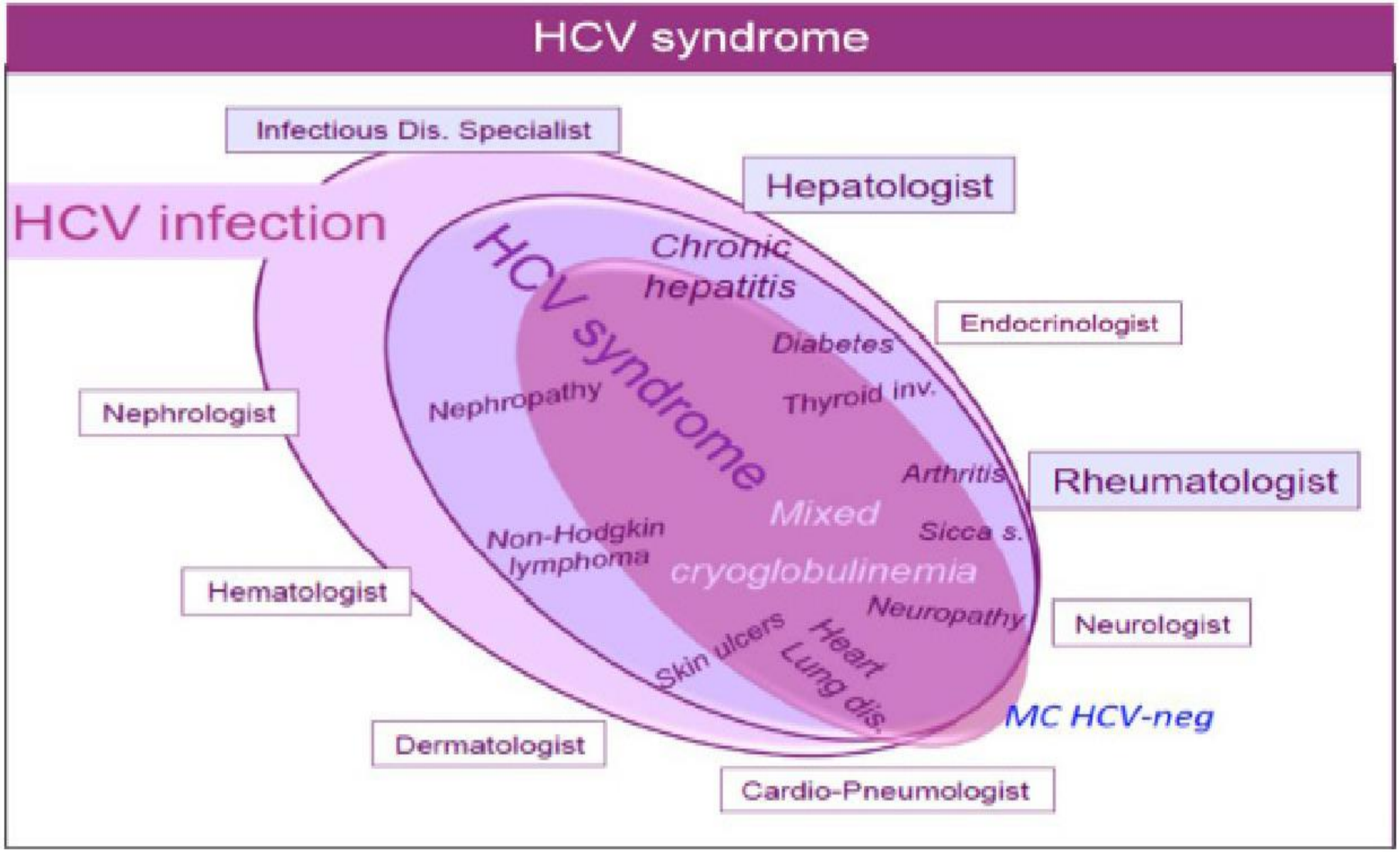
For people infected with the hepatitis C virus, WHO recommends:

- education and counselling on options for care and treatment;
- immunization with the hepatitis A and B vaccines to prevent coinfection from these hepatitis viruses and to protect their liver;
- early and appropriate medical management including antiviral therapy; and
- regular monitoring for early diagnosis of chronic liver disease.

https://www.who.int/news-room/fact-sheets/detail/hepatitis-c 9 JULY 2019


HCV-related diseases
Etiopathogesis
Treatment
HCV infection
HCV lymphotropism
Autoreactive T-cells
B-cell expansion
(Poly-oligoclonal)
oncogenesis
Immune-mediated organ inv.
Auto-Ab, RF, Cryo/non-Cryo IC
Complement
anti-HCV IgG
Arthritis, Sicca s.
Neuropathy, PCT
Nephropathy
Thyreopathy, Diabetes
Heart/Lung inv.
Mixed Cryog. syndrome
B-NHL HCC
ADVERSE PROGNOSTIC FACTORS
decompensated cirrhosis
severe cryoglobulinemic vasculitis, cancer
diabetes, cardiovascular/lung inv.
HBV/HIV co-infection
antivirals
etiological
anti-CD20 (RTX)
immunosuppressors
CPX, others
Corticosteroids
Plasma exchange
Pathogenetic
and/or
Symptomatic
chemotherapy
antivirals
etiological


Genetic & environmental cofactors
HCV infection
HCV genotypes
HCV proteins: core,
E2, NS3, NS4, NS5A
APC
Host autoantigens
CD81, LDL, HLA
sex hormones
CD8
CD4
Autoreactive
T-cells
B-cell
T(14; 18) translocation
Bcl2 activation
B-cell expansion
(Poly-oligoclonal)
Immune-mediated organ inv.
Anti-HCV IgG
Auto-Ab, RF, cryo-/non-cryo IC
complement
Nephropathy
Arthritis, sicca s.
neuropathy, PCT
thyropathy
diabetes type 2
heart/lung Inv.
Mixed
cryog.
syndrome
B-cell
NHL
Chronic hepatitis, cirrhosis, HCC


HCV syndrome
Infectious Dis. Specialist
Hepatologist
HCV infection
HCV syndrome
Chronic hepatitis
Endocrinologist
Diabetes
Nephrologist
Nephropathy
Thyroid inv.
Arthritis
Rheumatologist
Mixed cryoglobulinemia
Sicca s.
Non-Hodgkin lymphoma
Hematologist
Neuropathy
Neurologist
Skin ulcers
Heart
Lung dis.
MC HCV-neg
Dermatologist
Cardio-Pneumologist

Hepatitis D

Hepatitis D virus (HDV) is a virus that requires hepatitis B virus (HBV) for its replication. HDV infection occurs only simultaneously or as super-infection with HBV.

- The virus is most commonly transmitted from mother to child during birth and delivery, as well as through contact with blood or other body fluids.
- Vertical transmission from mother to child is rare.
- At least 5% of people with chronic HBV infection are co-infected with HDV
- HDV-HBV co-infection is considered the most severe form of chronic viral hepatitis due to more rapid progression towards liver-related death and hepatocellular carcinoma.
- Currently, treatment success rates are generally low.
- Hepatitis D infection can be prevented by hepatitis B immunization.

https://www.who.int/news-room/fact-sheets/detail/hepatitis-d, 8 July 2019

Hepatitis D-**Symptoms**

- **Acute hepatitis**: simultaneous infection with HBV and HDV can lead to a mild-to-severe or even fulminant hepatitis, but recovery is usually complete and development of chronic hepatitis D is rare (less than 5% of acute hepatitis).
- **Superinfection**: HDV can infect a person already chronically infected with HBV. The superinfection of HDV on chronic hepatitis B accelerates progression to a more severe disease in all ages and in 70–90% of persons. HDV superinfection accelerates progression to cirrhosis almost a decade earlier than HBV monoinfected persons, although HDV suppresses HBV replication
- The mechanism in which HDV causes more severe hepatitis and a faster progression of fibrosis than HBV alone remains unclear.

https://www.who.int/news-room/fact-sheets/detail/hepatitis-d, 8 July 2019

Hepatitis D-**Who is at risk?**

- **!!! Chronic HBV carriers are at risk for infection with HDV.**
- People who are not immune to HBV (either by natural disease or immunization with the hepatitis B vaccine) are at risk of infection with HBV which puts them at risk of HDV infection.
- High prevalence in persons who inject drugs (PWID) suggest that injecting drug use is an important risk factor for HDV co-infection.
- High-risk sexual activity (e.g. sex worker) is also an increased risk for HDV infection.
- Migration from high HDV prevalence countries to lower prevalence areas might have an effect on the epidemiology of the host country.

- https://www.who.int/news-room/fact-sheets/detail/hepatitis-d, 8 July 2019

Hepatitis D-**Treatment**

- Pegylated interferon alpha for at least 48 weeks irrespective of on-treatment response patterns. The overall rate of sustained virological response is low, however, this treatment is an independent factor associated with a lower likelihood of disease progression.
- **Liver transplantation** may be considered for cases of fulminant hepatitis and end-stage liver disease. New therapeutic agents and strategies are needed, and novel drugs, such as prenylation inhibitor or HBV entry inhibitors, have shown early promise.

https://www.who.int/news-room/fact-sheets/detail/hepatitis-d, 8 July 2019

Hepatitis D-**Prevention**

Prevention and control of HDV infection requires:

- - prevention of HBV transmission through hepatitis B immunization,
- - blood safety, injection safety,
- -and harm reduction services.

- Hepatitis B immunization does not provide protection against HDV for those already HBV infected.

https://www.who.int/news-room/fact-sheets/detail/hepatitis-d, 8 July 2019

Hepatitis E

Hepatitis E is a liver disease caused by infection with a virus known as hepatitis E virus (HEV).

- The virus is transmitted via the fecal-oral route, principally via contaminated water.
- Hepatitis E is found worldwide, but the disease is most common in East and South Asia.
- The virus has at least 4 different types: genotypes 1, 2, 3 and 4. Genotypes 1 and 2 have been found only in humans. Genotypes 3 and 4 circulate in several animals (including pigs, wild boars, and deer) without causing any disease, and occasionally infect humans.
- The virus is shed in the stools of infected persons, and enters the human body through the intestine. It is transmitted mainly through contaminated drinking water.
- Usually the infection is self-limiting and resolves within 2–6 weeks. Occasionally a serious disease, known as fulminant hepatitis (acute liver failure) develops, and a proportion of people with this disease can die.
- A vaccine to prevent hepatitis E virus infection has been developed and is licensed in China, but is not yet available elsewhere.

2019https://www.who.int/news-room/fact-sheets/detail/hepatitis-e 8 JULY

Hepatitis E-**Transmission**

- The hepatitis E virus is transmitted mainly through the fecal-oral route due to fecal contamination of drinking water. This route accounts for a very large proportion of clinical cases with this disease. The risk factors for hepatitis E are related to poor sanitation, allowing virus excreted in the faeces of infected people to reach drinking water supplies.

- Other routes of transmission have been identified, but appear to account for a much smaller number of clinical cases. These routes of transmission include:

-ingestion of undercooked meat or meat products derived from infected animals (e.g. pork liver);

-transfusion of infected blood products;

-vertical transmission from a pregnant woman to her baby.

- 2019https://www.who.int/news-room/fact-sheets/detail/hepatitis-e 8 JULY

Hepatitis E **Symptoms**

- The incubation period following exposure to HEV ranges from 2 to 10 weeks, with an average of 5 to 6 weeks. The infected persons excrete the virus beginning from a few days before to 3-4 weeks after onset of the disease.
- **Typical signs and symptoms of hepatitis include:**
- an initial phase of mild fever, reduced appetite (anorexia), nausea and vomiting, lasting for a few days; some persons may also have abdominal pain, itching (without skin lesions), skin rash, or joint pain. jaundice (yellow colour of the skin and whiteness of the eyes), with dark urine and pale stools; a slightly enlarged, tender liver (hepatomegaly).
- These symptoms are often indistinguishable from those experienced during other liver illnesses and typically last 1–6 weeks.
- In rare cases, acute hepatitis E can be severe, and result in fulminant hepatitis (acute liver failure); these patients are at risk of death. Fulminant hepatitis occurs more frequently when hepatitis E occurs during pregnancy. Pregnant women with hepatitis E, particularly those in the second or third trimester, are at increased risk of acute liver failure, fetal loss and mortality. Up to 20–25% of pregnant women can die if they get hepatitis E in third trimester.
- Cases of chronic hepatitis E infection have been reported in immunosuppressed people, particularly organ transplant recipients on immunosuppressive drugs, with genotype 3 or 4 HEV infection.
- 2019https://www.who.int/news-room/fact-sheets/detail/hepatitis-e 8 JULY

Hepatitis E- **Treatment**

There is no specific treatment capable of altering the course of acute hepatitis E.

- As the disease is usually self-limiting, hospitalization is generally not required.
- Most important is the avoidance of unnecessary medications.
  Acetaminophen/Paracetamol and medication against vomiting should not be given.
- However, hospitalization is required for people with fulminant hepatitis, and should also be considered for symptomatic pregnant women.
- Immunosuppressed people with chronic hepatitis E benefit from specific treatment using ribavirin, an antiviral drug.

2019https://www.who.int/news-room/fact-sheets/detail/hepatitis-e 8 JULY

Hepatitis E -**Prevention**

Prevention is the most effective approach against the disease.

At the population level, transmission of HEV and hepatitis E disease can be reduced by:

- maintaining quality standards for public water supplies; and
- establishing proper disposal systems for human faeces.
- On an individual level, infection risk can be reduced by:
- maintaining hygienic practices;
- avoiding consumption of water and ice of unknown purity.
- In 2011, a recombinant subunit vaccine to prevent hepatitis E virus infection was registered in China. It has not yet been approved in other countries.
- https://www.who.int/news-room/fact-sheets/detail/hepatitis-e 8 JULY 2019

Hepatitis E –**Diagnosis**

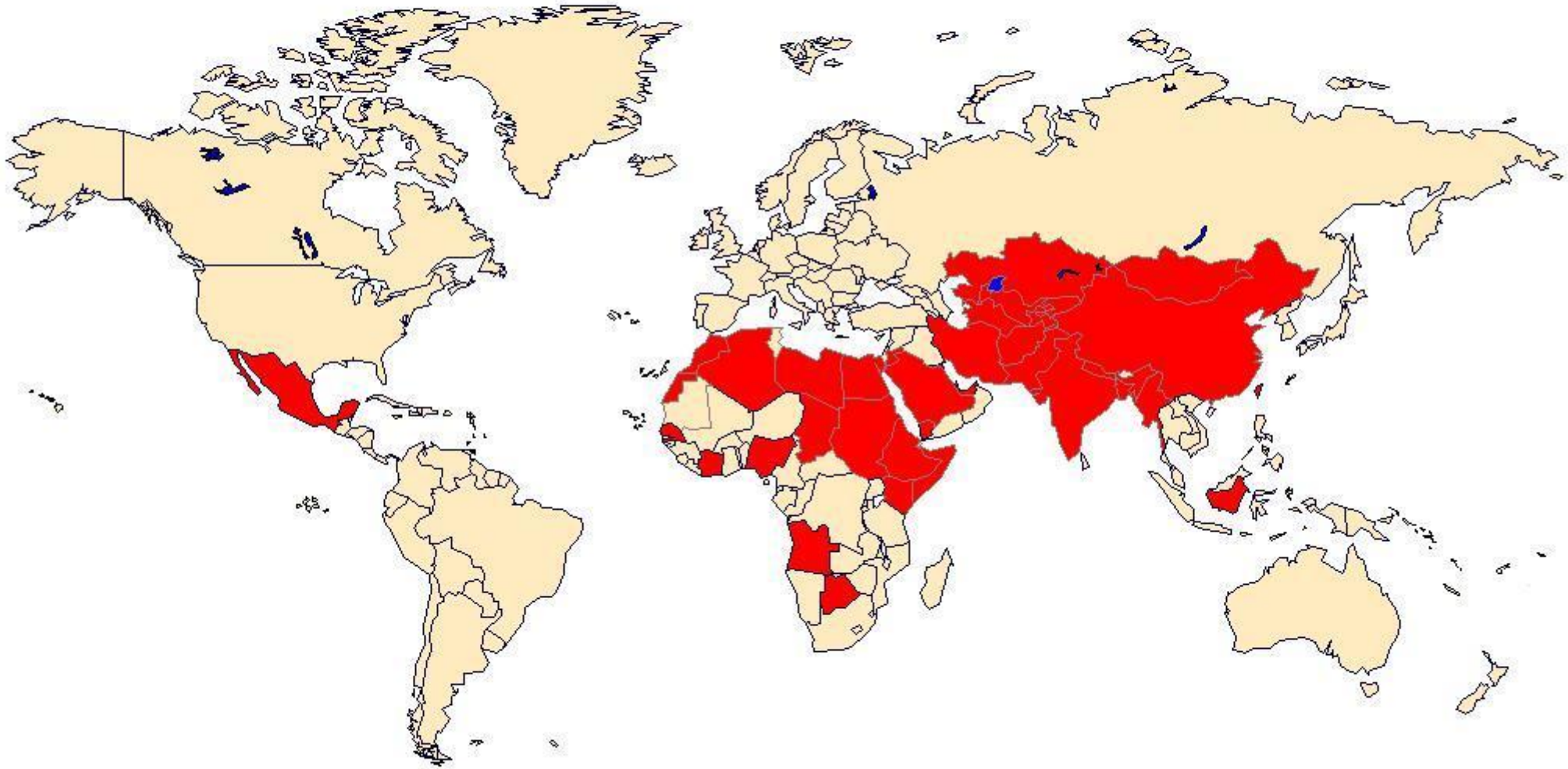
Cases of hepatitis E are not clinically distinguishable from other types of acute viral hepatitis.

- However, diagnosis can often be strongly suspected in appropriate epidemiologic settings, for example when several cases occur in localities in known disease-endemic areas, or in settings with risk of water contamination, when the disease is more severe in pregnant women, or if hepatitis A has been excluded.
- Definitive diagnosis of hepatitis E infection is usually based on the detection of specific IgM antibodies to the virus in a person's blood; this is usually adequate in areas where disease is common. Rapid tests are available for field use.
- Additional tests include reverse transcriptase polymerase chain reaction (RT-PCR) to detect the hepatitis E virus RNA in blood and/or stool; this assay requires specialized laboratory facilities. This test is particularly needed in areas where hepatitis E is infrequent, and in cases with chronic HEV infection.

- https://www.who.int/news-room/fact-sheets/detail/hepatitis-e 8 JULY 2019

Geographic Distribution of Hepatitis E

Outbreaks or Confirmed Infection in >25% of Sporadic Non-ABC Hepatitis

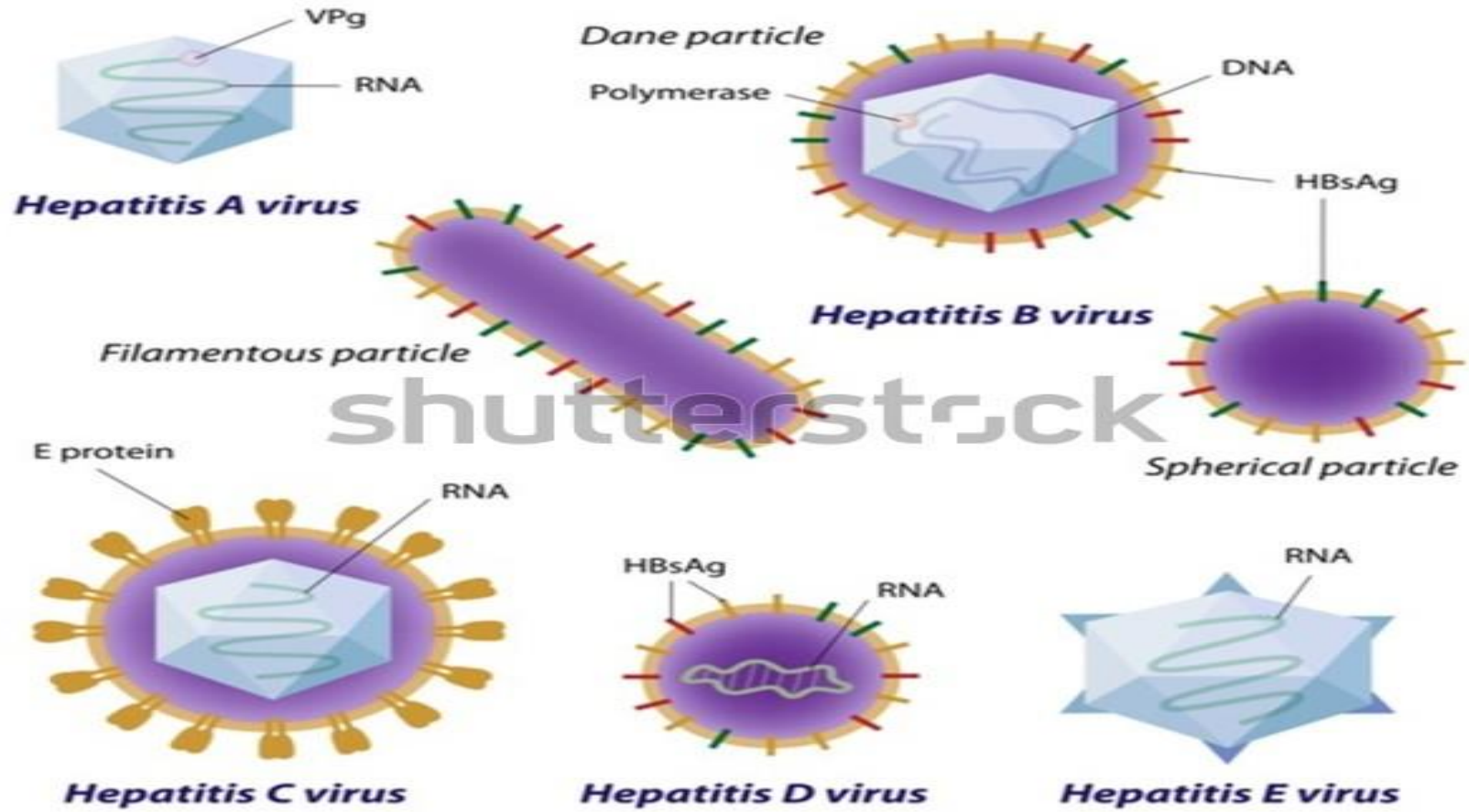


Hepatitis F

- Hepatitis F (non-A-E hepatitis) has recently been reported to occur in isolated cases in Western Europe, USA. and India.
- Hepatitis F virus (HFV) has been isolated from the feces of infected subjects, where it appears as 27-37 nm particles containing a double-stranded DNA molecule of approximately 20 kb.
- This virus differs substantially from HAV and HEV, both of which consist of a 7.5 kb single-stranded RNA molecule.
- There are no serological tests for the diagnosis of hepatitis F, but it can be performed after examination of the stool by electron microscopy.
- Those cases of hepatitis whose etiology cannot be determined after testing for other viruses are suspected of having the infection.

Hepatitis G

- Hepatitis G virus (HGV) - is commonly called the GB virus (the initials of the name of a surgeon with acute hepatitis, in 1967, whose case allowed the discovery of HGV after a long time).
- HGV belongs to the Flaviviridae family and has a genome represented by a single-stranded RNA molecule of approximately 9.5 kb.
- The route of transmission is parenteral;
- It is often associated with HCV infection;
- The prevalence among healthy donors is higher than that of HCV;
- The vast majority of carriers are asymptomatic;It is common among drug addicts, those who have received transfusions (hemophiliacs, patients with chronic hemodialysis);rarely, may cause fulminant hepatitis;
- The diagnosis of infection is molecular, by highlighting viral RNA by PCR.


VPg
RNA
Hepatitis A virus
Dane particle
Polymerase
DNA
HBsAg
Hepatitis B virus
Filamentous particle
Spherical particle
shutterstock
E protein
RNA
Hepatitis C virus
HBsAg
RNA
Hepatitis D virus
RNA
Hepatitis E virus
www.shutterstock.com · 98308451

Chronic autoimmune hepatitis

•Definition: abnormalities of the immune response, with production of autoantibodies

•type I: ANA and ↑γ-globulins
•type Iia : Antibody anti-LKM1 and ↑γ-globulin
•type IIb: Antibody anti-LKM1 and HCV ⊕
•type III: Antibody anti-ALS and its association with other immunological diseases
• type IV: the presence of ASMA isolated in large titers against actin F

Chronic autoimmune hepatitis

Simptoms: *- polymorphic, multisystemic manifestations*

-more noisy than in chronic viral hepatitis
-debut in a young woman with asthenia, fever, arthralgia

•. **Astenoneurotic sdr , algodispeptic sdr., acne, amenorrhea, arthralgia**
•cholestatic jaundice, embossed vascular purpura + necrotic manifestations and sdr. Raynaud
•various rashes: maculopapular, allergic, erythema "in vespertillo", livedo reticularis, erythema nodosum, stellar angiomas, palmar erythrosissdr. hemorrhagic, thrombocytopenia / pancytopenia, anti-erythrocyte antibody
•splenomegaly without PHT
•subfebrile + arthralgias and recurrent arthritis, ulcerative colitis
•pleurisy + transient pulmonary infiltrates - pulmonary alveolitis + PAH
•glomerulonephritis with nodular IgG deposits
•endocrine manifestations - sdr. Cushing (acne + hirsutism), bilateral gynecomastia, Hashimoto's thyroiditis, myxedema / thyrotoxicosis, type 1 diabetes

Chronic autoimmune hepatitis-treatment:

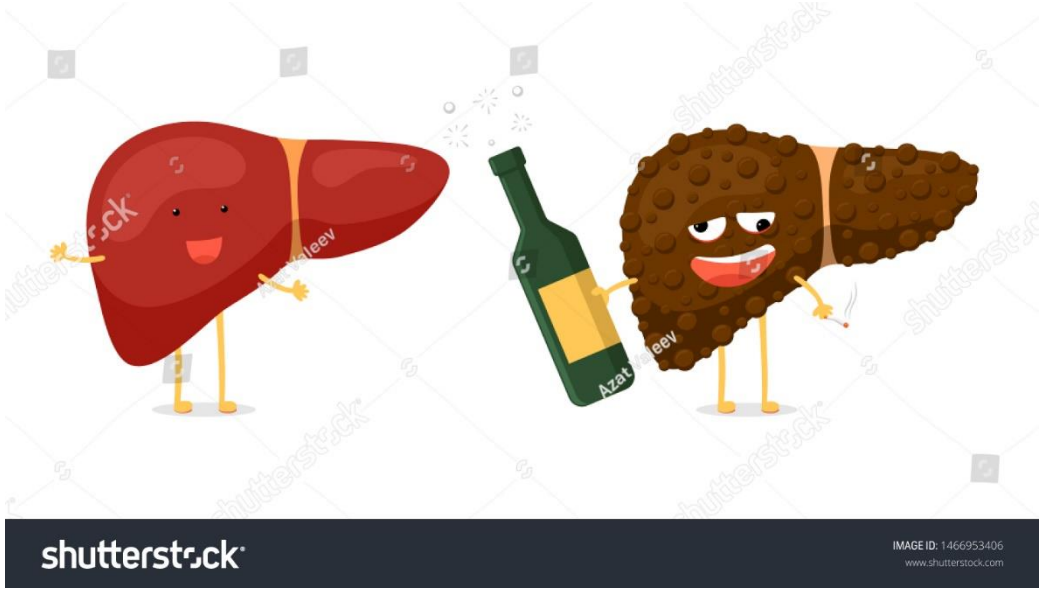
- It is started with Prednisone 30-60 mg / day for a few weeks, until the transaminases decrease, then the dose of Prednisone is reduced by 5 mg / week up to a minimum maintenance dose (10-15 mg / day) followed by a minimum of 6 months, until complete remission.

- -IMMUNOSUPPRESSORS: Azathioprine alone or in combination with Prednisone.

Alcoholic hepatitis

- Alcoholic hepatitis is the inflammatory response of the liver to alcohol intoxication, occurs in about 40% of alcohol users and is characterized by ballooning degeneration, inflammatory infiltrate, predominantly polymorphonuclear and Mallory bodies, perisinusoidal fibrosis

-When alcohol is processed in the liver, it produces extremely toxic chemicals.



Alcoholic hepatitis

Risk factors

- Ethanol consumption in doses exceeding 40 g / day, for men, and 20 g / day, for women.
- The duration of alcohol consumption is more than 5 years, on average 15-20 years.
- Sex - women are more susceptible than men to the progression of alcoholic liver injury.
- Genetic polymorphism of enzymes involved in alcohol metabolism.
- Obesity or nutritional deficiency.
- Liver virus infection (B or C).
- Use of medications that are metabolized in the liver.
- Immunological factors.

Alcoholic hepatitis

- Patients with alcoholic liver disease present various clinical simptoms, according to the variability of its morphopathology, influenced by the evolutionary stage of the disease, the presence of excessive alcohol consumption, alcohol-induced extrahepatic diseases, dependence and socio-professional context.

- Alcoholic liver damage may be assessed asymptomatically or with a non-specific clinical picture

Alcoholic hepatitis

Possible clinical symptoms:

- Asthenia, reduced work capacity, fatigue, emotional lability, insomnia, malaise, decreased ability to concentrate, headache - asthenovegetative sdr
- pain in the right hypochondrium, sensations of heaviness, compression in this area - are usually conditioned by the reaction of the liver capsule (serous tunic, visceral peritoneum) to the extension caused by hepatomegaly. Sometimes these complaint occur due to inflammation of the capsule, the adhesions between the fibrous tunic and the parietal peritoneum.
- Reduced appetite, nausea, less often vomiting, belching, feelings of heaviness and fullness in the epigastrium, intolerance to fatty foods, bloating of the abdomen, constipation, intolerance to alcohol and cigarette smoke - these form dyspeptic sdr
- Jaundice, itchy skin, xanthelasmas, xanthomas, stool and urine discoloration, darker, dry skin are noted in alcoholic hepatitis with cholestasis or complicated by Zieve sdr.

Alcoholic hepatitis

The symptoms of alcoholic hepatitis are similar to those caused by other liver diseases and vary depending on the degree of liver damage. In case of mild damage, it may be asymptomatic.

As more causes occur or the disease worsens, can be:

-changes in appetite

-dry mouth

-weight loss

-nausea and vomiting

-pain or swelling in the abdomen

- jaundice or yellowing of the skin or eyes

-fever

-changes in mental state, including confusion

-fatigue

- slight bleeding or bruising

Alcoholic hepatitis

Assessing the stigmas of systematic alcohol consumption:

- Characteristic exterior - facies aethylica characterized by swollen face, cyanotic, capillary, telangiectasia, hyperemic conjunctiva, edema; sweating, burns, bone fractures, frostbite.
- Trembling of fingers, eyelids, tongue.Weight loss, rarely obesity.
- Dupuytren-type contracture, the prevalence of palm retraction Dupuytren being similar to ethyl alcohol with or without liver damage (22-32.5%).
- Hypertrophy of the parotid glands.Muscular atrophy, especially in the scapular girdle.
- Signs of hypogonadism - gynecomastia, testicular atrophy, sexual impotence, altered distribution of body hair, signs of feminization in men, erythema palmar and vascular stars.
- Changes in behavior and emotional status - euphoria, familiarity, emotional instability, memory disorders, insomnia, often depression.

Alcoholic hepatitis

Clinical exam:

- Hepatomegaly
- Splenomegaly (15%)
- Jaundice (50%)
- Ascites, edema (30-60%)
- Signs of hepatic encephalopathy
- Fever (50%)
- Vascular stars, bruises, palmar erythema
- Hypotension

Alcoholic hepatitis

Markers of chronic excessive alcohol consumption:

- GGTP ↑↑↑ (significant reduction on abstinence background)
- AST> ALT↑
- TCD (carbohydrate transferrin deficiency) ↑
- IgA↑
- Erythrocyte macrocytosis
- HDLC ↑

Alcoholic hepatitis

Possible blood disorders:

- Macrocytic anemia due to folic acid and vitamin B12 deficiency.
- Hemolytic anemia, more common in acute alcoholic hepatitis, Zieve syndrome.
- Thrombocytopenia, leukopenia, anemia as a result of hypersplenism.
- Leukocytosis, sometimes with a leukemoid reaction, can be found in acute alcoholic hepatitis, in added infections or as a paraneoplastic manifestation in hepatocellular carcinomas.
- Leukopenia is most often the expression of hematological hypersplenism, but can also be caused by the suppressive effect of alcohol on the hematogenous marrow.

Alcoholic hepatitis -Treatment

- Stopping alcohol consumption and abstaining from alcohol for a long time
- Smoking cessation (for smokers)
- Maintaining an optimal body mass (BMI = 18.5-25.0)
- Exclusion of physical and mental overwork
- Exclusion of hepatotoxic drugs
- Rational diet, with additional vitamins and minerals, avoid heavy meals, fractional diet 4-5 times / day (meal 5, after Pevzner)
- Glucocorticosteroids
- Hepatoprotectors
- Antifibrotic

Chronic hepatitis-laboratory investigations

- CBC, platelets, reticulocytes
- ALT, AST, bilirubin, prothrombin time, albumin, GGTP, alkaline phosphataseSerum Fe, glucose, urea, total cholesterol
- Serological screening (HBsAg, anti-HBc, HBeAg, anti-HBe, anti-HCV, anti-VHD, etc. HBV DNA, HCV RNA, VHD RNA by PCR - as indicated),
- α-fetoprotein (for primary liver cancer screening),general analysis of urine.
- Autoantibodies: ANA, AMA, SMA, anti-LKM, anticardiolipin, cryoglobulinsTransferrin, ferritin, ceruloplasmin, with serum and urinary
- Lipidogram: HDLC, LDLC, triglycerides, phospholipids,
- Fibrinogen, Prothrombin Time (Quick), Ca, Mg
- Total protein and its fractions
- Uric acid
- Cellular and humoral immunological status: T lymphocytes (CD4, CD8) and B, IgA, IgM, IgG,circulating immune complexes,
- ·Thyroid gland hormone level (T3, T4, TSH, antiTPO)

Assessment of the degree of activity of the inflammatory process in liver pathology

The degree of activity of the pathological process in the liver is evaluated according to the expressiveness of the cytolysis syndrome:

- Minimum activity - ALT and / or AST ≤ 2 N.
- Moderate activity - ALT and / or AST from 2 to 5 N.
- Maximum activity - ALT and / or AST ≥ 5 N.

Chronic hepatitis-instrumental investigations

- FEGDS or R-scopy of the esophagus and stomach (for assessment of esophageal / gastric varices and assessment of the risk of bleeding)
- ECG, chest microradiography
- Doppler US of the portal system
- Hepatosplenic scintigram with Tc99 isotopes
- Upper digestive endoscopy
- Laparoscopy
- Liver biopsy:

-transcutaneous, "blind"

-transcutaneous, under USG control

-by laparoscopy·

- Computed tomography, Nuclear magnetic resonance·
- Retrograde endoscopic cholangiography

Hepatic cirrhosis (HC)

Liver cirrhosis is a progressive liver disease, which, from a morphological point of view, is characterized by diffuse fibrosis and disorganization of the liver architecture with the formation of regeneration nodules.

Hepatic cirrhosis

- More than 20 pathologies are known that can progress to cirrhosis

The main causes of HC:

Common causes:

· Chronic hepatitis B, C and D (≈ 25%)
· Alcoholic liver disease (≈ 20-40%)
· Cryptogenic (of unknown etiology) (≈ 10-40%)

Rare causes (<10%)·
Nonalcoholic steatohepatitis (≈10%)
· Autoimmune hepatitis
· Primary biliary cirrhosis
· Medicines and toxic chemicals (≈5%)Very rare causes (≈1%)
· Hemochromatosis
· Wilson's disease
· Insufficiency of α1-antitrypsin
· Secondary biliary cirrhosis (extra- or intrahepatic obstruction of the bile ducts)·
-Budd-Chiari syndrome

Classification of HC

International classification of CH, revision X (ICD 10):

K 74 Fibrosis and cirrhosis of the liver

K 74.0 Hepatic fibrosis

K 74.1 Hepatic sclerosis

K 74.2 Fibrosis and hepatic sclerosis

K 74.3 Primitive biliary cirrhosis

K 74.4 Secondary biliary cirrhosis

K 74.5 Biliary cirrhosis without specification

K 74.6 Cirrhosis of the liver (other and not specified)

K 70.3 Alcoholic cirrhosis of the liver

K 71.7 Toxic damage to the liver with fibrosis and cirrhosis

Clinical classification of HC

- By etiology:

- viral
- alcoholic
- drugs
- other (specify: primary biliary, secondary biliary, autoimmune, etc.)
- -cryptogenic

- By morphology:

- micronodular (parenchymal nodules less than 3-5 mm; are specific for alcoholic cirrhosis, biliary obstruction, hemochromatosis, prolonged venous congestion of the liver, Wilson's disease, etc.).
- macronodular (regeneration nodules over 5 mm, up to 2-3 cm; are specific for viral liver damage)mixed

- By degree of compensation:

- Compensated -subcompensated -decompensated ·

Clinical classification of HC

- By the activity of the inflammatory process in the liver:

- active phase

-inactive phase

-acute hepatitis against on the background of HC

- by evolution:

-stable

-slowly progressive

-rapidly progressive

- According to the degree of portal hypertension

Clinical classification of HC

The macroscopic classification of cirrhosis is made according to:

- a) Liver size:

-hypertrophic

-atrophicb)

- Liver morphology:

-Micronodular (usually alcoholic). There are numerous small regeneration nodules, 2-3 mm, extended to all lobes

-Macronodular (usually postviral, but also toxic, autoimmune). Uneven regeneration nodules with each other, with dimensions larger than 3mm.

-Micro-macronodular (found in biliary cirrhosis)

Clinical classification of HC

Liver cirrhosis can be:

* compensated (when missing - ascites and jaundice)

* decompensated:

- vascular (there is ascites and edema)

- parenchyma (there is jaundice)

HC classification - Child-Pugh score

In order to assess the CH prognosis, various scores were proposed.

- The most used is the modified Child-Pugh score.
- According to tab., the amount is calculated and classified:

-class A- 6-7 points;

-class B- 8-11 points;

-class C- ≥ 12 points

HC classification - Child-Pugh score

Parameters	Points		
	1	2	3
Serum Bilirubin(mg/dl)	2.0	2-3	>3.0
Serum Albumin(g/dl)	>3.515	2.8-3.5	<2.8
Prothrombin Time (Prolongation (s))	1-4	5-6	>6
Hepatic encephalopathy	None	Minimal	Advanced
Ascites	None	Slight	Moderate
One and two year survival based on CTP Score			
Class	1 yr	2 yr	
A (5-6 points)	100 %	85 %	
B (7-9 points)	80%	60%	
C (10-15 points)	45%	35%	

Data from Child CG, Turcotte JG.Surgery and portal hypertension. In: Child CG. The liver and portal hypertension. Philadelphia: Saunders; 1964.p.50-64

HC- risk factors for progression

- Mixed etiology of the disease (Mixed viral infection HBV + HDV, HBV + HCV, HBV + HDV + HCV)
- Infection + alcohol
- Alcohol abuse (> 150g week)
- Male sexIncreased activity of the inflammatory process in the liver
- Increasing the ALT level> 2 N
- Late detection of the disease
- Old age
- Presence of other serious concomitant pathologies
- Administration of potentially toxic drugs to the liver or the action of other toxic substances
- Inadequate nutrition (protein and vitamin deficiency
- Genetic factors
- Negative action of the environment, ecological factors (aflatoxins) - Obesity

HC- early diagnosis

In about 40% of cases, patients with compensated CH do not report and do not consult a doctor.

- Early detection of liver pathology requires active tactics
- First, it refers to patients in risk groups:

-patients with chronic hepatitis of different etiology-people with alcohol abuse

--patients with steatosis and nonalcoholic steatohepatitis-patients with long

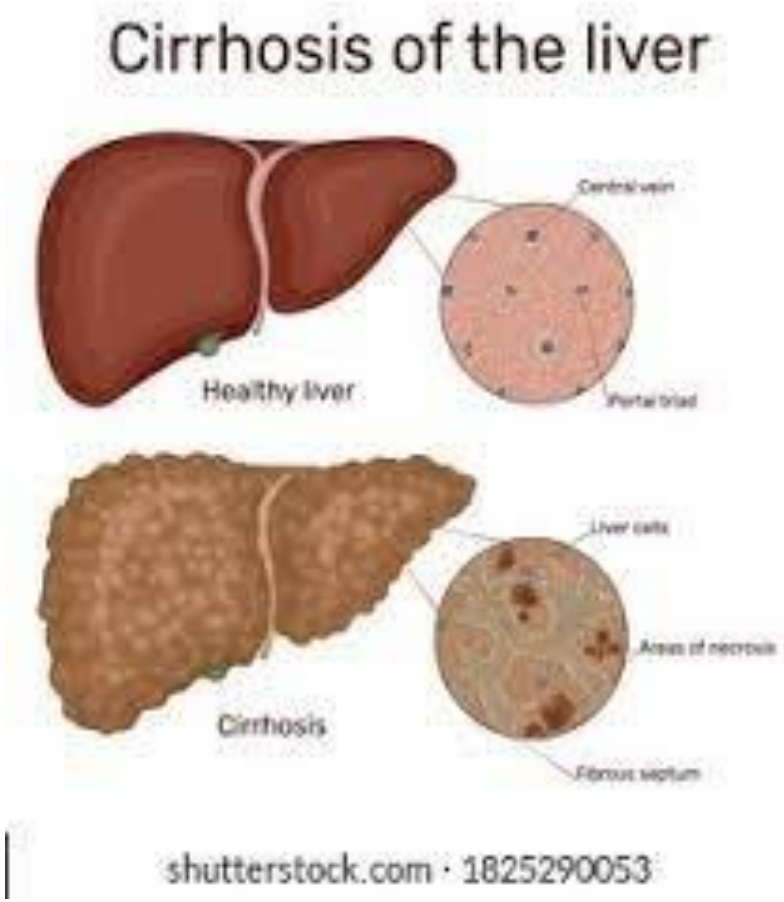
--term administration of hepatotoxic drugs (antituberculosis, non-steroidal anti-inflammatory drugs, neurotropic drugs, antihypertensive remedies, etc.).

HC-pathogenesis

1. Hepatocyte damage by toxic, viral, immunological factors - abnormal cellular energy metabolism with ATP deficiency - increased oxidative stress with lipid peroxidation of cellular structures

2. Liver fibrosis with nodular regeneration; consists:
   - Increased production and deposition in the Disse spaces of collagen (collagen type IV, III and I), proteoglycans (decorin, biglican, lumican, agrecan) and glycoproteins (fibronectin, laminin, tenascin, undulin)

3. Proliferation of extracellular matrix components ⇨ fibrosis ⇨ regeneration nodules



HC-pathogenesis

All liver cirrhosis has as a common and mandatory starting point cell death

It differs depending on the etiology

- More frequently - cell necrosis, a real violent death, following the direct aggressions of pathogens.
- Sometimes necrosis follows an inflammatory process and is the result of immune mechanisms.
- Cell death can also result from exacerbation of apoptosis (naturally programmed death of hepatocytes), as found in alcohol aggression.In order for cirrhosis to set in, it is necessary for the necrosis to occur over time and not be massive, otherwise fulminant liver failure occurs. Cell necrosis may be focal or may follow certain pathways similar to the inflammatory process (porto-portal, porto-central or centro-central).
- Following cell destruction, the parenchyma collapses, a real collapse of the lobes.
- Hepatocytes are framed in a collagen-supporting tissue, and following collapse, these collagen frames overlap and converge, creating the fibrous matrix of future cirrhosis.

HC-pathogenesis

The second element is fibrosis

- On the path of the matrix condensations, following the lobular collapse, fibrosis develops, which follows the path of necrosis

-Supportive liver tissue consists of collagen, structural glycoproteins, proteoglycans and elastin. All four of these components grow in cirrhosis.

-Fibrosis is the result of an intense process of fibrogenesis, which is mainly due to collagen.

- In the process of fibrogenesis are involved fibroblasts from the portal space, to cells, which are the precursors of myofibroblasts, and myofibroblasts from Disse spaces

HC-pathogenesis

Cell regeneration is the third constituent of the cirrhotic process

- The regeneration process is determined by cell death, but there is no balance between destruction and regeneration.
- Usually, the regeneration is excessive and forms nodules, which make compressions on the surrounding fibrous tissue.
- They cause a compression on the vascular system, contained in the connective tissue, and an increase in portal pressure.
- Through the process of destruction, regeneration and fibrosis, intrahepatic joints are born between the hepatic artery and the central vein, so between the arterial and the portal system, with consequences on the hepatic function.

CH-anamnesis

Key moments:

- Pre-existing liver or biliary diseases (hepatic colic, jaundice, etc.)
- Supported surgerie
- Transfusions of blood and / or blood substitutes
- Food features
- ·Metabolic diseases (diabetes, gout, lipid metabolism disorder)
- Alcohol abuse
- Use of medications
- Professional activity, occupations or hobbies, which can have a toxic effect on the liver (oil painting and various chemical dyes, paints, reuse of volatile lakes)
- Addiction, drug addiction
- Traveling abroad
- Sexual perversions
- Hereditary liver disease

HC- clinical examination

The clinical picture of HC depends on the stage of the disease in which the patient is and, in some cases, on the etiology

- About 40% of patients with compensated HC have no complaints and HC is established "occasionally" during the clinical, paraclinical examination or during abdominal surgery.
- The clinical symptoms of liver cirrhosis are determined by the two major consequences of morphological restructuring:

a) reduction of the liver parenchym

b) the presence of portal hypertension

CH - complaints (possible)

In the early stages, symptoms may be absent or there may be physical and mental asthenia

- Asthenovegetative syndrome: Asthenia, reduced work potential, fatigue, emotional lability, insomnia, suppressed mood, decreased ability to concentrate, headache
- pain in the right hypochondrium, sensations of heaviness, compression in this area - are usually conditioned by the reaction of the liver capsule (serous tunic, visceral peritoneum) to the extension caused by hepatomegaly.
- Dyspeptic syndrome: Reduced appetite, nausea, less frequent vomiting, belching, feelings of heaviness and fullness in the epigastrium, intolerance to fatty foods, bloating of the abdomen, constipation, intolerance to alcohol and cigarette smoke

CH - complaints (possible)

- Jaundice, itchy skin, xanthelasma, xanthoma, stool and urine discoloration, darker skin, dry
- Endocrine disorders - decreased libido, menstrual disorders, impotence, enlarged thyroid gland and / or dysfunction, diabetes, gynecomastia
- Hemorrhagic syndrome: nasal and rectal hemorrhages, gingivorrhages, subcutaneous hematomas, hemorrhagic vasculitis, gastrointestinal hemorrhages
- Psychoneurological disorders - reduced memory, disturbed sleep rhythm, inappropriate behavior, disorientation in time and space, precoma, coma

HC-Zieve syndrome

- Zieve syndrome occurs in alcoholics, but especially in alcoholic cirrhosis
- It is a special and complex clinical form, characterized by hyperlipemia and hemolytic anemia.
- Fat loading of the liver is mandatory, regardless of the type of liver disease.
- Clinical - fever, jaundice, abdominal pain, hepatomegaly.

HC - hepatic stigmas

The typical patient was described by Hvosteck (1922):

- The lack of pectoral hair on the abdomen, in the armpits, "bald abdomen" is found in about 70% of patients.
- The hair on the head is dull, often with growth on the forehead, bushy eyebrows, pubis in men of female structure.
- In women, pubic, axillary hair may be missing, breast atrophy, hair loss on the head is possible.
- "Cirrotic facies" - pale skin, with a yellow-gray hue, dark spots are possible due to melanin deposits, vascular stars, telangiectasias.
- Wrinkled, aged skin.
- The paraauricular glands are enlarged but painless.
- Jaundice of the sclera, mucous membranes, skin.

HC - hepatic stigmas

- Vascular asterisks (vascular angiomas) - occur as a result of increased content of estrogen hormones in the blood or activation of vasoactive substances (ferritin, histamine, bradykinin; change in the sensitivity of vascular receptors to these substances).

- they can be single or multiple with dimensions from a few mm to 2 cm and more (on the neck, face, shoulders, hands, chest, back, on the mucosa of the hard palate, pharynx, less often on the nose).

-they reduce or disappear with the improvement of the patient's condition.

- Palmar and plantar erythema (75%)

-a symmetrical hyperemia, in spots, of the palms and soles of the palms and hypotenuse, possibly of the fingertips.

at compression the erythema becomes paler.

- It is explained by arteriovenous aneurysms.

HC - hepatic stigmas

- White nails, "parchment" skin with an aged, wrinkled, dry, atrophic, yellowish appearance. more obviously on the chest, cheeks, behind the ears, on the hands, on the fingers with intensification from sun exposure.
- The tongue is smooth, red, slightly swollen, with dental imprints, furrowed by cracks, angular heliosis (cracks of the labial commissure), characteristic lips - red, smooth, "lacquered" can be conditioned by venous stasis and avitaminosis.
- In some patients the fingers take on the appearance of "drumsticks", the nails - the shape of "watch bottles".

HC - hepatic stigmas

- Gynecomastia

-men, combined with testicular atrophy reflects endocrine disorders caused by disturbed estrogen metabolism in the affected liver or reduced testosterone synthesis;

-in women - atrophy of the mammary glands, disorders of the menstrual cycle.

- Dupuytren's contracture is a flexor contracture of the fingers - as a result of tissue changes in the palmar aponeurosis and subcutaneous palmar tissue.

-Over time, due to this contract, the function of the hand is disturbed.

HC - hepatic stigmas

- The color of the skin can be changed

- bronze color, dark palm folds, hyperpigmentation of the axillary, inguinal, lumbar regions in hemochromatosis (storage of melanin and hemosiderin)- in porphyria, on the dorsal surface of the hand, blisters with epidermal exfoliation crusts or hyperpigmentation sectors appear

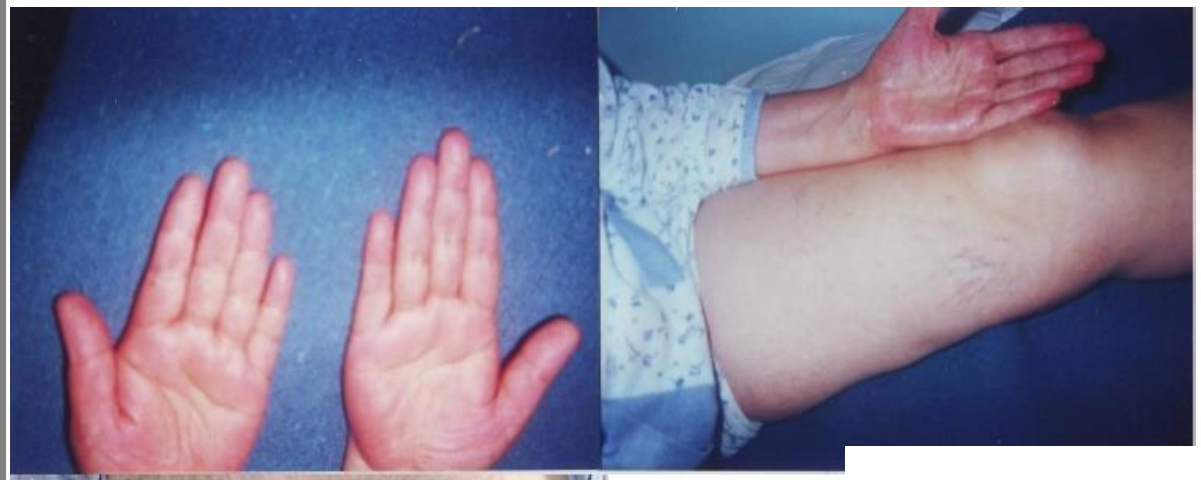
-in Wilson-Conovalov disease it acquires a silvery color (gray-bronze or gray-blue),nail lodges can have a cianotic color

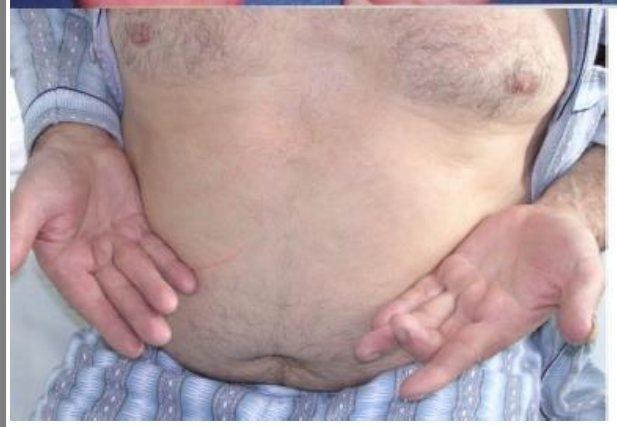
- On the skin - xanthomas, located intradermally, on the eyelids (xanthelasmas), on the hands, elbows, knees, soles, buttocks, in the armpits of hyperlipidemia, hypercholesterolemia,

- Skin itching (traces of excoriation, crusts, erosions, secondary bacterial dermatitis, hyperpigmented spots) increase in the level of bile acids in the blood and subsequent irritation of the skin receptors.

HC - hepatic stigmas

- Hemorrhagic manifestations - epistaxis, gingivorrhagia, petechiae eruptions, bruises, subcutaneous hematomas, gastrointestinal hemorrhages, hemorrhoids hepatocellular insufficiency.
- The odor of the liver (foetor hepaticus) is felt on the patient's breathing (sweating, urine, vomiting masses of the patient) accumulation of aromatic amino acids and methylmercaptan. In endogenous hepatic coma - smell of fresh liver, exogenous hepatic coma - smell of sulfur or ripe fruit.
- Ascites, dilation of the veins on the abdomen, edema of the lower limbs, scrotal portal hypertension.
- Psychoneurological disorders - drowsiness, reduced memory, sleep disturbance, inappropriate behavior, disorientation in time and space
-





Dupuytren 'S Contracture

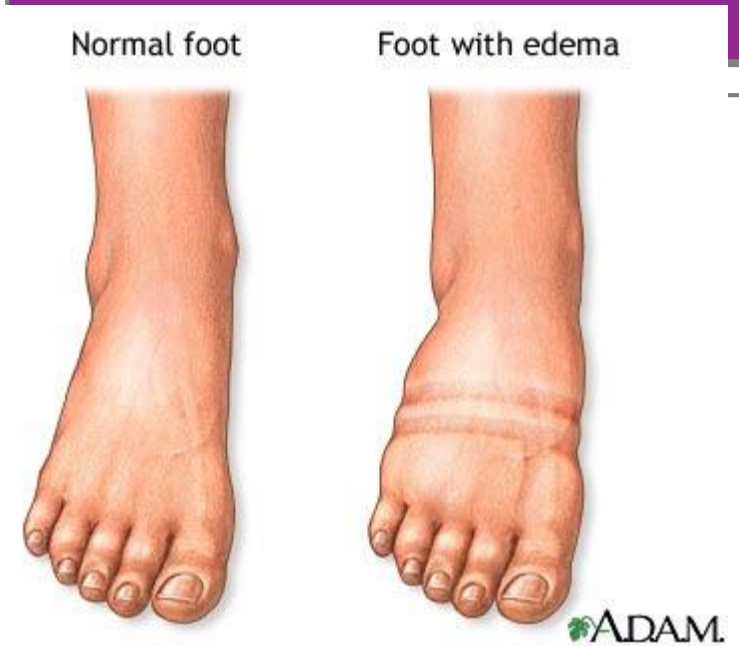
arthritis

easy stage of the disease

the average stage of the disease

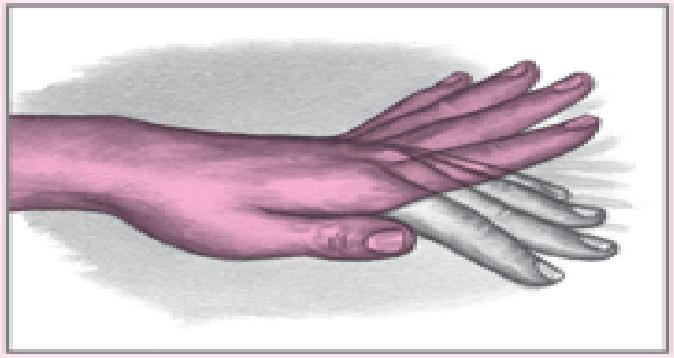
severe stage of the disease
fingers not unbend

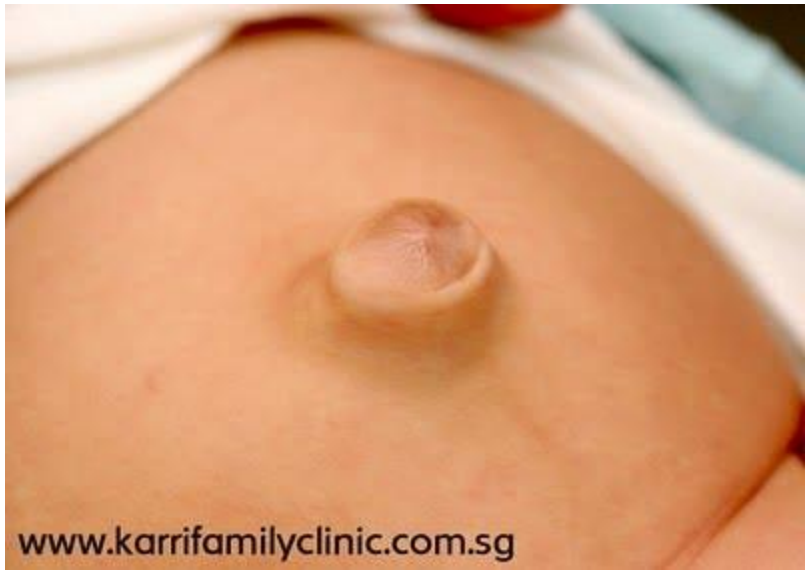
#178439594

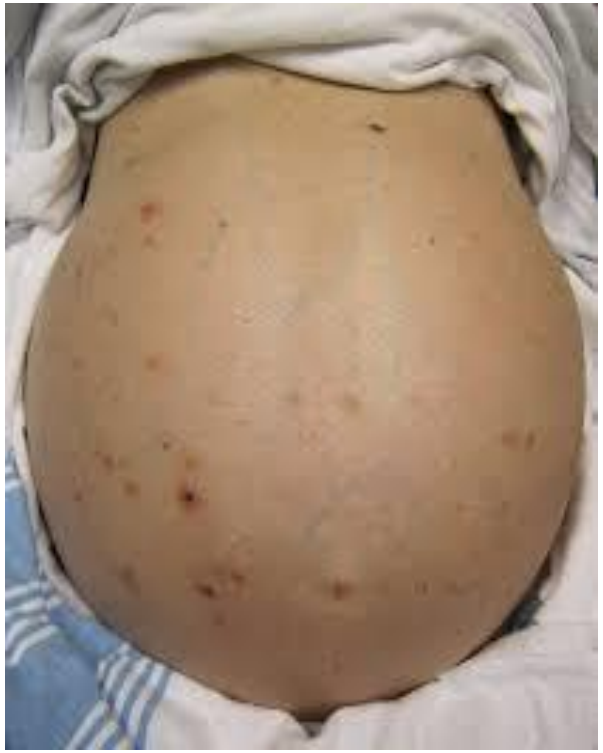


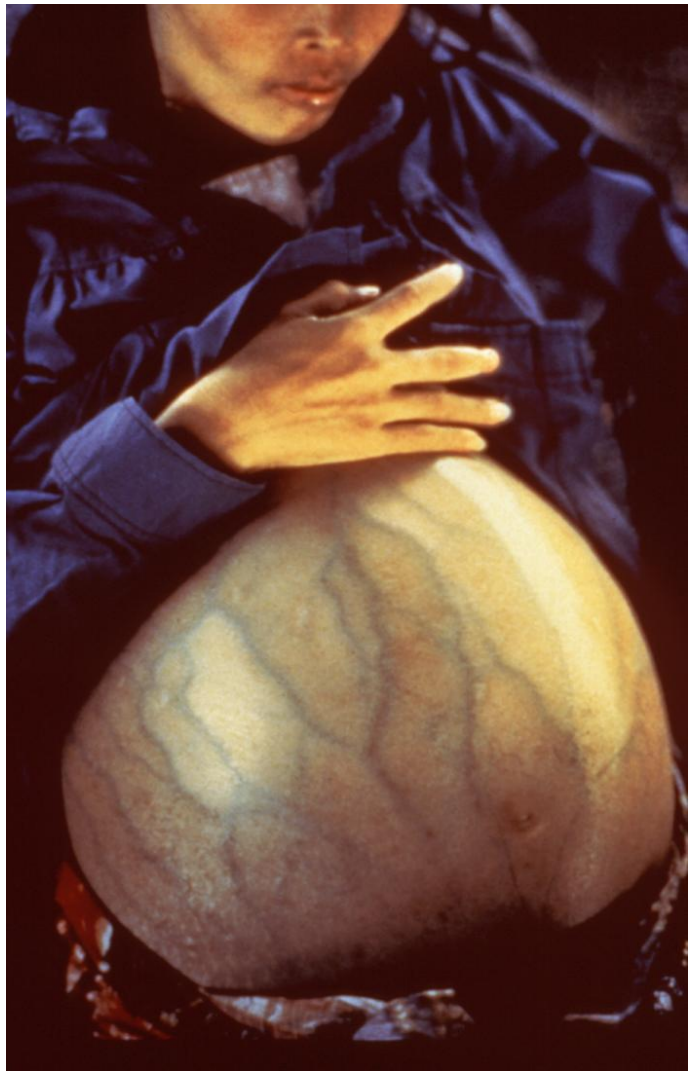
Recognizing asterixis

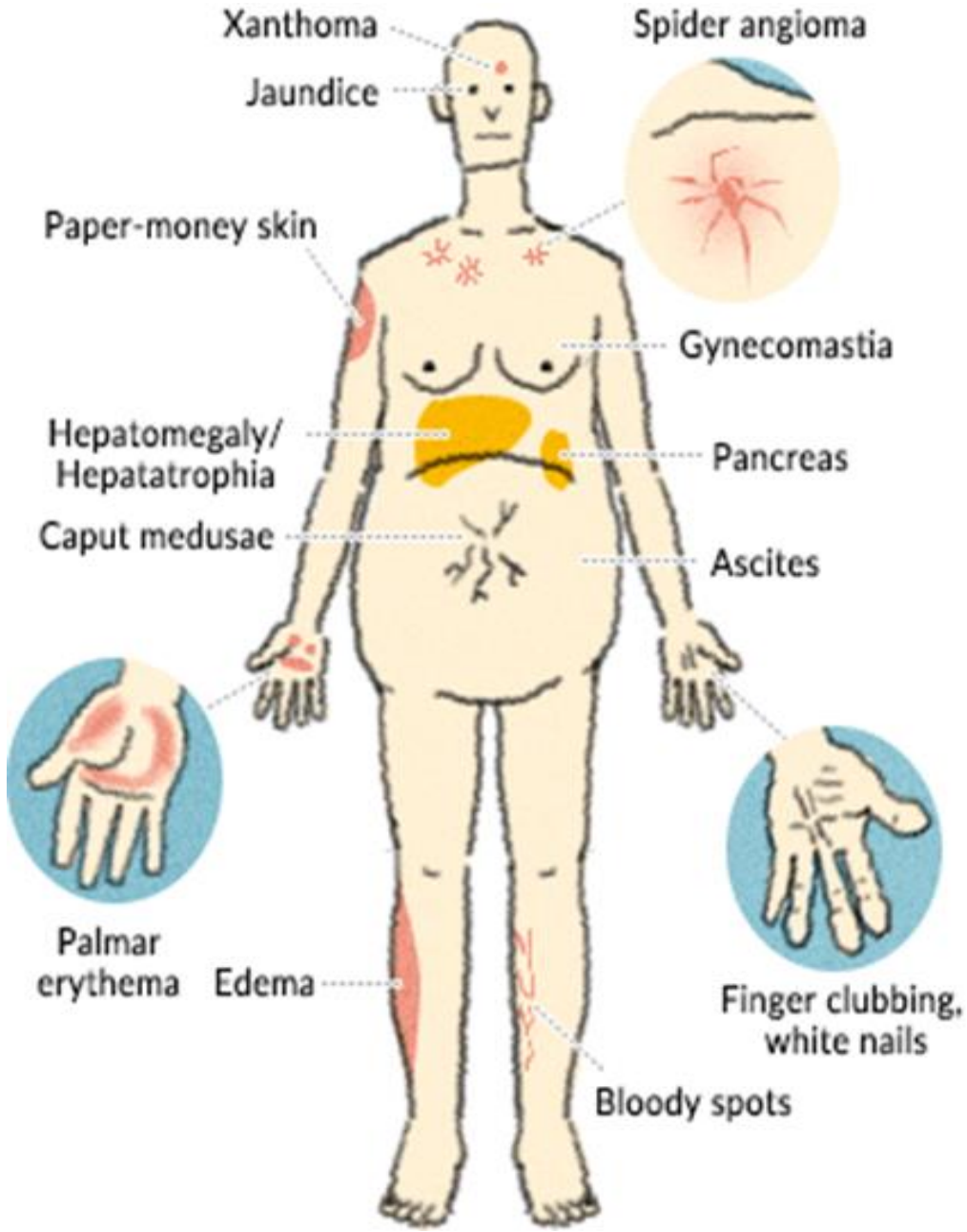
With asterixis, the patient's wrists and fingers are observed to "flap" because there's a brief, rapid relaxation of dorsiflexion of the wrist.



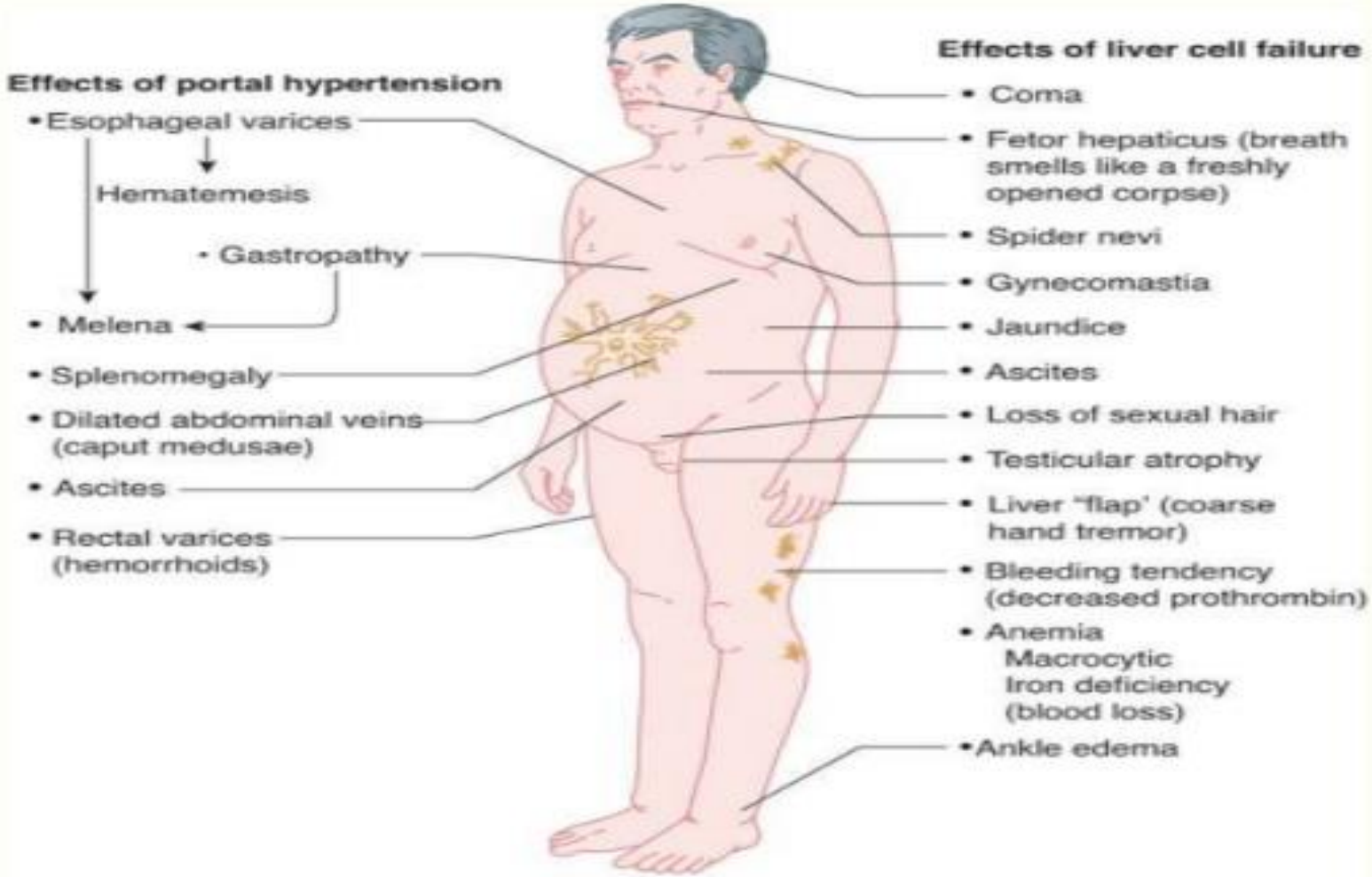







Xanthoma
Jaundice
Spider angioma
Paper-money skin
Gynecomastia
Hepatomegaly/
Hepatatrophia
Pancreas
Caput medusae
Ascites
Palmar
erythema
Edema
Finger clubbing,
white nails
Bloody spots

Clinical Manifestations



Source: McPhee SJ, Hammer GD: *Pathophysiology of Disease: An Introduction to Clinical Medicine, 6th Edition*: http://www.accessmedicine.com

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Hepatic cirrhosis

Changes in the liver and spleen

- Percussion of the liver (by Kurlov) - enlargement or, in advanced stages, decrease in organ size
- Palpation of the liver - change in the shape of the liver, hard consistency with the nodular surface and sharp edge of the organ
- Spleen palpation, percussion - splenomegaly

HC-extrahepatic manifestations

- Digestive system: gastroesophageal reflux disease with or without reflux esophagitis, portal gastropathy, gastric or duodenal ulcer, chronic pancreatitis with insufficient exocrine function, acute pancreatitis, gallstones, etc.
- autoimmune thyroiditis, type II diabetes mellitus, diffuse glomerulonephritis, secondary systemic vasculitis, cutaneous manifestations, hepatorenal syndrome, hepatopulmonary, etc.
- Nervous system: Peripheral neuropathy encephalopathy (alcoholics), Babinski sign, muscle stiffness
- Osteo-articular: osteoporosis and osteodystrophy.
- Cardiovascular: pericardial collections, hypotension, toxic (alcoholic) cardiomyopathy.

HC-extrahepatic manifestations

- Hematological:

* Coagulation disorders - all coagulation factors are synthesized in the liver, except factor VIII

* Thrombocytopenia occurs frequently in hypersplenism (epistaxis, gingivorrhagia, petechiae or bruising). Functional disorders may also occur with platelet aggregation disorders.

* Anemia can be hypochromic microcytic (result of small and repeated hemorrhages or massive hemorrhages from rupture of esophageal varices; hemolytic (n hypersplenism).

- Pulmonary:

* Pleural collections (hydrothorax) - in 10% of cirrhotic patients, most on the right

* Hepato-pulmonary syndrome (increase in plasma levels of vasodilators or lack of destruction or inhibition of circulating vasoconstrictors). -platypnea (improvement of dyspnea in decubitus) and orthodeoxia (decrease of SPO2 in orthostatism with improvement in clinostatism)

* Primary pulmonary hypertension

- Renal. Hepato-renal syndrome

HC-investigations

- CBC, platelets, reticulocytes
- · ALT, AST, bilirubin, prothrombin, albumin, GGTP, FA, urea, glucose
- Viral markers: HBeAg, anti-HBe, anti-HBcor IgM, anti-HCV IgM, anti-HDV IgM etc
- HBV DNA, HCV RNA, HDV RNA by PCR
- α-fetoprotein (for primary hepatic Cr screening)general analysis of urine,
- Autoantibodies: ANA, AMA, SMA, anti-LKM etc.
- Cryoglobulins, Serum Fe, transferrin, ferritin, ceruloplasmin,
- Serum and urinary, Lipidogram,
- K, Na, Urea, Creatinine, Fibrinogen, coagulogram

HC-investigations

- abdominal organs US
- Doppler of the portal system
- FGDS or R-scope of the esophagus and stomach (for assessment of esophageal / gastric varices and assessment of the risk of bleeding)
- ECG
- Chest X-ray,
- Hepatosplenic scintigram with Tc or Au isotopes
- CT
- MRI

PORTAL HYPERTENSION SYNDROME

- Definition: **represents the ↑ pressure in the portal vein above 10 mmHg**
- Causes:
- Portal HT can be determined by:

1. ↑ blood flow (very rare, because the increase in flow in the v. Porta causes a compensatory decrease in the flow in the hepatic artery to maintain a pressure N in the sinusoidal capillaries)

2. ↑ flow resistance in the gate circulation (!!!) as a result of an obstructive process located at one of the following levels: - presinusoidal: thrombosis, fibrosis or compression v. porte - sinusoidal: reduction of the vascular bed in liver cirrhosis

3. - postsinusoidal: compression of liver veins in liver cirrhosis due to nodular regeneration, thrombosis of suprahepatic veins or vena cava in BuddChiari syndrome, constrictive pericarditis, right heart failure

PORTAL HYPERTENSION SYNDROME-manifestations

Development of collateral circulation (porto-cave shunts):

- has the role of draining blood from the portal circulation in the vena cava system, bypassing the obstacle

anastomoses can come from the following branches of the port system:

- short gastric veins that anastomose with the esophageal submucosal plexus that flows through the azygos veins into the superior vena cava → esophageal varices

- inferior mesenteric vein that develops collaterals with hemorrhoidal veins that drain into the inferior vena cava → hemorrhoids

- the periumbilical veins that can be anastomosed with the epigastric vein that drains through the inferior vena cava or with the mammary veins that drain through the superior vena cava the periumbilical circulation in the → "jellyfish head"

PORTAL HYPERTENSION SYNDROME-manifestations

- Splenomegaly

-is the result of congestion, fibrosis and splenic siderosis

- causes hypersplenism by RES hyperplasia → ↑ the activity of sequestration and destruction of blood figurative elements

- Ascites - is an excessive accumulation of fluid in the peritoneal cavity

HYPERTENSION SYNDROME-diagnosis

- FEGDS is the method of choice for highlighting the signs of portal hypertension (esophageal and gastric varices, portal-hypertensive gastropathy, etc.).
- Esophageal varices are divided into 3 degrees:
- grade I - small in size and disappear when blown into the air;
- grade II - in the form of prominent columns occupying 2/3 of the esophageal lumen;
- grade III - completely covers the lumen of the esophagus.
- At the endoscopic examination, the extension of the varicose veins (in the lower third, up to the middle or upper third) and the signs of high risk of hemorrhage in the varicose veins: red spots, hemato-cystic dilatations, which are indications for endoscopic treatment: sclerotherapy or ligation of varicose veins.
- The presence of esophageal varices is a major sign that confirms PAH, however their absence does not rule out this diagnosis.

Portal HYPERTENSION SYNDROME-diagnosis

- Abdominal ultrasound is one of the most used imaging scans in the diagnosis of liver disease by highlighting changes in the liver parenchyma and signs of portal hypertension (increased size of the portal and splenic veins, splenomegaly, ascites).
- Doppler ultrasound allows not only the measurement of the diameter of the vessels in the spleen hilum, but also the establishment of the speed and volume of blood flow through the portal vein and spleen, through the hepatic artery.
- Barium radiological examination allows visualization of esophageal or gastric varices with lower sensitivity (II and III dgr. varices).

Ascites - is an excessive accumulation of fluid in the peritoneal cavity due to the following pathogenic mechanisms:

- Local mechanism:

✓ Increased hepatic lymph flow (is the main mechanism of ascites production) sinusoidal capillaries have a very high permeability ⇒ allow the passage of proteins through the capillary membrane in the interstitial ⇒ ascites

- -Hepatic lymph contains 90% of plasma proteins and hepatic lymph flow drained into the thoracic duct is 5 -10 times higher in cirrhotic than normal.

- Portal hypertension

-Systemic mechanisms:

✓ Hypoalbuminemia

✓ Hydro-saline retention triggered by:

- ↑ effective circulating volume (blood stagnates in the port system)
- activation of the RAA system (due to decreased renal perfusion)
- ↑ ADH level ⇒ ↑ distal reabsorption of H2O

HC-ascites

Classification of ascites according to severity

1. I degree ascites - ascites detectable only by ultrasonography
2. II degree ascites - ascites evidenced by moderate distension of the abdomen3.
3. III degree ascites - tense ascites, highlighted by marked abdominal distension

Classification of ascites, according to complications

- Uncomplicated ascites
- Refractory ascites
- Complicated ascites: spontaneous bacterial peritonitis

HC-ascites

Classification of ascites according to etiology

1. Ascites, without direct damage to the peritoneum

-Intrahepatic PAH: liver cirrhosis, acute ethanolic hepatitis, venoocclusive disease, massive liver metastases.

-Extrahepatic PAH: global heart failure, constrictive insufficiency, tricuspid insufficiency, inferior vena cava obstruction, hepatic vein obstruction

.-Hypoalbuminemia: nephrotic syndrome, enteropathy with protein loss, malnutrition.

-Pancreatic ascites (chronic and acute pancreatitis).

-Bile biliary ascites (traumas, biliary surgeries, percutaneous operations: ERSP)

.-Nephrogenic ascites.

-Chilosophyte ascites

.-Mixedema.

-Ovarian diseases (carcinoma, benign tumors)

2. Ascites, with primary peritoneal involvement

- Malignant ascites.
- -Peritoneal granulomatosis: tuberculous peritonitis, peritonitis with Chlamydia trahomatis, fungal peritonitis, parasitic peritonitis, sarcoidosis, iatrogenic granulomatous peritonitis.
- -Vasculitis: systemic lupus erythematosus, Henoch-Schonlein purpura
- .-Other conditions: eosinophilic gastroenteritis, Wipple's disease, endometriosis.

HC-ascites

- The inspection finds an enlarged abdomen in volume (through fluid, but also through the air in the intestine).

-In III degree ascites, the abdomen enlarged in volume is prominent,

-in II degree ascites - the abdomen hangs like a sack in orthostatism.

--The umbilicus is prominent, and as the amount of fluid increases, the protrusion of the umbilical or inguinal, femoral hernias is noticed.

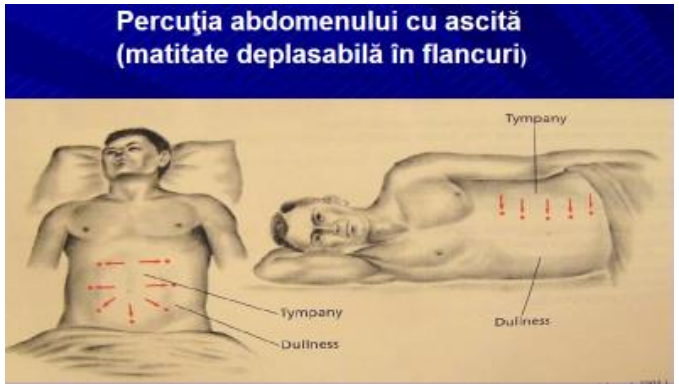
- Dilated abdominal veins that radiate from the umbilicus and do not disappear after the decrease of ascites or dilated veins on the flanks that appear as a result of compression of the inferior vena cava of ascitic fluid and disappear after ascites reduction (cavocava circulation).
- In liver cirrhosis with ascites, the liver and spleen can be palpated by baling.
- At an average amount of fluid in the abdomen (1 l - 5 l) - on palpation - the sign of floating ice - when performing sudden and intermittent compression in the liver a sensation as an object floating in a liquid.

HC-ascites

- Palpation and percussion highlight the sign of the wave in abundant ascites. It is caused by striking one of the flanks, and the transmission of the veil is perceived on the opposite flank.
- The percussion of the abdomen detects changes depending on the amount of ascites fluid: II degree ascites causes a declining dullness (on the flanks in dorsal decubitus, in the hypogastrium in orthostatism and peri-umbilical in the genupectoral position).
- Dullness is displaceable with position (by turning the patient in left lateral decubitus the left flank will become matte).
- Declining dullness can be detected clinically in the presence of more than 1000 ml of fluid. In III degree ascites, the abdomen becomes

  diffusely dull.

In 5% of patients with ascites in CH, hydrothorax may occur more frequently on the right, due to diaphragmatic defects that allow communication with the pleural cavity.



HC-ascites

Diagnostic:

- Clinical
- By Ultrasound
- Exploratory paracentesis: evaluates ascites-exudate, transudate, assesses the cellularity of the liquid (no. Leukocytes / ml)

Michelangelo Merisi, detto il CARAVAGGIO

Milano 1571 - Porto Ercole 610

Medusa
1595-1598 circa

Olio su tavola rivestita di tela
Inventario 1890 n. 1351

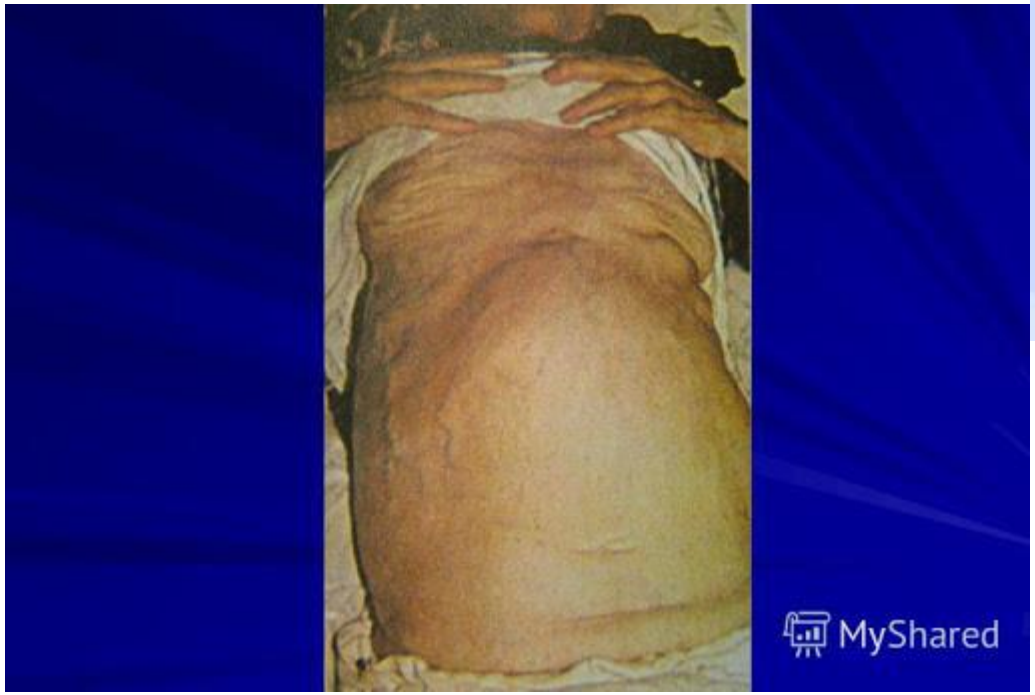
Donata nel 1598 al Granduca Ferdinando I dal Cardinale Francesco Maria del Monte e posta nell'"Armeria Nuova" di Galleria senza attribuzione, è citata come del Caravaggio nell'inventario del 1631, abbinata ad un'armatura persiana indossata da un manichino su cavallo di legno.

Medusa
ca. 1595-1598

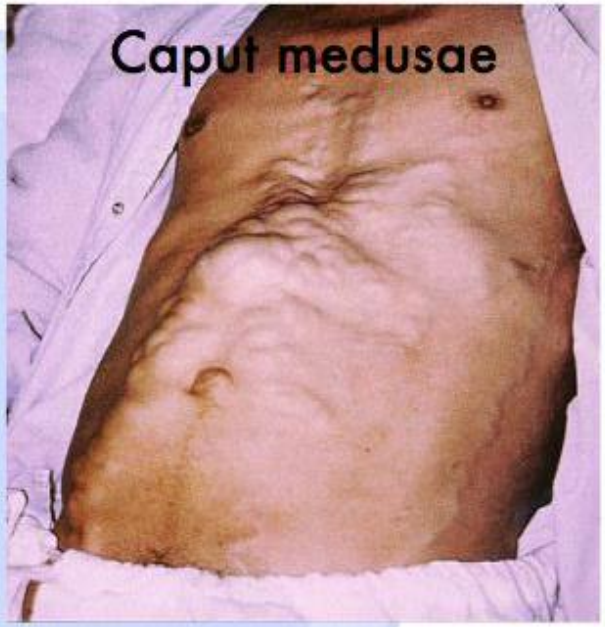
Oil on canvas-covered panel
Inventory 1890 no. 1351

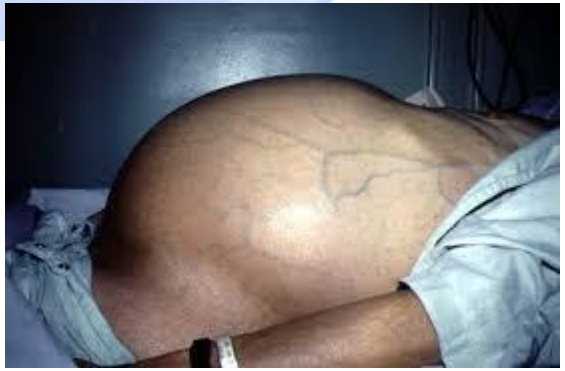
.In 1598 Cardinal Francesco Maria del Monte gave this painted shield to the Grand Duke Ferdinando I. It was put in the "Armeria Nuova" of the Uffizi Gallery, without any attribution, near a figure dressed in Persian armor mounted on a wooden horse. In the 1631 inventory it was listed as a work by Caravaggio.

HC-ascites

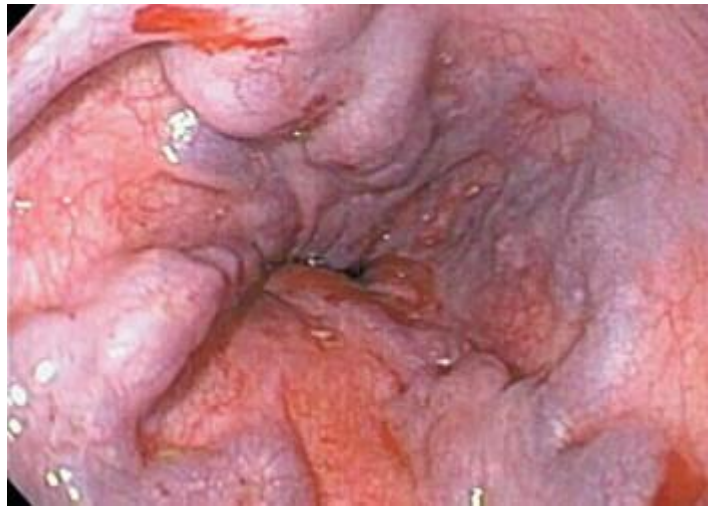


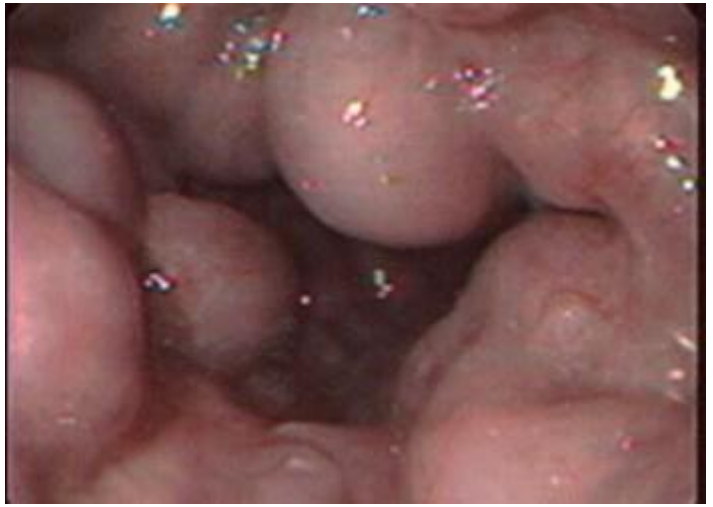
Very rare!

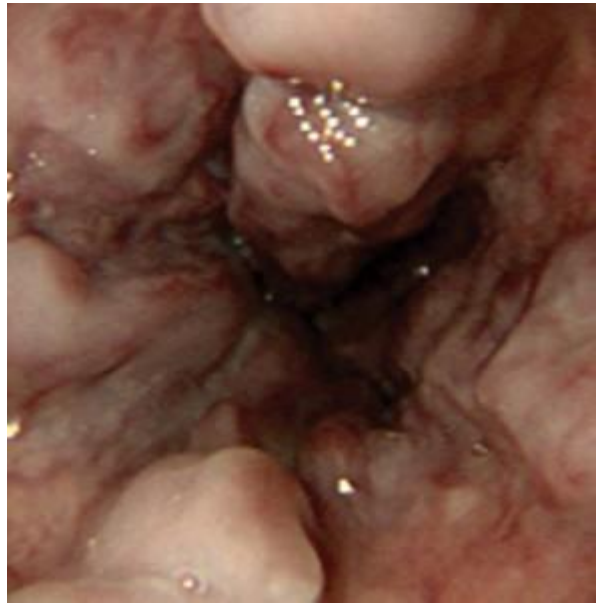


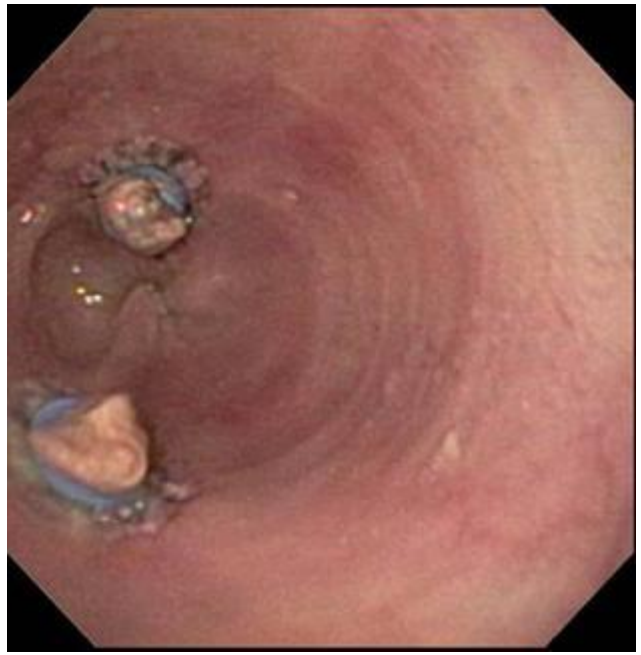


CH-PGT-esophageal varices







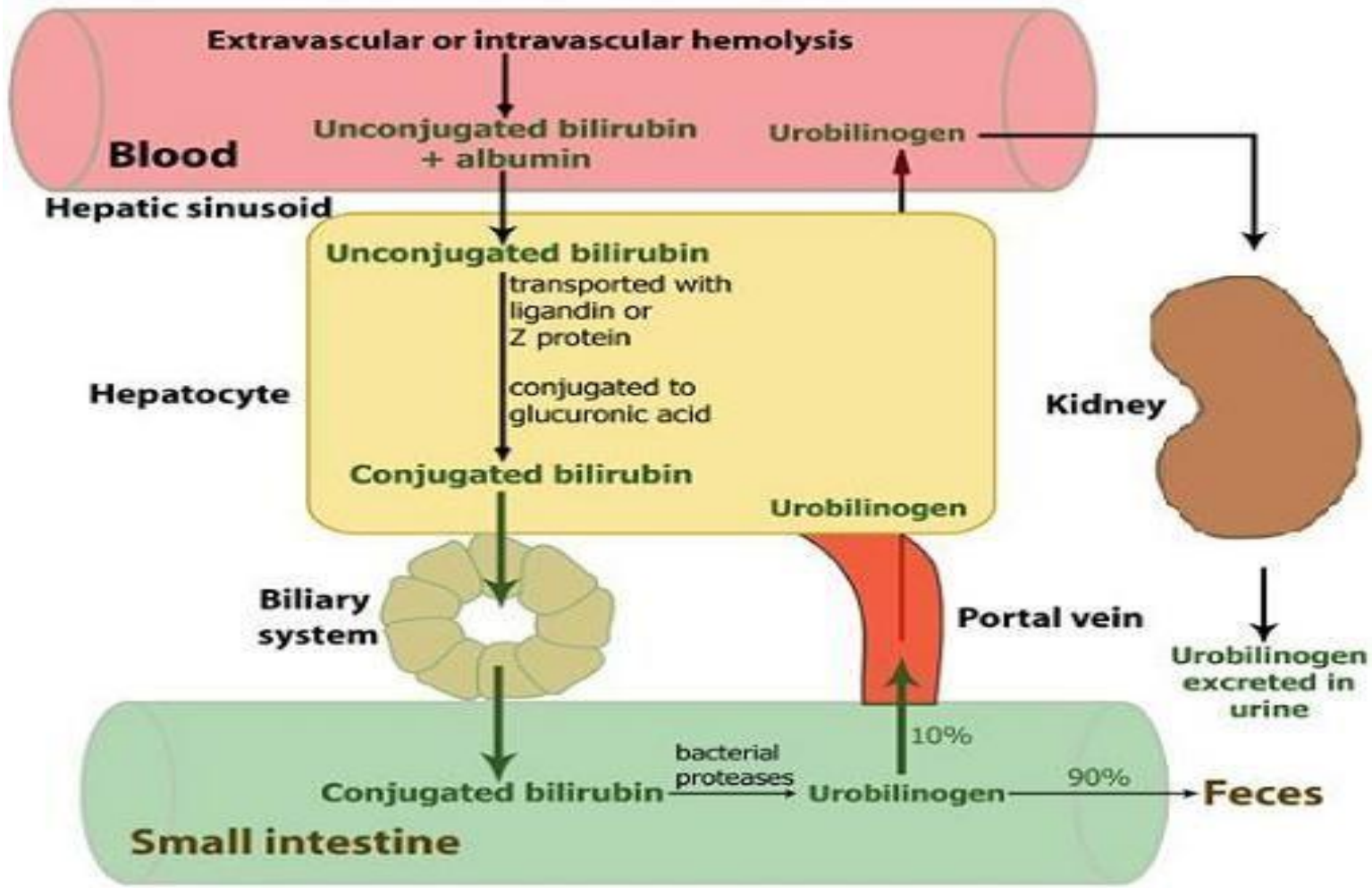


HC-jaundice syndrome

- Jaundice syndrome is the clinical expression of an increase in bilirubinemia due to hereditary, developmental or acquired abnormalities in the formation, transport, metabolism and disposition of bilirubin.

- It is characterized by the yellow coloration of the skin, sclera and mucous membranes, alteration of the chromatic aspect of the urine and by some digestive disorders.I
- increased bilirubin may occur not only in pathological circumstances but also in starvation, prolonged physical exertion, pregnancy or after excessive ingestion of alcohol, contraceptives or radiopaque substances.

HC-jaundice syndrome



HC-jaundice syndrome

Classification of jaundice

- Hemolytic jaundice results from the intensification of the processes of formation of unconnected bilirubin, as a result of an exaggerated destruction of erythrocytes and can be: congenital, manifested in thalassemia and other hereditary hemoglobinopathies, or acquired by autoantibodies, bacterial infectious agents, Clostridium welchii, infectious mononucleosis, parasites, malaria or toxoplasmosis, chemicals such as drugs, physical agents, burns. (↑ free serum bilirubin)

- Hepatocyte jaundice is found mainly in viral, toxic, alcoholic or halotic hepatitis, liver cirrhosis and in genetic defects in bilirubin transfer, in Gilbert syndrome, found in adults or Crigler-Najjar syndrome in children. (↑ free and conjugated serum bilirubin)

- Obstructive biliary jaundice is caused by biliary stasis caused by the mechanical action of obstacles such as stones, tumors, hematomas, lymphadenopathy, vascular abnormalities, stenotic papillitis or in rare cases parasites, located inside or outside the bile ducts. (↑ serum conjugated bilirubin)

HC-jaundice syndrome

- Normal serum bilirubin levels:

-Total bilirubin-8.5-20.5 mcmol / l

-Unconjugated (free) -2.14-5.13 mcmol / lConjugate -6.41-15.39 mcmol / l

Jaundice is considered to be:

-slight -when the level of total bilirubin in the blood serum is not> 85 mcmol / l;

-moderate - 86-170mcmol / l;-sever - > 171mcmol / l.

HC-hepatic failure syndrome

- Liver failure syndrome is a complex of clinical and biochemical signs and symptoms caused by acute / chronic ↓ of number and / or functional capacity of hepatocytes below the critical limit compatible with the full and adequate achievement of liver functions

* Installation of hepatic insufficiency (IH) → at ↓ 7/8 of the number of hepatocytes

- It is characterized by various hepatic and extrahepatic clinical signs as a result of affecting all liver functions

HC-hepatic failure syndrome

- Total protein-N-65-85 g / l ↓
- Serum albumin-N-35-50 g / l - ↓ hypoalbuminemia correlates with the degree of hepatic insufficiency
- Prothrombin index-N-90-105% - ↓ in liver cirrhosis, acute hepatitis, subacute hepatic dystrophy, is an unfavorable prognostic criterion.
- Urea-N-2,5-8,3 mmol / l ↓
- Fibrinogen –N-2.0 - 4.0 g / l ↓
- Pseudocholinesterase- N-5300-12900IU / l: Two types of enzyme have been described: acetylcholinesterase (nerve tissue, muscle, erythrocytes) and serum pseudocholinesterase (secreted by the liver). It has clinical value for the function of hepatic synthesis, progressive ↓ in CH, attesting to the lack of possibility of regeneration.

- **protrombin < 50%**
- **albumin < 35 g/l**
- **bilirubin > 35 mmol/l**

HC-hepatic cytolisis syndrome

- ↑ ALT- N-7-40 IU / l (0.1-0.45mcmol / l / hour - by the Reit man-Frenkel method))
- ↑ AsAT N-10-30 IU / l (0.1-0.68mcmol / l / h - by the unified Reit man-Frenkel method)
- Ritis coefficient (AST / ALT) - normal = 1.33.
- In cardiac pathology and alcoholic disease the coefficient ↑, and in liver diseases of other etiology - ↓

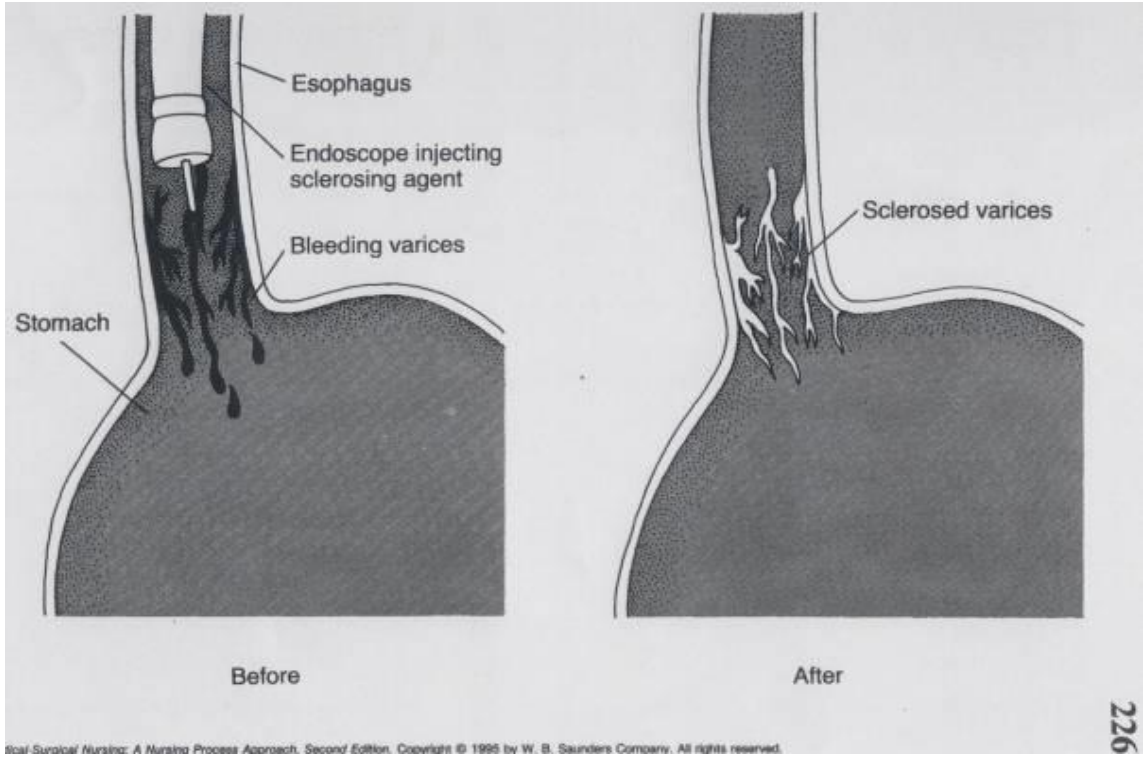
HC-complications

- Upper gastrointestinal bleeding
- Hepatic encephalopathy
- Spontaneous bacterial peritonitis
- Hepatorenal syndrome
- Acute tubular necrosis

HC-treatment

- Exclusion of physical and mental overwork
- Rational diet, avoiding heavy meals, divided into 4-5 times / day (meal 5 after Pevzner).
- Etiological treatment aimed at eliminating the cause (alcohol, toxic substances, hepatotoxic drugs, antiviral treatment in case of viral pathology, etc.)
- Pathogenetic treatment of primary reactions aims to interrupt the pathogenetic relationships induced by the etiological factor (immunosuppressants in case of autoimmune liver cirrhosis, penicillamine - in Wilson's disease, etc.).
- Treatment of pathological processes with potential for disease progression and aggravation - reduction of fibrogenesis (antifibrosants: pentoxifylline, silymarin, etc.), portal hypertension (beta-blockers, etc.), cholestasis (ursodeoxycholic acid, ademetionine, etc.).
- Symptomatic treatment - antioxidants, essential phospholipids, ornithine, cholestyramine

Sclerosis of the esophageal varices



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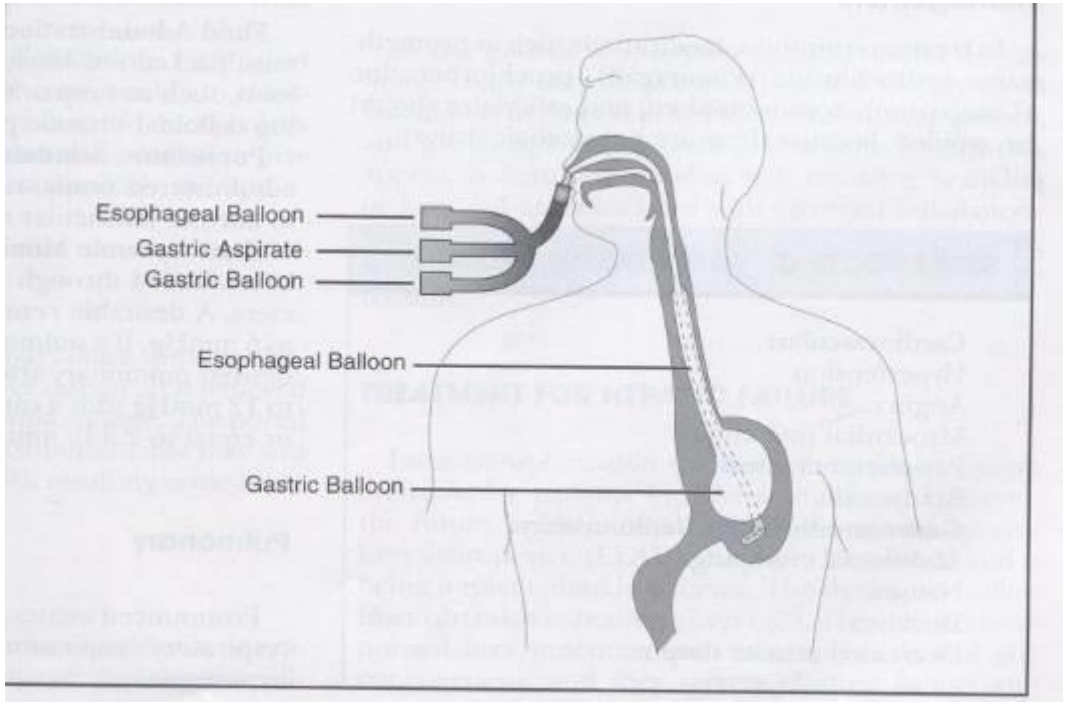
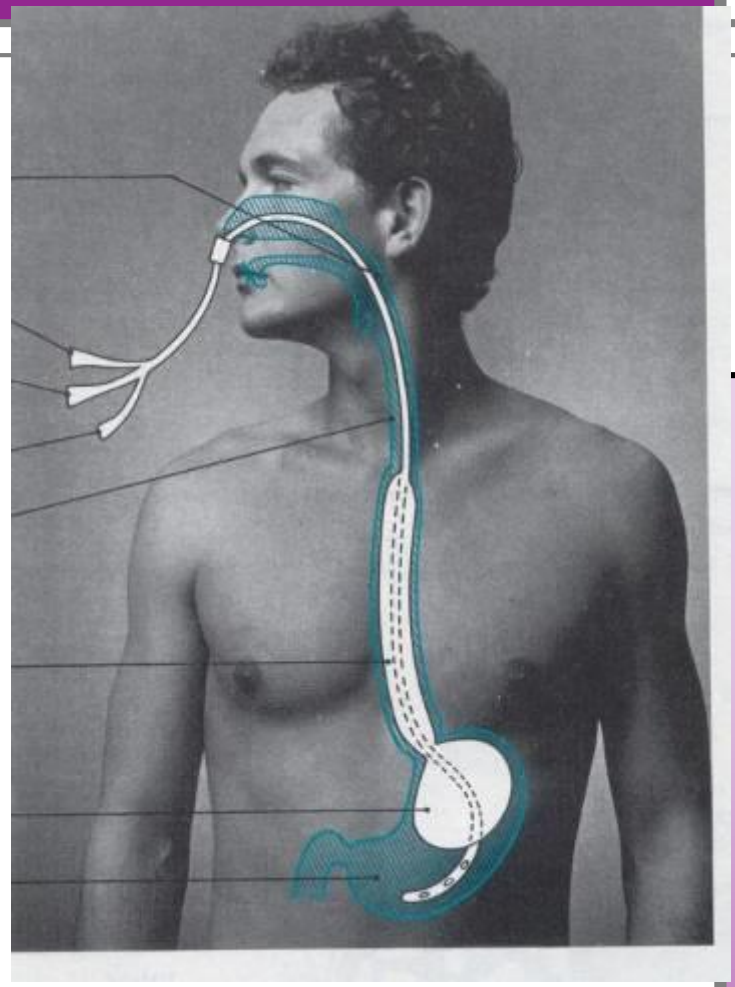
Blakemore probe



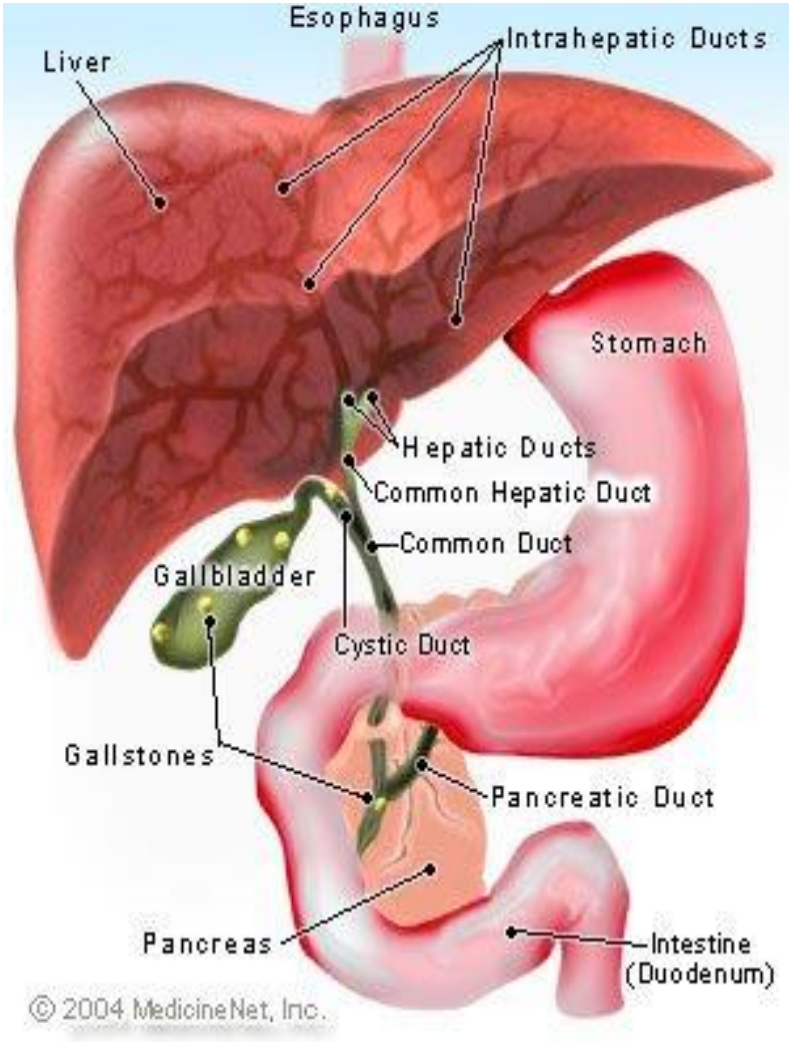


Cholelithiasis (gallstones)

- Gallstones or cholelithiasis - a pathology characterized by the formation of stones in the bile ducts and gallbladder due to alteration of the colloidal composition of bile

- Stones can form in any portion of the bile ducts (intrahepatic or extrahepatic ducts), but the predominant site of their formation is the gallbladder

- .predominantly in the sixth decade of life;F / M ratio = 2/1



Cholelithiasis – risc factors

- cholesterol stones (radiolucent
- old age, F sex, obesity
- CO treatment,
- lipid-lowering drugs (clofibrate) terminal ileum disorders / extensive ileum resections heredity pigment lithiasis:
- chronic hemolysis, liver cirrhosis
- estrogens, progesterone:
- increase bile lithogenesis (pregnancy, CO)
- high-cholesterol, low-fiber diet:
- lithogenic bile (HLP type IV)
- association with other conditions chronic occult hemolysis pigment lithiasis chronic liver diseases, strictures / dilatations of the bile ducts (b. Caroli) hiatal hernia, diverticular disease, parasitosis (ascarids) - pheochromocytoma

Cholelithiasis - clinical data

- Asymptomatic

✓ - ultrasound discovery biliary dyspepsia

✓ - bloating, flatulence, association with irritable bowel

- symptomatic lithiasis - biliary colic

❖ **Complications**

-Cholecystitis,

-choledochal lithiasis,

-cholangitis biliary-biliary / biliary-digestive fistulas,

- biliary ileus hemobilia (fistulas between the hepatic vessels and the bile duct, gallbladder carcinoma)

Cholelithiasis - clinical data

Abdominal inspection:

-bulging of the gallbladder region that evokes the presence of a gallbladder hydrops (by including a stone in the cystic duct)

-scar in the right hypochondrium (cholecystectomy)

- in a patient with biliary complaints: postcholecystectomy syndrome, gallstones remaining

- Palpation of the abdomen: superficial

-hyperesthesia in the right costal rim from the midline over the right hypochondrium to the right lumbar region

Cholelithiasis

painful points specific to biliary v. damage

Merphy - accentuation of pain in the right hypochondrium at the pressure of the right abdominal wall in the projection of the gallbladder during deep inspiration (usually the patient interrupts the expiration due to pain)

Kerhr - the appearance or intensification of pain in inspiration on palpation in the point of the gallbladder

Lepehne - pain on the percussion of soft tissues in the region of the right hypochondrium

Ortner - percussion pain on the right costal rim

Aizenberg II - pain occurs in the region of the right hypochondrium if the patient suddenly gets up on the toes and leaves on the sole

Volskii - pain, which appears at a slight paleness with the edge of the hand from top to bottom on the right costal rim

Krâmov - pressure pain in the upper right area of the umbilical region

Cholelithiasis

Reflective pain points in diseases of the biliary tract

Right reactive vegetative syndrome (irritant) - pain occurs on palpation of vascular and nervous points:

orbital point (Bergman symptom),

occipital point (Ionash symptom),

cervical point (Mussy's symptom),

interscapular point (Haritonov symptom),

femoral point (Lapinskii symptom),

plantar point (back of right foot)

Biliary colic

- Biliary colic (pain) - is the most characteristic sign of gallstones, caused by transient obstruction of the cystic duct or bile duct by a gallstone.
- The pain usually begins suddenly, postprandially, lasting several hours
- causes: gallstones, choliovascular dyskinesia, acute cholecystitis
- circumstances: heavy lunches, alcohol, exertion, mental stress
- character: permanent, with paroxysms (pressing, crushing, tearing) location and irradiation: right hypochondrium → at the base of the right hemithorax, right interscapulovertebral, right shoulder, Sometimes the pain radiates to the heart region, simulating an attack of angina pectoris ("cholecystoronary coronary syndrome" or Botkin's syndrome)

Biliary colic

- Clinical data:It is associated with nausea and vomiting which, as a rule, does not bring obvious relief
- Fever and sweating occur in infectious complications (cholecystitis, pancreatitis, cholangitis)
- Anxiety
- Jaundice of the sclera and skin
- Anterior flexion of the body
- +Murphy maneuver
- Tachypnea, tachycardia
- Urine hyperchrome

Biliary colic

Diagnostic

- Abdominal ultrasound - is a method with good accuracy that can visualize stones with dimensions up to 2 mm; false positive or false negative results in 2-3% of cases
- Empty abdominal radiography - can diagnose stones with calcium content
- Duodenoscopy
- Abdominal CT
- Abdominal MRI
- Endoscopic retrograde cholangiopancreatography
- Magnetic Resonance Cholangioancreatography (MRCP)
- Endoscopic ultrasonography

Biliary colic-treatment

- Diet 0;
- Infusion therapy with crystalloid or colloidal solutions;
- Spasmolytic drugs;
- Analgesics
- Antibiotics
- Installation of the nasogastric tube in case of persistence of nausea and vomiting;
- Non-steroidal anti-inflammatory drugs -indomethacin and diclofenac
- Cholecystectomy

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