Overview of Hepatitis C Virus: The Challenge & The Opportunity

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Disclosures

- Research supported by Gilead Sciences Inc.:
  - Site investigator for HIV/HCV SWITCH Registry Study
  - Key faculty personnel for Gilead FOCUS HCV Screening Program through Vanderbilt University Medical Center Emergency Department
Objectives

At the end of this lecture, the learner will be able to:

- Review key points and important trends in hepatitis C virus (HCV) epidemiology
- Describe appropriate screening criteria for HCV and apply to clinical practice
- Identify the clinical manifestations of HCV
- Understand the natural history of HCV
- Discuss the principles of and indications for HCV treatment
Outline

- Epidemiology
- Clinical Manifestations and Natural History
- When and Who To Treat
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Hepatitis C Virus (HCV)

- Single-strand, positive sense RNA flavivirus
- Spread through blood and body fluids
- Predominantly infects and replicates in liver cells
- No latent reservoir
The History of HCV

1989 - Discovery of Hepatitis C virus

1991 - First Hepatitis C treatment approved

1992 - Testing virtually eliminates Hepatitis C virus from U.S. blood supply

1996 - Hepatitis C infections continue to dramatically decline

1998 - CDC issues recommendations on Hepatitis C prevention and control

2007 - Deaths from Hepatitis C surpass HIV in U.S.

2010 - Institute of Medicine report issued on viral hepatitis

2011 - Action Plan released and July 28th declared World Hepatitis Day

2012 - First National Testing Day and CDC recommends testing all people born 1945-1965 for Hepatitis C

2014 - Realizing the potential of an all-oral cure

Elimination of Hepatitis C

www.cdc.gov/hepatitis
HCV Worldwide
HCV in the US

2.3-6 million Americans have chronic HCV infection

HCV and Mortality in the USA

Increases in Hepatitis C Virus Infection Related to Injection Drug Use Among Persons Aged ≤30 Years — Kentucky, Tennessee, Virginia, and West Virginia, 2006–2012

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Acute Cases of Hepatitis C in Tennessee by Case Count 2011-2015
A CASE STUDY
Ms. F: Presentation to Your Clinic

- 54 y/o woman presents to your clinic for follow up.
- Past Medical History:
  - Hypertension
  - Breast cancer
- Past Surgical History:
  - Tonsillectomy as a child
- Past Family History:
  - CAD, DM, lung cancer
- Past Social History:
  - On disability
  - Denies tobacco
  - Occasional social alcohol use
  - Experimental intranasal and inhaled drug use in distant past
Ms. F: Physical and Labs

- Physical:
  - General, HEENT, CV, lung, and skin examination are unremarkable
  - Abdominal exam reveals mild hepatomegaly two finger breadths beneath the R rib cage without splenomegaly or ascites

- Labs:
  - CBC notable for WBC of 3.7 and Platelets of 115
  - CMP notable for AST of 87 and ALT of 65 with a normal bilirubin and a normal albumin
What is this patient’s indication for HCV screening as per the USPSTF?
Who is at Risk for HCV?

- IV drug users
- Tattoo/piercing recipients
- Blood/clotting protein recipients prior to 1992
- Mother-to-child transmission from HCV+ mother
- Hemodialysis patients
- People with HIV
- Occupational exposures
- Born between 1945-1965 ("baby boomer" generation)
* 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 (66.9%); n=1,151,667.
§ Calculated as estimated number with access to outpatient care (1,151,667) x estimated percentage HCV RNA confirmed (62.9%); n=852,726.
‖ Calculated as estimated number with access to outpatient care (852,726) x estimated percentage who underwent liver biopsy (36.4%); n=314,632.
¶ Calculated as estimated number with access to outpatient care (314,632) x estimated percentage prescribed HCV treatment (36.7%); n=555,883.
** Calculated as estimated number prescribed HCV treatment (555,883) x estimated percentage who achieved SVR (58.8%); n=326,859.

Note: Only non-VA studies are included in the above HCV treatment cascade.
Diagnostics Review

- HCV Antibody
  - Tests for *exposure*
  - Near 100% sensitivity once >6 months after infection
- HCV RNA
  - Tests for *active infection*
  - ~20% of patients spontaneously clear HCV
- HCV Genotype
  - Defines genetic subtype for prognostic information and treatment guidance
Ms. F: The Diagnosis

- Ms. F’s HCV antibody is positive.
- HCV RNA is 600,000 copies/mL.
- You inform the patient of her laboratory testing and she returns to your clinic.
- Upon her return, the patient asks how this will impact her lifespan...
Outline

- Epidemiology
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Manifestations of HCV

- Acute HCV (~20%)
  - Fever
  - Fatigue and anorexia
  - Nausea and vomiting
  - Abdominal pain
  - Jaundice, dark urine, and clay-colored stools
  - Arthralgias

- Chronic HCV
  - Often asymptomatic
  - May cause fatigue, insomnia, depression, and mental status changes
  - May cause extrahepatic manifestations including vasculitis and renal disease
  - Long-term outcomes include cirrhosis, liver failure, and hepatocellular carcinoma
Natural History of HCV

- Cirrhosis usually takes years to develop in the absence of comorbidities
- Timeline may be accelerated by comorbidities
Factors Associated with HCV Accelerated Fibrosis Progression

<table>
<thead>
<tr>
<th>Host</th>
<th>Viral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonmodifiable</td>
<td>HCV genotype 3</td>
</tr>
<tr>
<td>Fibrosis stage</td>
<td>Coinfection with hepatitis B virus or HIV</td>
</tr>
<tr>
<td>Inflammation grade</td>
<td></td>
</tr>
<tr>
<td>Older age at time of infection</td>
<td></td>
</tr>
<tr>
<td>Male sex</td>
<td></td>
</tr>
<tr>
<td>Organ transplant</td>
<td></td>
</tr>
<tr>
<td>Modifiable</td>
<td></td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td></td>
</tr>
<tr>
<td>Nonalcoholic fatty liver disease</td>
<td></td>
</tr>
<tr>
<td>Obesity</td>
<td></td>
</tr>
<tr>
<td>Insulin resistance</td>
<td></td>
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</tbody>
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Updated February 24, 2016.
Ms. F: The Evaluation

- You reassure the patient that she is unlikely to imminently die of liver failure.
- The patient would like to be assessed for treatment.
Outline

- Epidemiology
- Clinical Manifestations and Natural History
- When and Who To Treat
Factors To Consider When Considering Treatment

- Manifestations of Disease
- Stage of Disease
- Rate of Progression
- Comorbidities
- Patient Readiness
- Financial Issues
Recommendations for Testing, Managing, and Treating Hepatitis C

Released January 29, 2014
Last updated September 16, 2016
Available at www.hcvguidelines.org
**Goal of treatment**

The goal of treatment of HCV-infected persons is to reduce all-cause mortality and liver-related health adverse consequences, including end-stage liver disease and hepatocellular carcinoma, by the achievement of virologic cure as evidenced by an SVR.

**Rating:** Class I, Level A
<table>
<thead>
<tr>
<th>Condition</th>
<th>Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrosis (Metavir F2)</td>
<td>Class I, level B</td>
</tr>
<tr>
<td>HIV-1 coinfection</td>
<td>Class I, level B</td>
</tr>
<tr>
<td>Hepatitis B virus</td>
<td>Class IIa, Level A</td>
</tr>
<tr>
<td>Other coexistent liver disease</td>
<td>Class IIa, Level A</td>
</tr>
<tr>
<td>Debilitating fatigue</td>
<td>Class IIa, Level A</td>
</tr>
<tr>
<td>Type 2 Diabetes mellitus (multiresistant)</td>
<td>Class IIa, Level A</td>
</tr>
<tr>
<td>Porphyria cutanea tarda</td>
<td>Class IIb, Level C</td>
</tr>
</tbody>
</table>
**Recommendations for When and in Whom to Initiate Treatment**

- Treatment is recommended for all patients with chronic HCV infection, except those with short life expectancies that cannot be remediated by treating HCV, by transplantation, or by other directed therapy. Patients with short life expectancies owing to liver disease should be managed in consultation with an expert.

Rating: Class I, Level A
Why Should We Treat HCV?

Van der Meer AJ et al. *JAMA* 2012.
Why Should We Treat HCV?

Jezequel C et al. EASL 2015.
HCV and “Nonhepatic” Manifestations

- Cryoglobulinemia → Resolution
- Immune complex related nephrotic syndrome → Reversal
- Diabetes → Decreased incidence, improved insulin sensitivity, better outcomes
- Fatigue → Improved, better QOL, better work productivity
- Dermatologic Conditions (i.e. Lichen planus, PCT) → Improved
- Others? (CAD, strokes, PVD, CKD...)

www.hcvguidelines.org
The Finances of HCV

- Cost effectiveness and savings
- Timing of cost vs. savings
- Lack of transparency
- Affordability
- “An intervention that is cost effective is not necessarily affordable.”
Cost Effectiveness of HCV Therapy

- HCV GT 1
  - Treatment naïve +/- cirrhosis \(\rightarrow\) <$0 - $31,452 per QALY
  - Treatment experienced +/- cirrhosis \(\rightarrow\) as high as $178,295

- HCV GT 2
  - $35,500 to $238,000 per QALY

- HCV GT 3
  - Data not pertinent to current regimens
“…the negotiated pricing and cost structure for pharmaceutical products in the United States are not transparent, and it is therefore difficult to estimate the true cost and cost-effectiveness of HCV drugs.”

“When new therapies for HCV are deemed cost effective, it indicates that such therapies provide excellent benefits for the resources invested in their use and that providing more therapy is a good investment in the long term. Determining the total resources that can be spent on HCV treatment, however, depends on political and economic factors that are not captured by cost-effectiveness determinations.”
Challenges

- Ongoing epidemic
- Effective screening
- Linkage of care
- Access to treaters
- Cost of therapies
QUESTIONS?