Hepatitis C Infection: Updated Information for Front Line Workers in Primary Care Settings

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Overview

- Hepatitis C Virus Prevalence
- Effects of Hepatitis C
- Prevention
- Diagnosis
- Education
- Treatment
- Financial Toxicity
Objectives

Review the screening and diagnosis of hepatitis C infection

Discuss the evaluation and monitoring of chronic hepatitis C infection

Describe updated treatment options for patients with chronic HCV infection
HCV Prevalence

UNITED STATES
HCV Statistics

- HCV infection is the most common blood borne infection in the USA.

- An estimated 3.7 to 5 million persons have HCV.

*Chou R. Screening for Hepatitis C Virus Infection: Systematic Evidence Review No. 24.*
HCV Statistics

In the 1980s, yearly incidence of HCV infection was around 230,000 cases/year but by 2001 this declined to 25,000 cases/year.
Prevalence of HCV by birth year

NHANES, 2002
Effects of Hepatitis C
HCV Mortality Exceeds HIV

The Increasing Burden of Mortality From Viral Hepatitis in the United States Between 1999 and 2007

Consequence: Hepatitis C Kills

- 1999 to 2007: HCV-associated mortality increased 50%
- 2013: 19,368 HCV-related deaths*
  - 73% in persons aged 45-64
  - Median age of death was 57 (or about 20 years less than average life expectancy)

*These represent a fraction of deaths attributable in whole or in part to chronic hepatitis C

http://www.cdc.gov/hepatitis/statistics/
Time from HCV infection until serious complications

About 30 years

Normal Liver → Fibrosis → Cirrhosis

Stable Disease

End Stage Liver Disease

Cure reduces but does not eliminate the risk of liver failure and hepatocellular carcinoma (HCC)
Hepatocellular Carcinoma (HCC)

Most common type of liver cancer

Chronic HCV increases the risk

Treated with surgery, medications or liver transplant

But poor prognosis:

- **Solution**: prevent development
How is HCV spread?

Source: CDC and Prevention
Guidelines: High Risk Groups to Screen

- Unexplained chronic liver disease or high ALT
- Injection-drug use (even once) or intranasal drug abuse
- Ever in jail
- Long-term hemodialysis (ever)
- Transfusions or organ transplants: before July 1992 or clotting factor given before 1987, HCV+ transfusion
- Tattoo in an unregulated setting
- Children born to HCV-infected women
- Healthcare/public safety workers exposed to HCV+ blood
- HIV infection
- Born in a high risk country
Risk-Based Screening is NOT Enough

Many people can live with HEPATITIS C FOR DECADES WITH NO SYMPTOMS

MORE THAN One Million people living with Hepatitis C DO NOT KNOW THEY ARE INFECTED
NEW US Preventive Services Task Force (USPSTF) Guidelines - 2012

- One time screening of all baby boomers (born 1945 through 1965) for HCV infection (USPSTF Rating: Class I, Level B)

- Enzyme immunoassay (EIA) is the initial screening test for anti-HCV antibodies.

- Followed by Polymerase Chain Reaction (PCR) for the virus
Diagnosing HCV

LAB TESTS AND CALCULATIONS
Preparing for HCV therapy

**HCV Evaluation and Staging**
- Treatment history (interferon therapy or DAA)
- Viral load (copies/mL)
- Genotype (1, 2, 3..) and subgenotype (1a vs 1b)
- Fibrosis score (i.e. Fib-4)
- Imaging
- Drug-drug interactions (DDIs)

Screen HCV Ab → Confirm Infection & Genotype → Stage Fibrosis → Treat? With What?

Treat?
Relevant History and Physical
Assess Compliance
Screening Tests for HCV Infection

Recommended Testing Sequence for Identifying Current HCV Infection

- **HCV Antibody**
  - **Nonreactive**
    - No HCV antibody detected
      - **STOP**
  - **Reactive**
    - **Not Detected**
      - No current HCV infection
      - Additional testing as appropriate
    - **Detected**
      - Current HCV infection
      - Link to care

* For persons who might have been exposed to HCV within the past 6 months, testing for HCV RNA or follow-up testing for HCV antibody is recommended. For persons who are immunocompromised, testing for HCV RNA can be considered.

† To differentiate past, resolved HCV infection from biologic false positivity for HCV antibody, testing with another HCV antibody assay can be considered. Repeat HCV RNA testing if the person tested is suspected to have had HCV exposure within the past 6 months or has clinical evidence of HCV disease, or if there is concern regarding the handling or storage of the test specimen.
HCV Genotype 1a: Most common in US and at Parkland

Infection by HCV genotype

N=512

HCV Genotype (% of total)

- 1a (60%)
- 1b (19%)
- 2 (9%)
- 3 (6%)
- 4 (4%)
- 6 (1%)
- ≥2 Genotypes (1%)
Four stages of liver fibrosis

Minimal fibrosis

Moderate fibrosis

Septal

F1 F2

F3 F4

mild fibrosis

Severe Fibrosis: Cirrhosis
Staging liver fibrosis

Liver biopsy is gold standard but excluding cirrhosis may also be possible with noninvasive estimates of liver fibrosis
- **Fib-4 or APRI score** or equivalent serum tests are widely available.
- FibroSure (# 550123 thru Labcorp)
- Imaging helpful (liver ultrasound)
- Elastography (shear wave) ultrasound
- **Fibroscan® (vibration Controlled Transient Elastography)** in special centers
- MRI elastography but not widely available.
Calculating FIB-4

Fibrosis-4 (FIB-4) Calculator

The Fibrosis-4 score helps to estimate the amount of scarring in the liver. Enter the required values to calculate the FIB-4 value. It will appear in the oval on the far right (highlighted in yellow).

\[
\text{FIB-4} = \frac{\text{Age (years)}}{\text{AST Level (U/L)}} \times \sqrt{\frac{\text{Platelet Count (10^9/L)}}{\text{ALT (U/L)}}}
\]

Interpretation:
Using a lower cutoff value of 1.45, a FIB-4 score <1.45 had a negative predictive value of 90% for advanced fibrosis (Ishak fibrosis score 4–6 which includes early bridging fibrosis to cirrhosis). In contrast, a FIB-4 > 3.25 would have a 97% specificity and a positive predictive value of 65% for advanced fibrosis. In the patient cohort in which this formula was first validated, at least 70% patients had values <1.45 or >3.25. Authors argued that these individuals could potentially have avoided liver biopsy with an overall accuracy of 86%.

Patients with cirrhosis need to have US screening

Ultrasound is the recommended modality for HCC surveillance

Advantages: cheap, safe, readily available, supported by data

Drawbacks: operator dependent, limited sensitivity, difficult in obese patients

Masses detected by ultrasound require further characterization with other modalities (CT, MRI)

Sonogram shows a small hypoechoic mass

Screening for HCC Improves Survival in Patients with Cirrhosis

- Surveillance (n=295) vs. other (n=779)
- Tumor size
  - 2.7 vs. 6.0 cm
- Early stage HCC
  - 61% vs. 21%
- Curative treatment
  - 57% vs. 32%
Education

PATIENTS DIAGNOSED WITH HCV
Patient Counseling

Effective patient counseling:

- **Educates patients on:**
  - HCV and how it affects the liver
  - Ways to avoid spreading to others
  - Strategies to reduce damage to the liver
Co-factors that worsen liver disease in person with chronic HCV infection

- Alcohol adds fuel to the fire

![Graph showing the effect of alcohol on Hepatitis C progression](image)

- Cirrhosis
- No Scarring

Years of Hepatitis C Infection:
- <10
- 15
- 25
- 35+

Legend:
- Heavy Drinker
- Light or Non-Drinker
Treatment As Prevention

NEW HIGHLY EFFECTIVE MEDICATIONS
Goal of Treatment

CURE!
Effectiveness of HCV medications

Rate of cure for each regimen varies depending on
- Genotype
- Presence of cirrhosis
- Prior treatment for HCV

Most of these have >90% cure rate

every 10 people who get treated, 9 will be cured
### All Oral HCV Treatments Available

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosing regimen</th>
<th>Typical duration</th>
<th>genotype</th>
<th>Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sofosuvir/ledipasvir (Harvoni)</td>
<td>1 pill once a day</td>
<td>12 weeks</td>
<td>1, 4, 5, 6</td>
<td>95%</td>
</tr>
<tr>
<td>Ombitasvir/paritaprevir/ritonavir and dasabuvir (Viekira Pak)</td>
<td>2 tabs once a day+ 1 tab twice a day+- Ribavirin twice a day</td>
<td>12-24 weeks</td>
<td>1, 4</td>
<td>95%</td>
</tr>
<tr>
<td>Daclatasvir, sofosbuvir (Daklinza, Sovaldi)</td>
<td>Two pills once a day</td>
<td>12 weeks</td>
<td>1, 3</td>
<td>95%, 90%</td>
</tr>
<tr>
<td>Elbasvir/grazoprevir (Zepatier)</td>
<td>One pill once a day</td>
<td>12-16 weeks</td>
<td>1, 4</td>
<td>95%</td>
</tr>
<tr>
<td>Sofosbuvir/Velpatasvir (Epclusa)</td>
<td>One pill once a day</td>
<td>12 weeks</td>
<td>1, 2, 3, 4, 5, 6</td>
<td>95%</td>
</tr>
<tr>
<td>Glecaprevir/pibrentavir (Mayvert)</td>
<td>3 pill once a day</td>
<td>8 or 12 weeks</td>
<td>1, 2, 3, 4, 5, 6</td>
<td>95%</td>
</tr>
<tr>
<td>Sofosbuvir/velpatasvir/voxilaprevir (Vosevi) (for prior failures)</td>
<td>One pill once a day</td>
<td>12 weeks</td>
<td>1,2,3,4,5,6</td>
<td>90-95%</td>
</tr>
</tbody>
</table>
Sofosbuvir/Velpatasvir:

Sofosbuvir is nucleoside NS5B inhibitor and pan-genotypic
Velpatasvir is NS5A inhibitor and pangenotypic
Can be used for all genotypes 1, 2, 3, 4, 5, and 6
One pill once a day
Sofosbuvir/Velpatasvir: Duration of Therapy

Without cirrhosis or with compensated cirrhosis (Child-Pugh A): 12 weeks (regardless of genotype)

Decompensated cirrhosis (Child-Pugh B and C) + ribavirin (weight-based) for 12 weeks

Can not use with Cr Cl <30 ml/min
Sofosbuvir/Velpatasvir: Efficacy

SVR (%)

Genotype 1a  Genotype 1b  Genotype 2  Genotype 3  Genotype 4  Genotype 5  Genotype 6

Epclusa 12 wk  sof + RBV 12 wk  Sof+ RBV 24 wk
Sofosbuvir/Velpatasvir: Drug Interactions

- Amiodarone - symptomatic bradycardia
- Rifampin, St. John’s wort, carbamazepine: may decrease concentration of drug
- Drugs decreasing velpatasvir dose
  - Antacids: take least 4 hours apart
  - H2 blockers: take 12 hours apart
  - No PPI: except take this drug with food at least 4 hours before omeprazole 20 mg
- HIV meds: do not use with Efavirenz, Tipranavir/ritonavir
Sofosbuvir/Velpatasvir: Side Effects

**SOFOSBUVIR/VELPATASVIR**
- Headache (22%)
- Fatigue (15%)
- Nausea (9%)
- Asthenia (5%)
- Insomnia (5%)

**WITH RIBAVIRIN**
- Fatigue (32%)
- Anemia (26%)
- Nausea (15%)
- Headache (11%)
- Diarrhea (10%)
Glecaprevir/Pibrentasvir:

Glecaprevir is a NS3/4a inhibitor, pangenotypic
Pibrentasvir is a NS5A inhibitor, pangenotypic

Can use with all genotypes: 1, 2, 3, 4, 5, 6
Take 3 tablets once a day, take with food
Glecaprevir/Pibrentasvir: 
Duration of Therapy

Treatment naïve or experienced with no cirrhosis: 8 weeks

Treatment naïve or experienced with cirrhosis, compensated (Child Pugh A): 12 weeks

Treatment experienced genotype 3: 16 weeks
Glecaprevir/Pibrentasvir: Duration of Therapy

Treatment experienced

- Genotype 1: NS5A inhibitor without NS3/4A—16 weeks
- Genotype 1: NS3/4A without prior NS5A—12 weeks
- Genotype 1, 2, 4, 5, 6: prior interferon/ribavirin/sofosbuvir—8 weeks (no cirrhosis); 12 weeks (compensated cirrhosis)
- Genotype 3: prior interferon/ribavirin/sofosbuvir—16 weeks
Glecaprevir/Pibrentasvir: Adverse Event

- Headache (9-17%)
- Nausea (6-14%)
- Diarrhea (5-7%)
- Nausea (9-12%)
Glecaprevir/Pibrentavir : Drug Interaction

Anti-convulsants
Rifamycins
Ethinyl estradiol (increased risk of ALT elevation)
St John’s Wort
Statins (atorvastatin, lovastatin, simvastatin)
Cyclosporine

HIV Medications
◦ Atazanavir
◦ Darunavir
◦ Lopinavir
◦ Ritonavir
◦ Efavirenz
Glecaprevir/Pibrentasvir: Efficacy

SVR 12 (%)

- 8 weeks, no cirrhosis
- 12 weeks, no cirrhosis
- 12 weeks, compensated cirrhosis
- 16 weeks, treatment exp, no cirrhosis
- 16 weeks, treatment exp, with cirrhosis
- 12 week, treatment exp, PI

Genotypes:
- geno1
- geno2
- geno3
- geno4
- geno5
- geno6
Acknowledgement

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Thank you for your Attention!

STOP HCC BY TREATING HCV