Hepatitis C Virus: National Trends and Prevention Recommendations

John W. Ward, M.D.
Division of Viral Hepatitis
Centers for Disease Control and Prevention
Goals

• Describe:

• Trends in HCV transmission, disease, and mortality
• Health benefits of HCV testing, care, and treatment
• Strategies to screen and link HCV infected persons to care
Hepatitis C Virus

• Discovered in 1989, RNA virus, family Flaviviridae
• 9600 nucleotide genome- single polyprotein
  – Non-structural protein- targets of therapy
  – High genetic diversity – intra-host variants- “quasispecies”
  – 7 major genotypes- varied response to treatment
    • Genotype 1- ~ 70% of infections in US
    – No vaccine

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

- 3-4 million new infections per year
- 130-150 million chronic infections
- 704,000 deaths/ 2010

### Prevalence of Current HCV Infection Among Persons in the United States

<table>
<thead>
<tr>
<th>Population Description</th>
<th>Prevalence (Million)</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence Civilian, Non-Institutionalized Populations (NHANES)</td>
<td>2.7 (2.2-3.2 million)</td>
<td>1.0% (0.8%-1.2%)</td>
</tr>
<tr>
<td>Estimated HCV Infection Among Homeless and Incarcerated Persons (Not Included in NHANES)</td>
<td>360,000-840,000</td>
<td>22%-52%</td>
</tr>
</tbody>
</table>

Natural History of HCV Infection

- 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

HIV, HBV, alcohol, and steatosis can accelerate disease progression

Modes of HCV Transmission

• Health care exposures- most common cause globally
• Injection drug use – highest risk population
• Other modes
  – Sexual
    • Heterosexual - rare
    • HIV+ MSM have eight fold higher risk than HIV-MSM
  – Perinatal - ~4% transmission risk; ~12% with high maternal viral load
• Others reported
  – Non-injecting drug use (e.g., inhaled drugs)
  – Household exposures
  – Unregulated tattooing

MSM: Men who have sex with men.
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/
Outbreaks of HCV in Residential Care Settings

- Investigation of residential care facility - North Dakota
- 35 HCV cases identified; >25% prevalence
- Highly related HCV quasispecies
- Associated with podiatry exposures
HCV Transmission Among Persons 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)

Discovery of HCV and Impact on HCV Incidence in US

- 1986 Indirect blood screening for HCV
- Anti-HCV test licensed 1992
- Discovery of HCV 1989
- Needle stick Safety and Prevention Act 2001

29,000 cases of incident HCV infection reported in 2013

The Growing Burden of Hepatitis C in the United States

- 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

Increases in Hepatitis C Mortality

Rate per 100,000 Persons

19,368
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)

## Staging of HCV-Related Liver Fibrosis Using FIB-4 by Birth Cohort, 2010-2013

<table>
<thead>
<tr>
<th></th>
<th>Born &lt;1945</th>
<th></th>
<th>Born 1945-1965</th>
<th></th>
<th>Born &gt;1965</th>
<th></th>
<th>Total</th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>Percent</td>
<td>Number</td>
<td>Percent</td>
<td>Number</td>
<td>Percent</td>
<td>Number</td>
<td>Percent</td>
</tr>
<tr>
<td>None</td>
<td>79</td>
<td>1</td>
<td>7,315</td>
<td>9</td>
<td>16,587</td>
<td>53</td>
<td>23,981</td>
<td>19</td>
</tr>
<tr>
<td>Moderate</td>
<td>1,543</td>
<td>19</td>
<td>32,996</td>
<td>38</td>
<td>8,949</td>
<td>29</td>
<td>43,488</td>
<td>35</td>
</tr>
<tr>
<td>Severe</td>
<td>2,982</td>
<td>37</td>
<td>22,448</td>
<td>26</td>
<td>2,172</td>
<td>7</td>
<td>27,602</td>
<td>22</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>2,865</td>
<td>36</td>
<td>17,875</td>
<td>21</td>
<td>1,315</td>
<td>4</td>
<td>22,055</td>
<td>18</td>
</tr>
<tr>
<td>Unknown/missing</td>
<td>508</td>
<td>6</td>
<td>5,253</td>
<td>6</td>
<td>2,189</td>
<td>7</td>
<td>8,164</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>7,977</td>
<td></td>
<td>85,887</td>
<td></td>
<td>31,212</td>
<td></td>
<td>125,290</td>
<td></td>
</tr>
</tbody>
</table>

Monina K, CROI 2015
The Evolution of HCV Therapy from Interferon to Direct Antiviral Agents

Potential to Avert 320,000 Deaths with Birth Cohort Testing Using Latest Treatments

PR = Pegylated Interferon plus Ribavirin for all genotypes, PRPI; PR = 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.
Testing of Persons Born 1945-1965 is Cost Effective (CE)

- Typical willingness-to-pay thresholds (<$50K-100K/QALY)
  - Treat all -$31,828-35,100/QALY at market price (Vikera-Pak-$31,828, Harvoni $35,100)
- Cost/QALY sensitive to stage of liver disease
  - F0- $173K; F2; $37K; F4- $13K; treat all $42K
- Drug costs are now lower than wholesale marker price
  - Payer/Pharma agreements- average ~46% decline
  - Medicaid- mandated 23% discount or to match best price
  - Lawsuits against health plans filed by patients denied treatment

*Quality adjusted life year.
Medicaid Reimbursement Criteria - HCV Therapy

- Minimum fibrosis score
- Prescription by specialist

Some states have few specialists; some states require biopsies for fibrosis scoring

Canary L, Ann Int Med, in press
The Quality of HCV Management Must Improve for Patients to Benefit from HCV Therapy

~ 3 million persons living with HCV

N.B.: HCV RNA test indicates whether patient’s infection is current or not.

Philadelphia HCV Testing and Care Coordination

• 5 community health centers - Philadelphia
• Underserved, largely Black / Hispanic population
  — ~75% homeless, 37% uninsured, 58% public insurance
• Interventions
  — Reflex HCV testing
  — Patient education
  — EMR prompts
  — Mid level provider conducting testing
  — Linkage to care coordinator
  — Uninsured: Referred to social worker

MMWR, May 2015
Philadelphia HCV Testing and Care Coordination

16% of 4514 tested

- 65% of anti-HCV+
- 89% informed of HCV RNA+
- 87% specialist referral
- 79% seen by specialist

MMWR, May 2015
Reports of Acute Hepatitis C Cases — United States, 2000–2013

Source: National Notifiable Diseases Surveillance System (NNDSS)
### Recent CDC, State, and Local Public Health Investigations of Young PWID

<table>
<thead>
<tr>
<th>Location</th>
<th>Year</th>
<th>Predominant Race/Ethnicity</th>
<th>Predominant Setting</th>
<th>Virus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Northern Plains</td>
<td>2008</td>
<td>American Indian</td>
<td>Rural</td>
<td>HCV</td>
</tr>
<tr>
<td>Erie County, NY</td>
<td>2007</td>
<td>White</td>
<td>Suburban</td>
<td>HCV</td>
</tr>
<tr>
<td>Massachusetts</td>
<td>2011</td>
<td>White</td>
<td>Suburban</td>
<td>HCV</td>
</tr>
<tr>
<td>Wisconsin</td>
<td>2011</td>
<td>White</td>
<td>Rural</td>
<td>HCV</td>
</tr>
<tr>
<td>Indiana</td>
<td>2011</td>
<td>White</td>
<td>Rural</td>
<td>HCV</td>
</tr>
<tr>
<td>Virginia</td>
<td>2012</td>
<td>White</td>
<td>Rural</td>
<td>HBV +/- HCV</td>
</tr>
<tr>
<td>Courtland County, NY</td>
<td>2014</td>
<td>White</td>
<td>Rural</td>
<td>HCV</td>
</tr>
</tbody>
</table>

Common Denominator: Prescription opioid misuse followed by early initiation to injection drug use

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Surveillance of Acute HCV Infection - 2013

• Estimated 29,000 new HCV infections
• 150% increase since 2010
• 28 of 34 states reported increases

• 66% of cases reported from 12 states
  • (CA, FL, IN, KY, MA, MI, NJ, NY, NC, OH, PA, TN)
  • KY has highest rate

• Case Rates
  • 61% report IDU
  • Equal Male (0.8): Female (0.7)
  • Highest rate
    • by age 20-29 years, 2.01
    • By race American Indian (1.7) and whites (0.82)
Tracking and Intervening to Prevent HCV Social Network of IDU- rural Kentucky- baseline
Understanding Transmission Among IDU Social Network of IDU- rural Kentucky- 24-Month
Regional Drug Injection Trends Among Persons <30 years old in KY, TN, VA, WVA

SAMHSA, Treatment Episode Data Set—Admissions
Heroin Use and Dependence is Increasing

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

SAMHSA NSDUH 2012
Analysis of Multiple Data Sources to Detect HCV Transmission and Related Risks

- Enhanced Surveillance Sites (mainly, acute)
- Real-time Commercial lab data
- TEDS-A, law enforcement data
- Death certificates, Overdose death, transplantation data
- NHIS, Drug prescription data
- Drug overdose data, Narcotic prescriptions
- Case reports 50 States (NNDSS)
Multi-Component Interventions Appear Most Effective in Preventing HCV Transmission

- In meta-analysis of single interventions, evidence only supports drug treatment
- 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: Opioid 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
### HCV Screening & Testing at Venues Serving PWID

*Prevention and Public Health Fund*  
January 2013—March 2014

<table>
<thead>
<tr>
<th>Location</th>
<th># of Tests</th>
<th>% anti-HCV+</th>
<th>% RNA Tested</th>
<th>% RNA+</th>
<th>% Referred to Care</th>
<th>% Attended First Appt.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arizona</td>
<td>938</td>
<td>17.3</td>
<td>15.4</td>
<td>76.0</td>
<td>84.2</td>
<td>26.3</td>
</tr>
<tr>
<td>Chicago</td>
<td>672</td>
<td>22.2</td>
<td>40.9</td>
<td>80.3</td>
<td>51.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Los Angeles</td>
<td>2175</td>
<td>8.7</td>
<td>29.6</td>
<td>89.3</td>
<td>100.0</td>
<td>82.0</td>
</tr>
<tr>
<td>Maine</td>
<td>795</td>
<td>28.1</td>
<td>51.1</td>
<td>60.5</td>
<td>98.6</td>
<td>52.2</td>
</tr>
<tr>
<td>New York City</td>
<td>2527</td>
<td>17.6</td>
<td>63.4</td>
<td>71.3</td>
<td>71.1</td>
<td>23.4</td>
</tr>
<tr>
<td>Oakland, CA</td>
<td>579</td>
<td>32.0</td>
<td>18.4</td>
<td>82.4</td>
<td>100.0</td>
<td>21.4</td>
</tr>
<tr>
<td>Seattle, WA</td>
<td>457</td>
<td>56.9</td>
<td>30.0</td>
<td>66.7</td>
<td>86.5</td>
<td>5.8</td>
</tr>
<tr>
<td>Virginia</td>
<td>761</td>
<td>36.8</td>
<td>75.4</td>
<td>78.2</td>
<td>99.4</td>
<td>27.3</td>
</tr>
<tr>
<td>Wisconsin</td>
<td>1127</td>
<td>16.1</td>
<td>107.1</td>
<td>73.3</td>
<td>100.0</td>
<td>100.0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>10031</strong></td>
<td><strong>20.7%</strong></td>
<td><strong>50.9%</strong></td>
<td><strong>73.5%</strong></td>
<td><strong>87.9%</strong></td>
<td><strong>42.0%</strong></td>
</tr>
</tbody>
</table>

Venues Include: Syringe Exchange Programs; Drug Treatment Centers; Health Departments; Methadone Clinics; Corrections; Shelters

*CDC unpublished data*
# HIV HCV Outbreak in Scott County, Indiana, 2014-2015

<table>
<thead>
<tr>
<th>Status</th>
<th># Patients</th>
<th>% among persons tested for both HIV and HCV</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-Positive/HCV-Positive</td>
<td>79</td>
<td>26%</td>
</tr>
<tr>
<td>HIV-Positive / HCV-Negative</td>
<td>3</td>
<td>1%</td>
</tr>
<tr>
<td>HIV-Negative / HCV-Positive</td>
<td>106</td>
<td>35%</td>
</tr>
<tr>
<td>HIV-Negative/HCV-Negative</td>
<td>111</td>
<td>37%</td>
</tr>
<tr>
<td>TOTAL SAMPLES</td>
<td>299</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Anti-HCV-positive</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-Risk Patients (reported IDU)</td>
<td>185 / 299</td>
</tr>
<tr>
<td>HIV-Coinfected</td>
<td>79 / 82</td>
</tr>
</tbody>
</table>

HCV antibody results

High-Risk Patients (reported IDU)
Activities to Improve Prevention of HCV Transmission in Scott County, IN

- Complete studies of social networks of HCV transmission
- Scale-up drug treatment, harm reduction
- Assess benefits of HCV cure and prevent (CAP)
  - Clinical capacity to treat target number of PWID
  - Ancillary prevention services
  - Drug availability
- Consider a CAP demonstration project
Legal Intervention-Syringe Services Programs

- On March 24, 2015 the Kentucky General Assembly gave municipalities authority to institute a syringe exchange program.

- Indiana passed a law in May allowing counties to seek state approval to run needle exchanges, if they are in the bottom two quartiles among Indiana Counties for average number of newly reported cases of hepatitis C before an exchange can be launched.

https://louisvilleky.gov/government/health-wellness/needle-exchange-program;
http://blogs.law.harvard.edu/billofhealth/2015/05/21/a-needle-in-a-haystack-finding-the-elusive-solution-to-indianas-hiv-outbreak/
Effective Prevention Strategies and Advent of Curative HCV Therapies Have Increased Considerations for HCV Elimination
Georgia as a Site to Model HCV Elimination

- ~4 million persons
- High burden of HCV- 5-7%
- Relatively small in-migration
- Mixed infection risks- healthcare, IDU
- Capacity- modest, good record in HIV prevention
- Motivated government and population
HCV Elimination in Georgia

- Phase I: Immediate introduction of curative treatments (0 – 12 months)
  - Reduce morbidity and mortality by treating persons with severe HCV associated liver disease
  - Build knowledge base for expanded access program
  - Develop broader elimination plan (Phase II)

- Phase II: Achieve HCV elimination (7-10 year time frame)
  - Define measurable/achievable goals
  - Interventions to prevent new infections
  - Expand access to treat all HCV infected persons
Proposals for HCV Elimination - United States

- **Increase priority** - widen public recognition of urgency of action
- **Increase screening** - follow USPSTF recommended screening
- **Improve testing algorithm** - simplify HCV screening and diagnosis
- **Enhance surveillance** - change policies to improve utility of data
- **Expand clinical workforce** - allow for primary care management
- **Increase treatment availability** - modify treatment regimens
- **Reduce payer restrictions** – increase number of therapeutics

Phil Coffin, UCSF, CDC National HCV Summit – 6/2014)
HCV Elimination in Cherokee Nation

- Small population (314,000) in defined 14 county area
- 95% receive care in CN Health Service- hospital, 8 clinics
- High prevalence- anti-HCV 6.0% (2013); 5160 current HCV infections
- Nascent test, care, and cure programs
- Tribal leadership commitment to HCV elimination
- Coalition of public health, clinical care, and academic medicine
Summary

• The burden of HCV mortality is large and growing
• HCV incidence is increasing in the US; IDU is major risk
• Effective interventions are available to prevent transmission and disease
  – Prevent mortality – Testing linkage to care and treatment
  – Prevent transmission – Infection control, harm reduction, drug treatment, cure and prevention strategies
  – HCV surveillance and monitoring data needed to guide interventions
• With capacity and commitment, elimination of Hepatitis C can become a feasible goal for the nation.
Contributors

• Dan Church
• Jennifer Havans
• Scott Holmberg
• Saul Karpen
• Anil Suryprasad
• Jon Zibbell