HCV Update:
Focusing on Testing, Simplification & Key Populations

Kristen Marks, MD
Assistant Professor of Medicine
Weill Cornell Medicine
Disclosure

• Dr. Marks has received grants for research support from Gilead Sciences.
Nov 6 2019 Update!

- Universal Testing
- Universal Treatment
  - Simplified algorithm
  - Children
  - Acute HCV
- Use of HCV-positive organs

HCV is underdiagnosed and undertreated

Need more testing

Management needs to be simpler

DAAs have helped here

Testing for HCV
Opioid Epidemic has changed the Epidemiology of HCV

**Number of newly reported cases, 2006**

**Number of newly reported cases, 2011**

**FIGURE 15. Age distribution of people reported with chronic hepatitis C in New York City, 2017**
Peer Review Plan For Recommendations for Hepatitis C Screening among Adults

Title: CDC Recommendations for Hepatitis C Screening among Adults

Subject of planned report: This document will summarize new recommendations for hepatitis C screening in adults and pregnant women in the United States, specifically:

- At least once in a lifetime hepatitis C screening for all adults aged 18 years and older, except in settings where the prevalence of HCV infection is less than 0.1%, and
- Hepatitis C screening for all pregnant women during each pregnancy, except in settings where the prevalence of hepatitis C infection is less than 0.1%.

Regardless of age or setting prevalence, all persons with risk factors should be tested for hepatitis C once, with periodic testing while risk factors persist.

- At least once in a lifetime hepatitis C screening for all adults aged 18 years and older, except in settings where the prevalence of HCV infection is less than 0.1%, and
- Hepatitis C screening for all pregnant women during each pregnancy, except in settings where the prevalence of hepatitis C infection is less than 0.1%.

Regardless of age or setting prevalence, all persons with risk factors should be tested for hepatitis C once, with periodic testing while risk factors persist.
Proposed USPSTF recommendations for HCV Testing

![USPSTF Website Screenshot]

**Draft Recommendation Statement**

**Hepatitis C Virus Infection in Adolescents and Adults: Screening**

This opportunity for public comment expires on September 23, 2019 at 8:00 PM EST

**Draft: Recommendation Summary**

<table>
<thead>
<tr>
<th>Population</th>
<th>Recommendation</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults ages 18 to 79 years</td>
<td>The USPSTF recommends screening for hepatitis C virus (HCV) infection in adults ages 18 to 79 years.</td>
<td>B</td>
</tr>
</tbody>
</table>

Newly updated IDSA/AASLD (hcvguidelines.org) Recommendations for HCV Screening

<table>
<thead>
<tr>
<th>RECOMMENDED</th>
<th>RATING</th>
</tr>
</thead>
<tbody>
<tr>
<td>One-time, routine, opt out HCV testing is recommended for all individuals aged 18 years and older.</td>
<td>I, B</td>
</tr>
<tr>
<td>One-time HCV testing should be performed for all persons less than 18 years old with behaviors, exposures, or conditions or circumstances associated with an increased risk of HCV infection</td>
<td>I, B</td>
</tr>
<tr>
<td>Period repeat HCV testing should be offered to all persons with behaviors, exposures, or conditions or circumstances associated with an increased risk of HCV exposure. Annual HCV testing is recommended for all persons who inject drugs and for HIV-infected men who have unprotected sex with men.</td>
<td>IIa, C</td>
</tr>
</tbody>
</table>

**Risk Behaviors**
- Injection drug use (current or ever, including those who injected only once)
- Intranasal illicit drug use
- Men who have sex with men

**Risk Exposures**
- Persons on long-term hemodialysis (ever)
- Persons with percutaneous/parenteral exposures in an unregulated setting
- Healthcare, emergency medical, and public safety workers after needlestick, sharps, or mucosal exposure to HCV-infected blood
- Children born to HCV-infected women
- Prior recipients of a transfusions or organ transplant, including persons who:
  - Were notified that they received blood from a donor who later tested positive for HCV
  - Received a transfusion of blood or blood components, or underwent an organ transplant before July 1992
  - Received clotting factor concentrates produced before 1987
- Persons who were ever incarcerated

**Other Conditions and Circumstances**
- HIV infection
- Sexually active persons about to start pre-exposure prophylaxis (PrEP) for HIV
- Unexplained chronic liver disease and/or chronic hepatitis, including elevated alanine aminotransferase (ALT) levels
- Solid organ donors (living and deceased)
A Can check RNA if want to r/o acute or if very immunocompromised

b Can repeat with different assay if want to r/o false +
Diagnosis needs simplification

Step 1
See the doctor

Step 2
To the lab for HCV Ab

Step 3
See the doctor for result

Step 4
To the lab for HCV RNA

Step 5
See the doctor for result

Step 6
Start DAA therapy (may be additional steps: fibrosis assessment, approvals etc)

Loss to F/U
Need improved Point of Care HCV Diagnostics that can detect viremia

• Have tests to determine seropositivity
  • E.g. OraQuick FDA approved HCV Rapid Test
  • Finger stick, or venipuncture whole blood
  • CLIA waived
  • 20 minute screening test
  • Clinical performance with >98% accuracy

Remember:
• Anti-HCV antibody positive = Ever infected
• Need HCV RNA to confirm active HCV infection

• Could use dried blood spot where no phlebotomy
Universal Treatment of HCV
HCV Therapeutics Timeline

1970s Non A, non B hepatitis
1989 HCV identified

- Consensus IFN
- Peg-IFNα-2b
- BILN-2061 Phase 1b
- HCV replication
- IFNα-2b in HCV/HIV
- Peg-IFNα-2a
- HCV replicons
- Peg-IFNα-2b + RBV
- IFNα-2b
- IFNα-2a

1995

2000

2005

2010

2015 by 2018

First IFN-free GT1 DAA regimens
Multiple Pan-genotypic regimens
Simeprevir Sofosbuvir
Boceprevir Telaprevir

SVR (%)

Relative misery
Strategy for Initial HCV therapy: Direct acting antivirals target life cycle

--- **PREVIR**
  - Protease inhibitors
e.g. telaprevir, boceprevir, faldaprevir, simeprevir, danoprevir, asunaprevir, paritaprevir, grazoprevir, voxilaprevir, glecaprevir

--- **BUVIR**
  - Polymerase inhibitors
    - Nucleos(t)ide analogs: e.g. tegobuvir, sofosbuvir,
    - Non-nucs: e.g. deleobuvir, dasabuvir

--- **ASVIR**
  - NS5A inhibitors
e.g. daclatasvir, ledipasvir, ombitasvir, elbasvir, velpatasvir, pibrentasvir
Currently used combinations of DAA classes

- NUC + PI
- NUC + NS5A
- NUC + PI + NS5A
- nonNuc

NUC-SPARING HCV
Renal insufficiency
Drug-drug interactions
Duration
Affordability/Access
Toxicity
Resistance

NUC-SPARING HIV
Toxicity
Resistance
Renal insufficiency
Drug-drug interactions
Affordability

+-/- RBV
First-line HCV Therapy: Distinguishing Among Recommended Options

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Regimen</th>
<th>Duration</th>
<th>Genotypes</th>
<th>RAS Testing</th>
<th>Decompensation</th>
<th>DDI Highlights</th>
<th>Approval Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>EBR/GZR</td>
<td>QD single tablet</td>
<td>12 wks</td>
<td>GT 1 or 4</td>
<td>Requires RAS testing for GT1a</td>
<td>Can be used in stage 4/5 CKD</td>
<td>glucocorticoids, statins, PDE inhibitors, rifampin</td>
<td>Requires RAS testing for GT1a</td>
</tr>
<tr>
<td>GLE/PIB</td>
<td>QD 3 tablets with food</td>
<td>8 wks</td>
<td>no cirrhosis or cirrhosis, GT 1-6</td>
<td>No RAS testing</td>
<td>Can be used in stage 4/5 CKD</td>
<td>statins, rifampin</td>
<td>No RAS testing</td>
</tr>
<tr>
<td>LDV/SOF</td>
<td>QD single tablet</td>
<td>8-12 wks</td>
<td>GT 1, 4, 5, or 6</td>
<td>No RAS testing</td>
<td>Safe in decompensation</td>
<td>acid-reducing agents, statins, rifampin</td>
<td>Now approved for stage 4/5 CKD</td>
</tr>
<tr>
<td>SOF/VEL</td>
<td>QD single tablet</td>
<td>12 wks</td>
<td>GT 1-6</td>
<td>Requires RAS testing for some GT 3</td>
<td>Safe in decompensation</td>
<td>acid-reducing agents, rifampin</td>
<td>Now approved for stage 4/5 CKD</td>
</tr>
</tbody>
</table>

DDIs are drug specific and there are many more to consider than are listed here. Always check! [https://www.hep-druginteractions.org/](https://www.hep-druginteractions.org/)
First-line HCV Therapy: Pangentotypic Recommended Options

**GLE/PIB** - QD 3 tablets with food
- 8 wks no cirrhosis or cirrhosis, GT 1-6
- No RAS testing
- Contains PI: *do not use* if decompensated
- Can be used in stage 4/5 CKD
- DDI highlights: statins, rifampin

**SOF/VEL** - QD single tablet
- 12 wks, GT 1-6
- Requires RAS testing for some GT 3
- Safe in decompensation
- *Now approved for* stage 4/5 CKD
- DDI highlights: acid-reducing agents, rifampin

DDIs are drug specific and there are many more to consider than are listed here.
Always check! [https://www.hep-druginteractions.org/](https://www.hep-druginteractions.org/)
Previously Challenging Clinical Scenarios – SVR now >95% with DAA combinations

- Black patients
- ESRD
- HIV/HCV
- Post-liver transplant
- G3 + cirrhosis
- PWID
- Children
Ending the HCV Epidemic: Depends on testing, treatment and prevention in “Key Populations”

• PWID
• Incarcerated persons
• HIV-infected MSM
Question: All PWID should be denied HCV treatment because...

1. Adherence to therapy is too bad
2. No treatment data with DAAs
3. Reinfection rates are too high
4. Interactions with illicit drugs too dangerous
5. None of the above
Question: All PWID should be denied HCV treatment because...

1. Adherence to therapy is too bad
2. No treatment data with DAAs
3. Reinfection rates are too high
4. Interactions with illicit drugs too dangerous
5. None of the above
Sof/vel for HCV infection in recent PWID
(SIMPLIFY)
SVR12 = 97/103 (94%)
Most People Treated for HCV do not get Reininfected – But Key Populations are Higher Risk

Studies included in meta-analysis
Simplification of HCV Management & Optimizing Delivery of Care
NOW AVAILABLE
One-Page Download: Simplified HCV Treatment* for Treatment-Naive Patients Without Cirrhosis
Click here to download the PDF, or read more.

PRETREATMENT ASSESSMENT

- Cirrhosis assessment
  Liver biopsy is not required. The cutoffs of the following tests suggest cirrhosis. If any test suggests cirrhosis, treat the patient as having cirrhosis.
  - FIB-4 > 3.25
  - Platelet count < 150,000/mm²
  - APRI > 2.0
  - Fibroscan™ stiffness > 12.5 kPa
- Pretreatment laboratory testing
  Within 6 months of initiating treatment
  - Complete blood count (CBC)
  - Hepatic function panel (i.e., albumin, total protein, total and direct bilirubin, alanine aminotransferase [ALT], aspartate aminotransferase [AST], and alkaline phosphatase levels)
  - Calculated glomerular filtration rate (eGFR)
  - Anytime prior to starting antiviral therapy
    - Consultation with IDSA/IDSA-KCVP

POST-TREATMENT ASSESSMENT OF CURE (SVR)

- Monitoring patients taking diabetes medication for hypoglycemia is recommended.
- Monitoring INR for patients taking warfarin is recommended.
- Assessment of quantitative HCV RNA and hepatic function panel are recommended 12 weeks or later following completion of therapy to confirm HCV RNA is undetectable (virologic cure) and transaminase normalization.
- Assessment for other causes of liver disease is recommended for patients with elevated transaminase levels after achieving SVR.

FOLLOW-UP AFTER ACHIEVING VIROLOGIC CURE (SVR)

- No liver-related follow-up is recommended for noncirrhotic patients who achieve SVR.
- Patients with ongoing risk for HCV infection (e.g., intravenous drug use or MSM engaging in unprotected sex) should be counseled about risk reduction, and tested for HCV RNA annually and whenever they develop elevated ALT, AST, or bilirubin.

FOLLOW-UP FOR PATIENTS WHO DO NOT ACHIEVE A VIROLOGIC CURE

- Assessment for disease progression every 6 to 12 months with a hepatic function panel, CBC, and international normalized ratio (INR) is recommended.
- Patients in whom initial HCV treatment fails to achieve cure (SVR) can be retreated, often successfully. Consult the AASLD/IDSA guidance for recommendations regarding the evaluation of patients for retreatment and selection of an appropriate HCV antiviral regimen. (https://www.hcvguidelines.org)

* More detailed descriptions of the patient evaluation process and algorithms used for HCV treatment, including the treatment of patients with cirrhosis, can be found at https://www.hcvguidelines.org. Updated: November 8, 2019
© 2019 American Association for the Study of Liver Diseases and the Infectious Diseases Society of America. All rights reserved.
Randomized controlled trial – intended sample size 72

Include: People 18-29y who are HCV Ab positive and injected drugs in past 30 days

Exclude: HIV, pregnancy, end-stage renal disease, decompensated cirrhosis

**Intervention**
1. Rapid Start Treatment*
2. Co-located at syringe service program
3. HCV-Care Coordination
4. Reinfection Prevention Training

**Control**
1. Referral to provider
2. Syringe service program HCV navigator

*Rapid Start: Pan-genotypic Sofosbuvir / Velpatasvir (SOF/VEL) given as 7d starter pack. If RNA +ve, start treatment via phone call.

Kapadia, INHSU poster, 2019.
Treatment as Prevention for HCV in PWID - Iceland

- Goal HCV elimination by 2020
- HCV Treatment emphasis: cirrhosis, active PWID, prison
- 680 treatments initiated 2016-18 (80-85% of total infected, 90% overall cure rate)
- Monitored HCV rates at Iceland addiction hospital (utilized by 7.4% of their adult population)

Similar studies showing effect of treatment as prevention in European MSM
Summary

• All adults should be tested for HCV once

• Persons with risk factors/exposures should be tested periodically (at least annually for PWID and MSM living with HIV)

• Remarkable advances in terms of HCV treatment tolerability & efficacy

• DAA therapy is safe and effective

• HCV reinfection will occur when treating HCV in PWID and other key populations (but does not in most people)

• Testing, diagnosis, and linkage to care remain a significant barrier that must be addressed

• Simplification of care will be essential to achieve HCV elimination

• Successful treatment prevents cirrhosis, end stage liver disease, and hepatocellular cancer for the individual treated and prevents spread to others

• Post cure – continue liver disease management/HCC screening, monitor HBV reactivation, and consider HCV RNA testing if ongoing risk
Resources

• https://www.hcvguidelines.org/
• http://necaaetc.org/
• http://www.hep-druginteractions.org

THANK YOU
for your time & the important work you do