Stable isotope techniques for assessment of micronutrient bioavailability and status

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Structure of presentation

1. Stable isotope techniques
2. Application of the stable isotope techniques
3. How the IAEA supports the application of these techniques
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“Atoms for Peace”

The Agency shall seek to accelerate and enlarge the contribution of atomic energy to peace, health and prosperity throughout the world.
The Division of Human Health

Nuclear Medicine and Diagnostic Imaging (NMDI)
Applied Radiation Biology and Radiotherapy (ARBR)
Dosimetry and Medical Radiation Physics (DMRP)
Nutritional and Health-Related Environmental Studies (NAHRES)
IAEA’s nutrition sub-programme objectives

To enhance Member State capabilities to combat malnutrition in all its forms:

1. Maternal, newborn and child nutrition
2. Management and prevention of obesity and non-communicable diseases
3. Nutrition and infectious diseases
IAEA’s work in nutrition

The IAEA’s work complements the work of other players in nutrition

Use of isotopic techniques to develop and evaluate interventions to combat malnutrition in all its forms
Stable isotope techniques are reference methods for nutritional assessment

- Body composition
- Exclusive breastfeeding
- Total daily energy expenditure
- Micronutrient bioavailability (vitamin A, iron, zinc)
- Micronutrient status (vitamin A)
Stable isotope methods

• Isotopes: atoms of an element containing the same number of protons, but different number of neutrons
• Unlike radioisotopes which are unstable, stable isotopes are safe and emit no radiation
• Stable isotopes occur naturally
• Suitable for all ages
• Non-invasive
• Can be used in community settings
Stable isotope dilution

A precise dose of concentrated isotopic compound equilibrates & the concentration measured – this enables calculation of the total quantity of exchangeable compound in the body.

- Can measure body water from 4 hour saliva samples to determine fat and fat-free body mass
- Can measure body vitamin A from 2 week blood concentrations - a non-invasive assessment of total stores
Using Stable Isotope Dilution to Measure Breast Milk Intake

Also estimates intake of non-milk fluids and body composition of the mother

To validate mothers’ reports

Saliva samples are collected from mother and baby over 14 days after dose was taken by mother
Fe isotopes (prepared as heme or nonheme Fe) added to food

Retention of isotopes after 2 weeks determined in blood; 80% of absorbed iron incorporated into RBCs

Measuring nonheme Fe absorption from beans in Rwanda
Zinc absorption with stable isotopes – Dual isotope method

- Two stable isotopes administered
  - Oral
  - Intravenous
- Equilibrates in plasma & urine after ~ 3 d
- Percent absorption determined from isotope enrichment in a convenience urine sample (iv retention represents 100% absorbed)
- Automatically corrects for endogenous excretion
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Vitamin A in breast milk - Senegal

- Infants’ vitamin A intake from breast milk sufficient for requirements for 6 months old infants in both groups
- Infants vitamin A liver stores better in supplemented group

<table>
<thead>
<tr>
<th></th>
<th>Supplemented group</th>
<th>Non-supplemented group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast milk intake, L/d</td>
<td>0.9 ± 0.1</td>
<td>0.8 ± 0.1</td>
<td>0.06</td>
</tr>
<tr>
<td>VA intake from full milk, µg/d</td>
<td>365 ± 215</td>
<td>389 ± 151</td>
<td>0.72</td>
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</tbody>
</table>

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>
</tr>
</thead>
<tbody>
<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
Isotope studies in Rwanda showed limitations of biofortified beans to combat Fe deficiency

- Amount of Fe absorbed only modestly improved
- Effects of polyphenol content on Fe absorption inconsistent

- Select for high iron, low phytate, and low polyphenol concentrations

PETRY N et al, J Nutr 142 (2012) 492-497
India: Zinc and iron in biofortified pearl millet bioavailable

- Quantities of iron and zinc absorbed greater than from non-biofortified grain
- Meet physiological requirements of young children if eaten as the major food staple

KODKANY BS et al, J Nutr 13 (2013) 1489-1493
Use of stable isotope techniques to monitor and assess the vitamin A status of children susceptible to infection in Africa

- 7 countries, 5 years
- Vitamin A body pool size, serum retinol, CRP, AGP, dietary intake

NEW Vitamin A regional project
Vitamin A Technical Meeting
March 2014

- Review of current knowledge of safety and effectiveness of large-scale interventions to prevent vitamin A deficiency

- Research agenda for assessing, monitoring, and preventing health risks of excessive vitamin A intake in populations

- Co-organized by the IAEA and BMGF
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The IAEA delivery mechanism

The IAEA Technical Cooperation Program
- Transfer nuclear technologies for peaceful uses, related to large scale interventions addressing national priority areas (national and regional projects)

The IAEA Coordinated Research Program
- Smaller, specific projects coordinated among investigator applicants from several countries
Technical Cooperation Programme

TC projects are not “research”
Should be related to large scale interventions addressing national priority areas

Applications have to come with government support

Implementation:

**National projects**
- Training Courses
- Experts
- Fellowships
- Scientific visits
- Equipment/consumables

**Regional projects**
- Training Courses
- Experts
- Coordination Meetings
- Consumables
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)
In 2010, St John’s Research Institute, Bangalore, India was designated the first IAEA Collaborating Centre for Nutrition.
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
IAEA’s nutrition publications
humanhealth.iaea.org

IAEA HUMAN HEALTH SERIES
No. 7
Stable Isotope Technique to Assess Intake of Human Milk in Breastfed Infants

IAEA HUMAN HEALTH SERIES
No. 21
Assessment of Iron Bioavailability in Humans Using Stable Iron Isotope Techniques

Analysis of Stable Isotope Data to Estimate Vitamin A Body Stores
Themes covered in presentation

1. Stable isotope techniques in micronutrient area
2. Examples of application of the stable isotope techniques
3. IAEA support mechanisms and examples of capacity development
Objectives of the presentation

• Raised awareness on the usefulness of stable isotope techniques for assessing micronutrient bioavailability and status
• Made aware of the IAEA mechanisms to develop capacity
• Opened opportunities for collaborations
Thank you