



Linkages between maternal and reproductive health

Trip Report

World AIDS Conference, Geneva, Switzerland

June 28–July 2, 1998

Jay Ross

**Academy for Educational Development
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Breastfeeding and Related Complementary Feeding and Maternal Nutrition**

BEST AVAILABLE

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Table of Contents

List of Acronyms	v
BACKGROUND	1
OUTCOMES	1
Annex A Selected Abstract	



List of Acronyms

CA	Cooperating Agency
MCT	Mother-to-Child transmission
NARESA	Network of AIDS Researchers in East and Southern Africa
OR	Operating Research
VCT	Voluntary Counseling and Testing

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I BACKGROUND

The 12th World AIDS Conference was held this year in Geneva from June 28–July 3. Given the risk of transmission of HIV during breastfeeding and LINKAGES efforts to promote breastfeeding at a global level including promotion in some countries where HIV prevalence among mothers exceeds 20 percent, it is important that we stay aware of technical developments in this area. In addition, LINKAGES was asked to make a short presentation on this issue for a satellite meeting organized by the the AIDS division of USAID's Global Bureau for representatives of missions and cooperating agencies in attendance at the conference. The conference also provided an opportunity to follow up on initiatives with NARESA and the multilateral agencies on efforts to promote confidential voluntary counseling and testing (VCT) within antenatal settings in Zambia.

II OUTCOMES

Given the large number of concurrent sessions and poster presentations, it was necessary to be very selective in what sessions I attended and therefore in what I can report here. Readers interested in greater scope or detail are referred to a) the annex to this report, containing published abstracts for selected presentations related to mother-to-child transmission of HIV, b) the full set of published abstracts in searchable form on CD (available in the LINKAGES resource center) and c) the AIDS98 website (www.AIDS98.ch).

In summary, there were no new breakthroughs reported. Although there was some progress on several fronts, as briefly summarized here, the outstanding “unanswered questions related to HIV and infant feeding” listed in the Preble and P1woz draft paper remain largely unanswered.

The greatest breakthrough is the UN announcement that they will proceed quickly with pilot projects to reduce MCT by offering VCT in pregnancy, together with a package of Zidovudine (ZDV=AZT) monotherapy, and counseling on infant feeding. However, since a) ZDV cannot yet be recommended with confidence for breastfeeding mothers (because the results of trials of ZDV for such mothers are not yet out) and b) replacement feeding supplies are not being provided as this is unlikely to be a sustainable option, the package of interventions to be provided is not yet clear.

The controversies are very much alive. The scientific community is committed to placebo controlled trials while the rights community objects. There is also a fear that the debate may slow or even halt such trials. The access to treatment debate that has plagued the HIV and infant feeding issue ever since the UN 1992 “dual standard” was the theme of the entire conference. “Bridging the gap” surfaced many times in discussions of the MCT issue, in relation to access to both drugs (ZDV as well as combination therapy) and replacement feeding. This problem will not go away. In a comment from the floor we were told that even Thailand, which has led the effort to reduce MCT through use of short course ZDV and free breastmilk substitutes, is faltering in this effort. The financial crisis has interrupted the free supplies of formula and thus threatened the AZT regimen that depends on replacement feeding.

Where is this all heading? The constraints are money, human resources, and community support. The money problem is enormous if “best practice” is considered as an option. A series of lower cost options needs to be spelled out from a package of low-cost interventions that should be offered to all pregnant mothers, regardless of HIV status through to the full package of VCT, AZT, and replacement feeding.



(for rich and middle-income countries) We heard much at the conference about how even California and Ontario cannot pull this off

Monday, June 29

A Session—Mother-to-Child Transmission

Nathan Shaffer (CDC) The Thailand Perinatal ZDV trial Shaffer presented the now well-known results of the randomized placebo-controlled trial of short course ZDV (=AZT) which provides 300mg of ZDV twice a day from 36 weeks of pregnancy 300 mg every three hours during labor, and requires replacement feeding The average number of doses per women in this study through delivery was 53 at a cost (drugs only) of \$50 This compares with \$800–\$1000 for the full ACTG 076 regimen Transmission rate in the treatment group was 9.4 percent vs 18.9 percent in the placebo group, suggesting a 50 percent reduction Additional point of note there were no new infections detected (using DNA PCR) after two months, indicating that any pre- or intrapartum infections are detectable by this time and that new infections detected after this time in a breastfeeding population could be attributed to breastfeeding

Based on the timing of the new infections and the differences observed between the treatment arms, most of the reduction is in intrapartum transmission Mode of delivery did not seem to be important, but there were few cesareans There was a strong correlation between viral load and transmission among both the treatment groups Treatment resulted in a large reduction in the viral load among both transmitters and non-transmitters (by a mean of 0.5 log copies) Viral load in the treatment group had returned to baseline by one month after delivery (This does not argue against a stronger “rebound” effect since the rebound is generally of shorter duration (20 days))

E Ekpini Short course ZDV trial (with BF) in Abidjan safety and compliance (efficacy results not yet in) Ekpini used the same regimen as in the Thai trial but a smaller sample (n=275) This trial is important, not only because it tests the short course therapy among breastfeeding mothers but also because adherence to therapy was poorer, reflecting the level of adherence that might be expected in a less tightly controlled clinical (rather than research) setting ZDV was well tolerated with no differences between treatment and placebo groups in any symptoms This and other similar trials (in Burkina Faso and elsewhere) should have results to report by the end of 1998

Jim Khan Analysis of placebo-controlled vs equivalence designs in trials of ZDV to reduce MCT Judged on the basis of validity (whether results would be conclusive), generalizability (whether results could be applied to other populations), or how quickly the result could be obtained and implemented, placebo trials are justified This was intended not as an ethical analysis but a technical analysis to inform the ethical one The issue of ethics and placebo trials was also mentioned in the discussion during the afternoon session This is still a controversial issue that threatens to slow progress towards better therapies by potentially halting the design and implementation of any kind of trial

W Fawzi Tanzania vitamin A and multivitamin trial This was reported recently in the Lancet The abstract and a comment have already been distributed to the LINKAGES HIV/BF group There was nothing new in the conference report that I noted

A Semprini European Multi-Center study of the efficacy of cesarean section in reduction of MCT Transmission rates among women randomly assigned to undergo elective cesarean section was 2 percent



vs 11 percent in mother delivering vaginally (In response to a question, it was revealed that, although the numbers were small, ARV used together with cesarean section resulted in zero transmission. We were not told how many mothers were in this group)

Chris Hudson (With Alan Smith South Africa) A high proportion of pregnant women test positive for p-24 antigen but are antibody negative. This implies that standard test for HIV will miss about one of five infected mothers, and the duration of infection before antibodies are detectable in this population is about 12 months (calculated assuming 10 percent of mothers newly infected each year)

B “Bridging” Session—Mother-to-Child Transmission

Isabelle de Vincenzi described components of a standard package of care for reducing MCT: antenatal care (general), VCT, ZDV short course, care in childbirth, and support for replacement feeding. Need practical recommendations on algorithms for rapid/simple HIV testing, efficacy of ZDV among breastfeeding mothers, and costs. Test kit available for \$1 from WHO [E. Marum, in comment from the floor, said that the rapid test they use, together with confirmation, quality control, and ongoing training, is \$14/test.]

The Zimbabwe pilot test site is the most advanced of 11 pilot sites now identified to test a MCT reduction protocol in Africa, Asia, and Latin America. A situation analysis was completed in March with main constraints revealed being the lack of human resources to do counseling. The development of materials for counseling will begin “this summer” at three sites and activities will start in September.

Philippe Van de Perre: What is the relevance of Short Course Trial results to breastfeeding? Three such trials underway: Abidjan (see Ekpini presentation above) and Burkina Faso. ZDV appears in breastmilk in slightly higher concentrations than in blood. Efficacy of this or any other dose in the infant is unknown. Rebound in viral load observed following ZDV lasts only about 20 days but given the strong correlation observed between viral load and transmission, short course ZDV may actually increase the risk of transmission for breastfed infants. Given these uncertainties, short course therapy cannot be recommended for breastfeeding women. We must continue to wait for the results of ongoing trials.

Other speakers:

- Dorothy Odhiambo (Representative of African NGOs)
- Peter Young (Glaxo Wellcome)
- Susan Moses (Caribbean community of women living with HIV)
- A. Amman (President of the American Foundations for AIDS research)

Comments from the floor

- Elizabeth Marum (AIDS information centre, Uganda) has used a rapid test with same-day results since January 1997 with good results. The total cost of the rapid test they use, together with confirmation, quality control, and ongoing training, is \$14/test.
- Prof. Ganapati Bhat is doing VCT in an antenatal setting in Zambia (UTH, Lusaka). Reports acceptance rate of 81 percent and no violence towards HIV positive women has been reported in follow-up. Prof. Bhat also stressed the need to involve the spouse in the process.



- Ruth Nduati (University of Nairobi) The avoidance of MCT is empowering for the mother since it relieves her of enormous time and financial costs of caring for the sick child
- Beatrice Tess (NIH) noted that although sample size was a problem for statistical inference in her Sao Paulo study, they observed increased transmission with cracked nipples and with mixed feeding (vs exclusive breastfeeding) Dr Tess also asked why there are no studies that look at these phenomena explicitly Reply (Philippe Van de Perre) These can be looked at in the ongoing short course trials among BF women

Official summary of Monday's MCT session (from the AIDS98 website)

Vertical transmission of HIV infection can occur before, during or after delivery, although most indirect evidence now suggests a limited role for the early intra-uterine route

With the advent of effective anti-retroviral therapy perinatal HIV infection has become a preventable disease, using a long regimen of zidovudine during pregnancy, at labour and in the neonatal period to reduce the risk by nearly 70%

Now, a cheaper short course of oral zidovudine has been shown to reduce transmission by 50% Reduction in maternal viral load at delivery was estimated to account for 80% of the reduction in vertical transmission rate

Adherence to and tolerance of prenatal and intra-partum zidovudine therapy in a randomised trial of a short course of zidovudine in a breastfeeding population in Cote D'Ivoire, showed that women could take the antenatal component of the regimen well However, adherence to the intra-partum component was a problem Zidovudine was found to be well tolerated by both mothers and children, with little evidence of serious adverse effects

Elective caesarean section delivery can also reduce vertical transmission by 50%, even after allowing for other risk factors known to be associated with increased risk

Other approaches to interventions include cleansing of the birth canal, and the administration of multivitamins Post-natal transmission through breastfeeding remains a problem, especially in countries where safe and affordable alternatives are not available and antenatal prevalence tends to be the highest Globally more than 40% of women do not have a skilled attendant during labour and delivery, while more than 30% of women do not receive adequate antenatal care essential to the general health and wellbeing of mothers and children

In a randomised-placebo controlled trial in Tanzania the administration of multi-vitamins, but not Vitamin A alone, was found to result in a decrease of adverse pregnancy outcomes, measured as fetal deaths, low birthweight, preterm birth and small for gestational age

Counselling to support women and to help them make informed decisions based on their individual circumstances is essential Studies in different geographical regions on current breast-feeding practices



and preferences are needed in addition to information on the impact on HIV transmission of possible options for women such as shorter duration of breastfeeding, mixed feeding, and breast milk substitutes

With respect to timely access to voluntary counselling and testing for pregnant women, the advantages and disadvantages of same day results need to be explored further. While rapid tests are now logistically and technically feasible, whether this approach is appropriate for pregnant women will require further debate. Women often may want and need to consult with spouses, family members and friends about whether to have an HIV test – and in some circumstances consent for such a procedure must be communal as opposed to individual.

Tuesday, June 30

A Session—HIV transmission Infant Feeding

This session focused on the infant feeding issue but provided very little in the way of new information or new perspectives to those already well-acquainted with the field. It did serve to emphasize the continuing difficulties in counseling mothers on infant feeding. Linda Francis, an AIDS activist and educator from Zimbabwe, delivered an impassioned plea for choice to be provided to HIV-positive mothers. She argued that safe alternatives to breastfeeding must be offered and that where formula was too expensive, animal milks and paps should be introduced, together with adequate education to make these alternatives safe. An official summary of this session follows.

Official Summary (from AIDS98 web site)

Although vertical transmission through breast milk was identified in 1985, there have been many complex issues surrounding the recommendation of artificial feeding.

For HIV-positive mothers, information on artificial breast-feeding is essential since it can prevent the child's infection. Each woman should have a possibility of informed choice. For artificial feeding to be effective mothers need clean water, the knowledge on the how to sterilise utensils and prepare the formula. The widespread use of artificial feeding by HIV-negative mothers and women unaware of their status can increase malnutrition and mortality. Infant mortality is 16 times more likely with artificial feeding than if a child is breast-fed.

The artificial feeding business should consider: Emphasis on replacement feeding as a medicinal practice, Procuring the formula centrally to control its distribution, Arrange for generic packaging so as not to promote the product.

For successful artificial feeding there is a need for education on alternatives such as cow and goats milk, expressing breast milk and boiling it and, if available, the use of an HIV-negative wet nurse. Making the change from the emotional rewarding act of breast feeding to artificial feeding often is an enormous burden for the mother to carry. Comprehensive education, emotional support and access to different options are needed.

B Poster Highlights (listed by abstract number and first author)



23266 Leroy A pooled analysis of transmission risk in four breastfed cohorts (from Rwanda (2) Cote d'Ivoire and Kenya) suggests a risk after 2.5 months of 3.2 percent in 100 child years of follow-up. Meaning among 100 children followed for a year 3.2 percent are expected to become infected through breastfeeding.

23270 Mioti 9.6 percent risk of transmission in the first 18 months. The report is confusing because it says that the risk remained constant over the period but elsewhere the monthly risk is lower as the child gets older.

23284 Whittle MCT in the Gambia is higher in the wet season. The authors suggest a possible role of malaria but since there are many other seasonal variations this is but one of many possible explanations.

23285 Tess Effect of obstetric factors in Brazil. MCT is associated with duration of rupture of membranes and maternal stage of disease but not with vaginal bleeding, fetal presentation, episiotomy, or genital warts.

23292 Burge In an observational study of effects of different patterns of adherence, ante-partum treatment seems more effective than intra-partum.

23295 In Brazil it is government policy to distribute free supplies.

23309 India ACTG-076 regimen is being used in Bombay, but due to the cost, which families must cover, this only serves an elite. The replacement feeding option recommended is unmodified cow's milk!

23310 Cartoux A study of the correlates and reasons given for test refusal in clinical trials of antenatal VCT and interventions. The greatest constraint faced in offering VCT was the shortage of trained counselors.

23319 Nduati Cracked nipples among HIV-positive breastfeeding mothers is associated with vaginal candida infection (RR=2.0) and poor vitamin A status (RR=3.2). Although confounding is not ruled out, authors suggest that Vitamin A supplements may prevent cracked nipples.

23323 Izazola-Licea Results of an "consensus workshop" on HIV and infant feeding in the LAC region: breastfeeding should be discouraged among HIV-positive mothers and breastmilk substitutes provided.

23325 Nyazema (Zimbabwe) There was no variation in antibody content of breastmilk during the course of a feed.

Wednesday July 1

A Session—Mother-to-Child transmission

Valeriane Leroy Oral presentation of yesterday's poster (see # 23266 above)

Mioti Oral presentation of yesterday's poster (see # 23270 above)



K Beckerman Risk of transmission can be reduced virtually to zero with double and triple combination therapy with antiretrovirals, protease inhibitors, and other drugs. This therapy is now standard “best practice” in the west and has largely replaced ZDV monotherapy where these drugs are affordable and where it is possible to monitor viral load.

R Steketee In preliminary analysis of an ongoing study in Kenya, observed a higher rate of transmission (+ve PCR before 2 months) among infants of mothers with malarial parasitemia (34.5 percent) than among those without (28.4 percent) but this difference is not yet statistically significant.

B Ad hoc Meeting

Ruth Nduati, Grace John, and Dorothy Mbori-Ngacha (NARESA), David Alnwick, and Eric Masse (UNICEF), Eric Van Pragg (WHO), Isabelle de Vincenzi (UNAIDS), Sam Kalibala (HORIZONS), Ganapati Bhat (UTH, Lusaka) held an ad hoc meeting. The purpose of this meeting was to update all parties about the NARESA initiative to introduce VCT in antenatal settings in Africa and to coordinate this activity with the similar pilot projects being launched in 11 countries as announced at this conference by UNAIDS. It was agreed that 1) coordination of these initiatives was essential, 2) efforts should not overlap or be duplicated, especially where they occur in the same country (e.g., Zambia) (UNICEF-Zambia is aware of both efforts in that country so can serve to avoid duplication), 3) WHO draft training guides can be made available for local adaptation when needed, 4) Sam Kalibala (HORIZONS, Nairobi) can act as a focal point for electronic networking and information sharing in the short term, 5) NARESA could act in this capacity but would need more resources (another half-time assistant position), 6) the UN could help with the Kenya arm of the OR effort but would require the willingness of the Kenya UNICEF office.

In further conversations with Ganapati Bhat, he expressed interest in assisting with the Zambia study. He has been conducting a similar pilot study for the last two years in three antenatal clinics in Lusaka (see abstract # 33282 in appendix) and has developed training materials and a VCT protocol that should be adapted for further OR or used as a basis for scaling up. He suggested that the next improvement needed is greater involvement of the spouse and would like to see this added to the protocol.

C USAID Satellite Meeting

The purpose of this meeting was to update mission staff on global bureau priorities and activities and to solicit feedback from the missions on what their needs were for technical and other assistance on HIV issues. In addition to representatives from about ten missions, many CAs working in the area had been invited to attend. I was asked to make a short (five minute) presentation on the infant feeding dilemma. After presenting the model and its policy implications (higher mortality if HIV-positive do not breastfeed, still higher if some HIV-negative do not), I made the case for shortened duration as an alternative to all or nothing, and closed by saying that this was hypothetical in most situations because mothers do not know their status, implying that the greatest programmatic need is for VCT. The Uganda mission (represented by Elizabeth Marum) was the only one to make specific mention of infant feeding as a priority issue. She also spoke of the availability of 70,000 patient records as a potential resource for research.

ANNEXES



Annex A Selected Abstracts

[30/33163] Randomized placebo-controlled trial of short-course oral ZDV to reduce perinatal HIV transmission, Thailand

Nathan Shaffer^{1,2} C Bhadrakom³ W Siriwasin⁴ R Chuachoowong¹ P Mock¹ N L Young² S Chearskul³ T Chotpitayasunondh⁵ J Karon⁶ R J Simonds⁶ T D Mastro² ¹HIV/AIDS Collaboration PO Box 139 Nonthaburi 11000 ²CDC & HIV/AIDS Collaboration Nonthaburi ³Mahidol University Bangkok ⁴Rajavithi Hospital Bangkok ⁵Children's Hospital Bangkok Thailand ⁶CDC Atlanta GA USA

Background Many developing countries with high burdens of perinatal HIV infection have not implemented the ACTG 076 regimen because of logistical and cost barriers. If proven safe and effective, a short-course oral zidovudine (ZDV) regimen administered to HIV-infected women late in pregnancy could become a widely implemented minimum alternative regimen for reducing perinatal HIV transmission. **Methods** A randomized, double-blind placebo-controlled trial is being conducted in Bangkok at Thailand's two largest maternity hospitals. The study regimen is oral ZDV 300 mg taken twice daily by HIV+ women beginning at 36 weeks gestation and every 3 hours during labor. No ZDV is given to the newborn. Mothers do not breast-feed, consistent with national guidelines. The target sample size is 392 women (196 in each arm), and has the power ($\alpha = 0.05$, $\beta = 0.2$) to detect a 50% decrease in transmission from a presumed background rate of 24%. Infants are tested by DNA PCR at birth, 2 and 6 months. Efficacy is based on estimated transmission rates at 6 months by Kaplan-Meier analysis of time to a positive PCR test. The study is monitored by an independent DSMB. **Results** Full study enrollment was completed from May 1996 through December 1997. Through 1997, there were 382 births (2 sets of twins). 313 children have been followed through 2 months and 222 children through 6 months. The median age of women at enrollment is 24 yrs (range 17-39) and the median CD4+ cell count is 412 cells/ μ L (range 6-1317). The median number of days on study drug before labor is 24 (range 3-58) and the median number of labor doses is 3. Weekly reviews of study drug, pill counts and qualitative interviews indicate a very high level of adherence (>95%) and tolerance. No woman has had to stop study drug. Thus far, more than 95% of expected study visits have been completed and <5% of children have been lost to follow-up. **Conclusions** Full study enrollment was completed in 1997. The study regimen, including the oral labor doses, has been well tolerated and adherence and follow-up have been >95%, suggesting that this short-course regimen would be feasible to implement in Thailand, and perhaps in other developing countries. There were two interim efficacy reviews by the DSMB. We expect to announce nearly final results by March 1998.

[31/23280] Study drug adherence and tolerance within a randomized clinical trial to evaluate a short-course regimen of zidovudine to reduce mother-to-child transmission of HIV-1 in Abidjan, Cote d'Ivoire

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Objective To evaluate adherence and tolerance to a self-administered prenatal and intrapartum drug regimen by HIV-1-positive women enrolled in a randomized clinical trial to evaluate a short-course zidovudine (ZDV) regimen to reduce mother-to-child transmission of HIV-1 in Abidjan, Cote d'Ivoire. **Methods** Since April 1996, all consenting eligible HIV-1-positive pregnant women attending a public antenatal clinic in Abidjan are enrolled at 36 weeks gestation and are randomized to receive either ZDV (300 mg tablets) or placebo. Women are instructed to take 1 tablet of study drug twice daily until the onset of labor, 1 tablet loading dose at the onset of labor, and then 1 tablet every three hours until delivery. Study drug adherence (number of tablets taken/expected number) is assessed by questionnaire and pill counts at biweekly prenatal visits and at delivery while tolerance to study drug is assessed by questionnaire, physical examination and laboratory evaluation. **Results** To date 272 HIV-1 seropositive women have been enrolled (mean age 26 years, range 15-42). Among the 259 women who have delivered the median duration of prenatal drug regimen was 26 days (range 1-80 days). The overall median study drug adherence during the prenatal period was 93% (range 29%-100%). The median duration of labor was 10 hours (range 1-44 hours). 11.6% of women delivered at home and 41% of women delivering in the clinic spent <1 hour in the delivery room. 82.2% (63.3% for home and 87.6% for clinic deliveries) of women took the loading dose at onset of labor.



Median intrapartum study drug adherence was 37% (10% for home and 43% for clinic deliveries) while 17.4% of the women took no study drug during labor and only 5.4% took all of the expected intrapartum dose. Tolerance to the drug regimen has been excellent with no permanent and only three temporary study drug interruptions due to clinical or laboratory adverse events. **Conclusion** Adherence to self-administered oral study drug by HIV-1-infected pregnant women is excellent during the prenatal period, is good for the oral loading dose at the onset of labor, but relatively poor for the remainder of the intrapartum period while tolerance is excellent. If this ZDV regimen proves effective, it will be critical to gain a better understanding to the barriers to intrapartum adherence.

[35/42201] Placebo control trials of short-course antiRetroviral regimens to reduce mother-to-child HIV transmission are essential to establish standard of care in Africa

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Objectives Trials in Africa of feasible short-course antiRetroviral (ARV) drugs to prevent mother-to-child HIV transmission have been criticized for using placebo-control designs instead of equivalence comparisons to AZT/ACTG 076. We compared the value of these 2 designs for determining local standard of care.

Design/Methods We review how statistical design and implementation issues affect trial validity, generalizability and rapidity in African settings. We estimate potential HIV infections prevented with faster trials. **Results** *Validity* An equivalence design requires a comparison with known efficacy. However, the efficacy of 076 cannot be confidently extrapolated to Africa due to differences in risk for HIV transmission that might affect efficacy, including immune status, HIV disease state, and breastfeeding practices. Natural history studies cannot serve as historical untreated controls due to the wide variability of observed transmission rates (25%-48%). If 076 were found to be better than short-course ARV, it would be unclear if the alternative were better than nothing. A

placebo trial provides direct information on efficacy. *Generalizability* An equivalence design has limited generalizability because the long 076 regimen requires women to enroll long before they usually seek prenatal care. These women may have atypical health practices, so that results may not apply well to the general population of pregnant women. Placebo trials enroll at the time when women usually seek prenatal care. *Rapidity of completion* An 076 equivalence trial is more time-consuming than a placebo trial, needing to recruit women by 30 weeks gestation (when 15-20% of women seek prenatal care) rather than by 34 weeks (when about 75% seek care) and with a 50% larger sample size. Study completion could take months to more than a year longer. A fast trial may save lives by speeding implementation of a perinatal ARV program. Africa has 200,000 mother-to-child HIV transmissions per year. Once implemented, a program reaching 50% of care sites, with 75% of women appearing by 34 weeks gestation, and 50% ARV efficacy would prevent 37,500 mother-to-child HIV transmissions per year.

Conclusion We believe that using placebo controls is essential to reliably establish an appropriate local standard of care. A placebo control trial of ARV is far more likely than an equivalence trial to produce results that are valid and generalizable for the African countries where these trials are being conducted. It also requires less time and therefore supports earlier implementation of ARV programs which may prevent nearly 40,000 mother-to-child HIV transmissions per year.

[11169] Analysis of Full-Length HIV-1 RNA genomic sequences in the genital tract of women

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Background To understand viral pathogenesis, vaccine design, and heterosexual and mother-to-child transmission, we studied HIV-1 in the genital tract of women. Because HIV-1 RNA represents replicating virus, we developed a technique based on reverse transcription and long PCR to clone full-length HIV-1 RNA genomes from infected individuals. **Methods** We used this technique to determine complete HIV-1 RNA sequences from virus in the genital tract, specifically the cervicovaginal lavage (CVL), and compare them to contemporaneous plasma sequences from the same individual. We performed these studies on two women who showed clear evidence of having reservoirs of viral replication in the genital tract. **Results** In each case, the level of HIV-1 RNA in CVL exceeded that in the plasma. Patient 1's viral load in plasma was 180,000 copies/ml while her viral load in a CVL sample was 2,500,000 copies/ml. Patient 2's viral load was 90,000 copies/ml and 200,000 copies/ml in her plasma and CVL, respectively. Both women were infected heterosexually and Patient 1 subsequently transmitted HIV-1 to a male partner. Preliminary computational analysis of multiple HIV-1 RNA sequences isolated from these subjects



show that the CVL and plasma sequences are related yet significantly distinct HIV-1 RNA sequences isolated from the CVL were also considerably more heterogeneous than contemporaneous plasma sequences. These sequence data confirm that the genital tract represents a distinct reservoir of infection and that comparison of HIV-1 sequences in blood and CVL is therefore necessary to understand HIV-1 pathogenesis in women

[12154] Viral load studies in untreated infants from Africa

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Objective To relate the viral load in untreated infants to the age at HIV-1 infection and to whether the mode of infection was perinatal (by cord blood (CB) status) or postnatal (breast milk) **Methods** Infants were enrolled at birth in Blantyre, Malawi in 1994. Infected infants were grouped by the time and probable route of infection. Infection (clade C) was assumed to be at birth for infants whose first postnatal sample was + if it was within 6 months of birth. These subjects were then stratified by CB+, CB- or CB? status. Infants with a negative test at > = 1 month but later + were considered infected by breast feeding, none had transfusions during the conversion window. The onset of infection for converters was the midpoint between the last negative and first + result. Sampling dates derived from this date and were then grouped for analysis. Levels (10x per ml) were measured from dried blood spots by a modified NASBA assay. Statistically, the exponents were averaged (+ SD) and compared by a T-test, and then re-translated. **Results** Viral loads were 100,000 (105 0 + 0 57) in 17 CB+ samples. In comparison, among 52 infants with CB- samples, the loads on the first + sample (average 9 5 wks) was 251,000 (105 4 + 0 61) (p =) Among 15 infants infected by breast feeding in the first 6 months, the first + sample (average time from estimated infection date 15 wks) was 158,000 (105 2 + 0 9), whereas in 9 infants infected later (average time from estimated infection date 65 wks), the average viral load was 79,000 (104 9 + 0 7). Viral loads appeared to rise to a plateau at 4-15 weeks after the estimated infection onset, even in infants who were CB+. **Conclusions** This work demonstrates clade C viral loads can be obtained from dried blood spots. CB+ infants showed a distinct rise from the CB to the first positive later sample, suggesting that infection is very recent. Since breast feeding exposure is continuous, it is difficult to establish exactly when breast feeding infections occurred. However, infants infected by breast feeding had a similar viral load profile to those infected perinatally, including those who were CB+ and could not have been infected by breast milk.

[12155] Reduction of maternal-infant transmission of Human Immunodeficiency Virus type 1 with Zidovudine (ZDV) treatment

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Objectives To compare the HIV vertical transmission rate between 2 groups of HIV+ women. **Design** Prospective, controlled study. **Methods** We offered zidovudine (ZDV) during pregnancy to all HIV+ women attending our service after september 1994, irrespective of their clinical status and CD4 count. The regimen followed is that described in ACTG 076 except all HIV+ women are eligible and some women discontinuing ZDV intrapartum or postpartum to the newborn. All babies are formula feed. Uninfected status was defined as at least one negative HIV-1 DNA polymerase chain reaction (PCR) beyond the neonatal period and 2 HIV-antibody negative ELISA performed at 6-18 months of age. Infected status was defined as one positive HIV-1 DNA PCR and 2 HIV-antibody positive ELISA performed after 18 months of age and confirmed by immunofluorescence assay. **Results** Out of 111 seropositive women, 58 agreed to the therapy and 53 did not. 8/58 (13 7%) infants whose mothers had received ZDV were found infected versus 18/53 (33 9%) whose mothers had not received (p = 0 022). This corresponds to a 59 6% relative reduction in the risk of HIV transmission. **Conclusion** The use of ZDV in pregnant women and newborn is well tolerated and reduces the maternal-infant transmission of HIV even though the complete protocol has not been used. This is very important for poor countries where all protocol is very expensive to be applied.

[12156] The potential role of intrapartum and neonatal Zidovudine treatment in reduction of perinatal HIV-1 transmission



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Objective To evaluate the efficacy of ZDV administered during labor and to the infants in the first 6 weeks of life in reduction of perinatal HIV-1 transmission **Design** This is a pilot non-randomized open label clinical trial **Method** A total of thirty five HIV-1 infected pregnant women with no prior antiRetroviral treatment who had either late or no prenatal care were given ZDV 300 mg orally every 3 hours during intrapartum period until delivery Maternal blood were tested for CD₄ cell count and plasma HIV-1 RNA (Chiron(r) assay and/or Amplicor(r) assay) before treatment Zidovudine 2 mg/kg orally every 6 hours were given to the infants immediately after birth for 6 weeks Breast feeding was not allowed HIV-1 DNA detected by the use of nested PCR was measured in infant's blood at age 1 day, 1, 3 and 6 months old Infants with positive PCR test performed at least twice were classified as HIV infected **Result** Twenty-five infants were analysed at 3 months old Short term toxic effect of ZDV with anemia and diarrhea were observed in one infant whose treatment had to be discontinued at age 7 days old HIV-1 DNA was detected in 2 infants The HIV-1 transmission rate is approximately 8% (95% CI, -2 to 18%) **Conclusion** This preliminary study suggests that intrapartum oral ZDV treatment in asymptomatic HIV-1 infected mothers together with ZDV treatment in their offsprings for 6 weeks, may reduce the rate of perinatal transmission to approximately 8 percent Further controlled trials in larger groups of pregnant women are needed

[12157] Use of Zidovudine to reduce the risk of perinatal transmission of HIV infection in the Washington Metropolitan Area

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Background Use of zidovudine (ZDV) for prevention of perinatal transmission of HIV was recommended in 1994 by the US Public Health Service Our study examined implementation of the recommendations and their effectiveness in the Washington, DC area **Methods** Chart review of HIV-exposed infants born between December 1994 and December 1996 enrolled in the Pediatric Spectrum of HIV Disease Project, who presented for follow-up prior to 1 year of age at the Washington, DC site HIV DNA PCR and/or cultures were used to determine the child's HIV status **Results** 248 infants were enrolled 24 of these were infected with HIV Of 126 children born between December 1994 and December 1995 (the 1995 birth cohort) 42 (33%) received the full regimen (ZDV antenatally, intrapartum and after birth), 63 (51%) of 122 children born in 1996 received the full regimen In the 1995 birth cohort, 15/126 children received only neonatal ZDV and 22 (17%) received no treatment In 1996 7 children (5%) received only neonatal ZDV and 7 (5%) received none The remaining children received partial or unknown treatment Overall, when 1995 and 1996 birth cohorts data were combined, of 105 children on full treatment only 3 (2.8%) were infected compared with 7 (9%) of 76 on partial treatment and 9 (31%) of 29 children who were not treated at all **Conclusions** ZDV administered in pregnancy, during delivery and neonatally prevents mother to-infant transmission of HIV Only half of the infants born in our area in 1996 received the full regimen which appears to be the most protective

[12175] Seroconversion in infants of positive mothers to HIV Total breastfeeding impact

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Objectives To estimate breastfeeding risk in the mother to infant transmission in a cohort of children born in Santos SP Brazil to analyse breastfeeding length effect in seroconversion to estimate survival of total breastfed versus non breastfed children **Methods** A historic cohort with HIV positives mother's infants was assisted at NIC - Santos SP Brazil (Nucleo Integrado da Crianca) from January 1993 to December 1997 The children were stratified in two groups Breastfed and Non breastfed The HIV infection was determined by the antibody test after 18 months of age or by AIDS clinical diagnosis at any age **Results** The results of antibody test in the two groups were



	HIV+	HIV -
Total Breastfed	45/64 (70.3%)	19/64 (29.6%)
Non breastfed	35/72 (48.6%)	37/72 (51.3%)
χ ² = 6.6 P value = 0.01		

25% of women had knowledge of their HIV positive status and decided to breastfeed their children despite of the strongly health professional warning to the risk of their choice. The total breastfeeding average was 30 days at seropositive group and 0 days at the seronegative group. **Conclusions** Breastfeeding is meaningful factor to HIV mother to infant transmission. The Kaplan - Meier analysis suggests greater survival of the total breastfed infants group, however the difference has not showed to be statistically meaningful. Would breast milk have a protector effect over HIV infected children?

[12179] Pediatric AIDS in a Brazilian Population 12 years of follow-up

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Background Since 1985 we have been following an increasing number of children, 294 affected by AIDS and 137 HIV-exposed infants, 43 of the latter have already been discharged as sero-reverted. This study describes clinical data and the evolution of pediatric AIDS in a Brazilian population. **Methods** The charts of every children with AIDS admitted to the "Instituto da Crianca" during the last 12 years were reviewed. **Results** The male gender represented 154 (52%) and the female 140 (48%) of the 294 cases, 241 (82%) patients were infected perinatally. 39 (13%) were infected by blood products and in 14 (5%) of the cases the source of HIV infection could not be determined. Among perinatally infected children, only 8 remain asymptomatic (range 25 to 126 months) in the symptomatic group, the median age at the first symptom was 11.5 months (range 1 to 82 months). The age distribution at diagnosis was 27.3% < 1 yr, 49.6% 1 yr-4 yr, 18.7% 4 yr-8 yr and 4.4% > 8 yr. The clinical manifestations at the time of diagnosis were failure to thrive (40%), hepatomegaly (39%), recurrent pneumonia (33%), adenomegaly (31%), diarrhea (26%), splenomegaly (25%), intermittent fever (23%), parotiditis (8%) and thrombocytopenia (5%). The most commonly seen complications were in the Respiratory Tract, followed by Gastrointestinal disorders, severe malnutrition and fungal infections. During this period 100 (34%) of the children died and only 18 (6%) abandoned the follow-up, while 12 (4%) patients were transferred. The other 164 cases are still being followed together with 94 exposed children whose diagnosis is still indetermined. The management is supported by anti-retroviral therapy, IVIG, and PPC prophylaxis when required. **Conclusions** This group represents 14% of the Pediatric AIDS in the State of Sao Paulo and these results may be comparable to the Brazilian total data. Sao Paulo is the state in Brazil with the higher number of HIV infected people (60% of the total), including HIV infected children.

[12209] Tolerance and acceptability of vaginal cleansing with Benzalkonium Chloride in HIV-infected African pregnant women 1996-1998 - ANRS 049b clinical trial

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Different interventions are tested in Africa to reduce mother-to-child transmission of HIV. Vaginal cleansing is one of these with the advantage of low cost and high feasibility. From a public health point of view, another interest is that HIV status of the pregnant women is not required before the intervention. **Objectives** 1) to study the tolerance of vaginal cleansing by Benzalkonium Chloride (BC) suppositories in HIV-infected pregnant women and of a bath with BC of the newborn 2) to assess the acceptability of this intervention in urban populations in West Africa. **Methods** After voluntary HIV testing and counselling to pregnant women in prenatal care units of Abidjan (Cote d'Ivoire) and Bobo-Dioulasso (Burkina Faso), HIV-infected pregnant women, who gave their informed consent, were recruited in a bicentric randomized phase II trial BC versus placebo. They self-administered daily a suppository of BC (1% concentration) from 36 weeks of pregnancy until labor, and the last one intra partum (IP).



The baby was washed with a BC solution within 300 after birth. Placebo was given similarly. Women were followed weekly with a speculum examination and wet mount and culture of cervico-vaginal secretions through 1 week post partum. Neonates were examined for irritations of the skin, mucosae and eyes. Data will be unblinded in February 1998. **Results** 112 HIV-infected pregnant women were enrolled in the trial from november 1996 to april 1997. They took the pre partum treatment for a mean duration of 20 days. The IP treatment was done in 71% of them and 87% of the babies were bathed with BC. The overall compliance was 91%. There were no major clinical event during the follow-up period extending up to 45 days post partum. In women, genital ulcers occurred in 1% and minor complaints in 17%. 12% of newborns presented with conjunctivitis and 2% with infectious dermatitis. In two children, there was a cutaneous exfoliation. **Conclusions** Vaginal cleansing with BC is a feasible intervention in Africa. It seems to be acceptable by the women. BC seems to have an acceptable tolerance in women and children (to be confirmed after unblinding). These data will help to determine whether BC can be considered for efficacy trials in the prevention of vertical transmission of HIV.

[12233] Lack of clinical or immunologic disease progression with transient use of Zidovudine (ZDV) to reduce perinatal HIV-1 transmission in PACTG 076

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Objective Evaluate and compare postpartum clinical and immunologic HIV disease progression and survival among women who received ZDV or placebo (PL) in the perinatal trial PACTG 076. **Methods** After completion of PACTG 076 study [6 months postpartum] women were enrolled in a three year follow up study, PACTG 288. Study visits were scheduled 12 months postpartum, and yearly thereafter. Each visit included HIV-related history, physical exam, lymphocyte subset analysis and stored plasma for future virologic assays. The primary endpoint was time from delivery to AIDS [defined as CDC Category C disease or CD4 count <200/mm³] or death. Comparisons were based on PACTG 076 randomization [ZDV vs PL]. This interim analysis describes 18 months of follow-up in this cohort. Chi-square, t-test, product-limit estimators and logrank test were used in the analysis. **Results** 226/513 [44%] of the women who enrolled in PACTG 076 were enrolled to PACTG 288. 112/226 [49%] were originally randomized to the ZDV arm. No significant differences were observed among women who had received ZDV or PL in age at enrollment, baseline CD4 count or length of follow-up in PACTG 288, mean follow-up was 2.4 years. More women in the PL arm received anti-retroviral therapy postpartum [38% ZDV vs 52% PL, p = 0.01]. 48 [21%] women had disease progression or death during the follow-up period [27 in ZDV vs 21 in PL arm, p = 0.42]. 8 women progressed to CDC Category C [5 ZDV vs 3 PL arm], 41 had CD4 < 200 [24 ZDV vs 17 PL arm], and 2 patients died [1 each group]. There was no significant difference in time to AIDS or death between the two arms. **Conclusions** Transient use of ZDV during pregnancy to prevent perinatal transmission in PACTG 076, which enrolled healthy women with CD4 > 200, was not associated with increased risk of clinical or immunologic disease progression following delivery. "Women for who therapy is optional (low HIV RNA/high CD4) & who wish to reduce fetal exposure to multiple drugs may consider use of ZDV alone during pregnancy to reduce perinatal transmission."

[12250] North Thailand Perinatal HIV Prevention Trial (NTPHPT) Design and study update

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Objective Compare the efficacy of a uniform three-month treatment for mothers and six-week treatment for infants with treatments shortened to one month in mothers and/or three days in infants for the prevention of perinatal HIV, assess the safety and tolerance of ZDV given to pregnant women and their infants, study the pharmacokinetics/dynamics of oral ZDV during pregnancy and labor, study factors associated with transmission. **Design** Multicenter, phase II/III, double-blind randomized, controlled equivalence trial, 4 arm factorial design. **Methods** Consenting HIV-positive women are randomized at week 28 of pregnancy. ZDV dosing in women begins with 300 mg per os bid during pregnancy, followed by 300 mg per os q3hr from labor until delivery. ZDV dosing in infants is 2 mg/kg q6 hrs. Infants are not breastfed and followed with their mother until 18 months old.



They are considered infected if 2 samples are positive by dried blood spot PCR analysis. 1 554 pregnant women will be enrolled in the northern and central regions of Thailand. **Results** As of January 27 1998 156 women have been confirmed HIV-positive. 121 (78%) agreed to participate. Of the other 35 women 14 (40%) arrived too late for enrollment and received open label ZDV from the study or alternative programs (Ministry of Public Health or the Thai Red Cross). 11 did not present for pre-enrollment. 7 chose to participate in alternative programs, and 3 decided to terminate their pregnancy. Of the 97 women who started the study treatment 31 have delivered. 11 infants are off study drug. One woman was reported lost to follow-up during pregnancy. In addition 24 women participated in the initial open label pharmacokinetic evaluation of oral ZDV during labor. **Conclusions** Study protocol compliance and coordination with other ZDV programs in Thailand appears to be excellent. The study results will have a decisive impact on policy decisions since the implementation of a shortened regimen if proven as efficacious as the ACTG 076 like regimen, would become a widely applicable option. Not only would overall effectiveness and cost-effectiveness of ZDV prophylaxis be increased, feasibility, safety and compliance would also be improved, while the risk of ZDV resistance would be decreased.

[12408] Modified ACTG- 076 protocol and its initial results in the largest ongoing perinatal HIV study in India

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Background With the HIV epidemic in its third phase affecting a large number of women, India ridden with poverty (GNP 150\$) illiteracy, double standards and multiple scandals has some activists for the cause of trees, animals and human rights. But strangely enough, a child in the womb is not covered under any of these causes and continues to be neglected. We decided to pursue 'Right to AIDS-Free Life' for the small creatures in the womb, before they breath in this morally and socially polluted world. To prevent perinatal transmission cost effectively by appropriately modifying the ACTG-076 protocol in Indian context, we initiated this study. **Methods** After sequential systematised HIV screening of the antenatal clinic attendees at a large Women's Hospital, seropositive women were counselled on preventing perinatal transmission through modified ACTG-076 to suit the cost and convenience in the 'IHO-Wadia' model. It has four wings. Locally produced AZT to mother for 8 weeks 400 mg/day, elective Ceasarean section for delivering the baby, no breast feeding or modified breast-feeding and AZT to the infant for first 40 days. Children are followed quarterly till 15 months and tested for HIV by ELISA at 9 and 15 months, the latest they can be certified infected or otherwise. Sero-negative babies are discharged from the study at the earliest revelation. **Result** Of the 81 babies born following our protocol, 26 have failed to follow-up. 35 are below 9 months. All the 20 babies who have completed 9 months have come 'HIV negative' (Zero prevalence but small sample size). It is a cost-effective study. Pool ELISA test per woman Rs 15/- (\$0.40). Cost of detection of one infection Rs 1500/- (\$40/-) (prevalence in women is 1%), Cost of prevention of one perinatal transmission Rs 5000/- (130\$) vis a vis cost of managing one HIV infected child with 'cocktail' Rs 100,000/- (2800\$). **Conclusion** AZT given to seropositive mothers in proportionately smaller doses (due to low average weight), for a shorter duration of 4 to 6 weeks has been equally efficient in preventing perinatal transmission. Such a cost-effective and user-friendly model needs to be replicated elsewhere. UNAIDS guidelines of 'no-breast feeding' for rich countries and 'breast-feeding' in poorer countries needs to be modified with indigenous solution of modified breast-feeding (heating breast milk).

[13378] Mother-to-child transmission Survival analysis of 1 066 cases from 1987-1994, Sao Paulo, Brazil

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Objective To determine changes in time until diagnosis (DDX), and risk factors for death, in AIDS-disease from mother-to-child transmission, from 1987 to 1994, in children aged 0-12 years at the date of diagnosis, in cases reported to the State of Sao Paulo epidemiological surveillance system. **Method** Cohort analytical study with secondary data. **Setting** The State of Sao Paulo, Brazil. **Entered the study** 1 066 children with AIDS-disease ascertained to be from mother-to-child transmission, diagnosed until December 31, 1994, and whose individual reporting forms reached the official system by December 31, 1995. They were followed up to June 30, 1996, 116 children were right-censored due to losses to follow-up. **Statistical methods** Kaplan-Meier and Cox proportional hazard analysis. **Were considered** time in months (mo) elapsed from birth (DOB) to DDX, according to year of



birth Eighteen-month survival time after DDX, according to gender year of DDX, and age at DDX Results The median time from DOB to DDX decreased from 31.6 mo for those born in 1987 and earlier, to 2.9 mo for those born in 1994 (p = 0.0000) For death in 18-months, the Hazard Ratios (and 95% CI) were

gender	year of DDX	age at DDX
male = 1.00	1987 = 1.00	<6 mo = 1.00
female = 1.26 (1.07-1.49)	1988-91 = 0.59 (0.37-0.96)	6-9 mo = 0.44 (0.33-0.58)
	1992-94 = 0.45 (0.28-0.72)	>=9 mo = 0.26 (0.22-0.31)

Conclusion There was a great reduction in the time until diagnosis of AIDS-disease from mother-to-child transmission from 1987 to 1994. Girls were at higher risk of death than boys. The risk of death in 18 months decreased with the diagnosis made in more recent years, and with increasing age at diagnosis.

[209/11214] Viral dynamics in neonatal macaques after oral inoculation with HIV-2₂₈₇
Implications for human transmission

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Background Fifty - 70% of human infants acquire HIV infection at the time of parturition, possibly by swallowing infected maternal secretions. HIV-2₂₈₇, a derivative of human isolate HIV-2_{EHO}, is pathogenic in adult macaques when administered by mucosal routes. Oral instillation of HIV-2₂₈₇ to neonatal macaques provides a unique model of peri-partum maternal-fetal transmission. An understanding of viral dynamics in early neonatal HIV infection will be crucial to the design of human anti-Retroviral regimens to prevent neonatal transmission. **Methods** A previous titration study determined an animal infectious dose (AID) for vaginal and rectal exposure in juvenile macaques corresponding to 10³ TCID₅₀. In this study 3 neonatal and 1 juvenile macaca nemestrina were orally, non-traumatically exposed to 10³ or 10⁴ TCID₅₀ of HIV-2₂₈₇. Viral load was initially monitored daily by plasma RT-PCR, other monitoring included weekly complete blood count/cellular subtypes, quantitative HIV-2 viral cultures and monthly HIV-specific serology. Lymph node biopsies obtained 2-3 weeks after acute infection and tissue from the time of necropsy were analyzed for viral presence by RT-PCR, DNA-PCR, and viral culture. **Results** In mucosally infected animals, regardless of age or route of exposure, HIV-specific RNA in plasma is first detected between days 6 and 10. Viral load peaks between days 14 and 21 and declines moderately thereafter. None of the animals orally exposed to 10³ TCID₅₀, but 100% of the animals exposed to 10⁴ TCID₅₀, became HIV-2 infected after exposure. This demonstrates an AID corresponding to 10⁴ TCID₅₀ for oral exposure of neonatal animals. All infected neonates developed prompt CD4 depletion. Both uninfected animals could subsequently be infected by re-inoculation with a higher dose or different mucosal route. **Conclusion** Viral replication in neonatal macaques after oral exposure to HIV-2₂₈₇ is rapid, with evidence of disseminated infection (by plasma RT-PCR) by 6-10 days and peak viremia by 14-21 days. HIV-infection is inoculum-dependent, but contrary to experience with SIV, oral exposure with HIV-2₂₈₇ is less infectious in neonatal macaques than HIV-2₂₈₇ by other mucosal routes in juvenile animals. Human implications of this study suggest that anti-Retroviral intervention in the newborn must be rapid and potent.

210/31131] Class I MHC polymorphism and mother to child HIV-1 transmission in Kenya

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Objectives We sought to determine whether specific class I Human Leucocyte Antigens (HLA) or the degree of maternal-child sharing of class I HLA were associated with differential risk of HIV-1 transmission. **Methods** HIV-1 infected mothers and their infants within the University of Nairobi Perinatal Transmission and Pediatric



AIDS Cohort, underwent serological class I HLA typing. Class I HLA matching between mother and infant was scored from 3/6 to 6/6. Class I determinants at a frequency of greater than 5% were examined for an association with differential risk of HIV-1 transmission. Serologically defined determinants associated with differential risk were molecularly confirmed and subtyped. HIV-1 status was determined by a combination of HIV-1 serology and PCR. **Results** One hundred and sixty infants born to 125 mothers were enrolled. Nineteen were classified as perinatally infected and 141 were uninfected at birth. Of these, 20 subsequently acquired HIV-1 during follow-up from breast feeding. HLA-A2 was strongly associated with a decreased risk of perinatal HIV-1 transmission (Odds Ratio 0.11, 95% CI, 0.02-0.55, $P = 0.06$ multivariate analysis). Molecular subtyping of HLA-A2 in this population revealed a number of allelic subtypes including A*0201, A*0202, A*0205 and A*0214. In addition, maternal-child class I HLA concordance was independently associated with an increased risk of perinatal but not breastmilk transmission of HIV-1 (OR = 2.63, 95% CI, 1.36-5.07, $P = 0.003$). **Conclusions** The HLA determinant HLA-A2 comprising a number of allelic subtypes, and class I HLA discordance were independently protective in perinatal HIV transmission but not breastmilk transmission. This points to independent but additive mechanisms of protection potentially mediated by both HLA restricted cellular effectors and anti-HLA alloimmune responses.

[211/11167] Co-receptor usage of HIV-1 isolates of different subtypes derived during pregnancy

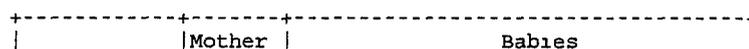
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Objectives To test the impact of genetic subtype and co-receptor usage on HIV-1 transmission from mother to child. **Design** HIV-1 isolates were obtained during pregnancy from eleven HIV-1 infected mothers from Cameroon. The majority of the mothers harbored HIV-1 of subtype A, one A/F and one B/D recombinant and one subtype G. **Methods** The isolates were characterized for co-receptor usage on the human osteosarcoma cell line (Ghost4) engineered to express CD4 and each of the chemokine receptors CCR3, CCR5, CXCR4, Bonzo and Bob. Infection of these cell lines was monitored by testing culture supernatants for p24 antigen content and for activation of the green fluorescent protein marker. **Results** Two viruses from transmitting mothers were multitropic and showed the X4R5 phenotype in addition to being able to use CCR3 and Bob, in one case (subtype G) and Bonzo and Bob, in the other (subtype A). Other viruses used CCR5 alone or in combination with Bob and/or Bonzo, regardless of transmission. The B/D recombinant was exceptional in using CCR3 and Bob only. Two isolates were available from four mothers three or six months apart (second or third trimester and partus). Changes in co-receptor usage - broadening or narrowing - were observed in three cases. **Conclusion** Transmission of HIV-1 infection to the child was associated with multitropic viruses in the mother. Repeated HIV-1 isolations during pregnancy revealed multiple changes in co-receptor usage of sequential isolates. It remains to be seen whether pregnancy predisposes to abrupt changes in the quasi-species leading to biologically important phenotypic differences.

214/12153] Influence of maternal HIV-1 and HIV-2 on child survival in Gambia

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Objective To compare the survival of children born to HIV infected and those born to HIV uninfected mothers. **Methods** 110 HIV-1 positive, 251 HIV-2 positive, 11 dually positive women, and 488 age/parity/health centre matched HIV negative controls, were enrolled in a perinatal transmission study. After delivery the children were seen at 2 and 6 months of age and subsequently followed 3 monthly up to 18 months of age. HIV infection in children was diagnosed by PCR at 2, 9 or 18 months and by antibody serology assays at 18 months. **Results** Transmission rates were 23.5% (95% CI 13.8-33.1) and 4.0% (95% CI 1.7-7.7) for HIV-1 and HIV-2 respectively. The rate of stillbirths did not differ between the groups but deaths in children of HIV-1 infected mothers (16%) were significantly higher than in HIV-2 infected (7%, $p = 0.04$) and control mothers (6%, $p = 0.008$). These differences were due to high mortality (35%) in HIV-1 infected babies whereas none of the 8 HIV-2 infected babies died. Maternal death increased child mortality significantly, independent of mother to child HIV transmission ($p < 0.001$).





Mother to child transmission			
		Infected	MCT rate % (95% CI)
HIV-1	90	17/81	23.5 (13.8 - 33.1)
HIV-2	217	8/201	4 (1.7 - 7.7)
HIV 1&2	11	0	0
Control	419	0	0

(continued table)

Babies		
Died		
	Infected n (%)	Uninfected
HIV-1	6 (35)	8 (11)
HIV-2	0 (0)	16 (7)
HIV 1&2	0 (0)	0 (0)
Control	0 (0)	27 (6)

Conclusions Maternal HIV-1 infection as well as maternal death independently contributed substantially to the mortality of children while maternal HIV-2 infection did not. To improve child survival, intervention measures to decrease mother-to-child HIV transmission and the HIV epidemic which is claiming lives of women at the child bearing age should be urgently applied.

[313/44266] Breast feeding in the HIV/AIDS era in Zimbabwe

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Issue An estimated 30% of pregnant women are HIV positive. Recent UNAIDS policy to devolve decision making about breast feeding to the individual woman challenges health workers to begin developing a dialogue once summarized simply as 'Breast is Best'. Can they meet this challenge? **Project** An analysis of activities and events around breast feeding was done. The activities included 2 public meetings where there were discussions by women PWAs (some of whom had children who died of AIDS), MCH service providers, AIDS activists, women NGOs and lactation specialists. There were focus group discussions held with women both infected and affected by HIV/AIDS. A national workshop was held for MCH service supervisors and reproductive health researchers. There were discussions with HIV/AIDS support groups on the draft policy document on breast feeding. Both print and electronic media provided fora for debate on the topic. **Results** All the women PWAs prefer not to breast feed their babies once they know that they are HIV positive. Most of them suffered a lot of guilt after their babies died of AIDS. MCH service providers, through the Baby Friendly Initiatives, continue to reinforce the view that good mothers breast feed. This manifests through prominent breast feeding posters in health institutions and breast feeding day celebrations. Generally, most women do not exclusively breast feed and by the third month of life supplementary foods are already introduced. **Lessons learned** Despite policy guidelines proposing discussion of personal circumstances and options, reinforcing breast feeding as good motherhood remains strong. Advocacy programs are needed to influence breast feeding policies so that they include discussion of alternatives. Health workers need guidance in presenting these complex issues. The presumption that women prefer to be protected from difficult decisions should be avoided. Women living with HIV must be involved in the policy discussion.

[316/24124] Breast or bottle? A cost-effectiveness evaluation of formula feeding for the prevention of post-natal transmission of HIV in an urban South African setting



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Introduction Mother-to-child transmission of HIV by breast feeding has now been well documented. Breastfeeding confers significant infant mortality and morbidity reductions and it is unclear whether the risk of HIV infection from breast milk outweighs the mortality and morbidity risks of formula feeding in developing countries. This study sought to evaluate the cost effectiveness of formula feeding as an intervention for the prevention of mother-to child transmission of HIV. **Methods** Data were taken from the actual community studied and where unavailable from a synthesis of studies from other developing countries. Weibull hazard functions calibrated to existing infection and mortality data, were used to simulate infection and mortality rates under various intervention assumptions. Intervention costs, the costs of care for HIV and non-HIV related conditions were estimated from data from the hospital serving the study community. Benefits were measured in terms of deaths averted and life-years gained. The simulated population was followed up for eight years, with costs and benefits discounted at 5% per annum. **Results** Prenatal screening and advocating formula for infected mothers with or without actually supplying formula was estimated to cost around \$5000/childhood death averted, or \$280/discounted life year saved. Estimates were sensitive to HIV sero-prevalence levels, non-HIV infant mortality rates and the relative risk of morbidity or mortality associated with formula feeding in non-infected children. Screening costs made up between 44% and 94% of total programme marginal costs suggesting that the combination of formula-feeding with perinatal interventions might be highly cost effective since the screening expense is only incurred once. **Conclusions** Compared to cost-effectiveness information in the 1993 World Development Report, formula feeding interventions appear less cost effective than most front-line public health programmes for children, but compare favourably with typical adult screening programmes, and are more cost effective than many curative clinical interventions recommended for middle income countries.

[23300] Prevention of mother-to-child transmission of HIV and its implications in developing countries. From research to programs

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Issues Randomised trials are ongoing in many developing countries to evaluate different approaches to prevention of mother-to-child transmission (MTCT) of HIV. The first of these trials will be completed in 1998. International and local public health strategies will need to be developed before implementation. **Project** To develop public health policy options for the local implementation of interventions to prevent MTCT of HIV into basic health and maternal and child care (MCH) services in developing countries. In 1997 the International Working Group on MTCT of HIV, supported by the European Commission and UNAIDS, undertook the following tasks: a critical review of completed, ongoing and planned randomised trials, a feasibility assessment of different preventive strategies including a survey on HIV voluntary counselling and testing of pregnant women, a review of the cost-effectiveness and cost-benefit of anti-retroviral therapy, the identification of requirements and research priorities for prenatal, obstetrical and paediatric care services, and an update of transmission of HIV through breastfeeding with an international pooled analysis of late postnatal transmission. These preparatory projects provided the background for a three-day workshop in Ghent, Belgium, in November 1997. **Results** A summary of relevant evidence and 10 public health recommendations to assist policy makers in implementing intervention strategies. **Lessons learned** Any specific intervention package to reduce MTCT should be fully integrated in the overall antenatal, obstetrical, and paediatric care, the prime goal of which is to reduce overall maternal and infant morbidity and mortality. Integration of HIV MTCT prevention into basic health services is a priority and should involve governments and donor agencies.

[23301] Mother-to-child transmission of HIV-1. Effect of preventive measures in full-term pregnancies

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Background Several studies have stated that transmission of HIV-1 from a pregnant woman to her fetus often occurs late in gestation or at delivery. We hypothesize that preventive measures, like prophylactic zidovudine (ZDV) and perhaps cesarean section, may be more effective in full-term pregnancies. **Design** Prospective study of children born to HIV-1-infected women in a university hospital in Barcelona, Spain. **Methods** Infants born to women with confirmed HIV-1 infection from January 1, 1987 to December 31, 1997 were selected and divided in two groups according to gestational age (<37 wk and ≥37 wk). Logistic regression was used to test the study variables against the risk of vertical transmission of HIV-1. **Results** A total of 248 children, 56 premature and 192 full-term, with confirmed HIV-1 infection or seroreverters were studied. Vertical transmission rates were 25% (95% CI 13.7%-36.3%) and 11.5% (95% CI 7.0%-16.0%), respectively, $p = 0.006$. Among premature infants HIV-1 infection was not associated with the variables of interest. However, at-term children born to symptomatic mothers (OR = 14.4, $p = 0.002$) and those delivered vaginally (OR = 9.0, $p = 0.04$) had an increased risk of becoming infected. In the latter group prophylactic ZDV was associated with a much lower risk of vertical transmission (OR = 0.03, $p = 0.003$). **Conclusions** Prophylactic ZDV and cesarean section seem to have a protective effect and decrease the risk of HIV-1 vertical transmission in children born at term. These results suggest that in addition to prophylaxis with ZDV, either alone or combined with other anti-retroviral drugs, elective cesarean section should be carefully considered especially for symptomatic women.

[23308] Mother-to-child transmission of Pol Mutant T215Y HIV-1 isolates related to a high viral load under AZT treatment

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Objective To predict AZT resistance in HIV-1 infected pregnant woman in relation with mutant Pol T215Y HIV-1 isolate detection prior treatment and the risk of transmission to child. **Methods** Six women have been followed during their pregnancy. CD4 cell count and viral load (VL) (NASBA system, Organon Teknika, France) were measured in the first 3 months of pregnancy, then during AZT treatment at 6 months and at the child birth. Pol T215Y mutation was detected in the plasma viral RNA extracted for the VL measure (Payan *et al.* CROI 1997). **Results** In the first case, VL was over 5 log/ml and did not vary under AZT treatment, in relation with T215Y mutation. This isolate was detected in the child plasma at birth, with a similar VL and AZT resistance. In 3 cases, VL was below 4 log/ml, reduced more than 1 log with AZT in relation with a wild T215Y isolate. In the 6th case, VL was higher (4.5 log/ml), with T215Y mutation but a combined AZT and ddI treatment was taken before pregnancy was declared. During pregnancy, CD4 cell counts were less than 50/mm³ in case 1 and 6 and about 400/mm³ in the 3 other cases, they were at about 2000/mm³ in children at birth. Five out of 6 children were free of virus, and for 2 cases get seronegative at 1 year, whereas, in case 1, the child died 8 months later, with a high VL (6.2 log/ml) and a decreasing CD4 (600/mm³). **Conclusion** It seems that Pol T215Y HIV-1 mutation detection related to a high VL during pregnancy could predict the risk of AZT resistance and viral transmission to child. Furthermore, a combined anti-retroviral therapy in pregnant women with VL higher than 4 log/ml and with a T215Y HIV-1 isolate may reduce the risk of viral transmission.

[23310] Acceptability of voluntary HIV Counselling and Testing (VCT) and interventions to reduce mother-to-child transmission of HIV in Africa

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Objective To assess acceptability of VCT and interventions to reduce Mother-to-Child Transmission of HIV (MCT) in different cities in Africa in the context of ongoing or completed clinical trials. **Method** In October 1997 thirteen studies located in west (Abidjan, Bobo-Dioulasso), east (Addis Abeba, Nairobi, Mombasa, Dar Es Salaam) and southern Africa (Blantyre, Lusaka, Harare, Soweto, Durban) were included in a cross-sectional mailing survey about the acceptability of VCT and interventions in antenatal clinics. Acceptance rate, return rates, overall acceptability of VCT (both acceptance of the pre- and post VCT sessions) and acceptability of intervention were obtained by a standardized questionnaire. **Results** The median overall acceptability of VCT was 65%, ranging from 33% to 95%. Overall acceptability of VCT most frequently depended on return rates as acceptance rates were



generally high. Where several studies were conducted in parallel in the same city or the same country, pregnant women had similar attitudes toward HIV testing even if the intervention programs differed. Five studies had an overall acceptability rates 970% with high return rates and a large number of VCT centres available for the whole population with the majority of the clinic staff of the projects involved in general antenatal care services as well.

The main common reason for refusing HIV testing was "want to discuss with the partner". In the 5 studies who provided the information, women who were finally included in the projects and who benefited from an intervention accounted for 1-4% of all women who were offered HIV testing and 11-35% of the HIV infected women (one of these studies offered vitamin A supplementation, four offered anti-retroviral therapy interventions). **Conclusion** Acceptability of VCT and interventions to reduce MCT are likely to be different if interventions were translated into a public health program with a real cost and known benefits. Increasing access to VCT and interventions to reduce MCT requires an offer of HIV services to both child and adults infected by HIV, a fight against HIV discrimination, VCT training of health care professionals and management of HIV+ persons, development of premarital counselling and education regarding MCT.

[23316] Vertical transmission of HIV-1 in the North of Portugal

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Objective to evaluate the risk of maternal transmission and the impact of the AZT therapy¹ during pregnancy and perinatal period on the rate of vertical HIV-1 infection. **Patients and methods** a 10-year retrospective study of the children with perinatal exposure to the HIV-1. Data comprising mode of delivery, clinical and immunological status of the mother, AZT therapy and child infection outcomes was reviewed. **Diagnosis** of the HIV infected child was based on the CDC criteria. **Results** the clinical records of 66 children, born to 63 mothers, were reviewed. Four children lost to follow-up and whose outcome is unknown were excluded. The type of delivery was known in 62 cases, being by vaginal route in 49 (79%) and by caesarean section in 13 (21%). None of the children was breastfed.

The maternal clinical and immunological status at childbirth was known in 41 cases. 7 (17%) women had ARC/AIDS, the others were asymptomatic, CD4 cell counts were >500/cmm in 21 (51%), 200 £ CD4 cells £ 500 in 17 (42%) and <200 in 3 (7%) cases. In 20 mother/child pairs AZT was begun before 34 weeks of gestation but in 2 of these AZT was not perfused during labour, in two cases AZT was administered *intrapartum* and to the child and in another two only the infant was treated.

Year of observation	No AZT (nr*)	Incomplete treatment (nr*)
1987-94	22 (9)	0
1995-97	16 (9)	6 (2)
Total	38 (18)	6 (2)
Transmission rate	47%	33%
* nr of infected children ¹ ACTG 076 protocol		

(continued table)

Year of observation	Complete treatment (nr*)	Total (nr*)
1987-94	0	22 (9)
1995-97	18 (3)	40 (14)
Total	18 (3)	62 (23)
Transmission rate	17%	37%



Conclusion high rate of vertical transmission in our study similar to the one in developing countries. As expected AZT treatment proved effective (χ^2 $p < 0.04$) in reducing the transmission rate, but this one remained significant emphasising the importance of the elucidation of the factors that determine mother-to-child HIV transmission for the development of better preventive interventions

[24199] Is antiRetroviral MCT prophylaxis provoking increased pregnancy incidence in women living with HIV?

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Objectives To compare pregnancy incidence and outcome in women participating in the Canadian Women's HIV Study for the periods before and after HIV diagnosis and before and after recommendations were made concerning prevention of mother-to-child transmission (MCT) using antiRetrovirals (ARV) **Methods** For 320 HIV-positive women age 15-44 years we documented pregnancy incidence pre- and post-HIV diagnosis per 100 person years (PY) and compared pregnancy outcome according to time of conception 12 months to 20 weeks before HIV diagnosis (period 1), the 20 weeks (maximum duration allowable for legal therapeutic abortion [TA]) prior to HIV diagnosis (period 2), and the time since HIV diagnosis to last study visit (period 3) The data were then stratified with respect to conception before March '94 and during/after March '94 to examine the impact of publication of results of the zidovudine prophylaxis trial (ACTG076) **Results** The incidence of pregnancy in the year before HIV diagnosis was 27.5/100 PY (95% CI 22.1-33.9) compared with 8.3/100 PY (95% CI 6.8-10.2) in the time since HIV diagnosis ($p < 0.001$), with the annual incidence post HIV diagnosis remaining stable The incidence of TA was 10.6/100 PY (95% CI 5.6-18.1) during period 2 versus 3.1/100 PY (95% CI 2.2-4.2) during period 3 ($p = 0.001$) After HIV diagnosis pregnancy incidence was similar before March '94 (8.5 per 100 PY) (58/681) to that during and after March '94 (8.1 per 100 PY) (39/483) The incidence of TA fell from 4.3/100 PY before March '94 to 1.4/100 PY ($p = 0.009$) after March '94 such that 50% (29/58) of HIV-aware women who conceived prior to March '94 underwent TA versus 17.9% (7/39) of HIV-aware women conceiving during and after March '94 ($p = 0.001$) **Conclusion** The advent of ARV prophylaxis of mother-to-child transmission of HIV has not lead to increased pregnancy incidence, however the incidence of therapeutic abortion has declined as more HIV-infected women opt to continue their pregnancies

[24200] Incidence of pregnancies in HIV-infected women between 1988 and 1996

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Background In order to describe the impact of HIV diagnosis and improvements in vertical transmission in women from different socio-cultural levels we compared the incidence in pregnancies before and after HIV diagnosis according to their geographical origin (sub-Saharan Africa versus others) **Methods** 533 women infected by HIV through sexual contact were followed in the French cohorts SEROCO and SEROGEST between 1988 and 1996 SEROCO is a cohort of HIV+ adults comprising 29% of women, mostly French SEROGEST is a cohort of HIV+ women enrolled while they are pregnant, this pregnancy having led to the HIV diagnosis or occurring thereafter, 40% of them were from sub-Saharan Africa Women enrolled in SEROGEST because of a pregnancy occurring after the HIV diagnosis were excluded from the analysis in order not to overestimate the incidence after The period surrounding the pregnancy having led to the test + (prenatal HIV testing being widespread in France) was excluded from the incidence estimation A multivariate Poisson regression analysis was conducted to compare incidence before and after diagnosis independently of the socio-economical level and geographical origin (fixed variable) and age and parity (time-dependent variables) **Results** In French women, the pregnancy incidence significantly fell from 11.2/100 person-years (p-y) before the test to 6.5/100 p-y after ($p = 0.02$) In contrast incidence remained stable in African women (15.5/100 p-y before vs 18.1/100 p-y after), the interaction term with geographical origin being significant After the test birth delivery as well as voluntary abortion rate was 3 times greater in African women than in others the % of sexually active women was similar in the 2 groups, but African reported less frequently having a contraception Finally in HIV+ French women the birth delivery rate increased in the 1994-96 period compared to before 1994, probably due to the large improvements in the prevention of mother-to-child transmission Such a trend was not observed in African women **Conclusion**



This description of behaviour of HIV-infected women towards pregnancy and contraception should allow improving counselling of HIV-infected women in France

[456/23266] Late post-natal mother-to-child transmission (LPT) of HIV-1 International multicentre pooled analysis

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Background Understanding the risk and timing of mother-to-child transmission of HIV-1 in the postnatal period is important for the development of public health strategies to reduce vertical transmission of HIV in the developing world **Methods** An international multicentre pooled analysis of individual data from prospective cohort studies of children born to HIV infected mothers followed from birth to estimate the rate of LPT of HIV All children diagnosed as uninfected by HIV DNA PCR and/or HIV serology were enrolled LPT was considered to have occurred if a child subsequently became infected Duration of follow-up for each child was calculated from the time of negative diagnosis to the date of the last laboratory follow-up, or for cases to the mid-point between the date of last negative and first positive results **Results** Fewer than 5% of the 2807 children enrolled in 4 cohorts from industrialized countries (USA, Switzerland France and Europe) were breastfed and no case of LPT was diagnosed In contrast there were 49 cases of LPT in 902 children enrolled in 4 cohorts from developing countries where breastfeeding was the norm (Rwanda [2], Ivory Coast, Kenya) yielding an overall estimated risk of LPT of 3.2 per 100 child-years of breastfeeding, with similar estimates in individual studies Exact information on timing of infection and breastfeeding was available for 20 of the 49 LPT cases Depending on assumptions about the timing of LPT in the interval between tests, LPT would have occurred in a minimum of none and a maximum of 2 cases if breastfeeding had ceased at 4 months, and 3 or 4 if breastfeeding had ceased at 6 months of age **Conclusion** The similarity in estimated risk of LPT between studies strengthens the reliability of the overall estimate, which shows that breastfed children born to HIV positive mothers are at substantial risk of LPT This risk should be balanced against the effect of early weaning on infant mortality and morbidity and maternal morbidity and fertility

[457/23270] HIV infection due to breastfeeding in a cohort of babies not infected at enrollment

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Objectives To determine the rate and timing of HIV infection due to breast feeding in a cohort of babies who tested HIV negative by polymerase chain reaction (PCR) at or immediately after birth **Methods** Babies born to HIV positive mothers were PCR tested in a large birth canal cleansing intervention trial in Malawi Children with negative PCR results were enrolled in a longitudinal study after counseling the mother and obtaining consent Follow-up visits were scheduled every 3 months to collect information on risk factors, and every 6 months to obtain a heel-prick blood sample on filter paper for PCR testing ELISA and Western blot tests were done at 15 months and every three months thereafter PCR conversion/sero-conversion was defined as a change from last negative to first positive HIV test result Survival analysis was used to estimate hazard and cumulative incidence based on an interval censoring weighted analysis **Results** 621 HIV negative babies were enrolled During a median follow-up of 32 months 47 conversions were first detected between 8 and 18 weeks (estimated incidence of 3.5%), 11 were first detected between 19 and 60 weeks (estimated incidence of 1.9%) and 23 were first detected after 60 weeks (estimated incidence of 3.8%) At enrollment, 98% of the converters and 97% of the non-converters were breastfed None of the babies who converted had blood transfusion Other risk factors such as cracked nipples and swelling of the breasts were infrequent 42 conversions which occurred between birth and 7 weeks are not included in the above estimates since the majority of these conversions could have been due to intrapartum factors **Conclusion** In this population the HIV transmission rate due to breastfeeding is at least 9.2% This risk needs to be compared with expected morbidity and mortality resulting from not breastfeeding

[458/23273] Missed opportunities to reduce perinatal HIV transmission Maternal and neonatal zidovudine (ZDV) use in Los Angeles County (LAC)

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Background In 1994 results of ACTG 076 showed that ZDV given to HIV+ pregnant woman prenatally during labor and delivery (L&D) and subsequently to the newborn for 6 weeks could significantly reduce HIV vertical transmission. In LAC, it is now standard of care to follow the 076 regimen. We examined maternal and neonatal ZDV (NZDV) use for HIV-exposed children born in '95-'96. **Methods** Pediatric HIV surveillance began in LAC in 1988 as part of CDC's Pediatric Spectrum of Disease (PSD) Study. Nurses identify new children through routine visits to all medical centers in LAC that treat HIV-infected and exposed children. Maternal and neonatal ZDV data are collected at baseline from pediatric hospital and clinic charts and reflect what is recorded in this record. Unknown data were excluded from the denominators. **Results** As of 10/97, 223 perinatally exposed infants born in 1995-96 were reported to PSD, 84% were identified at birth. 76% (148/195) of mother's received ZDV during pregnancy. 72% (136/190) during L&D and 78% (174/223) received NZDV. Of those with complete ZDV data on all three 076 treatment arms, 84% (151/179) received at least one intervention and 116 (65%) received all three arms. Of the 223 infants, 160 (72%) of the mothers had prenatal care, 20 (9%) did not, and for 44 (20%) data were unknown. Of the 160 with prenatal care, 149 (93%) were known to be HIV+ at the child's birth. Those with prenatal care, 90% (133/147) received ZDV during pregnancy, 82% (122/148) in L&D, 89% (143/160) got NZDV and 62% (111/140) received all three, 93% received at least one intervention compared to 53% (34/63) of those with unknown or no prenatal care (RR = 6.8, 95% CI = 3.5, 12.8). Race was not associated with prenatal care or ZDV during pregnancy. While not statistically significant, whites were more likely than non-whites to receive ZDV during L&D (RR = 2.9, 95% CI, 0.8 - 11.1) and receive NZDV (OR = 2.0, 95% CI, 0.9, 4.4). **Conclusions** Failure to receive prenatal care, and/or failure to complete all three 076 treatment arms, have created a significant number of missed opportunities for maternal and infant ZDV. Prevention efforts must continue to focus not only on offering pregnant women HIV testing, but developing interventions to keep them and their babies, particularly among non-whites, in treatment.

[459/12151] Control of maternal HIV-1 disease during pregnancy

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Issue Recently released Principles of Therapy of HIV Infection (NIH, 11/97) specify that women should receive optimal antiRetroviral therapy regardless of the pregnancy status. However reports of experience with the use of these therapies in pregnancy have not yet appeared. **Project** Areas Perinatal AIDS Center at San Francisco General Hospital (BAPAC) has cared for over 200 HIV-1 infected mothers and their exposed children since 1989 stressing continuity of care, case management and meticulous attention to basic principles of maternal and child health in conjunction with ongoing counseling, peer advocacy and education. The Center has been able to offer maternal viral load assessment and state-of-the-art combination drug therapy for treatment of maternal disease and control of maternal plasma viremia since 1995. **Results** Client choice of available therapies has shifted markedly during this period. The majority of clients delivered in 1996 elected to take ZDV monotherapy, while in 1997, 16/23 mothers delivered took double combination therapy and 6/23 took triple combination therapy. Ten of 12 women currently pregnant in 1998 have chosen triple combination therapy. At BAPAC, combination therapy has been well-tolerated and no maternal or pediatric complications have been observed. It has been possible to lower maternal viral burden in all mothers, usually to non-detectable levels. Multiple problems with maternal ability to adhere to therapy have been encountered, particularly during the late first trimester and the post-partum period. These therapies have also had a profound impact on vertical transmission rates. Of the 60 BAPAC infants born since May 1995 43 are uninfected with all DNA-PCR testing negative through 6 months of age. Of 17 infants less than 6 months who have not yet completed testing 9 are presumed uninfected with negative PCR at birth and 6 weeks while 8 are negative at birth with no evidence of infection. **Lessons Learned** Despite adherence problems associated with pregnancy and the post-partum period the use of combination antiRetroviral therapeutic strategies to treat maternal HIV-1 disease during pregnancy results not only in improved maternal health but also in rates of maternal-to-fetal transmission that approach zero.

[460/42210] Health care providers' awareness of the ACTG 076 findings and their adherence to government guidelines to reduce perinatal transmission of HIV

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Background Bureau of Primary Health Care funded programs provide care for over 230 000 pregnant women mostly through community health centers (CHCs) in the US Given CDC HIV seroprevalence estimates for pregnant women (1 6/1000 pregnant women) BPHC funded programs are caring for an estimated 360 HIV infected pregnant women The Bureau needed to know how well the funded providers are (1) adhering to current protocols to reduce mother-child transmission of HIV (ACTG 076 - administer a ZDV regimen to pregnant women and their newborn infants), (2) adhering to counseling and testing guidelines (all pregnant women should be offered HIV counseling and testing) as well as (3) the providers' comfort level with treating HIV/AIDS patients This information will then allow the Bureau to develop targeted training programs to help educate the providers and ensure that they provide the highest level of care to their patients **Methods** 2000 health care workers (73% response rate) from 77 CHCs in New Jersey, New York and Puerto Rico were surveyed by mail **Results**

- * Substantial numbers of health care providers lack confidence in the ACTG 076 research findings (16%)
- * Only 53% of respondents routinely offer HIV screening to pregnant women and 50% of respondents offer HIV screening to women of reproductive age
 - * Almost one in five CHC health care providers are uncomfortable with treating AIDS patients
- * Almost half of respondents felt that HIV infected individuals should receive care only from specialists in HIV
 - * Many health care providers refer *all* HIV infected patients for care (18%)

Conclusions These providers work in Federally funded public health clinics in high HIV/AIDS incidence areas and yet given the overwhelming medical evidence supporting the ACTG 076 findings and subsequent Public Health Service guidelines to perinatal transmission of HIV and to offer routine HIV screening to all pregnant women, it is surprising how many providers were unaware or skeptical of the findings and recommendations Additional education of health care providers must take place to ensure that treatment protocols are followed

[461/23268] Association between placental malaria infection and increased risk of mother-to-infant transmission of HIV-1 in western Kenya

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Background Malaria and HIV-1 are common infections in reproductive-age women in sub-Saharan Africa In Malawi infants born to HIV(+) women with placental malaria infection had a 3 4-fold increased risk of post-neonatal death compared with infants born to HIV(+) women without placental parasitemia, suggesting that placental malaria infection may promote mother-to-infant HIV transmission In August 1996 we began a prospective study to assess this possible interaction in western Kenya **Methods** Between August 1996 and September 1997, consecutive pregnant women attending an antenatal clinic in Kisumu Kenya, were counseled and offered HIV testing (CT) At delivery placental blood smears were examined for malaria parasitemia and infants born by spontaneous vaginal delivery to asymptomatic HIV(+) mothers were enrolled into the study Infants were seen monthly for a clinical exam, or more frequently for intercurrent illness Infant HIV DNA-PCR was drawn at 2, 3 and 6 months **Results** Among 2976 pregnant women who received CT, 790 (26 5%) were HIV(+) Overall, 18 2% (277/1521) of women had placental malaria infection, and HIV(+) women had higher rates of placental malaria than HIV(-) women (OR 2 06, 95% CI 1 55-2 73) Preliminary results of the 365 infants with follow-up indicate that infants born to HIV(+) mothers with placental malaria infection are more likely to be PCR(+) within the first 3 months of life compared with infants born to mothers without placental parasitemia, although the difference in HIV transmission rates does not yet attain statistical significance **Conclusions** HIV-1 and malaria are common in pregnant Kenyan women Preliminary results indicate that HIV(+) women are at increased risk for malaria and placental malaria may infant HIV transmission A safe, cost-effective strategy to prevent placental malaria is available and may reduce mother-to-infant HIV transmission in malarious areas Updated results from this study will be presented

[462/23265] Risk factors for perinatal HIV transmission in women/infants receiving standard zidovudine (ZDV) prophylaxis

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Background Determining factors associated with perinatal transmission in the presence of antenatal/intrapartum/neonatal ZDV prophylaxis (which is now standard in the US) may permit development of improved preventive interventions to further reduce transmission. **Methods** Risk factors were evaluated in 473 infected pregnant women enrolled in perinatal trial PACTG 185 [comparing efficacy of ZDV+HIV hyperimmune globulin (HIVIG) vs ZDV+IVIG], all mother/infant pairs received standard ZDV prophylaxis. Infant infection was determined by serial HIV culture through age 6 months. Stored plasma HIV RNA level was evaluated by NASBA assay. **Results** In univariate analyses, entry CD4 [$p = .016$, Odds Ratio (OR) 0.59 per 100 cell increment (-)] & HIV culture titer (IUPM) ($p = .04$, OR 1.7 per 1 log -) & HIV RNA (per 1 log -) both at entry ($p = .003$, OR 3.8) & delivery ($p = .005$, OR 3.3) were associated with transmission. Delivery IUPM, study arm (HIVIG/IVIG) gestational age, delivery mode, duration of membrane rupture & birthweight were not associated with transmission. 11% of women with entry CD4 in the lowest quartile ($<210/\text{mm}^3$) transmitted compared to 3% with CD4 in the other quartiles ($p = .001$). 12% of women with entry RNA in the highest quartile (>4.6 log) transmitted compared to 2% in the other quartiles ($p = .002$). Transmission was 0% (0/48) for delivery RNA <500 (below the level of detection of the assay) vs 5% for ≥ 500 ($p = .10$). In multivariate logistic regression models including {entry CD4 count, IUPM, & RNA} or {delivery IUPM & RNA}, only RNA remained significantly associated with transmission (at entry $p = .03$, OR 2.8, at delivery $p = .003$, OR 4.2). **Conclusions** Our results suggest that in women already receiving ZDV prophylaxis, attempts to reduce maternal viral load to <500 copies/mL may further reduce perinatal transmission. The effect of maximal RNA suppression by newer potent anti-retroviral regimens on perinatal transmission should be evaluated.

[463/12152] Combination therapy with nevirapine, zidovudine and a second nucleoside analog during pregnancy

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Objectives To determine the safety and efficacy of nevirapine given with 2 nucleoside analog reverse transcriptase inhibitors (NRTI) in HIV-infected pregnant women and evaluate the impact of this regimen on newborns. **Methods** We reviewed the records of 14 HIV-infected pregnant women who received nevirapine, zidovudine and another NRTI (9 DDI, 2 DDC, 2 3TC and 1 DDI later switched to 3TC) from 6/97 to 1/98. Exposure to nevirapine lasted from 2 to 31 weeks. 8 patients have delivered and 6 are near term. **Results** This regimen was well tolerated. Rashes (2 mild, 1 more severe) occurred in 3 cases. Zidovudine-induced anemia affected 1 patient. Of 11 patients who received ≥ 8 weeks of combination, 8 (mean baseline HIV RNA PCR = 16,000 copies/ml) reached an undetectable viral load (<200 copies/ml) within 8 weeks of treatment and continue to have a complete viral suppression (3 deliveries to date). Among the other 3 cases, 2 are failures (1 insufficient response, 1 relapse, mean baseline viral load = 47,000) and 1 had a decrease in viral load from 112,000 to 644 by 5 weeks prior to delivery and undetectable viral load after delivery. 7/8 newborns have negative HIV DNA PCR (1 pending). All newborns are without anomalies and with CD4 and other laboratory values within normal range. **Conclusion** In our experience a regimen of nevirapine, zidovudine and another NRTI is well tolerated in pregnancy, leads to a sustained undetectable viral load in 82% of cases and does not have detrimental effects on the newborn.

[528/23276] A randomized trial of STD control during pregnancy in Rakai, Uganda: Impact on maternal and infant health

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Objectives To evaluate effects of mass STD treatment on pregnancy outcome and maternal-infant infections. **Design** Prospective community-based single-blinded randomized trial of STD control. **Methods** In a randomized trial of STD Control for AIDS Prevention, pregnant women are enrolled into a maternal-infant follow up study. Single oral regimens are provided once during pregnancy: intervention arm women receive azithromycin, cefixime and metronidazole, and control arm receive iron/folate. Syphilis is treated with IM penicillin in both arms. Data are collected in the home during pregnancy and postpartum, and include interviews, HIV and syphilis serology, urinary LCR for gonorrhea (GC) and chlamydia (Ct), vaginal swabs for BV (gram stain) and trichomoniasis (Tv) culture, clinical exam for upper genital tract infection (UGTI), and placental histopathology.



Infant low birthweight (LBW) is based on anthropometry diagnosis of ophthalmia is by conjunctival LCR and HIV by PCR. Analyses examine rates (%) and relative risks (RR) in intervention vs control arm using statistical tests adjusted for cluster randomization. **Results** Between 1995-97 we enrolled 3635 pregnant women (1818 Intervention, 1817 Control) and 2973 mothers/infants (1576 Intervention 1397 Control). Compliance was 90%. Results are as follows

Maternal	Tv	BV	GC	Ct	UGTI	Infant GC	Ct	LBW	Mortality
Intervention (%)	5.7	37.6	0.9	1.1	2.2	0.6	0.8	9.8	4.6
Control (%)	17.3	52.4	2.1	3.6	3.6	1.5	1.3	12.6	4.7
RR (p < 0.05*)	0.30*	0.72*	0.43	0.31*	0.61	0.40*	0.60	0.78*	0.98
Data on STD infection, chorioamnionitis and mother-to-child HIV transmission will be available shortly									

Conclusions Mass treatment of STDs in pregnant women is feasible and results in substantial reductions of maternal and infant morbidity

[41147] Comparison of proviral DNA in HIV-1 and HIV-2 infected babies in relation to the mode of mother-to-child transmission and survival

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Objectives To compare proviral load in HIV-1 and HIV-2 infected babies and to relate proviral load to the mode of mother-to-child transmission peri-versus postnatal transmission, and to their survival. **Design** Community-based prospective study. **Methods** Twenty three HIV infected babies were recruited from the MRC transmission study 17 were HIV-1 of whom six died before the age of one year and six were infected with HIV-2. Perinatal mother-to-child HIV transmission was diagnosed if the baby was positive by PCR before 9 months of age and postnatally if negative by PCR before 9 months of age but positive at 18 months. Proviral DNA load in PBMC was quantitated by PCR using HIV-1 and HIV-2 specific primers and external controls. **Results** (Table)

Geometric mean (\pm SD) of proviral DNA copies/10 PBMCs (Log ₁₀)			
	2 month	9 month	18 month
HIV-1 infected babies (n=17)			
Perinatal			
Died (n=6)	2.962 \pm 1.343 ^a	2.375 \pm 0.046	
Survived (n=5)	1.171 \pm 1.209 ^a	2.207 \pm 1.741	1.501 \pm 1.124 ^b
Postnatal (n=5)			
Unclassified (n=1)	N D *	4.0	N D
HIV-2 infected babies (n=6)			
Perinatal (n=4)			
		2.554 \pm 0.409 ^c	2.107 \pm 0.535 ^d
Postnatal (n=2)			
		0.300 \pm 0.000 ^c	1.004 \pm 0.320 ^d
^a p < 0.05	^b p < 0.1	^c p = 0.002	^d p = 0.084 *Not done



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Conclusions No significant difference in DNA viral load between HIV-1 and HIV-2 infected babies. A high DNA viral load was strongly associated with poor survival within the first year of life in babies infected perinatally with HIV-1 ($p < 0.05$). Therefore, an early assessment of DNA viral load in children infected with HIV might be of use in estimating prognosis, and in management.

[60784] Evaluating the implementation of three programmes for preventing perinatal transmission of HIV

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The importance of the heterosexual transmission of the human immunodeficiency virus (HIV) is increasing worldwide and particularly in Brazil. Thus, it has been observed an increasing participation of the human population at child-bearing age in the AIDS epidemic in Brazil. Therefore, concern about vertical transmission (mother-to-child) has recently heightened in this country. It has been demonstrated the efficacy of the antiRetroviral therapy and of other preventive measures towards the reduction of mother-to-child transmission rates. These measures have been recommended by the Centers for Disease Control and Prevention (CDC) since 1994 and in Brazil by the Ministry of Health, since 1996. This study aimed at evaluating the implementation of the programmes for prevention of HIV perinatal transmission carried out in three different localities in Brazil. It also aimed at proposing strategies for increasing the effectivity of these programmes. Information was obtained from routine data and from questionnaires applied to the health workers involved in the programmes. The implementation of the programmes was not followed by adequate information systems. There is a need for some reorganization of the referral systems. Poor training and supervision were identified as the main limiting factors for the success of the programmes.

[12163] Morbidity and mortality among HIV-1 infected and uninfected Kenyan children

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Background and Objective To determine the excess morbidity and mortality experienced by HIV-1 perinatally and postnatally infected African children not receiving antiRetroviral therapy. **Design** Prospective cohort study. **Methods** The mortality and morbidity in HIV-1 perinatally, postnatally, and uninfected cohorts of children enrolled at birth to HIV-1 seropositive mothers and a concurrently enrolled cohort of infants born to HIV-1 seronegative mothers followed in The Nairobi Mother to Child HIV-1 Transmission and Pediatric AIDS Study were compared. **Results** There were 102 perinatally, 41 postnatally, 465 uninfected and 570 control children followed for 226, 144, 1217 and 1401 person years respectively. Cumulative mortality rates over 10 years were 40.2%, 31.2%, 4.2% and 4.6% respectively ($p < 0.001$). The following were significantly ($p < 0.001$) increased among perinatally infected children compared with controls: hospitalizations (3) and the incidence of sepsis/meningitis (2.5), tuberculosis (10), measles (3), pneumonia (2), acute otitis media (4.5), chronic otitis media (6.5), thrush (4.5), other mouth ulcers (3.5), skin rashes (2), and failure to thrive (1.5). Fewer illnesses were more frequent among postnatally infected children compared with controls and included hospitalizations (3), sepsis/meningitis (2.5), tuberculosis (5), acute otitis media (3.5), chronic otitis media (3.5), thrush (2.5), skin rashes (2.5) and failure to thrive (2). Only tuberculosis was increased among uninfected children compared with controls ($p < 0.05$). **Conclusion** Both perinatal and postnatal HIV-1 infection significantly affected childhood mortality and morbidity. The pattern of illnesses was slightly different for perinatal versus postnatal infection. There were no "AIDS" defining illnesses which would be useful for clinical screening in lieu of serological testing or which would be predictive of early infant mortality due to HIV-1 infection.

[12175] Seroconversion in infants of positive mothers to HIV Total breastfeeding impact

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Objectives To estimate breastfeeding risk in the mother to infant transmission in a cohort of children born in Santos SP Brazil to analyse breastfeeding length effect in seroconversion to estimate survival of total breastfed versus non breastfed children **Methods** A historic cohort with HIV positives mother's infants was assisted at NIC - Santos SP Brazil (Nucleo Integrado da Crianca) from January 1993 to December 1997 The children were stratified in two groups Breastfed and Non breastfed The HIV infection was determined by the antibody test after 18 months of age or by AIDS clinical diagnosis at any age **Results** The results of antibody test in the two groups were

	HIV+	HIV -
Total Breastfed	45/64 (70.3%)	19/64 (29.6%)
Non breastfed	35/72 (48.6%)	37/72 (51.3%)
X ² = 6.6 P value = 0.01		

25% of women had knowledge of their HIV positive status and decided to breastfeed their children despite of the strongly health professional warning to the risk of their choice The total breastfeeding average was 30 days at seropositive group and 0 days at the seronegative group **Conclusions** Breastfeeding is meaningful factor to HIV mother to infant transmission The Kaplan - Meier analysis suggests greater survival of the total breastfed infants group, however the difference has not showed to be statistically meaningful Would breast milk have a protector effect over HIV infected children?

[12408] Modified ACTG- 076 protocol and its initial results in the largest ongoing perinatal HIV study in India

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Background With the HIV epidemic in its third phase affecting a large number of women India, ridden with poverty (GNP 150\$), illiteracy, double standards and multiple scandals has some activists for the cause of trees, animals and human rights But strangely enough, a child in the womb is not covered under any of these causes and continues to be neglected We decided to pursue 'Right to AIDS-Free Life' for the small creatures in the womb before they breath in this morally and socially polluted world To prevent perinatal transmission cost effectively by appropriately modifying the ACTG-076 protocol in Indian context, we initiated this study **Methods** After sequential, systematised HIV screening of the antenatal clinic attendees at a large Women's Hospital, seropositive women were counselled on preventing perinatal transmission through modified ACTG-076 to suit the cost and convenience in the 'IHO-Wadia' model It has four wings Locally produced AZT to mother for 8 weeks 400 mg/day, elective Ceasarean section for delivering the baby, no breast feeding or modified breast-feeding and AZT to the infant for first 40 days Children are followed quarterly till 15 months and tested for HIV by ELISA at 9 and 15 months, the latest they can be certified infected or otherwise Sero-negative babies are discharged from the study at the earliest revelation **Result** Of the 81 babies born following our protocol, 26 have failed to follow-up, 35 are below 9 months All the 20 babies who have completed 9 months have come 'HIV negative' (Zero prevalence, but small sample size) It is a cost-effective study Pool ELISA test per woman Rs 15/- (\$0.40), Cost of detection of one infection Rs 1500/- (\$40/-) (prevalence in women is 1%), Cost of prevention of one perinatal transmission Rs 5000/- (130\$) vis a vis cost of managing one HIV infected child with 'cocktail' Rs 100,000/- (2800\$) **Conclusion** AZT given to seropositive mothers in proportionately smaller doses (due to low average weight) for a shorter duration of 4 to 6 weeks has been equally efficient in preventing perinatal transmission Such a cost-effective and user-friendly model needs to be replicated elsewhere UNAIDS guidelines of 'no-breast feeding' for rich countries and 'breast-feeding' in poorer countries needs to be modified with indigenous solution of modified breast-feeding (heating breast milk)

[23284] A community based study of perinatal transmission of HIV-1 and HIV-2 in The Gambia
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Objectives To determine rates of, and risk factors for mother to child transmission (MCT) of HIV-1 and HIV-2 in The Gambia **Methods** From January 1993 to March 1995 we screened 29 670 pregnant women attending antenatal clinics in The Gambia Mothers and babies were visited and examined by a clinician at 2 9 and 18 months of age when bloods were taken for immunology and virology **Results** We enrolled 109 HIV-1 seropositive women, 250 HIV-2 seropositive women and 448 seronegative controls Of the children born to HIV-1 seropositive women 7 of 64 were HIV-1 PCR positive at 9 months of age and 6 of 11 children who were dead or lost to follow-up by 9 months were HIV-1 PCR positive at 2 months of age Four children who were PCR negative at 9 months of age were HIV-1 seropositive and PCR positive at 18 months of age MCT rate was 17/81 i e 21 0% (95% CI 2 7, 31 5) Of the children born to HIV-2 seropositive women, 5 of 170 were HIV-2 PCR positive at 9 months of age None of the 22 children who were dead or lost to follow up at 9 months of age and who were tested at 2 months were HIV-2 PCR positive Three children who were PCR negative at 9 months of age were HIV-2 seropositive and PCR positive at 18 months of age MCT rate was 8/201 i e 4 0 (95% CI 1 7, 7 7) A low CD4% and birth during the malaria season were risk factors for transmission Plasma RNA HIV-2 viral load was higher in mothers who infected their babies than in those who did not (GM 4722 vs 973 copies/ml respectively, $p = 0 03$) The HIV-1 plasma RNA viral load is being measured Mother to child transmission rate which was influenced by season and state of disease as determined by CD4 level or plasma viral load, was higher in HIV-1 than HIV-2 infected mothers Late postnatal infection occurred in both infections

[23285] Comparative importance of obstetric factors for vertical HIV-1 transmission in Malawi and Brazil

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Objectives To assess the importance of obstetric factors on vertical transmission of HIV-1 comparing results from two large cohort studies in Malawi and in Brazil **Methods** A cross-validation approach was used to evaluate obstetric predictors similarly defined in Malawi (1359 mother-child pairs) and Brazil (434 mother-child pairs) A predictive model was built upon the Malawi data and was tested independently in the Brazilian data, controlling for the effect of maternal HIV disease We compared the risk of vertical HIV-1 transmission according to different indications of cesarean section (c-section) in the two settings **Results** Duration of ruptured membranes (ROM) (OR per hour 1 02, 95% CI 1 00-1 04), gestational age (OR per week 0 93, 95% CI 0 85-0 99) and maternal stage of HIV disease (OR 1 68, 95% CI 1 20-2 35) remained independently associated with child's HIV-infection status in a multivariate analysis based on the Malawi data and the model was fully validated in the Brazilian cohort ($p = 0 01$) where the effects of these three predictors were similar 14% of the deliveries were by c-section in Malawi vs 35% in Brazil In Malawi, the transmission risks for vaginal and c-section delivery were 26% (95% CI 24-29) and 19% (95% CI 14-25), respectively, whereas in Brazil these figures were 15% (95% CI 11-19) and 19% (95% CI 13-26) In Brazil, transmission risk was 21% (95% CI 13-30) for babies born by c-section for indications rarely used in Malawi but common in Brazil (tubal ligation, prolonged ROM, multiple birth, previous c-section, post-date delivery fetal distress and HIV infection) for indications which were equally common in the two countries (dystocia cephalo-pelvic disproportion hypertensive conditions, abnormal fetal presentation, placental and cervical emergencies) transmission risk was 13% (95% CI 4-27) **Conclusions** The effects of ROM, gestational age and maternal disease stage are consistent in Malawi and Brazil Differences in the crude effect of the mode of delivery on the risk of transmission may be partially due to differences in the indications for c-section in the two settings Such differences in indications need to be considered before addressing the issue whether c-section per se may or may not affect the risk of transmission

[23289] Assessment of the Programme of Serological Assistance to Pregnant Women (PASG) and the Programme of Assistance to Seropositive Pregnant Women (PAG+) in the City of Guarujá-Brazil

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Objectives To assess the impact of the introduction of the offering of anti-HIV test to pregnant women seroprevalence, and the difficulty of implementation of the ACTG-076 guidelines **Introduction** Guarujá is the 17th Brazilian city in incidence of the HIV-virus among the population being one of the first cities in Brazil to obtain AZT (intravenous), in June 1996 and to launch the PASG in July 1997 The programme consists in the universal offering (free) of anti-HIV tests to pregnant women in all public health centres by the obstetricians while the Infectious Diseases Division is responsible for the pre-test, the talks on STD/AIDS for the pregnant women and the personal filling-in of forms and questionnaires Fifteen days after the blood sampling, the pregnant woman returns for the post-test (orientation and the delivery of results individually), those women with a negative result go back to the public health centre for the pre-natal assistance while those with a positive result join the Programme of Assistance to Seropositive Pregnant Women (PAG+), following the ACTG-076 guidelines **Results** After the centralization of the programme in one department, these were results for information, blood sampling and the delivery of results the number of women who do the test increased 20 times (from 15 tests/month to an average of 300 tests/month) Of the 1264 pregnant women who used the service, sent by the basic healthcare system (pre-natal assistance), 89% had not received any information about STD/AIDS from their obstetricians, after receiving information and orientation in the central unit, all did the test that was offered and complained about their partners not getting involved in the programme Ten pregnant women (0.79%) are seropositive (confirmed by two samples) average age 22 years old, 4 married (40%), 3 single (30%) and 3 other marital status (30%), 5 sometimes use contraceptives 3 never used contraceptives (30%), 7 never did the anti-HIV test (70%), 2 had previously done the test (20%), 1 did not answer (10%), and 10 denied using intravenous drugs (100%) and 10 stated having only one partner (100%) **ASSESSMENT OF THE PAG+ (implementation of ACTG-076 guidelines)** Out of 10 pregnant women 5 (50%) did not return to receive the result of the second sample (positive), although they were invited by letter and visited by the service nurse, 2 (20%) followed all the procedures and are still under treatment 2 (20%) are using AZT (oral) and 1 (10%) did not use AZT (intravenous) during childbirth **Conclusion** After the implementation of the PASG in a centralized way, we considerably increased the amount of information about STDs/AIDS among women at the reproductive phase and there is less prejudice against maternal sampling for the HIV test in this population As for the PAG+ we have come across a lot of difficulty to keep it working the psychosocial aspect of the pregnant women when they receive the result, constant lack of test-kits (a long time passes before they receive the result increasing the stress), the obstetricians are very little involved lack of human and financial resources specifically for the programme We believe these must be common problems in many Third World cities where ACTG-076 guidelines are being implemented

[23292] The relative importance of antepartum antiRetroviral therapy versus intrapartum and neonatal treatment in preventing maternal infant HIV transmission

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Background AntiRetroviral therapy (ART) decreases rates of maternal infant (MI) HIV transmission when given ante and intra partum to the pregnant woman and post partum to the infant This study was undertaken to better define the relative importance of each component of ART in prevention of MI Transmission **Methods** All MI pairs cared for in our HIV centre from Mar 1993 through Dec 1997 were reviewed regarding HIV outcome, maternal characteristics obstetrical details and ART received Rates of MI Transmission were compared between (1) MI pairs that received full antepartum ART from 34 weeks (or earlier) through to term (regardless of intrapartum and postpartum ART), (2) MI pairs that did not receive full antepartum ART from 34 weeks till term but did receive other (intra or postpartum) ART (3) MI pairs that received no ART Statistical analyses were performed using chi square and Fisher's exact test and logistic regression modeling **Results** 73 MI pairs were reviewed Rates of MI Transmission were pairs receiving full antepartum ART (regardless of other ART received) 1/32 (3.1%), pairs that did not receive antepartum ART but did receive other ART (intra +/-postpartum) 4/19 (21%), pairs that received no ART 5/22 (22.7%) There was a statistically significant difference in transmission rates between MI pairs receiving antepartum ART and those receiving any other ART (P = 0.05) and those receiving no ART (P = 0.02) There was no significant difference between the groups receiving any ART other than the antepartum component and those receiving no ART After stepwise multivariate logistic regression, only the antepartum component remained significant (P=0.04, odds Ratio = 0.12) These parameters were not significantly changed when all components of therapy were forced into the model **Conclusions** These data suggest that the antenatal component of ART may be significantly more important in preventing maternal infant HIV transmission than the intrapartum and/or postpartum components of therapy Further study of ART in pregnancy is required in order to clarify this relationship and further improve maternal and infant outcomes



[23295] The challenge to reduce HIV vertical transmission in Brazil

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Issue HIV/AIDS epidemic in Brazil is growing fast among women in childbearing age resulting in an increase in the number of HIV infected children **Project** Based on the results of the 076 study, the Brazilian Ministry of Health established in July 1996 a special program to reduce vertical transmission The program includes 1- A policy to offer universally HIV testing to pregnant women (voluntary test with counseling), 2- Provision of AZT (capsules, IV and syrup) free of charge among the other antiRetroviral drugs, 3- A policy to discourage breast feeding for HIV infected women and provision of the milk formula to babies born from HIV infected women, 4- Training program for health care providers (obstetricians, pediatricians and nurses), 5- Publication of official guidelines to reduce HIV vertical transmission **Results** In spite of all efforts, the number of HIV infected pregnant women receiving IV AZT still low, even after 18 months of the program One of the major problem faced by this program is to deal with the deficiencies that characterize the maternal and perinatal care in Brazil The severity of this problem is reflected on the rate of maternal mortality which can be in some areas of the county as high as 160/100 000 born alive Some identified deficiencies 1- Overloaded health care services, 2- A very interventionist pattern of assistance to delivery 3- Lack of continuous education opportunities for health care providers Another problem identified during the training program is the lack of familiarity with HIV/AIDS issues by the maternal and child health (MCH) care providers **Lessons learned** In a developing country, a strategy to reduce HIV vertical transmission may face other problems no directly related with the HIV/AIDS epidemic These problems could be a significant barrier and should be addressed in the global strategy to manage the problem of HIV vertical transmission HIV/AIDS is a new issue for the majority of MCH care providers and this points out the need of training programs specially designed for them

[23297] AntiRetroviral drugs for pregnant women in rural South Africa cost-effectiveness and capacity

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Objective To estimate cost-effectiveness of, and capacity requirements for providing antiRetroviral drugs (ARVs) to pregnant HIV-infected women in rural South Africa **Setting** Hlabisa health district where HIV prevalence among pregnant women was 26 0% in 1997 **Methods** Calculation of number of paediatric HIV infections averted under three scenarios, and their cost No intervention compared with A zidovudine (ZDV, ACTG 076 protocol) delivered within current infrastructure, B ZDV delivered through enhanced and C short-course ZDV plus lamivudine (3TC) delivered through enhanced Cost effectiveness defined as cost/infection averted and cost/potential year of life gained Capacity in terms of staff and infrastructure required to effectively implement **Results** With no intervention 657 paediatric HIV infections are projected for 1997 In scenario A this could be reduced by 15% at a cost of about R2 7 million (1US\$ = R4 5), in scenario B by 42% at about R7 1 million, and in scenario C by 47% at about R3 6 million In scenario C, drugs account for 75 9% of costs, while additional staff account for 18 4% Cost per infection averted was RI 1,710 and cost per potential year of life gained (discounted at 3%) was R404 Cost of scenario C is equivalent to 14% of the 1997 district health budget At least 12 extra counsellors and nurses and one laboratory technician together with substantial logistical and managerial support would be needed to deliver an effective intervention **Conclusion** Although ARVs may be relatively cost-effective in this setting the budget required is currently unaffordable Developing the capacity required to deliver the intervention poses both a major challenge and an opportunity to improve maternity services

[23311] Main difficulties in the reduction of HIV vertical transmission in Rio de Janeiro, Brazil

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Objectives Investigate the factors which influence or hamper the access of HIV infected pregnant women to therapy with zidovudine (ZDV) to reduce the vertical transmission of HIV **Methods** We studied all the mothers of children classified in the categorie E (CDC) which were born between 1995 and 1997, in follow-up at the Pediatric Immunology Clinic The mothers were divided into two groups A - mothers that receive ZDV therapy during pregnancy/birth and B - mothers that were not treated with ZDV during pregnancy/birth We analysed



demographic characteristics access to pre-natal examination presence of STD during pregnancy offering of anti-HIV serology during pre-natal exam and knowledge of HIV diagnosis before pregnancy For statistical analysis we used Fischer's exact test **Results** We analysed 61 HIV infected women Twenty (32.8%) had been treated with ZDV during pregnancy/birth, of which 10 (50%) had previous knowledge of their HIV+ status 6 (30%) found out they were HIV infected during pregnancy via diagnosis of HIV infection in their sexual partner and 1 (5%) developed AIDS during pregnancy Median of age, ethnics and mode of acquisition of HIV were similar in both groups Twenty women (100%) in group A and 35 (85.4%) in group B ($p = 0.0810$ NS) performed prenatal exams where as 10 (50%) in group A and 10 (24.4%) in group B knew their HIV+ status before pregnancy ($p = 0.9883$ NS) The presence of STD during pregnancy occurred in 3 women (15%) of group A and 2 (4.9%) of group B ($p = 0.1931$ NS) Anti-HIV serology was offered during the pre-natal period to 3 women in group A and none in group B ZDV therapy for reduction of HIV vertical transmission was not offered to any of the 10 women in group B who knew they were infected by HIV **Conclusions** The main factors which hamper the reduction of vertical transmission were the non-identification of 49.2% of HIV infected pregnant women, due to reduced offering of anti-HIV serology during pre-natal exams, and the non-referral to ZDV therapy of 33.3% of pregnant women who already knew that they were HIV+ These data demonstrate the need for education/training of health providers who attend women

[23319] Nipple disease among lactating HIV-1 infected women

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Objectives Nipple disease a common problem in lactating women, may be associated with breast milk transmission of HIV-1 This study describes the incidence and correlates of cracked nipples (CN) among lactating HIV-1 infected women in Nairobi, Kenya **Methods** Pregnant HIV-1 seropositive women enrolled in a breast feeding versus formula feeding trial underwent an interview, physical examination, and laboratory evaluation of haemoglobin, CD4 counts, and plasma vitamin A level After delivery women were interviewed and examined for physical evidence of CN at each visit during a 2 year follow-up period **Results** Three hundred and seventy-one women were enrolled and followed for 582 person-years (p-yrs) Thirteen percent (31/242) of breast feeding women versus 3% (4/129) of formula feeders had CN ($p = .002$) Of these 35 women with CN, the first episode of CN occurred during the first month of lactation in 35% of breast feeders and 25% of formula feeders Mean vitamin A levels were significantly lower among women with CN (202 g/L vs 283g/L, $p = .001$) One third (10/30) of the women with CN experienced vaginal candidiasis during pregnancy compared to 17% (56/315) among women without CN (OR 2.3, 95%CI 1.02-5.2) Age previous parity, clinical disease status and immunosuppression were not associated with CN In a multivariate logistic regression CN were significantly associated with vaginal candidiasis (OR 8.7, 95% CI 4.1-19) and inversely related to vitamin A levels For every 10% decrease in vitamin A level there was a 1.4-fold increased odds of having CN (95% CI 1.2-1.7) **Conclusions** Vitamin A deficiency and vaginal candidiasis during pregnancy were associated with cracked nipples after delivery Supplementation with vitamin A maybe beneficial, particularly if cracked nipples are associated with increased risk of breast feeding transmission of HIV-1

[23322] The feasibility of short-course antiRetroviral therapy for the prevention of mother to child transmission of HIV in Soweto, South Africa

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Background Despite the success of zidovudine as standard treatment for the reduction of mother to child transmission in developed countries, current regimens may not be suitable for many developing countries, due to the cost infrastructure requirements and rates of breastfeeding Several trials of short-course antiRetroviral therapy are in progress, with early results expected in late 1998 If these prove successful this approach would provide a cost-effective alternative for some developing countries This paper discusses the requirements for the introduction of this therapy in South Africa's largest urban township These include access to maternity services, time of utilisation of antenatal care, laboratory facilities, drug supply logistics, testing and counselling services and infant feeding practices **Results** Chris Hanani Baragwanath Hospital in Soweto delivers 16 000 women annually with a further 7000 delivered at the associated midwife delivery clinics Antenatal care services are free and over 95% of pregnant women attend antenatal clinics and deliver in medical facilities The mean gestational age at first attendance is 23 weeks, with 88% of women attending before 36 weeks Uptake of voluntary HIV counselling and



testing currently only available at hospital level is over 95% The HIV seroprevalence was 18% in early 1998 giving an estimated 3200 HIV positive women per year who could be identified in time to start treatment at 36 weeks Laboratory facilities are available with the capacity to undertake sufficient HIV tests and other laboratory work A well-controlled drug distribution system is in place at hospital and clinic level Trained nurse counsellors are available at all clinics and the hospital, backed up by volunteer peer counsellors at the hospital Staffing levels would need to be increased to cope with the counselling workload At present, over 80% of identified HIV positive women formula feed their infants **Conclusions** The conditions and infrastructure for the implementation of short-course antiRetroviral therapy are largely available in Soweto Additional staff for counselling and funds for laboratory services and drug supply would be required Decisions on the introduction of such therapy will be made on the basis of efficacy results from the PETRA and other studies, and cost benefit analyses using local data

[23323] Recommendations from 11 Latinamerican AIDS programs to prevent HIV transmission through breastfeeding

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Problem It is estimated that between one-third to one-half of the total perinatal AIDS cases acquired HIV by their mothers milk (HIV transmission rate through breastfeeding 16-43%) The benefits of breastfeeding in reducing of infant mortality are widely acknowledged and promoted in developing countries **Project** A consensus workshop with directors of National AIDS Programs, officials of infant nutrition programs, and international organizations was organized to document current policies and practices regarding breastfeeding by HIV infected women in Latinamerica and to seek regional recommendations to promote the best alternative to prevent as many cases of HIV vertical transmission as possible **Results** Thirty-eight representatives of national AIDS and infant nutrition programs (Argentina, Brazil, Cuba Costa Rica, Chile, Dominican Republic, Honduras, Mexico Paraguay, Peru and Venezuela), of regional and national societies of pediatricians and from four international organizations dealing with AIDS were gathered (Brazil, Nov 1997) In all the participating countries, except Honduras and Dominican Republic, AZT was being provided (at different coverage rates) according to the ACTG 076 protocol using public funds All participating countries, except Honduras, contraindicated breastfeeding by HIV infected women and sought the sustained provision of milk substitutes or milk from other non-infected women (milk banks) as alternatives It was concluded that even when health personnel ignored the feasibility to substitute maternal milk, women should be adequately counselled about the risks of HIV transmission to their infants to make an informed decision In middle income countries in Latinamerica, adequate and sustained substitution of maternal milk is feasible using private (out-of-pocket) and public funds **Lessons Learned** It was concluded that ethically, breastfeeding must be contraindicated whenever alternative nutrition sources could be provided under a permanent basis The experience of nine countries in latinamerica showed the feasibility to limit the vertical transmission of HIV through the use of antiRetrovirals and substitution of maternal milk

[23325] Within feed analysis of HIV ABs in human breast milk Implication for breastfeeding policy and strategies

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Objective To investigate the variation of HIV specific immunoglobulins with respect to point of feed **Design** Prospective, follow-up study **Method** After a random selection, 20 pregnant women were recruited at an antenatal clinic where there was no mandatory test for HIV The women gave their consent to be followed up until the birth of the child All the ethical requirements were fulfilled Fore and hind samples of colostrum and mature milk were collected 5 and 21 days postpartum respectively and stored at -70 °C HIV specific antibodies were determined in all samples using 2 commercial Elisa kits **Results** Most women average age 24 yrs were between 26 and 32 weeks of gestation and received the standard care One of the assays detected HIV antibodies in 11 out of 20 colostrum samples and 3 out of 9 corresponding samples of mature milk The other assay showed that six quadruplicate samples i e 6 out of 20 milk samples had HIV antibodies Using the ODs obtained there appeared to be no statistically significant variation in the quantity HIV specific antibodies within feed **Conclusion** From the ODs obtained it would appear that there was no difference in the quality of fore and hind milk, as far as protective antibodies were concerned To change our breastfeeding policy and its strategies a bigger study which also looks at the viral load necessary HIV infection, lactation and breastfeeding is a complex issue



[23326] Zidovudine reduces HIV-1 perinatal transmission even if only the oral component administered to pregnant women is used

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Objective To evaluate the effectiveness of the different components of the zidovudine (ZDV) use in reducing the risk of perinatal transmission of HIV-1 in a cohort of vertically exposed infants in Belo Horizonte, Brazil **Design** Retrospective cohort study **Methods** A total of 103 infants born from HIV-1 infected mothers between January 1994 and August 1997 have been enrolled in a natural history study According to a standard protocol the baseline visit included information about ZDV use in antenatal, intrapartum and neonatal periods Infants were followed monthly for the first 6 months of life and every three months thereafter Infection status was defined in any of the following occurrences 1) development of AIDS-associated symptoms at any age, 2) persistence of serum HIV-1 antibodies beyond 18 months of age, or 3) serum or plasma p24 antigen detection in two occasions beyond neonatal period Seroreversion was established after 2 negative EIA performed in a three-month interval Infants <18 months who remained seropositive and had not presented clinical and laboratory evidences of infection had their HIV status classified as indeterminate **Results** At the time of analysis 33 (32.0%) of the 103 infants were infected 40 (38.8%) were serorevertors and 30 (29.1%) were indeterminate Infants whose HIV-1 status was indeterminate were excluded from the analysis Females comprised 50.5% of the population The mean age at entry in the study was 4.5 months (SD 3.8 months) Use of any combination of ZDV components was reported by 2 of 33 (6.1%) transmitting and 17 of 40 (42.5%) non-transmitting mothers {relative risk (RR) 2.10, 95% CI 1.49-2.97} Use of oral ZDV in the antenatal period alone was reported by 1 of 32 (3.1%) transmitting and 7 of 30 (23.3%) non-transmitting mothers (RR 2.05, 95% CI 1.37-3.08) The vertical transmission rate was 12.5% and 57.4% respectively in mothers reporting and not reporting ZDV use ($p = 0.024$) **Conclusions** In this observational cohort study, oral ZDV used only in the antenatal period was correlated to a 78.22% reduction in the vertical transmission rate These data indicated that a more simply approach of ZDV use, applicable in less developed countries, might have an efficacy comparable to the complete ACTG076 regimen

[23391] Changes in HIV-1 viral load after discontinuation of oral AZT given to pregnant Ugandan women

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Objectives To determine if significant post-partum HIV-1 viral load changes occur after cessation of a short course of oral AZT therapy in pregnant Ugandan women from 37 weeks gestation until delivery **Methods** Twenty HIV-1 infected pregnant Ugandan women with plasma HIV-1 RNA levels of >2000 copies/ml and equally distributed between CD4 cell count >500 cells/ μ l and CD4 cell count <500 cells/ μ l were enrolled Women received 300 mg AZT orally BID starting at 37 weeks gestation until the onset of labor A 600 mg oral AZT bolus was given at the onset of labor, followed by 300 mg every 3 hours until delivery Plasma HIV-1 RNA (Roche RT-PCR) CD4 cell counts and complete blood counts were monitored at enrollment delivery and post-partum A greater than three fold change in HIV-1 RNA was considered a biologically significant difference **Results** The study women delivered from 5 to 38 days (mean 21.9 days) after initiation of AZT therapy The median plasma HIV-1 RNA level was 10,119 copies/ml at baseline (37 weeks gestation), 3,720 copies/ml at delivery 24,000 copies/ml at 72 hours post-partum and 13,790 copies/ml at 6 weeks post-partum As compared to baseline - 8 of 19 women (42%) had >3 fold decrease in HIV-1 RNA by delivery (5 with CD4 < 500), - 6 of 20 women (30%) had >3 fold increase in HIV-1 RNA by 72 hours post-partum (2 with CD4 < 500), - 4 of 20 women (20%) had >3 fold increase in HIV-1 RNA by 6 weeks post-partum (2 with CD4 < 500) Overall none of the changes in plasma HIV-1 RNA levels associated with initiation or termination of oral AZT therapy were significant using log-transformed data **Conclusion** A short course of oral AZT in twenty pregnant Ugandan women produced variable changes in plasma HIV-1 RNA levels from initiation of therapy to timepoints after termination of therapy While a minority of women had persistent increased viremia up to six weeks post-partum, overall there was no significant viral overshoot response to termination of therapy

[31163] Study of cellular & humoral immune factors in colostrum of HIV infected & non-infected lactating mothers



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Background This study was done to quantify cellular & humoral immune factors in colostrum of HIV seropositive (Study group) & seronegative lactating women (Control group) **Methods** 15 ml colostrum was collected from 130 asymptomatic women 62 (Study) & 68 (Controls) in two sterile siliconised glass test tubes The total cell count cell viability differential count, T cell count by E rosette assay and phagocytic activity of macrophages as well as the IgA, IgM, IgG levels of colostrum were estimated in all **Results** The percentage phagocytosis and percentage T cell number in the study group was 57.3 ± 7.1 & 37.5 ± 5.4 as compared to 70.3 ± 7.1 & 50.5 ± 3.1 in controls ($p < 0.001$) The IgA & IgG content in the study group were 241.4 ± 110.3 & 9.6 ± 7.0 as compared to 289.3 ± 129.1 & 12.6 ± 7.9 in controls ($p < 0.05$) There was a statistically significant difference in the phagocytosis, T cell number as also the IgA & IgG contents in the two groups **Conclusion**, Results of this study indicate decrease in some cellular & humoral defence factors in colostrum of HIV seropositive women compared to seronegative ones Whether these reduce the overall beneficial effects of breast milk is a moot question The synergistic effect of not breast feeding & poor bottle hygiene can be disastrous in developing countries

[32232] Influence of maternal weight gain on vertical transmission and pregnancy outcome among HIV(+) women

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Objective To evaluate the influence of maternal weight gain among HIV-infected gravidas on vertical transmission, the length of pregnancy, intrauterine growth retardation (IGR), and birth weight **Material and Methods** Between 1988 and 1996, we studied 80 HIV-infected women delivering at School of Medicine of Ribeirao Preto-University of Sao Paulo that had at least 6 prenatal visits and had no exposure history to anti-retroviral agents (study group), matched with 80 uninfected normal gravidas (control group) We evaluated the pattern of weight gain of all pregnant women and compared those with low weight gain to those with normal weight gain in terms of vertical transmission rates, length of pregnancy and birth weight Vertical transmission was confirmed by HIV-PCR testing Maternal weight gain was evaluated according to Rosso's chart (zones A, B, and C) The newborns were classified by gestational age, (IGR), and birth weight **Results** Weight gain was found to be insufficient in 46.3% of HIV-infected pregnant women compared to 30.6% in HIV(-) gravidas Vertical transmission rate was numerically higher in newborns whose mothers had insufficient weight gain (18.9% vs 13.9%) There was a higher rate of preterm birth (32.4% vs 18.6%) and low birth weight newborns (35.1% vs 18.6%) comparing women infected by HIV with low vs normal weight gain No difference was observed on (IGR) rates **Conclusions** These data demonstrate worse pregnancy outcomes among HIV-infected women with poor maternal weight gain This suggests the need for nutritional support especially in indigent populations With more adequate nutrition, it may be possible to reduce the frequency of serious complications such as preterm delivery, low weight and vertical transmission of HIV-1

[32450] Is incomplete 076 ACTG protocol useful in reducing vertical HIV-1 transmission?

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Introduction ACTG 076 protocol decreased HIV vertical transmission from 25% to 8% Since 1995 it was initially offered to the HIV-1 infected pregnant women in Argentina However, different factors make a full compliance to the regimen a difficult matter **Objectives** to evaluate HIV-1 vertical transmission when incomplete ZDV treatment was prescribed **Methods** records of 95 children born to HIV-1 infected mothers were analyzed In order to assess vertical transmission 24 mothers and their corresponding children with complete treatment (CT) 17 mothers with incomplete treatment (IT) and 54 with no treatment (NT) were compared Treatment was considered incomplete when women were enrolled after week 34 of gestation and/or intravenous ZDV was not administered, and/or the baby did not receive the ZDV **Results** Transmission was 12.5% for CT, 41% for IT and 31.5% for NT Significant differences ($p = 0.03$) in decreasing perinatal transmission were observed between the IT versus CT groups with no significant differences between IT and NT groups Different types of incomplete treatment were not



analyzed separately due to the small number of patients in this group **Conclusions** Partial adherence to the ACTG 076 protocol did not result in decreasing HIV vertical transmission

[44124] Perinatal hiv transmission Ethical dilemma of a scientifically sound multi-micronutrients intervention study in Zimbabwe

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Issue Nutrition intervention studies in HIV/AIDS involving pregnant women have moral obligations that are complex but have to be addressed **Project** At the moment, in Zimbabwe the ACTG 076 regimen is not part of the standard care for pregnant women Nutrition intervention has always been felt to be useful in infection A double blind placebo controlled nutrition study was therefore carried out among pregnant women recruited at an ante-natal clinic Blood samples were collected and food frequency questionnaires administered after an informed consent form had been signed Each woman was counselled and given the choice concerning disclosure of her HIV status result Before leaving the clinic the women collected either 110 placebo or multi-micronutrients tablets They were visited at least once a month by the research team until birth of the child Each woman regardless of her HIV status was encouraged to breast feed and to use condoms **Results** HIV prevalence in the 1800 women recruited was 33% and average age was 24yrs Some of the women appeared to have no access to adequate nutrition Some mother and child pair have since died **Lessons Learnt** Young women were willing to know their HIV status However being ready to know was something else This made it difficult to advise on breastfeeding and use of condoms To put the women and their babies on the ACTG 076 regimen during the duration the study only would have been unethical

[33282] Same day HIV voluntary counselling and testing (VCT) improves overall acceptability among prenatal women in Zambia

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Objectives i) To evaluate the overall acceptability of HIV VCT, accompanied by pre- and post-test counselling and same day testing by using rapid HIV assays among women attending regular Prenatal Clinics (PNCs) ii) To determine factors associated with requesting or declining for VCT **Methods** Three clinics were chosen for the study The Nurse-Midwives and the Laboratory Technicians working at the PNCs were re-trained for the study purpose First 20-25 women arriving at the PNC participated in a group discussion led by a Nurse Counsellor Following the discussion the interested women were provided individual pre-test counselling After an informed consent the blood drawn for routine RPR testing was also tested for HIV using Capillus HIV-1/HIV 2 as a screening test All positive results were then confirmed using Dipstick HIV-1/HIV 2 The HIV result specific post-test counselling was offered after the prenatal check-up **Results** The results by each Clinic were as follows

NAME OF THE CLINIC	U T H	CHILENJE	CHIPATA	TOTAL
Attended Group Talk	320	287	271	878
Requested VCT	229	238	245	712
Overall Acceptability %	72	83	90	81
HIV Prevalence (%)	68 (30%)	60 (25%)	64 (27%)	192 (27%)

Conclusions Overall acceptability for HIV VCT was high (81%) among women attending Prenatal Clinics in Lusaka However, acceptance was low in women with higher educational and socio-economic status The use of two rapid diagnostic tests was userfriendly, convenient and cost effective



[60790] Changes in CD8 lymphocyte subset counts at different ages among HIV-1 perinatally and postnatally infected Kenyan children

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Background and Objective To describe the changes in CD8 subset counts over time in relation to the timing of HIV-1 transmission in African children not receiving antiRetroviral therapy **Methods** CD8 subsets were measured and compared in HIV-1 perinatally, postnatally and uninfected cohorts of children enrolled to HIV-1 seropositive mothers and infants of seronegative mothers followed in The Nairobi Mother to Child HIV-1 Transmission/Pediatric AIDS Study **Results** CD8 subsets were determined on ³1 occasion for 77 perinatally 38 postnatally, 398 uninfected and 366 control children and the mean values are presented in the graph Mean CD8 counts were significantly ($p < 0001$) higher among perinatally infected children compared with controls and uninfected children at all ages and higher than postnatally infected children until 4 years of age Postnatally infected children had higher counts compared with controls after 2 years of age ($p < 01$) **Conclusion** Perinatally infected children respond immediately to HIV-1 infection with a sustained CD8 response In contrast, the response of postnatally infected children is both less immediate and less dramatic, likely reflecting differences in immune system maturity at the time of initial HIV-1 infection

[12404] Avoidance of breast feeding by HIV infected women Strategy of a multiprofessional team in the developing world

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Issue The WHO has recommended breast feeding for HIV infected women even though it is a known risk for transmission of HIV from mother to infant Alternatives must be found which do not compromise the infants health **Project** As part of an "Integrated Program" for the care of HIV infected pregnant women and their children a multi-disciplinary team of health careworkers in the prenatal clinic of a public hospital in Rio de Janeiro Brazil have developed such a program At medical consultation and during "waiting room discussion groups" conducted by a nurse and psychologist, women are counseled on the risk of breastfeeding and practical alternatives they are additionally instructed on the safe preparation of formula Educational pamphlets are provided during these visits Women are encouraged to express their feelings and to raise questions regarding breastfeeding to the medical caretakers Formula donated by NGOs churches and by private donation is made available to these women free of charge for the first two years of the infants life **Results** Over the last 28 months, 68 women have participated in this program and 54 delivered their infants These infants have not been breastfeed, and are being followed in the pediatric outpatient clinic While initially frustrated at being unable to breastfeed women have accepted this with the understanding of its importance to their childs health No children in this time period have been admitted to the pediatric ward or required outpatient treatment for gastroenteritis Children are in good nutritional health with normal height and weight parameters **Lessons Learned** Even in a third world country limited resources, it has been possible to avoid breastfeeding of HIV exposed children, where mothers were adequately counseled and formula provided by their health care institution

[23400] Determination of viral load in breastmilk and plasma in HIV infected mothers

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Introduction In developing countries transmission of HIV by breastmilk could represent 30% of mother-child contamination Determinants of this mode of transmission remain unclear We describe here viral load in breastmilk and plasma among 42 mothers **Method** 8 days after pregnancy, blood and breastmilk specimens were collected and viral load has been determined by the branched-DNA (b-DNA) method (Quantiplex Chiron Diagnostic) since we have assessed this quantitative method for "in-breastmilk" viral load measurement **Results** Viral load average were 3 918 Eq/ml versus 28,196 Eq/ml in the breastmilk and the plasma respectively The mean ratio of matched viral loads "in-breastmilk" versus plasma was of 1 17 (range 50 1 to 1 180) No correlation between "in-breastmilk" versus plasmatic viral loads was observed Furthermore, no significant difference was observed between "in-breastmilk" viral loads in non-transmitter (NT) versus transmitter (T) mothers, even for 3



cases of late "mother-child" transmission suspicion. In contrast, a significant difference was observed at level of plasmatic viral loads (10 500 Eq/ml versus 85 000 Eq/ml) between NT and T mothers. **Conclusion** These data indicating low viral load in breastmilk could suggest a low rate of viral production by breastmilk cells. Quantification of intra-cellular viral load in breast cells is yet in progress and should be presented.

[24197] Determinants of contraceptive use and fertility decision-making among HIV-1 infected women

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Introduction Knowledge of HIV infection status has been postulated to result in a change in fertility behavior. This study examined contraceptive use and factors associated with subsequent pregnancies in women identified to be HIV-1 seropositive during pregnancy in an ongoing breast feeding trial. **Methods** Baseline sociodemographic and medical characteristics were obtained using a standardized questionnaire. After delivery, mother-infant-pairs were followed monthly for 2 years. Women were counseled to initiate contraceptive use from 6 weeks postpartum and data on contraceptive use and subsequent pregnancies recorded. In-depth interviews were conducted with women who had a subsequent pregnancy to explore possible factors associated with the occurrence of the pregnancy. **Results** As of September 1997, 353 women had delivered and been followed for more than 6 weeks. The median time to use of a reliable contraceptive (hormonal methods, IUD, and tubal ligation) was 17 weeks (95% CI 16-18). At the two year visit, current reliable contraceptive use was reported by 133 (86%) women. Age, marital status, parity and educational level did not correlate with contraceptive use. Women with HIV-1-discordant spouses were more likely to use a reliable contraceptive (P = 0.05). The prevalence of subsequent pregnancies was 19%. Death in the index child was significantly associated with second pregnancy (OR 2.3, 95% CI 1.2-4.3). Cessation of contraceptive use due to side effects and influence of the spouse were identified as contributing to the occurrence of subsequent pregnancy. **Conclusions** Although contraceptive use among this group of well-counseled women was high, a significant proportion still had subsequent pregnancies. There is need to evaluate whether targeting partners for fertility counseling will have a better impact.

[31106] Evaluation of the HIV-inhibitory activity of seven human mucosal fluids

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Objectives To determine levels of HIV-inhibitory activity of seven human mucosal fluids *in vitro*, whole parotid and submandibular/sublingual (sm/sl) saliva, breast milk, colostrum, seminal plasma and cervicovaginal secretions collected from HIV-seronegative subjects. **Methods** Samples were obtained from ten HIV-seronegative volunteers for each fluid type, and lectin from the plant *Galanthus nivalis* was used as a positive control. Anti-HIV activity was evaluated using a microtitre-based assay. The body fluids were incubated for 1 hr at 37°C with a cell free, laboratory adapted strain of HIV-1 which was attached to the microtitre plate with poly-l-lysine. The body secretions were subsequently washed off with PBS and C8166 cells were added to the fluid-treated virus. Cultures were incubated for 3 days and syncytia formation was assessed daily to monitor HIV replication. Final assessment of HIV infectivity was performed on day 3 by quantitation of p24Ag in the culture supernatant. **Results** Of the seven fluids tested, whole saliva, breast milk and colostrum samples demonstrated the highest levels of anti-HIV activity (60-100% inhibition). Seminal plasma samples showed moderate levels of activity (30-60%) and the cervicovaginal secretions, parotid and sm/sl salivas all demonstrated consistently low levels of activity (0-30% inhibition). **Conclusions** All seven body fluids assessed *in vitro* possessed HIV-inhibitory activity, with the highest levels being present in whole saliva, breast milk and colostrum. Identification and characterisation of these factors is important as they have potential for use in virucidal gel formulations that could have applications in minimising HIV-1 transmission.

[471/44123] Additional unethical aspects of vertical transmission studies in developing countries

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Issues After the publication of the ACTG 076 study, which demonstrated that zidovudine caused a 2/3 reduction in HIV transmission from pregnant women to infants, attention turned to identifying an affordable regimen for developing countries. In April 1997, we identified a total of 15 studies involving over 17,000 developing country women that sought to identify such regimens (e.g., regimens using zidovudine for 4-6 weeks antepartum) by



providing placebos or interventions not yet proved effective to at least some women. We initiated a campaign both in medical journals and in the popular press to redesign the studies so that all women had access to at least some antiRetroviral drugs. So far, one study in Ethiopia has been redesigned to eliminate its placebo group. **Project** To determine whether the studies violate additional ethical guidelines. **Results** There are three additional unethical aspects to these studies. 1. The informed consent form in at least one study fails to state that a pre-planned subanalysis of data from ACTG 076 showed a 2/3 reduction in HIV transmission among women receiving an average of only 7 weeks of zidovudine. 2. There is no provision for the women to continue on antiRetrovirals after the study is completed, even though noncompliance with antiRetrovirals (in this case, forced noncompliance due to zidovudine being unaffordable in most developing countries) is a known cause of HIV resistance. 3. There is also an observational study of 125 HIV-positive pregnant women conducted by the Thai and US Armies. Thai researchers and Johns Hopkins University, which has continued to provide the subjects with no zidovudine, even though zidovudine is so available that Thai researchers terminated their own placebo-controlled trial in January 1997. **Conclusion** The studies are unethical in a variety of ways beyond the provision of placebos. This highlights the need for the studies to be redesigned and for a renewed commitment to the conduct of ethical studies in developing countries.

[43114] Locally sustainable administration of HIV counseling and testing to young couples in rural regions of Western Kenya

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Objectives/(Issues) The Siaya AIDS Prevention study is designed to evaluate methods of preventing HIV infection utilizing pre-existing local health care systems in Western Kenya. An intervention based on counseling and testing of young couples was chosen based on previous studies. Local community health workers were trained in counseling and saliva sample collection. Demand for HIV counseling and testing was measured as the outcome of interest. **Project/Methods/Results** Households for interview were selected through multi-stage cluster sampling. The Participants were interviewed by specially trained local community health workers. HIV knowledge was measured by a 16 item index. Rapid testing utilizing a saliva sample was chosen for this study for 3 reasons: (1) collection of saliva is non-invasive, (2) samples remain stable for 21 days at ambient temperatures, hence facilitating transport and storage before analysis and (3) rapid testing technology is appropriate for analysis at a rural Kenyan laboratory. Data reported is from a pilot sample (n = 66). In the next 4 months, data on 500 couples will be available. The sample consisted of young couples with a mean age of 22 years. Seventy five percent of the sample had completed primary (8th grade) education or less. Household income was typically less than \$10/month, with this category accounting for 82% of those responding. All individuals had heard of AIDS, but knowledge regarding HIV/AIDS signs, symptoms and modes of transmission was low to moderate. On a knowledge scale of 1-16, the mean score was 11. If counseling and testing is offered free of charge, 95% of the sample said they would accept this service. When the counseling and testing is offered at a cost of \$4.00 (enough to cover the cost of the collector, the rapid test and analysis), between 31-40% of the sample responded they would take the test. Results suggest that HIV counseling and testing administered by local community health workers in rural Kenya is economically and culturally appropriate. These results carry important implications for HIV/AIDS prevention in rural Kenya. As AIDS interventions focused on vertical transmission and treatment of sexually transmitted infections are demonstrated effective in rural Africa, the need for practical HIV testing systems gains urgency.

[43571] When and where HIV-screening in pregnant women is a reasonable mode of action in prevention of HIV vertical transmission

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Background Since Protocol ACTG 076 and other preventive measures are effective in reduction of HIV vertical transmission, there is a need for effective method of identification of HIV-positive pregnant women in asymptomatic population. The question is, if HIV-mass-screening in pregnant women is an acceptable method of identification. **Methods** The simulation of HIV screening in population of 100,000 pregnant women was done with use of variety of percentage of HIV infection prevalence (range from 0.1% to 24%) and variety of percentage of specificity and sensitivity of the screening test (range from 99% to 99.7%). **Results** The study revealed that any screening test, regardless of its accuracy, performs poorly in low (0.1%-2.0%) prevalence population. In low-



prevalence population even an excellent test (sensitivity - 99.7% and specificity - 99.7%) has a relatively high false positive rate and low positive predictive value. Positive predictive value of the best screening tests in population of HIV-prevalence ranged from 2% to 4% is only in the range of 87.1%-93.3%. **Conclusion** As long as sensitivity and specificity of used HIV tests are below 100%, the HIV screening in asymptomatic pregnant women is not advisable and not acceptable in low-prevalence populations. With use of most sensitive and most specific HIV-tests, the HIV screening is a reasonable method of identification of HIV-infected pregnant women in high-prevalence (10% and more) populations.

[60815] HIV testing in pregnancy What happens in counselling

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Background Little is known about how HIV discussion is currently handled in the context of general maternity care. This study was conducted to examine the impact of HIV testing for pregnant women, the content of pre-HIV test counselling and the obstetric staff perspective of HIV discussion. **Method** The study was carried out in four phases. Consecutive attenders in four London antenatal clinics with different testing policies completed a questionnaire prior to an antenatal consultation (N = 697). A selection of the consultations were observed (N = 154) and a questionnaire was subsequently completed by a sub sample of women (N = 226) following the consultation. Finally a sample of obstetric staff (N = 345) completed a questionnaire. **Results** A average of 1.7 minutes was spent on discussing HIV infection and testing during the antenatal consultations which lasted a mean of 33.1 minutes. Although immediately before the consultation 31.4% of the women intended to have an HIV test the rate of intention decreased to 17.6% after the consultation. The mention of HIV risk factors during the consultation was infrequent, the most common being sexual behaviour, which was mentioned in 11.7% of the consultations. Where potential interventions to reduce vertical transmission were raised (20% of consultations) Retroviral treatment was mentioned for fewer than one in ten women and mode of infant feeding with one in five women. Discussion on possible mental health implications and future HIV risk reduction was infrequent. **Conclusion** The available time to discuss HIV issues within the context of antenatal clinics is limited. Although many women are already informed about HIV a drive to promote HIV testing is a disincentive for many to test. Strategies to promote HIV testing may be short-sighted and perhaps strategies aimed at women to provide them with more realistic information, update and a two way dialogue may be the better way forward.