HIV PRACTICE GUIDELINE

INTRODUCTION:

Since 10/2010 Ohio has adopted “opt-out” testing, supported by ODH, CDC, IOM, and ACOG, in which HIV-1 testing with patient notification is a routine component of prenatal care. One in 139 women will be diagnosed with HIV in her lifetime with African Americans and Latinos having the highest risk. Nearly all cases of childhood HIV is attributable to perinatal transmission. Early intervention and treatment is the key to decreased neonatal transmission, and Ohio is still far below national testing average for universal testing. Prevention challenges include the fact that women may not know her partner is infected with HIV, lack of personal awareness of HIV serostatus, limited access to resources, presence of other STDs increasing infectivity, sexual abuse, unprotected anal and vaginal intercourse, and engaging in high-risk behaviors including drug injection, which pose barriers to healthcare providers.

HIV is in the family of retroviruses and uses reverse transcriptase to convert viral RNA to DNA in a rapidly evolving process, creating further mutations and combination strains. HIV-2 infection is endemic in West African countries and not distinguished in most commercially available screening tests. From the PACTG 076 landmark trial, AZT therapy alone can decrease risk of HIV-1 transmission by 68% with a transmission rate of 8%. Antenatal anti-retroviral (ARV) prophylaxis antenatally has significantly impacted the transmission rates from 25% with no ARV to <2% with <200 infected neonates born each year. Scheduled cesarean sections prior to onset of labor can decrease transmission risk by 50%.

PRECONCEPTION:

- Educate patient on risk of transmission to partner and safe practice for prevention
- Ensure all immunizations are up-to-date (TDaP, Hepatitis B, Flu, and meningococcal)
- Maximal viral suppression prior to conception optimal
- Refer to IDX to ensure safest and most effective anti-retroviral (ARV) regimen prior to conception
- Sero-discordant couples should consider IDX and REI consultation for expert approach with regards to pre-exposure prophylaxis, transmission, safety and conception based in individual couples’ needs.

DIAGNOSIS:

Laboratory Criteria

1. Check HIV 4th generation testing with general initial prenatal panel. Must document if patient declines testing.
2. Recheck screening test in high risk populations in the 3rd trimester. Criteria includes but not limited to following:
   a. Lives in high HIV prevalent area
   b. Diagnosed other STD within last year
   c. Injection drug use or other high risk sexual behavior
   d. New or more than one sexual partner
   e. Declined testing earlier in pregnancy

Figure 1. Sequence of appearance of laboratory markers for HIV-1 infection. (CDC AidsInfo)
Causes of false (+) screen results include but not limited to specimen mix-up, mislabeling, and autoimmune disorders. Inconsistent or conflicting test results should be investigated with follow up testing with newly collected specimen. Cannot detect HIV infection immediately after required.

**Antepartum:** Individualized care

- Confirmation of pregnancy dating recommended
- Assess patient’s history, prior therapies & toxicities, previous ARV drug resistance testing, immunizations, barriers to care, social challenges, and obstacles for compliance. Explain importance of compliance, risks for drug resistance, and risk for perinatal transmission.
- Suggested initial labs: CBC, CMP, CD4 count, plasma HIV RNA level (VL), hepatitis C, PPD skin test, pap smear, early diabetes screen, and HIV resistance testing if it has not been previously performed (in addition to general prenatal labs).
  - For non-compliant patients, consider ordering HIV genotypic resistance testing
- *All women regardless of VL and CD4 count should be started on combination ARV drug regimen.*
  - Patients who require medications for her own health should start immediately regardless of gestational age
  - For perinatal transmission prevention, patients may start immediately in the first trimester or after the first trimester.
- ARV therapy should be managed by IDX physicians and involve complex, individualized assessments.
  - Do NOT discontinue therapy. If patient is not compliant with medications, discuss with the patient importance of compliance and notify IDX
- Check monthly VL until undetectable followed by VL & CD4 counts every 3 months; final labs at 34-36 weeks gestation to determine optimal delivery method
- Serial biometry ultrasound assessments
- ANFS is not indicated except for accepted obstetrical indications
- Mode of delivery discussion based on ARV drug compliance and regimen, VL, prior obstetrical history, and risks/benefits of procedures and transmission.
**Anti-Retroviral Medications:**

*Combination* ARV prophylaxis taken over longer duration is more effective than single short-course drug regimen to decrease perinatal transmission. Transmission can occur even with undetectable or low levels of HIV RNA, therefore, women should be counseled & administered ARV therapy.

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Risks</th>
<th>Recommended therapy</th>
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</table>
| - Decreases maternal viral load in blood & genital secretions            | - “Preferred” Drugs have no evidence of teratogenicity or established association with clinically significant adverse outcomes for mothers, fetuses, or newborn are present. - During the first trimester, current data are insufficient to support or refute the teratogenic risk of ARV drugs when administered but data does not suggest major teratogenic effects for the majority of such agents. | Combination of at least 3 agents (individualized): Two-NRTI backbone + either ≥1 PI or NNRTI  
  “Preferred” drugs: NRTI backbone: ABC/3TC, TDF/FTC or 3TC, or ZDV/3TC  
  PI: LPV/r (Kaletra) or ATV/r  
  NNRTI: EFV  
  ***Therapies individualized with IDX*** |
| - Infant pre-exposure prophylaxis                                        |                                                                     |                                                                                      |
| - Decrease sexual transmission to discordant partners if low VL maintained |                                                                     |                                                                                      |

**Specific Medications —**

1. Efavirenz (EFV) is classified as a FDA Pregnancy Category D with limited evidence to support use in pregnancy. Evidence of 2- to 3-fold increased risk for neural tube defect. Exposure risk of open neural tube defect occurs during specific period of time in the first trimester of pregnancy. Start after 8 weeks of gestation if needs to be started.
2. Nevirapine - Increases of hepatic transaminase levels associated with rash or systemic symptoms (hepatotoxicity) may be observed during the first 18 weeks of treatment with nevirapine.
   - Nevirapine-based regimens should be only initiated in women with CD4 T-lymphocyte (CD4-cell) counts >250 cells/mm³ if the benefits clearly outweigh the risks because of the drug’s potential for causing hepatic toxicity/hypersensitivity reaction
3. Tenovir – preferred in chronic HBV infections but alternative treatment in combination in pregnancy is advised due to high placental transfer to the fetus.
4. Protease inhibitors (PI) – **associated with hyperglycemia.** Patients need to be screened early in pregnancy and followed closely.
   - When methergine (ergot alkaloid drug) is co-administered with protease inhibitors (potent CYP3A4), this can lead to severe vasospasms with risk for cerebral and extremity ischemia.
5. Stavudine and didanosine (NRTIs) should not be prescribed during pregnancy with reports of lactic acidosis and maternal/neonatal mortality with prolonged use in pregnancy.

**Intrapartum:**

- Strictly continue combination ARV drug regimen throughout intrapartum & postpartum course unless absolutely unable to for medical indications
  - Collaborative discussion with IDX prior to discontinuation if patient has absolute indication to stop ARV
- Consult NICU physicians
- HIV RNA levels <1000 copies/mL → there is insufficient evidence to suggest perinatal transmission will be significantly lower for cesarean section versus a vaginal delivery, therefore, individual counseling should be performed of risks/benefits to determine mode of delivery.
  - Transmission may occur at very low HIV RNA levels. A cesarean section may theoretically decrease perinatal transmission even in women with RNA levels <1000 copies/mL who have a statistically lower risk for transmission. It is reasonable to offer a medically indicated cesarean section if the patient desires this method of delivery.
Pre-operative/Pre-induction/Immediate Zidovudine (AZT) 2mg/kg IV infusion over 1 hour followed by 1mg/kg continuous infusion for at least 3 total hours prior to cesarean section and continued throughout labor course for ALL known or suspected patients.

Unknown HIV status

1. HIV RNA level >1000 copies/mL
2. Unknown HIV RNA level
3. Late entry to care (3rd Trimester)
4. No prenatal ARV therapy/regimen

HIV RNA level <1000
Compliant with prenatal ARV therapy/regimen

Rapid HIV positive (send confirmatory test & presume positive)

Premature rupture of membranes >37 weeks gestational age

Continue Prenatal ARV therapy/regimen

Mode/timing of delivery to be individualized based on duration of rupture, obstetrical history, HIV RNA levels, and current ARV drug regimen.

Cesarean Section at 38 weeks gestational age

Vaginal delivery OR Cesarean section at 38 weeks gestational age††

1. AVOID INVASIVE MONITORING AND OPERATIVE-ASSISTED DELIVERIES unless emergently obstetrically indicated (Episiotomy, IUPC, FSE, AROM, vaginal instruments)
2. AVOID methergine as first line uterotonic
3. Notify Pediatrics/NICU for delivery
4. Notify & involve Infectious Disease as necessary

†† After thorough consultation of the risks/benefits of cesarean section vs. vaginal delivery and the patient desires vaginal delivery, delivery timing may be individualized considering the Bishop Score and cervical assessment.
**Special Considerations:**

- **Amniocentesis** – Optimally, women should have compliant ARV therapy and undetectable or low (<1000 copies/mL) viral load prior to receiving an amniocentesis. A theoretical risk exists for vertical transmission. Individualized counseling should be offered, with choice of plan for testing and risk/benefit discussion reviewed if amniocentesis for prenatal diagnosis is desired by an HIV infected gravida. Benefit of lung maturity amniocentesis usually outweighed by risk of infection.

- **Preterm premature rupture of membranes** – risks of vertical transmission must be weighed with risks of prematurity. Expectant management up to 32-34 weeks gestation is preferred in women with well controlled disease.

- **Betamethasone** – no contraindications in this population. Women receiving ARV therapy are at increased risk for glucose intolerance (see below). Follow post-corticosteroids glycemic monitoring per diabetes protocol.

- **Chemoprophylaxis** for women with CD4+ count of <200 cells/µL or a history of oropharyngeal candidiasis, CD4+ cell percentage of <14% or a history of an AIDS-defining illness, but do not otherwise qualify.

- **Gestational Diabetes Screening** – ARV therapy is an indication for screening early AND standard screening periods throughout gestation.

**Postpartum:**

- Breastfeeding is **NOT** recommended, including women receiving ART
- Discuss with IDX to establish management plans after delivery and to determine if prenatal ARV regimen requires dose adjustments postpartum.
- Contraceptive care should be thoroughly discussed and assess if current ART therapy will require hormonal adjustments
- Encourage compliance with ART and follow up with IDX to decrease risk for drug resistance and improve disease control

**Disclosure:** These care clinical guidelines follow ACOG and evidence of available literature. Clinical evaluation of each, individual patient to determine optimal management is recommended and MFM consultation is available for further assistance.

References:

## HIV Classification

<table>
<thead>
<tr>
<th>CDC Stage*</th>
<th>CDC T-lymphocyte (%)</th>
<th>WHO Stage</th>
<th>WHO T-lymphocyte (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage Unknown</td>
<td>Lab confirmation &amp; no CD4+ count available</td>
<td>Stage 1</td>
<td>CD4+ count ≥500 cells/µL</td>
</tr>
<tr>
<td>Stage 1</td>
<td>CD4+ count ≥500 cells/µL or (≥29%)</td>
<td>Stage 2</td>
<td>CD4+ count 350-499 cells/µL</td>
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<tr>
<td>Stage 2</td>
<td>CD4+ count 200-499 cells/µL or (14-28%)</td>
<td>Stage 3 (advanced)</td>
<td>CD4+ count 200-349 cells/µL</td>
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<tr>
<td>Stage 3 (AIDS)</td>
<td>CD4+ count &lt;200 cells/µL or (&lt;14%) or presence of AIDS-defining condition</td>
<td>Stage 4 (AIDS)</td>
<td>CD4+ count &lt;200 or (&lt;15%)</td>
</tr>
</tbody>
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*CDC requires laboratory confirmation of HIV infection at all stages


## AIDS Defining Conditions

- Bacterial infections, multiple or recurrent (<13y/o)
- Candidiasis of bronchi, trachea, or lungs
- Candidiasis of esophagus
- Cervical cancer, invasive (≥13y/o)
- Coccidioidomycosis, disseminated or extrapulmonary
- 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
- Lymphoid interstitial pneumonia or pulmonary lymphoid hyperplasia complex (<13y/o)
- Lymphoma, Burkitt (or equivalent term)
- Lymphoma, immunoblastic (or equivalent term)
- Lymphoma, primary, of brain
- *Mycobacterium avium* complex or *Mycobacterium kansasii*, disseminated or extrapulmonary
- *Mycobacterium tuberculosis* of any site, pulmonary (≥13y/o), disseminated, or extrapulmonary
- *Mycobacterium*, other species or unidentified species, disseminated or extrapulmonary
- *Pneumocystis jirovecii* pneumonia
- Pneumonia, recurrent (≥13y/o)
- Progressive multifocal leukoencephalopathy
- *Salmonella* septicemia, recurrent
- Toxoplasmosis of brain, onset at age >1 month
- Wasting syndrome attributed to HIV