Atomic Moms: using stable isotopes to measure the nutrition of children and mothers

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What to expect?

• What is the IAEA?
• What is IAEA‘s role in nutrition programmes?
• Examples of ongoing projects
• Examples of study findings
• How does the IAEA build capacity and reach out?
International Atomic Energy Agency

- IAEA is an specialized technical agency of the United Nations System;
- Established in 1957 as the world’s “Atoms for Peace” organization;
- Works with its Member States and multiple partners worldwide to promote safe, secure and peaceful nuclear technologies;
- Headquarters in Vienna with offices in Geneva, Tokyo, Toronto, and New York.
IAEA Mandate

“Atoms for Peace and Development”
To seek to accelerate and enlarge the contribution of nuclear techniques to peace, **health and prosperity** throughout the world.
Department of Nuclear Sciences & Applications

- Human Health
- Environment
- Food and Agriculture (Joint Division with FAO)
- Water Resources
- Radioisotope Production and Radiation Technology
- Nuclear Science
IAEA’s Sub-Programme ‘Nutrition for Improved Health’

Enhance Member State capabilities to combat malnutrition in all its forms and to address environment related nutrition issues for better health throughout the life course:

• Maternal, infant and young child nutrition;
• Prevention and control of obesity and non-communicable diseases;
• Health effects of the environment.
IAEA’s Contribution to the Global Efforts in Nutrition

The IAEA’s work complements the work of other players in nutrition through encouraging the use of stable isotope techniques (safe and non radioactive) in design and evaluation of nutrition interventions.
What is an Isotope?

• Isotopes of an element have the same the number of protons in the nucleus (atomic number)

  but

• Different atomic mass (the sum of number of protons + number of neutrons)
Isotopes of Hydrogen

Hydrogen has 3 isotopes:

- Protium ($^1\text{H}$)
- Deuterium ($^2\text{H}$)
- Tritium ($^3\text{H}$)

<table>
<thead>
<tr>
<th>Isotope</th>
<th>Mass Number</th>
<th>Abundance</th>
<th>Half-Life</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^1\text{H}$</td>
<td>1.00794</td>
<td>99.985%</td>
<td>Stable</td>
</tr>
<tr>
<td>$^2\text{H}$</td>
<td>2.0141</td>
<td>0.015%</td>
<td>Stable</td>
</tr>
<tr>
<td>$^3\text{H}$</td>
<td></td>
<td></td>
<td>$t_{1/2} = 12.32$ yrs</td>
</tr>
</tbody>
</table>
Summary on stable isotopes

• Unlike radioisotopes which are unstable, stable isotopes are safe and emit no radiation
• Stable isotopes occur naturally in our environment and our organism (natural abundance)
• We use stable isotopes that are less present in nature
• Need to collect baseline sample
• Suitable for all ages (pregnant women, lactating mothers, children)
• Can be used in community settings
Nuclear Applications in Nutrition

- Body composition
- Bone Density
- Total energy expenditure
- Micronutrient bioavailability and Vitamin A pool size
- Environmental enteric dysfunction
- Breastfeeding patterns
Support Mechanisms of IAEA

Coordinated Research Projects
- Call for research proposals
- Respond to research questions
- Small group of research institutes
- 4-5 years
- Small annual grants
- Regular coordination meetings

Technical Cooperation Programme
- Project submission from Member States
- Building and strengthening capacity to use stable isotope techniques
- Biannual planning and implementation cycle
- Training, expert advice, equipment, sample analysis, data management/analysis

No funding of field logistics!
Coordinated Research Projects

Areas of ongoing research projects:

- Infant feeding (breastfeeding), infant growth and body composition
- Childhood obesity
- Micronutrient nutrition (Vitamin A, Iron, Zinc)
- Optimizing nuclear techniques to assess vitamin A status and the risk of excess vitamin A intake
- Agriculture for improved nutrition
- Protein bioavailability from plant based diets
- Application of stable isotope techniques in EED assessment
- Link between Early Life Nutrition and Later Childhood Health
Application of stable isotope techniques in environmental enteric dysfunction (EED) assessment

No simple non-invasive methods to diagnose and classify EED.

New research project:
Develop non-invasive stable isotope based breath test using labelled sucrose

2 main phases:
1. Optimisation of existing 13C SBT protocol and validation by biopsy.
2. Assessment of the applicability of validated 13C SBT in EED diagnosis among children in settings where EED risk is high and linking it to growth pattern.

Exposure to unsanitary environment as found in many low and middle income countries leading to:
- Altered intestinal structure and function
- Reduced nutrient absorption
- More permeability to harmful microflora
Applying Nuclear Techniques to Understand the Link between Early Life Nutrition and Later Childhood Health

- To investigate the relationship between the first 1000 days and later childhood body composition
- To explore whether interventions during the first 1000 days can influence childhood body composition and associated NCD risk factors

Cohort A – mother received intervention from preconception and child from birth

| Preconception | Pregnancy | Infancy | Childhood |

Cohort B – mother received intervention in pregnancy

| Pregnancy | Infancy | Childhood |

Cohort C – Child received previous intervention in infancy

| Infancy | Childhood |

Cohort D – No intervention received

| Preconception | Pregnancy | Infancy | Childhood |
TC Projects

TC projects – national, regional:
• Childhood obesity/double burden of malnutrition
• Breastfeeding
• Recovery from malnutrition
• Vitamin A
• Iron bioavailability in context of food fortification
• Healthy Aging

1 Interregional:
• On stunting prevention in collaboration with UNICEF, IADB
Databases

Two pooled databases on breastfeeding practices and risk factors for childhood obesity from CRP and TC projects
Body composition by deuterium dilution – how does it work?

1. Collect baseline sample before drinking accurately weighed dose of deuterium that mixes with body water evenly within a few hours; collect 2 post-dose samples (3-4 h in saliva; 5-6 h in urine)
2. Measure deuterium abundance before and after equilibration of the dose
3. Calculate total body water and fat-free mass using appropriate hydration factor
4. Determine amount of fat mass as difference between body weight and fat-free mass (2-compartment model)
Assessment of interventions aimed at promoting exclusive breastfeeding – validating mothers’ reports and monitoring WHA target

![Graph showing percent rate of EBF by country and method]

- Sri Lanka [Bandara et al 2015]
- Cameroon [Medoua et al 2012]
- Kenya [Oiye 2015]
- Morrocco [Choua et al 2013]
- South Africa [Mulol et al 2016]
- Guatemala [Mazariegos et al 2016]
- Overall

Legend:
- Recall
- DTM
Results showed that infants who were exclusively breastfed for 6 months had a higher per cent fat-free mass at 12 months compared with infants who were not exclusively breastfed for 6 months (P<0.05).
Deuterium dose-to-mother technique – how does it work?

1. Mother consumes a single oral dose of deuterated water
2. Deuterium mixes with mother’s body water
3. Infant consumes deuterium through mother’s milk
4. Saliva is sampled from the mother and infant for 2 weeks
5. Amount of deuterium is analysed
6. Amount of breast milk consumed and amount of water from sources other than breast milk is calculated
IAEA’s Role in Breastfeeding Promotion

WHA targets 2025
Increase the rate of exclusive breastfeeding in the first 6 months up to at least 50%.
Fe absorption in Haitian women is 41% higher from NaFeEDTA than from FeFumarate.

Recommendation to use FeFumarate at 60mg/kg flour (vs 40mg/kg NaFeEDTA), because of lower cost.

<table>
<thead>
<tr>
<th></th>
<th>Fe fumarate</th>
<th>NaFeEDTA</th>
<th>Fe fum + NaFeEDTA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mothers</td>
<td>n=22</td>
<td>n=22</td>
<td>n=20</td>
</tr>
<tr>
<td>Fe absorption (%)</td>
<td>9.24 (6.35, 13.44)(^a)</td>
<td>13.06 (9.23, 19.10)(^b)</td>
<td>11.09 (7.45, 17.34)(^{a,b})</td>
</tr>
<tr>
<td>Fe absorbed (mg)</td>
<td>0.36 (0.26, 0.50)(^a)</td>
<td>0.51 (0.35, 0.72)(^a)</td>
<td>0.44 (0.30, 0.66)(^a)</td>
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</table>

Values are geometric means (95% CI). Values not sharing a common superscript letter differ significantly from each other (repeated measures ANOVA with post hoc bonferroni correction for the mothers, p<0.05)

HERTER-AEBERLI I et al, BJN 118 (2017) 273-279
Fortified extruded rice improved vitamin A status of school children in Thailand

Children’s vitamin A reserves doubled, with no change in serum concentrations

<table>
<thead>
<tr>
<th></th>
<th>Intervention</th>
<th>Control</th>
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<tr>
<td><strong>Serum retinol, µmol/L</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>1.21 ± 0.19</td>
<td>1.18 ± 0.26</td>
</tr>
<tr>
<td>Endline</td>
<td>1.28 ± 0.27</td>
<td>1.15 ± 0.23</td>
</tr>
<tr>
<td><strong>Total body reserves of VA, µmol retinol</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>153 ± 66</td>
<td>108 ± 67</td>
</tr>
<tr>
<td>Endline</td>
<td>269 ± 148*,**</td>
<td>124 ± 89</td>
</tr>
</tbody>
</table>

*Different from control group, p<0.05, **Different from baseline, p<0.05

PINKAEW S et al, J Nutr 144 (2014) 519-524
Validity of 24-h recalls in (pre-)school aged children: Comparison of energy intakes with energy expenditure

- Little is known about the validity of repeated 24-h dietary recalls as a measure of total energy intake (EI) in young children
- Evaluate the validity of proxyreported EI by comparison with total energy expenditure (TEE) measured by the *doubly labeled water (DLW) technique*

Fig. 2. Bland-Altman plot agreement between measured energy expenditure (TEE; kcal/day) and reported energy intake (EI; kcal/day). The mean of EI and TEE is plotted on the x-axis, the difference of both values (bias) on the y-axis accordingly. The solid line indicates the line of total agreement (zero differences between EI and TEE). Mean difference and upper/lower limits of agreement (mean difference ± 2 SD) are superimposed by broken line.
Purpose and objectives

- To strengthen understanding of how to tackle the DBM and address key gaps identified at the 2017 joint workshop.
- To highlight the role of stable isotopes in addressing gaps both in the measurement of malnutrition and in assessing the impact of interventions.
- To identify double-duty actions, new assessment tools, considerations for policies and action plans with an overall aim to support Member States in achieving their defined nutrition commitments within the Nutrition Decade.
Joint IAEA/WHO/UNICEF Symposium

Thematic areas:

- **Epidemiology**
  - Prevalence, causes and consequences of the DBM.
- **Biology**
  - Biological mechanisms contributing to the DBM.
- **Assessment**
  - How to assess the DBM in individuals and populations.
- **Interventions**
  - From biology to interventions targeting the DBM.
- **Policy implications**
  - From biology to policies addressing the DBM.

Audience:

- The symposium aims to bring together a broad range of stakeholders including UN organisations, policy makers, researchers, health professionals, NGOs and civil society.

Fee-free registration and abstract submission until 23 April 2018!

https://www.iaea.org/events/understanding-the-double-burden-of-malnutrition-symposium-2018
AFRA Regional Designated Centres

Regional Designated Centres in the field of deuterium dilution techniques in human nutrition:

- **Botswana** – National Food Technology Research Centre

- **Morocco** – Joint Unit for Nutrition and Food Research at the National Centre for Nuclear Energy, Sciences and Technology (CNESTEN)
Regional Centres In Africa
For Vitamin A Status Assessment

The IAEA is establishing capacity to measure vitamin A body pools using deuterated-retinol-dilution technique:

**Cameroon** – Centre for Food and Nutrition Research

**Zambia** - Tropical Diseases Research Centre at Ndola Central Hospital

**Morocco** – Joint Unit for Nutrition and Food Research at the National Centre for Nuclear Energy, Sciences and Technology (CNESTEN)
Regional Centres In Latin America

Regional Centres of excellence in assessment of body composition and energy expenditure:

- **Chile** – Institute of Nutrition and Food Technology (INTA), University of Chile
- **Guatemala** – Institute of Nutrition for Central America and Panama (INCAP)
- **Mexico** – Centre for Food Research and Development (CIAD) & University of Sonora
IAEA Collaborating Centre for Nutrition

In 2010, St John’s Research Institute, Bangalore, India was designated the first IAEA Collaborating Centre for Nutrition.
IAEA Human Health Series

Also available in Spanish and French!
More information: Human Health Campus

https://humanhealth.iaea.org/HHW/Nutrition/index.html

NEW! Elucidating Adverse Nutritional Implications of Exposure to Endocrine-Disrupting Chemicals and Mycotoxins through Stable Isotope Techniques
Thank you!

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Deuterium dose-to-mother technique – measurement points?

**Sampling points:**

Days 0, 1, 2, 3, 4, 13, 14 (7 samples x 2)

**Shorter protocol under validation:**

Days 0, 2, 7, 13 or 0, 2, 7, 14 (4 samples x 2)
**Deuterium dose-to-mother technique – costs?**

<table>
<thead>
<tr>
<th>Activity</th>
<th>Cost ($) per mother/baby pair</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inputs (consumables, deuterium)</td>
<td>15</td>
</tr>
<tr>
<td>Sample analysis</td>
<td>200</td>
</tr>
<tr>
<td>Training</td>
<td>?</td>
</tr>
<tr>
<td>Field logistics</td>
<td>?</td>
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Deuterium Dilution Technique For Body Composition Is Based On the Two-compartment Model

- Fat Mass
- Mineral matter
- Protein
- Total Body Water
- FM
- M + P
- TBW
- FFM

Four-compartment model
Three-compartment model
Two-compartment model