HIV Infection in Pregnancy: 2008 Update

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Wrangell-St. Elias Range - 2004

HIV Infection in Alaska: 2004

- Alaska has 1,002 total cases of HIV
- Alaska Natives accounted for 23% (n=228)
- Women accounted for 18% (n=175)
- AN/AI women accounted for 32% of these (n=56)
- Perinatal acquired cases 2% (n=7)

HIV in Pregnancy: Case 1

- Nellie Benally is a 22 y/o G3P0 at 11 weeks gestation whose routine prenatal HIV test (both EIA and WB) returns (+). She had a former partner who was an IVDU.

- What are the your next steps?

HIV in Pregnancy: Per-contact Risk of Infection

Exposure	Risk
Receptive vaginal	2-8/1000
Insertive vaginal	1-3/1000
Needle sharing	3-6/1000
Occupational needle stick	1/300

HIV Screening in Pregnancy Issues

- “opt-in” vs. “opt-out” (informed refusal)
  - removes the stigma
  - part of routine prenatal labs
  - 53% vs. 89% choose testing
  - current approach recommended by the CDC, ACOG, and AAP

HIV Screening in Pregnancy Issues

- Repeat testing in the 3rd trimester? Who?
  - Hx STD
  - IVDU
  - Multiple partners
  - Opportunistic infection
  - Previously declined testing

HIV Screening in Pregnancy Issues

- Rapid screening in labor?
  - Whole blood, done in L&D
  - Results in 20-40 minutes
  - OraQuick probably the best (CLIA-waived)
  - Sensitivity, specificity, PPV approach 100%
  - Initiate prophylaxis and order Western blot to confirm

HIV Screening in Pregnancy: ANMC Experience

- Use of “opt out” strategy
- 96% of women had a prenatal HIV screen done at the first visit
- 4% declined at the initial visit
- 2% eventually agreed to screening later
- 3% had no screen in labor (transfers in)

HIV Screening in Pregnancy Issues

- What about “indeterminate” results?
  - (+) EIA but WB (-): not infected
  - (+) EIA but WB “indeterminate” (<3 bands)
  - relatively common in multiparous women
  - risk factors? (low prevalence means more false positives…)
  - repeat the WB in 3 months
  - get a viral load

HIV in Pregnancy: Other Tests
Viral Load

- viral load is the key to preventing perinatal transmission
- goal is to reduce viral load to undetectable (<1,000 copies/mL)
- repeat q 2-3 mos, or at least q trimester
- 2 assay types:
  - -b-DNA (HIV-1 RNA)
  - -RT-PCR

HIV in Pregnancy: Other Tests CD4+ Count

- measure of host immune response
- if <500/mL, repeat every trimester
- if <200/mL, begin PCP prophylaxis
- CD4+ = wbc x %lymphs x %CD4
- eg. = 10,000 x .30 x .30 = 900

HIV in Pregnancy: Other Tests Baseline Labs

- CBC (anemia with ZDU)
- LFTs (mitochondrial disease with NRTI, elevated ALT w/ NNRTI and PI)
- amylase (pancreatitis with NRTI)
- early 1-hr OGT (GDM with PI)
- creatinine
- Hep B & C, CMV, toxo

Bridal Veil Falls
2004

HIV in Pregnancy: Treatment

- The goal in pregnancy is to reduce viral load to undetectable to minimize perinatal transmission.
- Is the woman willing and able to adhere to the regimen?
- What are the risks and benefits?
- Regardless of drug tx, should use condoms during pregnancy

HIV in Pregnancy: Therapy "The Milestone Study"

- ACTG 076 (1994)
  - Zidovudine (ZDU, formerly AZT) PO prenatally from 14-34 wks to term: 100 mg 5x/d
  - ZDU in labor IV: 2 mg/kg load, 1 mg/kg/h maintenance
  - ZDU to neonate: 2mg/kg/q6h x 6 wks
  - Reduced vertical transmission from 26% to 8%

HIV in Pregnancy: Therapy

- Any pregnancy regimen should include ZDU
- Combination HAART (3 drugs) is associated with vertical transmission rates of <2% and is considered standard of care (regardless of VL or CD4+)
- Safety of HAART in pregnancy is reassuring
- Patient choice should always be respected

HIV in Pregnancy: Therapy

- Pick the regimen that will be easiest to adhere to and have the fewest side effects
- "2 pills twice (or once) a day every day"
- ZDU 200 mg/lamivudine 150 mg (Combivir) + lopinavir 400 mg/ritonavir 100 mg (Kaletra) p.o. BID, -or-
- Combivir + nelfinavir (Viracept) 1250 p.o. BID.

- Side effects generally mild and treatable: anemia, headache, nausea, diarrhea

HIV in Pregnancy: Therapy

- Check viral load, CD4+, LFTs, CBC q trim
- Consider change of therapy if viral load still detectable in 3-6 months
  - Is she taking her meds??
- Baseline ARV resistance testing
  - HAART naïve (new) cases
  - HAART re-starts
  - if suboptimal viral suppression

HIV in Pregnancy: Therapy

- Avoid use of efavirenz (teratogen)
- Avoid use of nevirapine IF CD4+>250 (hepatotoxicity)
- Include ZDU if at all possible
- OK to initiate treatment in the 1st trimester
- (↑ duration of mat tx-→↓ transmission)
- Do resistance testing when starting tx
- Continue drugs during labor

HIV in Pregnancy: Case 2

- Adelina Low Dog is a 29 y/o G3P2 at 16 wks who is known to be HIV infected and is on triple therapy (ZDU, lamivudine, lopinavir/ritonavir) x 3 yrs. CD4+=373, HIV b-DNA = 490 copies/mL. Now that she is pregnant, is it safe to continue her current meds?

HIV Therapy in Pregnancy

- Recommended Agents (CDC):
- NRTIs:
- ZDU, lamivudine (emtricitabine, abacavir)
- NNRTIs:
- Nevirapine
- PIs:
- Lopinavir/ritonavir (nelfinavir, indinavir, squinavir)

HIV in Pregnancy: Therapy

- Are there any ART drugs that are NOT recommended during pregnancy?
  - Efavirenz, delaviridine, zalcitabine are teratogenic in *animals*
  - Atazanavir, tenofovir, fosamprenavir, enfuviritide, have insufficient data in human pregnancy

HIV Therapy in Pregnancy

- Are there any special precautions about ART in pregnancy?
- Indinavir, atazanavir: hyperbilirubinemia?
- Nevirapine: hepatotoxicity (if nl CD4+)
- Didanosine, stavudine: lactic acidosis
- Protease inhibitors: GDM? PTB?

HIV Therapy in Pregnancy

- Recommendations:
- Continue current HAART regimen if effective
- All pregnancy regimens should include ZDU
- Do NOT stop drugs in the 1st trimester
- Do NOT stop drugs in labor
- Avoid potential teratogens (efavirenz)
- Drug resistance testing recommended

HIV in Pregnancy: Therapy Issues

- Is HAART associated with an increased incidence of preterm birth/LBW?____
- Is combo HAART superior to ZDU alone?____
- If the patient has ZDU resistance, should it still be given during pregnancy?____
- Is lactic acidosis and fatty liver increased in pregnant patients?____

Ship Lake 2004

HIV in Pregnancy: Case 3

- Nora Koyukuk is a 32 y/o G5P4 w/o PNC who presents in false labor at 37 wks and has an HIV test drawn. When she returns the following week she is in active labor (cx 3 cm/75%/-1 sta, BOW-I) and the test is found to be positive. How should you manage?

HIV in Pregnancy: Is Cesarean Delivery Necessary?

- French Perinatal Cohort -1998 (n=2819)
- HIV(+) AND taking ZDU (n=902)
  - Emergent cesarean 11.4% transmission
  - Vaginal delivery 6.6% transmission
  - Elective cesarean 0.8% transmission

HIV in Pregnancy: Is Cesarean necessary?

- French Perinatal Cohort (1998) (n=2819)
- HIV(+)/ *NOT* taking ZDU (n=1917)
  - – Emergent cesarean 15.6% transmission
  - – Vaginal delivery 17.5% transmission
  - – Elective cesarean 17.2% transmission

HIV in Pregnancy:
Is Cesarean Necessary?

- International Perinatal HIV Group (1999)
- Meta-analysis – 15 studies (n=8533)
  - Cesarean alone 10% transmission
  - ZDU alone 7% transmission
  - ZDU + cesarean 2% transmission

HIV in Pregnancy: Is Cesarean Necessary?

- PACTG-367 – (2004) (n=2756)
  - Unknown viral load 11.6% transmission
  - >10,000 copies 4.6% transmission
  - <10,000 copies 2.3% transmission
  - Undetectable 0.9% transmission

HIV in Pregnancy
Is Cesarean Necessary?

- PACTG 367 (2004) n=2756):
- On HAART (all) 1.3% transmission
- On HAART/ VL<1000:
  - Cesarean 0.8%
  - Vaginal 0.5%
- It is unclear that scheduled cesarean delivery is of any benefit in women on HAART w/ VL <1000

HIV in Pregnancy: Is Cesarean Necessary?

- Elective cesarean delivery decreases perinatal HIV transmission, but…
- Women on HAART may not derive further benefit from cesarean delivery
- Women with undetectable viral loads may not derive benefit from cesarean delivery

HIV in Pregnancy: Is Cesarean Necessary?

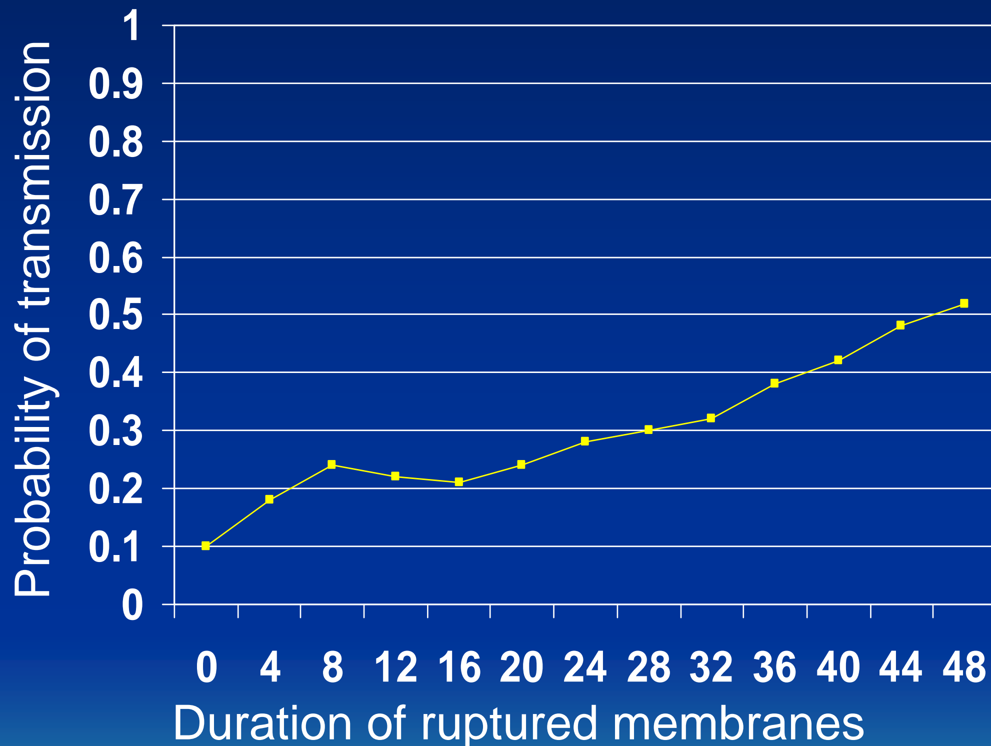
- Women with viral loads of <1,000 copies should be offered vaginal delivery
- Women with >1,000 copies should be offered elective cesarean at 38 weeks
- Women's autonomy should always be respected, especially in this situation where the data are insufficient

HIV in Pregnancy
Is Cesarean Necessary?

- Scheduled cesarean for HIV(+) women with:
  - VL>1000
  - unknown VL
  - not on HAART
  - not in labor or SROM >4 hrs
- Schedule at 38 wks by best estimate
- NO amnio for FLM
- Start ZDU 3 hrs pre-op-→continue til baby out!
- Prophylactic cefazolin
- (Increased risk of infectious complications)

Parking violation????

HIV in Pregnancy: How about ruptured membranes?



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HIV in Pregnancy: Management of Labor

- All patients should get IV ZDU per the ACTG 076 protocol:
- ZDU 2 mg/kg IV load → 1 mg/kg/hr IV maintenance throughout labor
- Continue usual oral HAART in labor
- No AROM, no IUM, no scalp electrodes, no forceps/VE, no episiotomy
- Augment labor if SROM
- Avoid ergotamine in women on a PI

Nevirapine (NVP) Intrapartum Therapy

- Resource-poor Settings :
  - Single-dose maternal NVP 200 mg p.o. x1 in labor
  - Single-dose infant NVP 2mg/kg p.o. x1
  - Significantly reduced transmission (30-40% efficacy)
- Resource-rich Settings (PACTG 316):
  - Did not offer benefit in women on HAART
  - Risk of promoting resistance to NVP (15%)
  - NOT recommended in the U.S.

Back to Case patient #3…

- She should receive IV ZDU during labor
- She may have a vaginal delivery
- Cesarean would convey no benefit to the infant in this situation
- Her infant should receive PO zidovudine x 6 wks
- The addition of single dose nevirapine (for mom or baby) is NOT recommended in the U.S.
- She needs a new patient HIV work up

There is no duty we so much underrate as the duty of being happy.“

Robert Louis Stevenson

HIV in Pregnancy: Case 4

- Sophie Aquino is a 34 y/o G8P7 who has had no PNC. She presents in active labor and is found to be completely dilated. She precipitously delivers a healthy newborn. The lab calls that on her screening labs she is HIV(+)….

- How should this infant be managed?

HIV: Management of the Newborn

- Infants should receive oral ZDU according to the ACTG 076 protocol:
- ZDU 2 mg/kg/dose q6h x6 wks beginning 6-8 h after birth
- CBC, LFTs, CD4+, WB, viral load
- Viral load at birth, 2-3 wks, 1-2 months and 4-6 mos
- PCP prophylaxis at 6 wks (SMX/TMP)

HIV: Management of the Newborn

Should the infant have other drugs added to its 6week ZDU regimen?

- High maternal VL despite ART and NSVD?
- Mother never received ART, or only IP therapy?
- Mother has known ZDU-resistant virus?
- Single dose nevirapine NOT rec in US
- Consult with your Peds HIV specialist

HIV and Breastfeeding African Data

- Overall risk of neonatal transmission is 14% over 2 years of nursing
- More diarrhea associated deaths
- Breast feeding mothers fare less well (11% vs. 4% death) at 2 years post del
- Short term ZDU or nevirapine po may decrease transmission 37-49%
- Breast feeding is contraindicated in the US

HIV: Postpartum Care

- Women with CD4+ <350/mm should be offered long-term HAART
- Keep it simple to foster adherence
- Women with low level viral loads should be followed q 3-6 mos for progression
- Breast feeding contraindicated in the U.S.
- Contraceptive issues + condoms
- Pap smear + HPV

HIV in Pregnancy References

- PHS Task Force Recommendations
- http://AIDSinfo.nih.gov
- www.hivatis.org
- http://www.apregistry.com

The End…