

VIRAL HEPATITIS

Dr Kulwant Singh

Dean: Faculty of Homoeopathy, V B University, Hazaribag

Principal: S H Medical College & Hospital, Jamshedpur

Kulwant1955@gmail.com

DEFINITION

Primary infection of the liver caused by a small group of viruses (hepatotropic viruses) having a particular affinity for the liver is known as Viral Hepatitis.

HEPATOTROPIC VIRUSES

- **HEPATITIS VIRUS A (HAV) :**

HAV causes benign self limited, acute, transient infectious hepatitis. It does not lead to chronic hepatitis or a carrier state and only rarely does it cause massive liver necrosis (Fulminant Hepatitis)

Year of Identification: 1973

Morphology: HAV is a small, non enveloped virus, 27nm(nanometer) in diameter, cubical in shape and contains single stranded RNA.

Epidemiology:

HAV occurs throughout the world and is endemic in countries with substandard hygiene and sanitation. Children are more commonly affected but severity increases with age. In India about 90% of children are serologically positive by 10 years of age. When the sanitation and hygiene is improved, the morbidity increases.

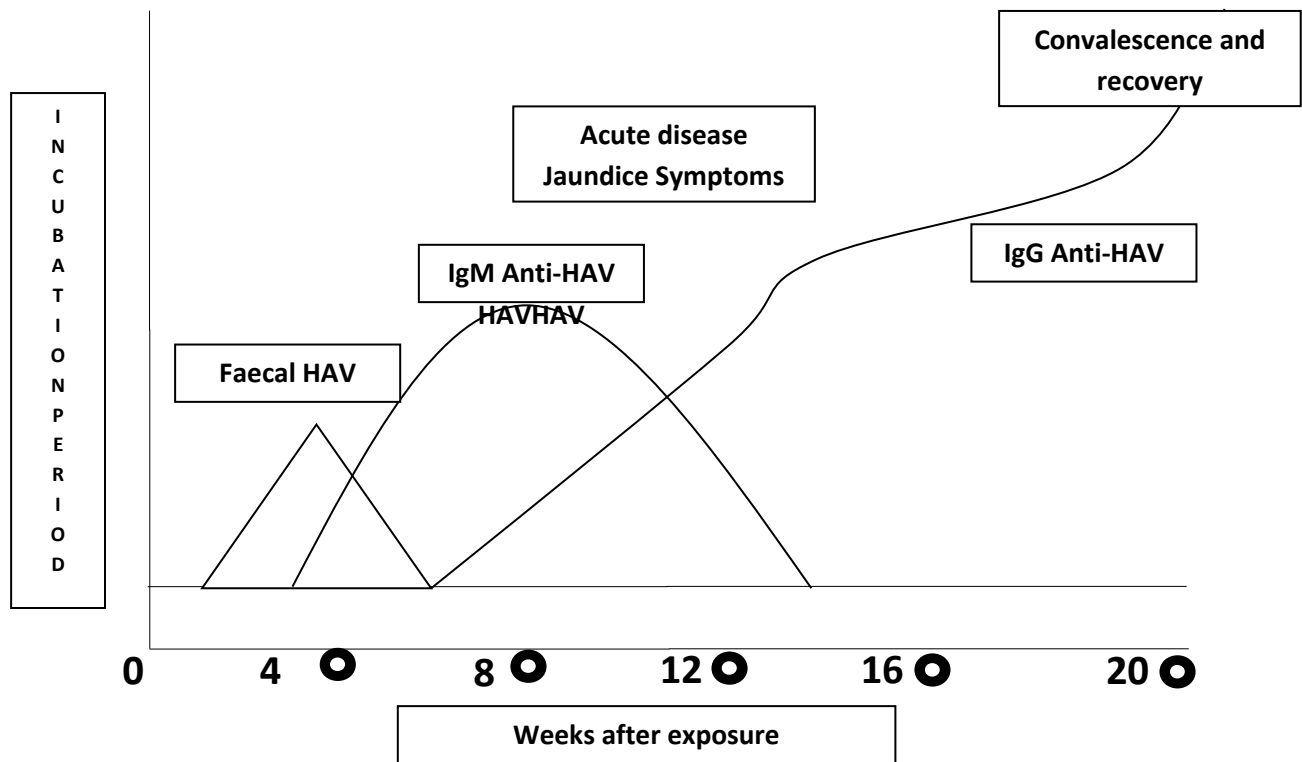
Incubation Period: 15-45 days

Mode of Infection:

- Faecal-oral route: HAV is shed in the stool for 2-3 weeks before and 1 week after the onset of Jaundice. Thus close personal contact with an infected individual or faecal oral contamination during this period causes infection. This explains the occurrence of outbreaks in institutional settings such as schools and nurseries. HAV is spread by ingestion of contaminated water and food (esp. sea food).
- Occasionally by infusion of infected blood or contaminated needle during the stage of transient viraemia.
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Immunological markers of HAV:

Specific antibody of IgM type appears in blood against the HAV at the onset of symptoms. It is a reliable marker of acute infection. As the IgM titer rises, the faecal shedding of the virus ends. The IgM response usually begins to decline in few months and is followed by the appearance of IgG anti HAV. During convalescent phase, the titer of IgG starts rising which persists for life time, proving protective immunity against reinfection by HAV.



Prevention and Control of HAV

1. Isolation of the patient
2. Disinfection of contaminated water and food
3. Disposal of night soil
4. Immunization: By human immunoglobulin derived from pooled plasma of healthy donors. It induces passive immunity. Immunoglobulin in 0.02 mg/kg IM should be given before exposure to the virus or during incubation period to the household and institutional contacts, elderly people and to pregnant women.

• HEPATITIS B VIRUS (HBV)

HBV is the most versatile of the hepatotropic viruses. It can produce the following:

1. Acute Hepatitis
2. Chronic nonprogressive hepatitis
3. Chronic active or progressive hepatitis ending in cirrhosis.
4. Fulminant hepatitis with massive liver necrosis.
5. Hepatocellular carcinoma

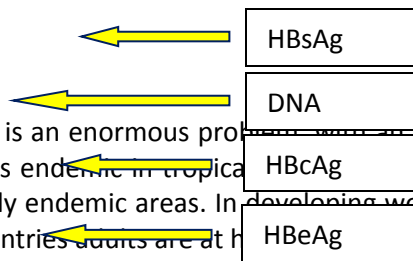
SCHEMATIC PRESENTATION OF THE POTENTIAL OUTCOME OF HEPATITIS B INFECTION IN ADULTS

ACUTE INFECTION WITH HBV	Subclinical Disease 60-65%	100%	Recovery
	Acute Hepatitis 20-25%	99% >1%	
	Healthy Carrier 5-10 %	*****	*****
	Persistent Infection 4%	67-90%	Recovery
		10-33%	Chronic Hepatitis: 20-50% Cirrhosis 10% of cirrhosis leads to hepatocellular carcinoma ---- death

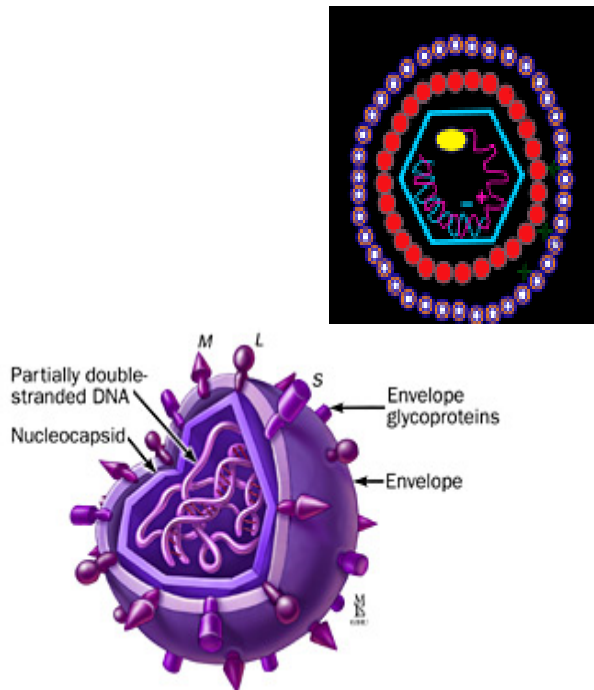
Year of identification : 1965

Epidemiology

Globally liver disease caused by HBV is an enormous problem with an estimated worldwide carrier rate of more than 300 million. HBV is endemic in tropical and subtropical countries. About 3/4th of the world population is living in highly endemic areas. In developing world HBV is more common in childhood whereas in developed countries adults are at high risk due to their life style.



MORPHOLOGY OF HBV



The mature HBV is a 42nm, spherical, double layered “Dane Particle”. It contains double stranded DNA in its core of 28 nm, enveloped with a capsule of Protein, Lipid and Carbohydrate. The antigenic activity of the core DNA is designated HBC(Core)Ag. The inner part of the envelope has its own antigen known as HBeAg. The outer surface of the envelop contains a surface antigen called HbsAg, which is also known as “Australian Antigen”, because it was first identified by Blumberg in the serum of an Australian aborigine in the course of genetic studies.

Incubation Period: 30-180 days (mean 100 days)

Reservoir of Infection: Man is the only source of infection

Period of communicability:

HBV is present in the blood in the last stages of incubation period and during active episodes of acute and chronic hepatitis. It is also present in all physiologic body fluids , with the exception of stool.

Infective material:

1. Blood : main source of infection
2. Body secretions: semen, saliva, sweat, tears, breast milk, vaginal secretions and path. effusions

Mode of transmission:

1. Parental Route: By infective blood and blood products
 - Blood transfusion
 - Contaminated needles
 - Accidental prick of skin
 - Handling of infected blood
 - Accidental inoculation of minute quantity of blood during surgical and dental operation
 - Immunization
 - Traditional tattooing
 - Ear piercing
 - Nose pricking
 - Ritual circumcision
 - Acupuncture
 - Accidental percutaneous inoculation by razors and tooth brush
2. Vertical Transmission: Spread from an infected mother to a neonate during birth is common. It often leads to the carrier state for life. Transplacental infection to foetus in uterus may occur rarely.
3. Sexual transmission: By intimate contact or sexual intercourse
4. By other route: saliva, sweat, tears, urine, menstrual blood, colostrums etc.

High Risk Group for HBV:

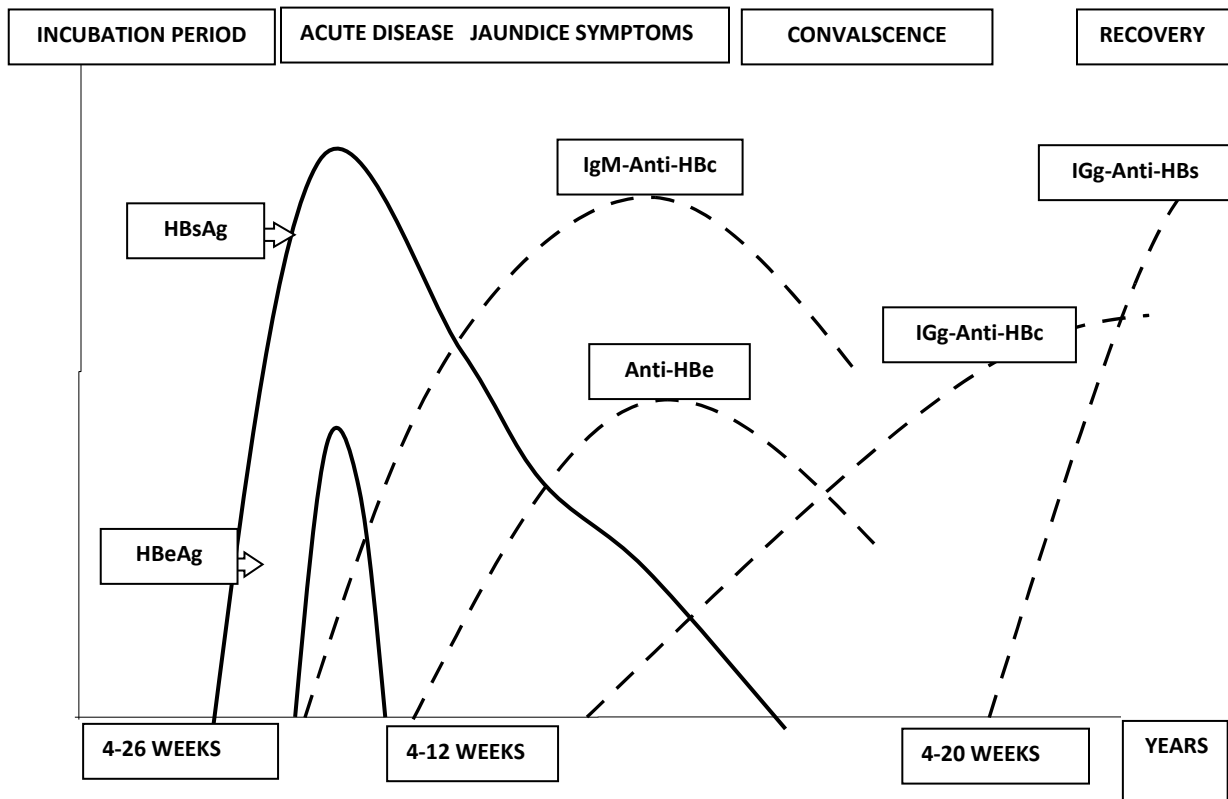
- IV drug users
- Gays-male homosexuals
- Close contact with infected person
- Chronic haemodialysis
- Medical / Nursing personnel, dentist, surgeon, intensive care unit staffs, liver unit, endoscopy unit, oncology unit and lab staff handling blood.

Immunological marker of HBV

1. HBsAg or Australia Antigen: it is the first antigen to appear in blood in HBV infection. It appears during the incubation period and peaks during the acute stage of the disease. It usually declines to undetectable level in 3-6 months. Presence of HbsAg in blood is the diagnostic hallmark of

HBV infection.

2. HBeAg: It appears in the serum soon after the HbsAg and indicates active viral replication. Persistence of HbeAg is an important clinical indicator of continued active viral replication , continued infectivity and probable progression to chronic hepatitis.
3. Anti-HBc Antibody: Antibodies against the viral core antigen, anti-HBc are the first to become detectable after exposure to HBV. Anti HBc of IgM type appears in the serum shortly before the onset of symptoms and coincides with the onset of elevated transaminases (SGOT, SGPT) , indicating hepatic injury. Over months the IgM antibody is replaced by IgG type of anti-HBc. So an elevated level of IgM anti-HBc indicates a recent acute infection.
4. Anti-HBe Antibody: It appears shortly after the disappearance of HbeAg, implying that the acute infection has peaked and the disease is on decline.
5. Anti-HBs Antibody: It appears in the patient's serum a few weeks to months after the disappearance of HbsAg. This interval is known as "window period", during which Anti-HBe and Anti-HBs are the only markers of the disease. In most of the patients , Anti-Hbs persists for life, confirming protection against any further HBV infection.



Prevention and control of HBV infection:

1. Isolation of the patient
2. Disinfection of contaminated material
3. Use of fresh needles
4. Adequate sterilization of all instruments
5. Detection of carriers and their treatment
6. Carriers should be advised to use barrier contraceptives
7. No sharing of razors, toothbrushes with the carriers

8. Immunization:

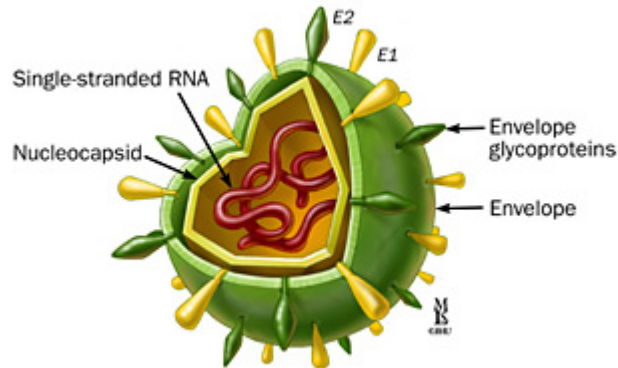
- Before Exposure: Hepatitis B vaccine at 0,1 and 6 months to high risk groups e.g. health workers, gay men, IV drug users, haemodialysis patients, hemophiliacs and all neonates in endemic areas .
- After Exposure: Hepatitis B immunoglobulin (HBIG) 0.06 ml/Kg I.M immediately after needle stick, within 14 days of sexual exposure, or at birth in case of HBsAg positive mother plus vaccine series.

3. HEPATITIS C VIRUS (HCV)

Persistent infection and chronic hepatitis are the hallmarks of HCV infection which usually leads cirrhosis of liver in more than 50% of cases.

Year of identification: 1989

Morphology: HCV is a small enveloped single stranded RNA virus with a 30-60 nm diameter.



Mode of transmission:

1. Parental: inoculations and blood transfusion
2. Vertical transmission
3. Close personal contact – sexual contact

Incubation Period: 20-90 days (mean: 6-12 weeks)

Immunological markers: presence of anti-HcV in the patient's serum. Episodic elevation of serum transaminase (SGOT, SGPT) with intervening normal or near normal periods.

4. HEPATITIS D VIRUS (HDV)

it is also known as “delta agent” and “hepatitis delta virus”. It is a unique virus with defective replication, causing infection only when it is encapsulated by HbsAg. This HDV is totally dependent on HBV for multiplication and causes hepatitis only in the presence of HBV.

Year of Identification: 1977

Morphology: HDV is a 35 nm, single stranded double shelled particle which resembles the “Dane

Particle" of HVB.

Mode of transmission: HDV infection occurs in the following ways:

- Acute co-infection: it occurs after exposure to serum containing both HDV and HBV. The HBV first becomes established to provide the HbsAg necessary for the development of complete HDV virions.
- Superinfection: Exposure of a chronic carrier of HBV with a new inoculation of HDV results in disease about 30-50 days later.

Incubation period: 30-50 days in superinfection

Immunological Markers of HDV:

1. Presence of IgM anti-HDV is the most reliable indication of recent HDV infection.
2. Presence of IgM anti-HDV and IgM anti-HbcAg in case of acute co-infection.
3. Presence of HbsAg and anti-HDV in case of superinfection.

Prevention: Hepatitis B vaccine (non carriers only)

5. HEPATITIS E VIRUS (HEV)

HEV hepatitis is an enterically transmitted infection occurring primarily in young to middle aged adults. A characteristic feature of HEV infection is the high mortality rate among pregnant women, approaching 20%. HEV does not cause chronic hepatitis or persistent viremia.

Year of identification: 1980

Morphology: HEV is an unenveloped single-stranded RNA virus, 32-34 nm in diameter

Mode of infection: water borne

Incubation period: 15-60 days (mean 6 weeks)

Immunological markers: a specific antigen (HEVAg) can be identified in the cytoplasm of hepatocytes during active infection.

Prevention:

1. Disinfection of contaminated water or food
2. Disposal of night soil
3. Improvement of personal and community hygiene.

ACUTE VIRAL HEPATITIS

Acute infection of the liver caused by hepatotropic viruses is known as acute viral hepatitis.

AETIOLOGY

1. Hepatitis A virus (HAV)
2. Hepatitis B virus (HBV)
3. Hepatitis C Virus (HCV)
4. Hepatitis D Virus (HDV)
5. Hepatitis E Virus (HEV)

Mode of transmission: as mentioned earlier

Incubation Period: as mentioned earlier

Period of Infectivity: Peak infectivity occurs during the last asymptomatic days of the incubation period and the early days of acute symptoms.

Pathology:

The morphologic changes in acute viral hepatitis are almost the same regardless of the causative agent.

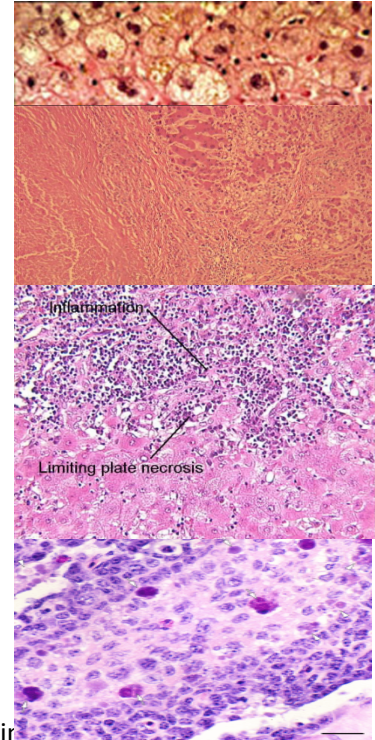
- (A) Macroscopically: The liver is enlarged and yellowish or greenish in colour.
(B) Microscopically:

- a) **Ballooning degeneration:** diffuse swelling of the hepatocytes, so that the cytoplasm looks empty and contains only scattered wisps of cytoplasmic remnants.
b) **Necrosis of Liver Cells :** The necrosis is variable in extent and degrees.

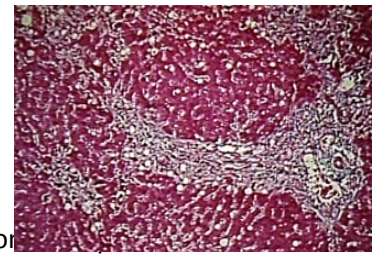
i) **Necrosis of isolated liver cell or Piecemeal necrosis**

ii) **Severe Necrosis**

- iii) **Bridging Necrosis:** Extensive necrosis connecting central or portal to central parts of the adjacent lobule. Necrotic hepatocytes may be evident as fragmental eosinophilic Councilman bodies or may be phagocytosed leading to accumulation of lymphocytes and



macrophages.



- c) **Hypertrophy and hyperplasia of Kupffer cells:** They often crowd out dead hepatocytes.
- d) **Infiltration of portal tract with inflammatory cells:** Lymphocytes, plasma cells and macrophages.
- e) **Evidence of hepatocytic regeneration :** during the recovery phase

Clinical Features:

A) PRE ICTERIC PHASE (1-2 weeks)

Symptoms:

1. Anorexia
2. Nausea and vomiting
3. Headache
4. Malaise
5. General Fatigue
6. Influenza like symptoms
7. Muscle and joint pains
8. Discomfort in upper abdomen
9. Diarrhea
10. Distaste for cigarettes
11. Fever, rash and arthralgia , in case of Hepatitis B due to circulating immune complexes.

Signs:

1. G/E: Pallor, Temperature 100-101 degree F
2. P/A: Liver slightly enlarged and tender

B) ICTERIC PHASE :

It is usual in adult (but not children) with HAV but is absent in about half of the cases of HBV and the majority of cases of HCV. It is usually caused by conjugated hyperbilirubinaemia due to intra hepatic cholestasis. Surprisingly with the onset of the icteric phase, the constitutional symptoms begin to abate and the patient feels better.

Symptoms:

1. Pain in Rt Hypochondrium
2. Pruritus due to retention of bile salts
3. High colored urine.

Signs:

1. G/E: Jaundice, Pulse: Bradycardia
2. P/A: Liver: enlarged and tender. Spleen: enlarged in 25% of cases
3. Urine: Dark due to presence of bilirubin
4. Stool: Pale , may be clay coloured due to cholestasis
5. There may be signs of glomerulonephritis, arthritis or systemic vasculitis in cases of Hepatitis B.

Investigations:

1. Liver Function Tests:

i) SGOT	Raised
ii) SGPT	Raised
iii) Serum Alkaline Phosphate	Mildly raised
iv) Serum Bilirubin	Increased
v) Prothrombin Time	Prolonged
vi) Hyperglobulinaemia	

Blood Count: Neutropenia and Lymphopenia followed by relative Lymphocytosis.

2. **Blood Count:** Neutropenia and Lymphopenia followed by relative Lymphocytosis.

3. **Urine:** Bilirubin present, Bile salts may be present.

4. Virology Tests:

- Hepatitis A: presence of IgM anti HAV in the serum
- Hepatitis B: Presence of IgM anti HBC in the serum
Presence of HbsAg in the serum
- Hepatitis C: Presence of anti HCV in the serum
Presence of HCV-RNA in blood
- Hepatitis D: Presence of anti HDV in the serum
- Hepatitis E: Presence of anti-HEV

Complications :

- Acute liver failure (Fulminant Hepatitis)
- Progression to chronic hepatitis
- Post necrotic liver cirrhosis
- Hepatocellular carcinoma
- Aplastic Anemia

Differential Diagnosis:

- Drug Jaundice
- Alcoholic Hepatitis
- Stone in the Bile Duct
- Carcinoma of Head of Pancreas
- Infectious mononucleosis

Treatment:

General Management:

- Bed rest
- High Caloric diet
- Avoidance of fat in the diet
- Intravenous feeding in case of severe nausea and vomiting
- Abstinence from alcohol until full recovery
- Vitamins: Vitamin B complex and Vit K should be given

Homoeopathic Treatment:

Treatment should be directed towards relief of acute symptoms, treatment of chronic miasm and prevention of further attacks by administration of proper constitutional medicines as per patient's totality. Following medicines may be helpful as and when indicated:

Sulphur: treatment of hepatitis should always be started with this medicine.

Cheidonium Maj: Constant pain under the lower and inner angle of Rt. Scapula. Tongue coated thick yellow with red edges, shows imprint of teeth. Desire for very hot drinks.

Bryonia: Burning , stitching pains in the Right Hypochondrium, worse from pressure, coughing and breathing; great thirst for large quantities of cold water at long intervals; aggravation from least motion and better by absolute rest.

Mercurius: stabbing pain in the liver region with chilliness. Tongue large and flabby, shows imprint of teeth, great thirst with moist tongue. Aggravation by lying on right side.

Natrum Sulph: Jaundice with vomiting of bile and sharp stitching pain in the Right Hypochondrium. Dirty greenish-grey or brown coating on tongue; aggravated by lying on left side and dampness.

Lycopodium: Pain goes from right to left side. Good appetite but a few mouthfuls fills upto the throat and he feels bloated. Red sand in urine. Aggravation from 4-8 PM. > warm food and drinks

Magnesia Mur: Pressing pains in liver when walking and touching it. Eructation tasting like rotten eggs, like onions. Constipation: stool difficult to pass, crumbling at verge of anus. Can pass urine by becoming down with abdominal muscles, Aggravated by lying on left side.

Podophyllum: Patient constantly rubs and shakes the region of liver with his hand. Diarrhoea specially morning, profuse stools with prostration.

Other important medicines are Hydrastis, Myrica, Carduus M, China, Arsenic Album, Carbo Veg etc.

Medicines for complications:

- Malignant Jaundice: Phosphorus, Crotalus H.
- Atrophy of Liver: Digitalis, Podophyllum, Phosphorus
- Enlargement of Liver due t Alcohol: Absinthium, Flouric Acid, Lachesis, Nux Vomica

C) FOLLOW UP

1. Patients with Acute hepatitis A , B or E should be followed until the LFT have become normal and the patient has made a full symptomatic recovery.
2. Patients with hepatitis B should be followed until HBsAg is eliminated. Persistence of HBsAg beyond 6 weeks suggests that a carrier state may be evolving.
3. For Hepatitis D, the prognosis depends ultimately on the outcome of the Hepatitis B infection.
4. Patients with Hepatitis C should be followed every 6-12 months unless evidence of

persistent Hepatitis C is lacking, i.e. disappearance of Hepatitis C virus antibody or RNA.

GLOSSARY:

- **Carrier:** *an individual who harbors an organism without manifesting any symptoms and therefore can transmit that organism to another person.*
- **Immunoglobulins :** *They are types of antibodies. They are of five types: IgG, IgA, IgM, IgD and IgE.*
- **Antigen :** *An agent which initiates the production of specific antibodies (Ab) against self.*
- **Dane Particle :** *HBV are also known as Dane Particle in recognition of the investigator who first discovered them.*
- **Kupffer Cell :** *A fixed phagocytic cell found in the sinusoids of liver*
- **Lipofuscin:** *partly insoluble lipid pigment.*