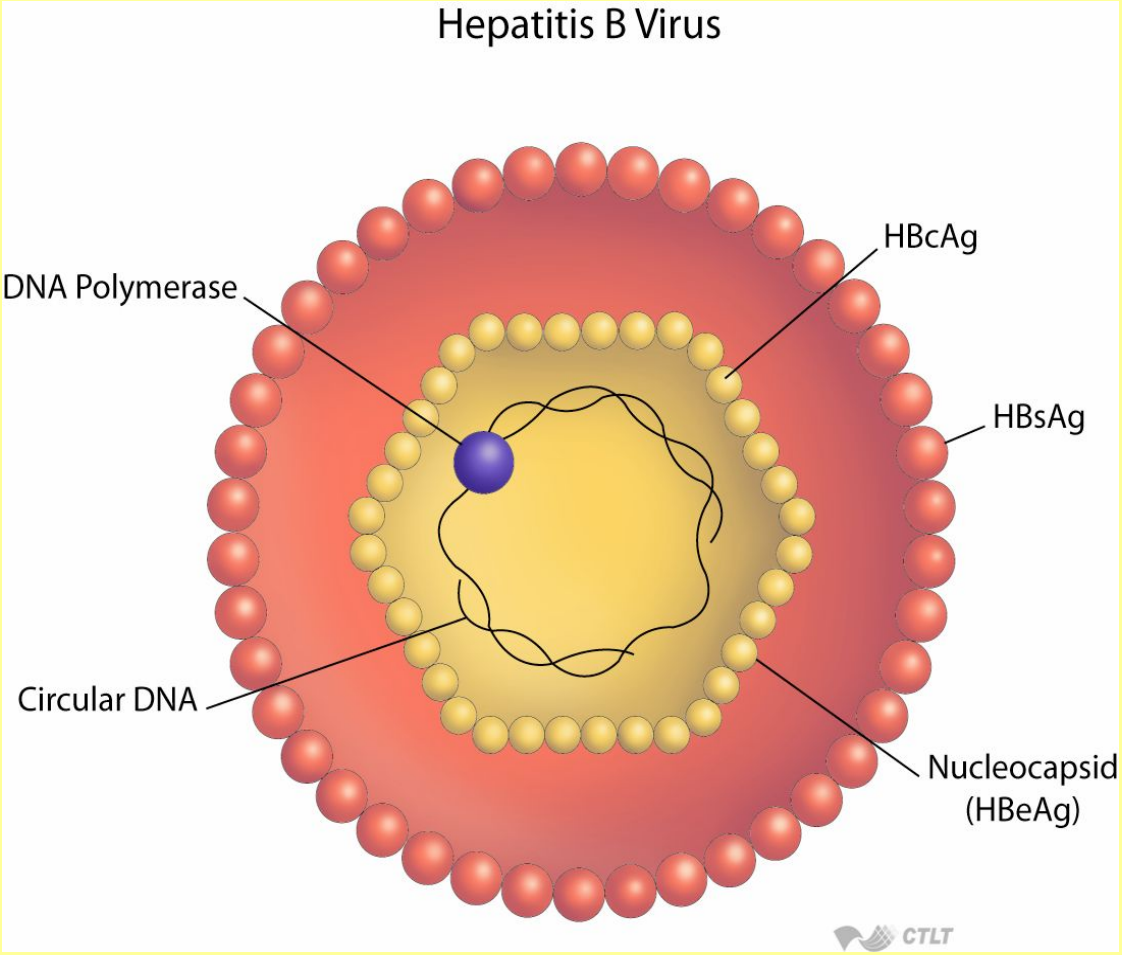
Hepatitis B

- Hepatitis B is caused by infection with the Hepatitis B virus (HBV), the prototype member of the hepadnavirus family
  - HBV is the only human representative of this family.
  - It has a circular DNA genome of 3.2 kb
- Currently, eight genotypes (A−H) are identified by a divergence of >8% in the entire genome

Hepatitis B Characteristics

- A Hepadnaviridae – partially double-stranded DNA virus
- HBsAg – stimulates protective antibodies, a marker for current infection
- HBcAg – localized within liver cells, identifies acute infection, anti-HBcAg persists for life and is a marker of past infection
- HBeAG – a marker of active replication and infectivity

Hepatitis B


Hepatitis B Virus
DNA Polymerase
HBcAg
HBsAg
Circular DNA
Nucleocapsid
(HBeAg)
CTLT

Hepatitis B Virus

- Hepadnaviridae family (DNA)
- Numerous antigenic components
- Humans are only known host
- May retain infectivity for more than 7 days at room temperature

Hepatitis B Virus Infection

- More than 350 million chronically infected worldwide
- Established cause of chronic hepatitis and cirrhosis
- Human carcinogen—cause of up to 80% of hepatocellular carcinomas
- More than 600,000 deaths worldwide in 2002

Hepatitis B Epidemiology

- Worldwide, HBV is the primary cause of liver cancer
  - For males, it is the third leading cause of cancer mortality
  - For females, it is the sixth leading cause of cancer mortality

Hepatitis B Epidemiology

- An estimated 800,000–1.4 million persons in the United States have chronic HBV infection.
- Chronic infection is an even greater problem globally, affecting approximately 350 million persons.
- An estimated 620,000 persons worldwide die from HBV-related liver disease each year.

Hepatitis B Epidemiology

- The incubation period from the time of exposure to onset of symptoms is 6 weeks to 6 months.
- HBV is found in highest concentrations in blood and in lower concentrations in other body fluids (e.g., semen, vaginal secretions, and wound exudates).
- HBV infection can be self-limited or chronic.

Hepatitis B

In adults, only approximately half of newly acquired HBV infections are symptomatic, and approximately 1% of reported cases result in acute liver failure and death.

Hepatitis B Diagnosis

- Hepatitis B is detected by looking for a number of different antigens and antibodies:
  - **Hepatitis B surface antigen (HBsAg):**
    - A protein on the surface of HBV; it can be detected in high levels in serum during acute or chronic HBV infection.
    - The presence of HBsAg indicates that the person is infectious.
    - The body normally produces antibodies to HBsAg as part of the normal immune response to infection.
    - HBsAg is the antigen used to make Hepatitis B vaccine.

Hepatitis B Diagnosis

- Hepatitis B is detected by looking for a number of different antigens and antibodies:
  - **Hepatitis B surface antibody (anti-HBs):**
    - **T**he presence of anti-HBs is generally interpreted as indicating recovery and immunity from HBV infection.
    - Anti-HBs also develops in a person who has been successfully vaccinated against Hepatitis B.
  - **Total Hepatitis B core antibody (anti-HBc):**
    - Appears at the onset of symptoms in acute Hepatitis B and persists for life.
    - The presence of anti-HBc indicates previous or ongoing infection with HBV in an undefined time frame.

Hepatitis B Diagnosis

- Hepatitis B is detected by looking for a number of different antigens and antibodies:
  - **IgM antibody to Hepatitis B core antigen (IgM anti-HBc):**
    - Positivity indicates recent infection with HBV (≤6 months).
    - Its presence indicates acute infection.
  - **Hepatitis B e antigen (HBeAg):**
    - A secreted product of the nucleocapsid gene of HBV that is found in serum during acute and chronic Hepatitis B.
    - Its presence indicates that the virus is replicating and the infected person has high levels of HBV.

Hepatitis B Diagnosis

- Hepatitis B is detected by looking for a number of different antigens and antibodies:
  - **Hepatitis B e antibody (HBeAb or anti-HBe):**
    - Produced by the immune system temporarily during acute HBV infection or consistently during or after a burst in viral replication.
    - Spontaneous conversion from e antigen to e antibody (a change known as seroconversion) is a predictor of long-term clearance of HBV in patients undergoing antiviral therapy and indicates lower levels of HBV.

Hepatitis B Clinical Features

- Incubation period 45-160 days (average 120 days)
- Nonspecific prodrome of malaise, fever, headache, myalgia
- Illness not specific for hepatitis B
- At least 50% of infections asymptomatic

Hepatitis B Complications

- Fulminant hepatitis
- Hospitalization
- Cirrhosis
- Hepatocellular carcinoma
- Death

Chronic Hepatitis B Virus Infection

- Chronic viremia
- Responsible for most mortality
- Overall risk 5%
- Higher risk with early infection

Hepatitis B Epidemiology

Reservoir	Human
Transmission	Bloodborne Asymptomatic infections transmit
Communicability	1-2 months before and after onset of symptoms Chronic infection

Hepatitis B Perinatal Transmission*

- **If mother positive for HBsAg and HBeAg**
  - 70%-90% of infants infected
  - 90% of infected infants become chronically infected
- **If positive for HBsAg only**
  - 5%-20% of infants infected
  - 90% of infected infants become chronically infected

*in the absence of postexposure prophylaxis

Global Patterns of Chronic HBV Infection

- **High (≥8%): 45% of global population**
  - lifetime risk of infection >60%
  - early childhood infections common
- **Intermediate (2%-7%): 43% of global population**
  - lifetime risk of infection 20%-60%
  - infections occur in all age groups
- **Low (<2%): 12% of global population**
  - lifetime risk of infection <20%
  - most infections occur in adult risk groups

Adults at Risk for HBV Infection

- **Sexual exposure**
  - sex partners of HBsAg-positive persons
  - sexually active persons not in a long-term, mutually monogamous relationship*
  - persons seeking evaluation or treatment for a sexually transmitted disease
  - men who have sex with men

* persons with more than one sex partner during the previous 6 months

Adults at Risk for HBV Infection

- **Percutaneous or mucosal exposure to blood**
  - current or recent IDU
  - household contacts of HBsAg-positive persons
  - residents and staff of facilities for developmentally disabled persons
  - healthcare and public safety workers with risk for exposure to blood or blood-contaminated body fluids
  - persons with end-stage renal disease
  - persons with diabetes mellitus

Adults at Risk for HBV Infection

- **Others groups**
  - international travelers to regions with high or intermediate levels (HBsAg prevalence of 2% or higher) of endemic HBV infection
  - persons with HIV infection

Hepatitis B Treatment

- For acute infection, no medication is available; treatment is supportive.
- For chronic infection, several antiviral drugs (adefovir dipivoxil, interferon alfa-2b, pegylated interferon alfa-2a, lamivudine, entecavir, and telbivudine) are available.
  - Persons with chronic HBV infection require medical evaluation and regular monitoring to determine whether disease is progressing and to identify liver damage or hepatocellular carcinoma.

Hepatitis B Elimination

- CDC's national strategy to eliminate transmission of HBV infection includes:
  - Prevention of perinatal infection through routine screening of all pregnant women for HBsAg and immunoprophylaxis of infants born to HBsAg-positive mothers and infants born to mothers with unknown HBsAg status
  - Routine infant vaccination
  - Vaccination of previously unvaccinated children and adolescents through age 18 years
  - Vaccination of previously unvaccinated adults at increased risk for infection

Hepatitis B Vaccine

- **Composition** — Recombinant HBsAg
- **Efficacy** — 95% (Range, 80%-100%)
- **Duration of Immunity** — 20 years or more
- **Schedule** — 3 Doses
- **Booster doses not routinely recommended**

Hepatitis B Vaccine Long-term Efficacy

- Immunologic memory established following vaccination
- Exposure to HBV results in anamnestic anti-HBs response
- Chronic infection rarely documented among vaccine responders

Hepatitis C

- Hepatitis C virus (HCV) infection is the most common chronic blood-borne infection in the United States; approximately 3.2 million persons are chronically infected
- By contrast to Chronic HBV, patients with chronic hepatitis C almost always develop HCC in the presence of established cirrhosis
- The annual risk of HCC development in HCV patients with cirrhosis is in the range of 1–4%, and an estimated 1–3% of patients chronically infected with HCV will develop HCC after 30 years

Hepatitis C Characterisitcs

- Flavivirus – small, enveloped, single-stranded RNA virus, six genotypes
- Replicates in liver cells, lymphocytes and monocytes
- Replicates >1 trillion progeny per day
- Mutates rapidly (error-prone RNA polymerase)
- Down-regulates stimulatory receptors on NK cells
- Increases inhibitory receptors on NK and CD8+ killer cells
- Produces TGF-beta, which blocks activation of T cells and inhibits production of IFN-gamma

Hepatitis C Epidemiology

- Transmission of HCV occurs through:
  - Percutaneous
    - Injecting drug use
    - Clotting factors before viral inactivation
    - Transfusion, transplant from infected donor
    - Therapeutic (contaminated equipment, unsafe injection practices)
    - Occupational (needlestick)
  - Permucosal
    - Perinatal
    - Sexual

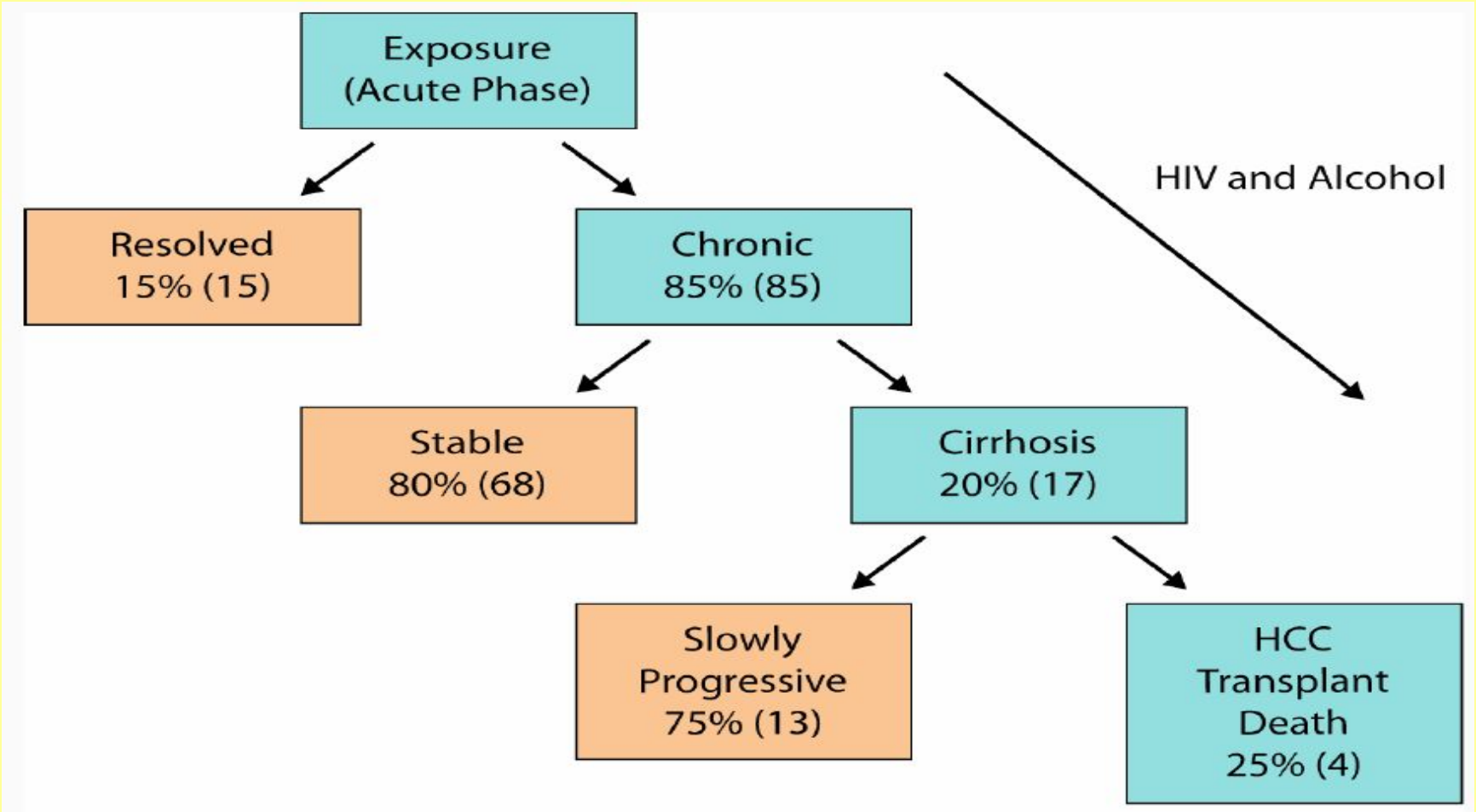
Hepatitis C Epidemiology

- The following persons are at known to be at increased risk for HCV infection:
  - Current or former injection drug users, including those who injected only once many years ago
  - Recipients of clotting factor concentrates made before 1987, when more advanced methods for manufacturing those products were developed
  - Recipients of blood transfusions or solid organ transplants before July 1992, when better testing of blood donors became available
  - Chronic hemodialysis patients
  - Persons with HIV infection
  - Children born to HCV-positive mothers

Hepatitis C

- Although only 850 cases of confirmed acute Hepatitis C were reported in the United States in 2010, CDC estimates that approximately 16,000 new HCV infections occurred that year, after adjusting for asymptomatic infection and underreporting.
- Persons newly infected with HCV are usually asymptomatic, so acute Hepatitis C is rarely identified or reported.

Hepatitis C
Natural History of Infection



Hepatitis C Diagnosis

- Sixty to 70% of persons newly infected with HCV typically are usually asymptomatic or have a mild clinical illness.
- HCV RNA can be detected in blood within 1–3 weeks after exposure.
- The average time from exposure to antibody to HCV (anti-HCV) seroconversion is 8–9 weeks, and anti-HCV can be detected in >97% of persons by 6 months after exposure.

Hepatitis C
Chronic Illness

- 75-85% of those infected with HCV will develop chronic infection.
- 60-70% of those infected with HCV will develop chronic liver disease.
- 5-20% of those infected will develop cirrhosis over a period of 20-30 years
- 1-5% will die from the consequences of chronic infection (liver cancer or cirrhosis)

Hepatitis C Treatment

- Interferon-based therapy is currently the standard of care for patients with chronic HCV, and has been proven to be effective in eliminating HCV.
- Both conventional and pegylated interferon (IFN) therapy have been used widely, with the aim of achieving a sustained virological response (SVR).

Hepatitis C Prevention

- Unlike HBV, there is currently no vaccine for HCV.
- However, with the screening of HCV in blood transfusion services, transfusion-related HCV infection has been lowered to almost zero.

Hepatitis C Prevention

- It may be possible to develop a preventive vaccine for HCV:
  - 30% of persons clear the virus spontaneously
  - The genome of HCV is not integrated into the host genome
  - After HCV infection, CD-8 CTL responses and antibodies appear, but the “protective immune response” or critical epitopes are not known
  - Persons who clear HCV and become re-infected have low viral loads and are more likely to clear HCV