Management of HIV on Labor and Delivery

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Disclosures

• I have no disclosures or conflicts of interest.

Learning Objectives

• Identify high-risk women who should be screened again for HIV in the third trimester.
• Counsel pregnant patients with HIV on optimal mode of delivery.
• Utilize available resources for clinical advice.
Outline

- **Perinatal Transmission: Background**
- Preventing Perinatal Transmission
  - Testing
  - Antepartum Treatment
  - Intrapartum Treatment
- Mode of Delivery
- Breastfeeding
- Neonatal Treatment
- Resources for clinical advice

Perinatal transmission: Background

1981: 270 reported cases, 121 died
1982
1983
1984
1985
1986
1987
1990

CDC: occupational exposure precautions for healthcare workers; identifies routes of transmission (blood-borne, sexual), and rules out other routes (casual, food, water, air, surfaces)

CDC reports AIDS in infant after blood transfusion

US Public Health Services: First recommendations for preventing perinatal transmission

HAART standard of care
Management of HIV on Labor and Delivery

Perinatal Transmission

1982: first reported pediatric AIDS cases:
1. Transfusion
2. Perinatal transmission
3. 2 cases: Parents unknown status
4. Mother with risk factors

CDC MMWR December 10, 1982.
CDC MMWR December 17, 1982.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Centers for Disease Control and Prevention
National Center for HIV, STD, and TB Prevention
Atlanta, Georgia  30333

Perinatally Acquired AIDS,* 1985-1998, United States
*Adjusted for reporting delays and unreported mode of HIV exposure.  Data reported through December 1999.

Acquired immunodeficiency syndrome (AIDS) is a specific group of diseases or conditions which are indicative of severe immunosuppression related to infection with the human immunodeficiency virus (HIV).

U.S. HIV and AIDS cases reported through December 1999 Year-end edition Vol. 11, No. 2

HIV/AIDS Surveillance Report
U.S. HIV and AIDS cases reported through December 1998

U.S. Pediatric HIV and AIDS Diagnoses

CDC Data
Question
Which intervention decreases perinatal HIV transmission rates the most?
A. Antiretroviral therapy
B. Scheduled cesarean delivery
C. Avoidance of breastfeeding
D. Treatment of infant

Perinatal HIV Transmission
- Transmission rates
  - pre-ART: 25% (~40% with breastfeeding)
  - With ZDV: 5-8%
  - With ZDV and scheduled CD: 2%
  - VL <1000/ml, <2% risk, even without CD

Timing of MTCT in the HAART era
- 1990-92: 18.1%
  - Antepartum (27%)
  - Intrapartum (73%)
- 1999-2000: 1.6%
  - Antepartum (80%)
  - Intrapartum (20%)
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HIV Testing in pregnancy

HIV Testing Recommendations

• ACOG Recommendations (CO#752, Sept 2018)
  • Screen all pregnant women as early as possible
    • Opt-out approach permitted everywhere in U.S.
  • Repeat testing in third trimester, preferably <36 weeks,
    in at-risk women
  • If unknown status, rapid screening should be done on L&D
    • Results should be available 24h/d, within 1h
HIV Testing Algorithms

• Traditional: Ab screening test (ELISA) with confirmatory Western blot

• Updated guidelines:
  • HIV-1/2 Ag/Ab combination immunoassay ("4th Generation Immunoassay")
  • If positive, differentiate between HIV-1 and HIV-2
  • If indeterminate/negative, HIV NAT (RNA)

CDC 2014: Lab testing for diagnosis of HIV; updated guidelines

Repeat third trimester testing

• Risk factors: (specified in ACOG update 2018)
  • IVDU or sex partner with IVDU
  • Exchange sex for money or drugs
  • Sex partner is HIV infected
  • New or ≥1 sex partner in pregnancy
  • Concerning signs/symptoms
  • Incarcerated
  • Health facility with screen positive incidence of ≥1/1000 pregnant women
  • Geographical

Note: Units for vertical axis are not noted because their magnitude differs for RNA, p24 antigen, and antibody.
Repeat third trimester testing

• Geographical area with high incidence (CDC 2004)

Rapid HIV Testing on L&D

• Unknown HIV status
• Results in <1 hour
• Available 24 hours a day
• Start ART immediately while waiting for confirmatory testing

• The HIV 1/2 antigen-antibody screen can be done in some hospitals within 1 hour
• Other rapid tests are for HIV-1 antibodies only – may require confirmatory testing

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Antepartum Treatment

Zidovudine treatment (antepartum + intrapartum + neonatal x 6 weeks) → 67% reduction in perinatal transmission from 25.5% to 8.3%

Maternal Plasma HIV RNA Level (viral load) at delivery is associated with Perinatal Transmission

Cooper E et al. JAIDS 2002;29:484-94

ART: the earlier the better for MTCT

Mandelbrot et al. CID 2015

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  • Neonatal Treatment
• Resources for clinical advice
Intrapartum management

Topics

• Another plug for Rapid HIV testing!
• Intrapartum treatment
• Mode of delivery
• Unanswered Questions:
  • Mode of delivery with low viral load when on HAART
  • Term PROM
  • PPROM

Intrapartum ARV

• Continue ART through labor/up until CD
• IV ZDV
  • Yes: HIV RNA > 1000 /ml, or unknown
  • No: HIV RNA < 50 /ml (<1% MTCT)
  • Maybe: HIV RNA 50-999/ml (1-2% MTCT)
• Start IV ZDV 3 h before scheduled CD

• CHIP: Only NO if undetectable VL x last 12 weeks,
  AND good adherence to ART throughout pregnancy
  • Also give a single dose of PO Nevirapine
Question

In which scenario is cesarean delivery definitely recommended?

A. Patient has undetectable viral load
B. Patient has viral load of 500 copies/ml and is not in labor
C. Patient has viral load of 1500 copies/ml and is not in labor
D. Patient has viral load of 1500 copies/ml and is in active labor
E. Both (C) and (D)

Mode of delivery - guidelines

- Scheduled CD at 38 w if HIV RNA > 1000/ml
  - If spontaneous labor or ROM, unclear
- If HIV RNA < 1000/ml:
  - If needs CD for other reason, do at normal time
  - Duration of ROM does not increase risk of transmission
  \[\text{VD still ok}\]

USDHHS, Nov 2017
ACOG, 2018

Early studies

- European Mode of Delivery Collaboration\(^1\)
  - RCT of elective CD at 38w vs planned VD
  - 1.8% transmission rate vs. 10.5% (significant)
  - By actual mode of delivery:

<table>
<thead>
<tr>
<th>Actual mode</th>
<th>MTCT rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elective CD</td>
<td>2.4%</td>
</tr>
<tr>
<td>CD after labor or ROM</td>
<td>8.8%</td>
</tr>
<tr>
<td>VD</td>
<td>10.2%</td>
</tr>
</tbody>
</table>

> NS

\(^1\) Lancet 1999; 353:1035.
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Early studies

• International Perinatal HIV Group
  - Meta-analysis of 15 studies

<table>
<thead>
<tr>
<th>Delivery Mode</th>
<th>Overall</th>
<th>No ARV</th>
<th>ARV ante/intra/post</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elective CD</td>
<td>8.4 %</td>
<td>10.4 %</td>
<td>2.0 %</td>
</tr>
<tr>
<td>All others</td>
<td>16.7 %</td>
<td>19.0 %</td>
<td>7.3 %</td>
</tr>
</tbody>
</table>


Unanswered Questions

• Is scheduled CD beneficial in cases of low viral load when on HAART?
• How does duration of ROM affect decision for CD?
• When to deliver in cases of PPROM?

Delivery Mode in era of ART

• 1983 mother-child pairs in HAART era (1/97-5/04)
• Transmission
  - 6.5% NSVD vs 2.5% emergent c/s vs 1.6% elective c/s
  - Undetectable viral load (n=560)
    • Elective c/section (univariate) OR 0.07 (0.02-0.31)
    • Bivariate analysis (adjusted for none vs. any ARV’s) OR 0.52 (0.14-2.03)
  - Women on HAART (n=759)
    • Elective c/section OR 0.64 (0.08-5.37)

European Collaborative Study CID 2005
### Table 1: Mother-to-child HIV transmission in women receiving cART, 2000–2010

<table>
<thead>
<tr>
<th>Variable</th>
<th>(1) Vaginal delivery</th>
<th>(2) Elective cesarean</th>
<th>(3) Nonelective cesarean</th>
<th>(4) Total vaginal</th>
<th>p value (1) vs (2)</th>
<th>p value (1) vs (3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>12,500</td>
<td>1,100</td>
<td>1,400</td>
<td>15,000</td>
<td>0.01</td>
<td>0.00</td>
</tr>
<tr>
<td>CD4 cell count</td>
<td>50–400</td>
<td>500–999</td>
<td>&gt;1,000</td>
<td>Total</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MTCT %</td>
<td>2.6 (1)</td>
<td>5.9 (1)</td>
<td>0.0 (0)</td>
<td>0.5 (0)</td>
<td>1.00</td>
<td>0.39</td>
</tr>
</tbody>
</table>

### Table 2: Maternal complications among women on combination antiretroviral therapy and delivering in 2010–2011.

<table>
<thead>
<tr>
<th>Maternal complication</th>
<th>Vaginal delivery</th>
<th>Elective cesarean</th>
<th>Nonelective cesarean</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delivery mode</td>
<td>n/N</td>
<td>n/N</td>
<td>n/N</td>
<td>n/N</td>
</tr>
<tr>
<td>Cesarean section</td>
<td>7,500</td>
<td>630</td>
<td>134</td>
<td>9,374</td>
</tr>
<tr>
<td>Vaginal delivery</td>
<td>10,000</td>
<td>960</td>
<td>1,386</td>
<td>12,346</td>
</tr>
<tr>
<td>VTE</td>
<td>2.5 (1)</td>
<td>0.0 (0)</td>
<td>0.0 (0)</td>
<td>2.5 (0)</td>
</tr>
</tbody>
</table>

### Risk of Cesarean Delivery for HIV+ Woman

- Maternal complications
  - Fever
  - Infections: wound, UTI, endometritis
  - VTE
  - Need for transfusion
  - Decreasing trends over time, but still higher than HIV(-)
- Early term deliveries: transient tachypnea of the newborn
- Future delivery options compromised

### Discussion

- **Delivery Mode in Era of ART**
- **Townsend et al 2014**

### Evolution of mode of delivery of HIV infected women

- **Figure 1:**
  - The MTCT rate in over 5500 pregnancies in diagnosed HIV positive women was 0.57% overall and 0.46% in 2010–2011.
  - Excluding five in-utero transmissions, the MTCT rate among women with viral loads at, or presumed to be at, specific assay detection limits, the MTCT rate was 0.47% (three of 637) for <50 copies/mL, 1.00% (82 of 82) for 50–400 copies/mL, 1.00% (37 of 37) for 400–1000 copies/mL, 1.00% (400–1000 copies/mL, 1.00% (143 of 143) for 1000–10,000 copies/mL, and 1.00% (201 of 201) for >10,000 copies/mL.

- **Risk of Cesarean Delivery for HIV+ Woman**
  - Maternal complications
    - Fever
    - Infections: wound, UTI, endometritis
    - VTE
    - Need for transfusion
    - Decreasing trends over time, but still higher than HIV(-)
  - Early term deliveries: transient tachypnea of the newborn
  - Future delivery options compromised
Info from Kourtis et al.

- CS rate = 58% for HIV(+) women vs 33% HIV(-)
- Kourtis et al, 2014: In 2010-2011, increased risks in HIV(+) CS of:
  - Infection (aOR 1.70)
  - Surgical trauma (aOR 2.71)
  - Extended hospitalizations (aOR 1.96)
  - Death (aOR 8.74)

Unanswered Questions

- Is scheduled CD beneficial in cases of low viral load when on HAART?
- How does duration of ROM affect decision for CD?
- When to deliver in cases of PPROM?

ROM Duration

- Minkoff et al, AJOG 1995
  - 1986-1991
  - <5% used ZDV at any time in pregnancy
  - 207 HIV(+) moms, 191 infants with data: MTCT 25%
  - Low CD4+ levels: ROM > 4h increased MTCT with RR 4.53.
  - If higher CD4+ levels, no such association (RR 1.11)
ROM Duration

- Int’l Perinatal HIV Group, NEJM 1999
- Elective CS: MTCT 8.4%
- VD with ROM < 1h: 11.7%
- VD with ROM < 4h: 13.5%

ROM duration

- 2007-2012, singleton live births in UK/Ireland
- Had to be on cART (3+ meds), and have data on VL, ROM duration, VD
- 2398 pregnancies in 1814 women
- No differences in MTCT with ROM <4h, 4-24h, and ≥24h

ROM duration

<table>
<thead>
<tr>
<th>VL</th>
<th>Mode?</th>
<th>ROM Duration</th>
<th>MTCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>VL &lt;1000</td>
<td>cART</td>
<td>&gt;4h (144/493)</td>
<td>0</td>
</tr>
<tr>
<td>VL &gt;1000</td>
<td>cART</td>
<td>&lt;4h ≥4h</td>
<td>3.8% 4.9% (NS)</td>
</tr>
<tr>
<td>VL &lt;1000</td>
<td>ZDV</td>
<td>2/45 (ROM 22h)</td>
<td>146 presented in labor, 55 had CD</td>
</tr>
</tbody>
</table>

Conclusion: Duration of membrane rupture not a risk factor for MTCT if VL <1000 and on cART.
ROM Duration - Summary

• ROM > 4h was felt to be a risk factor for MTCT in studies done before viral load data was reported.
• With low viral load, ROM duration is not a risk factor for MTCT.

Unanswered Questions

• Is scheduled CD beneficial in cases of low viral load when on HAART?
• How does duration of ROM affect decision for CD?
• When to deliver in cases of PPROM?

PPROM

• Cotter et al, 2012
• PPROM = 12, no MTCT
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PPROM

• Aagaard-Tillery et al, 2006
  • 7 patients with HIV and PPROM
    • IV AZT up to 48 h following PPROM, and then again just before delivery
    • Expectantly managed per obstetric management
    • 2/6 rate of MTCT (33%)
      • One mom without ART (was on placebo arm of PACTG 076)
      • Second mom only had AZT and VL not used to guide MOD
      • Others all had HAART, and CD if VL > 1000

<table>
<thead>
<tr>
<th>GA</th>
<th>GA delivery</th>
<th>Latency (days)</th>
<th>VL PPROM</th>
<th>VL Delivery</th>
<th>AP ART / IP AZT</th>
<th>MTCT HIV</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>30+5</td>
<td>31+5</td>
<td>1</td>
<td>1809</td>
<td>1809</td>
<td>Y / Y</td>
</tr>
<tr>
<td>2</td>
<td>31+2</td>
<td>30+2</td>
<td>92</td>
<td>7319</td>
<td>179</td>
<td>N / N</td>
</tr>
<tr>
<td>3</td>
<td>30+2</td>
<td>31+6</td>
<td>5</td>
<td>&lt;50</td>
<td>&lt;50</td>
<td>Y / N</td>
</tr>
<tr>
<td>4</td>
<td>31+4</td>
<td>31+6</td>
<td>2</td>
<td>&lt;50</td>
<td>&lt;50</td>
<td>Y / N</td>
</tr>
<tr>
<td>5</td>
<td>24+2</td>
<td>25+5</td>
<td>10</td>
<td>3710</td>
<td>971</td>
<td>Y / Y</td>
</tr>
<tr>
<td>6</td>
<td>31+0</td>
<td>31+1</td>
<td>3</td>
<td>--</td>
<td>--</td>
<td>N / N</td>
</tr>
<tr>
<td>7</td>
<td>23+4</td>
<td>24+4</td>
<td>7</td>
<td>--</td>
<td>--</td>
<td>N / Y</td>
</tr>
</tbody>
</table>

Aagaard-Tillery et al, 2006

PPROM

  • 19 HIV(+) with PPROM
    • 1 excluded (delivered at 24 weeks and had NND)
    • 2/18 surviving neonates were HIV+ at 6 months of age
    • All were expectantly managed
    • All had cesarean delivery
    • 0/10 HIV+ neonates if mom had antepartum HAART and intrapartum ZDV
    • 2/8 HIV+ neonates in moms without prenatal care: PO nevirapine + IV ZDV, CS
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**Table 1: Patients having had antenatal antiretroviral therapy.**

<table>
<thead>
<tr>
<th>Case</th>
<th>Gestational age (weeks)</th>
<th>Chorioamnionitis Other STDs</th>
<th>Clinical diagnosis</th>
<th>Neonatal outcome</th>
<th>MTCT</th>
<th>Blood culture</th>
<th>Time to diagnosis</th>
<th>HIV transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>38</td>
<td>No</td>
<td>None</td>
<td>Dead</td>
<td>No</td>
<td>None</td>
<td>2 days</td>
<td>HIV negative</td>
</tr>
<tr>
<td>2</td>
<td>37</td>
<td>Yes</td>
<td>Enterococci</td>
<td>None</td>
<td>No</td>
<td>None</td>
<td>2 days</td>
<td>HIV negative</td>
</tr>
<tr>
<td>3</td>
<td>36</td>
<td>No</td>
<td>None</td>
<td>None</td>
<td>No</td>
<td>None</td>
<td>2 days</td>
<td>HIV negative</td>
</tr>
<tr>
<td>4</td>
<td>35</td>
<td>Yes</td>
<td>None</td>
<td>None</td>
<td>No</td>
<td>None</td>
<td>2 days</td>
<td>HIV negative</td>
</tr>
<tr>
<td>5</td>
<td>34</td>
<td>No</td>
<td>None</td>
<td>None</td>
<td>No</td>
<td>None</td>
<td>2 days</td>
<td>HIV negative</td>
</tr>
<tr>
<td>6</td>
<td>33</td>
<td>Yes</td>
<td>None</td>
<td>None</td>
<td>No</td>
<td>None</td>
<td>2 days</td>
<td>HIV negative</td>
</tr>
<tr>
<td>7</td>
<td>32</td>
<td>No</td>
<td>None</td>
<td>None</td>
<td>No</td>
<td>None</td>
<td>2 days</td>
<td>HIV negative</td>
</tr>
<tr>
<td>8</td>
<td>31</td>
<td>Yes</td>
<td>None</td>
<td>None</td>
<td>No</td>
<td>None</td>
<td>2 days</td>
<td>HIV negative</td>
</tr>
<tr>
<td>9</td>
<td>30</td>
<td>No</td>
<td>None</td>
<td>None</td>
<td>No</td>
<td>None</td>
<td>2 days</td>
<td>HIV negative</td>
</tr>
<tr>
<td>10</td>
<td>29</td>
<td>Yes</td>
<td>Hepatitis C</td>
<td>None</td>
<td>No</td>
<td>None</td>
<td>2 days</td>
<td>HIV negative</td>
</tr>
</tbody>
</table>

**Table 2: Patients not having antenatal antiretrovirals, with nevirapine prescribed during labor.**

<table>
<thead>
<tr>
<th>Case</th>
<th>Gestational age (weeks)</th>
<th>Chorioamnionitis Other STDs</th>
<th>Clinical diagnosis</th>
<th>Neonatal outcome</th>
<th>MTCT</th>
<th>Blood culture</th>
<th>Time to diagnosis</th>
<th>HIV transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>32</td>
<td>No</td>
<td>None</td>
<td>Dead</td>
<td>No</td>
<td>None</td>
<td>2 days</td>
<td>HIV negative</td>
</tr>
<tr>
<td>2</td>
<td>31</td>
<td>Yes</td>
<td>None</td>
<td>None</td>
<td>No</td>
<td>None</td>
<td>2 days</td>
<td>HIV negative</td>
</tr>
<tr>
<td>3</td>
<td>30</td>
<td>No</td>
<td>None</td>
<td>None</td>
<td>No</td>
<td>None</td>
<td>2 days</td>
<td>HIV negative</td>
</tr>
<tr>
<td>4</td>
<td>29</td>
<td>Yes</td>
<td>None</td>
<td>None</td>
<td>No</td>
<td>None</td>
<td>2 days</td>
<td>HIV negative</td>
</tr>
<tr>
<td>5</td>
<td>28</td>
<td>No</td>
<td>None</td>
<td>None</td>
<td>No</td>
<td>None</td>
<td>2 days</td>
<td>HIV negative</td>
</tr>
<tr>
<td>6</td>
<td>27</td>
<td>Yes</td>
<td>None</td>
<td>None</td>
<td>No</td>
<td>None</td>
<td>2 days</td>
<td>HIV negative</td>
</tr>
<tr>
<td>7</td>
<td>26</td>
<td>No</td>
<td>None</td>
<td>None</td>
<td>No</td>
<td>None</td>
<td>2 days</td>
<td>HIV negative</td>
</tr>
<tr>
<td>8</td>
<td>25</td>
<td>Yes</td>
<td>None</td>
<td>None</td>
<td>No</td>
<td>None</td>
<td>2 days</td>
<td>HIV negative</td>
</tr>
<tr>
<td>9</td>
<td>24</td>
<td>No</td>
<td>None</td>
<td>None</td>
<td>No</td>
<td>None</td>
<td>2 days</td>
<td>HIV negative</td>
</tr>
<tr>
<td>10</td>
<td>23</td>
<td>Yes</td>
<td>None</td>
<td>None</td>
<td>No</td>
<td>None</td>
<td>2 days</td>
<td>HIV negative</td>
</tr>
</tbody>
</table>

**Table III: Mother-to-child transmission rate of HIV for patients getting antepartum ARVs.**

<table>
<thead>
<tr>
<th>Case</th>
<th>MTCT ( infection in baby</th>
<th>Latvia</th>
<th>Viral load</th>
<th>CD4 count</th>
<th>MTCT ( infection in baby</th>
<th>Latvia</th>
<th>Viral load</th>
<th>CD4 count</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10/10 MTCT in moms with antenatal ART</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>10/10 MTCT in moms with antenatal ART</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>10/10 MTCT in moms with antenatal ART</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>4</td>
<td>10/10 MTCT in moms with antenatal ART</td>
<td></td>
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</tbody>
</table>

**PPROM - summary**

- Need more data, but expectant management seems reasonable, especially if mom has been getting antepartum ART.

**Outline**

- Introduction: Definitions, Epidemiology, History
- Perinatal Transmission: Background
- Preventing Perinatal Transmission
  - Testing
  - Antepartum Treatment
  - Intrapartum Treatment
  - Mode of Delivery
  - Breastfeeding
  - Neonatal Treatment
- Resources for clinical advice
Breastfeeding considerations

CHIP Breastfeeding Protocol

- BF NOT recommended in resource-rich settings
- Counseling with 2 CHIP team members
  - Consider maternal reasons for desiring BF
  - Consider maternal feelings if infant does contract HIV
  - Risk of up to 1%

CHIP BF Protocol

- Infants > 36 weeks
- Start weaning at 6 months
- Mastitis increases risk
- Monthly visits:
  - Maternal: HIV VL on colostrum/BM and serum
  - Infant:
    - HIV NAT at birth, 2w, 4w, monthly, and then after weaning: 1, 3, 6 months (revising?)
    - Check for loss of antibodies at 12-18 months
    - Monitor for adverse effects of ART: CBC diff, LFTs
  - Standard ARV prophylaxis (6 weeks) and extended
- Stop BF if positive HIV VL at any time, and infant will receive full post-exposure prophylaxis (3 drug regimen)
Management of HIV on Labor and Delivery

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Take-home points

• Repeat third trimester testing in high-risk patients
• Rapid HIV testing on L&D if unknown HIV status
• Antepartum treatment is important!!
• Intrapartum treatment
    • Continue antenatal ART
    • Add IV ZDV if viral load > 1000
      • CHiP also does if any detectable VL in last 12 weeks, or if poor adherence in pregnancy
• Elective CD at 38 weeks if VL > 1000
• Breastfeeding not recommended

Neonatal treatment
Neonatal Treatment

• Antiretroviral prophylaxis (>1 ARV)
  • E.g. Mom on ART with viral suppression → 4 weeks of ZDV
  • If risk factors, multi-drug ARV
    • No antepartum/intrapartum ARV
    • Only IP ARV
    • AP ARV but no viral suppression
    • Primary/acute HIV in pregnancy/BF

• Empiric HIV therapy
  • High-risk infant, combination 3-drug ARV
  • If risk factors above, can also do this

• HIV Therapy
  • 3-drug ARV treatment doses (ART)
  • Risk Factors (multi-drug ARV ppx OR empiric HIV therapy)

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Resources

• Children’s Hospital Immunodeficiency Program (CHIP) Clinic
  • 24 hour Perinatal HIV Consult Line 303-281-9695
• National Perinatal HIV Hotline
  • 888-448-8765
  • http://nccc.ucsf.edu
• U.S. Department of Health and Human Services (USDHHS)
  • www.aidsinfo.nih.gov
Expanding the effort to decrease MTCT

- HIV positive woman
  - Preventing unintended pregnancy
  - Preconception care
- HIV positive woman in pregnancy
  - Antepartum: ARV to decrease VL
  - Intrapartum: C/S and ARV pm
  - Neonatal ARV
  - Avoid breastfeeding
- Testing in pregnancy + retesting 3rd tri and postpartum
- Preventing seroconversion: PrEP, condoms

HIV negative woman

Seroconversion in pregnancy

- Perinatal transmission rates higher if HIV acquired in pregnancy vs. pre-pregnancy
  - 22% vs 1.8% (2002-2005, NY)
  - 12.9% vs 1.6% (2005-2010, U.S.)

USC/HIV Guidelines 2018

HIV Transmission to Women in Pregnancy and Postpartum

- Thomson KA et al, JID 2018
Management of HIV on Labor and Delivery

Conception

- Consultation with Reproductive Endocrinology/Infertility
- Discordant couples (male +)
  - Treatment to reduce viral load
  - Donor sperm
  - IUI with washed sperm
  - IVF/ICSI with washed sperm
  - PrEP for female partner
- Discordant couples (female +)
  - IUI, or “home” insemination
- Natural conception:
  - Screen/treat both partners for other STIs
  - Treatment of HIV+ partner
  - PrEP for HIV(-) partner
  - Timed intercourse (ovulation predictor kits)

Selected References

- U.S. DHHS: www.aidsinfo.nih.gov
- CDC MMWR December 10, 1982.
- CDC MMWR December 17, 1982.
Extra slides
(Not for this talk)

AIDS-defining illnesses

- Infections
  - Bacterial
  - Fungal
  - Viral
- Malignancies
  - Kaposi Sarcoma
  - Lymphoma
  - Invasive cervical cancer
- Wasting syndrome
- Encephalopathy

- Bacterial infections, multiple or recurrent
- Candidiasis of bronchi, trachea, or lungs
- Candidiasis of esophagus
- Cryptococcosis, extrapulmonary
- Cryptosporidiosis, chronic intestinal (>1 month's duration)
- Cytomegalovirus disease (other than liver, spleen, or nodes), onset at age >1 month
- Cytomegalovirus retinitis (with loss of vision)
- Encephalopathy, HIV related
- Herpes simplex: chronic ulcers (>1 month's duration) or bronchitis, pneumonitis, or esophagitis, onset at age >1 month
- Histoplasmosis, disseminated or extrapulmonary
- Isosporiasis, chronic intestinal (>1 month's duration)
- Kaposi sarcoma
- Lymphoma, Burkitt (or equivalent term)
- Lymphoma, immunoblastic (or equivalent term)
- Lymphoma, primary, of brain
- Mycobacterium avium complex (MAC) or Mycobacterium kansasii, disseminated or extrapulmonary
- Mycobacterium tuberculosis of any site, pulmonary, disseminated, or extrapulmonary
- Mycobacterium, other species or unidentified species, disseminated or extrapulmonary
- Pneumocystis jirovecii pneumonia
- Pneumonia, recurrent
- Progressive multifocal leukoencephalopathy
- Salmonella septicemia, recurrent
- Toxoplasmosis of brain, onset at age >1 month
- Wasting syndrome attributed to HIV

https://www.cdc.gov/hiv/policies/law/states/

- Pregnancy provider is obligated to test for syphilis and HIV early in pregnancy.
- Patient may decline, and should document in chart.
- If HIV unknown in hospital, opt-out testing; document if declines.
- Birth/stillbirth certificates must state whether HIV and syphilis testing done (but not the result).
Antepartum Care (CHIP)

• Routine prenatal labs
  • Pap
  • TB, HCV Ab (if >12 months)
  • Hep A Ab
  • CMV IgG and IgM
  • Varicella status, HSV status

• Immunizations
  • Influenza, PCV 13, HBV, HAV, Tdap

Appendix A: CHIP Lab Evaluation Schedule for OB Client Management

<table>
<thead>
<tr>
<th>Test Year</th>
<th>After start or change of ARV</th>
<th>Q Months</th>
<th>2nd Trimester</th>
<th>3rd Trimester</th>
<th>HIV Clinical Indication</th>
<th>Repeat prior to transition</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV Ag/Ab</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>HIV quant</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td>(14-30 wks gest)</td>
</tr>
<tr>
<td>VDRL</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>CMV IgG</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>CMV IgM</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Lipase</td>
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<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>CBC/Diff</td>
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<td>X</td>
<td></td>
<td></td>
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<tr>
<td>CD4 count</td>
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<td></td>
<td></td>
<td>X</td>
<td></td>
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<td>CMP</td>
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<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Phosphorous</td>
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<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
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<tr>
<td>Non-fasting lipid profile</td>
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<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Venous Lactate</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Hep B sag</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Hep B sab</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Hep B cor ab</td>
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<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Hep B DNA</td>
<td>X</td>
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<td></td>
<td></td>
<td>X</td>
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</tr>
<tr>
<td>Hep C ab</td>
<td>X</td>
<td>X</td>
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<td></td>
<td>X</td>
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<tr>
<td>Hep C quant</td>
<td>X</td>
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<td>X</td>
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<tr>
<td>Hep C geno</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Quantiferon TB</td>
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<td>X</td>
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<tr>
<td>CMV IgG, IgM</td>
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<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Toxo IgG, IgM</td>
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<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>RPR</td>
<td>X</td>
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<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>VZV</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>HSV</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
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<tr>
<td>PK levels if available</td>
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<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Cervical Cytology</td>
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<td>X</td>
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<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>GC</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
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<tr>
<td>Chlamydia</td>
<td>X</td>
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<td></td>
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<td>X</td>
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<tr>
<td>Trichomonas</td>
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<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Urine or serum preg</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>UA</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
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</tr>
</tbody>
</table>

1 Unless prior results/source documentation are readily available
2 May have been performed at OB-obtain records, abstract to DB or EPIC depending on data source
3 If symptomatic or at risk
4 Defer if prior serology positive
5 Repeat Q pregnancy if prior seronegative and >12 months since last test
6 If uncertain hx of wild type disease or vaccine
7 Perform if screening serology positive for suspected disease
8 Until TND documented
9 Perform once after client is stable on ARV
10 If untreated, unsuppressed; HIV DNA genotype if HIV VL <1,000 cp/ml
11 For returning clients, rescreen if prior seronegative and travel to endemic region
12 If on TDF or TAF; recheck Q 6 months
13 Rescreen Q pregnancy if prior seronegative
14 If mother toxo IgG positive, desirable to send postpartum within 1 month of newborn toxoplasma testing for titer comparison

Antepartum ARV

- Backbone of 2 NRTI (nucleotide reverse transcriptase inhibitor)
  - Abacavir/lamivudine
  - Tenofovir/emtricitabine
  - Tenofovir + lamivudine

- Plus:
  - Protease inhibitor, or
    - Atazanir + ritonavir
    - Darunavir + ritonavir

- Integrase inhibitor
  - Dolutegravir (after 1st tri)
  - Raltegravir

USDHHS Guidelines 12/2018; aidinfo.nih.gov
Antiretrovirals in Pregnancy – risks?

- Antiretroviral Pregnancy Registry
  - 1-800-258-4263
  - www.APRegistry.com

Antiretrovirals in Pregnancy: Maternal concerns

- Mitochondrial toxicity → lactic acidosis
  - Avoid didanosine and stavudine if possible
  - 3 maternal deaths reported due to lactic acidosis (2 fetal deaths)
  - Nevirapine: skin rash, hepatotoxicity

Antiretrovirals in Pregnancy: Maternal concerns

- Protease inhibitors: glucose intolerance
  - Probably no increase in GDM rate
  - Routine screening vs early screening
- Dosing adjustments
  - TDF and atazanavir may decrease, esp in 3rd tri
  - Lopinavir-ritonavir; QD → BID in 2nd and 3rd tri

**Not recommended due to PK changes in pregnancy:**

- Atazanavir/cobicistat
- Darunavir/cobicistat
- Elvitegravir/cobicistat
Antiretrovirals in Pregnancy: Fetal concerns

- Growth restriction / SGA: ?? Conflicting results
  - Growth ultrasound vs follow fundal height
- Increased PTB, esp protease inhibitors: mild
  - OR 1.35 [1.08-1.70]
- Very PTB/NND
  - Tenofovir disoproxil fumarate + lopinavir-ritonavir
  - TDF alone still one of the preferred medications

Antiretrovirals in pregnancy: Fetal concerns - teratogenicity

- Antiretroviral Pregnancy Registry
  - Overall rate of 2.7% (1st tri), 2.8% (2nd/3rd tri) (baseline risk of 2.7%)
  - Dolutegravir
    - Recommended to avoid in 1st trimester (preconception and conception) due to increased risk of neural tube defects
    - Can use after first trimester
    - UPT prior to initiation
    - Don’t use if not on effective contraception
  - Efavirenz: use not restricted