Viral Hepatitis: A Global Snapshot of Challenges and Opportunities

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U.S. Centers for Disease Control and Prevention
Topics

• Disease burden

• Prevention options and impact
  • Primary
  • Secondary

• Steps in building prevention, care, and treatment capacity

• Setting elimination goals for HBV and HCV transmission and disease
Global HIV, HBV and HCV
Estimated Prevalence of Infection

- HCV: 130-150 million
- HIV: 36.9 million
- HBV: 248 million

Burden of HBV and HCV Infection - United States

740000-2.2M HBsAg+ persons
Increasing proportion of foreign born

3.5 M Persons with HCV
Seroprevalence Highest for Persons Born 1945-1965

- 5 fold higher prevalence than others (3.4%)
- 81% of all HCV-infected adults
- 73% of HCV-related deaths
Number of Deaths/Year from Selected Conditions, 2013

686,000 HBV and 704,000 HCV associated deaths
HCV Deaths and Deaths from Other Nationally Notifiable Infectious Diseases,* 2003-2013

* 60 infectious conditions reported to CDC

Mortality Rates for Hepatitis B, Hepatitis C and HIV infection - 2003-2013, United States

**Global Burden of Disease**

<table>
<thead>
<tr>
<th>Etiology</th>
<th>1990</th>
<th>2010</th>
<th>Percent Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>463,000</td>
<td>752,000</td>
<td>64%</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>210,000 (45%)</td>
<td>341,000 (45%)</td>
<td>62%</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>113,000 (24%)</td>
<td>196,000 (26%)</td>
<td>73%</td>
</tr>
<tr>
<td>Alcohol</td>
<td>93,000 (20%)</td>
<td>149,000 (20%)</td>
<td>59%</td>
</tr>
<tr>
<td>Other</td>
<td>46,000 (10%)</td>
<td>66,000 (9%)</td>
<td></td>
</tr>
</tbody>
</table>

Lozano R, Lancet 2012
Interventions to HBV and HCV Transmission and Disease

• Primary prevention (transmission)
  – Hepatitis B vaccination
  – Blood donor screening recruitment (e.g., voluntary donors)
  – Universal practices for infection control
  – Safer sex practices
  – Harm reduction/drug treatment
  – Testing and anti-viral therapy and cure

• Secondary prevention (disease)
  – Testing
  – Linkage to recommended care and treatment
Chronicity and age at HBV infection

Chronicity is related with age when HBV infection occurs.

<table>
<thead>
<tr>
<th>Age at infection</th>
<th>Chronicity</th>
<th>Symptomatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perinatal infection:</td>
<td>90%</td>
<td>rare</td>
</tr>
<tr>
<td>Infection at preschool age:</td>
<td>25%</td>
<td>~10%</td>
</tr>
<tr>
<td>Infection at adulthood:</td>
<td>&lt; 3%</td>
<td>~30%</td>
</tr>
</tbody>
</table>

Beasley et al.
Number of Countries Having Introduced Hep B Vaccine* and Global Infant Hep B3 Coverage, 1989-2011

*excluding 3 countries where Hep B administered for adolescence

Immunization Vaccines and Biologicals, (IVB), World Health Organization.
194 WHO Member States. Date of slide: 22 August 2012.
Deaths Averted Through Investment in Routine Infant Immunization

- Hepatitis B vaccination and cancer prevention
  - Cited by the United Nations as a best buy
  - WHO will soon monitor vaccination as a performance measure

Hepatitis B vaccination and cancer prevention

- Over 5.5 million
- Polio*: 40,000
- Yellow fever: 140,000
- Pertussis: 433,000
- Hib: 697,000
- Measles: 860,000
- Pneumococcal: 38,000
- Rotavirus: 2,000
- Hepatitis B: 3,696,000

ICVH 2016
INTERNATIONAL CONFERENCE ON VIRAL HEPATITIS
Countries Using Hep B Birth Dose Vaccine in National Immunization Schedule, 2011

Source: WHO/IVB database, 194 WHO Member States. Data as of October 2012
Date of slide: 01 October 2012

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement. © WHO 2012. All rights reserved
Prevalence of HbsAg by Age Group, China, 1979, 1992 and 2006

<table>
<thead>
<tr>
<th>Age Group (year)</th>
<th>1979</th>
<th>1992</th>
<th>2006</th>
</tr>
</thead>
<tbody>
<tr>
<td>1~4</td>
<td>0.96%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5~14</td>
<td>2.42%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15~59</td>
<td>8.57%</td>
<td></td>
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</tr>
</tbody>
</table>

Dramatic reduction in childhood prevalence but 93 million people with chronic HBV infection

Liver Cancer Rises from 12 to 6 in Rank of Causes of Years of Life Lost in China 1990 and 2010

<table>
<thead>
<tr>
<th>1990</th>
<th>2010</th>
<th>% Change in prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Lower respiratory infections</td>
<td>1. Stroke</td>
<td>21%</td>
</tr>
<tr>
<td>2. Stroke</td>
<td>2. Ischemic heart disease</td>
<td>81%</td>
</tr>
<tr>
<td>3. COPD</td>
<td>3. COPD</td>
<td>145%</td>
</tr>
<tr>
<td>4. Congenital anomalies</td>
<td>4. Road injury</td>
<td>64%</td>
</tr>
<tr>
<td>5. Drowning</td>
<td>5. Lung cancer</td>
<td>81%</td>
</tr>
<tr>
<td>7. Ischemic heart disease</td>
<td>7. Stomach cancer</td>
<td>-11%</td>
</tr>
<tr>
<td>8. Self harm</td>
<td>8. Self harm</td>
<td>-30%</td>
</tr>
<tr>
<td>9. Preterm birth complications</td>
<td>9. Lower respiratory infections</td>
<td>-81%</td>
</tr>
<tr>
<td>10. Road injury</td>
<td>10. Esophageal cancer</td>
<td>1%</td>
</tr>
<tr>
<td>11. Stomach cancer</td>
<td>11. Drowning</td>
<td>-64%</td>
</tr>
<tr>
<td><strong>12. Liver cancer</strong></td>
<td>12. Congenital anomalies</td>
<td>-66%</td>
</tr>
</tbody>
</table>
Countries reporting screening of 100% of blood samples for HBV and HCV 2002-2008

Source: WHO Global Database on Blood Safety (GDBS) and Blood Safety Indicators
## 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>
</tr>
</thead>
<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
Epidemics of HCV Transmission - United States

29,000 new HCV infections in 2013
150% increase since 2010

Regional Drug Injection Trends
Among Persons <30 years old in KY, TN, VA, WV

Suryprasad AG, et al. CID 2014  MMWR 2015; cdc.gov/hepatitis
Proportion of HCV infected Persons by Year of Birth- Part One
15 countries
• HBV testing and therapy
  – 56%-78% reduction in risk of liver cancer
  – Benefit for patients with and without cirrhosis
• HCV testing and curative therapy
  – 50%-74% reduction in all cause mortality
  – 75% reduction in liver cancer
  – 93% reduction in liver –related mortality

van der Meer JAMA 2012, Morgan Ann Int Med 2012
Knowledge of HCV Status is Low
Few HCV Persons are Diagnosed and Treated;
Forecasted Declines in Liver Related Deaths with Improved HCV Therapies Only Versus Improved Screening and Treatment

Gane E, JVH 2015; Alfaleh FZ, JVH 2015; Wedemeyer, JVH 2014
Steps Toward Building Capacity for Viral Hepatitis Testing, Care, and Treatment

- Strategic data
- Policy development (WHO normative guidance)
- Financing antiviral therapy
- Improved test technologies (FIND, CDC)
- Health system strengthening (Georgia, PEPFAR)
- Goal setting and accountability (elimination targets)
WHO 2012 Program Budgets Per Disease-specific Deaths (2010 GBD Study)

- Tuberculosis
- HIV
- Malaria
- Viral Hepatitis

Lozano et al, Global Burden of Disease Study 2010 Lancet 2012
WHO: unpublished data
Chronic Hepatitis B Virus Infection Prevalence, by Country, 2010

248 million HBsAg + individuals worldwide

Schweitzer A et al. Lancet 2015
Chronic Hepatitis C Virus Infection
Prevalence, by Country, 2010

115M anti-HCV + ; 80M current infections (Gower, 2014)

185M anti-HCV+ ; 130-150 M current infections (Hanafieh, 2013, WHO)
Improving Availability of Strategic Data - Vietnam

- Addition of HBV and HCV testing to Integrated Behavioral and Biologic Survey (IBBS)
- 2009-2010

<table>
<thead>
<tr>
<th></th>
<th>HIV</th>
<th>HBsAg</th>
<th>HCV Ag/Ab+</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSM (n=1588)</td>
<td>14.9%</td>
<td>12.4%</td>
<td>28.4%</td>
</tr>
<tr>
<td>MWID (n=3010)</td>
<td>28.1%</td>
<td>14.1%</td>
<td>53.8%</td>
</tr>
</tbody>
</table>

- IBBS 2012-2013 - Data analysis in progress
- Partnerships - PEPFAR, Abbott

WHO Normative Guidance

HCV (2014, 2016)  
HBV (2015)  
HEPATITIS TESTING GUIDELINES (2016)

- Who to screen?  
  Populations and setting  
- How to screen?  
  Diagnostics for hepatitis  
- Linkage to prevention & treatment
National Policies for HBV and HCV Testing - United States

- **HBV Testing Pregnant Women** – June 2009
- **HBV Testing** – June 2014
  - Foreign born persons from Asia, Africa (countries > 2% prevalence)
  - MSM, IDU
  - For populations > 2% HBsAg+ $31,600/QALY

- **HCV Testing - June 2013**
  - Persons born 1945-1965 - one time
  - Persons who inject drugs
  - Others (e.g., transfusion <1992)
  - Birth cohort testing- $31-35,000/QALY

Financing HCV Treatment

- Adversely affecting treatment access and drug compliance
- Encouraged drug counterfeiting which could create substantial public health hazards and cause safety concerns

Financing Cost of HCV Therapy
Country-By-Country Agreements

- Prices based on company-country negotiations
- Countries can require separate clinical trials
- Results vary and often lack transparency

HCV Drug Prices and Gross National Income

Financing Cost of HCV Therapy
Generic Manufacturing
Gilead and Medicines Patent Pool (MPP)

<table>
<thead>
<tr>
<th>Gilead</th>
<th>MPP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Announced September 15, 2014</td>
<td>Announced November 23, 2015</td>
</tr>
<tr>
<td>101 countries (looking to expand)</td>
<td>112 countries (looking to expand)</td>
</tr>
<tr>
<td>Production by 11 India companies</td>
<td>Broad base of manufacturers worldwide</td>
</tr>
<tr>
<td>FOCUS: low-income countries</td>
<td>FOCUS: low- and middle-income countries</td>
</tr>
<tr>
<td>Drug: sofosbuvir</td>
<td>Drug: daclatasvir and looking to expand</td>
</tr>
</tbody>
</table>

- Gilead:
  - Program could benefit as many as 103 million persons living with HCV
  - Price for generic Sovaldi (sofosbuvir) = $567 for 12 week treatment course
    Signed agreements for in-country production in Egypt and Pakistan

- MPP: Nearly two-thirds of all patients living with hepatitis C in the LMICs reside in the territory covered by this agreement.
Building HCV Prevention and Treatment Capacity

WORLD BANK

HCV Program

• Focus Countries: Egypt, Georgia, Mongolia
• HCV Area(s)
  – Injection safety
  – Safe blood supply
  – Health IT
  – Primary care training
  – Universal health coverage

THE GLOBAL FUND

At the 33rd Board Meeting (April 2015), an interim measure was approved for the financing of HCV treatment until the approval of a broader policy on co-infections and co-morbidities of HIV/AIDS, tuberculosis, and malaria. Financing includes treatment, diagnosis, and lab and clinic visits.
Building HCV Care and Treatment Capacity

UNITAID funded Médecins Sans Frontières (MSF) project
• Project launched May 2014
• FOCUS: HCV treatment in MSF HIV treatment sites in 7 LMIC countries
• Demonstrate feasibility of HCV testing and treatment

United Kingdom’s Department for International Development (DFID) funded Clinton Health Access Initiative (CHAI) program
• Project launched in April 2015
• Demonstrate feasibility of public sector hepatitis C treatment programs
• Activities: Simplify diagnosis and treatment
Promoting New Test Technologies and Strategies

Community health worker → Health post → Clinic → District hospital → Reference center

A. Screening with serological tests
B. Core HCV antigen test for POC diagnosis
C. Molecular tests for POC diagnosis & DBS for centralized testing
D. Test of cure

FIND’s 2015-2020 Hepatitis C Strategy | http://www.finddiagnostics.org
World Health Assembly Request of WHO to Develop Elimination Goals (2014)

WHO proposed global targets for eliminating HBV and HCV as public health concerns by 2030

- 60% reduction in HBV incidence
- 70% reduction in HCV incidence
- 60% reduction in mortality for both HBV and HCV

Preparing to present to WHA for adoption in May 2016
National HCV Elimination Project: Georgia

- ~ 4 million persons
- High burden of HCV (5-7%)
- Mixed infection risks - healthcare, IDU
- Strong political commitment
- Comprehensive elimination plan
- PPP - Gilead provides up to 20,000 treatment courses/yr
- Target: 90% diagnosed/95% treated/95% cured of HCV by 2020
Two Phases

Phase I (September 1, 2015 – April 1, 2016)
- Phase II, (April 15, 2016 – February 15, 2016)

Committee Charge:
- Determine feasible elimination goals for hepatitis B and hepatitis C
- Recommend a plan of action to reach incidence and mortality elimination goal(s) by 2030
Summary

The disease burden of HBV and HCV Infection is large

Proven interventions have reduced risk of transmission

Expanded access to HBV and HCV testing and treatment can prevent disease and mortality
  • Improve surveillance of Incidence and prevalence
  • Improve affordability of HCV treatments
  • Build capacity to test, care and treat HCV

With greater commitment, HBV and HCV can be eliminated as public health threats.