Vitamin B12 deficiency in Guatemala

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Outline

• Vitamin B12 deficiency is probably the most common MN problem in Guatemala.
• Across life span, male and female.
• Cause is low animal source food intake, and for infants, low maternal stores during pregnancy and lactation.
• Breast milk low in B12 and other MN.
Prevalence of B12 deficiency:
ENMICRON 2009-2010

Highest 20% women
Lowest 20% women
Highest 20% children
Lowest 20% children
Women
Children

% of sample

Deficient <150 pmol/L
Marginal 150-221 pmol/L
<table>
<thead>
<tr>
<th>Year</th>
<th>Group</th>
<th>Results</th>
</tr>
</thead>
</table>
| 1997   | Women 3 mo. lactation                  | 47% def/marginal  
Infants elevated MMA, milk low B12                                                                                                                                 |
| 2008   | Infants 7 mo.                          | 61% def/marginal  
RDA for 6 mo. no sig. benefit  
7 mo. correlated with 12 mo.  
Infant status negatively assoc. breastmilk                                                                                                           |
| 2003   | Schoolers                              | 33% def/marginal  
Not related to H pylori or bact. overgrowth                                                                                                                                 |
| 2007   | Women & child 12 -21 mo. lactation     | 49% infant, 68% mothers def/marginal  
Low milk B12, correlated with maternal serum B12  
Child B12 status neg. associated with breast milk  
Neither RDA or beef sig. effect improved child B12  
Child B12 at 12 mo. tracked to 21 mo.  
Child B12 at 21 mo. correlated with maternal B12                                                                                                           |
Continuum of mother-child B12 depletion

Maternal depletion in pregnancy

Low B12 stores in infant at birth & in colostrum, breast milk

Infant depletion at 3 months

Depletion at 7, and 12 months (r=0.49)

Breastfed freq (-)
Cows milk (+)

Depletion at 21 months (still correlated with early maternal B12 status)

↓ weight, length, motor development
B12 status at age 6 months (Santa Elena, n=127)

![Bar chart showing B12 status at age 6 months.

- Low (<148 pmol/L): 23.6%
- Marginal (148-221 pmol/L): 37.0%
- Adequate (>221 pmol/L): 1.8%]
Infant serum B12 at 7 mo. is inversely related to breast milk intake, and positively to cow’s milk intake.

Cows milk has much more B12 than breast milk, especially in Guatemala

Deegan, 2007
Anaya, 2008
Vitamin B12 in breast milk, by country

Cameroon: 67 pmol/L North, 287 pmol/L Cities

Maternal sB12
- NI: <220
- Mgl: <150
- Def: <150

Country: Oakland, Denmark*, Malawi, Bangladesh, India, Guatemala

Levels:
- 2 ug 0 to 6 PP
- 250 ug Preg to 3 PP
- 50 ug Preg to 1.5 PP

Comparison:
- Unsupplemented
- Supplemented

Sample sizes:
- n = 24
- n = 28
- n = 35
- n = 30
- n = 262
- n = 275
- n = 57
- n = 47
- n = 55
- n = 64
- n = 64
Guatemala: Infant B12 status predicts motor development (n≈80/group)

Factor score: Deficient lower than Adequate (P<0.01) adjusted for SES, environment etc.
Overlap between maternal and plasma B12 values in clinical cases of infant deficiency, and at 12 months in Guatemala
Other potential perinatal roles for B12

- NTD prevention
- Pre-eclampsia (homocysteine)
- Birthweight
- Epigenetic effects
- Postnatal insulin resistance
- Infant development

<table>
<thead>
<tr>
<th></th>
<th>V. deficient &lt;100 pmol/L</th>
<th>Deficient &lt;150 pmol/L</th>
<th>Marginal &lt;221 pmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>++</td>
<td>+/-</td>
<td>No</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>++</td>
<td>+</td>
<td>No</td>
</tr>
<tr>
<td>↑ Hcy, MMA</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Breast milk</td>
<td>++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Child devpt</td>
<td>++</td>
<td>Assoc.</td>
<td>Assoc.</td>
</tr>
<tr>
<td>Cognition</td>
<td>++</td>
<td>+/-</td>
<td>Assoc.</td>
</tr>
<tr>
<td>Depression</td>
<td>Assoc.</td>
<td>Assoc.</td>
<td>Assoc.</td>
</tr>
<tr>
<td>Bone mineral</td>
<td>+</td>
<td>Assoc.</td>
<td>Assoc.</td>
</tr>
<tr>
<td>NTD</td>
<td>?</td>
<td>?</td>
<td>Assoc.</td>
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</tbody>
</table>
BAN project: RCT of LNS (1 x RDA) and ARVs for first 6 months lactation. % of control values

LNS increased all but thiamin
ARVs abolished this effect
DOSE vs B12 in breast milk, by country

Pre- & post-fortification

2 ug
0 to 6 PP

250 ug
Preg to 3 PP

50 ug
Preg to 1.5 PP

Maternal sB12

Ni
<220

Mgl
<150

Def

No dose normalizes milk B12

Unsupplemented

+B12
Median relative concentrations in milk as % of value assumed to set Adequate Intake
Chilean elderly (high FA in flour)
B12 deficient
Nerve conduction baseline, 3 mo
Injected with B12
Higher serum folate at baseline → nerve function stays abnormal
and biomarkers of B12 status were more abnormal

Higher serum folate makes B12 deficiency worse
Conclusions

- B12 deficiency very common in Guatemala.
- Mothers, infants especially vulnerable.
- Supplements and LNS in pregnancy and lactation helpful but probably not enough.
- \( \uparrow \) Milk, eggs, poultry etc. where possible.
- Fortification likely best strategy:
  - Absorption highest from small amounts
  - Mothers will enter pregnancy with stores
  - Affects males and females across the life span
  - Good to provide with folic acid in flour