Hepatitis C Virus Laboratory Testing

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• 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

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

- Screening test for Anti-HCV
  - Negative*
  - OR
    - Positives* defined by s/co^1 ratios
      - Positives with high^3 s/co ratios
        - REPORT
      - Positives with low^3 s/co ratios
        - RIBA^4 for anti-HCV
          - Positive
            - REPORT
          - Negative
            - REPORT
          - Indeterminate
            - REPORT
    - All positives^*:
      - Nucleic acid test for HCV RNA
        - Negative
          - REPORT
        - Positive
          - REPORT

* Interpretation of screening immunoassay test results based on criteria provided by the manufacturer.
^1 Signal-to-cut-off.
^3 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.
^4 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/velpatasvir 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

Patients born between 1945 and 1965
“Baby boomers”

NHANES 1998-1994

NHANES 1999-2002

HCV Prevalence (%)

Age
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%.

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

1989
Discovery of Hepatitis C virus

1991
First Hepatitis C treatment approved

1992
Testing virtually eliminates Hepatitis C virus from U.S. blood supply

1996
Hepatitis C infections continue to dramatically decline

1998
CDC issues recommendations on Hepatitis C prevention and control

2007
Deaths from Hepatitis C surpass HIV in U.S.

2010
Institute of Medicine report issued on viral hepatitis

2012
First National Testing Day and CDC recommends testing all people born 1945-1965 for Hepatitis C

2014
Realizing the potential of an all-oral cure

2011
Action Plan released and July 28th declared World Hepatitis Day

Elimination of Hepatitis C

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

Acknowledgements

Dr. Nicole Tolan, PhD
Dr. Gary Horowitz, MD
Dr. Camilla Graham, MD, MPH
Disclosures/Potential Conflicts of Interest

Upon Pearl submission, the presenter completed the Clinical Chemistry disclosure form. Disclosures and/or potential conflicts of interest:

- **Employment or Leadership**: None Disclosed
- **Consultant or Advisory Role**: None Disclosed
- **Stock Ownership**: None Disclosed
- **Honoraria**: None Disclosed
- **Research Funding**: None Disclosed
- **Expert Testimony**: None Disclosed
- **Patents**: None Disclosed
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