HEPATITIS C VIRUS: TEST, TREAT AND CURE PART 2: DIAGNOSTICS, ASSESSMENT AND TREATMENT

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DISCLOSURE

Ms. Swan has no disclosures
LEARNING OBJECTIVES:

1. Diagnosing Hepatitis C Virus
2. Hepatitis C Virus: Pre-Treatment Assessment
3. Hepatitis C: Treatment Recommendations

HCV Care, Support, Education

Provide clear information about HCV transmission/risk, prevention, testing, natural history, prevention of liver disease progression, treatment

Alcohol assessment / counseling, treatment, support when indicated

HAV and HBV vaccination
Goal of HCV Treatment

A. To cure hepatitis C
B. To stop liver disease from getting worse
C. To improve overall health and quality of live
D. All of the above

Hepatitis C can be diagnosed:

A. With a single, rapid antibody test
B. By antibody and viral load testing
C. After a six month “window” period
D. None of the above
UNLIKE HIV,

A person can clear hepatitis C virus without treatment

A positive HCV antibody test result means:
That a person *has been* infected with HCV

That another test is needed (to look for the actual hepatitis C virus) to confirm or rule out whether they are *still* infected with HCV

**Hepatitis C Diagnostics**

![Flowchart](CDC: Recommended Sequence for Diagnosing Current HCV Infection 2014)
HCV RNA Testing

Anti-HCV “window” is 3 months
Hepatitis C viral load can be detected within 2 weeks

HCV RNA
May be needed in people who are:
• Recently infected
• Immunocompromised (including HIV+ people with CD4 cell count of <200 cells/mL)
• Re-infected


HCV Testing: By the Guidelines

• An anti-HCV test is recommended for HCV testing, and if the result is positive, current infection should be confirmed by a sensitive HCV RNA test.
  Rating: Class I, Level A

• Among persons with a negative anti-HCV test who are suspected of having liver disease, testing for HCV RNA or follow-up testing for HCV antibody is recommended if exposure to HCV occurred within the past 6 months; testing for HCV RNA can also be considered in persons who are immunocompromised.
  Rating: Class I, Level C

HCV Testing: By the Guidelines

• If found to have positive results for anti-HCV test and negative results for HCV RNA by polymerase chain reaction (PCR), persons should be informed that they do not have evidence of current (active) HCV infection.
  Rating: Class I, Level A

• Among persons at risk of reinfection after previous spontaneous or treatment-related viral clearance, initial HCV-RNA testing is recommended because an anti-HCV test is expected to be positive.
  Rating: Class I, Level C


HCV Assessment
People with chronic HCV

A. Can start treatment as soon as they are diagnosed—“test and treat”
B. Need to have other tests to see what type of treatment will work for them
C. Need to have a liver biopsy
D. B and C
Next Steps: HCV Genotyping

A blood test

- There are 6 HCV genotypes and many subtypes
- Each genotype assigned a number, in order of discovery
  - Each subtype assigned a letter, in order of discovery

HCV genotype (and subtype) determine type and length of treatment

Testing for HCV genotype is recommended to guide selection of the most appropriate antiviral regimen.

Rating: Class I, Level A


U.S. Distribution of HCV Genotypes

HCV genotypes 1, 2 and 3 are the most prevalent genotypes in the U.S., representing over 98% of all infections

Germer et al; *J Clin Microb* 2012
HCV Baseline Viral Load

- Quantitative HCV RNA testing is recommended prior to the initiation of antiviral therapy to document the baseline level of viremia (ie, baseline viral load).

Rating: Class I, Level A

Liver Disease Assessment

- Evaluation for advanced fibrosis using liver biopsy, imaging, or noninvasive markers is recommended for all persons with HCV infection, to facilitate an appropriate decision regarding HCV treatment strategy and to determine the need for initiating additional measures for the management of cirrhosis (eg, hepatocellular carcinoma screening).

Rating: Class I, Level B
What is an SVR?

*Sustained virologic response (SVR)* = undetectable HCV viral load 12 weeks after end of HCV treatment

**SVR is a cure for <99%**

- Being cured improves fatigue, quality of life, neurocognitive function and depression
- Being cured lowers the risk of liver-related illness, death and all-cause death – even in people with cirrhosis

Pearlman et al; *Clin Infect Dis* 2011; Kraus et al; *Hepatol* 2013; Smith-Palmer et al; *BMC Infect Dis* 2015; Morgan et al; *Ann Intern Med* 2013; Morgan et al; *Hepatol* 2013

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The HCV Treatment Revolution

A. New oral drugs can cure >90% of people, without interferon

B. Safe, and just as effective in HIV/HCV

C. Lasts for 8 to 24 weeks

D. All of the above
Pegylated Interferon + Ribavirin (PEG-IFN/RBV)

SOC until 2011
Low response rates, many side effects

<table>
<thead>
<tr>
<th>Genotype</th>
<th>HCV</th>
<th>HIV/HCV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype 1</td>
<td>40-50%</td>
<td>14-29%</td>
</tr>
<tr>
<td>Genotype 2/3</td>
<td>80%</td>
<td>44-73%</td>
</tr>
</tbody>
</table>


The U.S. HCV Treatment Cascade
2003 to 2013; interferon-based treatment

Slide courtesy of Dr. Kara Chew; Yehia et al; *PLOS One* 2014
Curing Hepatitis C, Without Interferon

Direct-Acting Antivirals (DAAs)

**NSSA INHIBITORS**
- Ombitasvir (in Viekira Pak)
- Ledipasvir (in Harvoni)

**NUCLEOSIDE/TIDE POLYMERASE INHIBITORS**
- Sofosbuvir (Sovaldi; in Harvoni)

**PROTEASE INHIBITORS**
- Simeprevir (Olysio)
- Paritaprevir/r (in Viekria Pak)

**NON-NUCLEOSIDE POLYMERASE INHIBITORS**
- Dasabuvir (in Viekra Pak)
HCV Treatment: Who and When

**TREATMENT SHOULD BE CONSIDERED FOR ALL**

Expected to benefit all HCV-infected persons, except those with limited life expectancy (<12 months)


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Federal Bureau of Prisons
Interim Guidance for the Management of Chronic HCV 6/2014; follows AASLD/IDSA guidelines

**PRIORITY GROUPS**
- Advanced liver disease (F3/F4)
- Transplant recipients
- HIV coinfection
- Comorbidities associated with HCV
- Continuity of care for newly incarcerated persons who were receiving treatment
HCV: Treatment as Treatment, and as Prevention

Persons at Elevated Risk of HCV Transmission and in Whom HCV Treatment May Yield Transmission Reduction Benefits (Class IIa, Level C)

- Men who have sex with men (MSM) with high-risk sexual practices
- Active injection drug users
- Incarcerated persons
- HCV-infected women of child-bearing potential wishing to get pregnant
- Persons on long-term hemodialysis

*Along with counseling on reducing transmission, reinfection risk

Slide courtesy of Dr. Kara Chew; AASLD/IDSA Recommendations for Testing, Managing and Treating Hepatitis C; www.hcvguidelines.org
Accessed May 25, 2015

HCV Treatment

1. Is the same for everyone with genotype 1
2. Is always longer for people who are being re-treated
3. Is always longer for people with cirrhosis
4. None of the above
What’s Great About DAA Treatment

• Cure rates generally over 90%
  – >95% in some groups

• Few discontinue treatment due to side effects
  – Usually mild

Common Side Effects and Lab Abnormalities from DAA Treatment

Common side effects: fatigue, insomnia, headache, nausea, diarrhea, irritability

Serious AEs are rare

Common Lab abnormalities: elevated bilirubin, sometimes ALT elevations (BUT NOT TOGETHER); anemia from ribavirin
DAAs and DDIs

- Acid-suppressing medications and SOF/LDV
  - Decreased absorption of ledipasvir
- Salmeterol and paritaprevir/ritonavir/ombitasvir + dasabuvir
  - Prolonged QT
- St. John’s Wort
  - St John’s wort will decrease ombitasvir/paritaprevir/ritonavir + dasabuvir levels and SOF/LDV levels
- HIV Antiretrovirals
  - DDIs with protease inhibitors
  - Effects on tenofovir levels and renal toxicity
- Statins
  - Increased levels with both SOF/LDV and paritaprevir/ritonavir/ombitasvir/dasabuvir
- AMIODARONE: RECENT FDA WARNING
  - SOF/LDV or SOF + another HCV DAA (daclatasvir or simeprevir)
  - Serious symptomatic bradycardia, including fatal cardiac arrest and cases requiring pacemaker intervention

Slide courtesy of Dr. Kara Chew

HCV Treatment Recommendations

<table>
<thead>
<tr>
<th>Genotype 1a, Treatment-Naive</th>
</tr>
</thead>
<tbody>
<tr>
<td>With or without cirrhosis:</td>
</tr>
<tr>
<td>12 weeks of <strong>sofosbuvir/ledipasvir</strong></td>
</tr>
<tr>
<td>No cirrhosis:</td>
</tr>
<tr>
<td>12 weeks of <strong>paritaprevir/ombitasvir + dasabuvir &amp; ribavirin</strong></td>
</tr>
<tr>
<td>Cirrhosis: treat for 24 weeks</td>
</tr>
<tr>
<td>No cirrhosis: 12 weeks of <strong>sofosbuvir/simeprevir with or without ribavirin</strong></td>
</tr>
<tr>
<td>Cirrhosis: treat for 24 weeks</td>
</tr>
</tbody>
</table>

### HCV Treatment Recommendations

#### Genotype 1b, Treatment-Naive

<table>
<thead>
<tr>
<th>With or without cirrhosis:</th>
<th>12 weeks of sofosbuvir/ledipasvir</th>
</tr>
</thead>
<tbody>
<tr>
<td>No cirrhosis: 12 weeks of</td>
<td>paritaprevir/r/ombitasvir + dasabuvir</td>
</tr>
<tr>
<td>Cirrhosis: add ribavirin</td>
<td></td>
</tr>
<tr>
<td>No cirrhosis: 12 weeks of</td>
<td>sofosbuvir/simeprevir</td>
</tr>
<tr>
<td>Cirrhosis: treat for 24 weeks</td>
<td></td>
</tr>
</tbody>
</table>


#### Genotype 1a, Treatment-Experienced (PEG-IFN + RBV; *PEG-IFN + HCV protease inhibitor*)

| No cirrhosis: 12 weeks of sofosbuvir/ledipasvir* | |
| Cirrhosis: 12 weeks of sofosbuvir/ledipasvir + ribavirin* | or 24 weeks of sofosbuvir/ledipasvir |
| No cirrhosis: 12 weeks paritaprevir/r/ombitasvir + dasabuvir & ribavirin | Cirrhosis: treat for 24 weeks |
| No cirrhosis: 12 weeks of sofosbuvir/simeprevir with or without ribavirin | Cirrhosis: treat for 24 weeks |

### HCV Treatment Recommendations

**Genotype 1b, Treatment-Experienced (PEG-IFN + RBV; *PEG-IFN + HCV protease inhibitor)*

<table>
<thead>
<tr>
<th>Condition</th>
<th>Treatment Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>No cirrhosis</td>
<td>12 weeks of sofosbuvir/ledipasvir*</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>12 weeks of sofosbuvir/ledipasvir + ribavirin*</td>
</tr>
<tr>
<td>or 24 weeks</td>
<td>sofosbuvir/ledipasvir</td>
</tr>
<tr>
<td>No cirrhosis</td>
<td>12 weeks paritaprevir/r/ombitasvir + dasabuvir</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>add ribavirin</td>
</tr>
<tr>
<td>No cirrhosis</td>
<td>12 weeks sofosbuvir/simeprevir with or without ribavirin</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>treat for 24 weeks</td>
</tr>
</tbody>
</table>


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**Genotype 2, Treatment-naive or Treatment-Experienced (PEG-IFN/RBV)**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Treatment Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>No cirrhosis</td>
<td>12 weeks of sofosbuvir + ribavirin</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>treat for 16 weeks</td>
</tr>
</tbody>
</table>

**PEG-IFN/RBV-experienced:** 12 to 16 weeks of sofosbuvir + ribavirin

If interferon-eligible, 12 weeks of PEG-IFN/RBV + sofosbuvir

### HCV Treatment Recommendations

<table>
<thead>
<tr>
<th>Genotype 3, Treatment-naive or Treatment-Experienced (PEG-IFN/RBV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>24 weeks of <strong>sofosbuvir</strong> + <strong>ribavirin</strong></td>
</tr>
<tr>
<td>If eligible for interferon, 12 weeks of PEG-IFN/RBV + <strong>sofosbuvir</strong></td>
</tr>
</tbody>
</table>

| PEG-IFN/RBV-experienced: 24 weeks of **sofosbuvir** + **ribavirin** |


<table>
<thead>
<tr>
<th>Genotype 4, Treatment-naive or Treatment-Experienced (PEG-IFN/RBV)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Treatment-naive:</strong></td>
</tr>
<tr>
<td>12 weeks of <strong>sofosbuvir</strong>/<strong>ledipasvir</strong></td>
</tr>
<tr>
<td>12 weeks of <strong>paritaprevir/r /ombitasvir</strong> &amp; <strong>ribavirin</strong></td>
</tr>
<tr>
<td>24 weeks of <strong>sofosbuvir</strong> &amp; <strong>ribavirin</strong></td>
</tr>
</tbody>
</table>

| **PEG-IFN/RBV-experienced:**                                  |
| 12 weeks of **sofosbuvir**/**ledipasvir**                     |
| 12 weeks of **paritaprevir/r /ombitasvir** & **ribavirin**    |
| 24 weeks of **sofosbuvir** & **ribavirin**                    |

If interferon-eligible, 12 weeks of PEG-IFN/RBV + **sofosbuvir**

**HCV Treatment Recommendations**

**Genotype 5, Treatment-Naïve or Treatment-Experienced (PEG-IFN + RBV)**

- 12 weeks of **sofosbuvir** + PEG-IFN/RBV
- If interferon-eligible, 48 weeks of PEG-IFN and RBV

**Genotype 6, Treatment-Naïve or Treatment-Experienced (PEG-IFN + RBV)**

- 12 weeks of **sofosbuvir/ledipasvir**
- If interferon-eligible, 12 weeks of **sofosbuvir** + PEG-IFN/RBV


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**More HCV Treatment Options Coming**

- Possibly one regimen for everyone!
- Retreatment options for people who weren’t cured by DAAs
- Shorter treatment (8 weeks—or maybe even less)
CLINICAL INQUIRY FOR: HIV • HCV • STD • PEP • PrEP

CEI LINE
1-866-637-2342
ASK AN EXPERT
Call for a clinical inquiry regarding your patient with an STD, HIV, HCV, or those in need of PEP or PrEP

866-637-2342  www.ceitraining.org

QUESTIONS?