Another look; Breastfeeding in the Era of HIV (and its Treatments…)

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I have no COI…
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What this talk will cover:
- Past history
- Current data
- Current recommendations
- Involving the community

A note about language
- People-first language for people with HIV
- Avoid stigmatizing, blaming language
- E.g. mother-to-child transmission
- Gender-inclusive language: Not everyone who gives birth or feeds a baby identifies as a woman.
- Breast and chestfeeding = the process feeding a baby your own human milk
Prior to antiretroviral therapy (ART), the risk of perinatal transmission was ~25%. Perinatal transmission refers to mother to child transmission during pregnancy, labor, and delivery (this does not include breastfeeding).

- With zidovudine (AZT) during pregnancy and labor and for the infant after delivery for 6 weeks: 8%
- With ART: <1%
- With ART and undetectable VL at conception, throughout pregnancy, and at delivery (5482 mother-baby pairs reported):

Once upon a time…

What has been the guidance around feeding choice for infants of people living with HIV?

1985: "HTLV-III/LAV-infected women should be advised against breastfeeding to avoid postnatal transmission to a child who may not yet be infected." (CDC and Public Health Service)

2015: In discussing the avoidance of breastfeeding as the strong, standard recommendation for HIV-infected women in the United States, the Panel notes that women may face social, familial, and personal pressures to breastfeed despite this recommendation and that it is important to begin addressing possible barriers to formula feeding during the antenatal period. (HHS Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States. 2015. Available from: https://clinicalinfo.hiv.gov/en/guidelines/archived-guidelines/perinatal-guidelines)
What's New in the Guidelines?

The former section, "Counseling and Managing Individuals With HIV in the United States Who Desire to Breastfeed," was revised and retitled to provide more comprehensive guidance on feeding infants born to individuals with HIV. Content about breastfeeding in other sections was revised to align with and refer to updated recommendations in this section.

What is the risk of HIV transmission via breastfeeding?

- Without maternal antiretroviral therapy (ART) or infant antiretroviral prophylaxis, the risk of an infant acquiring HIV through breastfeeding is 15% to 20% over 2 years.
- Achieving and maintaining viral suppression through ART during pregnancy and postpartum decreases breastfeeding transmission risk to less than 1%, but not zero.

Breast/chest feeding with HIV in the USA (?)

- What do we know about the risk of transmission during lactation?
- What is happening around the globe?
- How about in the USA?
- What should you look for in the future?

Does U=U for transmission through breastmilk?
Sexual: No transmissions if partner living with HIV is taking ART and has a viral load consistently <200 c/mL
Perinatal: No transmissions if pregnant person on ART before and during pregnancy and VL <50 c/mL during 3rd tri & at delivery
Lactational: Risk is very low but may not be zero. We don’t have enough information to know if there is a scenario where undetectable will equal untransmittable

Several other case reports of lactational transmission when breast/cheesfeeding parent seemed to have undetectable plasma HIV RNA ...

- At least 7 additional published cases of HIV transmission with a VL <50 c/mL close to the time of transmission
- One transmission with documented VL <50 c/mL at delivery and every 1-2 months postpartum (PP) (infant diagnosed with HIV at 3 months of life)
- Transmission may be related to late ART start in third trimester

Substantial Early Breast Milk HIV Transmission:
Nairobi & SAINT Trials: Difference Between Formula & Breast-Fed Infants

<table>
<thead>
<tr>
<th>Age (months)</th>
<th>Probability of LPT (Y/N)</th>
<th>Cumulative Probability of LPT (50% CI)</th>
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<tbody>
<tr>
<td>3</td>
<td>98.4%</td>
<td>1.6% (0.3-2.9%)</td>
</tr>
<tr>
<td>6</td>
<td>95.8%</td>
<td>4.2% (1.8-6.7%)</td>
</tr>
<tr>
<td>9</td>
<td>94.0%</td>
<td>5.9% (3.3-8.6%)</td>
</tr>
<tr>
<td>12</td>
<td>92.0%</td>
<td>7.2% (4.7-9.3%)</td>
</tr>
<tr>
<td>15</td>
<td>90.0%</td>
<td>9.3% (5.3-14.8%)</td>
</tr>
<tr>
<td>18</td>
<td>87.7%</td>
<td>10.3% (6.4-14.2%)</td>
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</tbody>
</table>

After 1 month, risk of vertical transmission is lower but persists ...

- Evaluated postnatal infection rate in 4,085 breastfed children uninfected at age 1 month

Metanalysis of trials before universal treatment ...

Late postnatal transmission 0.74%/month breastfeeding (8.9 per 100 child-years)
Breast Milk HIV RNA Viral Load is Associated with Risk of Postnatal Transmission

Evaluation breast milk RNA in 275 women over 2 years Kenya

HIV Incidence per 100 Child Yrs

First Breast Milk Sample HIV RNA...

Maternal plasma RNA VL, correlated with breast milk RNA VL, although breast milk RNA is lower. For every 1 log ↑ in plasma VL, there was estimated 0.58 log ↑ breast milk VL.

A model for transmission by breastmilk...

- Could be free virion or cell associated virus
- Breast milk enriched with lymphocytes
- ARV suppresses the release of virions in plasma, but only low levels of ARV are found in breastmilk
- Cells activated by extravasation or transepithelial migration in the mammary gland -> virus from stable reservoirs released in the breast milk?

Cellular Composition of Breastmilk During Lactation

- Macrophages
- Lymphocytes
- CD4+ T cells

Does Undetectable Plasma Viral Load Mean Undetectable Breast Milk Viral Load?

- BAN study: Postnatal maternal ART vs infant nevirapine (NVP) vs single-dose NVP for prevention of postnatal transmission (maternal ART and infant NVP similar efficacy).
- 221 mothers had paired plasma and breast milk specimens.
- Mothers with detectable plasma VL has adjusted 40-fold increased odds of detectable breast milk VL (95% CI 15-108).
- However, 2 (0.9%) had undetectable plasma VL at 6 weeks postpartum but detectable breast milk VL (56 and 77 c/mL).
Women with HIV and CD4 ≥350 cells/mm³ and their uninfected breastfeeding infants randomized to start either maternal ART (n=1220) or infant NVP (n=1211) at 6-14 days postpartum at 14 sites in 7 countries.

- Plasma viral load measured at baseline and 6, 14, 26, and 50 weeks postpartum.

Transmission rates were very low! (but not zero)

Vertical transmissions occurred to infants of women who had recently achieved virologic suppression...

- Time-varying maternal viral load was significantly associated with infant infection in the maternal ART arm (HR 11.0, 95% CI 2.5-56.1) but not the infant NVP arm.

HIV infections continue to occur in children, despite gains in antiretroviral coverage among pregnant women globally

Both detectable at delivery, then suppressed. Would this have happened if suppressed earlier?

We can do pretty well in clinical trials … but what is happening in “real world” settings where breastfeeding is recommended?
Half of vertical transmission occurs during breastfeeding
46% (2019)

Vertical transmission rate and the percent occurring during breastfeeding, by country

Source: UNAIDS, 2020 estimates

Mary Mahy (UNAIDS) and George Siberry (USAID) at PNP meeting 1, May 11, 2021

Where does this leave providers?

What is the risk of vertical transmission with longstanding virologic suppression? We don’t know but likely very low, < 1%

How well can we predict who will be able to maintain virologic suppression?

Will this be that unlucky infant?

Information we still need:
• Why do those rare cases occur?
• Are there biomarkers?
• Will better ARV treatment ensure durable suppression in breast/chest feeding parents?
• Does giving infants of women on treatment medication lower the risk further?

Why “risk’ it?

Not breastfeeding causes issues of stigma, privacy and unintended disclosure

Why “risk’ it? Breastfeeding is an investment in health. Not just a lifestyle decision

We don’t just want Zero Transmission, we want people affected by HIV to have the same choices and health outcomes as people without it …

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Where does this leave parents?

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Why “risk’ it? Not breastfeeding causes issues of stigma, privacy and unintended disclosure

Why “risk’ it? Breastfeeding is an investment in health. Not just a lifestyle decision

We don’t just want Zero Transmission, we want people affected by HIV to have the same choices and health outcomes as people without it …
Where does this leave providers?

The decision about whether or not to breast/chest feed is ultimately the parent’s... regardless of what providers and guidelines recommend.

“Tilting the Scale: Current Provider Perspectives and Practices on Breastfeeding with HIV in the United States”

- Survey in June/July 2021.
- 99 physicians, advanced practice providers, nurses, and lactation consultants.
- 10% had an institutional protocol.
- 1 transmission isn’t that enough?

Provider disagreement:
- Some of the providers in our small group believe that our guidelines should be liberalized. Other providers feel that we should not allow BFing among WLHIV under any circumstance. It has been difficult to get consensus.

Lack of guidelines or data:
- I would not feel comfortable because there aren’t specific guidelines or literature to support the care, however I’m very interested in learning more for those who are interested in breastfeeding to be able to support that decision.

European Guidelines?

Breastfeeding

Guidelines in USA

“Advise against but support if...”

New guidance in January 2023

https://www.eacsociety.org/guidelines/eacs-guidelines/

“Advise against but support if...”

Guidelines in USA


Tilting the Scale: Current Provider Perspectives and Practices on Breastfeeding with HIV in the United States

How often is breast/chest feeding happening in the USA?

Unknown

How many calls have we been getting at hotlines?

FY21 = 81
FY20 = 103

What to look for next?

• Better medications and long acting platforms, leading to better outcomes in women, lower risk of transmission, and new options for prophylaxis in infants
• HIV choosing to breast/chest-feed their infants
• More proactive and details guidance
• More data about the risk of transmission, the combined efficacy of maternal treatment plus different approaches to infant prophylaxis to get even closer to zero

What is the risk of HIV transmission via breastfeeding?

• Without maternal antiretroviral therapy (ART) or infant antiretroviral prophylaxis, the risk of an infant acquiring HIV through breastfeeding is 15% to 20% over 2 years
• Achieving and maintaining viral suppression through ART during pregnancy and postpartum decreases breastfeeding transmission risk to less than 1%, but not zero

Lets talk about the meds…

• Who is the patient?
  ▶ Its really both
• What is the setting?
  ▶ Moms who are HIV positive; high vs low risk
  ▶ Moms are risk for HIV acquisition
  ▶ Babies born to low risk moms
  ▶ Babies born to high risk moms
PrEP vs treatment

- What are our choices?
  - Oral vs LA meds
    - Lots of oral choices for treatment
      - Insurance coverage and switches
  - BUT for PrEP, fewer choices!!!
    - Descovy is a prime example!!!
    - Not enough LA meds yet
    - LA Cabo for PreP in women, but not while pregnant
  - Asked but not answered: bNABs for prevention or treatment...

Meds for breast feeding infants

- Among women with HIV:
  - AZT: worked
    - But in which setting
  - NVP works
    - But for how long?
    - Risks?
  - What else is out there for prevention?
    - DTG? Data in neonates?
    - Risks of post exposure prophylaxis (PrEP in infants)

How does one dose the baby meds?

- By gestational age
- By weight
- By confusion…
  - Daily calls with mom?

What data and studies do we need?

- How to dose LA meds (both for treatment as well as PrEP) post delivery
  - Data during breast feeding is very very limited
- Will women take oral PrEP during and after pregnancy?
  - Data from IMPAACT 2009 is pending
- How do we study which is best to use:
  - Meds in moms with HIV (long acting)
  - Meds in infants (long acting, daily oral, bNABs…combos)
So who is a high risk infant?

- Newborns are at an increased risk for HIV acquisition when their mothers do not receive ART during pregnancy
- When mothers start antepartum treatment late in pregnancy
- When antepartum treatment does not result in viral suppression (defined as at least two consecutive tests with HIV RNA level <50 copies/mL obtained at least 4 weeks apart)
- Higher maternal viral load, especially in late pregnancy, correlates with higher risk of transmission

Overview of counseling and management

For people with HIV who are not on ART and/or do not have a suppressed viral load at delivery, replacement feeding with formula or banked pasteurized donor human milk is recommended to eliminate the risk of HIV transmission.

<table>
<thead>
<tr>
<th>Individuals with HIV on ART with a consistently suppressed viral load during pregnancy (at a minimum during the third trimester) and at the time of delivery should be counseled on the options of formula feeding, banked donor milk, or breastfeeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>- The infant feeding options that eliminate the risk of HIV transmission are formula and pasteurized donor human milk</td>
</tr>
<tr>
<td>- Fully suppressive ART during pregnancy and breastfeeding decreases breastfeeding transmission risk to less than 1%, but not zero.</td>
</tr>
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</table>

Situations in Which to Consider Stopping or Modifying Breastfeeding...

- In the case of a detectable viral load, breastfeeding [should] be temporarily stopped. Options include giving previously stored breastmilk, pumping/flash heating, providing replacement feeding, or cessation of breastfeeding; repeating viral load; and reassessing continuation or cessation of breastfeeding.
- If the repeat viral load is detectable, the Panels advise immediate cessation of breastfeeding; this guidance is more directive than counseling for individuals on suppressive ART.

There is no consensus on ARV prophylaxis for infants of individuals with sustained viral suppression who are breastfed

- Most Panel members agree on only 2 weeks of infant zidovudine (ZDV)
- However, several Panel members prefer to extend the duration of ZDV prophylaxis to 4 to 6 weeks.
- Alternatively, some Panel members recommend 6 weeks of nevirapine (NVP), as currently recommended by WHO for breastfeeding infants at low risk of HIV transmission in resource limited countries.
- Some others opt to continue NVP dosing throughout breastfeeding.

Engaging Child Protective Services or similar agencies is **not** an appropriate response to the infant feeding choices of an individual with HIV

- Numerous pregnant people with HIV have reported that after expressing their interest/intention to breastfeed, their providers threatened to report them to CPS or actually did so.
- Such engagements can be extremely harmful to families; can exacerbate the stigma and discrimination experienced among people with HIV; and are disproportionately applied to minoritized individuals, including Black, Indigenous, and other people of color.


**What was new in process of developing the 2023 guidelines?**

- Integration of community input from members of The Well Project, International Community of Women Living with HIV - North America, and others
- Obtaining input from lactation specialists at CDC
- New level of collaboration between the Perinatal and Pediatric Panels
- CDC chose to refer any queries about infant feeding in the U.S. to the Perinatal Guidelines (rather than having their own recommendations)


**Support needed for birthing parents:**

- Primary care, HIV, and prenatal clinicians able to provide evidence-based, non-coercive counseling
- Knowledgeable lactation specialists
- Access to both a supportive clinical team and peer support in the postpartum period to address barriers to medication adherence and viral load monitoring
- Recommendations on how to deal with situations such as mastitis, maternal and infant illness, small elevations in viral load

**Data from a recent study**

- Assessed breastfeeding outcomes for a cohort of infants born to women living with HIV (WLHIV) at an urban health care center in the US.
- Ten infants were exclusively breastfed for a mean duration of 4.4 (1.0-8.6) months
  - 14 were approached
  - All had negative HIV RNA PCRs at a median age of 16 months

Yusef H. JPIDS jan 2022;https://doi.org/10.1093/jpids/piab116
### So, what did the study team do?

- Following delivery, infants were initiated on triple ART (zidovudine [AZT], lamivudine [3TC], and nevirapine [NVP]) in the newborn nursery and seen by a pediatric infectious disease specialist, neonatologist, pediatric nurse practitioners, and lactation consultant.
- At 6 weeks switched to NVP through 6 weeks post breastfeeding.
- PCR testing at birth, 2 weeks, 4 weeks, 8 weeks, 16 weeks, 24 weeks, 4 weeks post-cessation of NVP, monthly until cessation of breastfeeding, 4- to 8-week post-cessation of breastfeeding, 18 months.
- **IS THIS SUSTAINABLE?**

### Dissemination and Implementation of Updated Infant Feeding Recommendations

- **Dissemination of updated recommendations**
  - Guidelines website: [https://clinicalinfo.hiv.gov/](https://clinicalinfo.hiv.gov/)
  - CDC, AAP, ACOG, SMFM, Office of Women’s Health
  - HRSA/HAB, AETC Network, ANAC
  - Other organizations and websites e.g., [https://www.thewellproject.org/](https://www.thewellproject.org/), Academy of Breastfeeding Medicine
- **Updates and alignment of information from key trusted sources**
  - Identify information sources that conflict with updated recommendations for infant feeding and address discrepancies
  - Many excellent resources on breastfeeding list HIV as a contraindication
- **Anticipate questions/concerns from clinicians and consumers**
  - Guidelines provide a lot of information, but there are still grey areas
  - The Perinatal HIV Hotline anticipates a large increase in calls

Resources as you, your clinicians, and your staff navigate this new road …

- [www.hivinfo.nih.gov](https://www.hivinfo.nih.gov)
- 1-888-448-8766
- [https://ncc.ucsf.edu/](https://ncc.ucsf.edu/)

Questions??

Thanks for listening!