Is iron & zinc nutrition a concern for vegetarian infants and children?

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Outline

1. Consequences of iron & zinc deficiency during childhood
2. Adequacy of iron & zinc intakes from breast milk during early infancy
3. Assessing risk of iron & zinc deficiency in vegetarian children
4. Dietary and non-dietary factors that may affect absorption of iron & zinc in vegetarian children
5. Dietary practices to enhance adequacy of iron & zinc in vegetarian diets during childhood
6. Conclusions & recommendations
### Adverse health consequences of iron & zinc deficiencies during infancy and childhood

#### Post 1995 vegetarian studies

<table>
<thead>
<tr>
<th>Function affected</th>
<th>Iron</th>
<th>Zinc</th>
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<tbody>
<tr>
<td>Anemia</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Anorexia</td>
<td>+++</td>
<td>+++</td>
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<tr>
<td>Decreased resistance to infections</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Impaired growth</td>
<td>+</td>
<td>+++</td>
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<tr>
<td>Reduced activity</td>
<td>+++</td>
<td>++</td>
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<tr>
<td>Impaired cognition</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Behavioral deficits</td>
<td>+++</td>
<td>+</td>
</tr>
</tbody>
</table>

- **Nathan et al. 1996**: UK
- **Jory 1997**: Canada
- **Thane & Bates 2000**: UK
- **Leung et al. 2001**: Hong Kong
- **Taylor et al. 2004**: UK
- **Yen et al. 2008**: Taiwan
| | What is the adequacy of Fe & Zn intakes from breast milk (BM) during early infancy?
|
|---|---|
| - | [Fe] & [Zn] in BM unaffected by maternal status or use of supplements during lactation |
| - | Full term infants can meet requirements for Fe & Zn from BM alone up to 6 months of age, irrespective of maternal dietary practices |
| - | From ~ 6 months, liver Fe stores are depleted & BM [Zn] are very low so BM alone is no longer adequate |
| - | Hence, from ~ 6 months: additional Fe & Zn must be provided from complementary foods (CFs) |
| - | Plant-based CFs with a high phytate content may compromise bioavailability of Fe & Zn from BM |
Contribution that complementary foods must provide (as %) to meet iron & zinc requirements*

*For breastfed infants 9-11 mos of age
Major food sources of Fe & Zn (as %) for US & NZ infants & toddlers

- **Iron**
  - NZ 12-23 mos
  - US 12-23 mos
  - NZ 6-11 mos
  - US 6-11 mos

- **Zinc**
  - NZ 12-23 mos
  - US 12-23 mos
  - NZ 6-11 mos
  - US 6-11 mos

Legend:
- Red: Meat
- Yellow: Cereals
- Green: Milk
- Blue: Formula
How can we assess risk of Fe & Zn deficiency in vegetarian children?

### Dietary assessment
- Major food sources (as %)
- Percent with *usual* intakes < EAR (adjusted for bioavailability)

### Biochemical assessment
- Fe: Use a multi-parameter model to avoid misclassification
- Zn: Serum Zn as recommended by IZiNCG
- Select appropriate cutoffs; Consider confounders (eg: infection)

### Functional assessment
- e.g: cognition (Fe); linear growth (Zn): morbidity: all non specific
**Mean intakes of iron & zinc of vegetarian vs. omnivorous children**

*From Taylor et al. 2004; Thane & Bates 2000; Yen et al. 2008; Jory 1998; Nathan et al. 1996*
Recommended method for assessing risk of inadequate intakes of Fe & Zn

- Adjust nutrient intakes to usual intakes with PC-SIDE
- Select appropriate EAR for assumed bioavailability
- Use cutpoint method to assess percent with intakes < EAR
- Example: East Indian vegs vs. Omnivores
  - 18% vs. 0% Fe intakes < EAR
  - 35% vs. 16% Zn intakes < EAR

See IZiNCG Brief No. 3
Identifying risk of Fe deficiency in vegetarian children

Dietary indicator: Percent with Fe intakes < EAR

Biochemical indicators

Stage 1: Depleted Fe stores
- Low serum ferritin in the absence of infection
- Normal Hb

Stage 2: Fe deficient erythropoiesis**
- > 2 abnormal values: Ferritin, Transferrin receptor
- Normal Hb

Stage 3: Iron deficiency anemia**
- Fe deficient erythropoiesis
- Low Hb

Functional indicators
Prevalence (as %) of low serum ferritin in vegetarian vs. omnivorous children

Methods used to define iron deficiency

- Prevalence (95% CI) defined as serum ferritin < 12 µg/L in absence of infection & low Hb
- Prevalence (95% CI) with ≥ 2 abnormal values
  - Serum ferritin ≤ 12 µg/L; MCV (< 73 fL); Zn PP (≥ 70 µmol/mol heme) in absence of low Hb

![Graph showing storage Fe depletion and stage 2 Fe-deficient erythropoiesis](image-url)
Identifying risk of zinc deficiency in vegetarian children

- **Dietary indicator**
  - Percent with Zn intakes < EAR : risk of inadequacy
  - High risk: > 25% (IZiNCG, 2007)

- **Biochemical indicator**
  - Percent with low serum Zn (adjusted for infection)
  - Use IZiNCG procedures for blood collection & assay
  - High risk: > 20% (IZiNCG, 2007)

- **Functional indicator**
  - Length or height-for-age
  - Percent < 5 y HAZ-scores < - 2 SD ; High risk > 20%
  - Non-specific: use with Zn biomarker
Evidence for serum Zn as a biomarker for risk of Zn deficiency in populations

- Relation between mean dietary Zn intake & mean serum Zn from multiple adult studies

![Graph showing the relationship between zinc intake (mg/d) and serum zinc (ug/dL), with data points indicating supplementation, depletion, and repletion.](image-url)
Factors affecting serum/plasma Zn

**Technical factors**
- Adventitious contamination
- Refrigerate blood after collection
- Position of subject
- Time prior to centrifugation
- Hemolysis

**Biological factors**
- Fasting/ non-fasting state
- Time of recent meal
- Diurnal & circadian variation
- Infection
- Age; sex
- Use of OCA, hormones, steroids
- Physiological state: growth; pregnancy
- Concurrent nutrient deficiencies (protein; Vit A)
- Weight loss
- Disease states: eg. marasmus

**Effect of recent meal & time of day**

![Graph showing plasma Zn levels over time]
Prevalence of low serum Zn (as %) for vegetarian & omnivorous young women

Donovan & Gibson (1995)

Gibson et al. (2001)
Factors that may affect iron & zinc absorption in vegetarian children

- Fe & Zn status
  - Influence Fe & Zn absorption

- Genetic Hb disorders
  - Increase Fe absorption

- Parasitic infections
  - Deplete Fe stores via GI blood loss

- Hypochlorhydria
  - Reduces Fe & Zn absorption

- Inflammation
  - Reduces Fe absorption

- Overweight/obesity
  - Reduces Fe absorption

- Biological variation in absorption, metabolism, excretion
  - In health benefits of Fe or Zn

- Dietary factors
  - Absorption modifiers
## Dietary factors affecting iron & zinc absorption

<table>
<thead>
<tr>
<th>Iron</th>
<th>Zinc</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Enhancers</strong></td>
<td><strong>Enhancers</strong></td>
</tr>
<tr>
<td>Meat, poultry, fish, other seafood</td>
<td>Meat, poultry, fish, other seafood</td>
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<tr>
<td>Ascorbic acid</td>
<td>-----</td>
</tr>
<tr>
<td>Other organic acids</td>
<td>Organic acids</td>
</tr>
<tr>
<td><strong>Inhibitors</strong></td>
<td><strong>Inhibitors</strong></td>
</tr>
<tr>
<td>Phytate (IP-6) &amp; IP-5 to IP-3</td>
<td>Phytate (IP-6) &amp; IP-5</td>
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<tr>
<td>Polyphenols &amp; other flavanoids</td>
<td>------</td>
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<tr>
<td>Calcium?</td>
<td>Calcium?</td>
</tr>
<tr>
<td>Eggs</td>
<td>---</td>
</tr>
<tr>
<td>Other transition metals (Zn, Cu)</td>
<td>Other transition metals (Fe, Cu)</td>
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<tr>
<td>Certain processed soy products</td>
<td>Certain processed soy products</td>
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</tbody>
</table>
Non-dietary factors affecting iron & zinc absorption

<table>
<thead>
<tr>
<th>Factors</th>
<th>Mechanisms</th>
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</thead>
<tbody>
<tr>
<td>Low Fe &amp; Zn status</td>
<td>Fe absorption upregulated</td>
</tr>
<tr>
<td></td>
<td>Endogenous Zn losses reduced</td>
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<tr>
<td>Infection/inflammation</td>
<td>Reduces Fe absorption</td>
</tr>
<tr>
<td>Overweight/obesity</td>
<td>Induces inflammation: reduces Fe absorption</td>
</tr>
<tr>
<td>Hypochlorhydria</td>
<td>Reduces Fe &amp; Zn absorption; Exacerbates enteric infections &amp; diarrhea &amp; Zn loss via stool</td>
</tr>
<tr>
<td>Hookworm &amp; <em>T. trichiura</em> infestation</td>
<td>GI blood loss &amp; depleted Fe stores Diarrhea &amp; Zn loss in stool</td>
</tr>
<tr>
<td>Genetic Hb disorders in children of African, S or SE Asian descent</td>
<td>Fe absorption upregulated due to ineffective erythropoiesis: induces anemia &amp; Fe overload</td>
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Dietary practices to enhance adequacy of iron & zinc in diets of vegetarian children

<table>
<thead>
<tr>
<th></th>
<th>1. Reduce phytate content of cereals/legumes</th>
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<tr>
<td></td>
<td>2. Avoid tea &amp; coffee during/after meals</td>
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<td></td>
<td>3. Consume ascorbic-acid rich fruits or juices with meals</td>
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<td></td>
<td>4. Use cast-iron frying pans</td>
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<tr>
<td></td>
<td>5. Consume fortified cereal products: national/household</td>
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<tr>
<td></td>
<td>6. Consume fortified milk products</td>
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<tr>
<td></td>
<td>7. Use biofortified cereals &amp; legumes</td>
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<tr>
<td></td>
<td>8. Use supplements of iron and zinc when needed</td>
</tr>
</tbody>
</table>
Inhibitory effect of phytate on Zn absorption

From Sandberg & Sandström (1992)

Household strategies to reduce phytate content

- Use refined cereal flours (lower [Fe] & [Zn])
- Soak dried legumes & discard soaking water
- Use sprouted legumes
- Ferment porridges

Reducing phytate content of cereal/legumes
Adjustments to the requirement for Zn according to dietary phytate level in adults

From Hambidge et al. (2008)
Fractional Fe absorption from reference meal with or without tea & ascorbic acid in women with & without Fe deficiency anemia (IDA)

Thankachan et al. (2008)
Examples of fortification of cereal-based complementary foods

- Fortified cereal-based porridges
- Fortified spreads: plumpy-nut *
- Micronutrient powders: Sprinkles in serving size sachets *

*Mixed with prepared complementary foods in the home
Do cereal-based CFs fortified with Fe & Zn at recommended levels have a positive impact on anemia and Fe & Zn biomarkers?

Phy:Zn molar ratios Basal porridge = 19; Richly fortified porridge = 6
Effect of level of Zn fortification on total absorption of Zn in pre-school children

- Peruvian pre-schoolers given 2 meals of wheat flour products fortified with 3 levels of Zn
- Mean total absorbed Zn positively related to Zn intake
- No differences in Zn absorption from Zn0 or ZnS0\textsubscript{4} fortificants
- Additional Zn in fortified food contributes positively to total amount of absorbed Zn

From Lopez de Romaña et al. (2005)
Household Fortification

Efficacy of fortifying maize porridge with micronutrient powders + phytase for 23 wk on Fe & Zn status of S African school children

From Troesch et al. (2011)
2.5 mg Fe as NaFeEDTA;
2.5 mg Zn as ZnO
Biofortification of plant-based staples

Simulated impact of biofortified rice (+8 µg/g Zn) on *inadequate* Zn intakes (%) in Bangladeshi children & women

<table>
<thead>
<tr>
<th>Biofortification</th>
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<tbody>
<tr>
<td>- Fertilizers on soils low in Zn</td>
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<tr>
<td>- increase grain Zn (Turkey)</td>
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<tr>
<td>- Plant-breeding to increase:</td>
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<tr>
<td>- Zn in wheat, rice, maize</td>
</tr>
<tr>
<td>- Fe in beans, pearl millet</td>
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<tr>
<td>- Genetic modification to:</td>
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<tr>
<td>- reduce phytic acid in cereals</td>
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</tbody>
</table>

![Graph showing simulated impact of biofortified rice on Zn intakes]
Supplementation: adding zinc to iron
Effect on serum ferritin

Serum ferritin conc (g/L)

- **Iron alone**
- **Zinc & Iron**
- **Placebo**
Conclusions

- Overt Fe & Zn deficiency unlikely unless on very restricted diets
- Vegetarian children may have higher prevalence of low Fe stores than omnivores. Functional significance uncertain
- Very limited data on Zn status of vegetarian children
- Supplements may be needed for children on very restricted diets
- Fortified products increase intakes of absorbed Fe & Zn but only consistently improve Fe biomarkers: not Zn
## Recommendations

<table>
<thead>
<tr>
<th></th>
<th>Recommendation</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>More data urgently needed on Zn status of vegetarian children using IZiNCG procedures</td>
</tr>
<tr>
<td>2</td>
<td>Methods to assess Fe &amp; Zn status should be improved</td>
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<tr>
<td>3</td>
<td>Impact of health-related factors (e.g., inflammation) should be considered when interpreting data</td>
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<tr>
<td>4</td>
<td>Additional functional indices of Fe &amp; Zn status should be assessed</td>
</tr>
<tr>
<td>5</td>
<td>Vegetarian dietary guidelines should include phytate-reducing strategies</td>
</tr>
<tr>
<td>6</td>
<td>Recognition that Zn-fortified products may not necessarily have a positive impact on Zn status</td>
</tr>
</tbody>
</table>
Thank you

www.izincg.org/
Why comparing mean intakes with RNI does not provide data on inadequate intakes

- Compare mean/median nutrient intake of group with RNI

  - Prevalence of inadequacy depends on distribution of usual intakes. This is not taken into account when only mean/median are given:

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<thead>
<tr>
<th></th>
<th>5th</th>
<th>10th</th>
<th>15th</th>
<th>25th</th>
<th>50th</th>
<th>75th</th>
<th>85th</th>
<th>90th</th>
<th>95th</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.92</td>
<td>1.02</td>
<td>1.11</td>
<td>1.24</td>
<td>1.51</td>
<td>1.90</td>
<td>2.13</td>
<td>2.31</td>
<td>2.65</td>
</tr>
</tbody>
</table>

- Median intake of B-6 (1.51 mg/d) vs. RDA (1.5 mg/d): intake appears adequate
- BUT EAR (1.3 mg/d) is between 25th – 50th P of usual intake.
- Thus prevalence of inadequacy > 25%
Risk of Inadequacy

- Risk of inadequate intakes of Fe & Zn based on percent < RNI or < EAR for East Indian immigrant children

- Note the much higher prevalence estimates when intakes are compared with the RNI than with the EAR

- High risk for Zn: when at least 25% of individuals in the population have Zn intakes less than EAR
### Iron
- Appetite
- Cognitive development: longer looking times in infants
- Fine motor development in infants
- Alterations in sleep organization
- Eye-blinking rates
- Neurophysiologic methods

### Zinc
- Linear growth; weight gain
- Body composition
- Morbidity due to childhood illnesses
  - respiratory infections, diarrhea