

HIV, infant feeding, and maternal and child health

In 1997 the UN Policy Statement highlighted that, as a general principle and in all populations, irrespective of HIV infection rates, breastfeeding should be protected, promoted and supported. It also clearly emphasised that HIV-positive mothers have to be empowered to make a fully informed choice about infant feeding and have to be supported in implementing their decisions.

In October 2000, UNICEF, WHO and UNAIDS reviewed evidence that accumulated in the course of three years. There were research findings that required specific attention. The results published by Coutoudis et al. (The Lancet, 1999) suggested benefits of exclusive breastfeeding over mixed feeding, with exclusive breastfeeding carrying a similar risk of transmission compared to exclusive formula feeding (presented in BB 29). A follow up analysis of the data, published by Coutoudis et al. In 2001 (BB 31-32), also concluded that infants exclusively breastfed for 3 months or more had no excess risk of HIV infection over 6 months than those never breastfed. After analysing the data the UN clearly reiterated the 1997 Policy on HIV and Infant Feeding and specified in the recommendations that:

- When replacement feeding is acceptable, feasible, affordable, sustainable and safe, then avoidance of all breastfeeding by the HIV positive mother is recommended.
- In the absence of any of these conditions, exclusive breastfeeding is recommended during the first months of life.

Already at that time, the experts placed special emphasis on maternal health and recommended the inclusion of family planning services and nutritional support for HIV positive women.

This recommendation was again reviewed by WHO in 2001 in the light of the findings of Nduati et al which suggested that HIV positive mothers had higher mortality rates if they breastfed their infants. These results conflicted with findings of a South African study that found no increase in death among HIV nursing mothers. An editorial in the Lancet points out that these conflicting results must lead to further research, not to recommendations.¹ On 7 June 2001, WHO issued a statement that warned against rushing to quick conclusions leading to a shift in the policy.² WHO stated that the limitations of the Nduati data call for a cautious interpretation and reiterated again the importance of proper support, clinical as well as nutritional, to mothers who are HIV infected.

HIV and the infant feeding component of programmes on prevention of mother-to-child transmission of HIV has been most challenging. This is because research has not yet provided definite responses to issues such as the effect of exclusive breastfeeding and the impact of anti-retroviral therapy during lactation on the transmission rates. Much research that has looked at breastfeeding and HIV did not take into account the WHO 1991 definitions for individual infant feeding patterns (exclusive breastfeeding, predominant breastfeeding, partial breastfeeding etc). It was thus impossible to separate the data in this respect and provide useful guidance for programme managers. In 2001, WHO in collaboration with UNICEF and experts issued an assessment tool for research to assist scientists in designing research protocols.

The 2000 recommendation about using replacement feeding only when it is acceptable, feasible, affordable, sustainable and safe is certainly a step in the right direction. However, all these conditions are extremely situation specific. Therefore it is crucial that a proper detailed situation analysis is performed so that the counsellors for HIV positive mothers have a good understanding of the range of options and conditions and can effectively assist mothers in making an informed choice. The experience for counselling of HIV positive mothers in various parts of the world suggests that many counsellors are not fully equipped with knowledge and skills and are often acting on the basis of prejudice, personal experience and under time pressure.

¹ Newell ML. Does breastfeeding really affect mortality among HIV-1 infected women? Lancet 2001;357:1634

² WHO. New data on the prevention of mother-to-child transmission of HIV and their policy and implications. WHO, Geneva, 7 June 2001

Highlights

1. Nduati R, John G, Mbori-Ngacha D, Richardson B, Overbaugh J, Mwatha A, Ndinya-Achola J, Bwayo J, Onyango FE, Hughes J, Kreiss J. Effect of breastfeeding and formula feeding on transmission of HIV-1: a randomized clinical trial. *JAMA* 2000;283:1167-74

2. Nduati R, Richardson BA, John G, Mbori-Ngacha D, Mwatha A, Ndinya-Achola J, Bwayo J, Onyango FE, Kreiss J. Effect of breastfeeding on mortality among HIV-1 infected women: a randomised trial. *Lancet* 2001;357:1651-5

3. Mbori-Ngacha D, Nduati R, John G, Reilly M, Richardson B, Mwatha A, Ndinya-Achola J, Bwayo J, Kreiss J. Morbidity and mortality in breastfed and formula-fed infants of HIV-1-infected women: a randomized clinical trial. *JAMA* 2001;286:2413-20

OBJECTIVES. This study was conducted to determine the frequency of breast milk transmission of HIV-1, and to compare morbidity, nutritional status, mortality and HIV-1-free survival in breastfed and formula-fed infants. The same data were also used to examine the effect of breastfeeding on maternal death rates during two years after delivery.

METHODS. Four hundred and twenty five HIV-1-seropositive pregnant women never treated with antiretroviral drugs were enrolled from November 1992 to July 1998 in antenatal clinics in Nairobi, Kenya. Of these, 212 were randomized to breastfeeding (BF) and 213 to formula feeding (FF). Four hundred and one mother-infant pairs were followed-up for a median period of 24 months and were included in the analysis for the first two papers, while 371 infants were included in the analysis for the third paper.

RESULTS (1). Compliance with the assigned feeding mode was 96% in the BF arm and 70% in the FF arm ($p < .001$). Median duration of breastfeeding was 17 months. The cumulative probability of HIV-1 infection at 24 months was 36.7% in the BF arm and 20.5% in the FF arm ($p = .001$). The estimated rate of breast milk transmission was 16.2%, and 44% of HIV-1 infection in the BF arm was attributable to breast milk. Most breast milk transmission occurred early, with 75% of the risk difference between the two arms occurring by 6 months, although transmission continued throughout the duration of exposure. The 2-year mortality rates in both arms were similar (BF 24.4% vs FF 20.0%; $p = .30$), even after adjusting for HIV status. The rate of HIV-1-free survival at 2 years was significantly lower in the BF arm than in the FF arm (58.0% vs 70.0%, respectively; $p = .02$). The incidence of diarrhoea during the two years of follow-up was similar (155 vs 149 episodes per 100 person-years, respectively). The incidence of pneumonia was identical in the two groups (62 per 100 person-years), and there were no significant differences in incidence of other recorded illnesses. Infants in the BF arm tended to have better nutritional status, significantly so during the first six months of life. Mortality among mothers was higher in the BF than in the FF arm (18 vs 6 deaths, $p = .009$). The cumulative probability of maternal death at 24 months after delivery was 10.5% in the BF and 3.8% in the FF arm ($p = .02$). BF mothers had a 3.2 times higher risk of death compared to FF mothers; the estimated proportion of deaths due to breastfeeding among BF mothers was 69%. There was an association between maternal death and subsequent infant death, even after infant HIV-1 infection status was controlled for.

DISCUSSION. Infants assigned to FF or BF had similar mortality rates and incidence of diarrhoea and pneumonia during the first two years of life. However, HIV-free survival at two years was significantly higher in the FF arm. According to the authors, with appropriate education and access to clean water, formula feeding can be a safe alternative to breastfeeding for infants of HIV-infected mothers in a resource-poor setting.

4. Coutoudis A, Coovadia H, Pillay K, Kuhn L. Are HIV-infected women who breastfeed at increased risk of mortality? *AIDS* 2001;15:653-655

For the objectives and methods of this study, see summary in BB 29 and BB 31-32. A total of 566 HIV positive mothers were followed after delivery for 10.4 months among those who ever breastfed ($n = 410$) and for 10.6 months in those who never breastfed ($n = 156$). Two out of 410 (0.49%) women who ever breastfed died compared with three out of 156 (1.92%) who never breastfed, a non statistically significant difference. Among the breastfeeding group, the proportion with any morbidity was similar on those who breastfed for more than 3 months (14%) compared with those who breastfed for less than 3 months (11%), even after controlling for CD4 cell counts and hemoglobin levels. The authors were unable to confirm any deleterious effects of breastfeeding on the health of seropositive women.

Breastfeeding, why...

Tryggvadottir L, Tulinius H, Eyfjord JE, Sigurvinsson T. Breastfeeding and reduced risk of breast cancer in an Icelandic cohort study. *Am J Epidemiol* 2001;154:37-42

This case-control study used data from an Icelandic cohort of 80,219 women visiting a cancer clinic that offered population-based cervical and breast cancer screening in the years 1979-1995. The 993 parous cases of breast

cancer were aged 26-90 years at diagnosis were individually matched with 9,729 parous healthy controls on birth year, vital status at case diagnosis, and age when giving information on several potential risk factors for breast cancer. Confining the analysis to the 84 cases who were less than 40 years at diagnosis, a protective association was evident between total duration of breastfeeding and breast cancer, with a reduction of about

23% in risk per 6 months' increase in duration of breastfeeding, whereas for the remaining women a much weaker trend was observed. Ever breastfeeding was associated with about 67% reduction in risk for women diagnosed at all ages.

Zheng T, Holford TR, Mayne ST, Owens PH, Zhang Y, Zhang B, Boyle P, Zahm SH. Lactation and breast cancer risk: a case-control study in Connecticut. *Br J Cancer* 2001;84:1472-6

In a case-control study of breast cancer conducted in Connecticut, USA, between 1994 and 1998, 608 incident breast cancer cases and 609 age-matched controls aged 30-80 years were included. Parous women who reported ever lactation had a borderline significantly reduced risk of about 17%. Almost 50% reduction of risk was observed in those having breastfed more than 3 children compared to those who never lactated. Women having breastfed their first child for more than 13 months had also a risk reduced by about 50% compared to those who never breastfed. Further stratification by menopausal status showed a risk reduction related to lactation for both pre- and postmenopausal women, though the relationship was less consistent for the latter.

Wang B, Miller JB, Sun Y, Ahmad Z, McVeagh P, Petocz P. A longitudinal study of salivary sialic acid in preterm infants: Comparison of human milk-fed versus formula-fed infants. *J Pediatr* 2001;138:914-6

The saliva of preterm infants fed human milk contains twice the level of sialic acid as that in infants fed commercial formulas. The higher sialic acid level suggests greater viscosity and enhanced protection against infection of the mucosal surfaces in breastfed infants.

Breastfeeding, how...

Domellof M, Cohen RJ, Dewey KG, Hernell O, Rivera LL, Lonnerdal B. Iron supplementation of breastfed Honduran and Swedish infants from 4 to 9 months of age. *J Pediatr* 2001;138:679-87

In a randomized, placebo-controlled trial, term Swedish (n = 101) and Honduran (n = 131) infants were assigned to 3 groups at 4 months of age: 1) iron supplements, 1 mg/kg/d, from 4 to 9 months, 2) placebo, 4 to 6 months and iron, 6 to 9 months, and 3) placebo, 4 to 9 months. All infants were breastfed exclusively to 6 months and partially to 9 months. From 4 to 6 months, the effect of iron (group 1 vs 2 + 3) was significant and similar in both populations for haemoglobin, ferritin, and zinc protoporphyrin. From 6 to 9 months, the effect (group 2 vs 3) was significant and similar at both sites for all iron status variables except haemoglobin, for which there was a significant effect only in Honduras, where the prevalence of iron deficiency anaemia at 9 months was 29% in the placebo group and 9% in the supplemented groups. In Sweden, iron supplements caused no reduction in the already low prevalence of iron deficiency anaemia at 9 months (less than 3%). Iron supplementation from 4 to 9 months or 6 to 9 months significantly reduced iron deficiency anaemia in Honduran breastfed infants. The

unexpected haemoglobin response at 4 to 6 months in both populations suggests that regulation of haemoglobin synthesis is immature at this age.

Male C, Persson LA, Freeman V, Guerra A, van't Hof MA, Haschke F; Euro-Growth Iron Study Group. Prevalence of iron deficiency in 12-mo-old infants from 11 European areas and influence of dietary factors on iron status (Euro-Growth study). *Acta Paediatr* 2001;90:492-8

A prospective longitudinal cohort study was performed to assess the prevalence of iron deficiency in European infants at 12 months of age and to study the influence of socio-economic status, dietary factors, growth and morbidity on iron status. The cohort consisted of 488 normal term infants from primary healthcare centres in 11 European areas. The prevalence of anaemia at 12 months was 9.4%, of iron deficiency 7.2%, and of iron deficiency anaemia 2.3%. More than 40% of anaemia was associated with normal iron status and with an increased frequency of recent infections. Iron deficiency anaemia was significantly more frequent with low (5.1%) than high socio-economic status (0%). Dietary factors accounted for most of this variation in multiple regression analysis. Early introduction of cow's milk was the strongest negative determinant of iron status. Feeding of iron-fortified formula was the main factor positively influencing iron status. Other dietary factors, including breastfeeding, did not play a significant role as determinants of iron status at age 12 months.

Griffin JJ, Abrams SA. Iron and breastfeeding. *Pediatr Clin North Am* 2001;48:401-13

Given the importance of iron nutrition during the first year of life, there are surprisingly few true, randomized, controlled studies addressing this issue. However, it seems that iron deficiency is unlikely in full-term, breastfed infants during the first 6 months of life because these infants' body iron stores are sufficient to meet requirements. After this time, many infants exhaust their iron stores and become dependent on a secondary dietary iron supply. Although iron deficiency is a significant nutritional problem worldwide, most of the adverse effects of iron deficiency in this age group are hypothetical and rely on extrapolation from animal studies or studies at different ages. This, however, is also true of most of the adverse effects of iron excess in this age group. Given this uncertainty, it seems prudent to use the lowest dose of iron that prevents iron-deficiency anaemia. Currently, the best evidence is that this is achieved by prolonged breastfeeding, avoidance of unfortified formulas and cow's milk, and the introduction of iron-fortified and vitamin C-fortified weaning foods at approximately 6 months of age. There are many areas of uncertainty regarding iron supplementation of infants, including that: 1) The optimal age for introducing iron-fortified supplemental foods is poorly defined. 2) The natural history of iron deficiency and iron-deficiency anaemia during the first year of life is unclear, as are its possible long-term effects, especially on developmental outcome. 3) The biologic variability among infants and their mothers that allows many infants who do not receive iron-fortified foods to prevent iron deficiency while receiving only human milk throughout

the first year of life is intriguing and warrants additional study. 4) The iron requirements of small-for-gestational-age, term infants are unknown; their iron requirements are likely to be higher than those of average term infants, but whether iron supplements are required is unclear. 5) The optimum amount of dietary iron in the weaning diet needs to be further defined; similarly, the optimal source and amount of iron in infant formulas given to infants who receive a mixture of human milk and formula is unclear.

Auestad N, Halter R, Hall RT, Blatter M, Bogle ML, Burks W, Erickson JR, Fitzgerald KM, Dobson V, Innis SM, Singer LT, Montalto MB, Jacobs JR, Qiu W, Bornstein MH. Growth and development in term infants fed long-chain polyunsaturated fatty acids: a double-masked, randomized, parallel, prospective, multivariate study. *Pediatrics* 2001;108:372-81

To evaluate the effect of the intake of long-chain polyunsaturated fatty acids on infant growth, psychological, mental and cognitive development, intelligence, language, temperament and visual acuity, a double-masked, randomized trial was conducted with term infants fed formula (formula group; N = 239) with or without arachidonic acid (AA) and docosahexaenoic acid (DHA) for 1 year. Reference groups of breastfed infants (N = 165) weaned to formulas with or without AA+DHA were also studied. Infants in the formula group were randomized at 9 or less days of age to: 1) a control formula with no AA or DHA (N = 77); 2) a formula containing AA+DHA from egg (N = 80) at levels similar to the average in breast milk; or 3) a formula containing AA+DHA from fish or fungal oil (N = 82) at levels similar to the average in breast milk. All formulas contained 50% of energy from fat, including 10% from linoleic acid and 1% from alpha-linolenic acid (essential fatty acids). No developmental test results distinguished among these groups in the follow-up. These findings do not support adding AA+DHA to formulas containing 10% energy as linoleic acid and 1% as alpha-linolenic acid to enhance growth, visual acuity, general development, language, or temperament in healthy, term infants during the first 14 months after birth.

Pinelli J, Atkinson SA, Saigal S. Randomized trial of breastfeeding support in very low-birth-weight infants. *Arch Pediatr Adolesc Med* 2001;155:548-53

Does breastfeeding counselling improve the duration of breastfeeding in very low-birth-weight infants? A randomized trial with longitudinal follow-up at term, and ages 1, 3, 6, and 12 months, was conducted in a tertiary-level neonatal intensive care unit (NICU) in Ontario, Canada. The "counselling" consisted of viewing a video

on breastfeeding for preterm infants; individual counselling by the research lactation consultant; weekly personal contact in the hospital; and frequent post-discharge contact through the infants' first year or until breastfeeding was discontinued. The "standard" group had standard breastfeeding support from regular staff members confined to the period of hospitalisation in the NICU. The mean duration of breastfeeding was 26.1 weeks in the "counselling" group and 24.0 weeks in the "standard" group (not statistically significant). These results may be explained by the high motivation to breastfeed in both groups, a relatively advantaged population, and the availability of community breastfeeding resources, which may have diminished any significant differences that could have resulted from a breastfeeding intervention.

Valdes V, Labbok MH, Pugin E, Perez A. The efficacy of the lactational amenorrhea method (LAM) among working women. *Contraception* 2000;62:217-9

The authors assessed the efficacy of the lactational amenorrhea method (LAM) for family planning among mothers who are separated from their infants by work. 170 urban middle class women who planned to return to work before 120 days postpartum, were interviewed monthly for 6 months postpartum and contacted at 12 months. They received clinical support for expressing their milk and exclusively breastmilk feeding the infants, and for the use of LAM. The cumulative pregnancy rate by 6 months was 5.2%. LAM for working women might be associated with a higher pregnancy risk than LAM among non-working women. Women using LAM should be informed that separation from the infant might increase their risk of pregnancy.

Giuliani M, Grossi GB, Pileri M, Lajolo C, Casparini G. Could local anesthesia while breast-feeding be harmful to infants? *J Pediatr Gastroenterol Nutr* 2001;32:142-4

A nursing mother may need dental treatment. The purpose of this study was to determine the amount of lidocaine and its metabolite monoethyl-glycinexylidide (MEGX) in breast milk after local anesthesia during dental procedures. Seven nursing mothers (aged 23-39) received 3.6 to 7.2 mL 2% lidocaine without adrenaline. The concentration of lidocaine and MEGX in maternal plasma and maternal milk 2 to 6 hours after injection corresponded to daily infant dosages of 73.41 +/- 38.94 microg/L/day and 66.1 +/- 28.5 microg/L/day, respectively, considering an intake of 90 mL breast milk every 3 hours. This study suggests that a nursing mother undergoing dental treatment with local anesthesia using lidocaine without adrenaline can safely continue to breastfeed.
