Human Milk Banking: Considerations related to Human Immunodeficiency Virus

Kenneth L. Dominguez, MD, MPH
Epidemiology Branch
Division of HIV/AIDS Prevention, NCHHSTP, CDC

Outline

- Epidemiology of perinatal HIV in the U.S.
- Current recommendations around breastfeeding and HIV in the U.S.
- Pasteurization temperatures required to kill HIV
- Human milk banking procedures to reduce transmission of pathogens
- Summary

Epidemiology of Perinatal HIV in the U.S.

- **Estimated no. of HIV-infected women 13-44 years of age diagnosed and living with HIV or AIDS in 2006[1]:**
  - 181,872-185,475
- **Estimated No. of births to women 13-44 years of age diagnosed and living with HIV or AIDS in 2006[1]**
  - 8,650-8,900
- **Estimated No. of HIV-infected infants diagnosed in 2008[2]**
  - 141

References: (1) Whitmore, S., et al. **Estimated Number of Births to HIV-Positive Women, United States, 2006. Conference on Retroviruses and Opportunistic Infections, 2009. (2) CDC. HIV Surveillance Report, 2008; vol. 20. http://www.cdc.gov/hiv/topics/surveillance/resources/reports/ . Published June 2010. Accessed Nov . 29, 2010.**

Breastfeeding and link to HIV

- **Reports of probable breastfeeding transmission of the virus from a mother to her child**
  - Ziegler JB, et al.,*Lancet*, 1985. i: p. 896-98.
  - Lepage P, et al., *Lancet*, 1987. u: p. 400.
- **CDC has recommended against breastfeeding by HIV-infected women since Dec. 1985**
  - MMWR, 1985. **34**(48): p. 721-726, 731-732.
  - Ref: 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. May 24, 2010; pp 1-117. Available at http://aidsinfo.nih.gov/ContentFiles/PerinatalGL.pdf. Accessed Nov. 29, 2010

Should an HIV-infected woman with an undetectable HIV viral load be allowed to donate milk to a human milk bank? No

- **Can perinatal mother-to-child transmission occur vertically between an HIV-infected mother and her infant if the mother has un undetectable viral load? YES**
  - Transmission has been observed across the entire range of HIV RNA levels (including in women with undetectable viral load)
  - Although the risk of perinatal transmission in women with undetectable HIV RNA levels appears to be extremely low, transmission from mother to infant has been reported among women with all levels of maternal HIV RNA

Ref: 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. May 24, 2010; pp 1-117. Available at http://aidsinfo.nih.gov/ContentFiles/PerinatalGL.pdf. Accessed Nov. 29, 2010

Can HIV transmission still occur horizontally between an HIV-discordant couple when the HIV-infected individual in the relationship has an undetectable viral load? YES

- Sexual transmission of HIV from an infected partner who was on ART with a repeatedly undetectable plasma viral load has been documented
  - Ref: Sturmer M, et al. *Antivir Ther* 2008;13:729-732.
- Persistent virus is found in peripheral blood mononuclear cells even when individuals have sustained undetectable plasma viral load levels.
  - Ref. Ibanez A, et al. *AIDS* 1999;13:105-109.
  - Ref. Furtado MR, et al. *N Engl I Med* 1999;340:1614-1622.
- The potential for transmission exists despite sustaining undetectable viral load while on effective ART

Inactivation of Human Immunodeficiency Virus Type I in Human Milk: Effects of Intrinsic Factors in Human Milk and of Pasteurization

S. L. Orloff, J. C. Wallingford and J. S. McDougal
J Hum Lact 1993; 9; 13

- **Human milk inoculated with HIV-1 or HIV-1 infected cells**
- **Inoculated milk pasteurized at**
  - 62.5ºC for 30 minutes in a water bath (Holder pasteurization).
  - 56ºC for 30 minutes to better preserve some nutritional and protective components
- **Process of HIV-1 inoculation and pasteurization effectively inactivated the infectivity of both cell-free HIV-1 and HIV-1-infected cells**
- **No virus was recovered after the process at 62.5ºC or 56ºC, even after repeated subculturing in attempts to rescue the virus.**
  - HIV-1 Microculture assay: capable of detecting a single infected cell
  - Limit of detection = 1 cell/0.5 ml (2 cells/ml)

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- **Pasteurization reduced the infectious titer of cell-free HIV-1 and HIV-1 infected cells by > 5 logs and 6 logs respectively.**
- **Human milk contains ≥ 1 unidentified components that inactivate HIV-1**
- **The intrinsic activating activity of milk is enhanced at higher temperatures**
- **Pasteurization coupled with donor screening should alleviate any concerns about the safety of banked human milk with respect to HIV-1 transmission.**

Inactivation of HIV-1 in breast milk by treatment with the alkyl sulfate microbicide sodium dodecyl sulfate (SDS)

Sandra Urdaneta*[1,8], Brian Wigdahl[2], Elizabeth B Neely[1,3], Cheston M Berlin Jr[4,5], Cara-Lynne Schengrund[6], Hung-Mo Lin[7] and Mary K Howett[1,8]

Retrovirology 2005, 2:28 doi:10.1186/1742-4690-2-28

- **Alkyl sulfates (sodium dodecyl sulfate, SDS)**
  - **microbicidal against HIV-1 at low concentrations**
  - **Biodegradable**
  - **Have little/no toxicity**
  - **Inexpensive**

- **Human milk was artificially infected by adding HIV-I (cell free or cell-associated) and treated with ≤ 1% SDS (≤10 mg/ml) at 37ºC or room temperature for 10 min; SDS was them removed with resin.**
  - **Treatment concentration within safe limits for ingestion of SDS by children of 1 g/kg/day.**
  - **SDS listed in Generally Recognized As Safe (GRAS) list of chemicals of the U.S. FDA**

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- **SDS (≥ 0.1%) was virucidal against cell-free and cell-associated HIV-1 in breast milk**
- **SDS could be substantially removed from breast milk, without recovery of viral infectivity; milk was not infectious after SDS removal**
  - **Viral load determination via branched DNA (bDNA) VERSANT® HIV-1 RNA assay : sensitivity = 75-500,000 RNA copies/ml**

Flash-Heat Inactivation of HIV-1 in Human Milk

A Potential Method to Reduce Postnatal Transmission in Developing Countries

Kiersten Israel-Ballard, MPH, Richard Donovan, PhD,† Caroline Chantry, MD,‡ Anna Coutsoudis, PhD,§ Haynes Sheppard, PhD,† Lindiwe Sibeko, MSc,‖ and Barbara Abrams, DrPH**

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- **Heat flashing**
  - 50 ml of expressed breast milk placed in uncovered sterile 16-0z commercial glass food jar
  - Placed in 450 mL of water in a HART brand 1-qt aluminum pan
  - Water and milk heated together over a single burner butane stove, until the water reached 100°C and was at a rolling boil
  - Breast milk immediately removed from water and allowed to cool to 37° C.
  - Flash-heating typically reached temperatures > 56°C for 6 min. 15 seconds and peaked at 72.9°C
- **Sensitivity of RT assay = 400 copies/mL**
- **30 unheated breast milk samples had a**
  - mean of 8266 HIV copies/mL
  - Mean log of 3.45 HIV copies/mL
- **All corresponding flash-heated samples showed undetectable levels of HIV in the RT assay**

Human Milk Banking Procedures to Reduce HIV-Transmission

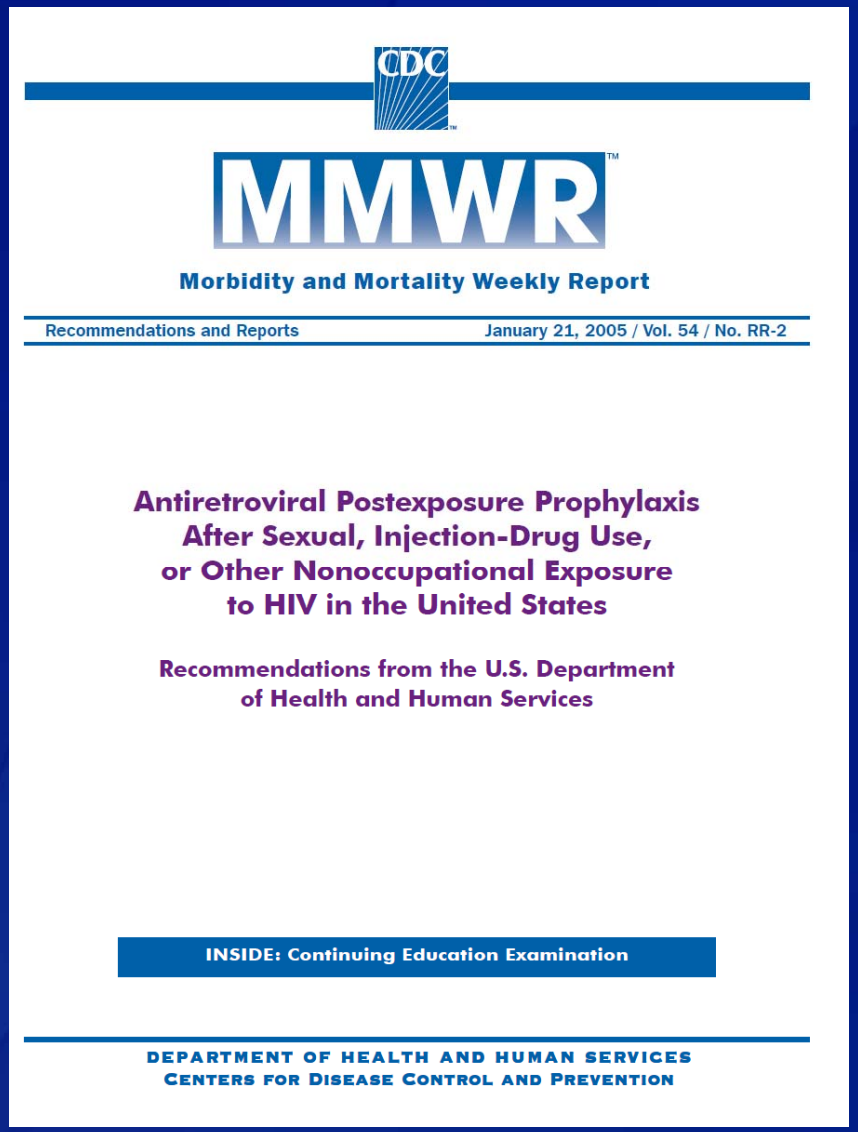
- **Donor Screening**
  - Written/verbal screening
  - educational materials high risk groups/behaviors
  - Statement of health/medical risk signed by provider
  - HIV serologically screened no > 6 mo. prior to the first donation
    - *Recommendation: Need minimum time period specified (prevent false negatives early on)*
    - *Recommendation: Consider: No < 4-6 weeks before donation using 3rd generation IgM-sensitive HIV-1 test or 4th generation HIV-1 Ag/Ab combination test*
  - Exclusions based on clinical issues unique to human milk and infants and current American Association of Blood Banks standards, when appropriate

Human Milk Banking Procedures to Reduce HIV-Transmission

- **Written Instructions for sanitary collection, handling, storage and transportation of human milk**
  - ***Recommdnation: If feasible, have donor donate milk at milk bank to guarantee identity of milk donor similar to blood donor procedure.***
- **Handling: Persons handling open containers of milk wear a hair covering, gloves, and a clean cover gown**
- **Heat processing**
  - **Milk placed in containers and submerged in water bath to a minimum of 62.5ºC x 30 minutes**
  - **Calibrated thermometer is placed in a control bottle**

Human Milk Banking Procedures to Reduce HIV-Transmission

- **Labeling of milk containers-Batch number, name of milk bank**
- **Procedures well outlined in case of accidental switching of milk bottles (notification of both parties, lab testing, etc.)**
  - ***Recommendation: Consider adding link to***
    - ***CDC Nonoccupational Postexposure Prophylaxis Guidelines***
    - ***American Academy of Pediatrics Postexposure prophylaxis Guidelines (Peter Havens)***
    - ***National Clinician's PEP Hotline 888-448-4911 link: http://www.nccc.ucsf.edu/about_nccc/pepline/***
      - ***Open 24 hours a day, 7 days a week***



Ref: Centers for Disease Control and Prevention. Antiretroviral postexposure prophylaxis after sexual injection-drug use, or other nonoccupational exposure to HIV in the United States: recommendations from the U.S. Department of Health and Human Services. *MMWR. 2005; 54(No. RR-2): 1-21.*

Link: www.cdc.gov/mmwr/PDF/rr/rr5402.pdf

NPEP Guidelines Summary

- **For persons seeking care ≤ 72 hours after unanticipated exposure to potentially infectious body fluid of HIV-infected person :**
  - Blood
  - Genital secretions
  - Other
- **Exposure must represent a substantial risk of transmission**
- **28 day course of highly active antiretroviral therapy is recommended**
- **Evaluate on a case-by-case basis**

Estimated per-act risk for acquisition of HIV, by exposure route

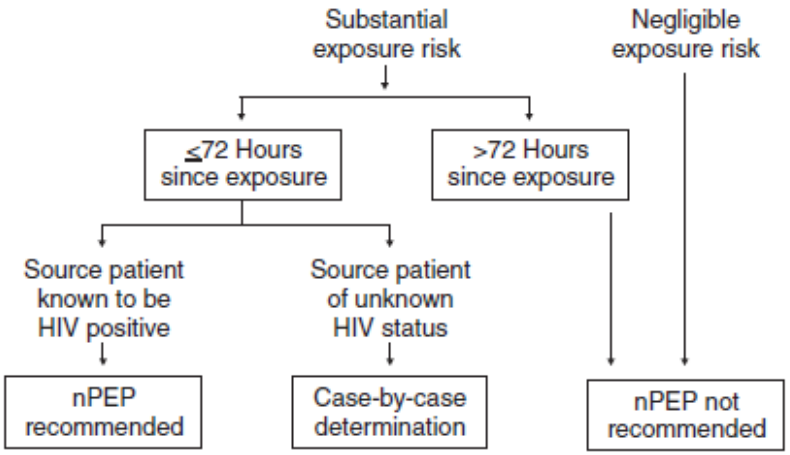
TABLE 1. Estimated per-act risk for acquisition of HIV, by exposure route*

Exposure route	Risk per 10,000 exposures to an infected source	Reference
Blood transfusion	9,000	74
Needle-sharing injection-drug use	67	75
Receptive anal intercourse	50	76, 77
Percutaneous needle stick	30	78
Receptive penile-vaginal intercourse	10	76, 77, 79
Insertive anal intercourse	6.5	76, 77
Insertive penile-vaginal intercourse	5	76, 77
Receptive oral intercourse	1	77†
Insertive oral intercourse	0.5	77†

* Estimates of risk for transmission from sexual exposures assume no condom use.
† Source refers to oral intercourse performed on a man.

Algorithm for evaluation and treatment of possible nonoccupational HIV exposures

FIGURE 1. Algorithm for evaluation and treatment of possible nonoccupational HIV exposures



Substantial Risk for HIV Exposure

Exposure of
vagina, rectum, eye, mouth, or other mucous membrane, nonintact skin, or percutaneous contact

With
blood, semen, vaginal secretions, rectal secretions, breast milk, or any body fluid that is visibly contaminated with blood

When
the source is known to be HIV-infected

Negligible Risk for HIV Exposure

Exposure of
vagina, rectum, eye, mouth, or other mucous membrane, intact or nonintact skin, or percutaneous contact

With
urine, nasal secretions, saliva, sweat, or tears if not visibly contaminated with blood

Regardless
of the known or suspected HIV status of the source

Antiretroviral regimens for nonoccupational postexposure prophylaxis of HIV infection

TABLE 2. Antiretroviral regimens for nonoccupational postexposure prophylaxis of HIV infection

Preferred regimens	
NNRTI*-based	Efavirenz† plus (lamivudine or emtricitabine) plus (zidovudine or tenofovir)
Protease inhibitor (PI)-based	Lopinavir/ritonavir (co-formulated as Kaletra) plus (lamivudine or emtricitabine) plus zidovudine
Alternative regimens	
NNRTI-based	Efavirenz plus (lamivudine or emtricitabine) plus abacavrir or didanosine or stavudine§
PI-based	Atazanavir plus (lamivudine or emtricitabine) plus (zidovudine or stavudine or abacavir or didanosine) or (tenofovir plus ritonavir [100 mg/day])
	Fosamprenavir plus (lamivudine or emtricitabine) plus (zidovudine or stavudine) or (abacavir or tenofovir or didanosine)
	Fosamprenavir/ritonavir¶ plus (lamivudine or emtricitabine) plus (zidovudine or stavudine or abacavir or tenofovir or didanosine)
	Indinavir/ritonavir¶** plus (lamivudine or emtricitabine) plus (zidovudine or stavudine or abacavir or tenofovir or didanosine)
	Lopinavir/ritonavir (co-formulated as Kaletra) plus (lamivudine or emtricitabine) plus (stavudine or abacavir or tenofovir or idanosine)
	Nelfinavir plus (lamivudine or emtricitabine) plus (zidovudine or stavudine or abacavir or tenofovir or didanosine)
	Saquinavir (hgc* or sgc*)/ritonavir† plus (lamivudine or emtricitabine) plus (zidovudine or stavudine or abacavir or tenofovir or didanosine)
Triple NRTI*	Abacavir plus lamivudine plus zidovudine (only when an NONRTI- or PI-based regimen cannot or should not be used)

* NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; sgc = soft-gel saquinavir capsule (Fortovase); hgc = hard-gel saquinavir capsule (Invirase).
† Efavirenz should be avoided in pregnant women and women of childbearing potential.
§ Higher incidence of lipoatrophy, hyoerlipidemia, and mitochondrial toxicities associated with stavudine than with other NRTIs.
¶ Low-dose (100–400 mg) ritonavir. See Table 4 for doses used with specific PIs.
** Use of ritonavir with indinavir might increase risk for renal adverse events.
Source: U.S. Department of Health and Human Services. Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents, October 29,2004 revision. Available at http://www.aidsinfo.nih.gov/guidelines/default_db2.asp?id=50. This document is updated periodically; refer to website for updated versions.

AMERICAN ACADEMY OF PEDIATRICS

CLINICAL REPORT

Guidance for the Clinician in Rendering Pediatric Care

Peter L. Havens, MD, and the Committee on Pediatric AIDS

Postexposure Prophylaxis in Children and Adolescents for Nonoccupational Exposure to Human Immunodeficiency Virus

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Summary

- **Significant numbers of HIV-infected women of reproductive age and delivering infants in the U.S.**
- **Breastfeeding still not recommended among HIV-infected women despite new medications due to low probability of transmissions**
- **Both heat- and chemical-related methods to rid human milk of HIV contamination**
- **Current Guidelines for Human Milk Banks of North America have several strategies in place to reduce likelihood for donor milk-related HIV transmission**
  - Made additional recommendations for reducing likelihood of transmission (donor procedure, HIV testing, PEP electronic links)

Thanks!

Contact Information:

Ken Dominguez

awh4@cdc.gov

(404) 639-8969