VIRAL HEPATITS

Viral Hepatitis

- Hepatitis is inflammation of the liver cells .
- Clinical picture varies widely from inapparent case up to severe hepatocellular dysfunction

Hepatitis may be acute or chronic.

- Acute hepatitis lasts for less than 6 months and ends by complete resolution / rapid progression to extensive , ultimately fatal necrosis.

- Chronic hepatitis persists for more than 6 and progresses to cirrhosis and sequelae.

Causes of Acute Hepatitis

- Viral infection, by hepatotropic and nonhepatotropic viruses.
- Toxic hepatitis, by for example carbon tetrachloride and mushroom poisoning.
- Drug-induced hepatitis.
- Alcohol.

Viral Hepatitis:

- Is the term given to involvement of the liver by infection with one of the hepatotropic viruses A, B, C, D (delta agent), E, F and G.

Etiologic Agents of Viral Hepatitis:

- Enterically transmitted hepatitis viruses: A and E.
- Parenterally transmitted hepatitis viruses: B, C, D, F and G.

- **No Cross immunity**

Nonhepatotropic Viruses

Hepatitis may be part of systemic infection with a number of viruses.

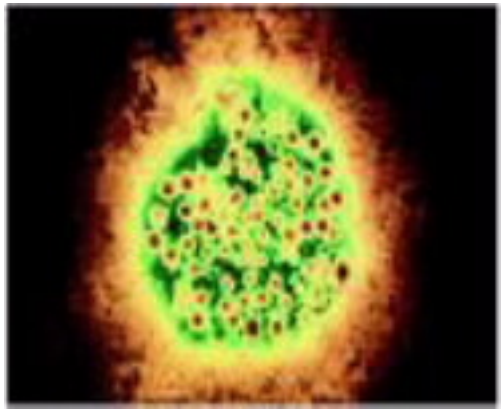
- Epstein-Barr virus (EBV), of infectious mononucleosis.
- Cytomegalovirus (CMV).
- Rarely : varicella virus, coxsackie virus, ECHO virus (enteric cytopathogenic human orphan virus), herpes simplex and herpes zoster viruses, and others.

Viral A Hepatitis

- It is a communicable food borne viral acute disease involving the liver and was formerly known as “Infectious hepatitis”
- Worldwide, in the form of sporadic cases, outbreaks and epidemics

Causative agent:

- Hepatitis A virus: RNA virus, relatively resistant outside the body.
- Single serotype.



Reservoir: Man

- **Cases:**
  - Main source of infection : clinical / subclinical
- **Carriers:**
  - Only incubatory (last wks of IP) before occurrence of the disease.

- **Foci of infection:**
  - Small intestine and blood.
- **Exit:**
  - Stools.
  - Blood in stage of vireamia.

Mode of Transmission

- **Feco-oral transmission .(main mode)**
  - Direct by contaminated hands. (hand to mouth)
  - Vehicle by contaminated water or food. (ingestion)
- **Parentral transmission:** rarely from blood during viremia.?
  - Due to short period of vireamia (only few days)

Period of communicability

- Around 4 weeks, including:
  - The last week of incubation period.
  - Preicteric and icteric stages of disease.
  - When jaundice appears, the virus persists in blood for few days, and in stools for about 1- 2 weeks
- **Incubation Period:**

  Up to 50 days

Clinical Picture

- **Unapparent cases**: mild anicteric cases, showing influenza-like picture and passes unnoticed.
- **Classical disease**.
- **Severe fulminant** rapidly fatal disease.

Stages of Classical Disease:

1-Pre-icteric Stage (before jaundice)

- Acute onset with fever, headache, malaise, myalgia and arthralgia.
- Tender liver.
- Gastroenteritis.
- Dark urine, with characteristic color that attracts attention of the case (or mother), just before jaundice appears

2. Icteric Stage: (jaundice)

- Jaundice appears, and is first noticed usually in sclera.
- Urine is still dark.
- Enlarged tender liver and spleen may be palpable

Post-icteric Stage : (convalescence phase)

- Jaundice disappears, but enlargement of liver persists for some time (3-6 wks)
- Urine become normal in color.
- Progressive improvement and clinical recovery.

- ***Complete recovery is the rule***

Susceptibility

- Age: all ages are susceptible.
- Sex: Both sexes are exposed.
- Environment: Poor sanitation favors spread of infection.
- Immunity:Clinical or subclinical infection gives long life immunity .

Diagnosis:

A) Clinical:

- Classical disease can be suspected :

  By dark-coloured urine and jaundice.

- Clinical diagnosis is thus difficult early in the disease, and in an-icteric cases.

B) Laboratory:

- Detecting the virus in stools, by electron microscopy, early in the disease.
- Serologic testing for IgM in acute disease.
- Liver function tests: elevated liver enzymes (not specific)

PREVENTION

A) General:

1- Environmental sanitation:

Food sanitation

Water sanitation

Sanitary waste and sewage disposal

Insect and rodent control

2- Health education of the public about good sanitation and personal hygiene.

3- Precautions to prevent parentral transmission.
(sanitary blood transfusion, disposable syringes)

B) Specific:

1-Active Immunization: The vaccine used is:

- Inactivated vaccine
- Two doses, 1 ml each, IM, in the deltoid, 4 weeks apart
- Given to: (**high risk groups**)
  - International travelers to endemic areas if they are going to stay for long time ie, more than 3 months
  - Persons in closed communities with insanitary conditions were the disease is endemic.

2- Seroprophylaxis:

- Human Normal Immunoglobulin is given, either before expected exposure, or within few days after exposure.
- **Given to:**
  - Household or other intimate contacts:
  - At-risk group, when outbreak spreads in closed community (camp, school, institute).

CONTROL

Control of reservoir is difficult because:

- **Large number of subclinical cases.**
- **Fecal excretion of virus is mostly during the IP.**
- **There is no specific treatment.**

Case Finding: clinically and lab.

Notification: should be done to local health authorities.

Isolation: Isolation: at home, though practically difficult with mild cases.

Disinfection: Sanitary disposal of feces, urine and blood

Treatment: Symptomatic treatment

- **General: Bed rest.**
- **Avoid drugs metabolized in liver.**
- **Release: After clinical recovery about one month after onset of disease.**

2) Contacts:

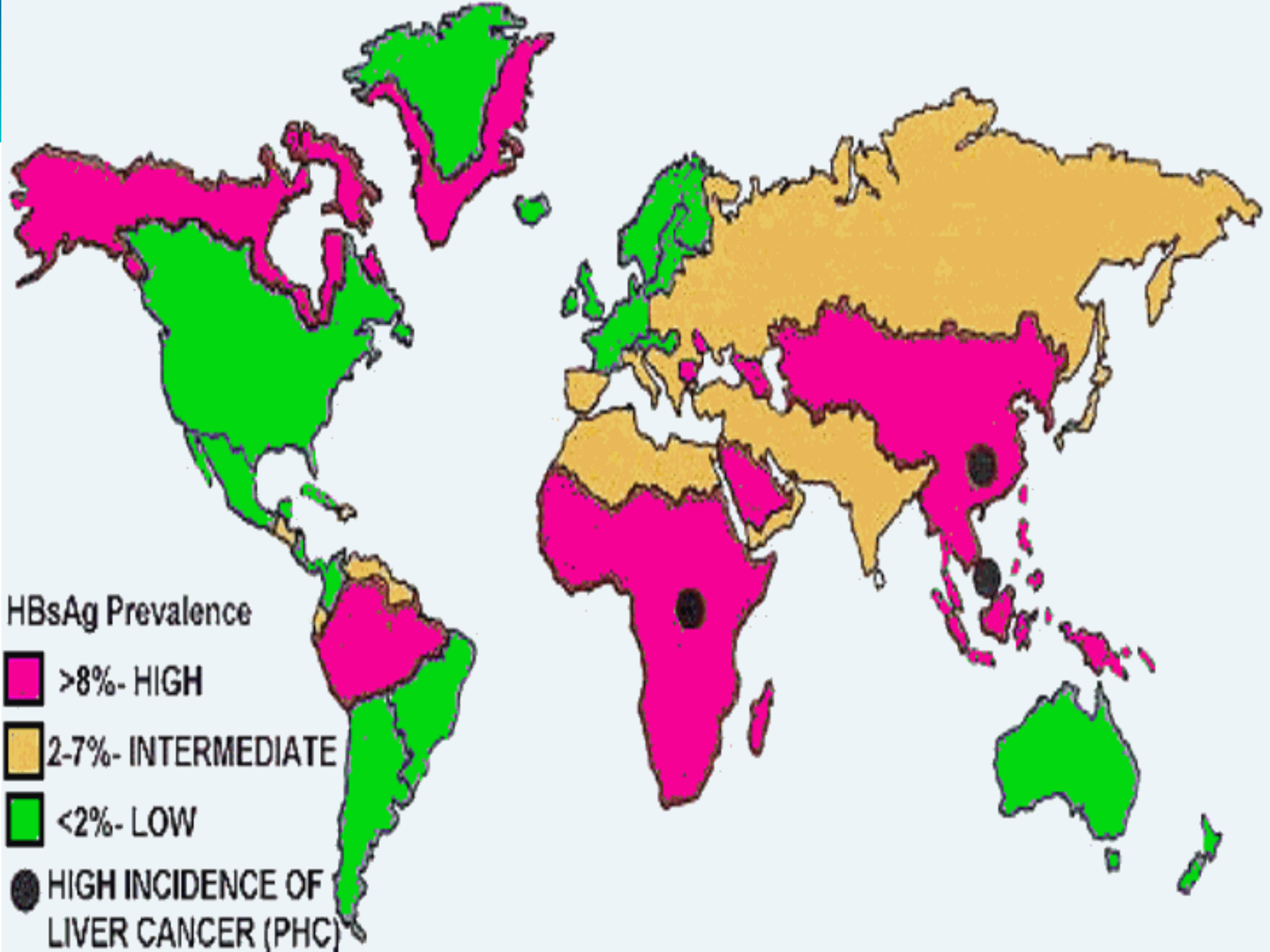
- **Enlistment**
- **Immunization:** Active and passive immunization should be given as soon as possible, within 2 weeks of exposure
- **Examination:** for early case finding
- **Surveillance:** for 6 weeks

3) Epidemic measures:

- Rules of food sanitation must be strictly followed.
- Seroprophylaxis of at-risk individuals or group
- Epidemiologic study, to trace sources and channels of infection.

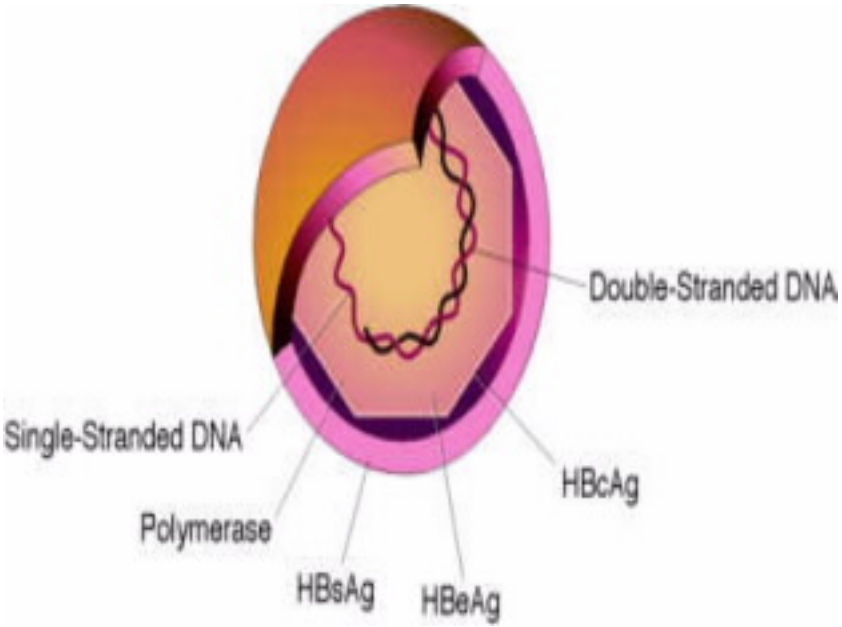
Viral B Hepatitis
"Serum hepatitis"

- It is a communicable blood borne viral disease involving the liver.
- It is has a worldwide distribution.
- WHO estimates that more than 2 billion persons have been infected with HBV (including 350 million chronically infected).
- Highest incidence in Africa & Asia.
- Every year about a million persons die as a result of HBV infection & over 4 million new acute clinical cases.


HBsAg Prevalence
>8%- HIGH
2-7%- INTERMEDIATE
<2%- LOW
HIGH INCIDENCE OF LIVER CANCER (PHC)

Causative agent

- (HBV): - **DNA** virus.
- More resistant than HAV to heat, boiling and disinfection. (double shell)
- The virus has three antigenic components, each stimulating formation of specific antibody.



- **Hepatitis B surface antigen (HBs Ag), also called Australia antigen (Au-antigen):**
  - Present in serum------ acute infection.
  - Persists in serum------ chronic infection
  - Its presence---------- denotes infectivity.
- **Hepatitis B core antigen (HBcAg):**

  Free core antigen cannot be detected in blood.
- **Hepatitis B e antigen (HBe Ag):**

  Can be detected in acute hepatitis. If found later, it signifies chronic liver disease, and infectivity of the case.

Reservoir: Man

Cases: throughout disease.

Carriers:

- **Incubatory carriers: infective for weeks.**
- **Convalescent carriers: 5-10% of recovered cases become chronic carriers, for years or lifelong.**
- **Healthy carriers: may be infective for *years*.**

Period of communicability :

- Infected persons who are HBs Ag positives are potentially infectious so long as the antigen is present in their blood
  - Starting late incubation period,
  - The course of the disease
  - The convalescent stage: until termination of carrier state which may extend for years.

- **Foci of infection:**

  Blood and tissue fluids (vaginal secretions, semen, saliva, breast milk)

- **Mode of Transmission:**

1) Per-cutaneous: (IM, IV, ID)

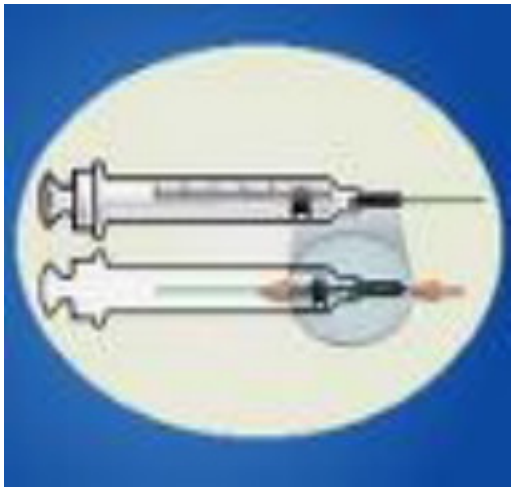
Infected syringes.

Haemodyalysis.

Acquipuncture.

Tatooing.

Dental instruments.



Mode of Transmission

- Per- cutanuous
- Infected blood transfusion.
- Organ transplantation, when donors are not accurately investigated
- Renal dialysis: if contaminated hemodialysis machine and instruments are used .
- Sexual contact with infected sex partners.
- Perinatal mother-to-infant transmission .
  - Provided that the mother is HBsAb-positive.
  - Breast feeding since virus is excreted in breast milk.

Susceptibility

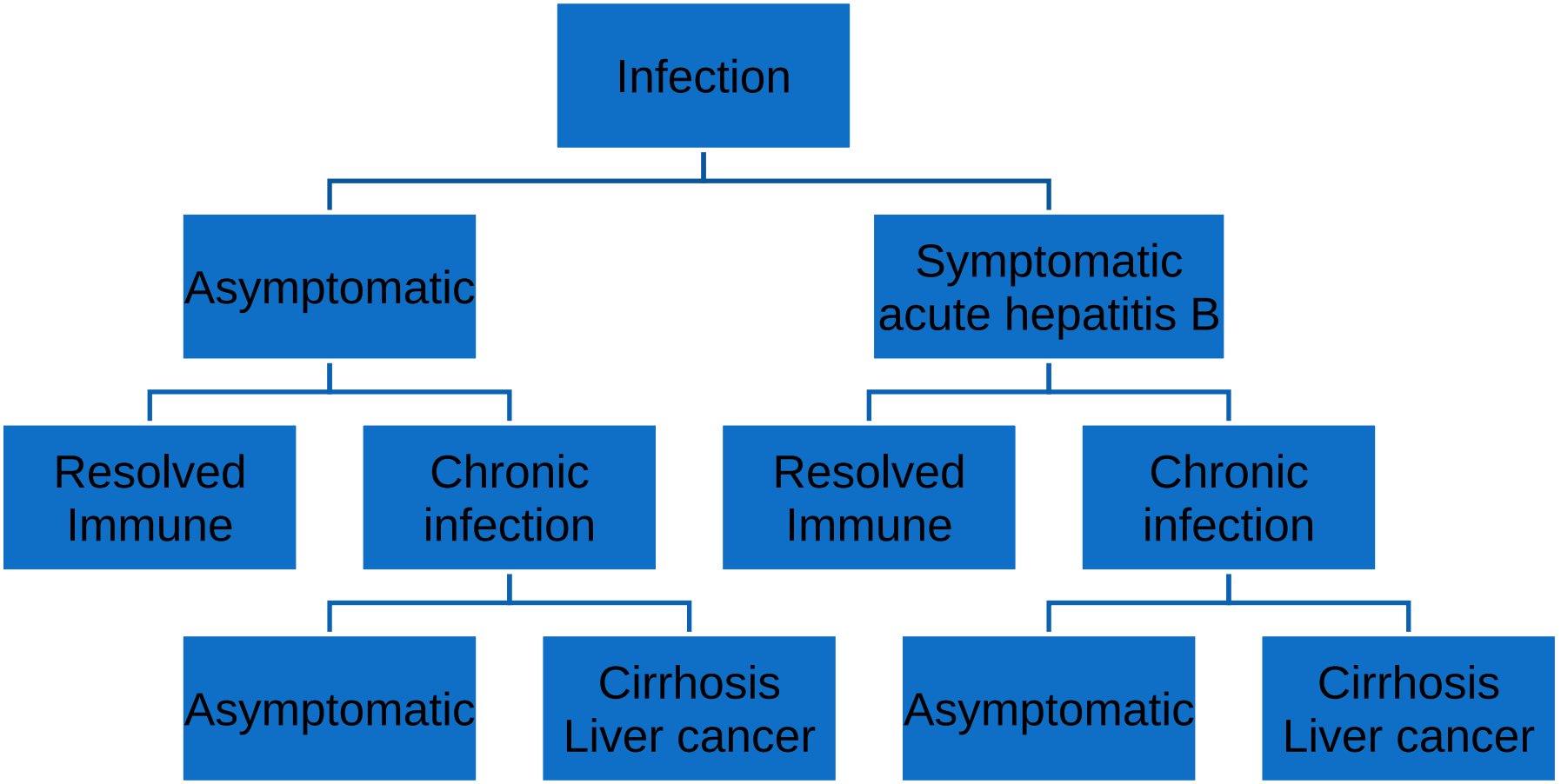
- **Age and sex:** susceptibility is general .
- **Immunity:**
  - Natural following infection (HBsAb is +ve)
  - Artificial following immunization.
- **Occupations:** Medical & paramedical staff.
- **Patients:** Blood transfusions, hemodialysis, during hospitalization.

- **Incubation Period:**

  Average 2-3 months

- **Clinical Picture:**
  - Only small portion of cases may manifest clinically.
  - Children---------- < 10%
  - Adults---------- 30-50%
- Clinical Picture (pre-ecteric / ecteric / post-ecteric) as VAH, with following differences:
  - Fever may be mild or absent.
  - Chronic HBV infection may occur in 1-20% of adult cases.
  - Complications are more common.(cirrhosis- carcinoma)

Outcome of HBV Infection



Sequelae and Complications:

- **Persistent HBs antigenaemia** (chronic carrier state and infectivity for years, or lifelong.)
- **Severe involvement of the liver:** (fulminant hepatitis), with high case-fatality, or (chronic hepatitis) and (liver cirrhosis).
- Increased risk of developing **hepatocellular carcinoma.**

Diagnosis

- **Clinical:**

  Non specific, may suggest viral hepatitis.

  Distinguished from VAH: insidious onset & afebrile.

- **Laboratory:**

  Detecting hepatitis markers in the blood.

Three clinically useful antigen –antibody systems are identified for hepatitis B:

1) HBsAg and its antibody (Anti-HBs)
2) HBcAg and its antibody (anti-HBc)
3) HBeAg and its antibody (Anti-HBe)

HBs Ag :

- Present in the serum during acute infection. (IP /active disease)
- Persists in the serum during (>6 m) chronic infection:(chronic carrier) potentially infective.
- Its presence denotes infectivity.

Anti-HBs:

- It denotes immunity.
- It appears late.

HBcAg:

- Cannot be detected in the blood.
- Present only in the liver cells.

Anti-Hbc:

- The first Ab to appear in the blood.
- Its presence signifies recent onset of infection.

HBeAg:

- It appears in the serum during late IP & during acute illness.
- Its presence indicates high infectivity of patients.

  - Its disappearance is a good prognostic sign.

Anti-HBe:

- Its detection------ a strong evidence of recovery.

Order of appearance of Ag & Ab:

Anti-HBc appears first in blood.	**Hbs Ag appears early blood.**
Anti-HBe appears next.	**Hbe Ag appears later blood**
Anti-HBs appears late	**Hbc Ag does not appear blood**

Prevention : General

1. **Prevention of blood-transmitted infection:**
   - Use disposable syringes, needles and any instruments whenever possible.
   - Sanitary precautions in dental clinics, during surgical operations, handling needles or sharp objects.
   - Sanitary precautions with blood transfusion: adequate screening of blood.
   - Sanitary disposal of sharp objects and body-fluid-contaminated objects. Avoid re-capping of syringes and needles.

2) Health education of the public and especially high risk groups.

Sources of infection.

Modes of transmission.

Preventive measures.

3) Prevention of sexual infection.

- Sex Education development & social welfare.
- Mental health promotion.
- Family welfare:
  - Providing facilities for marriage.
  - Premarital counseling
  - Social services

4) **Screening for HBV infection should be done for :**

- Blood and organ donors .
- Premarital examination of partners.
- Prenatal examination of pregnants.

Specific:

Immunization:

Active Immunization:

- ***Plasma- derived hepatitis B vaccine:***
  - Made of purified, (heat-or formalin)-(inactivated HBsAg), prepared from healthy HBsAg carriers.
- ***Yeast-recombinant hepatitis B vaccine: (Genetic engineering)***
  - Produced by recombinant DNA in yeast cells.
  - Used for mass vaccination.

Hepatitis B Vaccine:

- **Dose:** 3 doses, 0.5 ml each .
- **Route:** IM
- **Duration:** 0, 1, 6 months respectively.
- **Booster dose:** every 5 years ----- if there is continuous exposure.
- **Protective Value:** the vaccine is highly immunologic, giving protective neutralizing antibodies in at least 96% of the vaccinees.

Applications of Vaccination:

- **Compulsory vaccination of infants:** in Egypt it is given in 3 doses at 2, 4 and 6 months.
- **Medical and paramedical personnel,** in general, especially those exposed to the risk of professional infection .
- **Medical and paramedical students**, on starting hospital training.
- **Cases** in need of repeated blood transfusion or hemodialysis.
- **Sexual partners** and household contacts of HBsAg positive persons.
- **International travelers** to areas with intermediate to high rates of chronic HBV infection.

Combined Seroprophylaxis and Vaccination:

1- Infants borne to infected mothers :

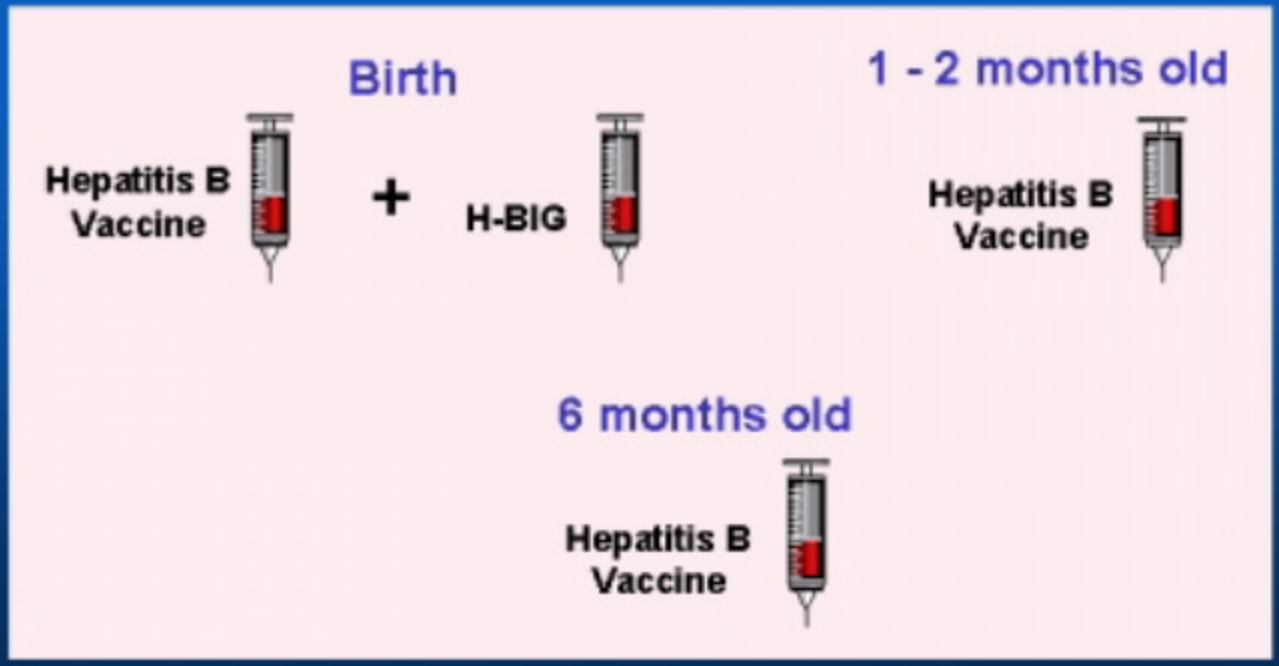
Within 12 hours from birth--------- a single dose of HBIG + first dose of the vaccine 0.5 ml, IM.

Then the two doses are given at 1 and 6 months of age.

2- Postexposure immunization: when an individual is exposed to infection.

Prophylaxis for Babies Born to HBV- Positive Mothers

- 95% of exposed infants will be protected by vaccination
- Exposed babies that are NOT immunized have 90% risk of being carriers for life
- 25% of carriers will die from liver problems



CONTROL

Cases:

- Case-finding: Serologic testing for hepatitis markers.
- Notification: to the local health office .
- Isolation: Universal precautions to prevent exposure to blood and body fluids
- Concurrent disinfection of equipment .
- Treatment: general, no specific therapy.
- Follow-up of cases, to detect and manage chronic disease

Contacts:

- Enlistment.
- Examination: for early case finding.
- Immunization. (combined vaccine and seroprophlaxis).
- Health education.

VIRAL HEPATITIS C

- It is a communicable parenterally tran[illegible] disease.

- It is found in every part of the world (31% of the world population, 170-200 million)
- It is highly endemic in Egypt (13%)

- **Causative agent:**

  Hepatitis C virus (HCV): an enveloped **RNA** virus.

- **Reservoir:** Man

  Case: 75% are un-apperant.

  Carriers: incubatory (temporary)

- **Focus:**

  Blood & blood products.

- **Period of infectivity:**

  Last days of IP and persist indefinitely.

- **Mode of transmission:**

  1) Exposure to infected blood or serum.

  (The majority of post-transfusion hepatitis cases is caused by HCV)

  2) Sexual and Peri-natal transmission are low.

- **Incubation period:**

  Ranges from **2weeks to 6 months**.

Clinical features

- **Wide clinical spectrum.**
  - **Asymptomatic cases.**
  - **Mild inapparent cases (75%)**
  - **Acute icteric disease. (indistinguishable from VBH)**
  - **Severe acute fulminant hepatitis.**
  - **Chronic cases: 5% of acute cases----------**
  - **Liver cirrhosis & hepatocellular carcinoma.**

- **Diagnosis: demonstration of antibodies to virus C in blood.**

Prevention :

- **General:** **same as HBV.**
- **Specific:** No vaccine is available yet .

Control:

Cases:

- Case-finding.
- General treatment, no specific therapy .
- Precautions with blood sampling .
- Follow-up of cases, to detect & manage chronic disease-

VIRAL D HEPATITIS
Delta viral hepatitis

- It is a communicable parentrally transmitted viral disease.

- The virus can not produce the disease by itself but if combined with virus B. It causes more severe illness.

Causative agent:

- **Hepatitis D virus (HDV)**

  Virus like particle unable to infect a cell by itself & requires co-infection with HBV to undergo complete replication cycle.
- **Reservoir:** human.

- **Mode of transmission**: same as HBV.
- **Susceptibility:** general as HBV
- **Clinical feature:** Clinical combination of HBV and HDV gives sever cases with high fatality.
- **Prevention and control:** as in HBV**.** Vaccination against HBV can prevent HDV.

VIRAL HEPATITIS E

- The clinical course is similar to that of hepatitis A .
- It occurs in sporadic cases, and out breaks especially in countries with law sanitary conditions.
- It occurs usually due to water borne infection.

- **Causative agent:** Hepatitis E virus (HEV).
- **Mode of transmission:** food-borne infection .
- **Clinical features:** like virus A.
- **Prevention:** general to prevent food borne infection.

Virus F Hepatitis

- Hepatitis F virus (HFV) has been recently identified.
- Disease is mainly transmitted by parenteral infection

Virus G Hepatitis

- **Causative Organism** : hepatitis G virus (HGV), single stranded RNA genome .
- **Reservoir of Infection** : man .
- **Transmission :** similar to that of HCV infection.
- **Prevention :** Similar to Hepatitis C virus .

Viral Hepatitis - Overview

	Type of Hepatitis				
	A	B	C	D	E
Source of virus	feces	blood/ blood-derived body fluids	blood/ blood-derived body fluids	blood/ blood-derived body fluids	feces
Route of transmission	fecal-oral	percutaneous permucosal	percutaneous permucosal	percutaneous permucosal	fecal-oral
Chronic infection	no	yes	yes	yes	no
Prevention	pre/post-exposure immunization	pre/post-exposure immunization	blood donor screening; risk behavior modification	pre/post-exposure immunization; risk behavior modification	ensure safe drinking water

CDC

Thank you