

# 1 Hepatitis C Virus

Hepatitis means inflammation of the liver

Most common types of viral hepatitis are A (vaccine), B (cancerous), and C (cancerous)

Related to other human pathogens (Yellow fever, Zika, Dengue)

Spread globally in 20th century due to novel medical practices

HCV is the cause of hepatitis cirrhosis (liver inflammation) and liver cancer in infected individuals

71 million people (1%) are currently living with Hepatitis C virus

## 1.1 Transmission

Blood contact

1. Intravenous drug use
2. Blood transfusions
3. Contaminated medical / dental instruments
4. Mother to baby (5% risk)

Higher risk if mother is HIV+

5. Low risk of sexual transmission (if blood is involved)
6. Unregulated tattoos or body piercings
7. Sharing personal item (glucose montors, razors, ...)

### 1.1.1 Egypt

Egypt is the country with the highest prevalence of the disease in the world (10% of Egyptians had chronic hepatitis C in 2008)

Campaign to rid the country of schistosomiasis, but needles were reused

## 1.2 Inflammation

Can cause both acute and chronic infection

New HCV infections are usually asymptomatic, but acute hepatitis C occurs within the first 6 months after exposure

→ Around 30% of infected people clear the virus within 6 months of infection without treatment

→ 70% of HCV-infected individuals will develop chronic HCV infection

Of those, the risk of cirrhosis ranges between 15-30% within 30 years

### 1.3 Liver Transplantation

Liver failure due to hepatitis C is one of the most common reasons for liver transplantation in the US

Chronic inflammation likely causes damage to cell DNA and affects growth / division, leading the the growth of tumors and cancer

Not fully understood

### 1.4 Estimates

1. 1.5 million new infections per year
2. 80% of infected people don't know
3. Less than 10 million people are being treated
4. Currently no effective vaccine against hepatitis C
5. Direct-acting antiviral medicines (DAAs) can cure more than 95% of cases, but access to diagnosis and treatment is low

## 2 Drugs and Vaccines

### 2.1 Viral Quasispecies

Hepatitis C exhibits significant genetic variability and exists as quasispecies within infected individuals

Quasispecies: a population of closely related but genetically diverse viral variants

Due to:

1. High mutation rate of the error-prone RNA-dependent RNA polymerase ( $10^{-4}$  substitutions per site per replication)
2. Rapid viral replication ( $10^{12}$  new virions produced daily)
3. Selective pressures from host immune system

Statistically, every genome that enters a cell, exits with 1 or more mutations

### 2.2 Direct-Acting Antivirals

Ribavirin and IFN-1

Work by targeting the virus directly, making them more effective than older treatments

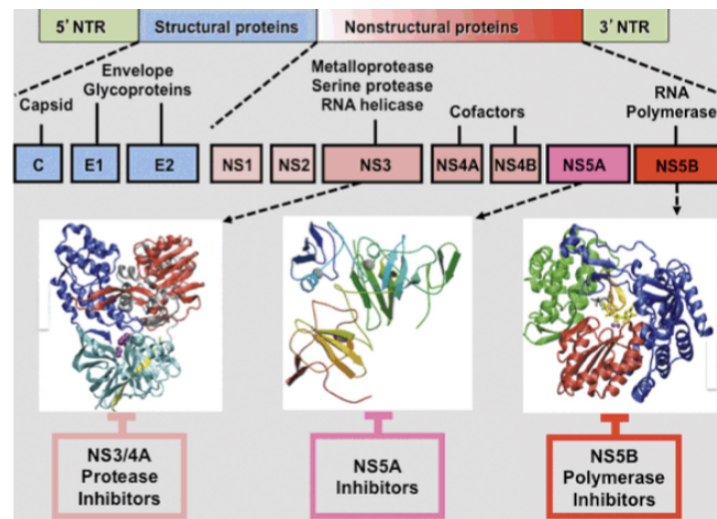


Figure 1: Direct-acting antivirals

Short-course oral treatment have few, if any side effects

DAAAs can cure most people within 8-12 weeks

## 2.3 Elimination

The WHO have committed to eliminate viral hepatitis by 2030

Only 11 countries are on track, with another 24 expected by 2050

Most countries, including the US, are unlikely to eliminate HCV by 2050

## 2.4 HCV in the US

The number of people infected with HCV in the US has increased dramatically

HCV disproportionately impacts minority and marginalized population

1. Substance use disorders
2. People of color
3. Incarcerated persons
4. People living in poverty

Hepatitis C treatment requires an antibody test to detect prior infection, followed by an RNA test to determine whether infection is active

Among those diagnosed, HCV coverage is far below what is needed to achieve elimination goals

1. 1/3 of HCV-infected individuals with insurance are treated (lower for patients without insurance)

2. High cost of DAAs

\$90,000 per patient initially; still around \$20,000 (As low as \$60 in low- and middle-income countries)

Requirement of sobriety

Requirement to document evidence of liver fibrosis

Access to treatment particular to field specialists

Currently plans to make treatment free for patients on Medicaid, uninsured, in the prison system, or on a Native American reservation