



# Hepatitis Viruses

Medical and Public Health Microbiology  
(BMS 4510)

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# Viral Hepatitis

- Caused by hepatitis viruses
- Disease caused is clinically indistinguishable
- Hepatitis viruses belong to different classes of viruses and are transmitted differently

## **Other viral infections associated with Hepatitis**

- Herpesviruses
  - HSV, EBV and CMV
- Adenoviruses
- Coxsackieviruses
- Measles and Rubella
- Yellow fever (Jaundice)
- Marburg, Ebola, Lassa, Rift Valley fever, Crimean-Congo hemorrhagic fever
- Neonatal HSV, varicella, CMV, congenital rubella

# Other causes of Hepatitis

- Viruses
- Bacteria
- Protozoa
- Drugs and Toxins
  - Isoniazid, Carbon Tetrachloride, ethanol
- Symptoms and course similar

# Viral Hepatitis

	Hepatitis A	Hepatitis B	Hepatitis C	Hepatitis D	Hepatitis E
<b>Virus family</b>	<b>Picornaviridae</b>	<b>Hepadnaviridae</b>	<b>Flaviviridae</b>	<b>Deltavirus</b>	<b>Caliciviridae</b>
Transmission	enteric	Parenteral, perinatal, sexual	Parenteral, sexual	perinatal	enteric
Acute disease	Mild to moderate	moderate	Mild to moderate	severe	Severe in pregnancy
Sero diagnosis	IgM	HBsAg	IgM	IgM	IgM
Chronic carrier state	No	5-10%	50%	>50%	no
Chronic hepatitis, cirrhosis	No	1-5%	20%	>50%	no
Liver cancer	No	Yes	Yes	No	No

# Hepatitis A Virus (HAV)

## Presentation Outline:

- I. Characterization of virus
  - a. Structure
  - b. Pathogenesis & Clinical Significance
- II. Diagnostics
- III. Treatment
- IV. Epidemiology
- V. Prevention/Vaccine

# HAV: Structure

- The hepatitis A virus is a positive-sense, single-stranded RNA virus of approx. 7.5 kb in length.
- It is the sole member of the genus Heparnavirus and part of the Picornavirus family.
- Like other members of the Picornaviridae, HAV is small with a naked, that is non-enveloped, capsid.
- There is only one serotype of HAV and it is only known to infect primates.

## PICORNAVIRADAE

### **Enterovirus**

Poliovirus

Coxsackie A virus

Coxsackie B virus

Echovirus (ECHO virus)

Enterovirus

### **Rhinovirus types**

### **Cardiovirus**

### **Aphthovirus**

### **Heparnavirus**

Hepatitis A virus

# HAV: Environmental Resistance

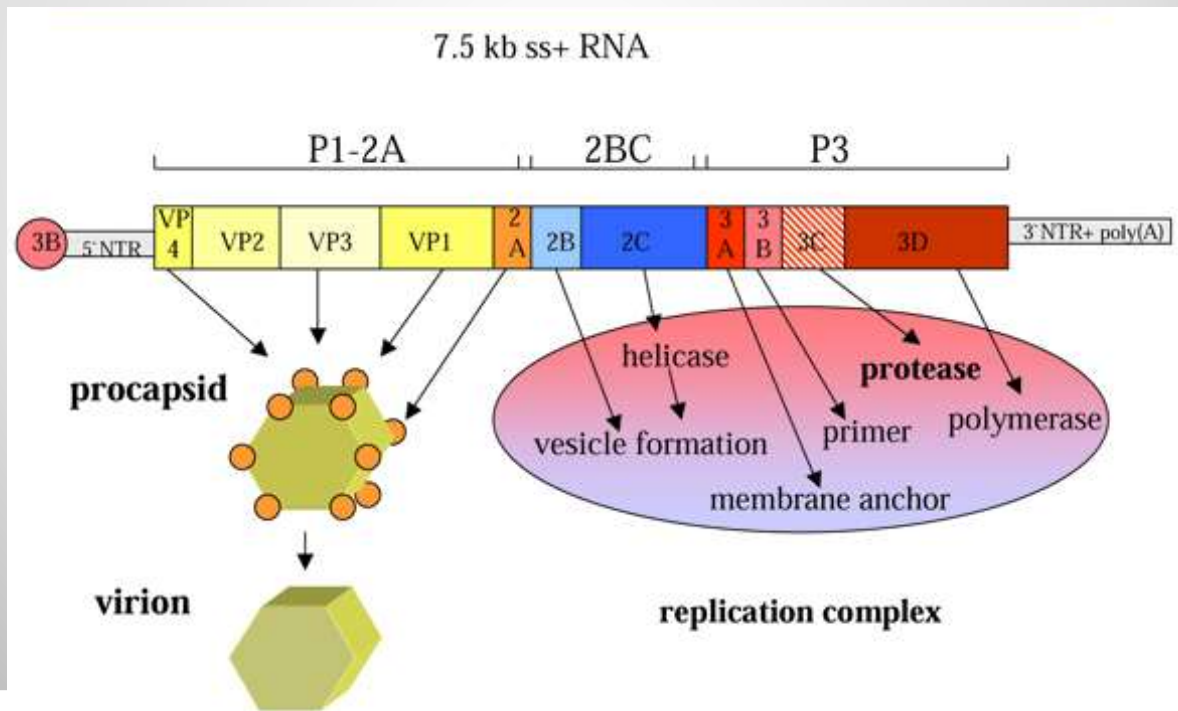
The capsid of Hepatitis A is icosahedral and extremely stable.

HAV is capable of survival in seawater, fresh water, and soil and shows long-term survival on hands and fomites, making them efficient vehicles of infectious transmission.

- Stable to:
  - Acid at pH 1
  - Solvents (ether, chloroform)
  - Detergents
  - Salt water, groundwater (months)
  - Drying (stable)
  - Temperature
    - 4°C: weeks
    - 56°C for 30 minutes: Stable
    - 61°C for 20 minutes: Partial inactivation
- Inactivated by:
  - Chlorine treatment of drinking water
  - Formalin (0.35%, 37°C, 72 hours)
  - Peracetic acid (2%, 4 hours)
  - $\beta$ -Propiolactone (0.25%, 1 hour)
  - Ultraviolet radiation (2  $\mu$ W/cm<sup>2</sup>/min)

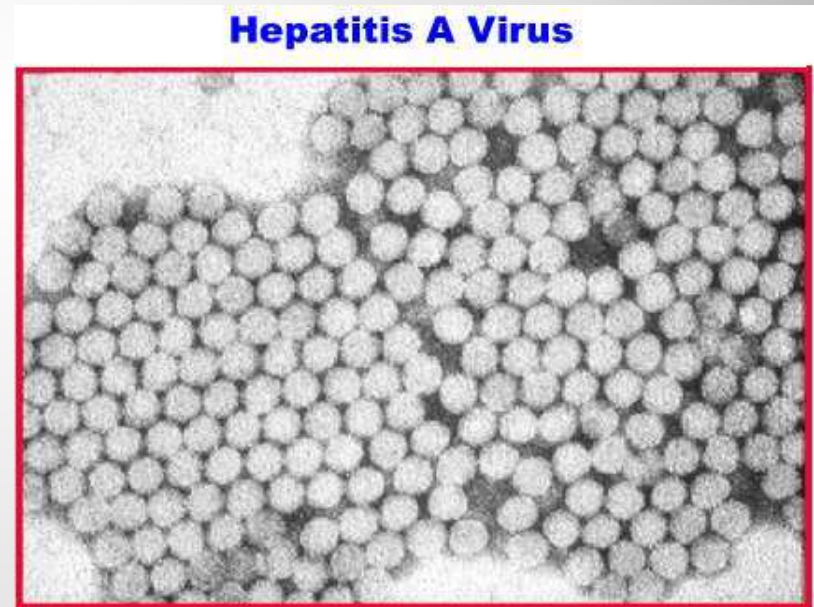
# HAV: Genomics

1. 5' noncoding region (NCR) is uncapped and covalently linked at the 5' end to the protein VPg which may be involved in initiation of RNA synthesis.
2. Single open-reading frame encodes all viral proteins, both structural and non-structural.
3. Short 3' NCR ends in a poly(A) tail.



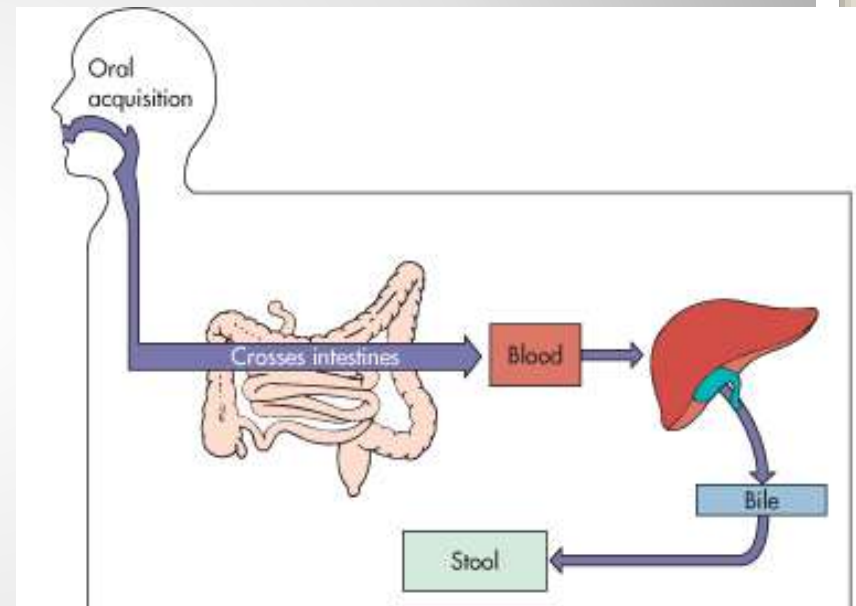
# HAV: Transmission

- Close personal contact
  - Household member
  - Sex contact
  - Childcare centers
- Contaminated food or water
  - Fecal – oral contact
  - Contaminated shellfish
  - Infected food handlers
- Blood exposure
  - rare



# HAV: Transmission

- Upon ingestion, viral particles reach target, the parenchymal cells of the liver.
- HAV replicates in hepatocytes and gastrointestinal epithelial cells and is released through exocytosis (rather than cell lysis) into bile and from there into stool.

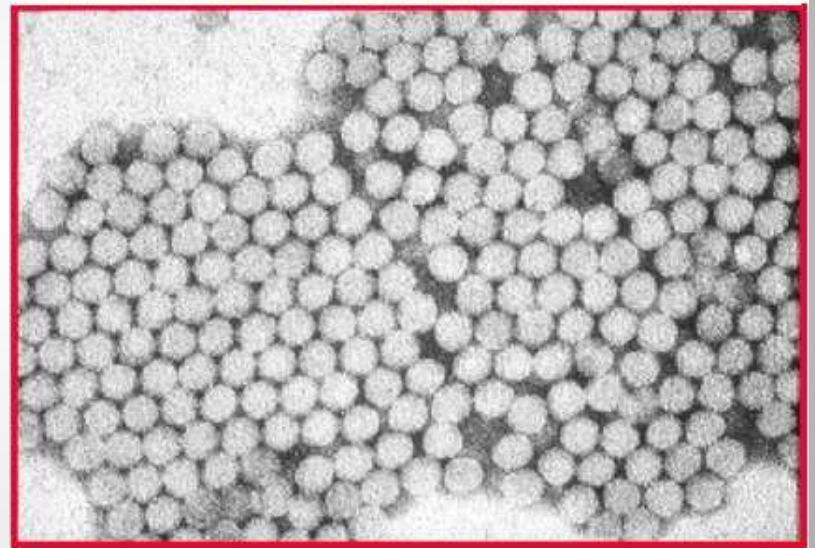


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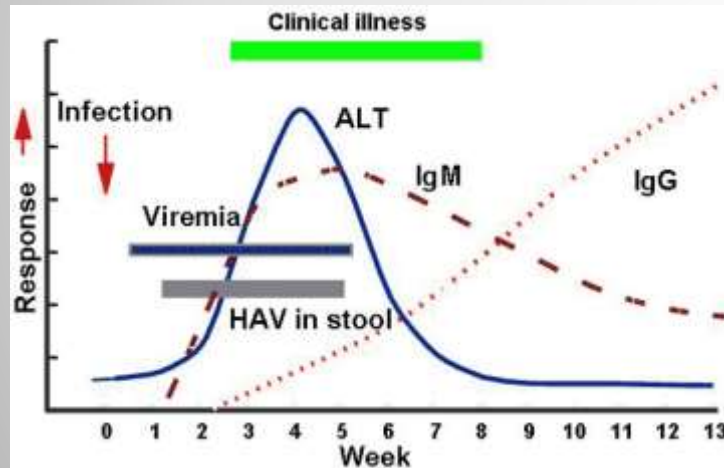
# HAV: Clinical Features

- Incubation period is usually about 30 days after exposure, range is 15 – 50 days
- Jaundice (turning yellow) is most commonly seen in the older patients
  - Under 6 years old (10%)
  - 6 to 14 years old (40 – 50%)
  - Greater than 14 years old (70 – 80%)
- Fatigue
- Dark urine
- Fever
- Nausea and vomiting
- Abdominal pain
  - Complications of this type of viral infection include rare liver failure and relapsing hepatitis
  - Chronic sequelae are not seen
- 33% of the US population has evidence of past infection and thus immunity

**Hepatitis A Virus**



# HAV: EVENTS IN INFECTION



ALT = Alanine transaminase

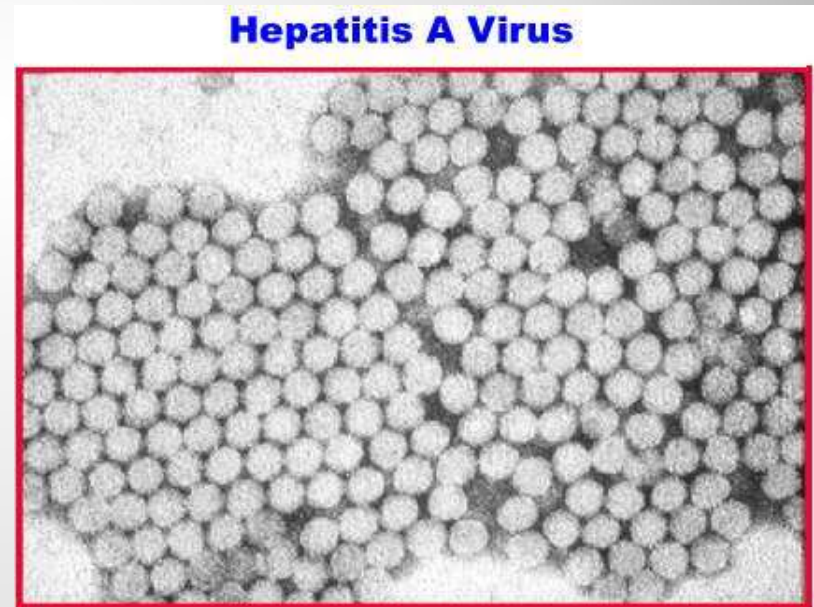
- As the immune system responds to the infection, the amount of virus in the blood (viremia) and in the stool (HAV in stool) disappears. The liver enzyme, ALT goes up at the beginning of the infection, but decreases to normal at about 8 weeks. IgM shows acute infection and IgG is positive long-term.

# HAV: Diagnosis

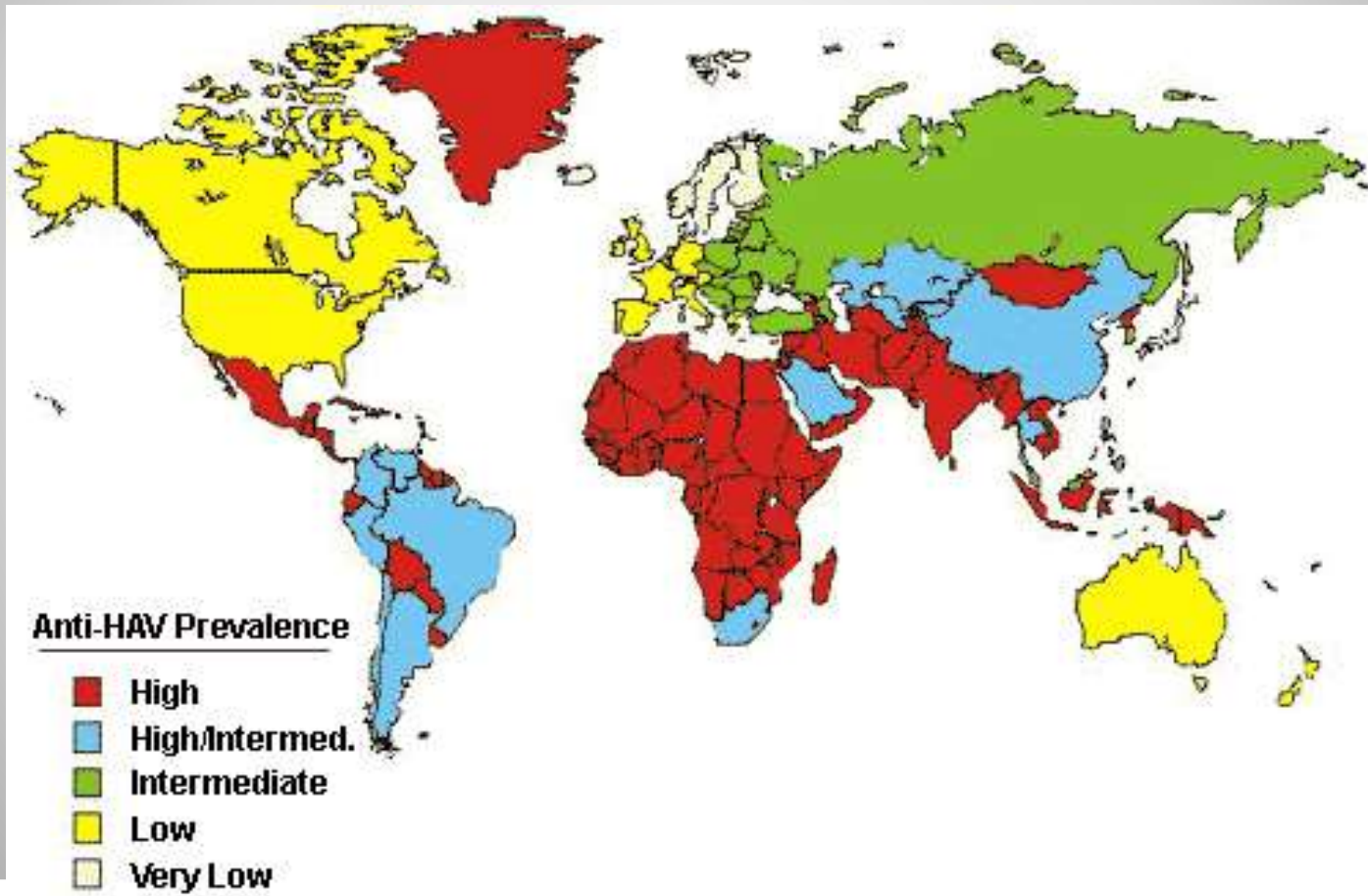
- Time course of clinical symptoms
- Identification of known source
- Hepatitis Panel
  - IgM anti-HAV detectable in blood as early as 2 weeks after the initial infection. Antibodies disappear 3 to 12 months after the infection.
  - IgG anti-HAV appear approximately 8 to 12 weeks after initial infection. Antibodies remain in the blood for lifelong protection (immunity) against HAV and indicate previous infection.

# HAV: Treatment

- HAV Treatment
  - No specific medical treatment
  - Avoid alcohol and all medications that are metabolized in the liver
  - Manage symptoms
  - If the spleen is enlarged avoid activities that could lead to abdominal pressure or injury

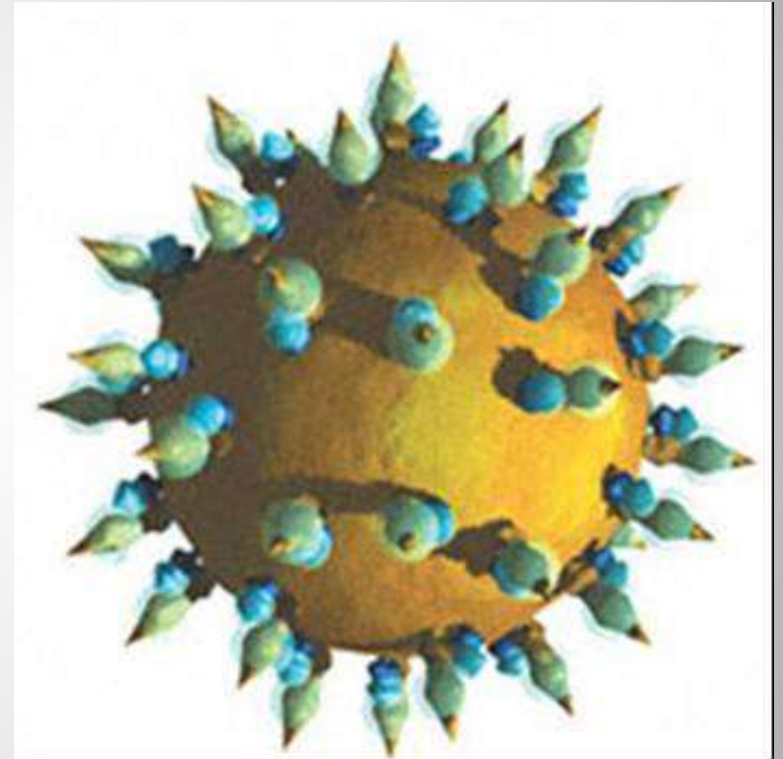


# HAV: Worldwide Prevalence



# HAV: Prevention

- Wash hands
- Use gloves when appropriate
- Risk reduction if involved in oral/anal sexual practices
- Risk reduction if involved in intravenous drug use
- Vaccination



Hepatitis A virus. Courtesy of PRN Notebook Online ([www.prn.org](http://www.prn.org)). Model created by Dr. Louis Henderson PhD, Frederick Cancer Research Center.

# HAV: Prevention (continued)

- Immune Globulin (IG)
  - Sterile preparation of concentrated antibodies (immunoglobulins) made from pooled human plasma
    - Only plasma tested negative for hepatitis B, HIV, and hepatitis C are used
  - Provides protection against hepatitis A through passive transfer of antibody
  - When administered within 2 weeks after an exposure to hepatitis A virus, IG is 80 – 90% effective in preventing hepatitis A
  - IgA deficiency has been known to cause anaphylaxis after repeated intramuscular administration of IG

# HAV: Vaccination

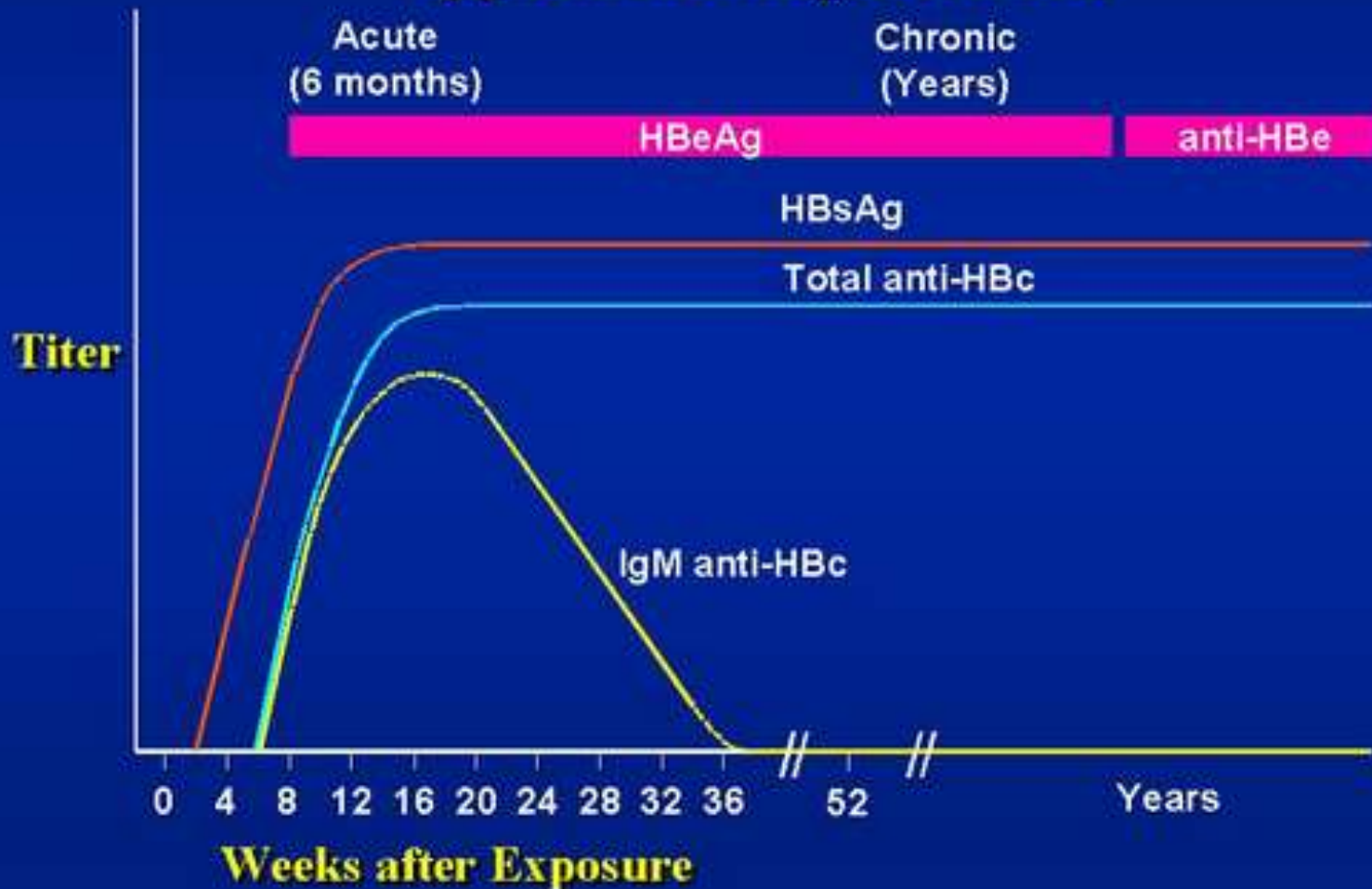
- HAV Vaccines first licensed in 1995 in the US (1992-1994 in other places)
  - Vaccines created from inactivated virus
  - Vaccines are highly immunogenic where 100% of those vaccinated with 2 doses will seroconvert to a protected level
  - 2005 recommendations: routine vaccination of all children in US beginning at 1 year of age
- Pre-exposure Vaccination
  - Persons at increased risk for infection:
    - Travelers to intermediate and high HAV-endemic countries
    - Homosexual and bisexual men (men who have sex with men)
    - Persons with HIV/AIDS
    - Drug users
    - Persons with chronic liver disease including Hepatitis C
    - Persons with a diagnosis of clotting factor disorder
    - Persons with occupational risks
  - Communities with high rates of hepatitis A [e.g., Alaska Natives, American Indians]
  - Routine childhood vaccination

# Hepatitis B Virus

- A hepadnavirus
- Established chronic infections
  - Especially in those infected as infants
  - Causes acute and chronic hepatitis and permanent carrier state
- Major cause of liver disease and hepatocellular carcinoma
- Structure:
  - Three morphological forms of HBsAg
    - Spherical (22nm in diameter)
    - Tubular form (200nm long)
    - Larger spherical virions (42nm in diameter)



# Progression to Chronic Hepatitis B Virus Infection Typical Serologic Course



# Geographic Distribution of Chronic Hepatitis B Virus (HBV) Infection

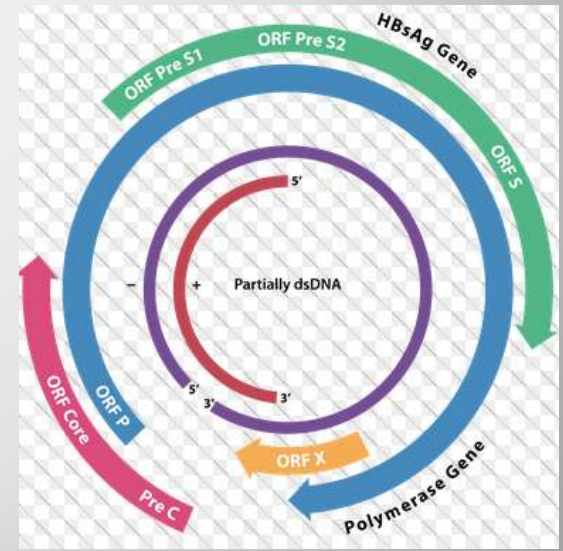


## HBsAg Prevalence

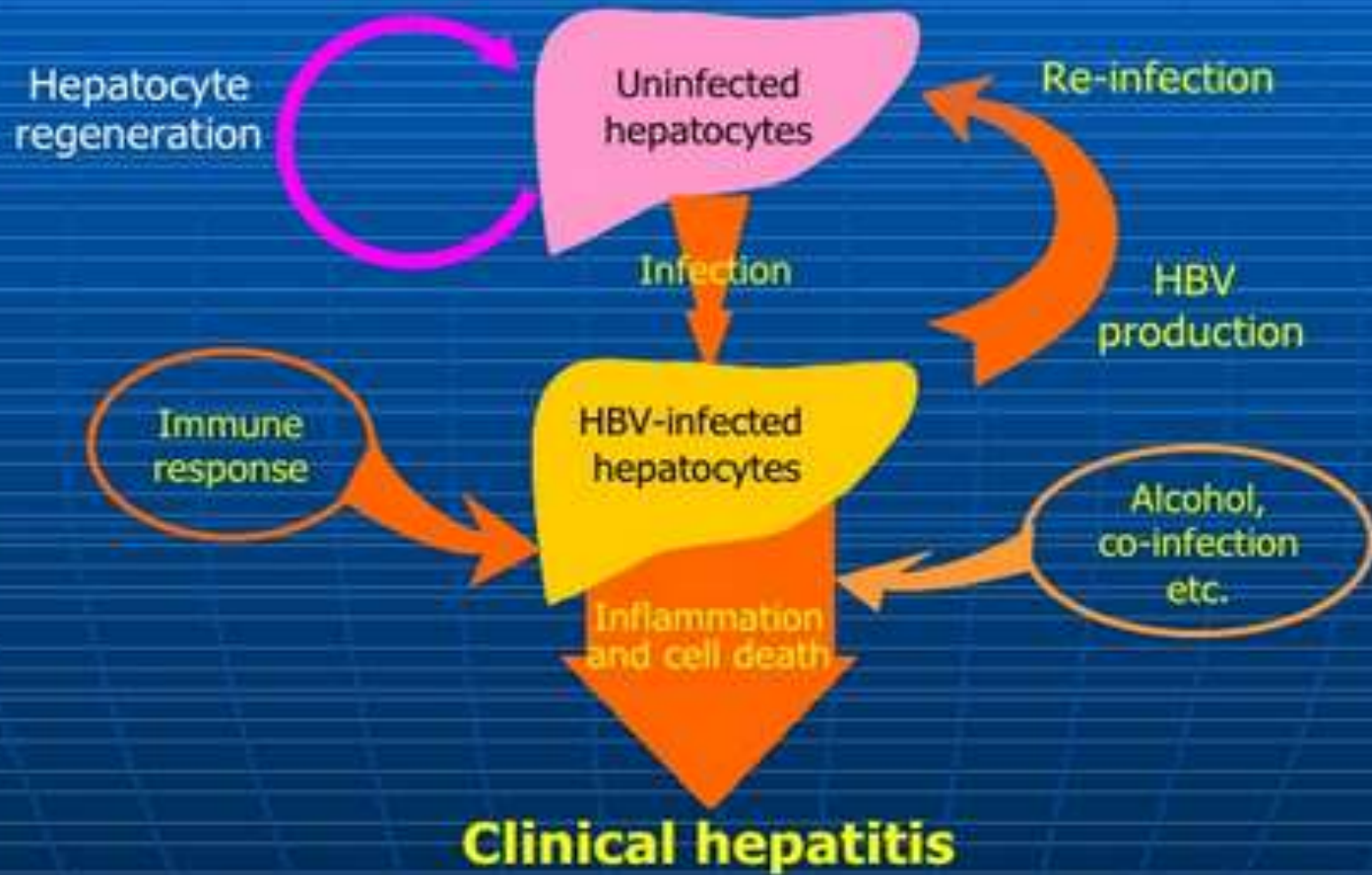
- $\geq 8\%$  – High
- 2%–7% – Intermediate
- $< 2\%$  – Low

# Hepatitis B Virus

- Virions
  - Average size is 42nm in diameter
- Genome: one molecule of circular dsDNA, 3.2kbp
- Proteins
  - HBsAg
  - Envelop contains HBsAg and lipid
- Replication
  - Forms intermediate RNA



# Pathogenesis of HBV Infection



# SIGNS AND SYMPTOMS OF HEPATITIS-B

➤ Jaundice



➤ Fever



➤ Fatigue in a short period

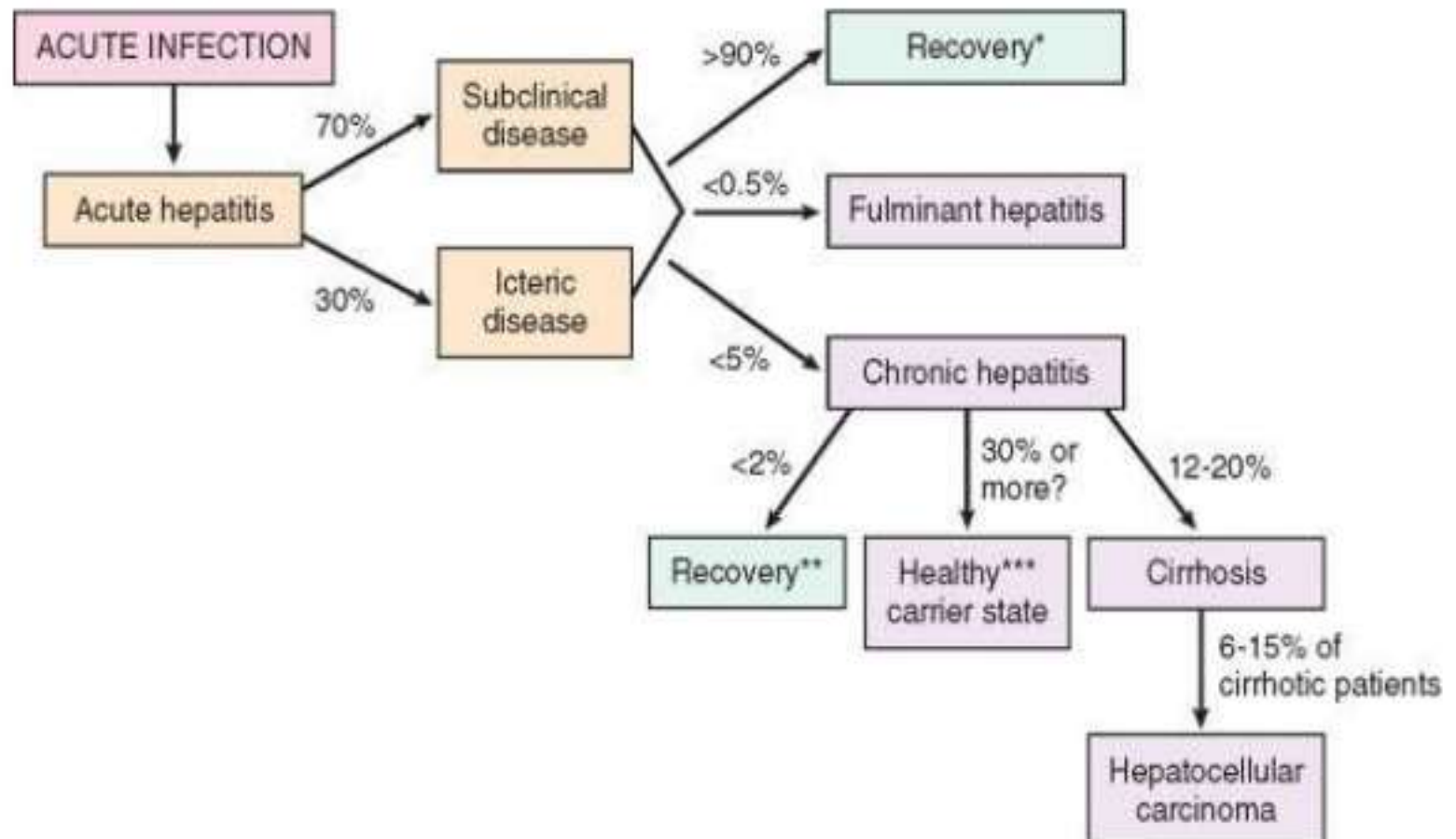
➤ Abdominal Pain

➤ Gastrointestinal problems

➤ Loss of appetite



# Natural History

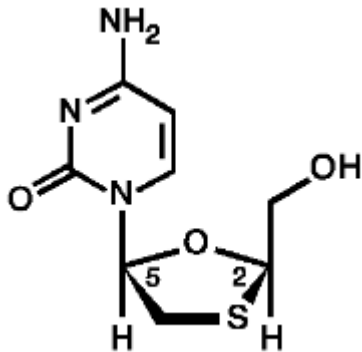


# Hepatitis B: Treatment Options

- Pre-exposure vaccination is better than any treatment option
- Option 1: Chemotherapeutic
- Option 2:  
Biotherapeutic/Immunotherapeutic

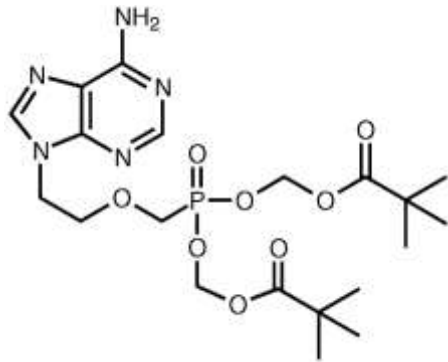
# Chemotherapy

- Lamivudine is a nucleoside analogue
- Lamivudine linked to mutations in YMDD motif of polymerase
- Lamivudine is relatively non-toxic
- Lamivudine may restore T-cell responsiveness in chronic Hepatitis B patients (open doorway to vaccination in previous carriers)



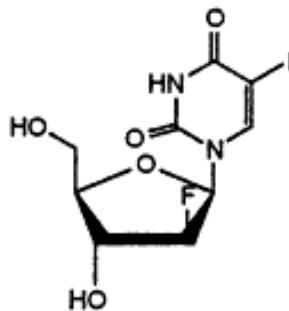
# Chemotherapy

- Adefovir is a newer nucleoside analogue
- Shown to be more effective than Lamivudine
- Alternative when Lamivudine resistance occurs
- Drawback: Toxic to kidneys
- Lamivudine + Adefovir combination appears to have synergistic effect but overall not greatly enhanced



# Chemotherapeutic (failures)

- Fialuridine was found to poison the mitochondria
  - dysfunction or death attributed to lactic acidosis



FIAU: 1-2'deoxy-2'fluoro-1-β-D-arabinofuranosyl 5-iodouracil

# Chemotherapeutic (potentials)

- Tenofovir
  - nucleoside analogue approved for HIV
  - shown to be effective against HBV (4 log reduction in viremia)
  - increased HBeAg seroconversion

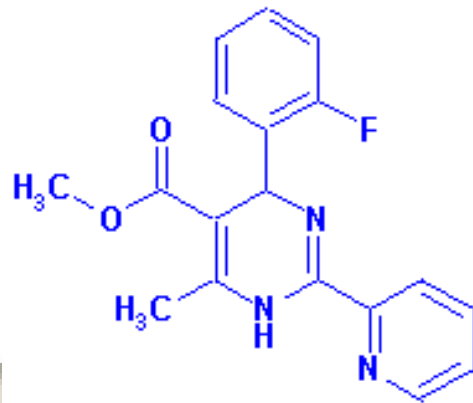
## OTHER NUCLEOSIDE ANALOGUES

- Entecavir (G analogue)
- L-deoxythymidine (T analogue)
- Emtricitabine
- Clevudine

# Chemotherapeutic (potentials)

- BAY 41-4109 (Methyl (R)-4-(2-chloro-4-fluorophenyl)-2-(3,5-difluoro-2-pyridinyl)-6-methyl-1,4-dihydro-pyrimidine-5-carboxylate); Abstract from Intersci Conf Antimicrob Agents Chemother (Bayer, 2001)

- Novel Non-Nucleosidic and Highly Potent Inhibitor of Human Hepatitis B Virus



# Biotherapeutic/Immunotherapeutic

- Interferon Alpha (IFN  $\alpha$ ) used for many years
- Minor benefit; mainly immunomodulatory
- Effectiveness depends on E antigen status, Liver enzyme level, level of viremia, mutations
- Activity can be boosted by covalent attachment of polyethylene glycol moiety (pegylated INF)

# Biotherapeutic/Immunotherapeutic

- Thymosine  $\alpha$  1 is a hormone that enhances T cell maturation and function
- Activity alone is relatively weak but might prove useful in combination therapies

# Biotherapeutic/Immunotherapeutic

- Hepatitis B Immunoglobulin (HBIG)
- HBIG used to prevent allograft infection
- HBIG cost is very high
- Early efforts into viral gene suppression by antisense DNA oligos
- HBV specific ribozyme complexes (ribozymes found to block nucleotide complementary sequence sites)
- Efforts in transfection with recombinant vectors (antiviral Abs to interfere with replication)

## Biotherapeutic/Immunotherapeutic

- In vitro studies found applicability of siRNA for treatment of persistent HBV (therapeutic potential)
- dsRNA interferon induction (immunomodulatory)
- Therapeutic vaccines to break persistent infections

# Prevention of Hepatitis B

- 'Safe' sex practices
- Avoidance of needlestick injuries or injection drug use
- Active and passive prophylaxis

## Prevention of exposure to hepatitis B virus

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### Preventing direct exposure

Avoidance of mucosal contact or parenteral intrusion with/by

Infected body fluids and secretions

Infected blood or blood products

Needle sharing, intravenous drug use

Unprotected sex

Infected patient–doctor contact

Contact via abrasions and open lesions

### Preventing indirect exposure

Renal dialysis

Fomites

Medical instruments, acupuncture, needle stick

Environmental exposure—wounds and scratches

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# Passive prophylaxis

- ISG
  - Anti-HBs (HBIG)
    - Prepared from persons with high titers of HBsAg but are free of the antigen itself.
    - Reduces disease if administered immediately after exposure
    - Postexposure passive prophylaxis must be followed by active immunization with vaccine

# Active Prophylaxis (Immunization)

- Inactivated Hepatitis B vaccine
  - Have been available for several years
  - First developed by purification and inactivation of HBsAg from blood of chronic carriers
    - No longer in use
- Recombinant HBsAg grown in yeast
  - Current vaccine
  - Excellent protection has been shown in MSM/Medical personnel
    - High risk groups should be vaccinated
      - Laboratory workers, Injection drug users, Children (Recently)

# Prevention of vertical transmission

- Combination active and passive prophylaxis
  - Most effective approach to prevent neonatal acquisition and development of chronic carrier state in neonate
- Routine screening of pregnant women for HBsAg
  - Infants born to HBsAg<sup>+</sup> women are given HBIG immediately followed by three doses of Hepatitis B vaccine within 24hrs of birth
  - Similar combination is used for unimmunized persons exposed by needlestick or similar injuries.
    - Procedure varies depending on the Hepatitis B status of the 'donor' linked to the injury

## Research and development of hepatitis B vaccines

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Hepatitis B virus does not grow in cell culture

- 1965 Blumberg discovery of surface antigen opens door to vaccine
  - 1968 Pioneering studies initiated in our laboratories to purify antigen and to inactivate all life forms
  - 1971 Process developed, safety established in vitro, antigen formulated in alum, potency shown for plasma-derived vaccine
  - 1973 Safety and efficacy established in chimpanzee studies
  - 1975 Clinical safety shown
  - 1980 High-level protective efficacy shown in clinical trials
  - 1981 Plasma-derived vaccine licensed
  - 1975 Collaborative venture started to attempt recombinant expression in yeast. Success achieved
  - 1980 Process developed for purification of antigen from yeast
  - 1982 Yeast-derived antigen substituted for plasma-derived antigen in vaccine
  - 1986 Yeast-derived vaccine licensed
-

## Performance of hepatitis B vaccine

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Paradigm for a safe and effective vaccine

In adults, protection in near 100% of antibody responders.

Overall efficacy 95%

In newborn infants born to *e* antigen positive mothers — vaccine overcomes tolerance and immunizes in at least 75%

In babies from non-carrier mothers, protection is near 100%

Lasting immunity, with strong anamnestic memory

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## Economic analysis for vaccination benefits

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Great societal benefits may derive from vaccination, but policy for vaccine use is based on cost effectiveness

Cost effectiveness is based on the savings in medical treatment and time lost per dollar spent for vaccination. Thus, the cost per unit of benefit

The World Bank measures benefit in terms of cost for each disability adjusted life year saved. Thus, DALY

Six vaccines used by the Expanded Program on Immunization cost less than \$25.00/DALY

The cost for universal infant immunization against hepatitis is estimated at \$25–50 per DALY using purchased vaccine

General view by World Bank:

A cost of less than \$100 per DALY is a good buy

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## Utilization of hepatitis B vaccine

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Universal immunization of all newborn — at least 90 nations

Immunization of all high-risk persons and adolescents — some nations

Worldwide immunization — will gradually reduce the 350 million carrier pool and the deaths from liver disease

Worldwide focus on newborn alone — will require at least one generation to bring hepatitis under substantive control

Nationwide immunization program in Taiwan — reduced liver cancer in 12–14-year-old children by 75%

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## The legacy and future of hepatitis B vaccine

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Hepatitis B is a disease for which a solution already exists

The solution lies with global immunization of all susceptibles

Elimination/eradication of the infection could bring huge cost savings

High cost of disease and disability eliminated

High cost for research could be diverted to medical problems that still need to be solved

United Nations General Assembly — declaration that protection by vaccines is a basic human right

Global Alliance for Vaccine Initiatives (GAVI): current major force to develop and bring vaccines to all peoples

Gates Foundation brings economic reality to vaccine initiatives

Real value is given when medical science brings health to all nations for the betterment of mankind

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# Hepatitis C Virus

- Causes of Hepatitis
- Hepatitis C Virus
  - Virology
  - Genome Organization
  - Viral Replication
- Hepatitis C Disease
- Transmission
- Clinical Manifestations
- Diagnosis
- Prevention and Treatment

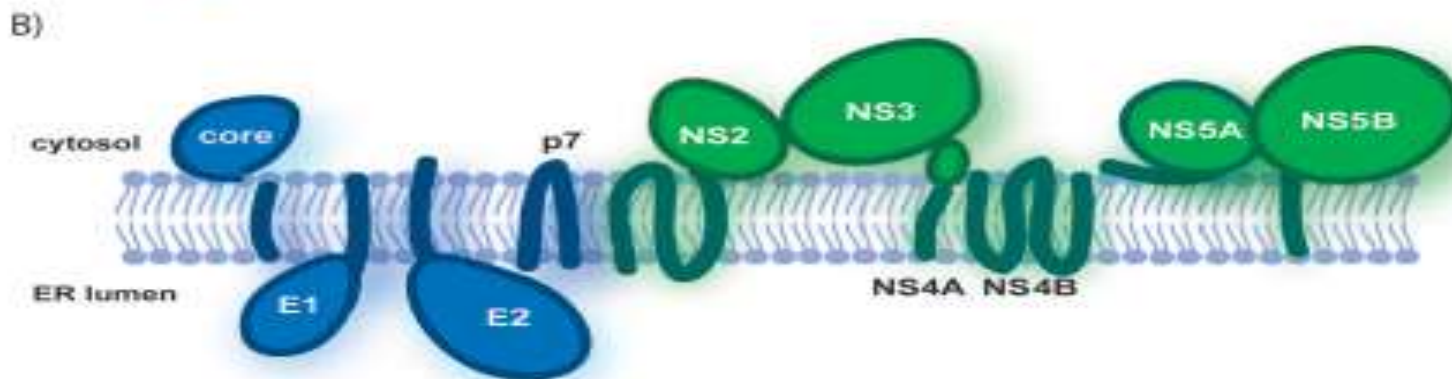
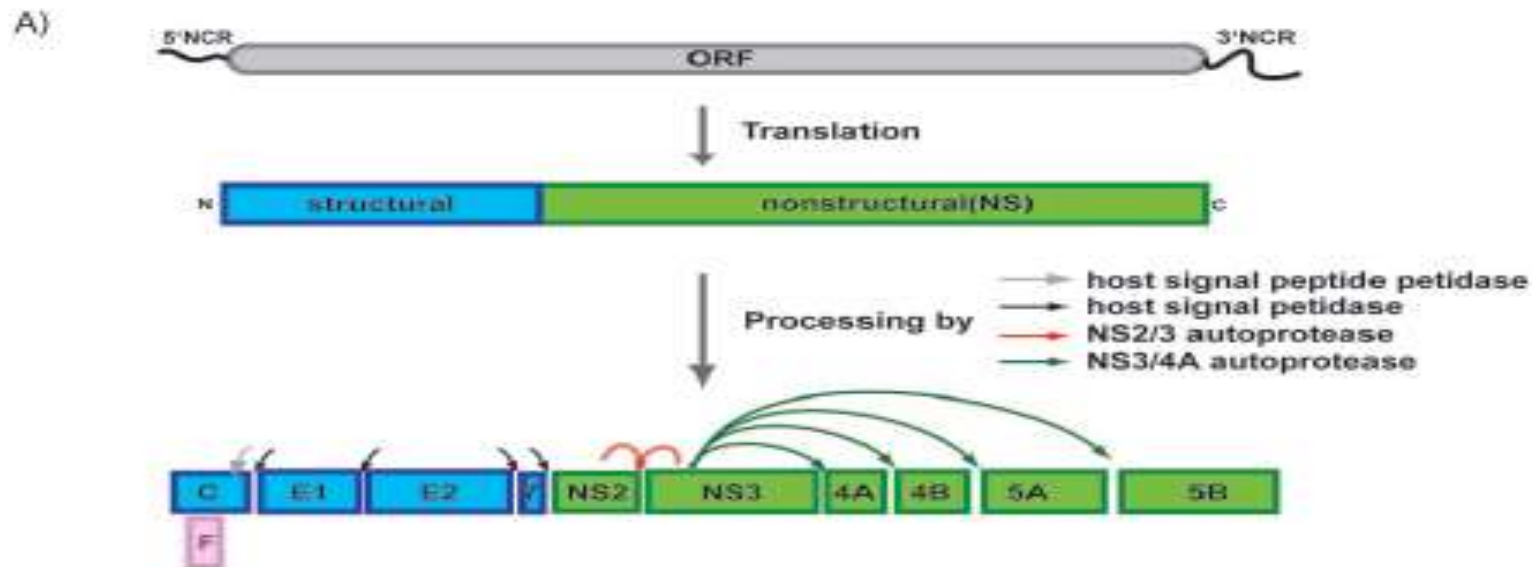
# Hepatitis C

- Positive sense single stranded RNA Virus
- RNA and nucleocapsid are enveloped in host derived membranes
- Existence and role in etiology identified by cDNA clones from RNA in infectious serum
- Peptides encoded by clones tested with sera from cases highly specific
  - Basis for a serological test

# Hepatitis C Virus Virology

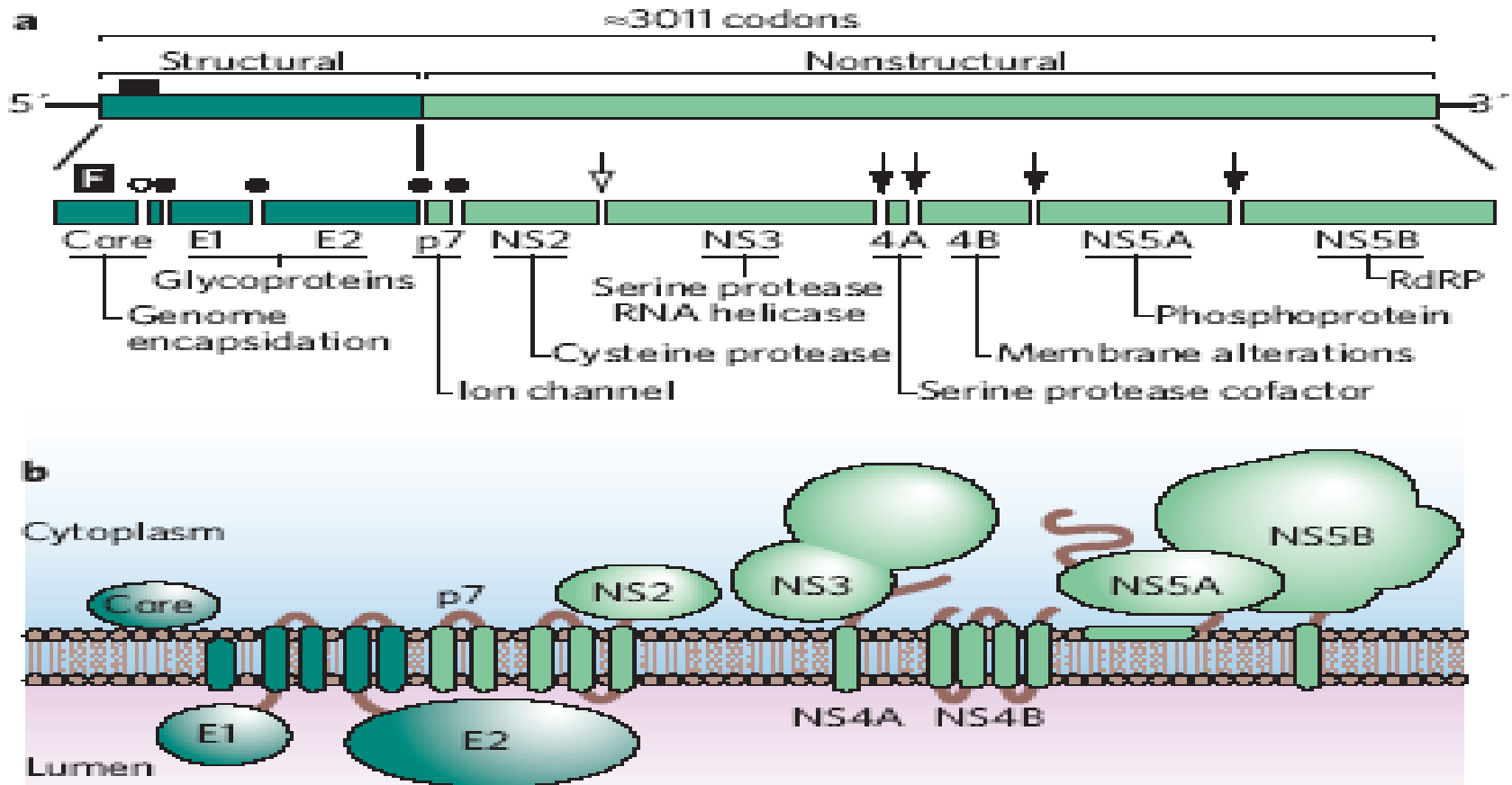
- Flavivirus (Other members: yellow fever, dengue)
  - RNA virus
- Simple genome
  - Three structural genes
  - Five non-structural genes
- Six major genotype, multiple subtypes
  - Genotype have different geographical distributions
  - Associated with different severity of disease and response to therapy

# Hepatitis C Genome Organization



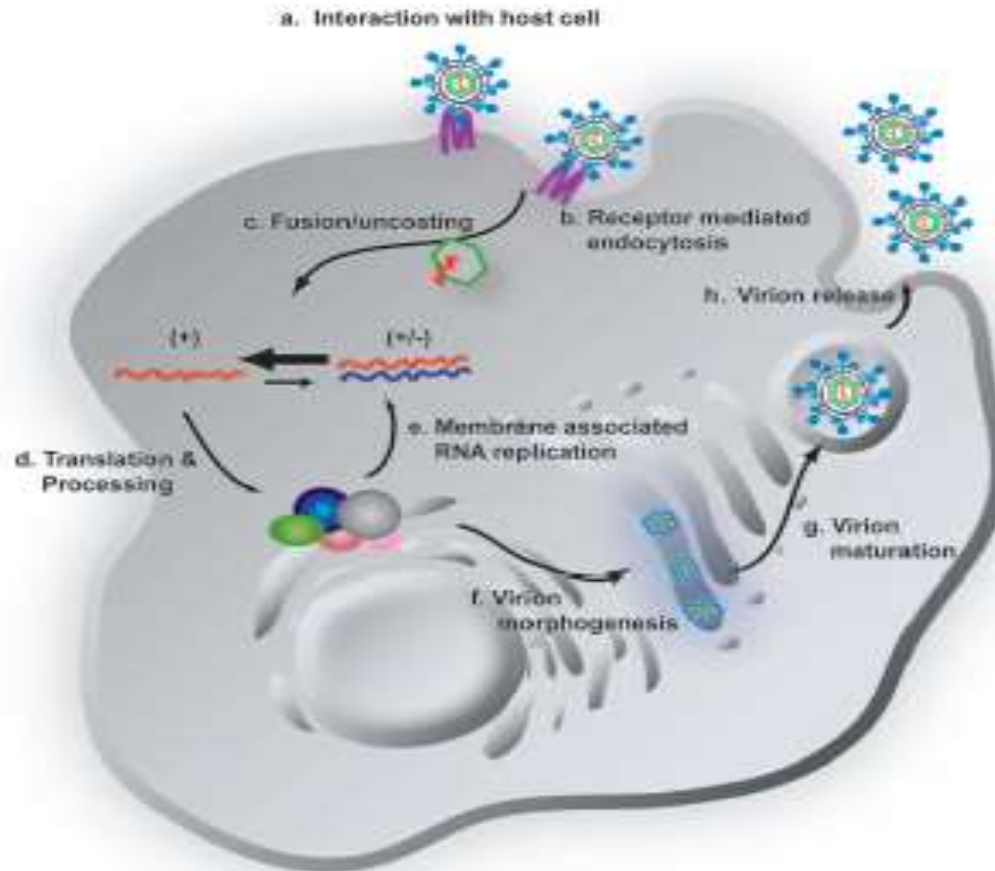
HCV genome organization, polyprotein processing, and protein topology. (A) The HCV genome is a single-stranded RNA encoding a single large open reading frame (ORF) of roughly 3,000 amino acids, flanked by structured 5' and 3' NCRs. The translation of the open reading frame, via the activity of an IRES element in the 5' NCR, generates a large polyprotein that is organized with structural proteins in the amino-terminal third of the polyprotein, followed by the NS replication proteins. The polyprotein undergoes a complex co- and posttranslational series of cleavage events, catalyzed by both host and viral proteases, to produce the 10 individual HCV proteins. (B) The topology of the HCV proteins relative to the ER membrane.

# Hepatitis C Genome Organization



**Figure 2 | HCV genes and gene products.** **a**, The structure of the viral genome, including the long open reading frame encoding structural and nonstructural genes, and 5' and 3' NCRs. The polyprotein processing scheme is shown below. Closed circles refer to signal peptidase cleavage sites; the open circle refers to the signal peptide peptidase cleavage site. All other terms are defined in the text. **b**, The topology of HCV proteins with respect to a cellular membrane.

# Hepatitis C Replication



1. Schematic diagram of the HCV life cycle. The life cycle of HCV is similar to that of other members of the *Flaviviridae* family. Extracellular HCV virions interact with receptor molecules at the cell surface (a) and undergo receptor-mediated endocytosis (b) into a low-pH vesicle. Following HCV glycoprotein-mediated membrane fusion, the viral RNA is released into the cytoplasm (c). The genomic RNA is translated to generate a single large polyprotein that is processed into the 10 mature HCV proteins in association with a virus-derived ER-like membrane structure termed the membranous web (d). The mature HCV proteins replicate the RNA genome via a minus-strand replicative intermediate to produce progeny RNA. A portion of this newly synthesized RNA is packaged into nucleocapsids and associated with the HCV glycoproteins, leading to budding into the ER (f). Virions follow the cellular secretory pathway (g) and, during this transit, maturation of particles occurs (g). Mature virions are released from the cell, completing the life cycle (h). +, positive-sense genomic RNA; +/-, minus-strand replicative intermediate associated with positive-strand genomic RNA.

# Hepatitis C Disease

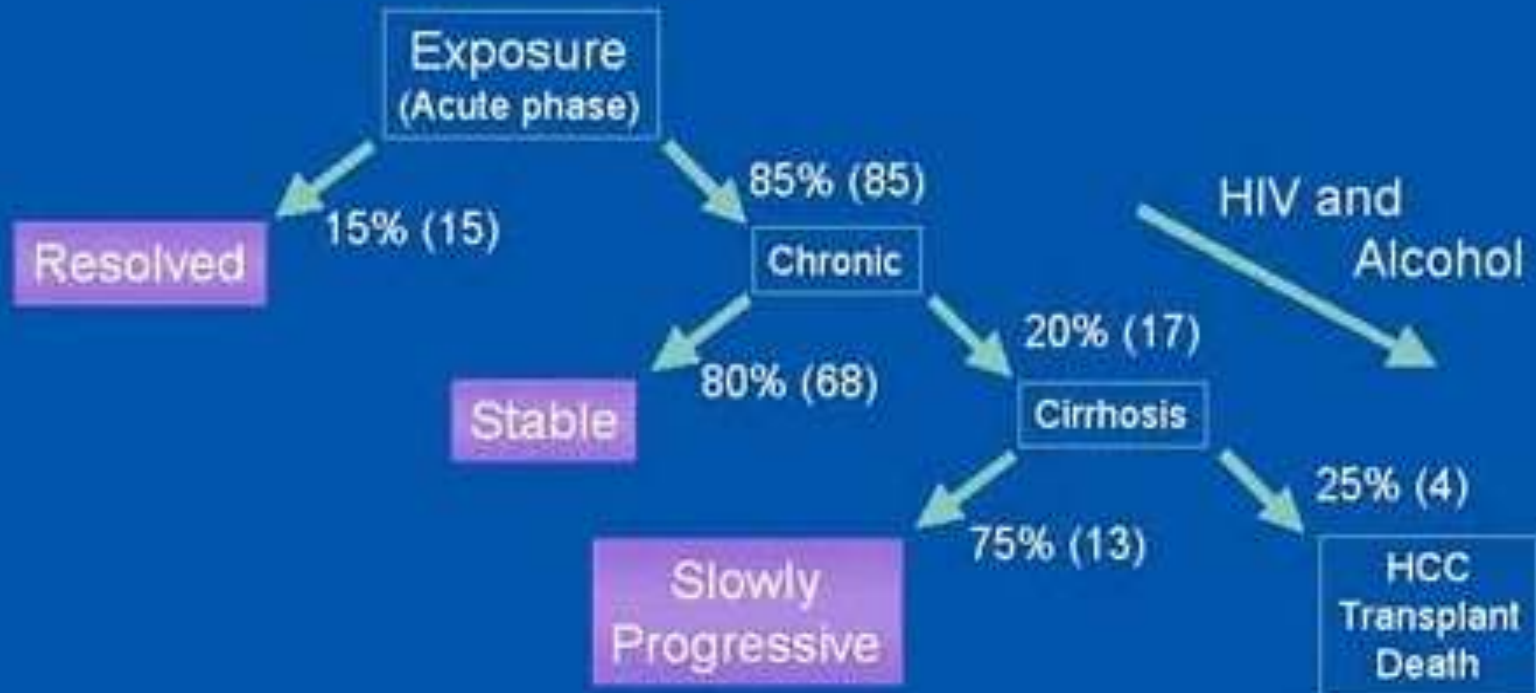
- Insidious disease
  - No clinically evident acute illness
- In about 25% of cases there is smoldering chronic hepatitis that ultimately leads to liver failure

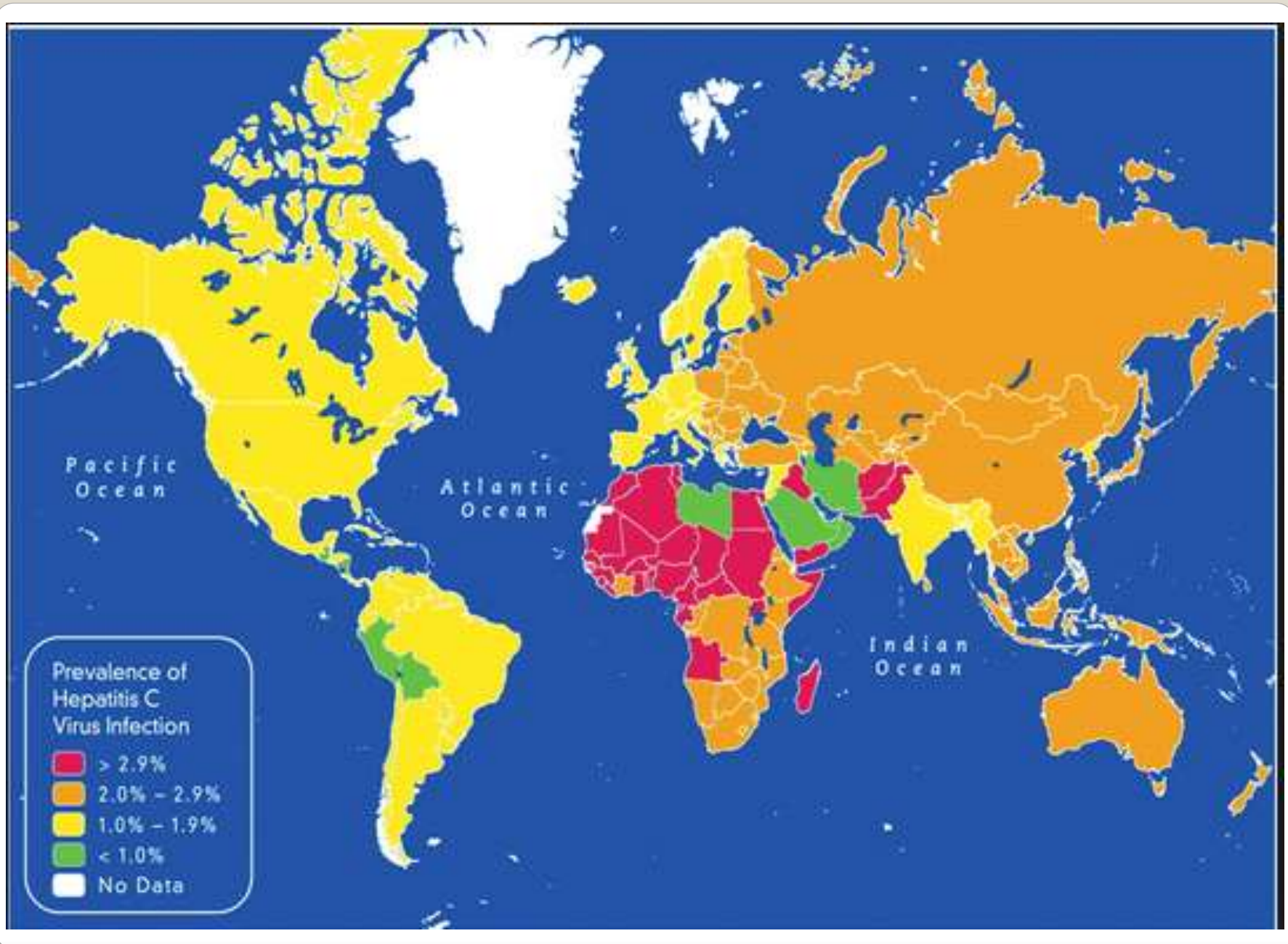
# Co-infection with HIV

- Increases risk of sexual transmission
- More severe liver disease



# Natural History of HCV Infection





# Transmission

- Less well understood than A,B,D
- Major cause of posttransfusion hepatitis until serological test was developed
- Transmission by blood well documented
- May be transmitted sexually, needle sharing (40% of cases)
- Vertical transmission very low (6%..Japan)
- In the US 1.8% of people have antibody to Hep. C (3% worldwide)
  - Screening of blood products
    - Reduced posttransfusion hepatitis by 80-90%
  - Outbreaks associated to IVIG

# Symptoms

- Incubation period is 6-12 weeks
- Assymptomatic or mild
  - Results in chronic carrier state in up to 85% of adult patients
- 10-18 years to develop chronic hepatitis
- Cirrhosis and hapatocellular carcinoma are late sequaleae of chronic hepatitis
- Elevated alanine aminotransferase (ALT) in serum
- Leading cause of liver transplantation in the US

# Diagnosis

- Antigens not detected in blood
  - Diagnostic tests test for antibody
- Unfortunately, antibody tests test negative in acute disease
  - IgG to Hep. C may not develop till 4 months
- Current tests
  - Enzyme immunoassays or immunoblots
- Quantitative RT-PCR assays for Hep. C RNA may be used for
  - Diagnosis
  - Estimating prognosis
  - Predicting interferon responses
  - Monitoring therapy
- No good correlation between viral load and histology

# Treatment

- Combination therapy
  - Pegylated Interferon alpha
  - Ribavirin
    - Poorly tolerated
- Corticosteroids not beneficial
- Responses better in individuals with genotypes other than 1 and those with low viral RNA titers
- Criterion to start therapy controversial
  - Elevated liver enzymes and abnormal liver histology

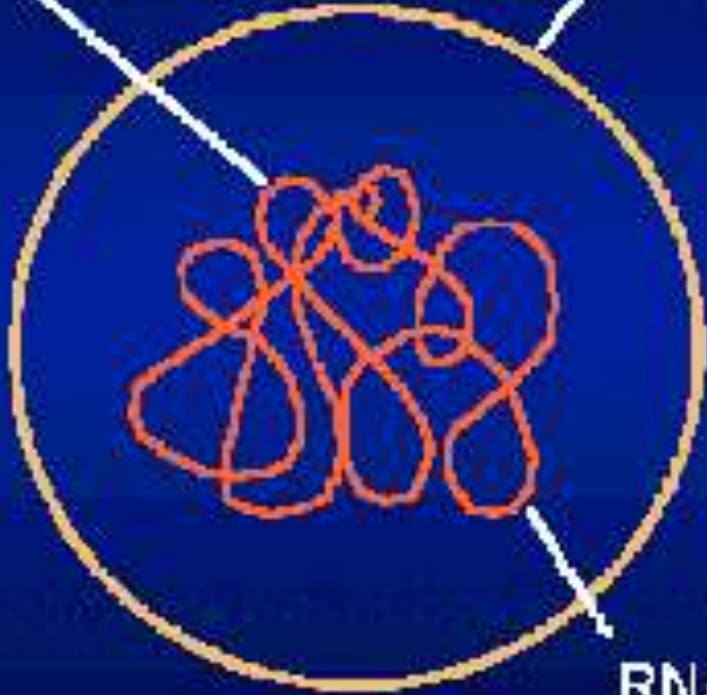
# Prevention

- Avoid injection drug use and sharing needles
- Avoid illicit sex
- Screening of all blood products
- Prophylactic ISG???
- Vaccine???
  - Patients may be infected with wild-type virus

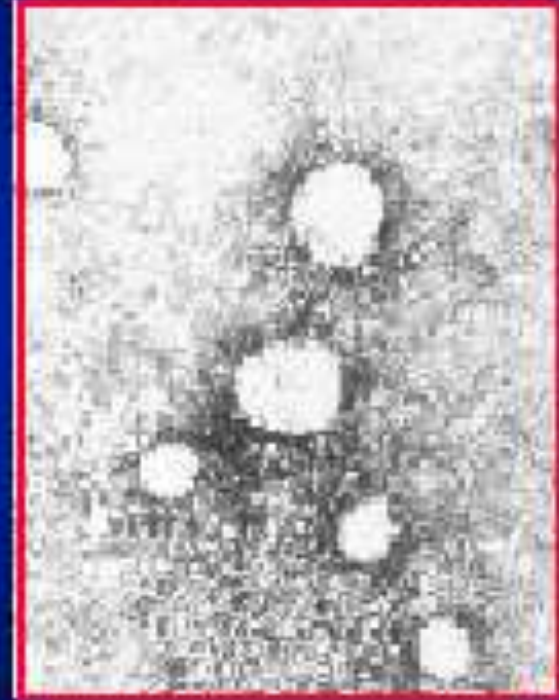
# Hepatitis D (Delta) Virus

$\delta$  antigen

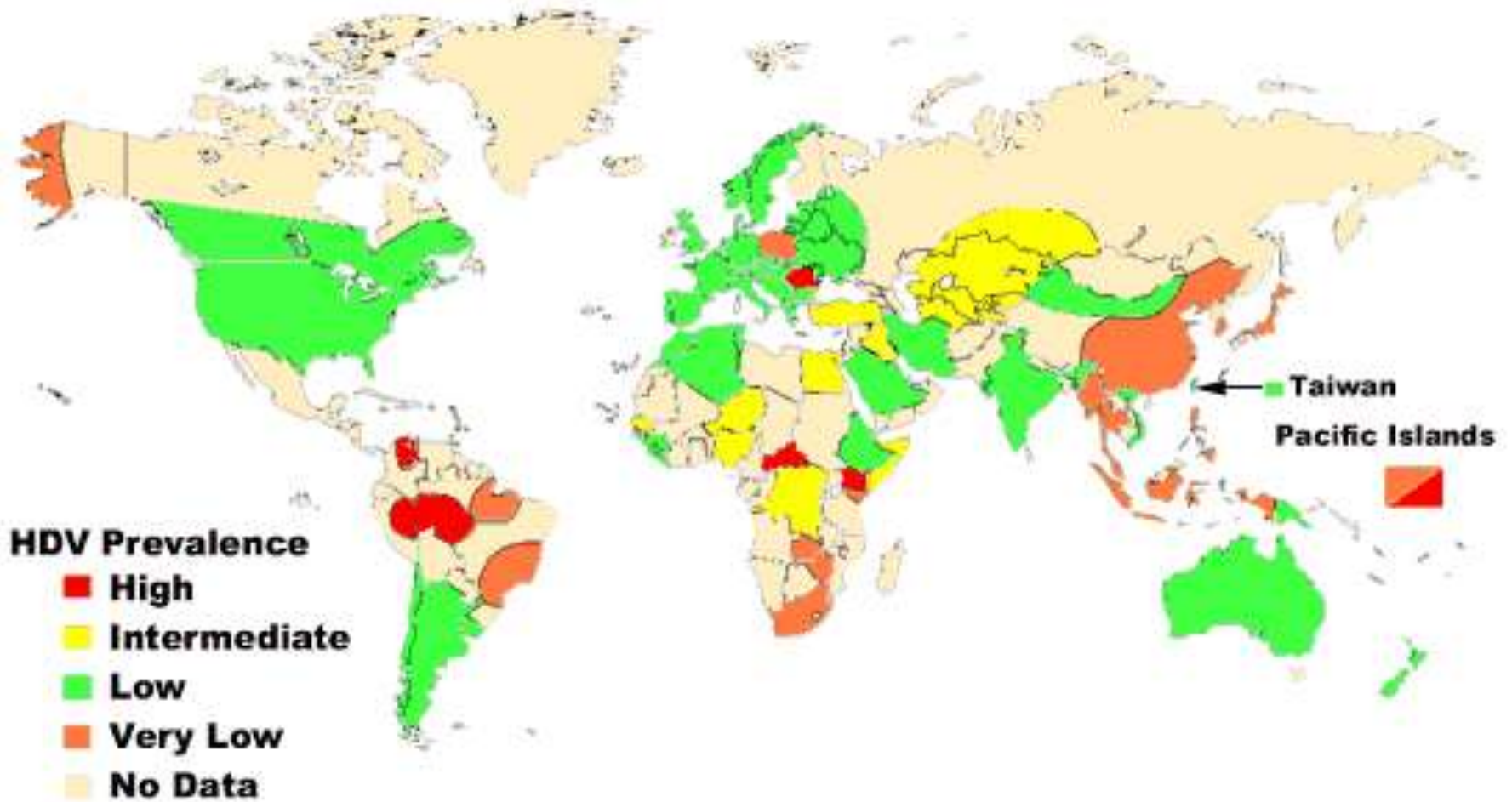
HBsAg



RNA



## Geographic Distribution of HDV Infection



# Virology

- Small circular negative sense single stranded RNA virus
  - No RdRP
- Viral genome serves as ribozyme
  - Self-ligation, cleavage
- Required HBsAg for transmission
  - Found in Hep. B infection
- RNA associated with delta antigen
- Three genotypes
  - Geographical distribution

# Disease

- **Most prevalent in Hep B high risk groups**
  - Injection drug users
  - Dialysis patients
  - Nonparenteral and vertical transmission
- Rapidly progressive liver disease causing death in up to 20% of infected people
  - More severe disease
- **Simultaneous Delta and Hep. B infection**
  - Clinical hepatitis indistinguishable from Hep. A or B
- **Delta superinfection**
  - Relapses of jaundice and high likelihood of chronic cirrhosis

# Diagnosis

- Demonstration of IgM and/or IgG antibodies to delta antigen in serum
- IgM appear within 3 weeks of infection and persist for several weeks
- IgG persists for years

# Prevention and Treatment

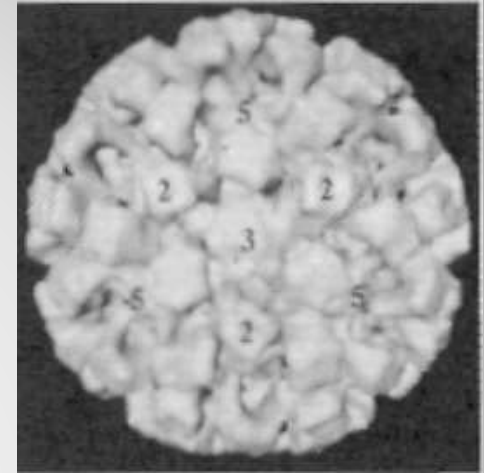
- Because of association with Hep. B virus
  - Hep. B Vaccination, blood screening.... Prevent transmission of delta virus
  - Safe sex
  - Avoid needle sharing
  - Needle safety by HCWs
- Interferon alpha....effect less in people with Hep. B alone
  - Higher doses are recommended and may produce improvement in 10%-15% patients

# Hepatitis E

- Hepatitis E virus causes another form of hepatitis spread by fecal-oral route
- Resembles Hepatitis A
- Hepatitis E
  - RNA virus similar to but distinct with caliciviruses
  - Viral particles in stool are
    - Spherical 27-34nm in size
    - Unenveloped
    - Have spikes on the surface

# Family Caliciviridae

- The family name comes from the Latin word, *caliculus*, meaning "cup-shaped." In electronmicrographs these viruses have the appearance of a small cup in the shape of the Star of David, i.e., a six-pointed star.
- These are naked icosahedral viruses containing linear single-stranded RNA coding for four to six genes.
- These viruses are morphologically similar to the Picornaviridae but about 25% larger.
- The members of this family causing human disease are:
  - Norwalk agent - the cause of epidemic viral gastroenteritis, also called summer diarrhea
  - Hepatitis E virus - the agent of endemic hepatitis, a disease with a high mortality rate among pregnant patients



Hepatitis E  
Virus

# Clinical Manifestations

- Like Hepatitis A infections with Hepatitis E are frequently sub-clinical
- When symptomatic
  - Causes only acute disease in especially pregnant women
- High attack rate in young adults in endemic areas

# Transmission

- Infections usually associated with drinking contaminated water
- Does not appear to be transmitted from person to person transmission
- Risk factors
  - Poor sanitation
  - Endemic areas
    - Asia, Africa, India (Rarely in US...immigrants)

- Incubation Period
  - 40 days
- Diagnosis
  - Presence of IgM antibody
- Treatment
  - ISG (likely but not proven to be protective)
  - No treatment
  - Liver transplant for seriously ill patients

# Hepatitis G

- Hepatitis C is the major cause of hepatitis
  - Other etiological agents continue to be sought
- In 1995 Hepatitis G was identified in the sera of two different patients
- Hepatitis G
  - RNA virus similar to Hepatitis C
  - Member of Flaviviridae

# Diagnosis

- Antibody assay
  - Past infection not present
  - Acute infection diagnosis requires RT-PCR assay for viral RNA in serum
- 2% of volunteer blood donors are seropositive for Hepatitis G RNA
- Transmission
  - Blood borne

# Association with Hepatitis C

- Majority of people infected with Hepatitis G are co-infected with Hepatitis C
- Because of this association
  - Difficulty to certain contribution of Hepatitis G to clinical disease
  - Patients infected with both viruses do not appear to have worse disease than those infected with Hepatitis C alone

# Currently

- No useful diagnostic test
- No therapy is established