

## RNA Hepatitis Viruses (Hepatitis A, Hepatitis C, Hepatitis E and Hepatitis G)

Reading: Schaechter's Mechanisms of Microbial Disease, Fourth Edition, Chapter 43.

I. **Overview.** Hepatitis viruses are one of the few groups of viruses that are characterized by the disease that they cause. While they all share a similarity in their tropism for the liver, the severity of infection and the ability to persist varies greatly among these viruses.

### II. Hepatitis A virus – 1.5 million cases worldwide

#### A. Properties of the virus:

1. Picornavirus, (+) ssRNA genome
2. Icosahedral capsid (non-enveloped)
3. Virions very stable in the environment
  - a) heat stable at 60°C
  - b) can survive in water for months
4. Only one serotype of virus is known

#### B. Clinical features (“infectious hepatitis”)- 40% of acute cases of hepatitis

1. Oral ingestion and primary replication in oropharynx and intestinal epithelial cells
2. Virus spreads from intestine to blood stream (viremia) which results in infection of the liver.
3. Incubation period is 2 – 6 weeks
4. Most infections worldwide occur in children and are subclinical- 90%
5. Severity of infection increases with age (2/3 of adult infections are icteric)
6. Large amounts of virus can be isolated in feces, virus is cytopathic in intestine with lots of virus released; smaller amounts in blood, saliva and the throat. Virus is shed 10-14 days before symptoms
7. *No chronic carrier state*
8. Case-fatality rate is low (0.5%)
9. Virus is not cytopathic in liver, where damage caused by cell mediated immune response.

#### C. Epidemiology and Control

1. Spread from person to person by fecal-oral route
2. Can cause wide-spread epidemics when water and/or food supply is contaminated. Largest US outbreak 2003 over 600 people had hepatitis from green onions in fast food restaurant. 9000 people who ate at the restaurant were given immune globulin.
3. Control primarily depends on high standards of personal and public hygiene.
4. Prior to vaccine, immune globulin given and effective for 6 months
5. The first hepatitis A vaccines (inactivated virus) were licensed in 1992. 4 different vaccines, give 2 doses 1 yr apart.

## II. Hepatitis C virus

### A. Properties of the virus:

1. Member of the *flaviviridae* family
2. (+) ssRNA genome
3. *Enveloped* icosahedral capsid

### B. Initial discovery of the infectious agent- ~200 million carriers worldwide

1. A substantial number of the post-transfusion cases of non-A, non-B hepatitis remained after sensitive screening assays for HBV were introduced in the late 1970s.
2. Causative agent could not be cultured *in vitro* or visualized by EM.
3. Molecular biologic approach was used in 1989 to clone and identify the agent, developed screening test. 6 genotypes identified now.
4. The first infectious clone was reported by Dr. Charles Rice in 1997.

### C. Clinical features:

1. Incubation period averages 6 – 8 weeks. 75% are asymptomatic.
2. Clinical infections are usually less severe than with HBV.
3. Chronic infections with HCV are more common than with HBV.
4. 85% of patients with HCV have chronic infections for a year or two or longer.
5. 20% of chronic infections progress to cirrhosis of the liver.
6. Chronic HCV infection correlates with the development of hepatocellular carcinomas.

### D. Epidemiology and Control

1. Transmitted by contaminated blood, blood factors and intravenous drug use in US.
2. Sexually transmitted world wide, but more rare in US. Perinatal transmission rare.
3. Recurrence of HCV infection is very common in liver transplant patients.
4. In the US HCV more important cause of cirrhosis than alcoholism.
5. Interferon can be effective for treatment, but only for certain genotypes.

## III. Hepatitis E virus

### A. Properties of the virus:

1. (+) ssRNA genome
2. Icosahedral capsid; stable virion
3. Member of the *Hepevirus* unclassified family

### B. General features

1. Fecal-oral route of transmission (mainly water-borne).
2. Mainly seen in under-developed countries.
3. The virus initially multiplies within the intestinal epithelial cells.
4. After entering the bloodstream, it infects the liver

### C. Clinical features:

1. Incubation period averages 2 – 8 weeks
2. Mostly a sub-clinical infection in children.

3. Acute Hepatitis E is clinically similar to HAV *except*:
    - a) Bilirubin levels are higher.
    - b) Jaundice is deeper and more prolonged.
  4. Normal case-fatality rate is 0.5 – 3%, BUT in pregnant women it is 10 – 20%
  5. There is no chronic carrier state.
  6. Diagnosis is on the basis of the exclusion of HAV and HBV (and specific sera).
- D. Epidemiology and Control
1. Cook foods and avoid contaminated water when traveling to endemic regions.
  2. Ig from western countries not helpful.
  3. Protein vaccine in clinical trials.

#### IV. Hepatitis G virus

- A. Properties of the virus:
1. (+) ssRNA genome, 9.1 – 9.4 kb
  2. Icosahedral capsid
  3. Member of the *flaviviridae* family
- B. General features
1. Newly characterized NANBH (non-A, non-B hepatitis).
  2. Occasionally referred to as “GBV-C” virus.
  3. Parenteral transmission (especially i.v. drug use).
  4. Sexual transmission?
- C. Pathogenesis:
1. Estimated to cause 0.3% of acute viral hepatitis
  2. 900 – 2000 infections per year, mostly asymptomatic.
  3. Chronic disease? controversial.
  4. Analysis by RNA detection
- D. Risk groups
1. Transfusion recipients.
  2. Injection drug users.
  3. May be a frequent co-infection with HCV?
- E. Prevention/treatment
- None until virus can be grown.