Hepatitis C Virus: An Overview

IHS/CCUIH Hepatitis C Warmline

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May 11, 2016
The Challenge: Hepatitis C Virus (HCV) in 2016

3.5 million infected

New treatments which are safe and curative

Opportunity to end the epidemic
We Are: The Clinician Consultation Center

The Clinician Consultation Center (CCC) at the University of California at San Francisco provides immediate, state-of-the-art HIV/AIDS clinical consultation to health care providers (physicians, nurse practitioners, physician assistants, pharmacists and other health care professionals) across the country through four telephone and online consultation services:

- HIV/AIDS Management Consultation Service: 6:00 a.m.-5:00 p.m. PST
- Perinatal HIV Consultation and Referral Service: 24/7
- Post-Exposure Prophylaxis Consultation Service (PEPline): 6:00 a.m. – 11:00 p.m. PST
- Pre-Exposure Prophylaxis Consultation Service (PrEPline): 6:00 a.m.-5:00 p.m. PST

Health Resources and Services Administration (HRSA) HIV/AIDS Bureau
AIDS Education and Training Centers (AETCs)
and
Centers for Disease Control and Prevention (CDC)
Indian Health Services
Hepatitis C Consultation Service
9 am – 8 pm EST, Monday - Friday

Hepatitis C Mono- and Co-infection Consultation: 844-437-4636

The Clinician Consultation Center (CCC) provides IHS clinicians of all experience levels free, confidential, and timely expert consultation by physicians and clinical pharmacists with expertise in HIV and HCV care.

Advice is based on Federal treatment guidelines, VHA guidelines, current medical literature, and clinical best practices.

Our team includes: Betty Dong, Joanna Eveland, Rena Fox, Alex Monto, Marion Peters
Objectives

Understand HCV..

Natural history

Epidemiology

Screening

Staging of liver disease
HCV Has a Broad Reach

1.0% US prevalence

~3.5 million Americans

11.5-36% in IHS Clinics

22-52% in Health Care for the Homeless programs

12-35% in incarcerated populations
Chronic HCV Infection May Lead to Chronic Liver Disease and Liver Cancer

Fibrosis

Chronic HCV infection can lead to the development of fibrous scar tissue within the liver.

Cirrhosis

Over time, fibrosis can progress, causing severe scarring of the liver, restricted blood flow, impaired liver function, and eventually liver failure.

Fibrosis Cirrhosis Hepatocellular Carcinoma

(with cirrhosis)

Cancer of the liver can develop after years of chronic HCV infection.
Natural History of HCV
HCV Warmline Case

65 year old man recently co-infected with HIV (now well controlled) and HCV. Drinks 6-12 beers on weekends. No evidence of cirrhosis on labs or ultrasound. Patient is requesting HCV treatment but caller not sure if it’s indicated as patient has no liver disease.
Risk Factors for HCV Progression

- HIV or other co-infection
- Alcohol use
- Older age at infection
- Male gender
- Insulin resistance
Hepatitis C and Opioid Epidemics Intersect

30-90% of IDUs infected with HCV

Opportunities for harm reduction, substance use disorder treatment

HCV testing and treatment of active drug users prevents new infections
Post-exposure Hotline Case

Prison guard stuck with homemade tattoo needle recently used by 55 year old inmate with history of injection drug use. Inmate is HIV negative but should they worry about HCV?
The USPSTF recommends...

Screening for HCV infection in persons at high risk

1-time screening for HCV infection to adults born 1945-1965
Birth Cohort Screening

Persons Born Between 1945 and 1965\textsuperscript{1,2}

- The 1945-1965 birth cohort was selected on the basis of HCV prevalence and disease burden
- One-time screening for HCV infection in the birth cohort may identify infected patients at earlier stages of disease

Risk Factor–Based Screening

Important Risk Factors\textsuperscript{1,2}

- Past or current injection drug use
- Receiving a blood transfusion before 1992
- Long-term hemodialysis
- Being born to an HCV-infected mother
- Incarceration
- Intranasal drug use
- Getting an unregulated tattoo
- Other percutaneous exposures
While HCV Incidence Has Peaked, Cirrhosis Is Projected to Peak in the Coming Decades

Incidence of Hepatitis C by Year
United States, 1982-2009

Estimated Peak Incidence: 23-31 years ago

Historical and Projected % Prevalence of Cirrhosis Among HCV Patients

- 1989: 5%
- 1998: 10%
- 2006: 20%
- 2010: 24.8%
- 2020: 37.2%
- 2030: 44.9%
HCV Cure Associated with Decreased All-Cause Mortality

530 patients with advanced fibrosis, treated with interferon-based therapy, and followed for 8.4 (IQR 6.4-1.4) years

Van der Meer et al. JAMA 2012; 308:2584
History of HCV Treatment: In a New Era

Recombinant type I IFN-based therapy in chronic hepatitis C

- 1989: IFNα
- 1998: IFNα and ribavirin
- 2001: pegIFNα and ribavirin
- 2011: pegIFNα and ribavirin, telaprevir or boceprevir
- Future: IFN-free combination of direct-acting antiviral drugs
The National HCV Treatment Cascade

**Diagram: The National HCV Treatment Cascade**

- Chronic HCV-Infected: 3,500,000
- Diagnosed and Aware: 50%
- Access to Outpatient Care: 43%
- HCV RNA Confirmed: 27%
- Underwent Liver Biopsy: 17%
- Prescribed HCV Treatment: 16%
- Achieved SVR**: 9%

*Chronic HCV-Infected: N=3,500,000.
† Calculated as estimated number chronic HCV-infected (3,500,000) x estimated percentage diagnosed and aware of their infection (49.8%); n=1,743,000.
‡ Calculated as estimated number diagnosed and aware (1,743,000) x estimated percentage with access to outpatient care (86.9%); n=1,514,667.
§ Calculated as estimated number with access to outpatient care (1,514,667) x estimated percentage HCV RNA confirmed (62.9%); n=952,726.
|| Calculated as estimated number with access to outpatient care (1,514,667) x estimated percentage who underwent liver biopsy (38.4%); n=581,632.
¶ Calculated as estimated number with access to outpatient care (1,514,667) x estimated percentage prescribed HCV treatment (36.7%); n=555,683.
** Calculated as estimated number prescribed HCV treatment (555,683) x estimated percentage who achieved SVR (58.8%); n=326,859.

Note: Only non-VA studies are included in the above HCV treatment cascade.
## Types of HCV Tests

<table>
<thead>
<tr>
<th>Test</th>
<th>Comments</th>
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<tr>
<td>HCV Antibody</td>
<td>• Screening test&lt;br&gt;• Positive in past or current infection</td>
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<tr>
<td>HCV Viral load</td>
<td>• RNA PCR test&lt;br&gt;• Does not correlate with degree of liver disease&lt;br&gt;• Only recheck if treating&lt;br&gt;• Quant&gt;Qual</td>
</tr>
<tr>
<td>HCV Genotype</td>
<td>• “Strain” of HCV&lt;br&gt;• 1-6&lt;br&gt;• NOT like HIV genotype</td>
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# HCV Genotypes: Common in US

<table>
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<tr>
<th>Genotype</th>
<th>Notes</th>
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| 1        | • Most common in US (75%) and worldwide (45%)  
          | • Used to be hardest to treat with Interferon (IFN)  
          | • Includes subtypes 1a + 1b |
| 2        | • 13-15% of US Infxns  
          | • Used to be “the good one” (easier tx with IFN) |
| 3        | • 10% of US Infxns  
          | • Used to be grouped w/ geno 2  
          | • May progress faster  
          | • Now the hardest to treat |
# HCV Genotypes: Rare in US

<table>
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<th>Genotype</th>
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<tr>
<td>4</td>
<td>Predominant in Egypt, Middle East, Central Africa</td>
</tr>
<tr>
<td>5</td>
<td>Predominant in South Africa</td>
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<tr>
<td>6</td>
<td>Predominant in Asia</td>
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Liver Disease Staging Modalities

- Biopsy
- Ultrasound
- Clinical findings
- MR Elastography
- Biomarkers
- Fibroscan
Fibroscan

Castera Transient Elastography Breakpoints

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<tr>
<th>2.5</th>
<th>7.0</th>
<th>9.5</th>
<th>12.5</th>
<th>75kPa</th>
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- **Metavir**
  - F0-F1: Absent or mild fibrosis
  - F2: Significant fibrosis
  - F3: Severe fibrosis
  - F4: Cirrhosis
# Staging with Serum Biomarkers

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<th>Serum Markers of Fibrosis/Cirrhosis</th>
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| APRI                               | APRI >1 = advanced fibrosis  
APRI >2 = cirrhosis  
(sensitivity 76%, specificity 72%) |
| FIB-4                              | FIB-4 >3.25 =advanced fibrosis/cirrhosis  
(specificity 98%)  
FIB-4 <1.4= no significant fibrosis  
(sensitivity 74%, specificity 80%) |
| Fibrosure  
Fibrotest  
Fibropect | Combos of biomarkers  
Proprietary |

Adapted from VA HCV Guidance
FIB-4: Fibrosis 4

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

28 year old man infected with HCV 2 years ago. History of heavy EtOH use and recent UGIB due to esophageal varices by verbal report. Ultrasound is WNL, FIB-4 score 0.6, Fibroscan not available.
Should HCV be treated as if this patient has cirrhosis?
HCV Warmline Case

40 year old woman with history of IDU recently tested HCV+ at local ED, now presenting to begin primary care. What to do next?
Primary Care for HCV Patients

Education to prevent transmission and progression
Assess EtOH
Vaccinate for HAV/HBV
Treat comorbidities
HCC screening if cirrhotic
## Conclusions

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<th>SCREEN</th>
<th>Implement age cohort and risk based screening</th>
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<tr>
<td>STAGE</td>
<td>Stage liver disease for HCV+ patients and prioritize treatment</td>
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<tr>
<td>PROVIDE PRIMARY CARE</td>
<td>Educate, assess EtOH use, offer vaccinations, treat comorbidities, screen for HCC</td>
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<tr>
<td>TREAT</td>
<td>Build capacity for treatment or enhanced referrals</td>
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Thank you!