Global Burden of Viral Hepatitis: Implications for the US and CDC Response

David M. Bell, MD
Division of Viral Hepatitis
Centers for Disease Control and Prevention
Atlanta, GA USA
Acknowledgements

CDC
Veronica Allen
Susan Goldstein
Dale Hu
Eric Mast
Tarissa Mitchell
Anne Moorman
Joseph Perz
John Ward
Cindy Weinbaum

WHO
Steven Wiersma
Asian Liver Center at Stanford University
Alena Groopman
David Hutton
Samuel So
University of Texas at Galveston
Miriam Alter
Outline of Presentation

- Global burden of viral hepatitis (B and C)
- Implications for US
- Future challenges and directions
Hepatitis B Burden: 
Difficulties in Assessment

- Most new infections occur at birth or in early childhood—usually asymptomatic
- Sequellae occur in adulthood (hepatocellular CA & cirrhosis)
- Etiology of liver disease often unrecognized, especially in developing countries
- Models using serosurveys and other data are needed to estimate HBV burden and impact of preventive measures
  - WHO Global Burden of Disease estimates are now being updated using models
Chronic HB Prevalence from Seroprevalence Surveys

Source: CDC, WHO
HBV Burden of Disease Estimates, 2000

- Total HBV infection: 2 billion
- Chronic HBV: 370 million
- Deaths annually: 500-700,000
- Second only to tobacco in causing the most cancer deaths worldwide
- 60-80% of primary liver cancer (hepatocellular carcinoma) is caused by chronic hepatitis B infection
- Other blood-borne infections (# prevalent cases)
  - Chronic HCV: 98.1 million
  - HIV: 40 million

1 CDC. Available at: www.cdc.gov/ncidod/diseases/hepatitis/b/faqb.htm
2 WHO. Available at: www.who.int/csr/disease/hepatitis/en
# Leading Causes of Infectious Disease Deaths Worldwide

<table>
<thead>
<tr>
<th>Disease</th>
<th>Est. Deaths per Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower respiratory tract infections</td>
<td>~3.5 million</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>~3.0 million</td>
</tr>
<tr>
<td>Diarrheal diseases</td>
<td>~2.2 million</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>~2.0 million</td>
</tr>
<tr>
<td>Malaria</td>
<td>~1-3 million</td>
</tr>
<tr>
<td>Measles</td>
<td>~888,000</td>
</tr>
<tr>
<td>Hepatitis B Virus</td>
<td>~620,000</td>
</tr>
<tr>
<td>Hepatitis C Virus</td>
<td>~366,000*</td>
</tr>
<tr>
<td>Pertussis</td>
<td>~355,000</td>
</tr>
<tr>
<td>Neonatal tetanus</td>
<td>~300,000</td>
</tr>
</tbody>
</table>

Source: CDC, WHO, UNICEF, UNAIDS  
*Perz et al, J Hepatology, 2006
China has the Greatest Burden of Hepatitis B and Liver Cancer in the World

1/3 of all chronically infected persons live in China

- Adult HBsAg prevalence 9.1%\(^7\)

China accounts for about 54% of the 600,000 worldwide deaths from liver cancer each year\(^2\)

More deaths from HBV (263,000-300,000) than HIV/AIDS, TB and Malaria combined

- 200,000 from TB, 39,000 from HIV/AIDS, and 0 from malaria\(^3-6\)

1 WHO. Available at: [www.who.int/csr/disease/hepatitis/en/](http://www.who.int/csr/disease/hepatitis/en/)
4 MMWR 2007; 56(18):441
7 [http://www.gov.cn/xwfb/2008-04/21/content_950425.htm](http://www.gov.cn/xwfb/2008-04/21/content_950425.htm)
Model: Global HBV-Related Deaths by Age at Acquisition of Infection

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

- **Perinatal Period**

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

1 Future deaths, without vaccination
Estimated Global Burden of Disease Associated with Unsafe Injections

- Overuse of injections
- Reuse of equipment
- Estimated annual incidence in 2000
  - > 21 million HBV infections
    - 32% of new infections
  - > 2 million HCV infections
    - 40% of new infections
  - > 260,000 HIV infections
    - 5% of new infections

88% of countries have hep B programs
65% of infants born in 2007 vaccinated

- 27% got birth dose (36% in countries with chronic infection rate >8%)

Source: MMWR 2008;57:1252; WHO/IVB (August 2008)
Impact of Hep B Vaccine in China: Reduced HBsAg Prevalence in Children (Still Large Reservoir in Adults)

Examples of CDC Support for Global Hepatitis B Control

- CDC Division of Viral Hepatitis is a WHO collaborating center
  - Epidemiology, surveillance, outbreak investigation, prevention/control, laboratory support, training
- Global Immunization
  - Strategy, implementation, assessment, certification
- Global Burden of Disease Project
- Safe Injection Global Network
  - Technical support, funding
- Management of chronic HBV infection in resource poor settings
  - WHO consultation February 2009
- Integration with HIV Prevention/Treatment Programs
Impact on U.S. of Global HBV Infection

- Chronic hepatitis B infection in foreign born citizens/residents: A Ticking Time Bomb
  - Progression to chronic liver disease
  - Potential transmission to newborns, household, and sexual contacts
- Many foreign-born children (and adults) not immunized
Changing Patterns of U.S. Immigration, 1820-2000

Number (millions)

Decade


Source: Yearbook of Immigration Statistics, 2004

- 61% of the 27.2 million immigrants to US in 1973-2007 were from countries of intermediate (2-8%) or high (>8%) chronic HBV infection prevalence

- Estimated 90% of new US cases of chronic hepatitis B are imported
  - 49,000 cases imported vs. 3000-5000 new US cases annually

- Imported cases are increasing with time
  - Mean annual number 18,000 (in 1973-77); 49,000 (in 2003-07)

Source: Mitchell T et al unpublished CDC data
Estimated Cases of Chronic Hepatitis B Importation to U.S. by WHO Region, 1973-2007

Source: Mitchell T et al, unpublished CDC data
Estimated Number of Imported Hepatitis B Infections from Top 10 Countries, 2003-2007

Burden

Source: Mitchell T et al, unpublished CDC data
Vaccine-based Strategy to Eliminate HBV Transmission in U.S.

- Prevent perinatal HBV transmission (1982-88)
  - Maternal screening
  - Newborn vaccination
  - Universal birth dose (2005)
- Universal infant vaccination (1991)
- Catch-up vaccination
  - Adolescents 11-12 years (1995)
  - All persons <19 years (1999)
- Adults at risk and household contacts (1982)

Source: CDC Advisory Committee on Immunization Practices, MMWR
Success of US Hep B Childhood Vaccine Programs:  
Hepatitis B Incidence in Persons <19 Yrs  
By Race/Ethnicity, 1990-2004

Overall decline ~ 93%  
Decline among API ~ 95%
Chronic Infection is Now the Major Domestic HBV Challenge (and a Source of Health Disparities)

- Estimated 805,000-1.4 million total, of which 375,000-975,000 foreign born
- Foreign-born women account for ~80% of HBsAg positive pregnant women in CA and NYC
- 10% of Asian/ Pacific Islander (API) adults in US have chronic HBV
  - 2/3 are foreign born
  - 2/3 are unaware of their HBV infection - cannot benefit from rx or preventive measures (eg vaccinate contacts)
- Liver cancer incidence 3x higher among API males than white males
- 60-80% of liver cancer cases in APIs are attributable to HBV infection
Hepatitis B Screening of Immigrants and Refugees

- Not required by US law for immigration or resettlement
- 1992 CDC/ACIP: Screen all persons from high endemicity (>8%) countries for HBsAg
  - Related to vaccination of contacts
- 2008 CDC: Also from intermediate endemicity (2-8%) countries
  - New focus on management of chronic infection
- 2008 CDC: “Refer HBsAg-positive persons to a clinician experienced in management of chronic hepatitis B”
  - No CDC resources for screening programs
Hepatitis B Vaccination of Contacts: A Mixed Record

- Recommended by CDC/ACIP since 1982
- 1997 San Diego study: 55% of providers advised contact vaccination; <20% of contacts initiated vac.
  
- 2005: 26% of contacts of HBsAg + pregnant women were tested and evaluated by public health depts*
- 2005: Up to 85% of contacts evaluated in model (funded) adult hepatitis B prevention programs*
- 2008: Most states and cities have little to no capacity for contact identification and management

*MMWR 2008;57(RR-8)
HBsAg Testing of Pregnant Women in the United States

- CDC supports perinatal hepatitis B prevention coordinators in all states (funding for the position only)

- In 2004, immunization programs reported that 85-100% of pregnant women in their jurisdictions were screened for HBsAg

- However, in 2004,
  - 23,919 expected births to HBsAg-positive women
  - 11,967 HBsAg-positive women identified by perinatal hepatitis B prevention programs (50% of expected)
Identified and Expected Births to HBsAg-Positive Mothers, United States, 1993-2005

- **Expected Number**
  - Year: 1993 to 2005
  - Expected Number: 0 to 25,000

- **Percent Identified**
  - Year: 1993 to 2005
  - Percent Identified: 0 to 100

The graph shows the trend of expected births and the percentage identified from 1993 to 2005.
Completion of Follow-up For Infants of HBsAg-Positive Mothers, 1993-2005

Source: National Immunization Program, CDC
Cost-effectiveness of HBV Screening, Treatment, Vaccination Strategies for Asian/Pacific Islander (API) Adults in US

Compared with status quo (voluntary screening):

- Universal vaccination of API adults
  - Not cost-effective

- Screen; treat carriers with antivirals if indicated
  - $36,288 per QALY

- Screen; treat carriers, ring vaccinate contacts
  - $36,500 per QALY

Estimated Prevalence of Anti-HCV
Total 150 million people
HCV: Major Patterns of Transmission

- Developed countries
  - Primarily injection drug use
- Developing countries
  - Primarily unsafe medical practices and transfusions
- Not major concern among US immigrants, but some groups may be at increased risk
# HCV Seroprevalence, US NHANES Surveys, 1999-2002

<table>
<thead>
<tr>
<th>Category</th>
<th>% HCV + (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All participants</td>
<td>1.6 (1.3-1.9)</td>
</tr>
<tr>
<td>(N=15079)</td>
<td></td>
</tr>
<tr>
<td>Born in US</td>
<td>1.8 (1.4-2.1)</td>
</tr>
<tr>
<td>Born in Mexico</td>
<td>0.5 (0.3-0.9)</td>
</tr>
<tr>
<td>Born elsewhere</td>
<td>0.6 (0.2-1.6)</td>
</tr>
</tbody>
</table>

Possible High Rates of HCV Infection among Immigrants from Certain Regions

- Community HCV screening of immigrants from former Soviet Union in NYC (Brooklyn & Queens)
- 28.3% of 283 subjects were HCV+
- Seropositivity rates by country: 11% Russia; 29% Uzbekistan; 31% Ukraine; 37% other
- Only risk factors identified were history of:
  - Intramuscular injections: OR 9.1 (2.0-42.4)
  - Blood transfusion: OR 3.2 (1.2-9.0)

Source: Batash et al. Am J Gastroenterol 2008;103:922-7
Summary (1 of 2)

- Large global burden of viral hepatitis has direct domestic implications for US
- Estimated 375,000-975,000 foreign-born persons in US have chronic hepatitis B infection acquired in their country of birth; numbers are increasing over time
  - Most do not know their status
  - Even for known carriers, management is erratic
- **Ticking time bomb** for these people, their susceptible contacts, and public health because of risk of transmission and progression to liver cancer & cirrhosis
Summary (2 of 2)

- New strategies & programs are needed in the US to implement CDC recommendations to:
  - Identify persons with chronic hepatitis infection
  - Ensure appropriate management of cases and contacts
- US engagement in global hepatitis control programs promotes domestic and global health
Possible Future Directions

- Novel comprehensive strategies, e.g., family-oriented approaches
  - Counseling and testing
  - Preventing Transmission
    - Vaccine for household, sexual, and injection drug use contacts
    - Perinatal case management
  - Management of chronic infection
- Engagement of many partners (community, business, healthcare providers, etc.)
- Resources to implement strategies
Thank You!