Viral Hepatitis: A Global Health Threat

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### Types of Viral Hepatitis

<table>
<thead>
<tr>
<th>Source of virus</th>
<th>A</th>
<th>E</th>
<th>B</th>
<th>D</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feces</td>
<td>Feces</td>
<td>Blood/blood-derived body fluids; requires HBV</td>
<td>Blood/blood-derived body fluids</td>
<td>Blood/blood-derived body fluids</td>
<td></td>
</tr>
<tr>
<td>Feces (blood rarely)</td>
<td>Fecal-oral</td>
<td>Percutaneous permucosal</td>
<td>Percutaneous permucosal</td>
<td>Percutaneous permucosal</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Route of transmission</th>
<th>Fecal-oral</th>
<th>Fecal-oral</th>
<th>Percutaneous permucosal</th>
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<th>Percutaneous permucosal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic infection</td>
<td>No</td>
<td>Yes- immuno-compromised</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Severity</td>
<td>Acute disease severity increases with pre-existing liver disease and age at infection</td>
<td>Most infections are clinically silent; can cause liver failure</td>
<td>15-25% of chronically infected develop chronic liver disease, including cirrhosis, liver failure, or liver cancer</td>
<td>Co-infection can increase disease severity; Superinfection can accelerate progression to cirrhosis and hepatitis decompensation</td>
<td>60-70% of chronically infected develop liver disease; 1-5% will die from cirrhosis or liver cancer</td>
</tr>
</tbody>
</table>
Hepatitis A Virus 2005

- 212 million incident infections globally
- 103,000 deaths/yr

Hepatitis A

- Incidence is strongly correlated with socioeconomic factors and access to safe drinking water
- In highly endemic areas, young children have highest incidence but no or mild disease
- Improved living standards delay infection until later life and increases risk for clinically significant hepatitis A
- For some countries in transition, hepatitis A has become a leading cause of fulminant hepatic failure (e.g., Argentina, Brazil, Korea)

Epidemiologic Shift in Prevalence of Antibodies to Hepatitis A Virus

WHO position paper, WER 2012
Hepatitis E

- 2005 estimates
  - 21 million incident infections globally
  - 3.3 million symptomatic cases
  - 57,000 deaths
Hepatitis E

- **Genotype 1,2- Infect humans only**
  - A common cause of endemic and epidemic acute hepatitis in east and southern Asia, Africa
  - Up to 20% mortality risk for pregnant women
- **Genotype 3,4- infect humans, pigs, other animals**
  - Cause of hepatitis E in developed countries
  - Transmission associated HEV+ meat products; unknown source for many cases
  - Incidence of clinical disease appears highest for middle-aged men (>60 yrs.)
  - Can persist as chronic infection in liver, kidney, heart transplant recipients
Hepatitis B Burden and Geographic Distribution 2005

- 4.5 million new infections
- 240 million living with chronic infection
- 786,000 deaths
- United States
  - 700K-1.4M
  - ~2000 deaths

Global HBV-Related Deaths By Age at Acquisition of Infection

- **Late Period**
  - children >5
  - adolescents
  - adults

- **Perinatal Period**
  - 31%

- **Early Childhood Period**
  - children ≤5
  - 48%

- **Early Adolescents Period**
  - 21%
Countries Using HepB Birth Dose Vaccine in National Immunization Schedule, 2010

Source: WHO/IVB database, 193 WHO Member States. Data as of July 2011
Date of slide: 21 September 2011

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Number of imported hepatitis B cases by country of origin

- **CHINA**: 50,000 cases
- **PHILIPPINES**: 40,000 cases
- **VIETNAM**: 30,000 cases
- **KOREA**: 20,000 cases
- **INDIA**: 10,000 cases

2004—2008
**HCV Disease Burden and Global Distribution**

- 3-4 M new infections /year
- 130-170 M persons living with chronic HCV
- ~499,000 deaths/year

**United States**
- 3.2 M (2.7-3.9)
- 15,000 deaths/yr
HIV and HCV Co-infection

- 4-5 million coinfected persons globally

- Prevalence of co-infection varies by region
  - 25% of HIV infected persons in US
  - 80% in countries with large IDU related epidemics (e.g., China, Vietnam, Ukraine)
  - Sexual transmission among HIV+ MSM

- HIV hastens progression of HCV related liver disease

- Liver disease is second leading cause of deaths for persons with HIV/AIDS

HHS Viral Hepatitis Action Plan

- EDUCATING PROVIDERS AND COMMUNITIES TO REDUCE HEALTH DISPARITIES
- IMPROVING TESTING, CARE, AND TREATMENT TO PREVENT LIVER DISEASE AND CANCER
- STRENGTHENING SURVEILLANCE TO DETECT VIRAL HEPATITIS TRANSMISSION AND DISEASE
- ELIMINATING TRANSMISSION OF VACCINE-PREVENTABLE VIRAL HEPATITIS
- REDUCING VIRAL HEPATITIS CASES CAUSED BY DRUG-USE BEHAVIORS
- PROTECTING PATIENTS AND WORKERS FROM HEALTH-CARE-ASSOCIATED VIRAL HEPATITIS
World Health Assembly Resolution 63.18: Comprehensive Hepatitis Prevention and Control- 2010

• 2010 World Health Assembly adopted resolution 63.18 as sponsored by Brazil, Columbia, and Indonesia calling for WHO to develop a comprehensive approach to hepatitis prevention and control

• WHO
  – Formed Global Hepatitis Programme
  – Developed Strategic Framework
Global Hepatitis Framework

Axis 1: Partnerships, resource mobilization and communication

Axis 2: Data for policy and action

Axis 3: Prevention of virus transmission

Axis 4: Screening, care and treatment
Axis 1: Partnerships, resource mobilization and communication
About Hepatitis Testing Day

May 19, 2012 is the first ever national Hepatitis Testing Day. It is a day for people at risk to be tested, and for health care providers to educate patients about chronic viral hepatitis and testing. Millions of Americans have chronic hepatitis; most of them do not know they are infected.

This new national Hepatitis Testing Day in the United States is part of an educational initiative related to CDC’s Know More Hepatitis campaign and the U.S. Department of Health & Human Services’ Combating the Silent Epidemic of Viral Hepatitis: Action Plan for the Prevention, Care & Treatment of Viral Hepatitis.

Brought to You By

KNOW MORE HEPATITIS™

CDC

NPIN

Find Hepatitis Testing Year Round Near You

Locate organizations offering Hepatitis testing, and additional services including vaccines and treatment in the NPIN Organizations database.

Are You at Risk for Hepatitis?

We can help you find out with CDC’s assessment tool.

Spread the Word about Hepatitis Testing Day

Add buttons and badges to your Web and social networking sites to promote Hepatitis Testing Day.
Airport Diorama

Space donated at airports and transit stops, > 100 placements, worth > $4 million
Cirrhosis moving up among leading causes of deaths (12th)
- 1.2 million new deaths in 2010

Liver cancer - 600,000 HBV and HCV-assoc cancers/yr
- 77% of liver cancer, third leading cause of cancer deaths
- Liver cancer rates increasing in US and other countries

References:

Division of Viral Hepatitis

Center M M, Jemal A Cancer Epidemiol Biomarkers Prev 2011;20:2362-2368

©2011 by American Association for Cancer Research
Mortality associated With Hepatitis B, Hepatitis C, and HIV
United States, 1999 – 2008

Future Burden of Hepatitis C Related Morbidity and Mortality in the US

- Markov model of health outcomes
  - Of 2.7 M HCV infected persons in primary care
    + 1.47 M will develop cirrhosis
    + 350,000 will develop liver cancer
    + 897,000 will die from HCV-related complications

Prevalence of HCV among Persons Born 1945-1965 United States

- 74% of 2.7-3.9 M HCV infected
- Prevalence 5.3 times higher than other ages (3.29% vs 0.55%) \(^2\)
- 73% of all HCV-associated mortality \(^4\)

HCV Prevalence by Age - Selected Countries

HCV Prevalence - Japan

HCV Prevalence - China

HCV Prevalence - Romania

HCV Prevalence - Pakistan

Gheorghe, L., et al., J Gastrointestin Liver Dis, 2010; Qureshi, H., et al., E Mediterr Health J,
Vaccine-based Prevention Strategies

- **Hepatitis B immunization**
  - “The infrastructure to eliminate HBV transmission is in place”
  - All infants should receive HepB vaccine preferably ≤ 24 hrs. of birth
  - Regions should adopt elimination goals (e.g., WPRO, EMRO)

- **Hepatitis A immunization**
  - “The elimination of HAV transmission is epidemiologically feasible”
  - Hepatitis A vaccination recommended for children ≥1 year of age
  - National immunization programs may consider one dose schedule

- **Hepatitis E vaccine**
  - 94-100% efficacy (Gen 1,4)
  - Licensed in China- 2011
  - Studies needed to guide indications
  - WHO prequalification pending

References:
Deaths Averted Through Investment in Routine Infant Immunization

- 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

Over 5.5 million

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

- **Improve sanitation**
  - 37% of world population lack access to sanitation facilities
  - 780 million lack access to water from improved sources
- **Improve patient safety**
  - > 2 M HCV infections attributable to unsafe injections in health-care settings
- **Prevent drug use associated transmission**
  - HCV prevalence among persons who use injection-drugs is high\(^1\) at \(~64\%\) (95% CI 63.4-64.7%)
- **Promote adoption of safer sexual practices**
  - Increases in HCV incidence among HIV+ MSM

Screening, Care and Treatment for Persons Living with Chronic Infection

- Quality diagnostics
- Screening, care and treatment guidelines
- Training for health care providers
- Access to treatment and drugs
## Therapies for Hepatitis B

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Date US licensure</th>
<th>HBV DNA not detected</th>
<th>Improved hepatic histology</th>
<th>Resistance &gt; 1 yr</th>
<th>Cost USD/yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamivudine</td>
<td>1998</td>
<td>36%-44%</td>
<td>49%-62%</td>
<td>70%</td>
<td>2,500</td>
</tr>
<tr>
<td>Adefovir</td>
<td>2002</td>
<td>13%-21%</td>
<td>53%-68%</td>
<td>30%</td>
<td>6,500</td>
</tr>
<tr>
<td>Pegylated Interferon</td>
<td>2005</td>
<td>25%</td>
<td>38%</td>
<td>---</td>
<td>18,000</td>
</tr>
<tr>
<td>Entecavir</td>
<td>2005</td>
<td>67%</td>
<td>72%</td>
<td>&lt;1%</td>
<td>8,700</td>
</tr>
<tr>
<td>Telbivudine</td>
<td>2006</td>
<td>60%</td>
<td>65%</td>
<td>25% (2 yrs.)</td>
<td>6,000</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>2008</td>
<td>80%</td>
<td>74%</td>
<td>&lt;1% (2 yrs)</td>
<td>6,000</td>
</tr>
</tbody>
</table>

IFN
6 m
16%
6%
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%
Peg/RBV/
+ new DAA- 3 m
>90%

Sustained Virologic Response (%)

Advances in HCV Therapy

CDC Recommends One-Time HCV Testing for Persons Born 1945-1965

- 74% of 2.7-3.9 M HCV infected
- Prevalence 5.3 times higher than other ages (3.29% vs 0.55%)
- 45%-85% unaware of their infection
- HCV testing linked to care and treatment reduces risk of:
  - HCC by 70%
  - all-cause mortality by 45%
## Health Impact of Birth Cohort Recommendations

<table>
<thead>
<tr>
<th>Outcome</th>
<th>PegIFN-Riba + Telaprevir</th>
</tr>
</thead>
<tbody>
<tr>
<td>Additional identified cases</td>
<td>809,000</td>
</tr>
<tr>
<td>Cirrhosis cases averted</td>
<td>203,000</td>
</tr>
<tr>
<td>Decompensated cirrhosis cases averted</td>
<td>74,000</td>
</tr>
<tr>
<td>Hepatocellular carcinoma cases averted</td>
<td>47,000</td>
</tr>
<tr>
<td>Transplants averted</td>
<td>15,000</td>
</tr>
<tr>
<td>Deaths from hepatitis C virus averted</td>
<td>121,000</td>
</tr>
<tr>
<td>Medical costs averted</td>
<td>$2.5B</td>
</tr>
<tr>
<td>Cost/QALY gained</td>
<td>$35,700</td>
</tr>
</tbody>
</table>

Potential Impact on Future Burden of Hepatitis C Related Mortality in the US

D. Rein, et al, unpublished data
“Today, my husband and I are attending the funeral of one of our favorite patients. He died Saturday of hepatitis C. He was 35 years old and the father of two little boys.

By the time he became my patient, he had HIV and hep C. As his CD4 cell count was excellent, we opted to treat his hep C first. However, his liver was so fibrosed at the time he was diagnosed, he wasn't a candidate for therapy.

We enrolled him in hospice care, and he declined rapidly and died peacefully at home with his family at his side.

It was the best we could do, but doesn't feel like anywhere near enough.”

Donna Miller Potts, MD
Anderson Free Clinic, SC
Removing Barriers to Hepatitis C Testing, Care, and Treatment

- Policy development
- Capacity building
- Simplification of diagnosis and care
  - New diagnostic technologies and therapies
  - Care models
- Integration in other services (e.g., HIV, primary care)
- Reach vulnerable populations (e.g., corrections)
- Monitor outcomes
- Access to affordable services
- Build donor and political commitment

Summary
Global Burden of Viral Hepatitis

- 150 million new infections each year
- 400 million living with chronic infection
- 1.2 million deaths per year

Global Control of Viral Hepatitis

• Requires comprehensive primary and secondary prevention strategies
• Vaccination and other prevention strategies can reduce and potentially eliminate transmission of HAV and HBV
• HCV therapies are powerful prevention tools
  – Prevent cirrhosis and liver cancer
  – Treatment as prevention
• Prevention infrastructure must be strengthened to realize health gains of interventions
• Collaborations are essential among public health, clinical care providers, laboratories, payers and industry to improve HCV testing, care and treatment
Thank you

For more information please contact Centers for Disease Control and Prevention
1600 Clifton Road NE, Atlanta, GA 30333
Telephone, 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
E-mail: cdcinfo@cdc.gov  Web: www.cdc.gov

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