HIV, Hepatitis and Women
What Do We Know – What Do We Need To Know

Sally L. Hodder M.D.
November 6, 2015
Disclosures

• Consulting
  • BMS
  • Gilead Sciences
  • Janssen
  • Viiv

• Stock Options
  • Merck (Spouse)
Overview

HIV
• The US Epidemic (Then and Now)
• Perinatal Management Issues
• Prevention

Hepatitis C
• The US Epidemic (Then and Now)
• Perinatal Management Issues
• Prevention

Hepatitis B
• The US Epidemic Prevention
• Perinatal Management Issues
• Prevention

• Conclusions
Rates of Diagnoses of HIV Infection among Adult and Adolescent Females, 2013—United States and 6 Dependent Areas

N = 9,479            Total rate = 6.9

Note. Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. All displayed data have been statistically adjusted to account for reporting delays, but not for incomplete reporting.
Diagnoses of HIV Infection and Population among Adult and Adolescent Females, by Race/Ethnicity, 2010—46 States

Diagnoses of HIV Infection
N=9,868

- American Indian/Alaska Native: 1%
- Asian: 1%
- Black/African American: 1%
- Hispanic/Latino*: <1%
- Native Hawaiian/Other Pacific Islander: 4%
- White: 64%
- Multiple races: 18%

Female Population, 46 States
N = 122,842,284

- American Indian/Alaska Native: 1%
- Asian: 1%
- Black/African American: 1%
- Hispanic/Latino*: <1%
- Native Hawaiian/Other Pacific Islander: 12%
- White: 68%
- Multiple races: 14%

Note: Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. All displayed data have been statistically adjusted to account for reporting delays, but not for incomplete reporting.

* Hispanics/Latinos can be of any race.
Diagnoses of HIV Infection among Adult and Adolescent Females, by Race/Ethnicity and Transmission Category 2013—United States and 6 Dependent Areas

Note. Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. All displayed data have been statistically adjusted to account for reporting delays and missing transmission category, but not for incomplete reporting.

- Hispanics/Latinos can be of any race.
- Heterosexual contact with a person known to have, or to be at high risk for, HIV infection.
- Includes blood transfusion, perinatal exposure, and risk factor not reported or not identified.
Southeast Indiana: Recent Scott County HIV Outbreak
Southeast Indiana: Recent Scott County HIV Outbreak

• Investigation initiated January 2015 after 11 cases reported
  • Scott County has ~4200 residents and ≤ 5 cases HIV annually

• 181 cases reported to date
  • Age 18–57 years (mean = 35 years)
  • 54.8% male.
  • 80.0% reported injection drug use (3.0%) have reported no injection drug use
  • 84% coinfection with hepatitis C.

• Scott, Indiana:
  • 8.9% unemployment
  • 21.3% < high school education
  • 19% live below the poverty line
HIV Prevalence in Adults
Selected US Cities and African Countries

HIV Prevalence in Adults from Selected Countries in Sub-Saharan Africa and Subpopulations in the United States.
New HIV Testing Algorithm

+HIV 1 & 2 4\textsuperscript{th} generation immunoassay

- HIV-1 Ab +
- HIV-2 Ab +
- HIV ½ Ag+

RNA

RNA+: Acute HIV
RNA-: HIV Neg

http://www.cdc.gov/hiv/pdf
HAART Impact on Survival

Excellent Treatment Options in 2015

NRTIs
- Abacavir (ABC)
- Didanosine
- Emtricitabine (FTC)
- Lamivudine (3TC)
- Stavudine
- Tenofovir (TDF)
- Zidovudine
- Truvada (TDF+FTC)
- Epzicom (ABC+3TC)

NNRTIs
- Delavirdine
- Efavirenz
- Nevirapine
- Etravirine
- Rilpivirine

Protease Inhibitors (PIs)
- Atazanavir
- Darunavir
- Fosamprenavir
- Indinavir
- Lopinavir
- Nelfinavir
- Saquinavir
- Tipranavir

Entry Inhibitors
- Enfuvirtide
- Maraviroc

Integrase Inhibitors
- Raltegravir
- Elvitegravir
- Dolutegravir

NRTI = nucleoside analog reverse-transcriptase inhibitor; NNRTI = non-nucleoside reverse transcriptase inhibitor.
Single Tablet, Once-Daily HIV Regimens

• Currently available
  • Efavirenz/TDF/FTC
  • Rilpivirine/TDF/FTC
  • Elvitegravir/cobicistat/TDF/FTC
  • Dolutegravir/ABC/3TC
  • Elvitegravir/cobicistat/TAF/FTC

• In advanced development
  • Darunavir/cobicistat/TAF/FTC
Mother-to-Child Transmission

• 25–35% of HIV positive pregnant women not on antiretroviral treatment will pass HIV to their newborns

• In the absence of breastfeeding:
  • 30% of transmission in utero
  • 70% of transmission during the delivery
  • Meta-analysis showed 14% transmission with breastfeeding and 29% transmission with acute maternal HIV infection or recent seroconversion

Estimated Number of Perinatally Acquired AIDS Cases, by Year of Diagnosis, 1985-2004 – United States

- CDC HIV screening Recs
- PACTG 076 & USPHS ZDV Recs

~95% reduction

Year of Diagnosis

Number of cases
Change in HIV MTCT Over a Decade in the U.S.

<table>
<thead>
<tr>
<th>Year</th>
<th>Study</th>
<th>Transmission Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1993</td>
<td>WITS</td>
<td>24.5%</td>
</tr>
<tr>
<td>1994</td>
<td>PACTG 076</td>
<td>7.6%</td>
</tr>
<tr>
<td>1997</td>
<td>PACTG 185</td>
<td>5.0%</td>
</tr>
<tr>
<td>1999</td>
<td>WITS</td>
<td>3.3%</td>
</tr>
<tr>
<td>2001</td>
<td>PACTG 247</td>
<td>2.0%</td>
</tr>
<tr>
<td>2002</td>
<td>PACTG 316</td>
<td>1.5%</td>
</tr>
<tr>
<td></td>
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</tr>
</tbody>
</table>

**AZT Era**

**Combination ARV Era**
Perinatally Acquired HIV Infections in Children Born During 2011—United States and 6 Dependent Areas

N = 53

Note: Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. All displayed data have been statistically adjusted to account for reporting delays, but not for incomplete reporting.
Time of Maternal HIV Testing among Infants with Perinatally Acquired HIV Infection
Birth Years 2008–2011—United States

N = 327

- 38% Before pregnancy
- 19% During pregnancy
- 10% At birth
- 10% After birth
- 23% Unknown

Note. Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. All displayed data have been statistically adjusted to account for reporting delays, but not for incomplete reporting.
Interventions to Reduce Mother-to-Child Transmission

• HIV testing in pregnancy
• Antenatal care
• Antiretroviral agents – Start as soon as possible after obtaining resistance testing
• Obstetric interventions
  • Avoid amniotomy
  • Avoid procedures: Forceps/vacuum extractor, scalp electrode, scalp blood sampling
  • Restrict episiotomy
  • Elective cesarean section (HIV RNA >1000 copies/ml)
• Newborn feeding: Formula
## Initial ART for ARV-Naive Pregnant Women

### Preferred 2-NRTI Backbone Regimens

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Comments</th>
</tr>
</thead>
</table>
| ABC/3TC          | • Available as FDC, can be given once daily  
• Potential HSR: ABC should not be used in patients who test positive for HLA-B*5701 because of risk of hypersensitivity reaction  
• Not recommended with ATV/r or with EFV if pretreatment HIV RNA >100,000 copies/mL |
| TDF/FTC or TDF + 3TC | • Available as FDC, can be given once daily  
• TDF has potential renal toxicity, use with caution in patients with renal insufficiency |
| ZDV/3TC          | • Most experience for use during pregnancy  
• Available as FDC. Twice-daily administration  
• Higher risk of hematologic toxicity |
## Initial ART for ARV-Naive Pregnant Women

### Preferred PI Regimens

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Comments</th>
</tr>
</thead>
</table>
| ATV/r + preferred 2-NRTI backbone | • Once daily administration  
|                                 | • Extensive experience in pregnancy  
|                                 | • Maternal hyperbilirubinemia                             |
| DRV/r + preferred 2-NRTI backbone | • Better tolerated than LPV/r.  
|                                 | • PK data available. Increasing experience in pregnancy  
|                                 | • Must be used twice-daily in pregnancy.                  |

DHHS Perinatal Guidelines August 2015
### Initial ART for ARV-Naive Pregnant Women

#### Preferred NNRTI Regimen

<table>
<thead>
<tr>
<th>EFV + preferred 2-NRTI backbone</th>
<th>Comments</th>
</tr>
</thead>
</table>
| **Note:** May be initiated after the first 8 weeks of pregnancy | • Birth defects in primates; risk in humans is unclear.  
• Postpartum contraception must be ensured. |

DHHS Perinatal Guidelines August 2015
## Initial ART for ARV-Naive Pregnant Women

### Preferred Integrase Inhibitor Regimen

<table>
<thead>
<tr>
<th>RAL + preferred 2-NRTI backbone</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• PK data available and increasing experience in pregnancy.</td>
</tr>
<tr>
<td></td>
<td>• Rapid viral load reduction.</td>
</tr>
<tr>
<td></td>
<td>• Useful when drug interactions with PI regimens are a concern.</td>
</tr>
<tr>
<td></td>
<td>• Twice-daily dosing required.</td>
</tr>
</tbody>
</table>

DHHS Perinatal Guidelines August 2015

August 2015
Antiretroviral Pregnancy Registry: Birth Defects With First Trimester Exposure

- Enrolls ~ 1300 women exposed to ART each year (80% US)
- 18,488 live births with follow-up data through July 2013
  - 7790 with first trimester exposure
- Overall birth defect prevalence comparable to CDC population–based surveillance data: 2.9 per 100 live births vs 2.7
- Commonly used PIs not associated with increased birth defect rate
- Register pregnant women at http://www.APRegistry.com

<table>
<thead>
<tr>
<th>Drug</th>
<th>Defects/Live Births, n ( &gt; 200 First Trimester Exposures)</th>
<th>Prevalence, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NRTIs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABC</td>
<td>27/905</td>
<td>3.0 (2.0-4.3)</td>
</tr>
<tr>
<td>ddI</td>
<td>20/416</td>
<td>4.8 (3.0-7.3)</td>
</tr>
<tr>
<td>FTC</td>
<td>34/1400</td>
<td>2.4 (1.7-3.4)</td>
</tr>
<tr>
<td>3TC</td>
<td>136/4360</td>
<td>3.1 (2.6-3.7)</td>
</tr>
<tr>
<td>d4T</td>
<td>21/805</td>
<td>2.6 (1.6-4.0)</td>
</tr>
<tr>
<td>TDF</td>
<td>46/1982</td>
<td>2.3 (1.7-3.1)</td>
</tr>
<tr>
<td>ZDV</td>
<td>129/4000</td>
<td>3.2 (2.7-3.8)</td>
</tr>
<tr>
<td>PIs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATV</td>
<td>19/878</td>
<td>2.2 (1.3-3.4)</td>
</tr>
<tr>
<td>DRV</td>
<td>5/212</td>
<td>2.4 (0.8-5.4)</td>
</tr>
<tr>
<td>IDV</td>
<td>7/289</td>
<td>2.4 (1.0-4.9)</td>
</tr>
<tr>
<td>LPV</td>
<td>26/1125</td>
<td>2.3 (1.5-3.4)</td>
</tr>
<tr>
<td>NFV</td>
<td>47/1211</td>
<td>3.9 (2.9-5.1)</td>
</tr>
<tr>
<td>RTV</td>
<td>52/2260</td>
<td>2.3 (1.7-3.0)</td>
</tr>
<tr>
<td>NNRTIs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EFV</td>
<td>18/766</td>
<td>2.3 (1.4-3.7)</td>
</tr>
<tr>
<td>NVP</td>
<td>31/1061</td>
<td>2.9 (2.0-4.1)</td>
</tr>
<tr>
<td>INSTIs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RTV</td>
<td>Insufficient data</td>
<td></td>
</tr>
</tbody>
</table>
Controversial Association of Antiretroviral Therapy and Preterm Birth

- Multiple observational studies through 2008 detected small increases in preterm birth with combination antiretroviral therapy (cART):
  - Odds ratio 1.2–1.8 in largest studies.\(^1-4\).

- Meta-analysis of 14 studies demonstrated cART during pregnancy did not increase the overall risk of preterm birth.\(^5\)
  - A subgroup analysis demonstrated small increased risk of preterm birth with Protease Inhibitor-based cART:
    - Odds Ratio 1.35 [95% CI 1.08–1.7]

- Mma Bana Study of HAART for PMTCT in Botswana, N = 530
  - PI-based HAART (ZDV/3TC + LPV/RTV) associated with 2-fold higher rate of preterm delivery than triple-NRTI HAART, but no increase in infant morbidity or mortality through 6 mos of life\(^6\)

Barriers to Elimination of MTCT

- Failure to diagnose HIV in pregnancy
- Acute infection in pregnancy
- Adherence issues
- Drug resistance
- Mistakes in ARV management
  - Stopping ART in the 1st trimester
  - Changing ART regimens in 1st trimester
  - Pharmacokinetic issues
  - Lack of infant prophylaxis
- Breastfeeding
HIV Incidence in the U.S. 25 Years of Data

≥ 40,000 infections annually despite improvements in therapy!

## Recent HIV Pre-Exposure Prophylaxis (PrEP) Studies in Women

<table>
<thead>
<tr>
<th>Study</th>
<th>Agent</th>
<th>Efficacy % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FemPrEP¹</td>
<td>Oral TDF/FTC</td>
<td>- Study Stopped</td>
</tr>
<tr>
<td>Partners PrEP²*</td>
<td>Oral TDF</td>
<td>62% (34, 78)</td>
</tr>
<tr>
<td>Partners PrEP²*</td>
<td>Oral TDF/FTC</td>
<td>73% (49, 85)</td>
</tr>
<tr>
<td>TDF2³</td>
<td>Oral TDF FTC</td>
<td>62.6% (21.5, 83.4)</td>
</tr>
<tr>
<td>VOICE⁴</td>
<td>Oral TDF/FTC</td>
<td>- Arm stopped</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- No efficacy</td>
</tr>
</tbody>
</table>

*Partners PrEP: TDF Arm Efficacy: 68% in women; 55% in men
TDF/FTC Arm Efficacy: 62% in women; 83% in men

1. FHI360, Press Release 4/18/11
4. Mezzaros J. CROI 2014
PrEP: Current Status in US

• Truvada® (tenofovir+emtricitabine) approved by FDA for pre-exposure prophylaxis of HIV in July 2012

• Baseline Patient Assessment
  • Acute or Chronic HIV Infection
  • Pregnancy
  • Renal Function
  • STDs
  • Harm Reduction and Adherence Counseling

• Concerns remain
  • Emergent resistance
  • Long-term toxicity
  • Behavior disinhibition
  • Cost
# CDC Guideline: Follow-up and Monitoring

<table>
<thead>
<tr>
<th>Follow-up</th>
<th>At Least Every 3 Months</th>
<th>After 3 Months &amp; at Least Every 6 Months Thereafter</th>
<th>At Least Every 6 Months</th>
<th>At Least Every 12 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All patients</strong></td>
<td>HIV test</td>
<td>Assess renal function</td>
<td>Test for bacterial STIs</td>
<td>Evaluate need to continue PrEP</td>
</tr>
<tr>
<td></td>
<td>Medication adherence counseling</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Behavioral risk reduction support</td>
<td></td>
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<tr>
<td></td>
<td>Adverse event assessment</td>
<td></td>
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<tr>
<td></td>
<td>STI symptom assessment</td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Women</strong></td>
<td>Pregnancy test (where appropriate)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HBsAg+</strong></td>
<td></td>
<td></td>
<td>HBV DNA by quantitative assay*</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>*Every 6-12 mos.</td>
<td></td>
</tr>
</tbody>
</table>

*Every 6-12 mos.*

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Overview

HIV
  • The US Epidemic (Then and Now)
  • Perinatal Management Issues
  • Prevention

Hepatitis C
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Hepatitis B
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• Conclusions
HCV Prevalence by Selected Groups in the United States

- Hemophilia: 87%
- Injecting Drug Users: 79%
- Hemodialysis: 10%
- STD Clients: 6%
- General Population Adults: 3.5%
- Surgeons: 2%
- Pregnant Women: 1%
- Military Personnel: 0.3%

Centers for Disease Control and Prevention, 2003.
Incidence of acute hepatitis C among persons aged ≤30 years
Kentucky, Tennessee, Virginia, and West Virginia, 2006–2012

Zibbel, et al. MMWR May 8, 2015
Acute Hepatitis C cases 2006-2012
Kentucky, Tennessee, Virginia, West Virginia
n=1,377

• 44.8% < 30 years of age
• Median age of persons with acute infection was 25 years
• Among new cases in persons aged ≤30 years
  • Nonurban: 78.4% non-Hispanic whites; 49.5% males
  • Urban: 82.7% non-Hispanic whites, 51.5% males.
• 73.1% reported intravenous drug use (IDU)

Zibbel et al, MMWR May 8, 2015
Percentage of all admissions to substance abuse treatment centers for persons 12–29 years (N = 217,789) attributed to injection of opioids and other drugs in Kentucky, Tennessee, Virginia, and West Virginia, 2006–2012

Zibbel, et al. MMWR May 8, 2015
Chronic HCV is #1 reason for liver transplantation in the U.S.

Mother to Child Transmission of HCV

- Leading cause of childhood HCV infection
- Up to 4,000 new cases each year in the U.S.
- 40-70% of HCV-infected pregnant women do not initially report major risk factors for HCV
- ~85%-95% of HCV-infected children have not been identified*
- Transmission rate variable, and is higher in moms with HIV co-infection

Most Recent Estimates of MTCT Risk

- Review and meta-analysis of observational studies published since the last review in 2001
- Goal: define proportion of infants diagnosed with HCV at ≥18 months born to HCV AB+ and RNA+ women
- Estimates of HCV vertical transmission:

<table>
<thead>
<tr>
<th></th>
<th>HIV- moms</th>
<th>HIV+ moms</th>
</tr>
</thead>
<tbody>
<tr>
<td>range of MTCT risk</td>
<td>1.1%-10.7%</td>
<td>4.2%-28.5%</td>
</tr>
<tr>
<td>pooled risk (all studies)</td>
<td>5.8%</td>
<td>10.8%</td>
</tr>
</tbody>
</table>

Effect of Interventions to Reduce HCV Mother to Child Transmission

- Systematic review of primarily observational studies*
- Assessed mode of delivery, labor management practices and breastfeeding
- No intervention clearly reduced risk of MTCT
- Prolonged rupture of membranes, internal fetal monitoring, HIV co-infection, higher viral load seemed to be associated with higher risk
- Avoidance of breastfeeding does not seem to be indicated for reducing transmission risk

Effect of Maternal HCV on Pregnancy Outcomes

- Retrospective study, 2005-08
- >2 million births in CA
- HCV/HIV coinfection excluded
- HCV+ moms had higher rates of:
  - prematurity OR 1.44 (1.28-1.61)
  - fetal anomalies OR 1.37 (1.19-1.77)
  - cesarean section OR 1.30 (1.10-1.54)
- Term babies had lower birth weight, p<0.001
- No data on perinatal transmission

Long-term Outcome of HCV MTCT

• Most children asymptomatic with mild liver abnormalities
• Both chronic and transient infection occurs
• Studies following patients for 10 to 20 years after perinatal acquisition show that 5%-12% have Significant fibrosis and 5% have cirrhosis*

Consequences of Failure to Identify HCV+ Mothers

- Methadone program in Australia showed that more than 70% of the pregnant women were HCV+, but <20% of babies examined for HCV
- Due to lack of awareness of HCV in this high-risk population, many of these children lost to follow-up and not diagnosed

Anti-HCV Antibody Testing for HCV

ELISA screening tests

- Detect circulating HCV antibodies
- Sensitivity: 97% to 100%
- Positive predictive value
  - 95% with risk factors and elevated ALT
  - 50% without risk factors and normal ALT

<table>
<thead>
<tr>
<th>False Positives More Likely in:</th>
<th>False Negatives More Likely in:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with low risk of HCV infection</td>
<td>Severely immunosuppressed patients</td>
</tr>
<tr>
<td></td>
<td>Transplantation recipients</td>
</tr>
<tr>
<td></td>
<td>Patients with chronic renal failure on dialysis</td>
</tr>
<tr>
<td></td>
<td>HIV-positive patients</td>
</tr>
</tbody>
</table>

Testing Strategy in Clinical Practice: Diagnosis of Chronic HCV Infection

Immunocompetents

HCV antibody screening

If positive

- HCV RNA qualitative
- HCV RNA quantitative

HCV Genotype
A Negative Anti-HCV Test Does Not Exclude HCV Infection in Patients with Suspected Liver Disease in:

- Acute HCV infection
- HIV infection
- Chronic hemodialysis

In immunosuppressed individuals, HCV RNA testing should be performed regardless of a negative anti-HCV test
The management of HCV coinfection in pregnancy is complex

- Currently approved medications for HCV not recommended during pregnancy, and no safety data exist for use of the recently approved HCV oral medications in pregnant women.

- Expert advice should be sought to assess stage of fibrosis

- Decisions concerning mode of delivery should be based on standard obstetric indications alone; HCV coinfection does not necessitate cesarean delivery, if not otherwise indicated.
Hepatitis C – Considerations in Infants

• Infants born to women with HCV infection should be evaluated for HCV infection with anti-HCV antibody testing after age 18 months.
• Infants who screen positive should undergo confirmatory HCV RNA testing.
• HCV RNA virologic testing can be done after age 2 months, if earlier diagnosis is indicated.
  • Because HCV viremia can be intermittent, 2 negative HCV RNA test results at or after age 2 months, including 1 test at or after age 12 months, are needed to definitively exclude HCV infection.
  • Children are considered to be HCV infected if they have 2 or more positive HCV RNA results or are HCV antibody positive beyond age 18 months.
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Acute Hepatitis B: 2009-2014

Rates of Acute Hepatitis B Infection, Hamilton County and Ohio, 2009-2014

<table>
<thead>
<tr>
<th>Year of Report</th>
<th>Rate per 100,000 Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>2.7</td>
</tr>
<tr>
<td>2010</td>
<td>3.7</td>
</tr>
<tr>
<td>2011</td>
<td>3.9</td>
</tr>
<tr>
<td>2012</td>
<td>4.7</td>
</tr>
<tr>
<td>2013</td>
<td>7.6</td>
</tr>
<tr>
<td>2014</td>
<td>10.1</td>
</tr>
</tbody>
</table>

Hamilton County
Ohio

2009: 3.3
2010: 6.5
2011: 6.8
2012: 7.0
2013: 12.3
2014: 17.1
Risk Factors Associated With Acute HBV Infection in the United States (2006)

- Unknown: 57%
- Multiple Sex Partners: 34%
- IDUs: 16%
- MSM: 15%
- Iatrogenic Related to Occupation: 10%
- Household Contact: 5%
- Unknown: 2%

Risk factors do not total 100% because of multiple risk factors in some patients.

Acute Hepatitis B Virus Infection with Recovery

Typical Serologic Course

Weeks after Exposure
Progression to Chronic Hepatitis B Virus Infection
Typical Serologic Course

<table>
<thead>
<tr>
<th>Titre</th>
<th>Weeks after Exposure</th>
<th>Years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute (6 months)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HBeAg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>anti-HBe</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Chronic (Years)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HBsAg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total anti-HBc</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IgM anti-HBc</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Typical Serologic Course

- Acute (6 months)
- Chronic (Years)
- HBeAg
- anti-HBe
- HBsAg
- Total anti-HBc
- IgM anti-HBc

Weeks after Exposure:

- 0
- 4
- 8
- 12
- 16
- 20
- 24
- 28
- 32
- 36
- 40
- 44
- 48
- 52

Years:
Outcome of Hepatitis B Virus Infection by Age at Infection

Chronic Infection (%)

Symptomatic Infection (%)

Age at Infection

- Birth
- 1-6 months
- 7-12 months
- 1-4 years
- Older Children and Adults
Long-term Outcome of HBV MTCT

• Up to 90% of neonates born to moms with acute HBV or HbsAg & HBeAg become infected.
• Most infants are asymptomatic but become chronic carriers due to failure to make HBsAB or cell-mediated responses.
• 95% will develop chronic disease, with 40% lifetime risk of cirrhosis or hepatocellular carcinoma.
Prevention of HBV vertical transmission

passive + active immunization provides 95% efficacy

Birth

Hepatitis B vaccine + HBIG

1 month old

Hepatitis B vaccine

6 months old

Hepatitis B vaccine
Hepatitis B Virus in Pregnancy

- Mode of delivery in HBV-coinfected pregnant women based on standard obstetric indications alone. HBV coinfection does not necessitate cesarean delivery, if not otherwise indicated.
- Within 12 hours of birth, infants should receive hepatitis B immune globulin and should initiate the HBV vaccine series.
  - Timing of later doses in series differs between infants > 2,000 g and < 2,000 g. The regimen is 95% effective in preventing HBV.
  - Post-vaccination testing for anti-HBs and HBsAg should be performed after completion of the vaccine series, at age 9 months to 18 months.
### HBV Immunoprophylaxis Failure in Infant Associated with Maternal HBV DNA Level

<table>
<thead>
<tr>
<th>HBV DNA &lt; 6 Logs</th>
<th>HBV DNA &gt; 6 Logs &lt; 6.99 Logs</th>
<th>HBV DNA &gt; 7 Logs &lt; 7.99 Logs</th>
<th>HBV DNA &gt; 8 Logs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion of Infants with Immunoprophylaxis Failure</td>
<td>0%</td>
<td>3.2%</td>
<td>6.7%</td>
</tr>
</tbody>
</table>

Minimizing Risk of HBV MTCT

- Antiviral therapy to suppress high levels of maternal HBV in the third trimester
  - lamivudine
  - tenofovir
  - telbivudine
- Post-exposure prophylaxis (PEP) to neonate

Hepatitis B Virus in Pregnancy

• All pregnant women should be screened for hepatitis B virus (HBV) and unless they are known to be coinfected or have already been screened during the current pregnancy.

• All pregnant women who screen negative for HBV (surface antigen, core antibody and surface antibody) should receive the HBV vaccine series.

• Women with chronic HBV (or HCV) who have not already received the hepatitis A virus (HAV) vaccine series should be screened for immunity to HAV because they are at increased risk of complications from coinfection with other viral hepatitis infections.

• HAV vaccine series if negative for HAV IgG.
Maternal Risk Factors for HIV, HBV & HCV Are Similar

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>HIV</th>
<th>HBV</th>
<th>HCV</th>
</tr>
</thead>
<tbody>
<tr>
<td>unprotected sex</td>
<td>+</td>
<td>+</td>
<td>+*</td>
</tr>
<tr>
<td>injection drug use</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>tattoos, piercings, needlesticks</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>hemodialysis</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>transfusion/organ transplant</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>foodborne</td>
<td></td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>household contact</td>
<td></td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>institutionalized</td>
<td></td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>

*more common among MSM
Impact of HIV Co-infection with Chronic Viral Hepatitis

• There is bilateral synergy between HIV and chronic viral hepatitis, esp HCV
  • HIV augments the clinical progression of HCV
  • HCV augments the clinical progression of HIV

• For example, if progression to cirrhosis/end-stage liver disease takes ~25-30 years in HCV mono-infection, this typically occurs in ~10-15 years (or faster) in HCV/HIV co-infection

• Urgency to prevent/treat/cure chronic viral hepatitis in HIV co-infected persons
Conclusions

• HIV, Hepatitis B and Hepatitis C are increasing in certain areas and may have dire consequences for mother and infant

• Diagnosis and treatment of these infections (particularly HIV and Hep C) is critically important before pregnancy ensues

• HIV treatment during pregnancy greatly decreases MTCT

• Pregnant women with Hepatitis B or C should be assessed for evidence of chronic liver disease

• Currently, approved agents to treat hepatitis C have not been adequately assessed for safety in pregnancy

• Hepatitis B treatment during the third trimester may be indicated

• All infants born to Hepatitis B infected mothers require immunoprophylaxis
Acknowledgments

• Judith Feinberg MD
• AETC
• Clinical Care Options