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Better health through laboratory medicine.

PEARLS OF LABORATORY MEDICINE

Hepatitis C Virus Laboratory Testing

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DOI:

CCTC Clinical Chemistry Trainee Council

Hepatitis C Virus Laboratory Testing

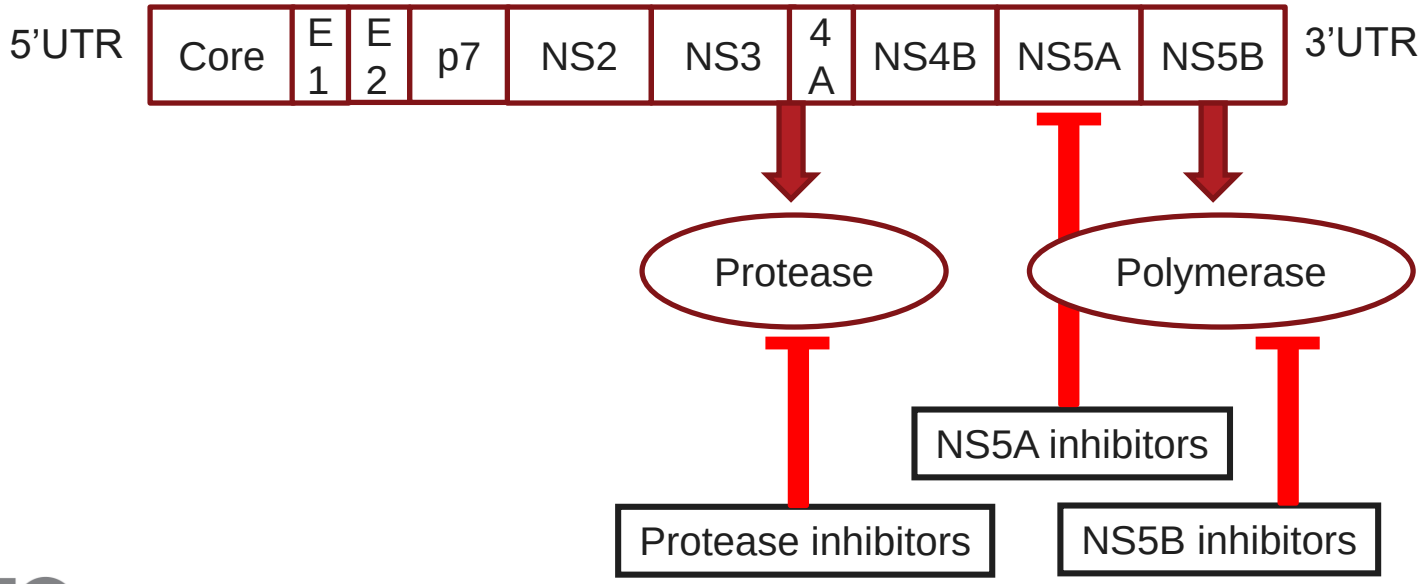
- Hepatitis C Virus (HCV)
- Serologic Pattern of Infection
- Clinical Manifestations
- Laboratory Testing
- Incidence and Prevalence of HCV
- CDC Recommendations: Screening Baby-Boomers

Hepatitis C Virus (HCV)

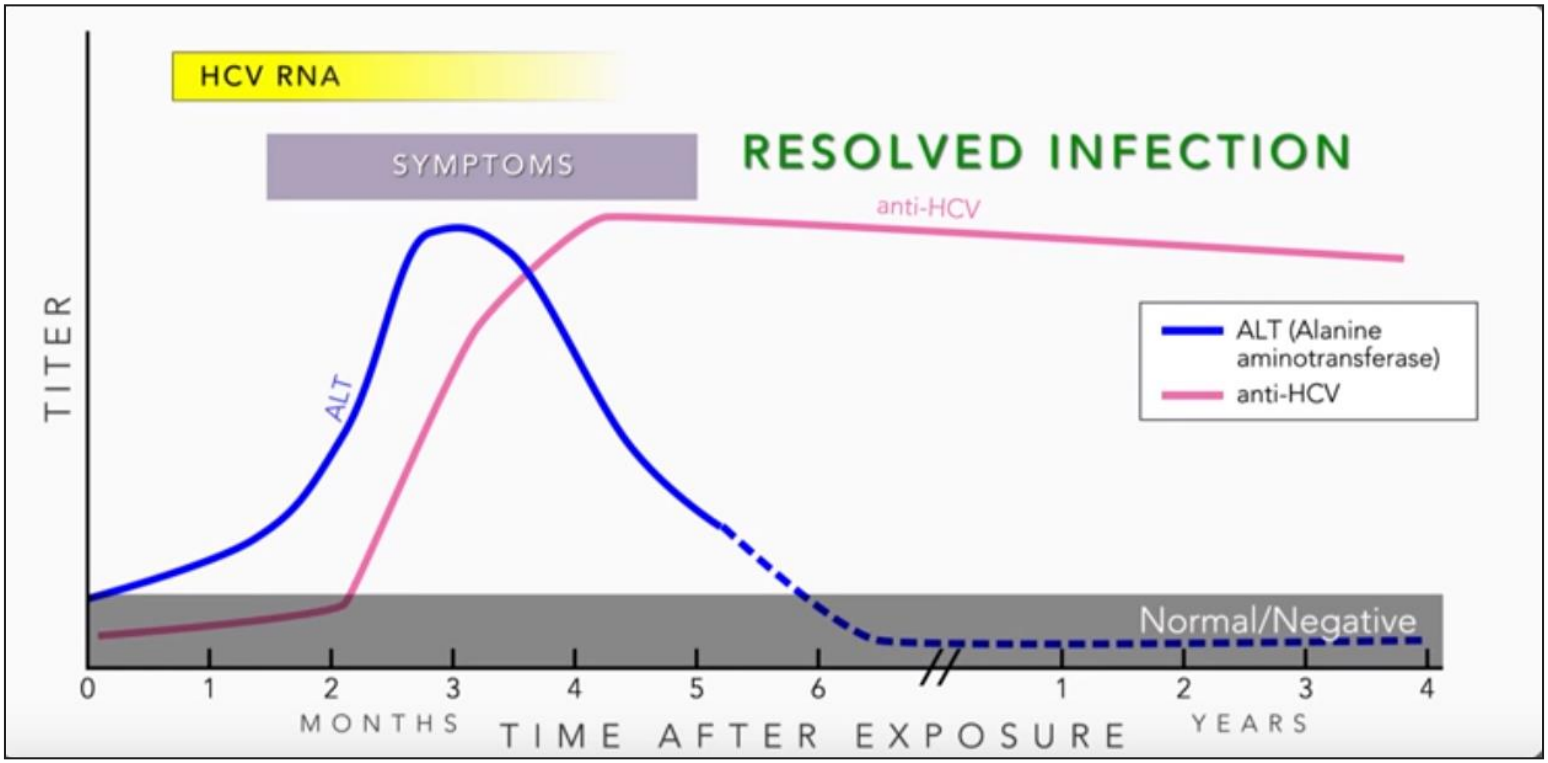
- Positive strand RNA virus
  - 9600 nucleotides
- Polyprotein cleaved into structural and non-structural proteins
- RNA polymerase lacking proofreading: leading to many minor genetic variations
  - Genetic diversity increases chronicity, no vaccine
  - Requires continuous replication

Genome and Therapeutic Targets

- Six major genotypes: genotype 1 is most common
- Antiviral agents include: NS3/4A protease inhibitors, NS5B polymerase inhibitors (nucleoside and non-nucleoside), NS5A inhibitors

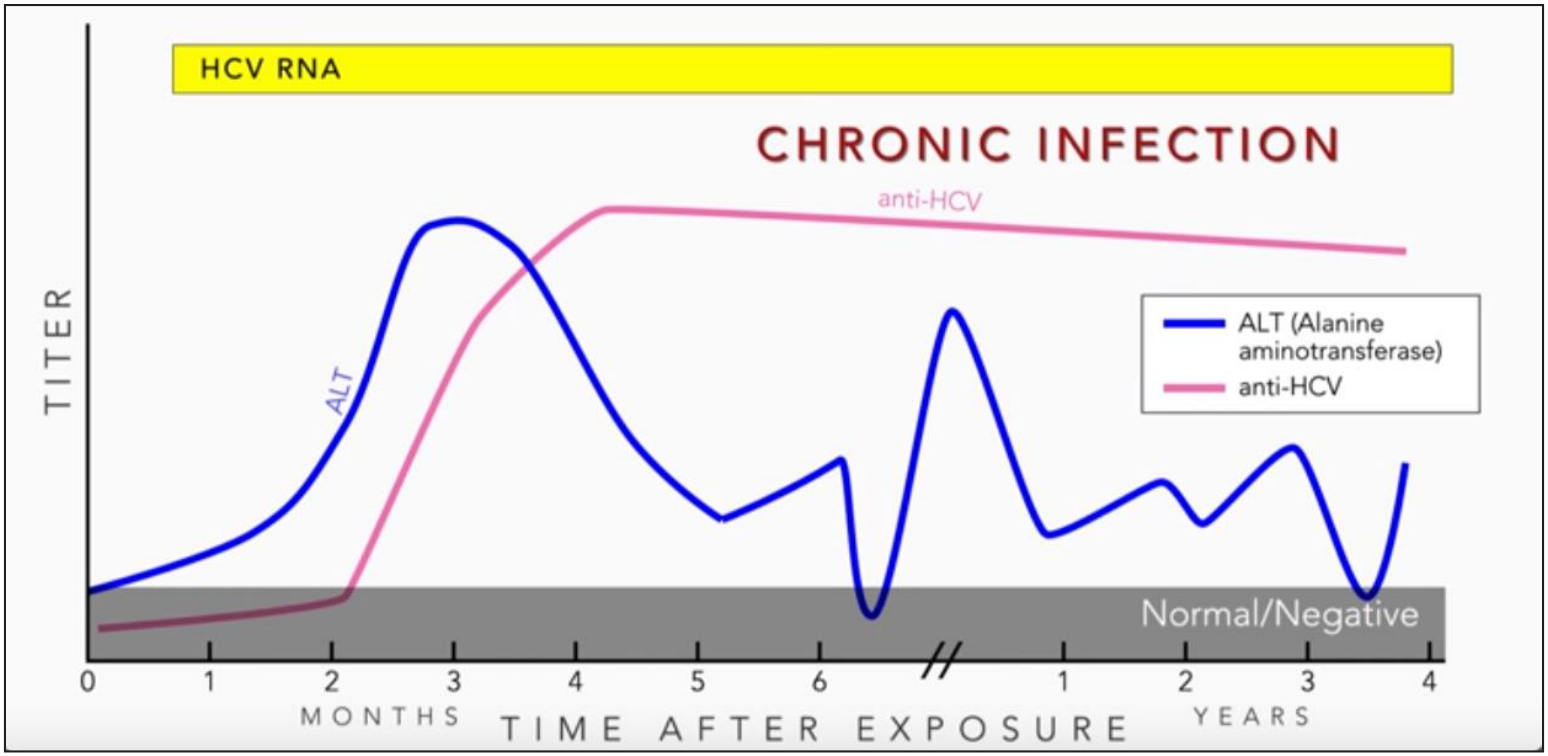


Serologic Pattern: Acute, Resolved Infection



http://www.cdc.gov/hepatitis/resources/professionals/training/serology/training.htm

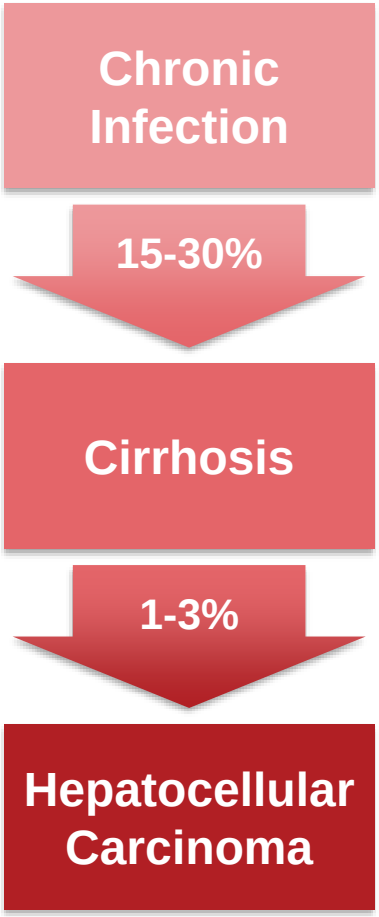
Serologic Pattern: Chronic Infection



http://www.cdc.gov/hepatitis/resources/professionals/training/serology/training.htm

Clinical Manifestations of Chronic Infection

- Disease progression is silent
- Over a 20 year period, may progress to cirrhosis, end-stage liver disease, hepatocellular carcinoma
- Extrahepatic manifestations
  - Mixed cryoglobulinemia
  - Autoimmune disease
  - Insulin Resistance/Diabetes
  - Porphyria Cutanea Tarda
  - Parkinson's Disease

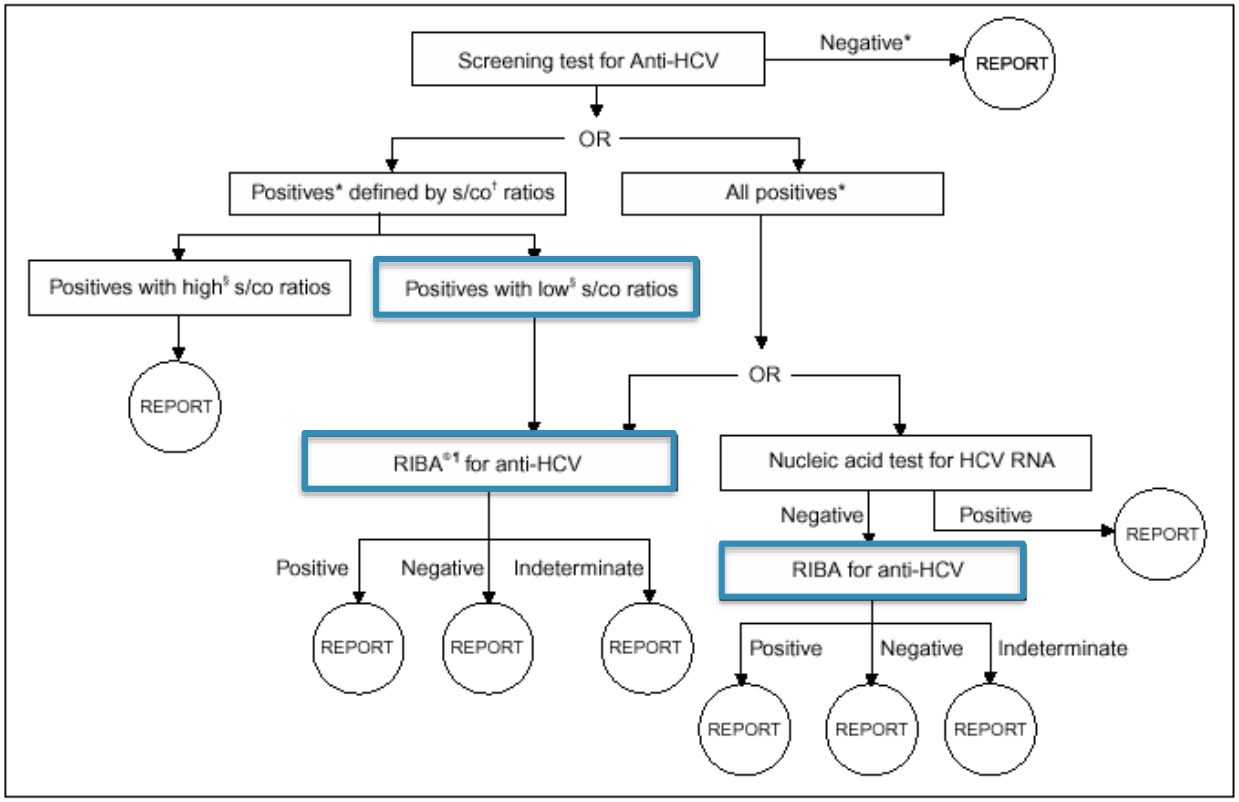


Laboratory Testing

- Screening immunoassays for anti-HCV antibodies:
  - Enzyme Immunoassay (EIA, ELISA)
  - Chemiluminescence Immunoassay (CIA)
  - Point-of Care Rapid Immunoassays
- Confirmatory tests:
  - HCV Total Antibody by Recombinant Immunoblot Assay (RIBA) (previously)
  - HCV RNA by molecular tests
- Testing prior to antiviral therapy:
  - Genotyping by molecular tests

Testing Algorithm (2003)

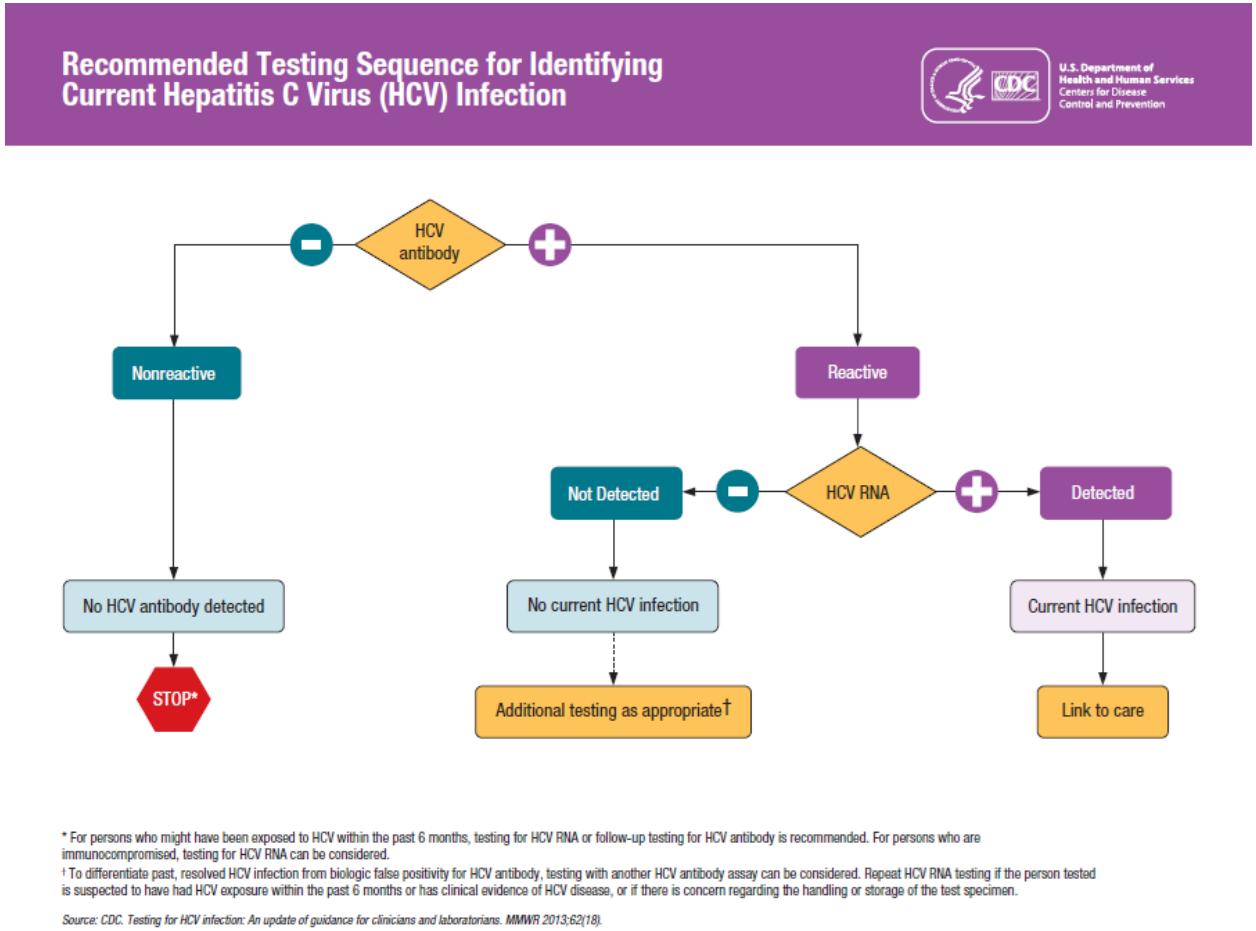
FIGURE 4. Laboratory algorithm for antibody to hepatitis C virus (anti-HCV) testing and result reporting



* Interpretation of screening immunoassay test results based on criteria provided by the manufacturer.
† Signal-to-cut–off.
§ Screening-test–positive results are classified as having high s/co ratios if their ratios are at or above a predetermined value that predicts a supplemental-test–positive result ≥95% of the time among all populations tested; screening-test–positive results are classified as having low s/co ratios if their ratios are below this value.
¶ Recombinant immunoblot assay.

http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5203a1.htm (public domain)

Testing Algorithm (2013)



http://www.cdc.gov/hepatitis/hcv/pdfs/hcv_flow.pdf (public domain)

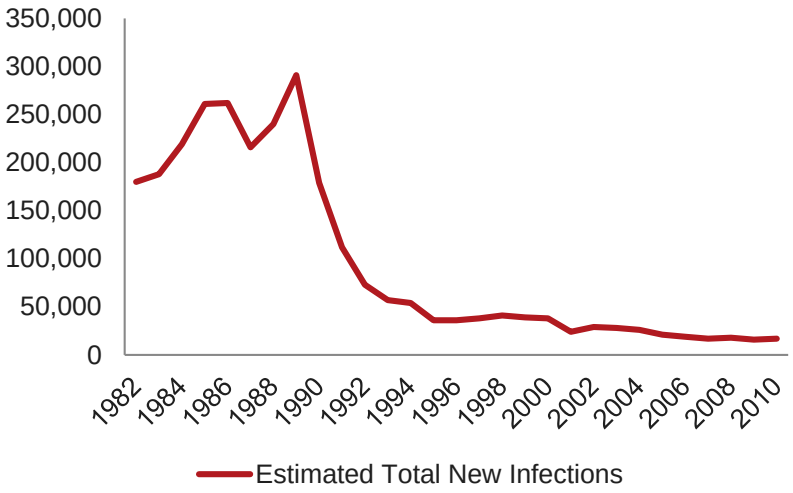
Incidence of HCV Infection in the US

1986: Indirect blood screening for HCV/HIV prevention measures

1989: Discovery of HCV

1992: Anti-HCV serologic test licensed

2001: Needlestick Safety and Prevention Act



CDC: Division of Viral Hepatitis: Statistics and Surveillance.

Worldwide Prevalence of HCV (2005)

National Health and Nutrition Examination Survey (NHANES)

- Worldwide HCV Infection: ~130-170 million (3%)
  - Egypt: 7.5 million (10%)
  - United States: ~2.7 million (1%)
- An estimated 45-85% of individuals worldwide are unaware of their infection.
- Exclude individuals with and unproportionately high incidence of infection.

Risk-Based HCV Screening (1998)

- Past or present injection drug use
- Blood transfusion/solid organ transplant before July 1992
- Clotting factors before 1987
- Chronic hemodialysis
- Infants of HCV infected mothers
- Healthcare workers with needlestick injuries
- Signs of liver disease
- HIV infection

Treatment for HCV (2013 - present)

Sustained Virologic Response (SVR): undetectable HCV RNA 12 - 24 weeks after treatment

- PEG-IFN + Ribavirin: SVR in ~45% of patients
- Direct acting antiviral agents: SVR in >90% of patients

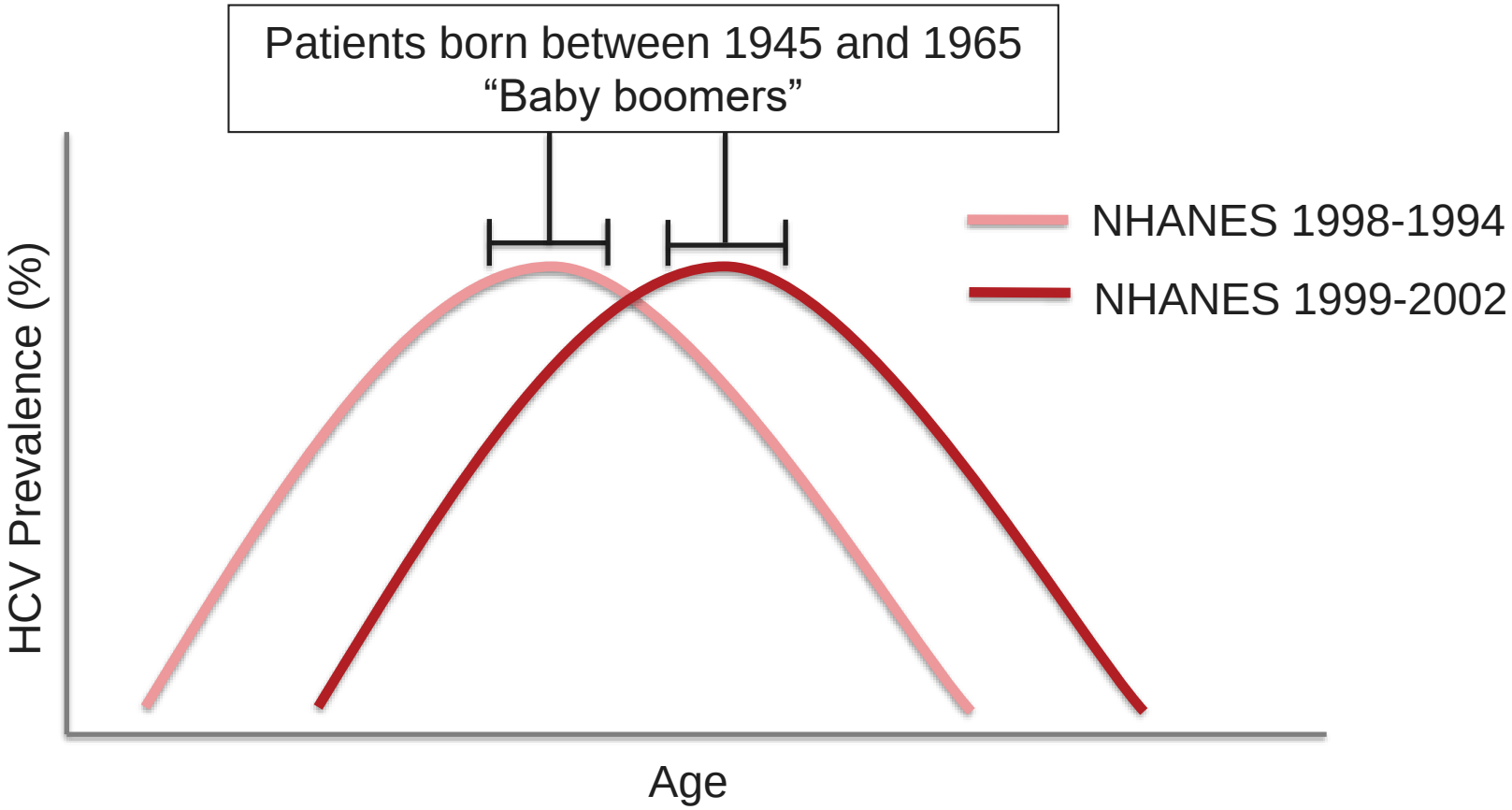
Increasingly effective antiviral therapy is rapidly evolving

Genotype and subtyping essential to identify the most effective regimen, dosing, duration of therapy

Sofosbuvir/veltapasvir approved by FDA (June 2016)

More information through the American Association for the Study of Liver Disease (AASLD) and the Infectious Disease Society of America (IDSA) is available: http://www.hcvguidelines.org/

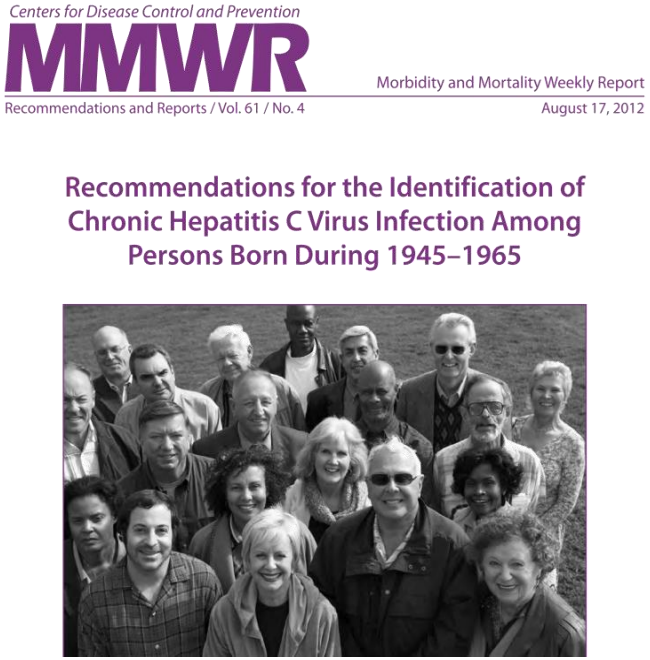
CDC Birth Cohort Studies



One-Time Screening: Baby Boomers

- All adults born between 1945-1965 should receive one-time testing for HCV without prior ascertainment of HCV risk factors.

- Anticipated to reduce the risk of HCC by 70%, liver disease by 90% and all-cause mortality by 50%.


Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 61 / No. 4
August 17, 2012

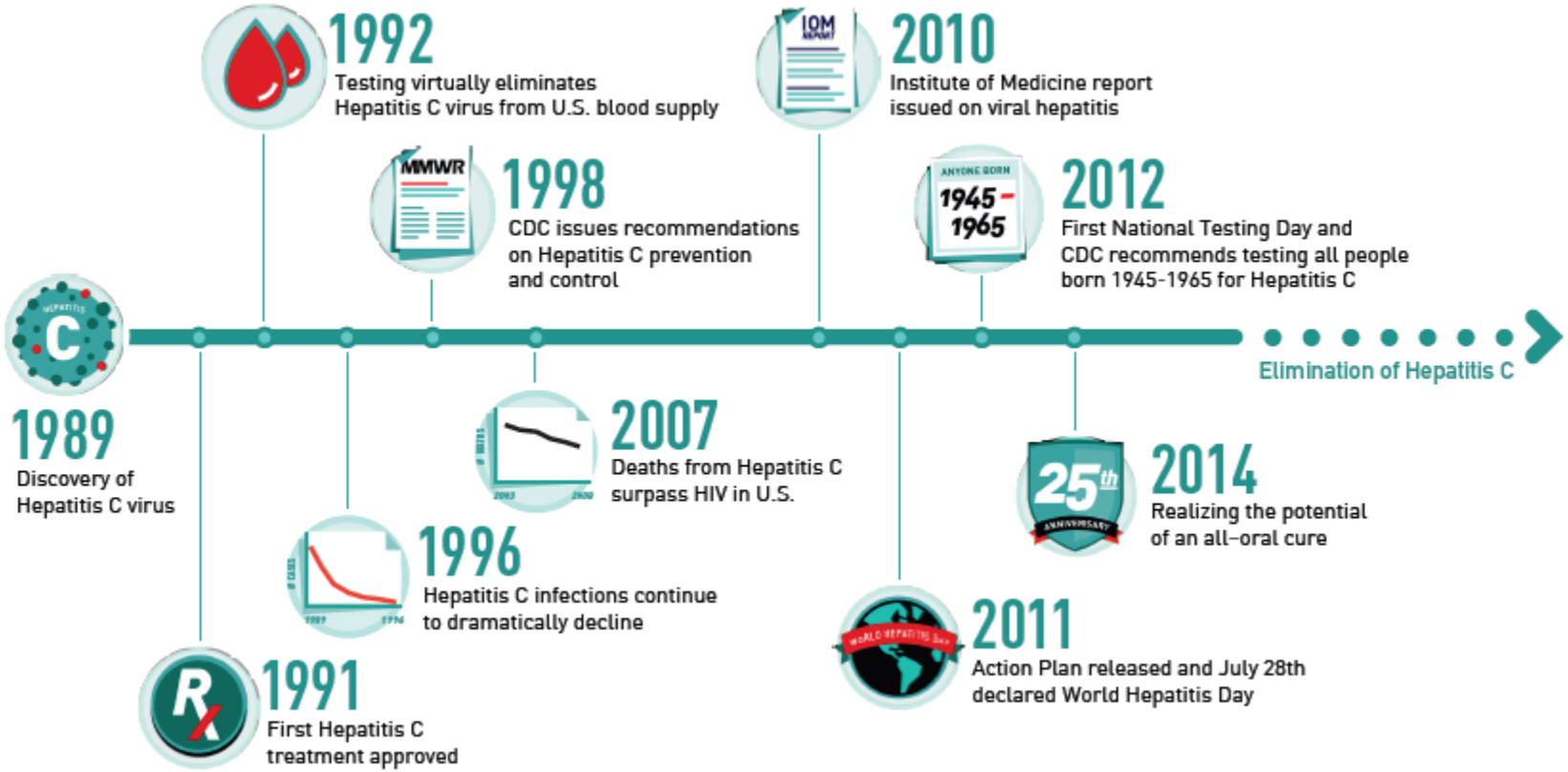
Recommendations for the Identification of Chronic Hepatitis C Virus Infection Among Persons Born During 1945–1965

http://www.cdc.gov/mmwr/pdf/rr/rr6104.pdf (public domain)

Limitations

- Positive HCV antibody screens may not receive confirmatory HCV RNA testing.
  - CDC report: approximately 50% of HCV Antibody tests did not receive a follow-up HCV RNA
- Considerations for new HCV treatments
  - Cost of therapy when some may not progress to liver failure or HCC in their lifetime
  - Potential for long-term adverse effects of treatment

Summary



http://www.cdc.gov/knowmorehepatitis/media/pdfs/hepc-timeline.pdf (public domain)

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