HEPATITIS
A &E

What is Viral Hepatitis ?

- Viral hepatitis is a group of systemic infection affecting the liver predominantly caused by 5 kinds of viruses at least
- Viral hepatitis may be divided into 5 types according to etiology, that is hepatitis A, B, C, D and E
- Although the agents can be distinguished by its antigenic properties, the 5 kinds of viruses may produce clinically similar illness

- Clinical manifestations are characterized by anorexia, nausea, lassitude, enlarged liver and abnormal liver function, a part of cases may appear jaundice. Subclinical infection is common

- Hepatitis A and E shows acute hepatitis, hepatitis B, C and D predispose to a chronic hepatitis and is related to liver cirrhosis and hepatic cancer

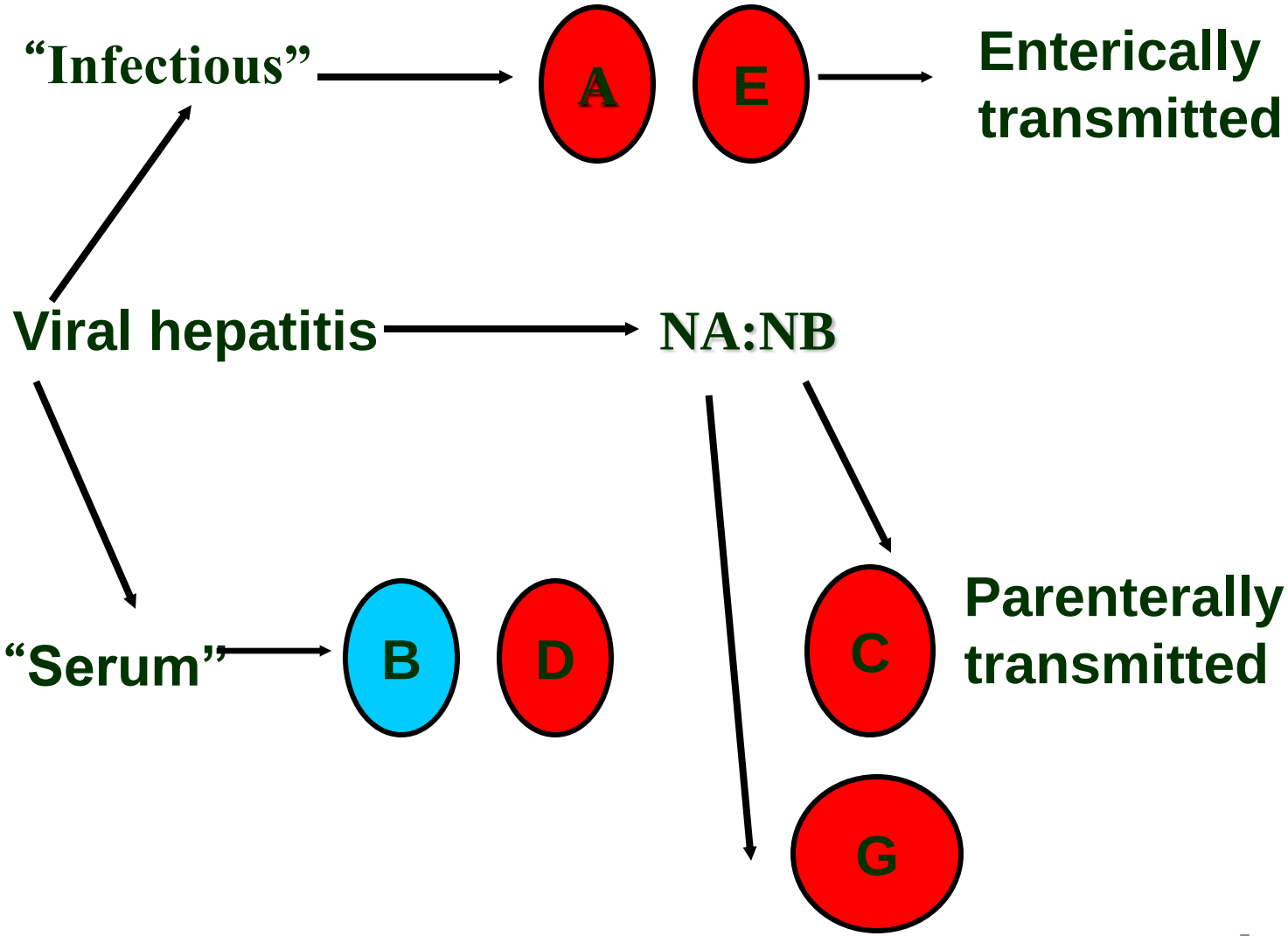
- The course of acute hepatitis is about 2-4 months generally.

- Recently, 2 kinds of viruses named HGV and TTV are discovered and considered to relate to viral hepatitis

HEPATITIS VIRUSES

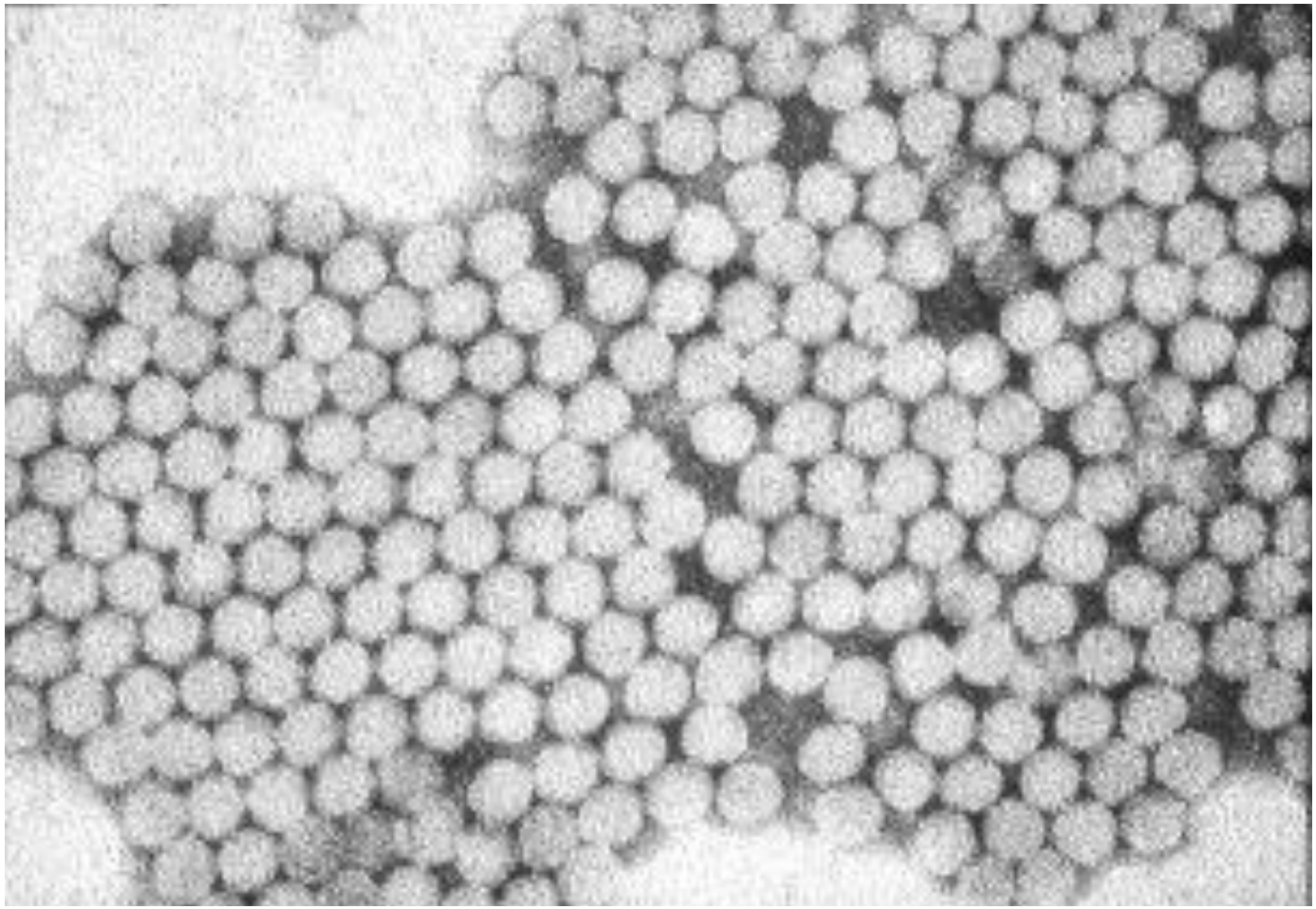
- **Hepatitis A (HAV) Picornaviridae (1973)**
- **Hepatitis B (HBV) Hepadnaviridae (1970)**
- **Hepatitis C (HCV) Flaviviridae (1988)**
- **Hepatitis D (HDV) ? (1977)**
- **Hepatitis E (HEV) (Caliciviridae-like) (1983)**
- **Hepatitis G (HGV) Flaviviridae (1995)**

Viral Hepatitis - Historical Perspectives



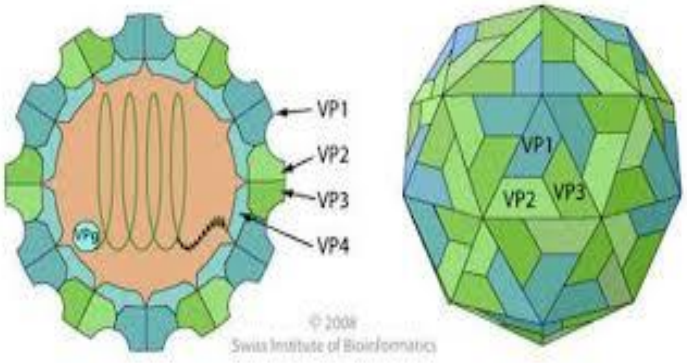
Hepatitis viruses					
	HAV	HBV	HCV	HDV	HEV
Transmission	Enteral	Parenteral	Parenteral	Parenteral	Enteral
Classification	Picornavirus	Hepadnavirus	Hepacivirus	Deltavirus	Hepevirus
Genome	+ssRNA	+dsDNA	+ssRNA	−ssRNA	+ssRNA
Antigens		HBsAg,HBeAg	Core antigen	Delta antigen	
Incubation period	20–40 days	45–160 days	15–150 days	30–60 days	15–60 days
Severity/ Chronicity	mild; acute	occasionally severe; 5–10% chronic	subclinical; 70% chronic	exacerbates symptoms of HBV; chronic w/ HBV	normal patients, mild; pregnant women, severe; acute
Vaccine	10 year protection	3 injections, lifetime protection	none		

HAV



Hepatitis A Virus

- Naked +ve sense, single stranded RNA virus with icosahedral symmetry



- Related to enteroviruses, formerly known as Enterovirus 72, now put in its own family: picornaviridae; genus: hepatovirus

- One stable serotype only
- Capsid comprises 4 proteins VP1-4
- VP1 is the spike used for attachment to receptors on target cell.

- Difficult to grow in cell culture: primary marmoset cell culture and also in vivo in chimpanzees and marmosets

- 4 genotypes exist, but in practice most of them are group 1
- Resistant to inactivation by heat at 60^0 C for one hour, ether & acid at pH 3.
- Inactivated by boiling for one minute, 1: 4,000 formaldehyde at 37^0 C for 72 hours & chlorine 1 ppm for 30 minutes.

Epidemiology

- The anti-HAV seroprevalence rate is presently decreasing in many parts of the world, but in less developed regions and in several developing countries, HAV infection is still very common in the first years of life and seroprevalence rates approach 100%.
- Hepatitis A is the most common form of acute viral hepatitis worldwide.
- The highest risk areas: the Indian subcontinent (in particular India, Pakistan, Bangladesh, and Nepal), Africa, parts of the Far East (except Japan), South and Central America, and the Middle East.
- Approximately 1.5 million clinical cases of hepatitis A occur worldwide annually (actual rates X10)
- The incidence rate is strongly related to socio-economic indicators and access to safe drinking water.
- In developed countries, reduced encounters with HAV in the young have resulted in a decline in herd immunity.
- Pts mostly contagious in 1-2 weeks before onset of clinical disease.

Risk factors and transmission

- Personal contact.
- Certain occupations (e.g., residential institutions, sewage workers).
- Travel to high-risk areas.
- Male homosexuality with multiple partners.
- Intravenous drug abuse.
- People with clotting factor disorders who are receiving factor VIII and factor IX concentrates.

- Close personal contact
  (e.g., household contact, sex contact, child day care centers)
- Contaminated food, water
  (e.g., infected food handlers, raw shellfish)
- Blood exposure (rare)
  (e.g., injecting drug use, transfusion)
- Many cases occur in community-wide outbreaks
  - no risk factor identified for most cases, highest attack rates in 5-14 year olds
  - children serve as reservoir of infection

PATHOGENESIS - HAV

- **Causes subacute disease in children & young adults.**
- Humans appear to be the only reservoir for the HAV.
- The incubation period usually lasts 2-6 weeks. The time to onset of symptoms may be dose-related.
- HAV invade into human body by fecal-oral route, multiplies in the intestinal epithelium & reaches the liver by hematogenous spread.
- After uptake, the viral RNA is uncoated, and host ribosomes bind to form polysomes.
- Viral proteins can then be synthesised with the viral genome being copied by a viral RNA polymerase.
- Assembled virus particles are then shed through the biliary tree into the faeces.
- Shedding of the HAV is greatest during the pre-icteric prodrome of infection (between 14 and 21 days after infection). This corresponds to the time when transmission is highest.

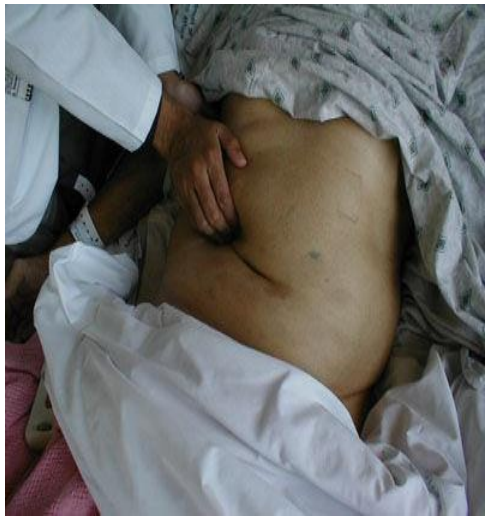
PATHOGENESIS – HAV

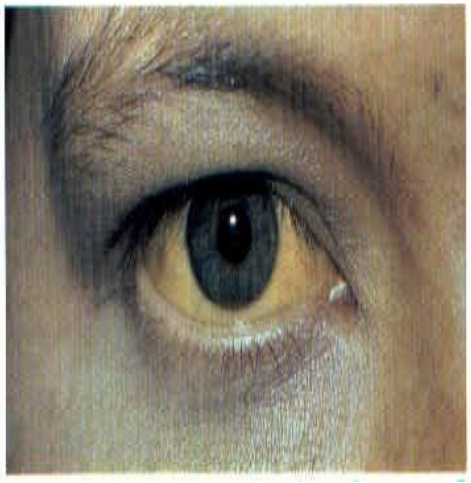
- After HAV replicating and discharging, liver cells damage begin
- Lymphoid cell infiltration, necrosis of liver parenchymal cells and proliferation of kuppfer cells
- Complement level reduce the pathogenesis by the following:
  - activated T cell secrete γ-INF that promote the representation of HLA on the liver cells, CTL may kill the target cell that is infected with HAV

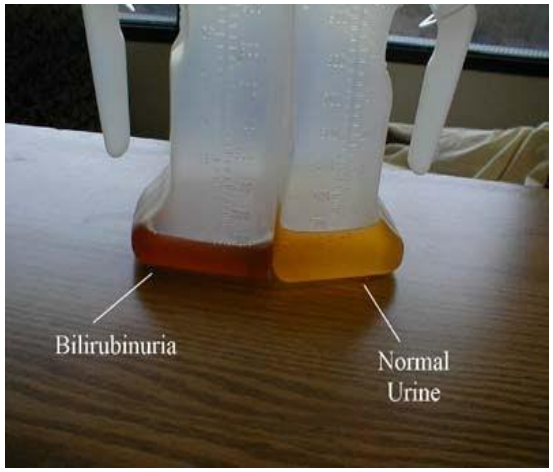
Clinical features

- Pre-icteric phase:
  - There is a prodrome of mild flu-like symptoms (anorexia, nausea, fatigue, malaise and joint pain) preceding the jaundice. Diarrhoea can occur, particularly in children.
  - Fever is not usually common.
- This can progress to the icteric phase with:
  - Dark urine (appears first).
  - Pale stools (not always).
  - Jaundice occurring in 70-85% of adults with acute HAV infection.
  - Abdominal pain occurring in 40% of patients.
  - Itch or pruritus (usually with jaundice but can occur without).
  - Arthralgias and skin rash. These occur less often
  - Tender hepatomegaly, splenomegaly, and lymphadenopathy may occur.
- Complete clinical recovery may take up to six months after the onset of the illness.
- Anorexia, malaise, and weakness may persist for some weeks after biochemical recovery.

- Prodromal or Preicteric phase : (symptoms: fatigue, joint- and abdominal pain, malaise, vomiting, lack of appetite, hepatomegaly)
- Icteric phase: Icterus: jaundice (skin, sclera, mucous membranes, cause: elevated bilirubin level, bilirubinuria: dark urine, pale stool)

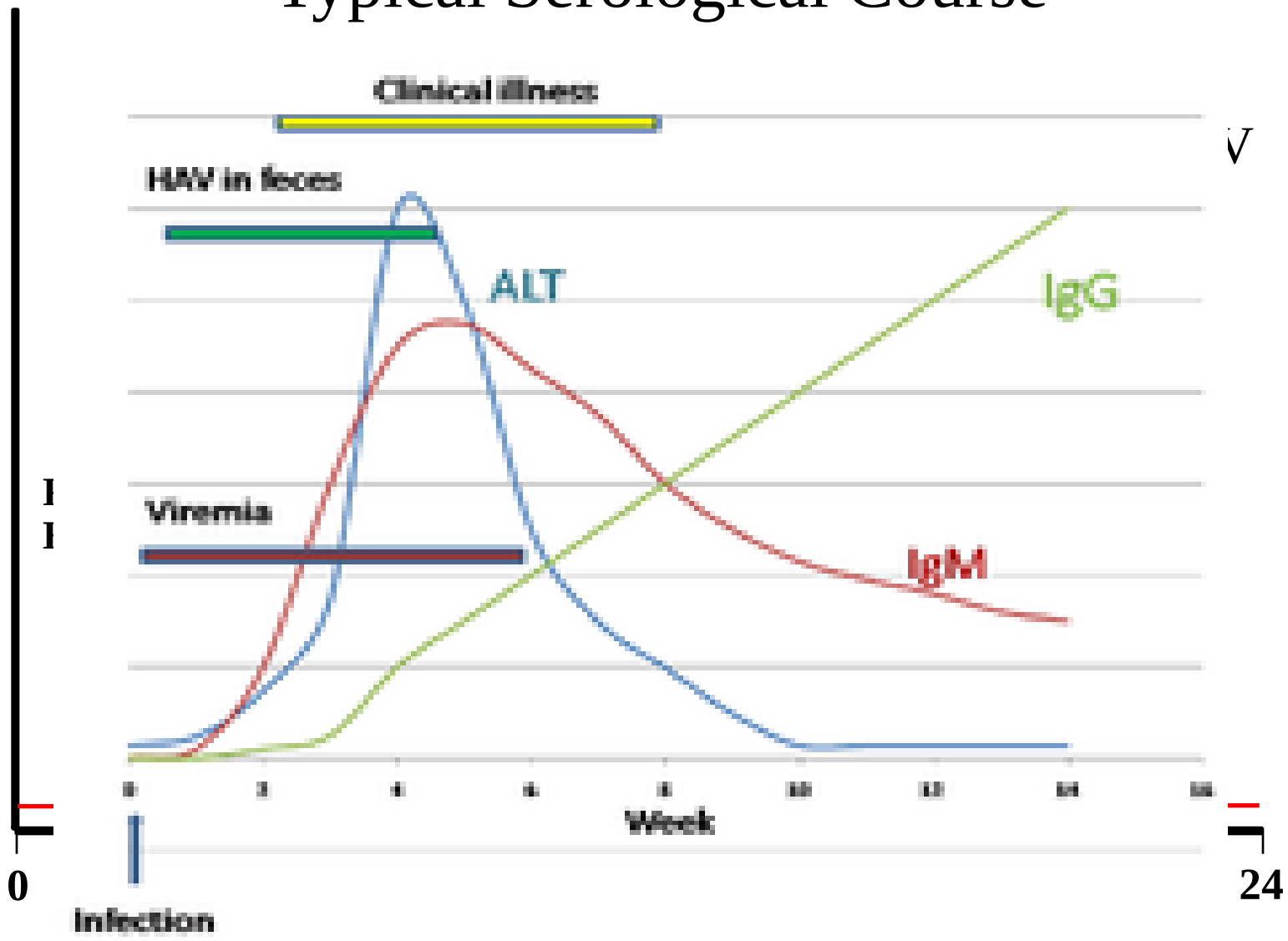






Hepatitis A Infection

Typical Serological Course



LAB DIAGNOSIS

1. Demonstration of Virus in feces: Immunoelectron microscopy
2. Virus Isolation:
3. Detection of Antibody : ELISA
   - IgM antibody: The test is sensitive and specific. It is positive with onset of symptoms (3 to 6 weeks after exposure). It remains positive for between 3 and 6 months (up to 12 months). It remains positive in relapsing hepatitis.
   - IgG antibody: Appears soon after IgM and persists for many years. In the absence of IgM it indicates past infection or vaccination rather than acute infection. IgG remains detectable for life
4. Biochemical tests:
   i) ALT and AST: raised
   ii) Alkaline phosphatase: raised
   iii) Bilirubin: raised
   iv) Mild lymphocytosis
5. Molecular Diagnosis : RT PCR of feces

Treatment and prevention

- Mainly supportive with treatment of symptoms (fluids, antiemetics, rest).
- Avoid alcohol until liver enzymes are normal.
- Admit patients with severe systemic upset or intractable vomiting for rehydration and observation.

- Good hygiene and sanitation are of fundamental importance. Tap water should be avoided in high-risk areas.
- Public education about transmission and prevention are needed, particularly in communities where HAV is endemic.
- Immunisation is effective and should be appropriately used:

Passive immunization (ISG)

- Protective if given before or during incubation period

Active immunization

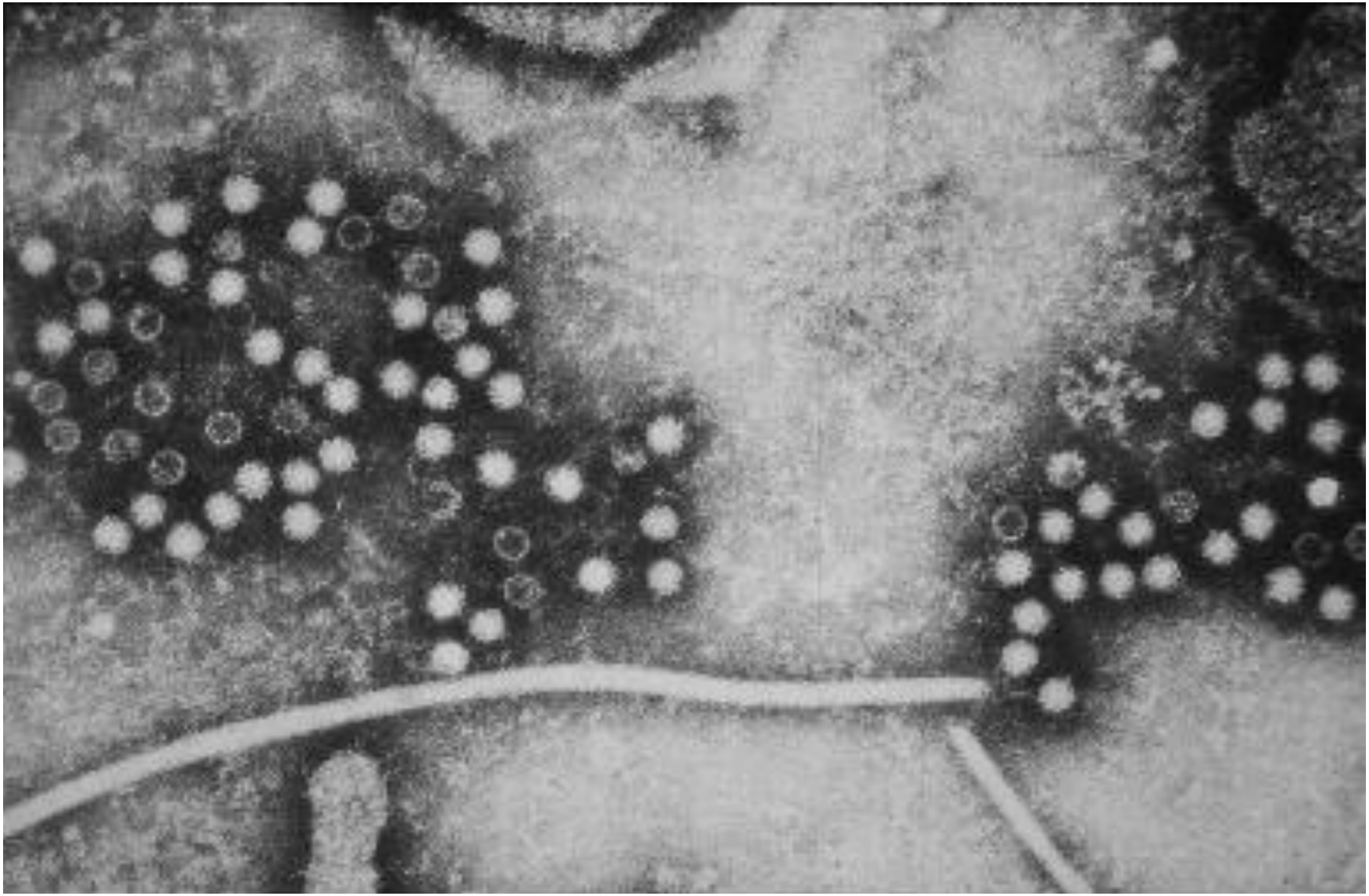
- Formalin killed HAV
- 100% protective
- 2 doses 6-12 months apart

Complications and prognosis

- Cholestatic hepatitis (8%). Features may include severe pruritus, diarrhoea, weight loss, and malabsorption. However, they usually fully recover.
- Death (mortality 0.2%)
- Fulminant liver failure (0.4%). Manifests during the first four weeks of illness. It is more common in those with concurrent chronic hepatitis B or C.
- Relapsing HAV infection (up to 15%). It can occur at an interval of 4-15 weeks after the original illness. More than once.

- Excellent. It is usually self-limiting with no long-term sequelae.
- There is no carrier state and chronic liver disease does not occur.

Hepatitis E Virus



Hepatitis E Virus

- Calici-like virus
- Unenveloped RNA virus, 32-34nm in diameter
- +ve single stranded RNA genome, 7.6 kb in size.
- The main reservoir is pigs
- HEV genotype 3 and 4 can cause liver disease in humans.
- In humans, the infection may vary in severity from inapparent to fulminant. The mortality is between 1% and 4%
- In resource-limited countries, HEV infection is endemic and spreads mainly through contamination of water supplies.
- Transmission of virus from domestic pigs to humans is common and higher rates of HEV seroprevalence are detected in slaughterhouse workers and vets.
- It is evaluated that one third of the worldwide population has been in contact with the virus
- Was cultured only recently

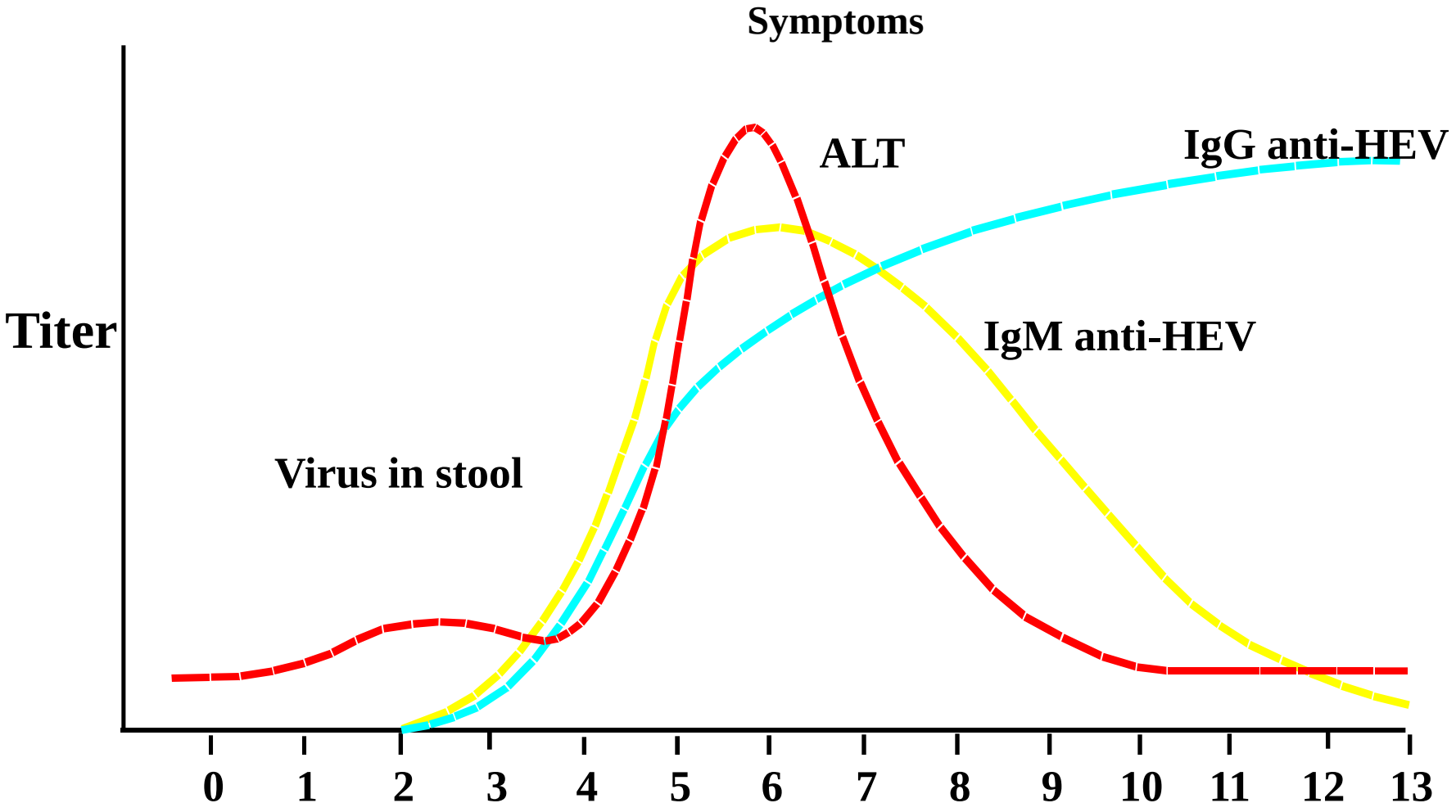
Hepatitis E - Clinical Features

- These are also similar to HAV with no apparent risk of chronic liver disease.
- Incubation is 2-9 weeks (average 40 days)
- It is usually a self-limiting illness.
- There are no reports of chronic infection with HEV.
- HEV usually causes an acute self-limiting illness like HAV. Fulminant disease occurs in about 10% of cases.
- In pregnancy, the mortality rate may be as high as 15-20%.
- Illness severity increases with age

- In immunocompromised patients, particularly in solid organ transplanted patients, hepatitis E may cause a chronic infection. Occasionally this may cause liver fibrosis and cirrhosis.

Hepatitis E Virus Infection

Typical Serologic Course



Hepatitis E - Epidemiologic Features

- Most outbreaks associated with faecally contaminated drinking water.
- Several other large epidemics have occurred since in the Indian subcontinent and the USSR, China, Africa and Mexico.
- In the United States and other nonendemic areas, where outbreaks of hepatitis E have not been documented to occur, a low prevalence of anti-HEV (<2%) has been found in healthy populations. The source of infection for these persons is unknown.
- Minimal person-to-person transmission.

Prevention and Control Measures for Travelers to HEV-Endemic Regions

- Avoid drinking water (and beverages with ice) of unknown purity, uncooked shellfish, and uncooked fruit/vegetables not peeled or prepared by traveler.
- IG prepared from donors in Western countries does not prevent infection.
- Unknown efficacy of IG prepared from donors in endemic areas.
- Vaccine? (HEV 239). The first vaccine batches came out in late October 2012 in China