MEDICINE

432 Team

23 Acute Viral Hepatitis

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COLOR GUIDE: • Females' Notes • Males' Notes • Important • Additional

Objectives

1. Clinical presentation of Acute Viral Hepatitis.
2. Diagnosis.
3. Epidemiology of viral hepatitis infection A, B, C in KSA.
4. Management.

Viral hepatitis

Definition [1]:

Hepatitis is inflammation of the liver. It can be caused by viruses, alcohol or substance use, exposure to toxins, and certain diseases. Viral hepatitis refers to liver inflammation caused by one of several types of viruses that attack the liver. In the United States, these are primarily hepatitis A virus (HAV), hepatitis B virus (HBV), and hepatitis C virus (HCV), but other types of hepatitis viruses do exist. Hepatitis can be acute, which means that the infection does not last longer than **6 months.** If the body's immune system cannot fight off the virus within 6 months, the disease is considered chronic.

Symptoms [1]:

Pre-icteric (jaundiced) phase:

- Fatigue (tiredness).
- General feeling of being unwell (malaise).
- Flu-like symptoms (e.g., headaches, muscle aches, low-grade fever).
- Lack of appetite, weight loss.
- Nausea and vomiting, abdominal pain.
- Diarrhea.

Icteric phase:

- Jaundice (new yellow tinge to skin and mucus membranes).
  - Itching of the skin.
  - Tea- or dark-colored urine.
  - Pale bowel movements.
- Tender RUQ + discomfort.
- Enlarged liver & spleen.
- General adenopathy.

Complications of Hepatitis:

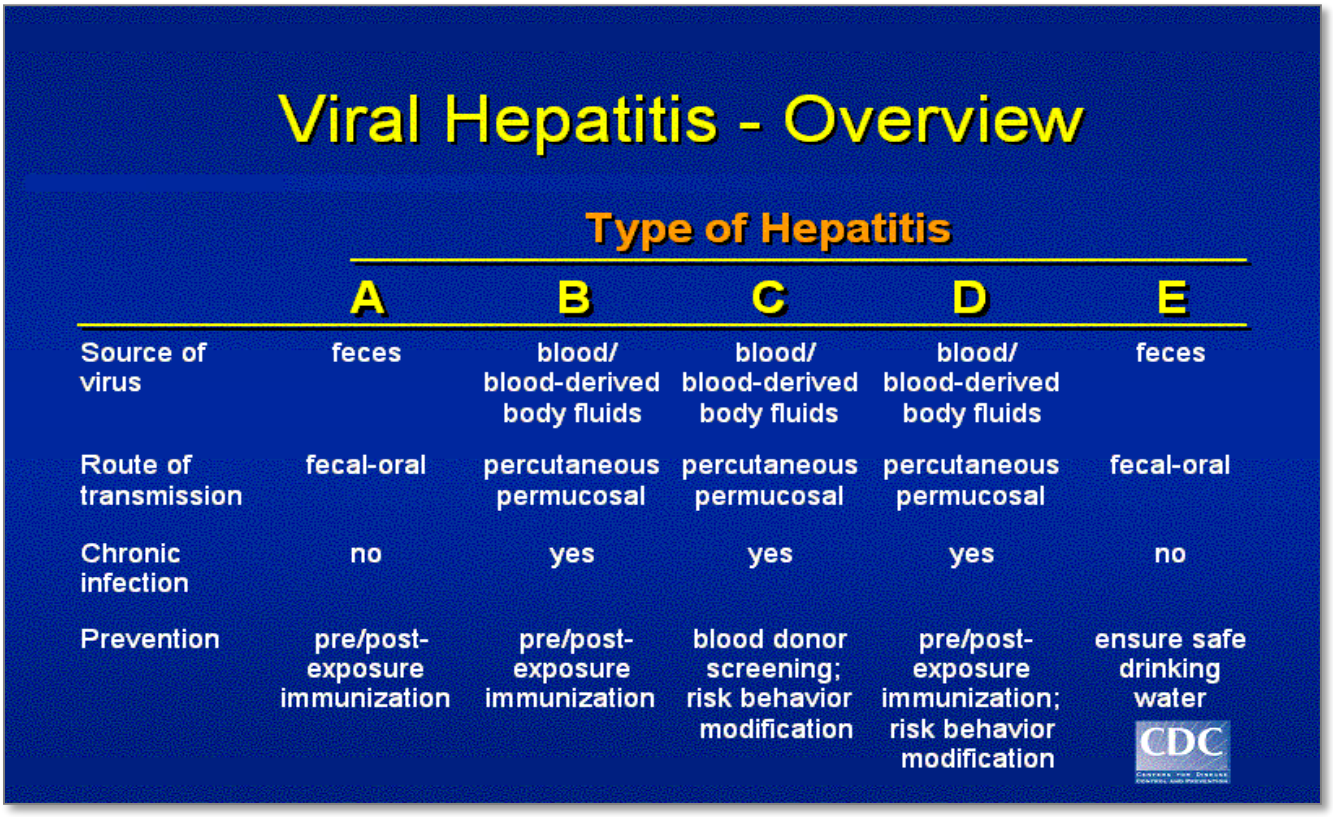
1- Cirrhosis - HCC (with chronic hepatitis = C + B + D)

2- Fulmnant hepatitis:

- Definition: Hepatic Failure within 8 weeks of onset of illness.
- Manifestation: Encephalopathy, Prolonged PT (prothrombin time)
- Histopathology: Massive Hepatic Necrosis.

Types of viral hepatitis:

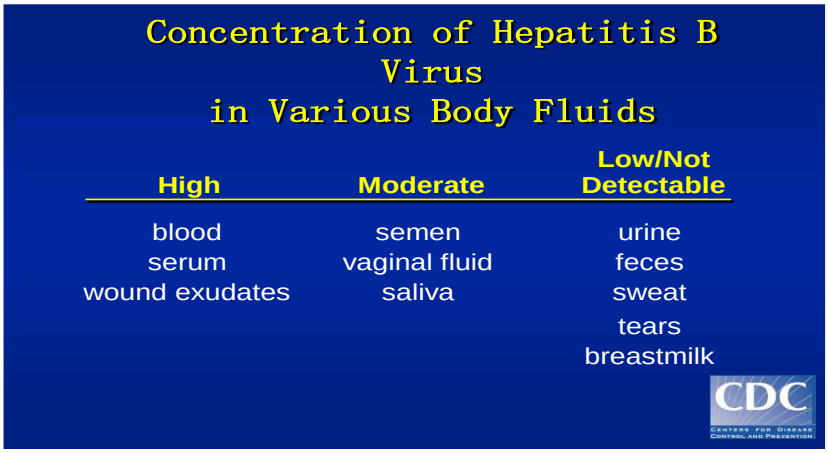
- The most important types are A, B and C.
- Hepatitis B is the only DNA virus.
- All can become chronic exp A + E
- Vaccine can be given for A, B and D

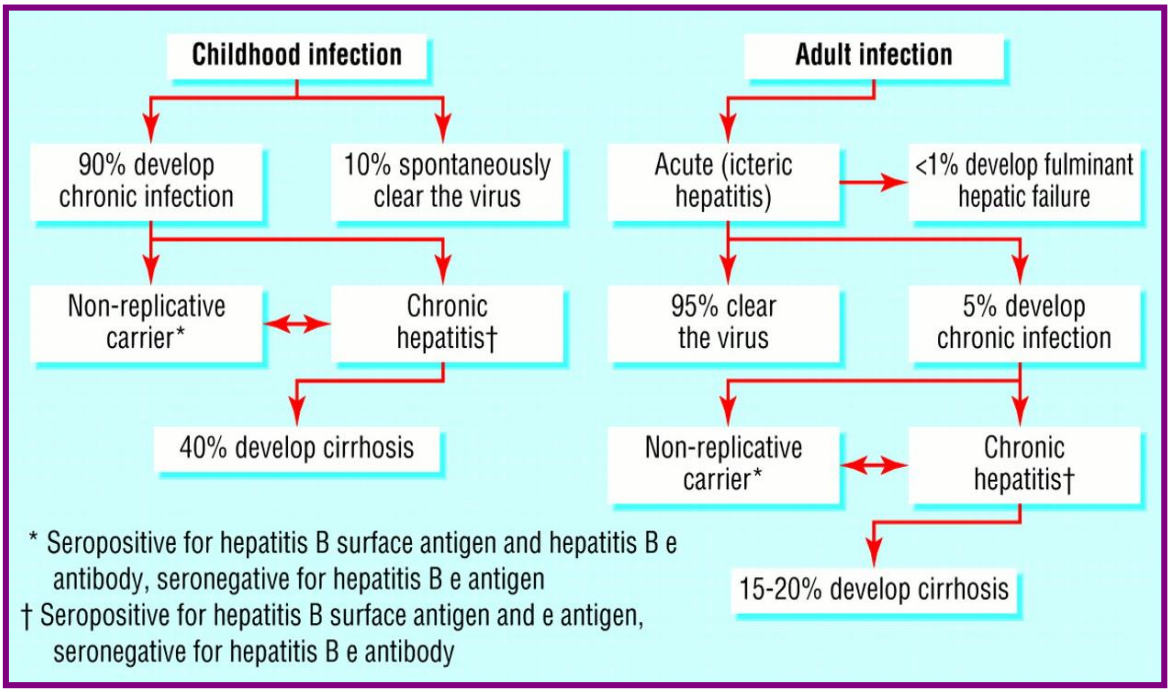


HBV Infection: (DNA double-stranded)

IP: 2-3 months

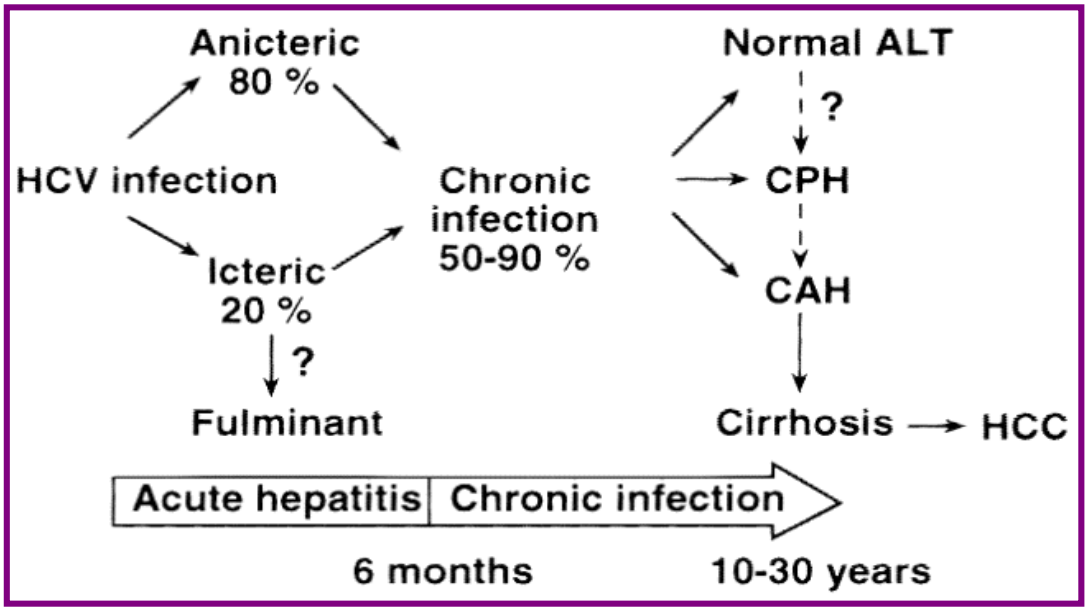
- Chronic infection: Children 90% , Adults 5% (low but still have it)
- Clinical illness (jaundice): 60% (most with chronic HBV).
- Mode of transmission: Sexual, parenteral (contaminated injections) and perinatal (positive HBSAG mothers).
- PREVENTION STRATEGIES:
  - Health education especially among medical personnel.
  - Mandatory screening of blood donors and expatriates.
  - Vaccination of risk groups.





HCV Infection: (Single-stranded RNA virus)

- IP: 2 months.
- Chronic infection: 80% (High).
- Clinical illness (jaundice): 20%
- Cirrhosis: 20%
- Mode of transmission: Sexual, parenteral and perinatal.
- Household Transmission (rare but not absent) through percutaneous/mucosal exposures to blood (sharing personal articles)
- Nosocomial Transmission through contaminated equipments (endoscopy, dialysis, unsafe injections).
- PREVENTION STRATEGIES:
  - Health education especially among medical personnel.
  - Avoiding shared use of Razors or brushes and any item that pierces the skin.



HAV infection: (Single-stranded RNA)

- Hepatitis A is the most common viral hepatitis occurring worldwide, often in epidemics.
- IP: 1 month
- Chronic infection: No (*A = Acute)
- Clinical illness (jaundice): 80%
- Mode of transmission: **Fecal-oral** (contaminated water or food) Sexual, parenteral (rare) and close contact (Household Transmission).
- PREVENTION STRATEGIES:
  - Personal hygiene & sanitation of water.

HEPATITIS A VACCINES

Recommended Dosages of Hepatitis A Vaccines

Schedule Vaccine	Age (yrs)	Dose	Volume (mL)	2-Dose (mos)
HAVRIX ®*	1-18	720 (EL.U.*)	0.5	0, 6-12
	>18	1,440	1.0	0, 6-12
VAQTA ®**	1-18	25 (U**)	0.5	0, 6-18
	>18	50	1.0	0, 6-18

  - Vaccination:
    - 1- HA vaccine (pre-exposure) "active vaccine"
    - 2- Immunoglobulin (pre & post-exposure) "passive"

HDV infection: (Single-stranded RNA)

It requires HBV for replication and to become stronger, it can cause acute severe hepatitis and relieved with HBV treatment.

HEV infection:

It's endemic in India & Middle-east, very similar to HAV (acute and usually from feco-oral route), during pregnancy it can lead to acute liver failure and death.

Diagnosis of Viral hepatitis

Based on the history, physical examination, liver function tests and serologic tests.

Note(s):

From "*Essentials of Kumar and Clark's Clinical Medicine 5th edition"***:**

Clinically the patient may be jaundiced, with an enlarged and tender liver, and there is laboratory evidence of hepatocellular damage with raised serum aminotransferase levels.

Liver function tests: >5-10 times of normal

There are increased levels of serum transaminase in an acute infection. The plasma bilirubin reflects the degree of liver damage. The alkaline phosphatase **(ALP)** rarely exceeds twice the upper normal limit. Prolongation of prothrombin time **(PT)** indicates the severity of the hepatitis. (2)

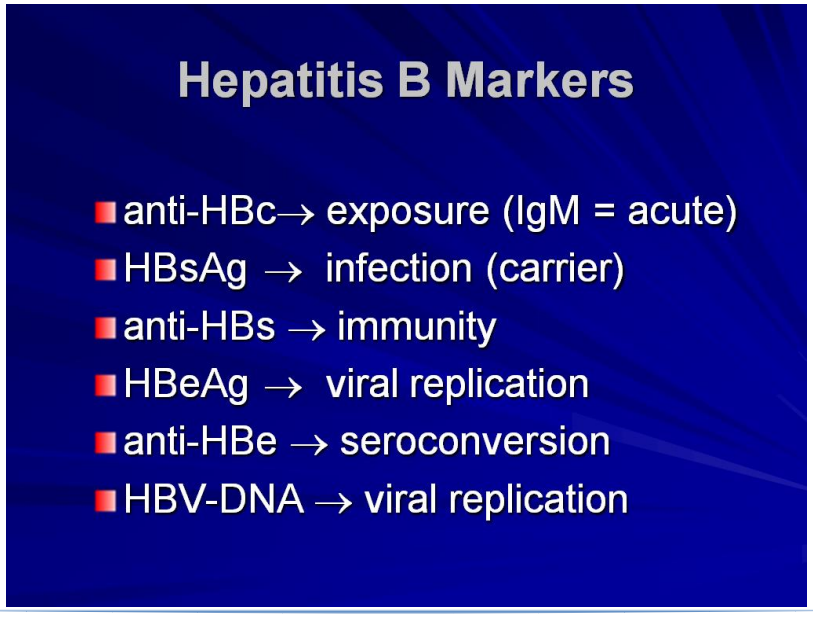
Serologic tests: imp!

1. Hepatitis A virus

The diagnosis of acute hepatitis A virus (HAV) infection is made by the detection of **anti-HAV antibodies** in a patient with the typical clinical presentation. Serum IgM anti-HAV is **the gold standard** for the detection of acute illness. Anti-HAV is positive at the onset of symptoms, peaks during the acute or early convalescent phase of the disease, and remains positive for approximately four to six months.(3)

2. Hepatitis B virus

Hepatitis B surface antigen (HBsAg) is the serologic hallmark of HBV infection. HBsAg appears in serum 1 to 10 weeks after an acute exposure to HBV, prior to the onset of hepatitic symptoms or elevation of serum alanine aminotransferase (ALT). Persistence of HBsAg for more than six months implies chronic infection. The disappearance of HBsAg is followed by the appearance of hepatitis B surface antibody (anti-HBs). In most patients, anti-HBs persists for life. In some patients, however, anti-HBs may not be detectable until after a window period of several weeks to months, during which **neither** HBsAg nor anti-HBs can be detected. At this time, the serologic diagnosis may be made by the detection of IgM antibodies against hepatitis B core antigen (IgM anti-HBc).(4)



3. Hepatitis C virus

Hepatitis C RNA can be identified in the blood as early as 2-4 weeks after infection. Anti-HCV antibodies persist in serum even after viral clearance, whether spontaneous or post-treatment. (2)

4. Hepatitis D virus

Due to the dependence of HDV on HBV, the presence of HBsAg is necessary for the diagnosis of HDV infection. The additional presence of **IgM antibody to hepatitis B core antigen (IgM anti-HBc)** is necessary for the diagnosis of acute HBV/HDV co-infection. (5)

5. Hepatitis E virus

The diagnosis of hepatitis E virus (HEV) is based upon the detection HEV in serum or stool by **polymerase chain reaction (PCR)** or by the detection of IgM antibodies to HEV. Antibody tests against HEV alone are less than ideal since they have been associated with frequent false positive and negative results. (6)

Treatment and management:

Hepatitis	Treatment
A	Supportive therapy.
B	Acute: supportive
C	Dual therapy with pegylated interferon-alpha given as weekly subcutaneous injection, together with oral ribavirin, a synthetic nucleotide analogue. (2)
D	There is no specific treatment for acute hepatitis D.(7)
E	Treatment of hepatitis E virus (HEV) infection remains supportive, as the disease appears to be self-limiting in nonimmunocompromised patients.(6)

Summary of hepatitis serology markers: imp

Agent	Marker	Definition	Significance
Hepatitis A virus (HAV)	Anti-HAV IgM type IgG type	Antibody to HAV	Current or recent infection or convalescence Current or previous infection, confers immunity
Hepatitis B Virus (HBV)	HbsAg	HBV surface antigen	Positive in most cases of acute or chronic infection
	HbeAg	e antigen; a component of HBV core	Transiently positive in acute hepatitis B May persist in chronic infection Reflect presence of viral replication, whole Dane particles in serum and high infectivity
	Anti-HBe	Antibody to e antigen	Transiently positive in convalescence Maybe persistently present in chronic cases Usually reflects low infectivity
	Anti-HBc (IgM or IgG)	Antibody to HBV core antigen	Positive in all acute and chronic cases Reliable marker of infection; past or current IgM anti-HBc reflects active viral replication Not protective
	Anti-HBs	Antibody to HBV surface antigen	Positive in late convalescence in most acute cases Confers immunity
Hepatitis C Virus (HCV)	Anti-HCV	Antibodies to a group of recombinant HCV peptides	Positive on average fifteen week after exposure; not protective Persists in chronic infection
Hepatitis D Virus (HDV)	Anti-HDV (IgM or IgG)	Antibody to HDV antigen	Acute or chronic infection; not protective

FULMINANT HEPATIC FAILURE (FHF): (Extra topic but important)

This is defined as severe hepatic failure in which encephalopathy develops in under 2 weeks in a patient with a previously normal liver (occasionally in some patients with previous liver damage; e.g. D virus superinfection in a previous carrier of HBsAg, Budd–Chiari syndrome or Wilson's disease). Cases that evolve at a slower pace (2–12 weeks) are called subacute or subfulminant hepatic failure. FHF is a rare but often life-threatening syndrome that is due to acute hepatitis from many causes. The causes vary throughout the world; most cases are due to viral hepatitis, but paracetamol overdose is common in the UK (50% of cases). HCV does not usually cause FHF although exceptional cases have been reported from Japan and India.

AUTOIMMUNE HEPATITIS: (Extra topic but important), (Dr. said it is the most common type nowadays in Saudi)

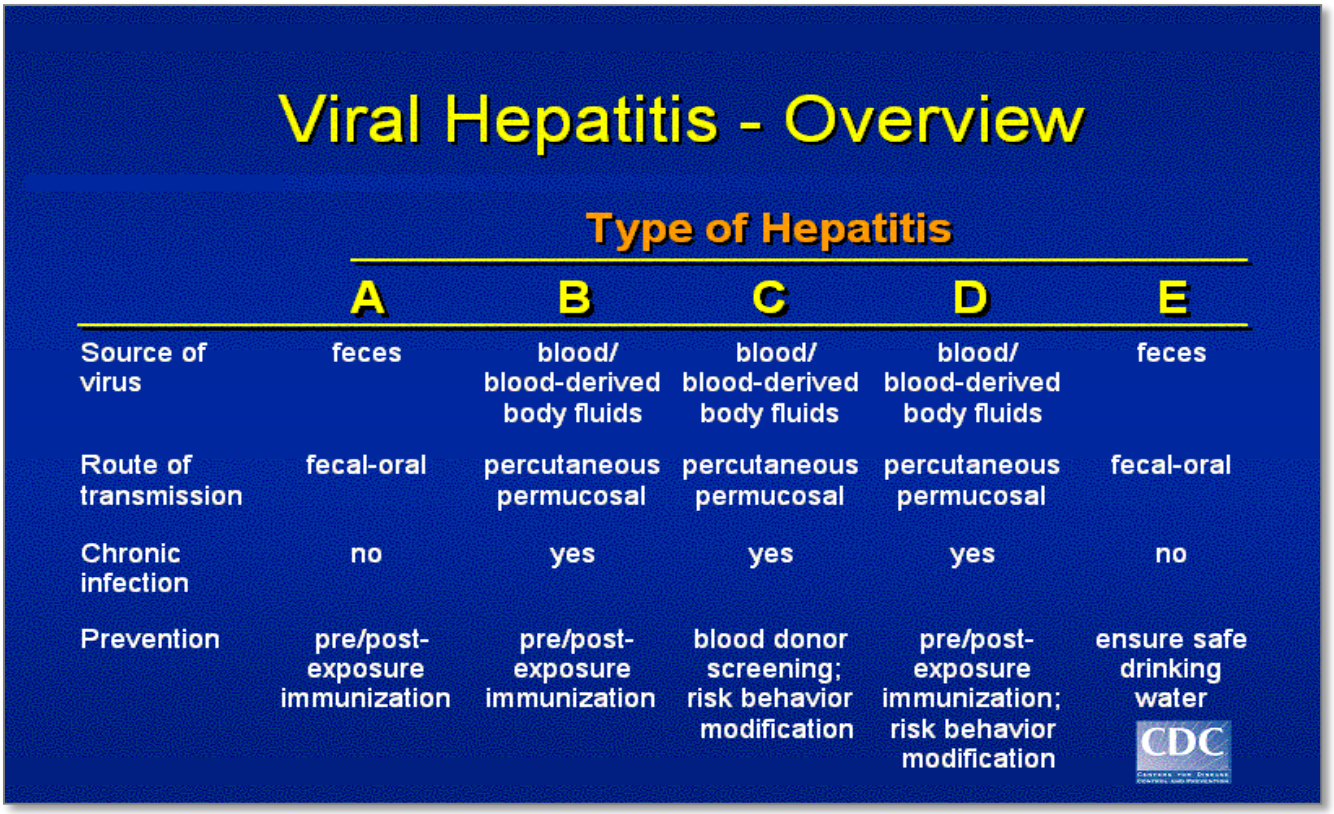
This condition occurs most frequently in women. In type I (see below) there is an association with other autoimmune diseases (e.g. pernicious anaemia, thyroiditis, coeliac disease and Coombs'-positive haemolytic anaemia) and 60% of cases are associated with HLA-DR3, DR52a loci, HLADRB1* 0301 and HLA-DRB2*0401. In Asians, the condition is associated with HLA-DR4.

Pathogenesis

The cause is unknown. It is proposed, in a genetically predisposed person, that an environmental agent (perhaps a virus) causes a sequence of T cell mediated events against liver antigens, producing a progressive necroinflammatory process which results in fibrosis and cirrhosis.

Treatment

Budesonide 3 mg × 2 or 3 daily has fewer side-effects than prednisolone and is now the preferred treatment.



List of references

(1)http://www.ncbi.nlm.nih.gov/books/NBK92038/

(2) Davidson's Principles and Practice of Medicine 22nd edition, viral hepatitis, page 948

(3) http://www.uptodate.com/contents/overview-of-hepatitis-a-virus-infection-in-adults#H8

(4) http://www.uptodate.com/contents/diagnosis-of-hepatitis-b-virus-infection?source=machineLearning&search=hepatitis+b&selectedTitle=1%7E150&sectionRank=2&anchor=H2#H2

(5) http://www.uptodate.com/contents/diagnosis-of-hepatitis-d-virus-infection#H2

(6) http://www.uptodate.com/contents/hepatitis-e-virus-infection#H10

(7) http://www.uptodate.com/contents/treatment-and-prevention-of-hepatitis-d-virus-infection?source=machineLearning&search=hepatitis+D&selectedTitle=3%7E32&sectionRank=1&anchor=H10#H10

SUMMARY

1. **Hepatitis** is inflammation of the liver. It can be caused by viruses (most common here), alcohol (west) or substance use, exposure to toxins, and certain diseases.
2. Hepatitis infection can be **acute** or **chronic**. Chronic hepatitis can lead to **Cirrhosis & HCC**.
3. **HBV** is mostly **acute** for adults. It can be transmitted sexually, parenteraly and perinataly. It can be prevented by **vaccination**.
4. **HCV** is mostly **chronic.** It can be transmitted sexually, parenteraly and perinataly. It can be prevented by **avoid sharing personal items**.
5. **HAV** is **always acute.** It usually spread through **fecal-oral route**. It can be prevented by personal **hygiene**, drinking from **clean water** and active and passive **vaccination.**
6. The diagnosis done by history, examination and **liver function & serology tests**.
7. The treatment for most infections are **supportive.**(exp HCV)

Questions

1) A 34-year-old male found to have ALT 130, AST 120, AIP 101, GGT 50, and Total bilirubin 18, INR 10, with strong family history of HBV.
Which ONE of the following is the most appropriate test to confirm HBV diagnosis?

a. HBsAg
b. HBcAg
c. HBsAb
d. HBeAg

2) A 40 years old male presented with jaundice, progressive abdominal distention and lower limp edema .He was diagnosed to have a chronic liver disease.
Which one of the following hepatitis can lead to the current presentation?

a. HAV
b. HBV
c. Herpes virus
d. HEV

Answers:

1st Questions: A

2nd Questions: B