Conflicts of Interest/Financial Disclosures

• None
Hepatitis C Update: Outline

- Epidemiology and Transmission
- Screening and Diagnosis
- Treatment Options and Guidelines 2018
- Assessing Candidates for Treatment
Resources

AASLD/IDSA Guidelines
http://hcvguidelines.org

UW Hepatitis Online Modular Course
http://hepatitisc.uw.edu
A patient with hepatitis C asks you what their chance of cure would be with currently available oral treatment options. What would you say?

- A. 0%, hep C can’t be cured
- B. 20-25%
- C. 45-50%
- D. 70-75%
- E. 90-95% or greater
Key Take-Home Points

• Very high chance of cure (>90-95%) with hep C therapy

• Treatment requires pills only for 2-3 months (never use interferon anymore; oral ribavirin rarely indicated)

• Need for labs at baseline and during treatment is minimal

• Treatment reduces mortality and risk of transmission

• Treatment is cost effective!
A 55-year-old man has a positive hepatitis C virus (HCV) antibody test, followed by a detectable HCV RNA (viral load) of 8 million copies/ml. An HCV genotype test determines that he has genotype 1a HCV. He last used injection drugs approximately 25 years ago (and started using 35 years ago). He drinks 1-2 beers daily and binge drinks on weekends.

How would you counsel him about preventing progression of liver disease and preventing transmission to others?

What would you do to assess his stage of liver fibrosis and the urgency of treatment?

What are his options for treatment and his chance of cure?
Hepatitis C Transmission, Screening, and Epidemiology
Hepatitis C - Transmission

- Blood – Blood – Blood
  - IV drug abuse (68%)
  - Occupational exposure
  - Transfusions (before 1992)
  - Tattoos, piercings (unsanitary)
- Mother-to-child (rare)
- Sexual exposure *(not so rare!)* (18%)

- No vaccine or immunity for hepatitis C

Who Should be Screened for Hepatitis C?

CDC Guidelines

- Ever injected illegal drugs or used intranasal cocaine (even once)
- Received clotting factors before 1987
- Received blood/organs before July 1992
- Ever on chronic hemodialysis
- Evidence of liver disease/elevated LFT’s
- Infants born to HCV-infected mothers
- HIV infection (up to 1/3 also have hep C)
- After hep C exposure
- History of non-sterile tattoo/piercing
- Baby boomers (born 1945-1965)
Hepatitis C in the United States

- Estimated 3-4 million people in the US are infected with hepatitis C

Up to 75% of people living with Hepatitis C DO NOT KNOW THEY ARE INFECTED.

Many people can live with Hepatitis C for DECADES WITH NO SYMPTOMS.

CDC recommends anyone born from 1945-1965 GET TESTED.
Recent Surge of New Hep C Infections in US

- 4-fold rise in rate of # new infections/year since 2011
- Majority in individuals <30 years old
- Majority related to the opioid epidemic

Source: CDC, UW Hepatitis C Online (Editor Dr. David Spach)
Who Needs Repeat HCV Screening?

- **Annual** testing for people who inject drugs (PWID) and men who have sex with men (MSM) who have HIV

  - Also repeat if new elevation in AST/ALT, STI diagnosis, other suggestion of elevated risk or new infection

- “Periodic” testing for others who have ongoing risk factors

Source: hcvguidelines.org
Hepatitis C – Diagnostic Testing

HCV Antibody (EIA), ‘HCV Ab’
• Indicates past or active infection

HCV RNA test (PCR), ‘Viral Load’
• Confirms active infection & infectivity to others
• Need *quantitative* for making treatment decisions and for treatment monitoring

HCV Genotype
• Important for treatment decisions

Source: hcvguidelines.org
Natural History of Hepatitis C
HIV-Negative Exposure
(Acute Hepatitis)

Resolution
15%

Persistence (chronic)
85%

Cirrhosis
20%

ESLD
3%/yr

HCC
4%/yr

Transplant
Death

Time (yrs):
10
20
30

Alcohol greatly accelerates this progression

Mandell: Principles & Practice of Infectious Disease, 7th Ed;
Natural History of Hepatitis C
HIV-Positive

Exposure
(Acute Hepatitis)

Resolution
5%

Persistence
(chronic)
95%

Cirrhosis
20%

ESLD
3%/yr

HCC
4%/yr

Transplant?

Death

Time (yrs): 5

Mandell: Principles & Practice of Infectious Disease, 7th Ed;
Forecasted 2010-2060 Annual HCV-Related Deaths in the US Persons with Chronic Hepatitis C and No Cirrhosis in 2005

“Why screen if I’m not ready to treat?”

• **Counsel to prevent progression of liver disease**
  - Avoidance of alcohol
  - Vaccinate for hep A/B

• **Evaluate for cirrhosis; if cirrhosis present:**
  - EGD to screen for varices
  - Every 6-month ultrasound to screen for HCC

• **Counsel to decrease risk of transmission**
# Recommendations for All HCV+ Individuals

- Abstain from alcohol
- Evaluate for conditions that accelerate liver fibrosis (HBV, HIV, NAFLD/NASH)
- Manage obesity, insulin resistance, etc
- Vaccinate against HAV, HBV
- Offer pneumococcal vaccination
- Evaluate stage of liver fibrosis; management of cirrhosis to prevent complications
- Educate regarding how to prevent transmission to others
Measures to Prevent HCV Transmission

Avoid sharing dental and shaving equipment; cover bleeding wounds

Abstain from intranasal or injection drugs; avoid sharing needles & equipment (syringes, water, cotton, cookers)

Advise persons with HIV, multiple sexual partners, or STI’s to use barrier protection

Counsel other persons with HCV that risk of sexual transmission is low and “may not warrant barrier protection”

Wear gloves should to clean blood spills; household surfaces and implements can be cleaned with 1 part bleach:9 parts water

Source: hcvguidelines.org
Hepatitis C Treatment Options in 2018
The biggest barrier to hepatitis C treatment in my practice/clinic/community is:

A) Lack of screening/testing – patients/clients don’t know if they have hepatitis C or not

B) Individuals with hep C have other priorities and aren’t interested in treatment

C) Providers need more knowledge about current treatment options or how to access them

D) The cost/staff resources necessary to access current treatment options is prohibitive
Who Should Be Treated?

- HCV treatment reduces liver-related complications (ESLD, HCC, decompensation events) and all-cause mortality
  - Also improves symptoms, liver inflammation, and liver fibrosis
  - And eliminates the risk of transmission to others!

- Goal of treatment is sustained virologic response (SVR)

- Treatment is recommended for all individuals with HCV (unless very limited life expectancy)

Source: hcvguidelines.org
Who Should be Treated More Urgently?

- **Advanced stage of fibrosis**
  - Especially stage 3 or compensated stage 4 fibrosis
  - If decompensated, need co-management with a specialist

- Symptomatic or systemic complications (cryoglobulinemia, porphyria, lichen planus, arthritis, fatigue, etc)

- HIV or HBV co-infection; other causes of liver disease

- High risk of transmitting to others
Who Should be the Treater?

Equivalent results when treater is specialist, PCP, or advanced practitioner!
What Evaluation Do We Need Before Treating?

1) Need to know treatment-naïve or experienced?

2) Labs:
   - Hepatitis C RNA (viral load) and genotype
   - Baseline CMP (consider CBC, INR)
   - Hepatitis B serology panel
   - Very rarely need a resistance test at baseline

3) Assessment of fibrosis stage
Assessment of Fibrosis Stage

Liver biopsy
- Also provides assessment of other causes of liver disease (NASH, iron, autoimmune hepatitis, etc)
- Subject to observer variability, sampling error

or...

Non-invasive markers
- Elastography (Fibroscan)
- Direct biomarkers (Fibrosure, Fibrotest)
- Indirect markers (APRI, FIB-4)
- *Usually combine 2 of the above

Source: hcvguidelines.org
Another Pre-Treatment Consideration:
Risk of Hepatitis B Reactivation

• FDA warning (October 2016)

• 24 cases of hep B reactivation during hep C DAA therapy
  - 2 deaths; 1 liver transplant

• Check hep B serology panel prior to treatment
  - If surface Ag+ start hep B treatment first
  - If only core Ab+ monitor AST/ALT monthly during hep C tx
TREATMENT OF CHRONIC HEPATITIS C

Guidelines for Treatment-Naïve Individuals (hcvguidelines.org)
Treatment Regimen Depends on Genotype and Treatment Experience

Genotype Prevalence in the US

- Genotype 1: 74%
- Genotype 2: 15%
- Genotype 3: 7%
- Genotypes 4-6: 4%

DAA: Directly Acting Antiviral

- **“PREVIR”**: protease inhibitors (e.g. glecaprevir, grazoprevir, voxilaprevir)
- **“BUVIR”**: polymerase inhibitors (e.g. sofosbuvir)
- **“ASVIR”**: NS5A inhibitors (e.g. ledipasvir, elbasvir, velpatasvir, pibrentasvir)

Adapted from talk by Dr. Kristen Marks (April 2018, IAS-USA Webinar)
Therapy for Hepatitis C
Rapid Improvement in SVR Rates in Recent Years

Timeline

1986 2002 2011 2013

<table>
<thead>
<tr>
<th>Year</th>
<th>SVR Rate (%)</th>
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<tbody>
<tr>
<td>1986</td>
<td>10%</td>
</tr>
<tr>
<td>2002</td>
<td>60%</td>
</tr>
<tr>
<td>2011</td>
<td>95%</td>
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<tr>
<td>2013</td>
<td>&gt;90-95%</td>
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<table>
<thead>
<tr>
<th>Treatment Regimen</th>
<th>Duration - No Cirrhosis</th>
<th>Duration - Compensated Cirrhosis</th>
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</thead>
<tbody>
<tr>
<td>Sofosbuvir/velpatasvir (<em>Epclusa</em>) 1 tab daily</td>
<td>12 weeks</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Sofosbuvir/ledipasvir (<em>Harvoni</em>) 1 tab daily</td>
<td>*12 weeks</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Glecaprevir/pibrentasvir (<em>Mavyret</em>) 3 tabs daily</td>
<td>8 weeks</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Elbasvir/grazoprevir (<em>Zepatier</em>) 1 tab daily</td>
<td>No NS5A resistance: 12 weeks NS5A resistance: not recommended</td>
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*8 weeks may be sufficient if HCV RNA <6 million, no HIV infection, and not African American

Source: AASLD/IDSA/IAS-USA ([www.hcvguidelines.org](http://www.hcvguidelines.org)).
HCV Treatment Recommendations, Updated Sept. 2017
Treatment Naïve Genotype 1b Chronic HCV

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<table>
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<th>Duration-Compensated Cirrhosis</th>
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Source: AASLD/IDSA/IAS-USA ([www.hcvguidelines.org](http://www.hcvguidelines.org)).
## Treatment Regimen, Treatment Duration for Chronic HCV Genotype 3

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*CConsider resistance testing at baseline and if Y93H mutation present, consider adding ribavirin or using sofosbuvir/velpatasvir/voxilaprevir x 12 weeks*

Source: AASLD/IDSA/IAS-USA (www.hcvguidelines.org).
Choosing Between the Regimen Options

• A lot depends on the payer (i.e. state Medicaid)

• Factors may indicate need for one regimen over another:
  - Decompensated cirrhosis: avoid PI’s (so avoid G/P or E/G, use a sofosbuvir-based option) *treat with help of a transplant center
  - Stage 4/5 CKD: avoid sofosbuvir (so use G/P or E/G ok)
  - Some drug-drug interactions (DDI’s) may be a factor
Drug-Drug Interactions

• A comprehensive assessment of all prescribed & OTC meds is recommended prior to initiating treatment


• Examples:

  - Ledipasvir & velpatasvir interact with PPI’s

  - HCV PI’s interact with rifampin, some statins, some anti-epileptics, etc.

  - There are some interactions with HIV ART (that are surmountable)
HCV Treatment Recommendations for HIV/HCV Coinfected Individuals

“HIV/HCV-coinfected persons should be treated and retreated the same as persons without HIV infection, after recognizing and managing interactions with antiretroviral medications.”
Monitoring During and After Hep C Treatment

- **Hep C RNA (viral load) at two time points: end of treatment and 12-24 weeks post treatment**
  - Optional at 4 weeks of treatment (mostly to assess adherence)
  - Optional 12 months after treatment (consider if cirrhosis or HIV+)
  - Repeat if concern for reinfection at later timepoint

- **CMP at 4 weeks**
  - Then q4 weeks if concern or if hep B surface Ag+ or isolated core Ab+

- **Ongoing surveillance for HCC if cirrhosis present pre-treatment**
  (such as q6 months US)
Medicaid Access to Hep C Treatment: Varies by State

Examples of requirements in some states:

- May require documented hep C diagnosis based on HCV RNA levels, and other labs (genotype, HBV & HIV status, CBC, INR) & fibrosis test

- May require documentation/testing to show free of illicit drug use and alcohol or receiving treatment from an addictions provider

- May require consult with a hepatologist, gastroenterologist, or ID specialist (telemedicine or Project ECHO consults generally allowed)

- May require HCV RNA level check on week 4

- May require documentation of adherence to scheduled visits
Medication Access and Patient Assistance


- Patient assistance programs for uninsured through drug companies

- Patient Access Network (PAN) Foundation for high deductibles

- HepEducation project (Seattle)
Suggestions for Accessing Hep C Meds

• Prescriber:
  - Clearly describe in notes the indications for treatment/specific regimen
  - Review DDI’s and document how these are addressed
  - Document adherence to appointments/meds and any substance use/addictions treatment or negative drug screens

• Support team (RN, pharmacy team, etc):
  - Complete specialty pharmacy referral
  - Print relevant labs/imaging documentation
  - Keep templates of letters of appeal
  - Help with applications to patient assistance programs

Adapted from talk by Dr. Kristen Marks (April 2018, IAS-USA Webinar)
Case

- A 55-year-old man has a positive hepatitis C virus (HCV) antibody test, followed by a detectable HCV RNA (viral load) of 8 million copies/ml. An HCV genotype test determines that he has genotype 1a HCV. He last used injection drugs approximately 25 years ago (and started using 35 years ago). He drinks 1-2 beers daily and binge drinks on weekends.

- How would you counsel him about preventing progression of liver disease and preventing transmission to others?

- What would you do to assess his stage of liver fibrosis and the urgency of treatment?

- What are his options for treatment and his chance of cure?
SUMMARY

• Hepatitis C is common, but underdiagnosed

• Treatment is expensive but patients CAN BE CURED and treatment is cost effective

• Oral DAA’s are now the standard of care

• Patients with advanced liver disease, complications, or high transmission risk should be prioritized for treatment

• Goal is a day when all persons can be treated without fibrosis testing and without a lengthy approval process – we are getting there!