Hepatitis C: Where Are We Now?

Local Health Departments and Hepatitis C: Webcast 1.1

Presented by:
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Changing Epidemiology of HCV Transmission and Disease

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Discovery of Hepatitis C Virus (HCV)

- Discovered in 1989, RNA virus, family Flaviviridae
- 9,600 nucleotide genome-single polyprotein
  - Structural proteins
  - Non-structural proteins - viral replication and targets of therapy
  - High genetic diversity leads to intra-host variants “quasispecies”
  - 7 major genotypes that predict treatment response
    - Genotype 1 accounts for ~ 70% of infections in US
  - No vaccine candidates for licensure

Natural History of HCV Infection

In 20 years, 15-30% progress to cirrhosis. Progression accelerated by HIV, HBV, alcohol use, and fatty liver.

- Acute HCV infection
- Chronic infection 55-85%
- Mild fibrosis
- Moderate to severe fibrosis
- Cirrhosis 15-30%
- Decompensated Cirrhosis
- Hepatocellular carcinoma (2-4% per year in cirrhosis)
- Extrahepatic disease
- Liver Transplant or Early Death


Global Hepatitis C Burden is Large and Highest in Asia and Africa

- 3-4 million new infections per year
- 130-150 million chronic infections

Six HCV Genotypes and Subgenotypes Vary by Region: Important Predictor of Treatment Response

WHO.org.
### Hepatitis C is a Leading Cause of Infectious Disease Deaths Worldwide, 2010

<table>
<thead>
<tr>
<th>Disease</th>
<th>Estimated Deaths per Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower respiratory tract infections</td>
<td>~ 2.65 million</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>~ 1.34 million</td>
</tr>
<tr>
<td>Diarrheal diseases</td>
<td>~ 1.26 million</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>~ 1.29 million</td>
</tr>
<tr>
<td>Malaria</td>
<td>~ 855 million</td>
</tr>
<tr>
<td>Hepatitis C Virus</td>
<td>~ 704,000</td>
</tr>
<tr>
<td>Hepatitis B Virus</td>
<td>~ 602,000</td>
</tr>
<tr>
<td>Meningitis</td>
<td>~ 304,000</td>
</tr>
<tr>
<td>Measles</td>
<td>~ 96,000</td>
</tr>
<tr>
<td>Hepatitis E Virus</td>
<td>~ 50,000</td>
</tr>
</tbody>
</table>

A Large Number of Persons Are Living with Hepatitis C in the United States; Many Are Unaware of Their Infection

<table>
<thead>
<tr>
<th>Virus</th>
<th>Prevalence</th>
<th>% Unaware of Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV</td>
<td>2.7 million (2.2 – 3.2 million)</td>
<td>45%-60%</td>
</tr>
</tbody>
</table>

Estimated HCV Infection Among Homeless and Incarcerated Persons (Not Included in NHANES)

360,000-840,000
22%-52%

HCV Transmission Risks Globally
HCV Transmission Among People Who Inject Drugs

- Transmission risks
  - Injection duration
  - Frequency of injecting
  - Equipment sharing, not just sharing needles

- Incidence declined in response to harm reduction for HIV (e.g., syringe access programs)


Kwon et al., JAIDS 2009
HCV Infections among Persons Who Inject Drugs

• Anti-HCV antibody + among PWID between 30% and 70%

• Anti-HCV prevalence among younger injectors (18—29 yo) between 10% and 36%

• Anti-HCV incidence among PWID between 5-42/100 person years

• HCV prevalence ~ 1.5 million HCV + PWID in United States

Healthcare-associated HCV Transmission

- Larger contributor to transmission before viral discovery
- Prevention measures have reduced not eliminated transmission risk
- Total 18 outbreaks reported to CDC 2008-2013
  - 223 outbreak-associated cases
  - >90,550 at-risk persons notified for screening
- Settings
  - Outpatient (e.g., surgical centers), dialysis
  - Hospitals
  - Long term care
- Modes of transmission
  - Syringe reuse
  - Other poor infection control
  - Drug diversion

http://www.cdc.gov/hepatitis/
Sexual Transmission

- Heterosexual
  - Attributable risk for 14% of cases of incident HCV
  - Low risk among discordant couples- 0.07%/ 100 pyrs.
- Men Who Have Sex With Men (MSM)
  - HIV+ MSM have eight fold higher risk than HIV-MSM
    - Swiss Cohort Study- 4.1/100 pyrs.
    - U.S. cohort studies .26-.40/100 pyrs.
    - Boston clinic- 1.63/100 pyrs; 70% non IDU
- Risks
  - Unprotected rectal intercourse
  - Non injection drug use (e.g., XTC)
  - Other STIs
- CDC recommends annual HCV testing

Perinatal Transmission of HCV

• Transmission from HCV RNA + mothers
  – Mono-infected 6.5%
  – HIV –infected- 13.6%

• Transmission risks
  – HCV viral load
    o < 6 log viral load- 3.9%
    o > 6 log viral load – 14.3%
  – Prolonged rupture of membranes( > 6 hours; OR 9.3)
  – Often cited but poor or no supportive data
    • Internal fetal monitoring
    • Vaginal versus cesarean delivery

• No risk from breast feeding
• No recommendations for maternal testing
• Role of new antivirals yet to defined

Other Exposures Associated with HCV Transmission

- Non-injecting drug use - (e.g. cocaine); 0-17% HCV+
- Household exposures: 9% HCV+
- Unregulated tattooing: 2–3 times higher likelihood of HCV infection

Trends in HCV-Associated Disease and Mortality in the United States
HCV is a Major Cause of Liver Disease and Associated Health Care Costs

- HCV is a major cause of liver disease
  - 40,000 (36%) of persons on liver transplant waitlist
  - 50% of persons with liver cancer; 2.5% annual increase

- Substantial HCV-related costs
  - Three-fold higher disability days (1.36 vs 0.34) than others
  - $21,000 in annual health costs vs $5,500 for others
  - From 2002 to 2010, HCV-positive patients aged 50-59 years had largest increases in hospital admissions (164%) and charges (341%)

- Successful hepatitis C treatment reduces health costs ($900 vs $1,378 per patient per month)

In the United States, at a Time of Declines in HIV Deaths, Mortality From HCV is Increasing

In Absence of New Interventions, the Burden of Hepatitis C is Projected to Continue to Grow in the United States

- Markov model of life-time health outcomes
  - Of 2.7 million HCV-infected persons in primary care:
    - 1.47 million will develop decompensated cirrhosis (DCC)
    - 350,000 will develop hepatocellular carcinoma (HCC)
    - 897,000 will die from HCV-related complications

Discovery of HCV and Impact on HCV Incidence in US

22,000 cases of incident HCV infection reported in 2012

Two of Three Americans Living with HCV Were Born During 1945-1965

- Reflects high HCV incidence in distant past
- Five-fold higher prevalence than others (3.39% vs .55%)
- 81% of all HCV+ adults
- 73% of all HCV-related mortality

CDC and USPSTF Updated Recommendations for HCV Testing

• **One time screening test for persons born 1945-1965**

• **Major risk**
  – Past or present injection drug use

• **Other risks**
  – Received blood/organs prior to June 1992
  – Received blood products made prior to 1987
  – Ever on chronic hemodialysis
  – Infants born to HCV infected mothers
  – Intranasal drug use
  – Unregulated tattoo
  – History of incarceration

• **Medical**
  – Persistently elevated ALT
  – HIV (annual testing)

http://www.hcvguidelines.org
Advances in HCV Therapy

Sustained Virologic Response (%)

- 1991: IFN 6 m - 6%
- 1999: IFN 12 m - 16%
- IFN/RBV 6 m - 34%
- IFN/RBV 12 m - 42%
- Peg-IFN (PEG) 12 m - 39%
- PEG/RBV 12 m - 54 - 56%
- Peg/RBV DAA 6 m - 67-72%
- All oral DAA - >90%

HCV Deaths Averted with Birth Cohort Testing Using Different Treatments

No treatment | PR | PRPI,PR | PRS/SR | SS/SR, Harvoni, Vikera-Pak

PR = Pegylated Interferon plus Ribavirin for all genotypes, PRPI = PR plus a protease inhibitor for genotype 1, PR for genotypes 2/3; PRS/SR = pegylated interferon, ribavirin, and sofosbuvir for genotype 1, and sofosbuvir plus ribavirin for genotypes 2 and 3; SS/SR = Sofosbuvir and Simeprevir for genotype 1, and sofosbuvir and ribavirin for genotypes 2 and 3.
HCV Test, Care, and Cure Continuum

~ 3 million persons living with HCV

- All HCV infected: 50%
- anti-HCV tested: 38%
- HCV care: 23%
- HCV RNA: 11%
- Treated: 6%

Reports of Acute HCV infection 2007-2013

Number of acute hepatitis C cases

- 2007: ~800
- 2008: ~800
- 2009: ~900
- 2010: ~950
- 2011: ~1200
- 2012: ~1500
- 2013: ~2000
Recent Increases in New HCV Infection

• Between 2007 and 2013
  – Estimated 29,000 new HCV infections
  – 150% since 2010
  – 12 states report 66% of cases
   - (CA, FL, IN, KY, MA, MI, NJ, NY, NC, OH, PA, TN)
Risks Among Persons 18-29 Years of Age with Acute HCV Infection

• 1202 cases of acute HCV investigated
  – 52% female
  – 85% white
  – 77% persons injected drugs
    o 57% shared needles/syringes
    o 82% shared equipment

• Percent use and mean age of drug use initiation
  - Powder cocaine: 71%, 17.4 yrs.
  - Prescription opioids 76% : 17.9 yrs.
  - Heroin: 61%: 19.7 yrs.
Hepatitis C Incidence by Urbanicity and Year of Diagnosis

Suryprasad AG, et al. CID 2014

- 2006: Non-Urban 0.45, Urban 0.15
- 2007: Non-Urban 0.42, Urban 0.17
- 2008: Non-Urban 0.49, Urban 0.18
- 2009: Non-Urban 0.56, Urban 0.17
- 2010: Non-Urban 0.65, Urban 0.17
- 2011: Non-Urban 0.99, Urban 0.33
Heroin Use and Dependence is Increasing

Estimated # of persons 12 years and older reporting abuse/dependence (in thousands)

- Opioids
- Heroin

SAMHSA NSDUH 2012
## Interventions to Prevent HIV and HCV Among Persons Who Inject Drugs

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Decrease Injection Risks</th>
<th>Prevent HIV</th>
<th>Prevent HCV</th>
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<tbody>
<tr>
<td>Syringe exchange</td>
<td>++</td>
<td>+</td>
<td>±</td>
</tr>
<tr>
<td>Pharmacy access</td>
<td>+</td>
<td>±</td>
<td>*</td>
</tr>
<tr>
<td>Drug preparation equipment</td>
<td>+</td>
<td>*</td>
<td>±</td>
</tr>
<tr>
<td>Opioid substitution</td>
<td>++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Education</td>
<td>+</td>
<td>±</td>
<td>±</td>
</tr>
<tr>
<td>Supervise injection</td>
<td>+</td>
<td>±</td>
<td>±</td>
</tr>
</tbody>
</table>

++: sufficient data; ++ tentative data; ±: Inconclusive; *: no data

Multi-Component Interventions for HCV Prevention

A combination of *readily-available* and *low threshold* OAT (with methadone and/or buprenorphine) and SEPs have been shown to:

- Reduce syringe sharing
- Lower injecting risk
- Reduce incidence of HIV and HCV
  - Up to 80% in UK
  - Three fold - New York

OAT: Opiod Agonist Treatment  
SEP: Syringe Exchange Programs
Antiviral Therapy Might Be Used to Reduce HCV Prevalence Among Injecting Drug Users

- Annually treating 10 HCV infections per 1000 IDU and achieve SVR of 62.5%
- Projected to result in a relative decrease in HCV prevalence over 10 years of 31%, 13%, or 7% for prevalences of 20%, 40%, or 60%, respectively
- Can the HIV model of “Treatment as Prevention” be applied to HCV?

Martin et al. Journal of Hepatology 2011 vol. 54 j 1137–1144
Blood-borne exposures to HCV are major transmission risks

The burden of HCV-related disease is large and growing

Reports of acute HCV infection are increasing

Many if not most persons living with HCV are undiagnosed

CDC and USPSTF recommend HCV testing for persons born 1945-1965, past or present injection drug users, and others at risk

Access to HCV prevention, testing, care, and treatment must improve to reduce HCV transmission and disease
IT TOOK US 25 YEARS TO BRING HIM TO HIS KNEES... NOW LET'S FINISH HIM OFF...
Local Health Departments and Hepatitis C
NACCHO Educational Series

Webcast 1.1  Hepatitis C: Where Are We Now?
Webcast 1.2  The National Viral Hepatitis Action Plan
Webcast 1.3  Viral Hepatitis C Testing Recommendations for Persons Born 1945-1965
Webcast 1.4  Leveraging Partnerships to Address Hepatitis C: Philadelphia’s Model

All materials available at www.naccho.org/hepatitisc

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