INTERNATIONAL SYMPOSIUM ON
Understanding the Double Burden of Malnutrition for Effective Interventions

How to Use Stable Isotope Techniques for Assessment of Breastfeeding Patterns

Christine Slater
Retired IAEA Nutrition Specialist
Objectively measured breastfeeding

- Deuterium oxide dose-to-mother technique (DTM)
  - Accurately assesses the amount of human milk consumed by breastfed infants
  - Provides an estimate of the water intake from sources other than human milk
  - Provides an objective measure of the exclusivity of breastfeeding
  - Does not disturb the baby’s normal feeding pattern
Deuterium oxide dose-to-mother technique

- The mother consumes an accurately weighed dose of deuterium oxide ($D_2O$)
- The deuterium mixes with the mother’s body water
- The baby consumes deuterium during breastfeeding
- Saliva is sampled from the mother and from the baby over 2 weeks
Two-compartment steady-state model of water flux in a mother-baby pair

Mother’s TBW: $V_m$

- $F_{mo}$ to the baby from the mother
- $F_{om}$ to the mother from the baby
- $F_{bm}$ to the outside from the baby
- $F_{ob}$ to the baby from the outside

Infant’s TBW: $V_b$

- $F_{bo}$ to the mother from the outside
- $F_{ob}$ to the baby from the outside


The subscripts m, b, p refer to mother, baby, outside. The combined subscripts indicate the direction of water flow e.g. bm is to the baby from the mother, and bo is to the baby from the outside.
If the baby is breastfed, deuterium enrichment in the baby’s body water gradually increases and then decreases:

- The higher the enrichment in the baby’s body water, the more human milk it has consumed.
- The more milk the mother produces, the faster the deuterium disappears from her body water.
Assessing Intake of Human Milk in Breastfed Infants

Nutritional and Health-related Environmental Studies
Division of Human Health

http://humanhealth.iaea.org
Applications

- Assessment of the amount of milk consumed by breastfed infants
- Assessment of nutrient intake (e.g. vitamin A, Zn)
- Assessment of intake of potentially toxic chemicals (As, Hg, Pb, pesticides)
- Validation of EBF data collected from maternal recall
How much milk do breastfed babies consume?

Data from 12 countries on 5 continents. Mean intake 780 g/d. Increased over first 3-4 m, remained above 800 g/d until 6-7 m. Dedicated to the memory of Andy Coward: pioneer of the DTM technique

How Much Human Milk Do Infants Consume? Data from 12 Countries Using a Standardized Stable Isotope Methodology

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J Nutr (2010) 140, 2227-2232
IAEA database

- **Latin America**: Argentina, Brazil, Chile, Cuba, Dominican Republic, Ecuador, Guatemala, Uruguay (n = 301)
- **Asia**: India, Sri Lanka, Thailand (n = 258)
- **Africa**: Benin, Central African Republic, Ghana, Kenya, Morocco, South Africa, Tanzania (n = 691)
- Some projects collected longitudinal data at 6 weeks, and 3, 6, 9, 12 months
Human milk intake over time

Mean human milk intake (95% CI)

<table>
<thead>
<tr>
<th>Age</th>
<th>Breastmilk intake (g/d)</th>
<th>Breastmilk intake (g/d/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5 months</td>
<td>(N = 213)</td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>(N = 827)</td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>(N = 465)</td>
<td></td>
</tr>
<tr>
<td>9 months</td>
<td>(N = 133)</td>
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</tbody>
</table>

0 100 200 300 400 500 600 700 800

Breastmilk intake (g/d)
Nutrient intake: Zinc

Zinc Transferred through Breast Milk Does Not Differ between Appropriate- and Small-for-Gestational-Age, Predominantly Breast-Fed Bangladeshi Infants¹–³

M. Munirul Islam⁴* and Kenneth H. Brown⁵

¹Centre for Nutrition and Food Security, International Centre for Diarrhoeal Disease Research, Bangladesh, Dhaka, Bangladesh; and
²Department of Nutrition, Program in International and Community Nutrition, University of California, Davis, Davis, CA

J Nutr (2014) 144, 771-776

- Breast milk zinc concentration was similar to that of wealthier countries
- There was no relation between infant birth-weight and milk zinc concentration or transfer.
VAD is still a public health concern in Mexico. Infants from urban areas receive 66% of their dietary adequate intake from BM; Infants from rural areas receive only 49%
Vitamin A Status: Senegal

- Vit A intake through breastfeeding measured using DTM; Vit A conc by HPLC
- Infants’ milk VA intake was close to estimated requirements (375 mg/d)
- No correlation was found between infants’ plasma retinol and MRDR value
- Low VA liver stores at the beginning of the complementary feeding

Breastfeeding reduces the intake of As in infants living in contaminated areas

- There was less As in human milk than the local drinking water.
Chile: former copper mining area

Maternal–Child Transfer of Essential and Toxic Elements through Breast Milk in a Mine-Waste Polluted Area

Francisca Castro, MSc¹  Florencia Harari, MD²  Miguel Llanos, PhD¹  Marie Vahter, PhD²  Ana Maria Ronco, PhD¹

Am J Perinatol (2014) 31, 993-1002

• Lower amounts of toxic elements were transferred to exclusive breastfed infants compared with those who additionally received non-maternal milk.
EBF: Which cut-off for non-milk water intake should we use?

• The IAEA guidelines use 25 g non-milk water per day, based on a theoretical threshold supported by empirical data from Haisma et al. (2003)*

• This is the value used in most of the IAEA supported projects

Validation of EBF data


- Reported EBF 45%; Measured (DTM) 11%, infants 1-4 months
- Mothers’ self-reports may be subject to social desirability and social approval biases (N=44)
Guatemala Example

- Reported EBF 61%; Measured (DTM) 36%
- Infants 3 months (N=36)
South Africa Example

- HIV –ve mothers, infants 3 months (N=74)
- Reported EBF 88%; Measured (DTM) 32%
Kenya Example

- HIV-infected mothers are more likely to EBF compared with HIV-uninfected mothers.
- At 6 months EBF rates by DTM were 43% among HIV +ve (N=68) and 24% among HIV -ve mothers (N=68).
- Reported EBF 75% and 60%
Regional differences

Latin America (N = 230)  |  Asia (N = 49)  |  Africa (N = 425)
---|---|---
Reported EBF: 61%  |  Reported EBF: 90%  |  Reported EBF: 60%
Measured EBF: 27%  |  Measured EBF: 35%  |  Measured EBF: 16%
EBF: Which cut-off for non-milk water intake should we use?

• The IAEA guidelines use 25 g non-milk water per d
• In 2007, the Cambridge group used a Monte Carlo modelling approach for data from infants age 3-4 m
• Infants whose mothers reported EBF had non-milk water intake 40 ± 81 g/d

Conclusions
• The DTM technique can be applied to validate reported feeding behaviour
• Reports of feeding practices were accurate at the group level, but it is not adequate to distinguish between feeding practices in individual infants
Validation by direct observation

- New validation study based on direct observation of infant feeding practices and pharmokinetic modelling
- Published on-line 14 November 2018
Validation study 2017-2018

• The validation study was conducted in Indonesia; supervised by Rosalind Gibson and Lisa Houghton, University of Otago, New Zealand

• 121 mother-infant pairs were recruited

• Infant feeding practices were determined using the DTM technique and by direct observation

• Feeding practices were observed in the mother’s homes by trained field assistants, recruited from the local community, from 6 am to 6 pm on 6 non-consecutive days over the two week protocol
Validation study 2017-2018

- A non-linear hierarchical model within a Bayesian frame-work was developed for the description of deuterium oxide kinetics in exclusively breastfeeding mother–infant pairs
- The cut-off based on the 90th percentile of the posterior distribution of non-milk water intake was 86.6 g/day
- This cut-off can be use to categorize any new cohort of mother-infant pairs as EBF or non-EBF
Potential reduced protocol

• Objective: To develop a field-friendly DTM protocol to categorise infants as EBF or not and assess human milk intake
• Bayesian approach comparing potential reduced protocols with the full protocol (6 post-dose samples)
• Three samples required: 1 baseline + 2 post-dose
**Reduced protocol**

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<tr>
<th>No</th>
<th>Design</th>
<th>Specificity</th>
<th>Sensitivity</th>
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<td>22</td>
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</table>

- Best sensitivity and specificity was with post-dose sample collection on Days 9 +13 compared with the full protocol (97%)
- Data collection and analysis tool expected release date: March 2019
Acknowledgements

• Everyone who contributed data to the IAEA database and the validation study for a simplified protocol: project counterparts for IAEA Technical Cooperation Regional projects (RAF6039, RLA6071) and Research contract holders for Coordinated Research Project E43026

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THANK YOU!