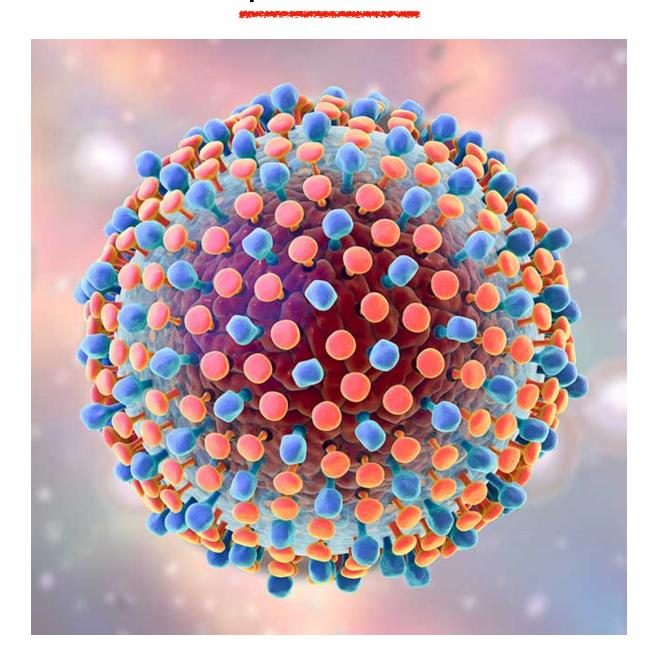
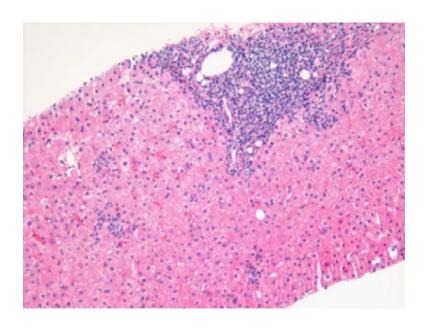
# Hepatitis C virus

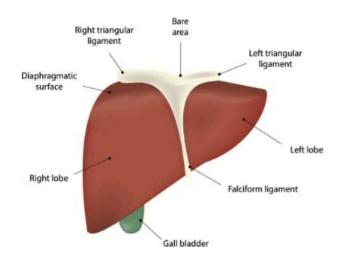


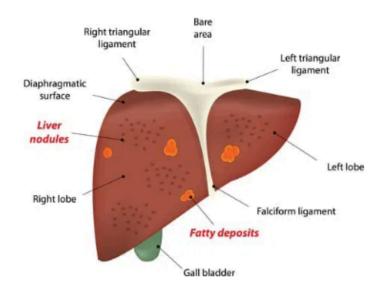
# Hepatitis means inflammation of the liver.

Hepatitis is most often caused by a virus. In the United States, the most common types of viral hepatitis are hepatitis A, hepatitis B, and hepatitis C.



#### **Healthy Liver**



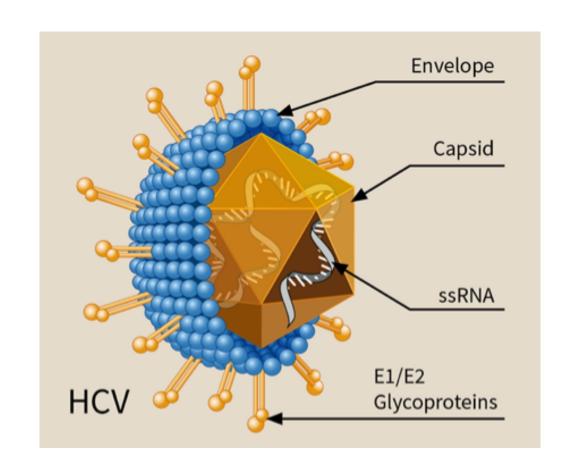


### Hepatitis C virus

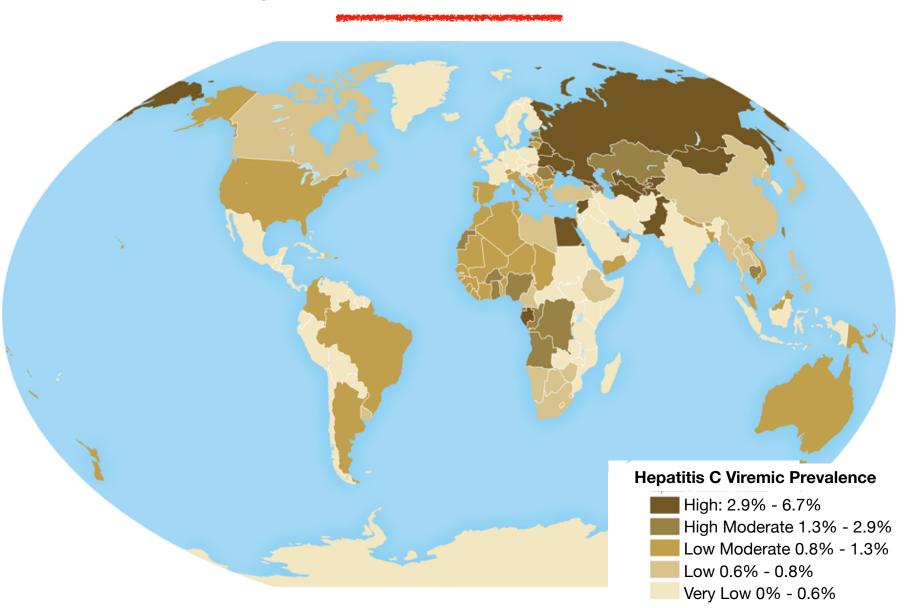
HCV related to other human pathogens (Yellow fever virus, Zika virus, Dengue virus.....)

Spread globally in the twentieth century due to novel medical practices

HCV is the cause of hepatitis, cirrhosis and liver cancer on infected individuals.



# 71 million people are currently living with Hepatitis C virus infection



### **HCV** Transmission

HCV is transmitted via blood contact.

- 1. Intravenous drug use
- 2. Blood transfusions
- 3. Contaminated medical/dental instruments
- 4. From mother to baby at birth (about 5% risk), risk are higher if mother is HIV+
- 5. Sexual transmission that involve blood, overall the risk of sexual transmission is very low
- 6. Unregulated tattoos or body piercings.
- 7. Sharing personal items (glucose monitors, razors.)...

### The case of Egypt

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





# Hepatitis C virus causes both acute and chronic infection

Acute hepatitis C occurs within the first 6 months after someone is exposed to the hepatitis C virus.

New HCV infections are usually asymptomatic. Some persons get acute hepatitis which does not lead to a life-threatening disease.

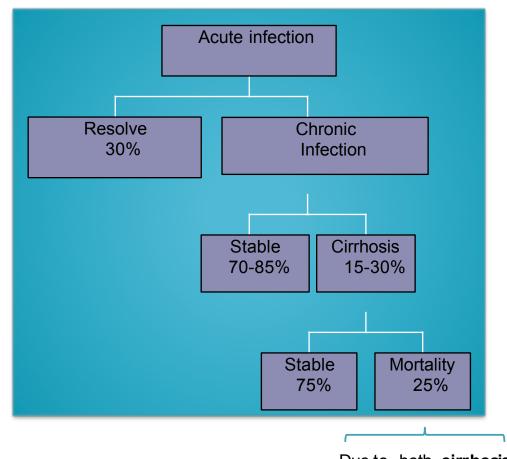
Around 30% of infected persons spontaneously clear the virus within 6 months of infection without any treatment.



# Hepatitis C virus causes both acute and chronic infection

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

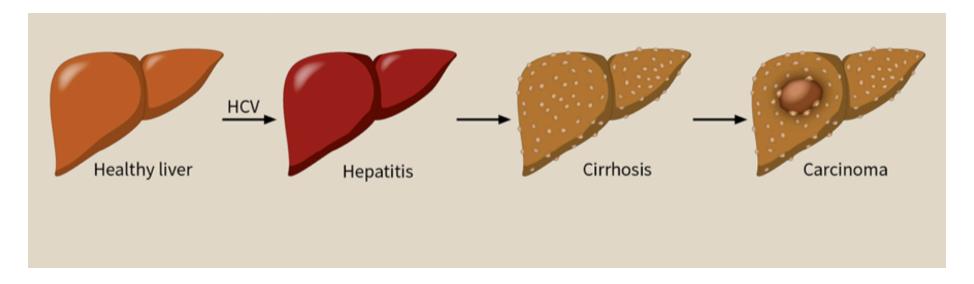
Of those with chronic HCV infection, the risk of cirrhosis ranges between 15% and 30% within 20 years.



Due to both cirrhosis and liver cancer

#### Liver transplantation

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



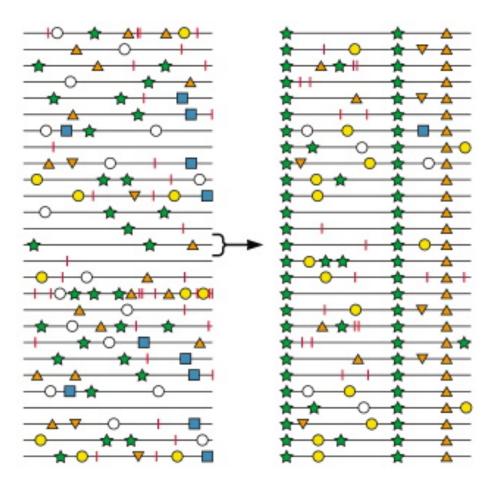
An estimated 1 to 5 out of 100 people with chronic hepatitis C that will die of cirrhosis or liver cancer (if they are not treated with DAAs).

How HCV cause cancer is not fully understood but it is thought that over time, chronic inflammation (due to the infection) causes damage to cell DNA and affects the way cells grow and divide leading to the growth of tumors and cancer

#### The last estimates

- about 60 million people are currently infected worldwide 2.4 million people in the U.S
- 1.5 million new infections per year
- 80% of people infected with HCV don't know their status
- less than 10 millions are currently being treated.
- There is currently no effective vaccine against hepatitis C
- Direct-acting antiviral medicines (DAAs) can cure more than 95% of persons with hepatitis C infection, but access to diagnosis and treatment is low.

## Viral quasispecies



Hepatitis C virus (HCV) exhibits significant genetic variability and exists as quasispecies within infected individuals.

Quasispecies refers to a population of closely related but genetically diverse viral variants that coexist within an infected host

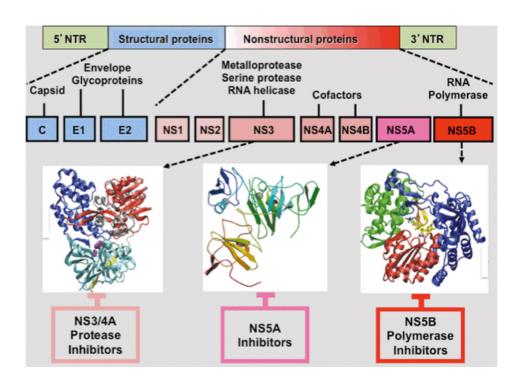
HCV forms quasispecies due to:

- High mutation rate (10^-4 substitutions per site per replication) of the error-prone RNAdependent RNA polymerase<sub>2</sub>
- Rapid viral replication (up to 10<sup>12</sup> new virions produced daily)
- Selective pressures from the host immune system

What are the consequences for vaccine development and for the development of antivirals?

### Direct-acting antivirals (DAAs)

Direct-acting antivirals (DAAs) are a newer class of drugs used to treat hepatitis C. DAAs work by targeting the virus directly, making them more effective than older treatments. (DAAs) that can cure hepatitis C in more than 95% of people infected



The short-course oral, curative DAA treatment regimens have few, if any side effects. DAAs can cure most persons with HCV infection, and treatment duration is short (usually 8 to 12 weeks).

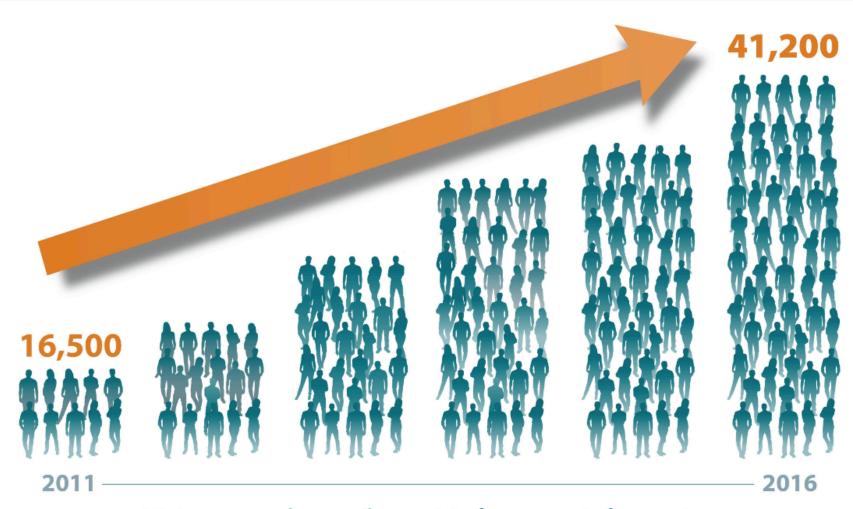
#### Toward the elimination of HCV?

World Health Organization have committed to eliminate viral hepatitis by 2030



- Only 11 countries are on track to meet all HCV elimination targets by 2030
- Another two dozen are expected to meet these targets between 2031 and 2050.
- Most countries, including the United States, are unlikely to achieve hepatitis C elimination until after 2050.

# In the US, the number of people infected with HCV has increased dramatically





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#### In the US.

HCV infection disproportionately impacts minoritized and marginalized populations. Many people with hepatitis C have poor access to health care and experience other chronic health and social inequalities

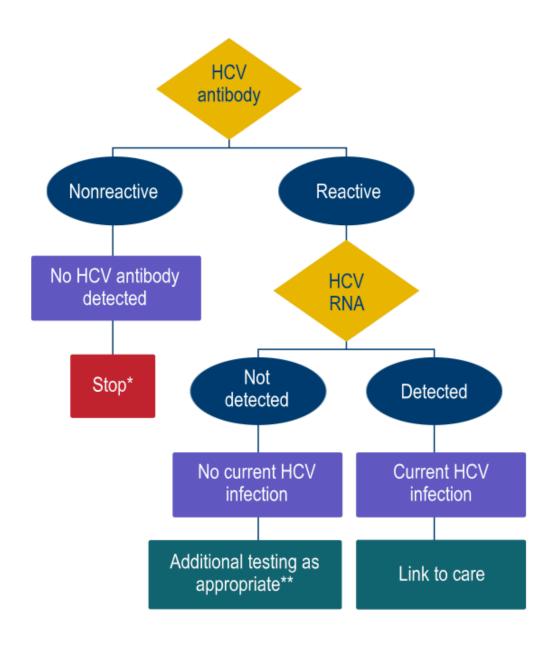
- Individuals with substance use disorders
- People of color
- Individuals with interactions with the Corrections system
- Persons living in poverty



#### In the US.

An estimated 40% of those chronically infected with hepatitis C

One major limitation is that testing for hepatitis C requires 2 steps: initiating treatment starts with an antibody test to detect prior infection, followed by an RNA test to determine whether infection is active. Return of those test results can take days or weeks, and then a third visit is needed to initiate treatment.



### In the US.

Among those diagnosed, hepatitis C treatment coverage is far below what is needed to achieve elimination goals.

1/3 of HCV-infected individuals with insurance are treated (the proportion is probably even lower for those without insurance).

- high cost of DAAs (\$90 000 per patient initially, still around \$20 000)
  - requirements for patient sobriety,
  - requirements to document evidence of liver fibrosis,
  - access to treatment only to those seen by specialists,
- Low rates of treatment may also reflect the complexity of traversing the full cascade of care in our health care delivery system.

In low- and middle-income countries, a 12-week course of DAAs can be obtained for as low as \$60, thanks to pricing agreements aimed at making treatment more accessible

The president's Administration has proposed a National Hepatitis C Elimination Program, led by Dr. Francis Collins, former director of the National Institutes of Health.

The plan proposes a subscription model to increase access to hep C drugs, in which the government would negotiate with drugmakers to agree on a lump sum payment, "and then they would make the drugs available for free to anybody on Medicaid, who's uninsured, who's in the prison system, or is on a Native American reservation," Collins says, adding that this model for hep C drugs has been successfully piloted in Louisiana.

The five-year, \$12.3 billion program is currently under consideration in Congress.

