Viral Hepatitis

By

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What is Viral Hepatitis?

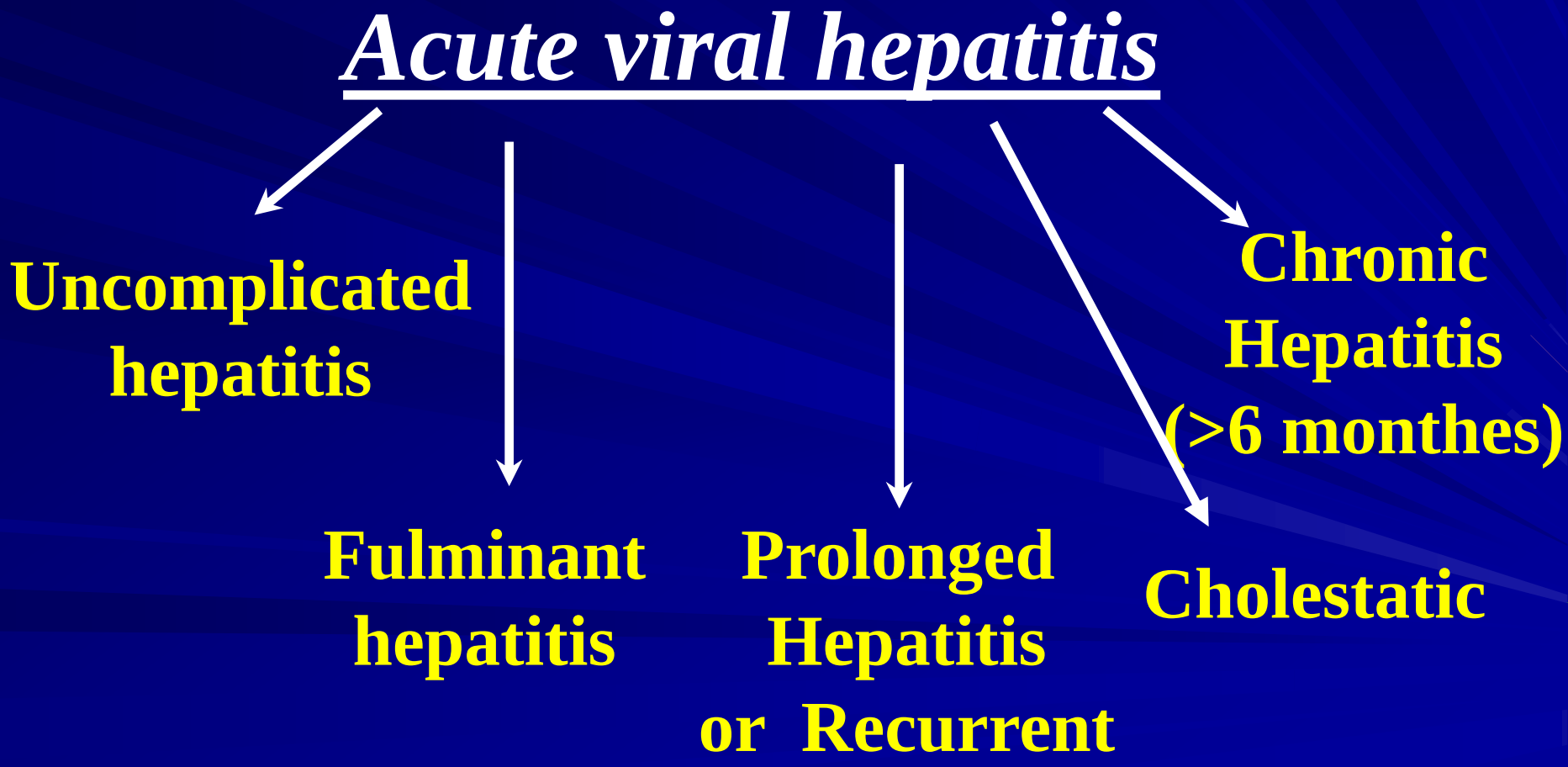
- Viral hepatitis is a systemic disease with primary inflammation of the liver by any one of a heterogeneous group of hepatotropic viruses.
- The most common causes of viral hepatitis are the five unrelated hepatotropic viruses Hepatitis A, Hepatitis B, Hepatitis C, Hepatitis D, and Hepatitis E.
- In addition to the nominal hepatitis viruses, other viruses that can also cause liver inflammation include Herpes simplex, Cytomegalovirus, Epstein-Barr virus, or Yellow fever.

Clinical Stages

- ***Incubation period***
- ***Prodromal (preicteric) phase***
- ***Icteric phase***
- ***convalescence***

Jaundice

Sequelae of acute viral hepatitis



Hepatitis A (HAV)

Acute "infectious" hepatitis- picornavirus

- **not blood-borne**
- **occurs in epidemics**
- **no animal reservoir**
- **effective vaccine since 1995**

Hepatitis A Virus Transmission

- 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)

Hepatitis A - Clinical Features

- Incubation period: Average 30 days
  Range 15-50 days
- Jaundice by age group: <6 yrs, <10%
  6-14 yrs, 40%-50%
  >14 yrs, 70%-80%
- Complications: Fulminant hepatitis
  Cholestatic hepatitis
  Relapsing hepatitis
- Chronic sequelae: None

Laboratory Diagnosis

- Acute infection is diagnosed by the detection of HAV-IgM in serum.
- Past Infection i.e. immunity is determined by the detection of HAV-IgG.

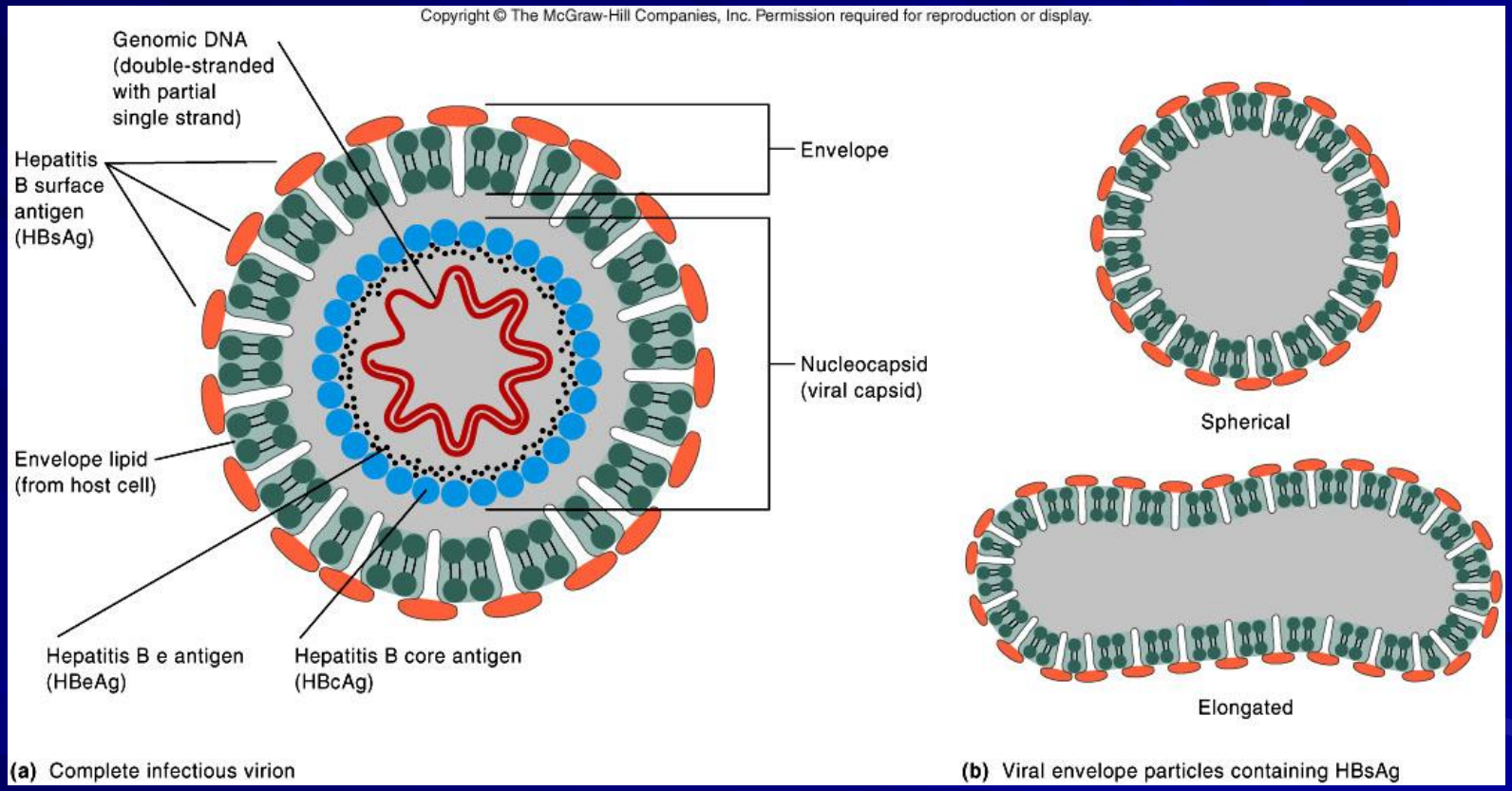
HAV prevention and control

- sanitation- separate waste from water source and foods
- handwashing, avoidance of contaminated foods
- inactivated virus vaccine is effective (2 doses 6 monthes apart n before age of 12 monthes)(1995)
- human IgG(0.02ml/kg IM) given as passive immunization
- vaccine to travellers or higher risk workers, healthcare or sewer workers, food handlers and those with chronic liver disease

Hepatitis B Virus (HBV)
Hepadnaviridae

- **originally called "serum hepatitis”**
- **epidemiology –** major worldwide prevalence and impact
- **blood borne** transmission
- **unique virion structure and biology**
  - enveloped particle
  - lipid + HBsAg, nucleocapsid protein, HBcAg
  - circulating HBsAg "Australian antigen" (22nm)
  - incomplete ds DNA genome in particle
  - unique polymerases include a reverse transcriptase

Hepatitis B virus structure



Hepatitis B Virus
Modes of Transmission

- Sexual - sex workers and homosexuals are particular at risk.
- Parenteral - IVDA, Health Workers are at increased risk.
- Perinatal - Mothers who are HBeAg positive are much more likely to transmit to their offspring than those who are not. Perinatal transmission is the main means of transmission in high prevalence populations.

Hepatitis B - Clinical Features

- Incubation period: Range 45-180 days
- Clinical illness (jaundice): <5 yrs, <10%
5 yrs, 30%-50%

0.5%-1%

- Chronic infection: <5 yrs, 30%-90%
5 yrs, 2%-10%
- Premature mortality from chronic liver disease: 15%-25%

Diagnosis

Table 7.7 Significance of viral markers in hepatitis B

Antigens	
HBsAg	Acute or chronic infection
HBeAg	Acute hepatitis B Persistence implies: continued infectious state development of chronicity increased severity of disease
HBV DNA	Implies viral replication Found in serum and liver
Antibodies	
Anti-HBs	Immunity to HBV; previous exposure; vaccination
Anti-HBe	Seroconversion
Anti-HBc	
IgM	Acute hepatitis B (high titre) Chronic hepatitis B (low titre)
IgG	Past exposure to hepatitis B (HBsAg-negative)

HBV prevention and control

- **highly protective vaccines**

  - HBsAg from serum of carriers (1980's)

  - yeast recombinant HBsAg since 1986 (3 doses , 0,1,6 monthes) .

  - recommended for all, especially healthcare and high risk

  - approved combination vaccine for HAV and HBV

- **treatment and control**

  - HBIG hepatitis B immune globulin(0.06ml/kg IM) is protective

  - education of vaccine and avoiding contact with transmitting agents

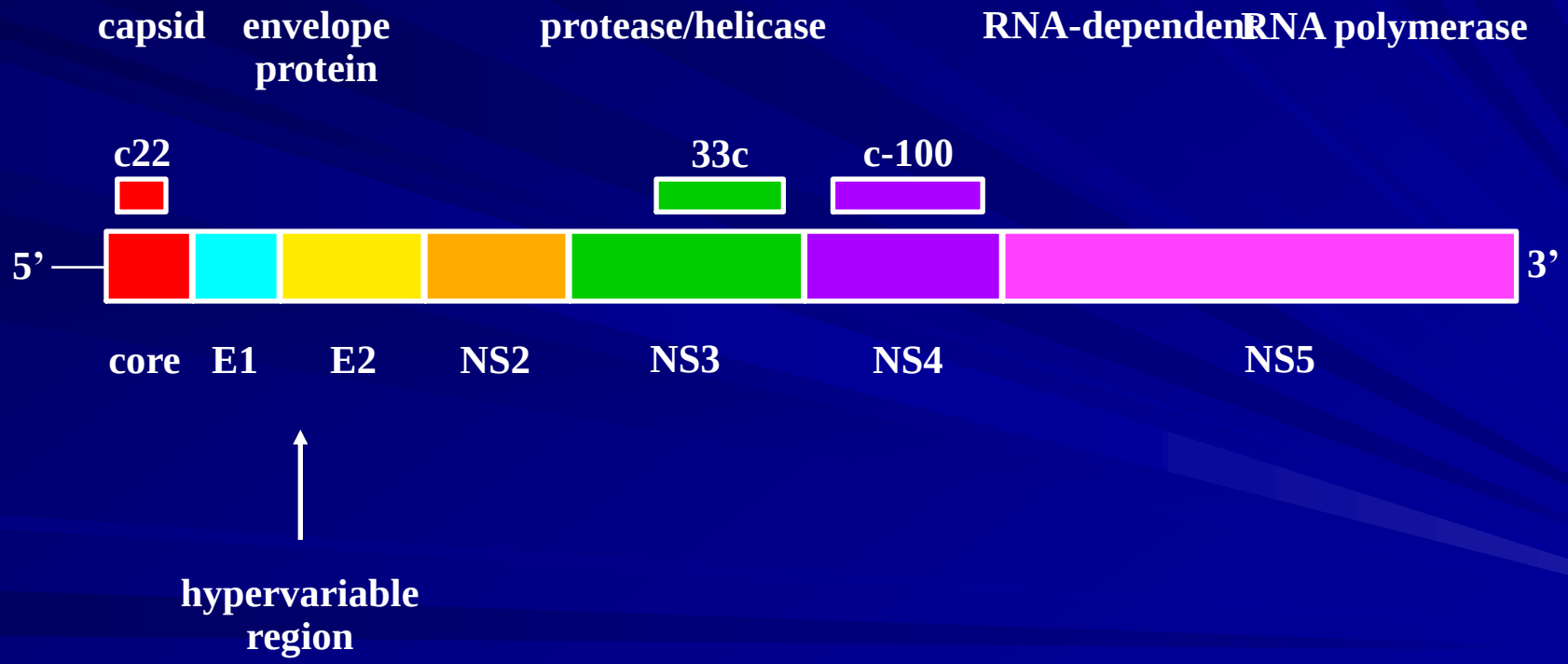
Treatment of chronic HBV

- Pegylated interferon weekly for one year or
- First line antivirals:Daily tablet of Entecavir(0.5,1 mg) or Tenofovir(300mg) or Tenofovir alafenamide (For renal and bone diseases,25 mg) or
- Second lines antivirals:Daily tablet of Lamivudine(100mg) or adefovir(10 mg).

Hepatitis C Virus (HCV)

- **major cause of "nonA, nonB hepatitis"**
  - genome cloned from transfusion-associated hepatitis patients in 1989
  - most common chronic blood borne infection in USA
- **Flavivirus family**
  - ss (-) RNA genome
  - envelope with glycoproteins
  - core protein
  - several nonstructural proteins
  - family of closely related viruses, 6 genotypes, >90 subtypes
  - HCV is not easy to grow in tissue culture

Hepatitis C Virus



Hepatitis C - Clinical Features

Incubation period:	Average 6-7 wks Range 2-26 wks
Clinical illness (jaundice):	30-40% (20-30%)
Chronic hepatitis:	70%
Persistent infection:	85-100%
Immunity:	No protective antibody response identified

Extrahepatic Manifestations

Hematologic	cryoglobulinemia B-cell lymphoma Plasmacytoma MALT lymphoma
Autoimmune	Autoantibodies Thyroiditis Sjogren's syndrome ITP
Renal	GN Membranous GN
Dermatologic	Leukocytolastic vasculitis Lichen planus Porphyria cutanea tarda
Rheumatologic	Inflammatory arthritis

Laboratory Diagnosis

- HCV antibody - generally used to diagnose hepatitis C infection. Not useful in the acute phase as it takes at least 4 weeks after infection before antibody appears.

- HCV-RNA - various techniques are available e.g. PCR and branched DNA. May be used to diagnose HCV infection in the acute phase. However, its main use is in monitoring the response to antiviral therapy.

Prevention of Hepatitis C

- Screening of blood, organ, tissue donors
- High-risk behavior modification
- Blood and body fluid precautions

HCV prevention and control

- no vaccine
- diagnosis is important
- transmission means is not always obvious
- milder clinical symptoms than HBV
- major area of study is biology of virus

Direct Acting Antiviral treatment of chronic HCV

- Protease inhibitors: Simeprevir(Olyseo),Paritaprevir(Qurevo,Viekera pak), grazoprevir(Zepatier),Glecaprevir(Mavyret),voxilaprevir(Vosevi).
- NS5B Polymerase inhibitors: Sofosbuvir(Sovaldi,Harvoni,Epclusa,Vosevi),Dasabuvir(Viekera pak).
- NS5A inhibitors: Ledipasvir(Harvoni),Daclatasvir(Daklinza),Ombitasvir(Qurevo,Viekera pak), elbasivir(Zepatier),velpatasvir(Epclusa, Vosevi), Pibrentasvir(Mavyret).

Hepatitis D (Delta) Virus

- antigen

Hepatitis D - Clinical Features

- Coinfection
  - severe acute disease
  - low risk of chronic infection
- Superinfection
  - usually develop chronic HDV infection
  - high risk of severe chronic liver disease

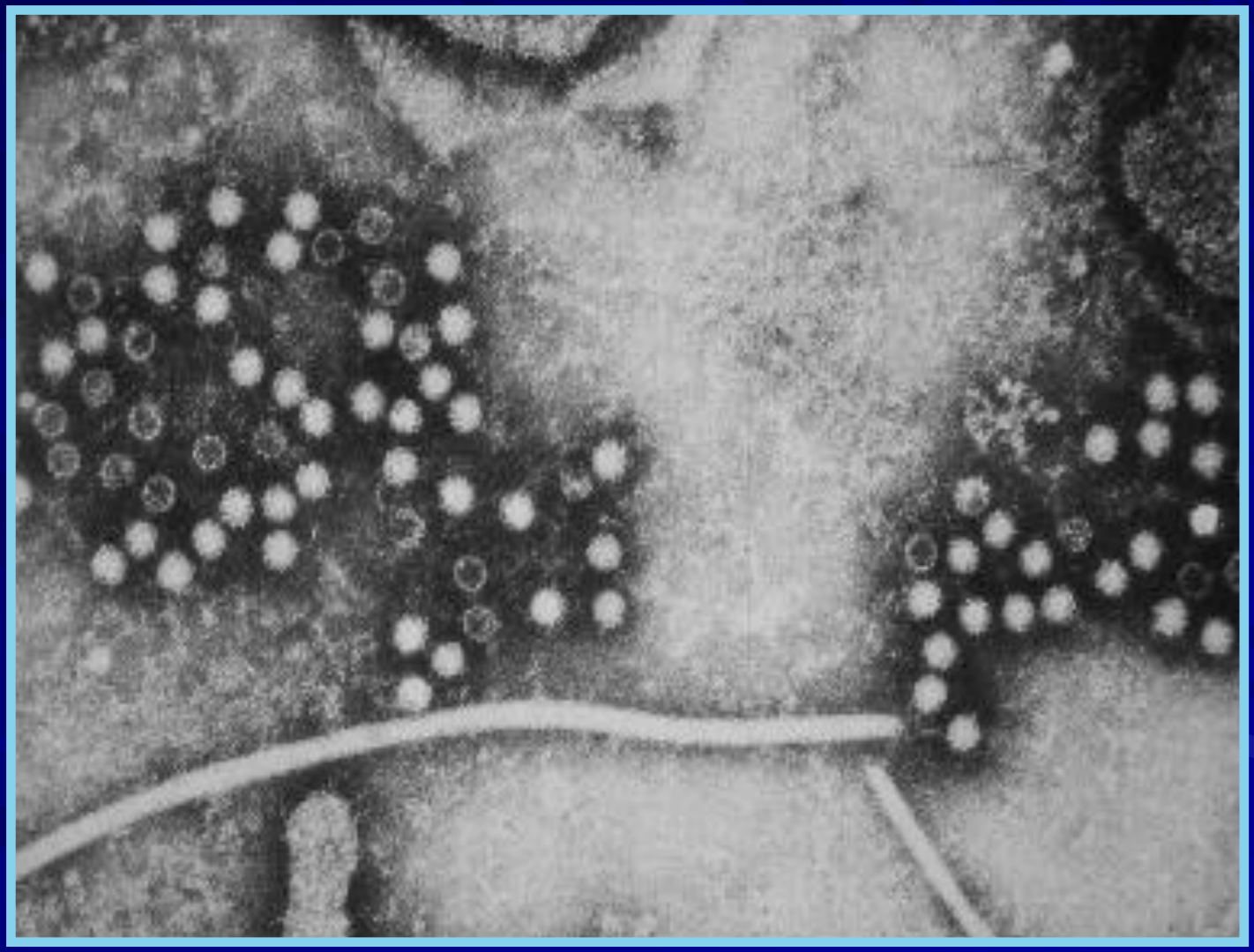
Hepatitis D Virus
Modes of Transmission

- Percutanous exposures
  - –injecting drug use
- Permucosal exposures
  - –sex contact

Treatment of chronic Hepatitis D

- Pegylated interferon alpha

Hepatitis E Virus



Hepatitis E - Clinical Features

- Incubation period: Average 40 days
  Range 15-60 days
- Case-fatality rate: Overall, 1%-3%
  Pregnant women, 15%-25%
- Illness severity: Increased with age
- Chronic sequelae: In liver transplant recipient

Hepatitis E - Epidemiologic Features

- Most outbreaks associated with fecally contaminated drinking water
- Minimal person-to-person transmission
- Cases usually have history of travel to HEV-endemic areas
- May be zoonotic with animal reservoir.


THANK YOU