Hepatitis C: Revolutionary New Drugs and Barriers to Care and Treatment

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11/3/15
Learning Objectives

• Recognize the scope of the HCV epidemic and impact on AI/AN populations
• Identify the recommended screening guidelines for HCV
• Identify current medications available to treat HCV
• Recognize barriers to HCV treatment
• Recognize the potential for HCV elimination
HEPATITIS C IS A GLOBAL HEALTH PROBLEM

Estimated 170 million persons with HCV infection worldwide

Prevalence of infection
- > 10%
- 2.5%-10%
- 1%-2.50%
- NA

Estimated 170 million persons with HCV infection worldwide

World Health Organization 2008 (http://www.who.int/ith/es/index.html)
HCV Deaths and Deaths from Other Nationally Notifiable Infectious Diseases,* 2003-2013

* TB, HIV, Hepatitis B and 57 other infectious conditions reported to CDC

HEPATITIS C PREVALENCE (NHANES ESTIMATE)

3.2 Million HCV Antibody positive

Possibly up to 7.1 Million HCV Antibody positive in US

Chak E, et al. Liver Int. 2011;31:1090-1101
What is the true HCV prevalence?

<table>
<thead>
<tr>
<th>Population</th>
<th>Estimated Size</th>
<th>HCV Prevalence</th>
<th>Number of Infected Persons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incarcerated</td>
<td>2,186,230</td>
<td>23.1%</td>
<td>7.5%-44.0%</td>
</tr>
<tr>
<td>Homeless</td>
<td>691,899</td>
<td>32.1%</td>
<td>7.5%-52.5%</td>
</tr>
<tr>
<td>Hospitalized</td>
<td>478,054</td>
<td>15.6%</td>
<td>4.0%-38.0%</td>
</tr>
<tr>
<td>Nursing homes</td>
<td>1,446,959</td>
<td>4.5%</td>
<td>2.1%-8.4%</td>
</tr>
<tr>
<td>Military</td>
<td>1,404,060</td>
<td>0.5%</td>
<td>0.48%-0.84%</td>
</tr>
<tr>
<td>Indian reservations</td>
<td>1,069,411</td>
<td>11.5%</td>
<td>7.8%-16.2%</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

What is the true HCV prevalence?

"Without knowing the true scope and scale of the epidemic, we can't appropriately plan or argue for necessary resources."

Discovery of HCV and Impact on HCV Incidence in US

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

22,000 cases of incident HCV infection reported in 2012

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

Source: National Notifiable Diseases Surveillance System (NNDSS)
Surveillance of Acute HCV Infection - 2013

- Estimated 29,000 new HCV infections
- 150% increase since 2010
- Case Rates
  - 61% report IDU
  - Equal Male (0.8): Female (0.7)
  - Highest rate
    - By age 20-29 years, 2.01
    - By race AI/AN (1.7) and whites (0.82)
Regional Drug Injection Trends Among Persons <30 Years Old in KY, TN, VA, WVA

Proportion of All Admissions

- Any Opioid Injection < 30
- Other Drug Injection < 30

Source: National Notifiable Diseases Surveillance System (NNDSS)
HCV Screening for American Indians

- **Clinic-based screening**
  - 243 patients in Omaha Nebraska; 30 tribes
  - 11.5% anti-HCV positive
  - Risks included use of cocaine and injected drugs

- **Screening of pregnant women**
  - 205 pregnant women in northern plains (median age 22 years)
  - 6% anti-HCV positive
  - Injection drug use only risk factor

- **Screening of persons born 1945-1965**
  - 31% of cohort screened by IHS; 267% increase in testing
  - HCV testing data pending
## Results of an Enhanced Screening among one North Dakota Tribal Area

<table>
<thead>
<tr>
<th></th>
<th>No. Tests Positive</th>
<th>No. Tests Ordered</th>
<th>Percent Positivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlamydia</td>
<td>218</td>
<td>2,041</td>
<td>10.7%</td>
</tr>
<tr>
<td>Gonorrhea</td>
<td>71</td>
<td>2,041</td>
<td>3.5%</td>
</tr>
<tr>
<td>Syphilis (RPR)</td>
<td>59</td>
<td>1,933</td>
<td>3.1%</td>
</tr>
<tr>
<td>HIV</td>
<td>0</td>
<td>1,916</td>
<td>0.0%</td>
</tr>
<tr>
<td>Hepatitis C Ab</td>
<td>126</td>
<td>1,108</td>
<td>11.4%</td>
</tr>
</tbody>
</table>

Sarah Weninger, Viral Hepatitis Prevention Coordinator, North Dakota sweninger@nd.gov
A 300% Increase in Hepatitis C–related Hospitalization for AI/AN – 1995-2007

Byrd KK, et al Pub Hlth Rep 2011
HCV –Related Mortality by Race/Ethnicity- 2007 compared to 2011

Byrd KK, et al Pub Hlth Rep 2011
WHO SHOULD BE SCREENED FOR HCV?
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/organisms prior to June 1992
  - Received blood products 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)

NHANES SURVEY, UNITED STATES, 2001-2008
AWARENESS OF HCV INFECTION STATUS

Knowledge of HCV Infection

Unaware 50%  Aware 50%

Forecasted Annual Incident Cases of Decompensated Cirrhosis (DCC), Hepatocellular Carcinoma (HCC), Liver Transplants, and Deaths Associated with Persons with Chronic Hepatitis C Infection and No Liver Cirrhosis in the United States in 2005

Twin Epidemics of HCV Transmission and Disease

- 5 fold higher prevalence than others (3.39%)
- 81% of all HCV infected adults
- 73% of HCV related deaths
HCV Treatment
The Evolution of Highly Effective Treatment

- **1991**: Standard IFN
- **1998**: RBV
- **2001**: PegIFN
- **2011**: BOC and TPV
- **2013**: SMV
- **2014**: SOF/LDV 3D

**SVR (%)**

- **IFN 6 mos**: 6%
- **IFN 12 mos**: 16%
- **IFN/RBV 6 mos**: 34%
- **IFN/RBV 12 mos**: 42%
- ** PegIFN 12 mos**: 39%
- ** PegIFN/RBV 12 mos**: 55%
- ** PegIFN/RBV/BOC or TPV 6-12 mos**: 70%
- ** PegIFN/RBV/SMV 24-48 wks**: 80%
- ** PegIFN/RBV/SOF 12-24 wks**: 89%
- ** SOF/LDV 8-12 wks**: 93%
- **Ombit/P ar/r + Das + RBV 12-24 wks**: 92%
Sofosbuvir

- Approved 12/2013
- NS5B polymerase inhibitor (chain terminator)
- Potent activity against genotypes 1–6
- Once-daily, 400-mg tablet
- Safe and well tolerated
- Wholesale acquisition cost for a 12-week course $84,000
> 90% SVR 12 Across Treatment-Naïve Genotypes 1, 2, 3, 4, 5, 6

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Patients with HCV RNA &lt;LLOQ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GT 1, 4</td>
<td>90%</td>
</tr>
<tr>
<td>GT 2</td>
<td>97%</td>
</tr>
<tr>
<td>GT 3</td>
<td>93%</td>
</tr>
<tr>
<td>GT 5/6</td>
<td>100%</td>
</tr>
</tbody>
</table>

Ledipasvir/Sofosbuvir: A Single Tablet Regimen (S1R)

- **Approval Status:** FDA approved October 10, 2014
- **Dosing:** One tablet daily (fixed dose 90 mg ledipasvir/400 mg sofosbuvir)
- **Wholesale Acquisition Cost in United States:** $1125 per pill
  - 8-week course = $63,000
  - 12-week course = $94,500
  - 24-week course = $189,000

Source: Harvoni Prescribing Information. Gilead Sciences
ION Phase 3 Program (ION-1, ION-2, ION-3)

Efficacy Summary

- 97% (1886/1952) overall SVR rate

Error bars represent 95% confidence intervals.

Viekira pak

- Approved 12/2014
- HCV Genotype 1
- 2 tablets of Ombitasvir/paritaprevir/ritonavir every am
- 1 Dasabuvir tablet every am and pm
- Wholesale acquisition cost for a 12-week course $ 83,319
Daclatasvir

- Approval 7/24/15
- HCV genotype 3
- 60 mg daclatasvir with sofosbuvir for 12 weeks
  Available as 60 mg tablet and 30 mg tablet
- Mechanism of action: NS5A inhibitor
- Wholesale acquisition cost for a 12-week course $63,000
HCV Direct Acting Agents

• NS3-4A Protease inhibitors “previr”
  – Simeprevir licensed 2013
  – Paritaprevir licensed 2014
  – Grasoprevir January 2016

• NS5B Polymerase inhibitor “buvir”
  – Nucleoside – Sofosbuvir licensed 2013
  – Non-nucleoside – Dasabuvir licensed 2014

• NS5A replication complex inhibitor “asvir”
  – Ledipasvir licensed 2014
  – Ombitasvir licensed 2014
  – Daclatasvir licensed 2015
  – Elbasvir January 2016
DAA short pipeline

- Sofosbuvir/Velpatasvir STR – pangenotypic NS5A inhibitor (genotypes 1-6)
- 1 pill once per day all genotypes
Who should be treated for HCV?
Persons with chronic HCV infection
HCV IS NOT JUST A LIVER DISEASE
Extrahepatic Manifestations

• Diabetes (70% increase)
• Renal Disease
• Peripheral Neuropathy
• Dermatologic Manifestations
• Lymphomas
Hepatitis C virus infection: a risk factor for Parkinson’s disease


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Common Symptoms of HCV in the Absence of Cirrhosis

- Fatigue
- Impaired cognitive function
- Migratory arthralgia or myalgia
- Depression
What do we get with HCV Treatment?

• SVR (cure) of HCV is associated with:
  • 70% Reduction of Liver Cancer
  • 50% Reduction in All-cause Mortality
  • 90% Reduction in Liver Failure

Lok A. NEJM 2012; Ghany M. Hepatol 2009; Van der Meer AJ. JAMA 2012
Cirrhosis Regression and Fibrosis Reduction Following SVR

“Strong and accumulating evidence argue against deferral”

• Decreased all-cause morbidity and mortality
• Prevention of onward transmission
• Improve or prevent extrahepatic complications, including diabetes mellitus, cardiovascular disease, renal disease, and B-cell non-Hodgkin lymphoma which are not tied to fibrosis stage.
• Quality-of-life improvements for patients treated regardless of baseline fibrosis
• **Deferral practices based on fibrosis stage alone are inadequate and shortsighted**
• **Prioritization tables are now less useful and have been removed**

HEPATITIS C CASCADE OF CARE IN UNITED STATES

Medicaid Reimbursement Criteria - HCV Therapy

- Minimum fibrosis score
- Prescription by specialist

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

Medicaid Reimbursement Criteria - HCV Therapy

- Illicit drug abstinence before treatment
- Alcohol abstinence before treatment

Some states require blood/urine tests; some states deny payment for patients who test positive for methadone, and marijuana.

The numbers

*IF* other barriers addressed - the lack of medical providers becomes a severe limitation

Adapted form Whyles ID week 2015.
Role of the Primary Care Team in HCV

- Screening for HCV
- Counseling on modifiable risk factors important in disease progression
- Staging of liver disease
- HCC surveillance
- Recognition of extra-hepatic manifestations
- HCV treatment (with mentoring) or referral
Effective Prevention Strategies and Advent of Curative HCV Therapies Have Increased Considerations for HCV Elimination
Cherokee Nation Hepatitis C Elimination Project

Hepatitis C Free
Cherokee Nation Health Services
The Cherokee Nation’s Jurisdiction is comprised of 14 counties in NE Oklahoma. The Jurisdiction includes 6 full and 8 partial counties within the Oklahoma Tribal Statistical Area (OTSA). The Jurisdiction is estimated to be 7,000 square miles.
80% of HCV Transmission Occurs in PWID

PWID: People who inject drugs
Goals Needed For HCV Elimination

• Eliminate the burden of liver disease
  – Screen 85 %
  – Link to care 85 %
  – Treat 85%

• Eliminate transmission
  – Treatment as prevention
  – Syringe and needle exchange programs
  – Opioid substitution programs
  – Determine the impact of other risk factors and plan for interventions
HCV Elimination Cherokee Nation: Action Plan

- Increase patient/community/HCW awareness
- Increase screening (age 20-69)
- Centralized linkage to care
- Expand the treatment workforce
  - Train PCP in the evaluation and management of HCV
  - Incorporate pharmacists in the treatment of HCV

PCP: Primary Care Providers
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
Summary

• There are two HCV epidemics
  – rapidly rising mortality related to prevalent disease
  – incidence is increasing; IDU is major risk

• AI/AN populations disproportionately affected by HCV
Summary

• HCV is curable in > 90% of people
• Dire need to test and treat
• Many barriers to treatment
  – Need to address drug pricing
  – Need to address restrictions on treatment
  – HCV must be treated in the primary care setting
• HCV elimination may be a possibility in the future
Slide Acknowledgments

• John Ward, CDC
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• Jorge Mera, MD
• Paulina Deming, PharmD
Questions?