VIRAL HEPATITIS

Hepatitis Virus	Family	Type	Trans-mission	Incubation	Age preference	Chronicity	Carrier	HCC Risk	Prognosis
A	picorna	ssRNA	**Feco-oral**	15-45 days	**Children**, young adults	No	No	NO	Excellent
B	hepadna	dsDNA partial ssDNA	**Blood** & **Sex**	30-180 days	Young adults, babies, toddlers	Yes (mainly in neonates)	Yes	Yes	Worse with age
C	Flavi-virus	ssRNA	**Blood** "percutaneous"	15-160 days	**Any age** but MC in **adults**	Yes	Yes	Yes	Moderate
D	Delta-virus	ssRNA	**Blood** & **Sex**	30-180 days	**Any age** Like HBV	Yes	Yes	Yes	Acute "good " Chronic "poor"
E	Hep-virus	ssRNA	**Feco-oral**	14-60 days	**Young adults**	No	No	No	Good

Always remember that

HAV & **HEV** have similarity

HBV & **HCV** have similarity

HDV always co-infected with **HBV** infection so HDV is a defective virus depending on HBV surface coat for entry into hepatocytes

No vaccine for ***HCV***

The same serotype for HAV

HBeAg is a truncated form of the major **core** polypeptide "the presence of pre-core convert HBc to HBe "

HBeAg is a secretory protein & marker for replication

Case (1): A 32 year old man develops fever, nausea, vomiting, malaise, anorexia& RUQ pain within a few weeks of returning to the U.S from a developing country. He also mentioned that his **urine** appears particularly **dark** &**light stool**. The patient states that he ate some shellfish that were harvested from a bay in which sewage enters. On physical examination, he is jaundiced & has tender hepatomegaly. Laboratory studies reveal marked elevations of AST& ALT. A hepatitis profile reveals (+)anti HAV-IgM ,(-) anti HAV-IgG &(-) HBsAg

1. What is the diagnosis?

Acute Hepatitis A infection. Hepatitis A is an enterically transmitted picornavirus that is highly endemic in the developing world where sanitation is poor. Hepatitis A virus enters hepatocytes, where it replicates & leads to immune-mediated damage of the cells

➔ Keep in mind that viral infection of the hepatocytes isn't cytopathic, but the cytotoxic T cell response results in cell death.

2. Explain how the results of the hepatitis profile facilitate the dx of an acute infection rather than a chronic one.

IgM is the 1st antibody isotype produced in response to a new infectious agent & can persist for several months. A previous infection would have been negative for anti-HAV IgM & positive for anti-HAV IgG because the IgG is produced later in the infection providing lifelong immunity

3.Should the patient be concerned about developing a chronic infection or hepatic cirrhosis ?

No, because hepatitis A doesn't develop into a chronic infection or lead to cirrhosis. The prognosis is excellent & only supportive therapy is required

4. What are the complications followed by this infection?

Cholestasis – relapsing disease& fulminant hepatitis are rare &commoner in older patients

5. Can hepatitis A be prevented?

Yes, an inactivated vaccine for hepatitis A exists

Also can be inactivated by boiling for 1 minute, UV light, chlorine, formaldehyde

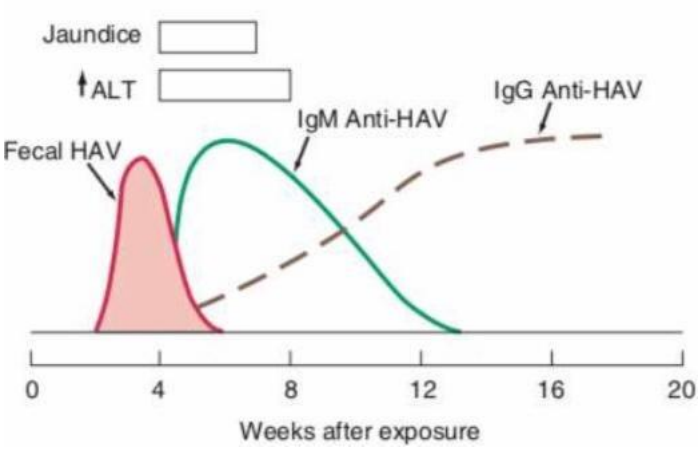
Note: infection with hepatitis A confers lifelong immunity against future HAV infections

6. What is the treatment of hepatitis A?

- ✓ Symptomatic "avoid paracetamol &alcohol" 85% have full recovery by 3 months &nearly all after by 6 months
- ✓ Fulminant hepatitis should be treated by supportive therapy
- ✓ Fatalities are commoner with advancing age& in those with HCV co-infection

*subclinical in children <5 years

*acute hepatitis more frequently with increasing age



Important notes: The patient start shedding in feces before symptoms appear

Anti HAV IgM antibody appears when ALT peaks & shedding decreases

Then IgG will predominate & providing protection

Morphology of HBV

i. **Double shelled spherical virion (complete) →42 nm →surface& core**
ii. **Nucleocapsid core only** HBcAg & HBeAg
iii. **Spherical &filamentous** representing excessive virus coat material → only HBsAg

Case (2): A 45 year old woman presents to the clinic with complains of a flu like illness. The patient is currently employed as a nurse. She states that approximately 1 month ago, she started feeling fatigued& feverish. Soon she developed RUQ pain. Last week she noticed that her urine was darker than usual. She claimed **needlestick** exposure a few months earlier. Checking liver enzymes & serologic findings for viral hepatitis, ALT& AST are markedly elevated, hepatitis serologic assays reveal the following findings

*HBsAg (+) *Anti HBs negative *Anti HBc IgM (+) *Anti HBc IgG (-) *Anti- HCV (-)

1. What is the diagnosis?

Acute hepatitis B infection

2. What other viruses would you consider screening for in this patient?

HDV, it requires co-infection with HBV for replicating

3. What are the chronic phases of hepatitis B?

Replicative immune tolerant phase (perinatal infection only)→high levels of virus "HBeAg +" but no hepatitis, normal ALT & a largely normal liver

Replicative immune clearance "HBeAg seroconversion may occur" mainly associated with exacerbations which may be misinterpreted as acute hepatitis B

Inactive carrier state →remission &patients are HBeAg (-), anti HBe (+)& ALT usually normal

*several ALT & HBV viral loads over 12 months are required to confirm someone is inactive

*complications of chronic hepatitis B →end stage liver disease &HCC

4. What are the extrahepatic manifestations of chronic HBV

Serum sickness, polyarteritis nodosa (PAN) , glomerulonephritis, with most cases seen in children (presents as nephrotic syndrome)

5. How is HBV treated?

Avoiding alcohol, practice safe sex, hepatitis A vaccination "in low prevalence areas" , HBV immunization of household members

- Tx to prevent HBV after exposure with no previous vaccination →immunoglobulin (Anti HBs) within 12 hours + vaccine
- Tx of acute HBV → supporative care unless sever cases/ patients with underlying illness→ Antiviral drugs
- Tx of chronic HBV → lifelong tx to reduce risk of complications &transmission

Antiviral medications include tenofovir, lamivudine, entecavir→ all help reduce the virus amount& liver damage

- Interferon injection mainly for younger patients/ women who wants to get pregnant "can't be used in pregnancy"
- Liver transplant

6. How HBV can be prevented?

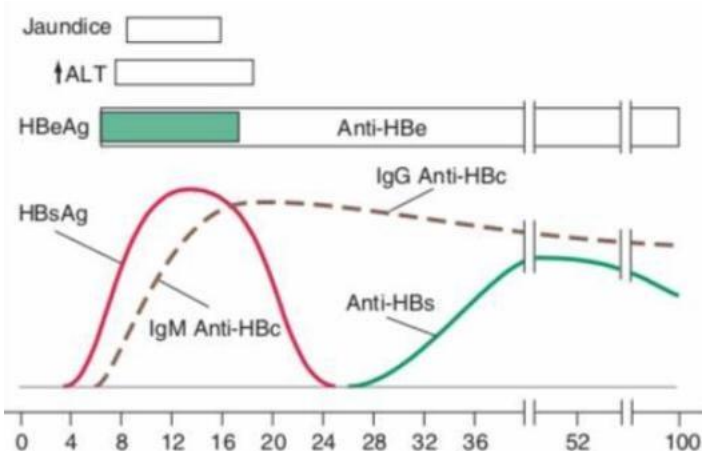
Education – screening of blood products – immunization for high risk groups including health care workers (YOU!) , who always receives blood, haemodialysis recipients …..Hepatitis B immunoglobulin should be given to neonates born to HBsAg + mothers (unless anti HBe +) & needlestick recipient

Dx of HBV

The 3 types of antigens associated with this infection are **surface antigen HBsAg, core antigen HBcAg, HBeAg "**that circulates in blood during viral replication **"**

HBcAg isn't clinically useful **because it's not detectable in serum (intracellular antigen)** so we don't have to be worry about this one**. HBsAg is the most important of the 3** because it's the 1st antigen to appear after infection & the last antigen to disappear, and if it's present in serum the patient is infected with HBV (although you can't tell yet whether this indicates acute, chronic, or carrier state infection) **HBeAg** is your infectivity marker→ this is important in pregnant women→the presence of HBeAg indicates a high infectivity rate. 90% of neonates will acquire HBV from mom if she is **(+)**HBeAg while (10-15%) if the mom is **(-)**HBeAg

- Anti-HBsAg are deemed the protective antibody → susceptible people are given this antibody
- Resolution of HBeAg predict resolution of the disease ,having it +ve for >3 months →chronic state
- Anti-HBc is a non-protective antibody



HBsAg as early as 1-2 weeks **detected before elevated ALT & symptoms** by as much as 2-6 weeks, undetectable after 1-2 months. HBeAg appear with HBsAg (refer to high replication & DNA) &anti HBc appears within 1-2 weeks before Anti HBs & after HBsAg.

- ➔ If a patient is positive for anti HBcAg of the IgM isotype it indicates acute/recent infection
- ➔ If anti HBcAg-IgG is present the patient has chronic disease **or** he has recovered from disease (we need to look at anti-HBs levels to determine this)

Window period →No HBsAg & Anti HBs →the only marker detected is Anti HBc

Isolated Anti HBc may be seen in 2 other situations →years after recovery from acute HBV (anti HBs fallen to undetectable levels)

→years after chronic HBV (HBsAg fallen to undetectable levels)

After window period Anti HBs & Anti Hbe antibodies will become detectable in the serum

- ➔ Vaccinated person against HBV will be positive **only** for **anti HBs** & **not** anti HBc

The question is how to distinguish between a cured patient vs an immunized patient as both are Anti HBs positive? Look for **anti-HBc-IgG** " positive in recovered patient "

For HBsAg → those who clear infection become negative after 4-6 months → positivity beyond this period indicates chronic HBV

→Patients who are positive to HBsAg & Anti Hbs (the antibody can't neutralize the virus)→**Carriers**

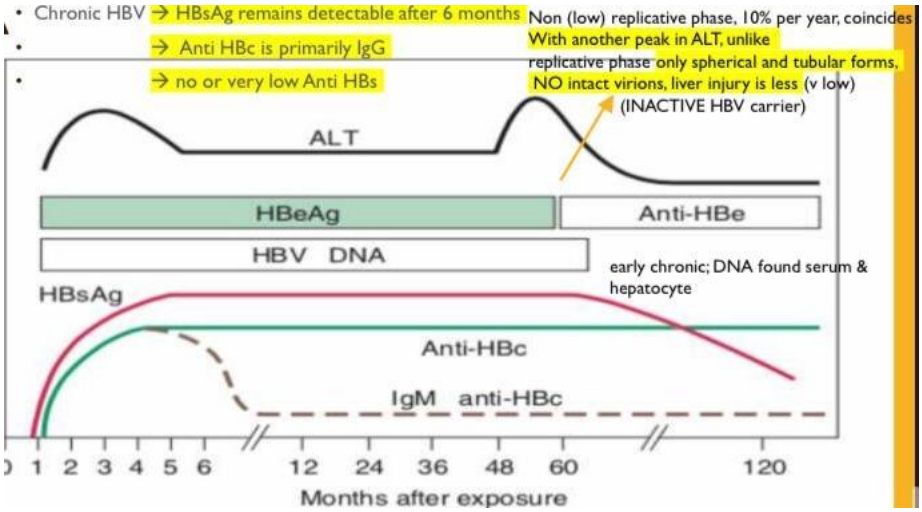
- Markers of replication : HBV DNA "quantitative & HBeAg "qualitative"

The prevelance of hepatitis B is in China & Sub-Saharan Africa

In **acute** infection **Anti-HBc-IgM** should also be detected

Table 8.3 Diagnosis of hepatitis B virus

	HBsAg	Anti-HBs	HBeAg	Anti-HBe	Anti-HBc IgM	Anti-HBc IgG	HBV DNA
Acute infection	✓		✓				+++
Window					✓		+
Prior infection		✓				✓	
Vaccinated		✓					
Chronic (high infectivity)	✓		✓			✓	+++
Chronic (low infectivity)	✓			✓		✓	±
Pre-core mutant	✓			✓		✓	++



This is the chronic HBV

Having HBsAg & Anti HBc

After 3-4 months class switching of IgM to IgG happens

10% esch year converting from high infectivity to low infectivity → ALT is elevated another time like if he has a new acute hepatitis →after decreasing sero-conversion takes place from HBeAg to Anti-HBe & HBV DNA disappears

---

Hepatitis C virus

- Envelope proteins are coded in hypervariable region, core is conserved →so when detection is needed look for the core
- 7 genotype
- Commoner in **Egypt, Japan, Italy**
- Cytotoxic T lymphocytes (cellular) →suppressing HCV RNA
- Also humoral response but aren't sufficient to clear the virus
- Acute HCV → most infections are anicteric (non jaundice)→if diagnosed early tx is appropriate
- Fulminant HCV commoner in HBV co infection
- Chronic HCV →ALT levels fluctuate independently of symptoms, whereas **HCV RNA** levels remain constant (which helps in Dx)
- Dx →serology detection of antibody to recombinant HCV peptides
  →HVC RNA quantitative to treat & qualitative to confirm dx& to achieve sustained virological response
- Tx → aims to reach SVR "absence of HCV RNA by PCR at 6 months after finishing tx "

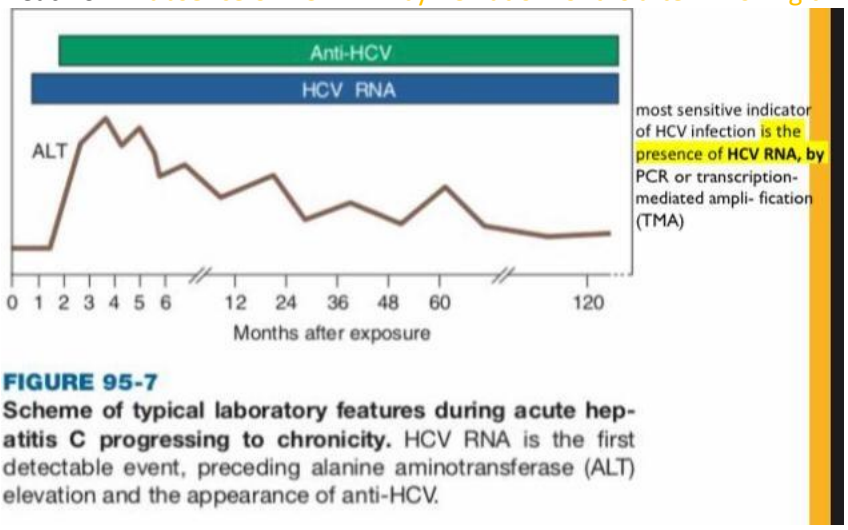


FIGURE 95-7
Scheme of typical laboratory features during acute hepatitis C progressing to chronicity. HCV RNA is the first detectable event, preceding alanine aminotransferase (ALT) elevation and the appearance of anti-HCV.

Hepatitis D

- consist of a core of delta & single stranded circular RNA enclosed in an envelope provided by HBV (HBsAg)
- 8 genotypes
- Most patients with delta antigen in the liver have anti delta in their serum
- HDV superinfection results in suppression of HBV replication (HBsAg & HBV DNA levels drop)
- Higher incidence of HDV infection in HBsAg + patients with acute& chronic hepatitis compared with asymptomatic
- Symptoms range from asymptomatic to fulminant liver failure 5-20%(ten times commoner than in other hepatitis)
- Western countries see higher rates of fulminant disease related to genotype 1 (dominant in these areas)

- May cause liver flare → 80% become chronic
- Causes acute hepatitis indistinguishable from classic acute HBV→5% develop chronic HDV
- HDV exacerbates the pre-existing liver disease due to HBV with potentially rapid progression of cirrhosis

---

HEV" icosahedral non-enveloped"

- Commonest cause of acute hepatitis in certain parts of Asia (prevention for travelers)
- Fulminant disease is more common in the third trimester of pregnancy & elder men →carries high mortality (up to 20%)
- 4 genotypes →3 (milder)&4 infect humans & animals
- Waterborne mainly & some food-borne
- Perinatal transmission &severe neonatal disease can occur
- Similar to HAV but more severe
- Dx by RT-PCR in blood & **stool** (viremia is short but may be prolonged in some patients)

→in stool it appears week before illness onset remaining until 2 weeks after

- HDV antibodies appear late (4 weeks) & may vanish after resolution
- Supportive – transplant for liver failure – reduction in immunosuppressive therapy

Done By: RAND ASSAF

You deserve to be the best