Issues Related to the Prevention and Control of Hepatitis B Virus (HBV) Infection in the U.S.

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IOM Orientation - December 4, 2008

"The findings and conclusions in this presentation are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention."
Outline

• **Key features of HBV infection**
• General epidemiology based on different data sources to guide and evaluate prevention services
• Strategies for preventing new HBV infections
• Strategies for reducing morbidity and mortality from chronic HBV infection
# Features of Newly Acquired HBV Infection

<table>
<thead>
<tr>
<th>Feature</th>
<th>Details</th>
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<tbody>
<tr>
<td><strong>Incubation period</strong></td>
<td>Mean: 60-90 days</td>
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<td>Range: 45-180 days</td>
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<tr>
<td><strong>Fulminant liver failure</strong></td>
<td>1-2% of symptomatic cases</td>
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<tr>
<td><strong>Case fatality rate</strong></td>
<td>Overall: 0.5-1%</td>
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Outcome of HBV Infection by Age at Infection

15-25% of infants who acquire chronic HBV infection will die prematurely from HBV-related chronic liver disease.
HBV Infection and Immunity

• To cause chronic infection, HBV must avoid both innate and acquired host immune defenses
  - Type I interferons
    • HBV core & polymerase proteins inhibit interferons
  - Immune recognition of viral antigens by major histocompatibility complex (MHC) peptides
    • HBeAg can cross the placenta and induce tolerance to itself and related HBV proteins

• Therefore, acquired humoral immunity (from immunization) with antibodies targeted to HBV surface protein is the best protection
Outline

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Global Disease Burden

- Estimated 2 billion people infected with HBV
- More than 350 million have chronic HBV infection
- Estimated 500-700K HBV-related deaths/year
- Almost 90% of the world's population live in areas where the prevalence of chronic HBV infection was high or moderate prior to immunization
U.S. Immigration since 1820

Decade

Number (millions)

Africa
Asia / Pacific
LatAm / Caribb
Mexico
Canada
Europe

Source: Yearbook of Immigration Statistics, 2004
Disease burden in the United States

- National Health and Nutrition Examination Survey (NHANES) 1999–2004 estimates:
  - Prevalence of lifetime HBV infection (presence of markers of resolved or active HBV infection) in the U.S. pop. - 4.8% (95% CI 4.2%-5.5%)
  - HBsAg prevalence 0.3% (95% CI 0.2% - 0.4%)
NHANES: Limitations

- Excludes incarcerated and homeless persons
- Prevalence estimates are less precise for certain populations like Asian-American & Pacific Islanders
- Cross-sectional design prevents determination of sources of infection for individuals
- Possible under-reporting of injection drug use and other risk behaviors
Decline in New Cases of Acute Hepatitis B with Increased Vaccination

Vaccine for certain groups (1982)

Recombinant vaccine licensed (1986)

All Infant Immunization (1991)

All Adolescent Immunization (1995)

All birth dose (2005)
Rapid Increase in Hepatitis B Vaccination Coverage 19-35 Months of Age (US)

- Success factors
  - All infants strategy
  - Routine immunization schedule
  - Large increase in federal support
    - Vaccine for Children, 1993
    - 42% of birth cohort

HBV Vaccine Coverage

- 0% 8% 16% 37% 64% 82% 84% 87% 88% 90% 89% 90% 92%
Incidence of Acute Hepatitis B, by Age, United States, 1990-2006

Reported cases per 100,000

- <15 yrs
- 15 - 24 yrs
- 25 - 44 yrs
- 45+ yrs

Year:
- 1990
- 1992
- 1994
- 1996
- 1998
- 2000
- 2002
- 2004
- 2006
Reported Risk Factors for Acute Hepatitis B, United States, 2001-2005

- Heterosexual (33%)
- MSM (23%)
- IDU (12%)
- Other (5%)
- No Identified Risk (27%)

1 Other: Household contact, institutionalization, hemodialysis, blood transfusion, occupational exposure
Source: Sentinel Counties Study of Acute Viral Hepatitis, CDC
Estimated Age at Infection of Persons With Chronic HBV Infection Before Childhood Vaccination, United States

Newborn 18%
Children 18%
Adolescent 6%
Adult 59%

Sources: National Health and Nutrition Examination Survey III
Pediatrics 1992;89:269-73
Pediatrics 1995;96:1113-6
Estimated New Chronic HBV Infections by Place of Acquisition, United States, 1990-2005

- Immigrants from other countries
- United States
Overall Challenges due to Population Trends

• Ongoing immigration from intermediate and high HBV-endemic countries

• Successful case management for immigrant populations requires addressing
  - Culture and customs
  - Language barriers
  - Access to health care

• Support for immunization and disease reduction globally will reduce disease burden in the U.S.
Burden of Chronic HBV Infection
United States

- Conservative estimate of 1.0 - 1.4 million prevalent infections but **may be up to 2 million**
- ~45,000 new cases of chronic HBV infection
  - ~40,000 (90%) are foreign born
  - >50% are **Asian-Americans**
  - Many are unaware of infection
- Improved therapies increase potential benefit of counseling and testing programs
- CDC guidelines for chronic HBV screening and referral
National Chronic Hepatitis Surveillance

- Very high volume
- Widely variable in quality
- Essentially unfunded system
Data Sources for Directing State and Local Prevention

- Surveillance data maintained in chronic hepatitis B registries at state and local health departments
- Outbreak investigations
- Mortality data
- Cancer registries
- Patient care populations
  - Population-based vs. convenience sample
  - Private insurance vs. uninsured
  - Specialty vs. primary care
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Activities Supporting Prevention of Hepatitis B Infection

- Conduct surveillance and outbreak investigations
- Immunization
- Education for prevention of exposures
- Identify chronically infected persons and refer to treatment and care
- Prevention research
Primary Prevention of HBV Transmission

• Immunization
• Decrease transmission from risk activities - IDU, high risk sex
• Reduce nosocomial, occupational, transfusions and transplant transmission
Hepatitis B Vaccines

• Safe, immunogenic, and effective protection against acute HBV and chronic HBV
  • 85->95% efficacy with anti-HBs titers>10 mIU
• Long-term protection despite decline in anti-HBs titers (need for boosters will require research)
• Need measurable correlates of long term protection
Factors Associated with Decreased Immunogenicity of Hepatitis B Vaccine

- Age
- Host immune and other genetic factors
- Immunosuppressive illnesses (HIV infection, chronic liver disease, chronic renal failure, diabetes)
- Obesity
- Smoking
Long-Term Immunogenicity & Efficacy: Children & Adults

- Alaska:
  - Alaskan Native children, adolescents, and adults
    - Fiore, Pediatrics 2007;120:373-81
- Micronesia:
  - 105 adolescents followed up 15 years after vaccination as infants
    - Bialek, Ped Infect Dis J 2008; 27: 881-5
- Other and ongoing studies
US Strategies to Eliminate HBV Transmission

- Universal infant vaccination (1991)
- Catch-up vaccination
  - adolescents 11-12 years (1995)
  - all persons <19 years (1999)
  - Adults at risk for HBV (1982)
- Universal birth dose (2005)
- Universal vaccination in settings serving adults at high risk (e.g. MSM, STD, IDU, contacts, HCW, dialysis patients, HIV+) (2006)
2005 ACIP Hepatitis B Vaccine Recommendations for Infants, Children, and Adolescents

- Past focus on increased maternal screening
- New focus on hospital as safety net to eliminate perinatal (as well as early childhood) hepatitis B transmission through use of standard orders for
  - universal birth dose administration
  - universal verification of maternal HBsAg screening
- Associated with higher rates of on-time completion of hepatitis B vaccine series as well as for other vaccines
- New recommendation to refer HBV-infected mothers for medical care
Estimated New Perinatal Chronic HBV Infections
United States

Program successes:
- >85% pregnant women screened for HBsAg
- >85% decline in perinatal chronic infections

Program challenges:
- ~24,000 HBV+ preg. women (1/2 identified)
- Not all receive public health management
- 900 infants develop chronic HBV
  - Testing omissions, failures
- 100-150 infants at risk for HBV-mortality

Improved prevention can protect all children
Ongoing and Future Considerations for Perinatal HBV Prevention

- **Ongoing need for prevention programs**
  - number of HBsAg-positive mothers increasing as a result of immigration from countries with high endemicity

- **Future considerations:**
  - Improve maternal referrals for care
  - Role of antivirals in perinatal HBV prevention
  - Evaluate the need for booster doses
  - Ongoing and expanding role of health departments
### Hepatitis B Vaccine Coverage
#### Is Lowest for Adults with Behavioral Risks

<table>
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<tr>
<th>Group</th>
<th>Coverage</th>
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<tr>
<td>Children (19-35 mos.)</td>
<td>92-93%</td>
</tr>
<tr>
<td>Adolescents age 13 yrs</td>
<td>50-60%</td>
</tr>
<tr>
<td>Adults -(self reported, NHIS)</td>
<td>30-45%</td>
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<tr>
<td>Adults at risk for infection</td>
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<tr>
<td>Occupationally-exposed workers</td>
<td>95%</td>
</tr>
<tr>
<td>Dialysis patients</td>
<td>56%</td>
</tr>
<tr>
<td>Men who have sex with men</td>
<td>16%</td>
</tr>
<tr>
<td>Injection drug users</td>
<td>6%</td>
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<tr>
<td>STD clinic clients</td>
<td>10%</td>
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**Adults represent 95% of new HBV infections (2006)**
Universal Hepatitis B vaccination recommended for settings serving adults at risk:

- STD Clinics
- HIV testing/care
- Correctional facilities
- Substance abuse treatment
- Other
Barriers to HBV Vaccination for Adults

- Cost of vaccine purchase and administration
- Provider priority and training
- Patient/client concerns
  - Perception of personal risk
  - Willingness to disclose risk behaviors
  - Vaccine safety
- Insurance reimbursement
Adult Hepatitis B Vaccination Initiative

- No federal program to support adult vaccination

- Increased availability of general immunization funds (Section 317)
  - Savings from changes in ordering/distribution
  - Increases in Congressional funding
  - Funds available only for purchase of adult hepB vaccine

- 2008 - Distributed $20M to 51 project areas

- FY 2009 - Distributed $16M for adult hepB vaccination

- Future funding uncertain
Non-hospital healthcare-associated HBV infection

- Failures to adhere to enhanced infection control precautions caused outbreaks in hemodialysis settings
- Injection safety (or lack of) have contributed to outbreaks in outpatient settings
- At least 15 outbreaks of acute HBV in nursing homes/extended living facilities in the last 10 years (case fatality rate ~ 4%)
- Poor infection control practices when performing blood glucose monitoring caused outbreaks in long-term care settings
- These outbreaks continued despite available recommendations
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Secondary Prevention
Prevention of Disease and Death

- Identify, test, counsel, medical management
- Includes access to care
- Linkage to care
- Provision of therapy
- Adherence to therapy
- Ancillary services

- What are the barriers and facilitators to each of these steps?
Reasons to detect and control chronic liver disease

- Medical management
  - Evaluate for chronic liver disease
  - Treatment if indicated
  - Substance abuse treatment (alcohol, drugs) if appropriate
  - Immunization (HAV, influenza, pneumonia)

- Counsel to prevent disease transmission
  - Household contacts
  - Sexual contacts
  - Drug use contacts
Recommendations for Identification and Public Health Management of Persons with Chronic HBV Infection

- Testing recommendations
  - Populations with >2% prev
    - Foreign born- (e.g. Asia, Africa)
    - MSM, IDU
    - HIV
  - Persons with certain conditions
    - Immunosuppressed
    - Elevated liver enzymes

- Management guidance
  - Patient counseling
  - Contact management
    - Screening
    - Vaccination
  - Care referral
Outstanding Issues

• Improve and expand national surveillance for HBV
• Assess transmission in focused settings (health care, IDU, and other outbreak situations)
• Continued focus on infant, child, and adult immunization
• Expand testing/screening programs and contact management
• Expand provider and patient education
• Improve medical management of chronic hepatitis B
• Continue long-term studies of vaccine immunogenicity
• Research into host genetic factors associated with both:
  - susceptibility to transmission and progression as well as
  - responses to vaccine and therapies