Hepatitis C: Making an Impact in Our Community Health Centers

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Objectives

- Provide an overview and update on HCV infection
  - Clinical aspects of HCV
  - Epidemiology
  - Transmission
  - Screening
  - Care and treatment
  - Resources
Viral Hepatitis

- Hepatitis A Virus (HAV, fecal-oral transmission, vaccine available)
- Hepatitis B Virus (HBV, blood-borne, vaccine available)
- Hepatitis C Virus (HCV, blood-borne)
- Hepatitis D Virus – (blood-borne, only causes problems for people infected with HBV)
- Hepatitis E Virus (fecal-oral, occurs rarely in U.S.)
Case

- 65 yo African-American real estate lawyer presents for physical, with no complaints.
- H/o HTN, appendectomy age 13, cholecystectomy age 25 c/b hemorrhage
- Remote h/o MJ use; no h/o IVDU, cocaine, unsupervised medication use
- Divorced, sexually active with one new F partner, total of 5 F lifetime sexual partners
- Pt requests STD screening, and you send HIV, HBV, syphilis, and HCV tests
- HCV antibody testing comes back positive

- What is the clinical significance of Hepatitis C?
- What further testing is indicated?
- What is the natural history of Hepatitis C infection?
Hepatitis C: Clinical Significance

- 3.9 million in U.S. with positive antibody
- Most common cause of end-stage liver disease and liver cancer
- Acute infection usually asymptomatic, and usually leads to chronic infection; less than half of those infected are aware of being infected
- Bulk of infected patients (>2/3) born between 1945 and 1965, and contracted HCV more than two decades ago
- 20-30 year time course to development of cirrhosis and its complications
- HCV-related mortality rising (~15,000/yr in 2007) and has now surpassed HIV-related mortality

Mortality trends: HIV, HCV, HBV

Workup of Hepatitis C

- **Diagnose and characterize infection, predict treatment response:**
  - HCV Antibody
  - HCV RNA (viral load)
  - HCV genotype
  - HIV, HBV, HAV serologies
  - Lipids, blood sugar, BMI

- **Assess for HCV-related disease:**
  - ALT
  - Bilirubin, PT, and Albumin
  - RUQ ultrasound
  - Liver biopsy or non-invasive alternative (e.g., HCV Fibrosure)
Natural History of Hepatitis C

- **Acute infection**
  - Ab+ or Ab-, VL+, ALT↑↑
  - 2-12 wk incubation period
  - 80% asymptomatic

- **Chronic infection (75-85%)**
  - Ab+, VL+, ALT↑

- **Viral clearance (15-25%)**
  - Ab+, VL-, ALTnl

- **Cirrhosis (30%/30yrs)**
  - Decompensation or Hepatocellular carcinoma (1-4% per year)

More common with:
- Young patients
- Females
- Icteric acute infection (occurs in 15-20%)

Promoted by:
- Alcohol use
- Older age, male gender
- HBV or HIV infection
- High BMI, DM, or fatty liver
HCV Prevalence

- **NHANES (1999-2008)**
  - General US Population: 1.5%
  - Gender: ~2/3 of all cases are male
  - Born between 1945-1965: 3.25%
    - Non-Hispanic black males: 8%
    - Non-Hispanic white males: 4%
    - Mexican-American males: 3.4%

- **Injection Drug Users (IDUs):**
  - 70% - 90% (Alter, 1998; Hagan, 2008)

- **Incarcerated:**
  - 12% - 35% (Boutwell, et al, 2005)
HCV Transmission

- Bloodborne pathogen
- Asymptomatic still potentially infectious
- Most people infected through:
  - Injection drug use (sharing drug injection equipment)
  - Blood transfusions/clotting factors/organ transplants prior to 1992
  - Chronic hemodialysis
  - Sexual transmission - inefficient but does occur
  - Vertical transmission – 4-7% of births to infected mothers (20% in HIV/HCV co-infected)
Possible Transmission Risks

- Occupational exposures
  - Risk from needlestick:
    - HIV=3/1000  HCV=2/100  HBV=3/10
  - Prevalence of HCV in health care workers is the same as the general population
- Sharing personal/household items with blood
- Intranasal drug use
- Tattoo/body piercing: nonsterile practices
HCV – Injection Drug Users (IDU)

- IDU accounts for 68% of all new infections (CDC)
- As many as 32% of IDUs are infected with HCV within 1 year of first injecting; 53% within 5 years (Hagan, et al, 2008)
- Sharing of syringes, cookers, cottons, rinse water, etc. from injection drug use is the greatest risk for HCV transmission
- HCV infection CAN be prevented among injection drug users
  - Access to sterile injection equipment and multi-component prevention programs is critical
Sexual Transmission of HCV

- Occurs, but efficiency is low
- Low prevalence (0.6-1.8%) among monogamous long-term partners (Terrault, et al, 2012)
- May account for 15-20% of acute and chronic infections in the United States (CDC)
- Increased transmission among HIV+ MSM (CDC, 2011)
CDC Risk-based HCV Screening Recommendations (1998)

- Ever injected illicit drugs
- Received a transfusion or blood products before July 1992
- Received clotting factor prior to 1988
- Children >18 months born to HCV-positive women
- Ever on hemodialysis
- HIV-positive
- Healthcare, emergency, public safety workers after needlestick/mucosal exposures to HCV-positive blood
Changes to HCV Screening Recommendations (2012)

- Move to focus on age-based screening
  - 2/3 of HCV cases among “baby-boomer” population

- Recommendation: One-time HCV screening for all people born between 1945-1965
  - Alcohol use screening and treatment for HCV+

- Risk-based screening still important
Why test this age cohort?

Annual age-adjusted mortality rates from hepatitis B and hepatitis C virus and HIV infections listed as causes of death in the United States between 1999 and 2007

Ly, et al, 2012
HCV among youth in Massachusetts 2007-2011

- Starting in 2007 an increase of newly diagnosed HCV infection has been noted among youth ages 15-25
- Between 2002 and 2011, an increase of 62 to 132 cases per 100,000 population was reported in this age group
- Data suggest that the increase is due to youth injecting drugs (mostly heroin)
- Other jurisdictions have also seen this trend (CT, HI, KY, ME, MN, NY, PA and others)
MMWR: Rates of newly reported cases of hepatitis C virus infection (confirmed and probable) among persons aged 15--24 years and among all other age groups --- Massachusetts, 2002--2009
MMWR: Age distribution of newly reported confirmed cases of hepatitis C virus infection --- Massachusetts, 2002 and 2009

* N = 6,281; excludes 35 cases with missing age or sex information.
† N = 3,904; excludes 346 cases with missing age or sex information.

Source: Onofrey et al MMWR: May 6, 2011 / 60(17);537-541
## Treatment regimens

<table>
<thead>
<tr>
<th>HCV Genotype</th>
<th>Treatment Regimen</th>
<th>Success (SVR*) rate</th>
<th>Side-effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Peginterferon SC qwk • Ribavirin PO BID • 12 week “boost” with a Direct Acting Antiviral (DAA): NS3 protease inhibitor (Telaprevir or Boceprevir) Duration: 24-48 weeks depending on early response</td>
<td>62-80%</td>
<td>• Flu-like sx • Mood changes • Pancytopenia • Autoimmunity • Hemolytic anemia • Teratogenicity For protease inhibitor regimens: • More severe anemia • Pruritus and rash • Dysguesia</td>
</tr>
<tr>
<td>2 and 3</td>
<td>Peginterferon SC qwk • Ribavirin PO QD Duration: 24 weeks</td>
<td>78-82%</td>
<td></td>
</tr>
</tbody>
</table>

* Sustained Virologic Response = negative HCV viral load 24 weeks after treatment

### And coming very soon:

#### More DAAs:
- More protease inhibitors
- NS5A inhibitors
- Nucleotide polymerase inhibitors (e.g., Sofosbuvir)

#### Interferon-free regimens?

#### Human pharmacogenetics
- IL28B polymorphisms
**Factors in favor of treatment:**
- HCV VL positive
- Histologic evidence of chronic hepatitis with significant fibrosis
- Compensated liver disease
- Acceptable baseline hematologic and biochemical indices (e.g., Hgb > 12, GFR > 50)
- Willing to be treated and able to adhere to requirements

**Contraindications to treatment:**
- Uncontrolled depression
- Ongoing EtOH use
- Active autoimmune disease
- Pregnancy or risk thereof
- Severe comorbid medical disease that would make treatment dangerous (e.g., CAD, seizure d/o)
- Known Hypersensitivity to one or more of the anti-HCV medications

**When decision to treat should be individualized:**
- Failed previous treatment
- Current active illicit drug users
- Quasi-stable psychiatric disease
- Unstable social situation / housing / follow-up
- Decompensated cirrhosis
- Genotype 2,3 (given promise of DAAs)?
Barriers to Treatment

Reasons for non-treatment

Referral and treatment rates

- Referred for treatment: 88%
- Pre-treatment visit: 72%
- Treated: 37%
- Completed treatment: 15%
- Sustained viral response: 9%

Young adults (20-39)
- No identified reason: 12%
- Active substance abuse: 21%
- Patient preference: 13%
- Waiting for new tx: 6%
- Medpsych comorbidity: 4%
- Unstable housing: 2%
- Active etoh use: 2%

Older adults (40+)
- No identified reason: 15%
- Medpsych comorbidity: 15%
- Loss to follow up: 23%
- Active substance abuse: 5%
- Active etoh use: 2%
- Min fibrosis: 12%
- Patient preference: 14%
- Waiting for new tx: 14%

** denotes significant differences from the other group.
Harm Reduction

- HAV and HBV vaccination
- EtOH cessation
- Avoidance of hepatotoxic medications or OTC products
- Hepatitis C education
- Counseling about transmission
- Referral to psychiatric or addiction treatment when appropriate
- Referral to Hepatology for cirrhotics
- Collaboration w/ Hepatology on cirrhosis harm reduction (e.g., liver cancer screening, fluid mgmt)
HCV Harm Reduction for IDUs

To reduce spread of HCV, IDUs should:

- Be provided information on drug treatment options
- Be informed about existing needle exchange programs and pharmacy access
- Have access to harm reduction education
  - Clean works
  - Safe injection practices
  - Overdose prevention
  - Opioid replacement therapy
Roles of Primary Care

Harm reduction:
- Hepatitis A and B immunization
- Alcohol cessation
- Avoidance of hepatotoxic meds
- Recognition and management of comorbid conditions

Co-management of advanced liver disease:
- Co-management of ascites, encephalopathy, and varices with Hepatology
- Assisting w/ HCC screening

Identification and Characterization of the infection

Management of barriers to antiviral treatment
- Identification and removal of surmountable barriers
- Referral for antiviral treatment when appropriate

Primary Care Team
Telemedicine project enabling HCV treatment by PCPs at 21 rural sites in New Mexico

- Key personnel identified at each site
- Development of “knowledge networks” for review of cases, dissemination of best practices, and community-building
- Prospective comparison of SVR rates between 261 patients treated locally and 146 patients treated at the University of New Mexico
- Equivalent success rates seen for all patients (58.2% at ECHO sites vs. 57.5% at UNM)
- Lower side-effect and dropout rates at ECHO sites
On-site, Team-based HCV Care

Community Education/Screening Team

Hospital-Community Connections

“Knowledge Networking” w/ specialists

Feedback to PCPs

Health Center Registries

MGH Community Hepatitis C Program
Resources: Provider Education

- CDC  http://www.cdc.gov/hepatitis/
- Hepatitis Web Study:  
  http://depts.washington.edu/hepstudy/
- National Training Center for Integrated Hepatitis, HIV and STD Prevention Services  
  www.knowhepatitis.org
- Treatment Action Group  
  www.treatmentactiongroup.org/hepatitis
- Caring Ambassadors Program: Hepatitis C  
  http://www.hepcchallenge.org/index.htm
Resources: Patient Education

  - “Know Hepatitis” campaign
- Treatment Action Group  [www.treatmentactiongroup.org/hepatitis](http://www.treatmentactiongroup.org/hepatitis)
Resources: Policy

- US Department of Health and Human Services Viral Hepatitis Action Plan (2011)
- Institute of Medicine Report on Hepatitis and Liver Cancer (2010)
  http://www.cdc.gov/hepatitis/IOMnews.htm
- National Viral Hepatitis Roundtable www.nvhr.org
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