The role of health status: Infections

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Outline

• Prevalence and variation of infections in developing versus developed countries.
  o Overview of influence on nutrient requirements.

• Protein and Vitamin A as case study of influence of infections on nutrient requirements

• Implications of inter-country variations of infections for the global harmonization

• Conclusions
Infectious diseases remain common worldwide

Source: UNICEF, 2015
% of deaths in chn < 5 y attributable to pneumonia, 2015

Source: UNICEF
% of deaths in chn < 5 y attributable to diarrhea, 2015

Globally, there are nearly 1.7 billion cases of childhood diarrheal disease every year.

Source: UNICEF
Global distribution of malaria, 2016

Source: WHO database
Other common infectious diseases

• Tuberculosis (New cases in 2015, in thousands)
  o Europe: 323; Africa: 2,720; SE Asia: 4,740

• Typhoid fever
  o Rate in S. Asia >10 times the rate in N. America

• Helicobacter pylori infection
  o 8.9% in Switzerland to 87.7% in Nigeria.

• Neglected Tropical Diseases (NTDs)
  o All low-income countries have >5 NTDs simultaneously
  o 7 of most common NTDs found primarily in Africa, Asia, and Latin America
  o Generally rare/absent in developed countries
Infections influence nutrient requirements via:

1. Decreased food intake.
2. Impaired nutrient absorption or re-absorption.
3. Absolute/ direct losses (i.e. wastage) of body nutrients
   - Eg. muscle protein/ vitamin A
4. Uptake, diversion and sequestration of various body nutrients.
Role of infections/infestations in the establishment of dietary intake values:

A case study of protein and vitamin A
1. Infection decrease food intakes via:

- Anorexia – loss of appetite
- Cultural tendency to withdraw solid foods
- Advice for liquid (often thin, less nutritious) gruels without emphasizing solid foods during recovery
- Other adverse effects of treatments, eg purgatives.
Decreased food intakes: Guatemalan preschool children with selected common symptoms

Energy: 19%
Protein: 18%

Source: Martorell et al., 1980
Decreased energy intakes: Kenyan children with measles

Source: Duggan and Milner, 1986
Decreased total energy and non-breastmilk energy intakes: **Peruvian infants with fever and diarrhea**

![Chart showing energy intake percentages for fever and diarrhea]

- Symptom-free:
  - Total energy intake: 94.3%
  - Non-BM energy intake: 71.8%

- Symptom:
  - Total energy intake: 95.5%
  - Non-BM energy intake: 76.6%

Brown et al., 1990
Decreased nitrogen and fat intakes: Bangladeshi pre-school children with cholera and rotavirus infection

Mean nutrient intakes, g/kg/d

- Nitrogen, g/kg/d
  - Cholera: 0.32 ± 0.57
  - Rotavirus: 0.25 ± 0.32

- Fat, g/kg/d
  - Cholera: 2.03 ± 2.09
  - Rotavirus: 1.88 ± 2.99

Source: Molla et al., 1991
Decreased food/nutrient intakes in pre-school Zambian children with Malaria

Source: Bresnahan et al., 2014
2. Infections impair nutrient absorption/re-absorption via:

- Inflammatory lesions interfering with absorption
- Damage to epithelia/intestinal mucosa
- Parasites’ competition with absorptive mechanisms
- Interference from antibiotics/purgatives
- Reduction transit time
- Alteration of mucosal transport mechanism
Gastrointestinal protein loss: Pre-school Nigerian children with measles

- Mean fecal $^{59}$Fe-labelled iron dextran clearance in acute stage was 5.7% ($n = 5$) → 1.7 g/day mean absolute loss of albumin.
- Values of $^{59}$Fe-labelled iron dextran clearance on recovery higher than normal (<1%)
- Xylose absorption depressed in acute phase of infection

Source: Dossetor and Whittle, 1972
Decreased nitrogen absorption: Pre-school Bangladeshi children with cholera and rotavirus infection

Source: Molla et al., 1991
Decreased protein re-absorption: **3-9 mo olds with or without diarrhea, USA**

Source: Ghadimi et al., 1973
Vitamin A malabsorption, excretion, and retention: Indian 1-4 y olds with or without diarrhea

Source: Reddy et al., 1986

* statistically significant
3. Infection cause absolute loss of body nutrients through:

• Depletion of muscle protein => increased amino acid requirement

• Fever factor → Urinary losses
  
  o Impaired glomerular reabsorption (amino acids, vitamin A)
    ▪ Damage to renal tubules, e.g. by tumor necrosis factor
    ▪ IL-6 down-regulation of hepatic TTR synthesis
    ▪ Decreased affinity between retinol-RBP vs. TTR
Increased loss of nitrogen due to sandfly fever

Source: Beisel et al, 1972
Magnitude of catabolic loss of protein

- 2.5 to 3.5 g protein/kg of muscle: typhoid fever (MacCallum, 1910)
- 2.5 to 3.5 g protein/kg of muscle in patients with erysipelas (Kocher, 1914)
- 0.6 g protein/kg of muscle per day in patients with acute infection (Scrimshaw, 1977)
- 0.9 g protein/kg of muscle per day during diarrhea (Scrimshaw, 1977)
- Negative nitrogen balance may last for days or weeks; recovery 2-4 times longer
- Data on impact of longer periods of infection are lacking
Urinary retinol excretion during pneumonia and sepsis: adults, USA

Geometric mean Vit A excretion:
Pneumonia/Sepsis = 0.78 µmol/d
Control = 0.002 µmol/d

Geometric mean Vit A excretion:
Fever = 0.78 µmol/d
Acute Phys Score= 0.002 µmol/d

Source: Stephensen et al., 1994
Urinary retinol excretion during diarrhea: 6-36 month olds, Peru

Source: Alvarez et al., 1995

Rotavirus-associated diarrhea

Source: Alvarez et al., 1995
Urinary retinol excretion during shigella dysentery: chn < 5 y, Bangladesh

- Urinary retinol loss in 59% of chn
- Urinary retinol loss >0.1 µmol/d in 8% of chn
- More severe disease $\rightarrow$ greater mean urinary retinol concentration excreted
- Body temperature $\geq 48$ °C $\rightarrow$ greater mean urinary retinol concentration excreted

Source: Mitra et al., 1998
% of chn with inadequate liver VA stores following chickenpox infection, Brazil

Source: Campos et al., 1987
4. Infections cause the uptake, diversion and sequestration of various body nutrients:

• Demand for substrates => increased requirement
  – Production of positive acute phase proteins
  – Synthesis and function of phagocytic cells / immunoglobulins
  – Glutathione synthesis
  – Cellular proliferation
  – New secretory protein synthesis
  – Amino acids for energy
Increased synthesis of plasma proteins during typhoid fever

Bostian, et al, 1976
Maintaining the status quo

• Are metabolic responses purposeful defensive mechanisms?
• Are increased absorption and efficiency of utilization during recovery sufficient?
• Focus on elimination of infections?
• “Safe level of intake” supports reserves – offsets increased requirements for infections.
Increasing nutrient requirements for infections

- Benefit for individuals with prior borderline status
- Usual marginal diet inadequate for rapid repletion => longer recovery period.
- Rapid repletion needed before “next” disease episode.
- Part of catabolic response can be reduced/eliminated with ↑energy/protein
- Supportive therapy during the illness
- Nutrients for growth
Increasing nutrient requirements for infections: Developed countries vs. Developing countries (1)

- Differences background characteristics
  - Developed countries:
    - Low rates of infections/infections
    - Aging populations
  - Developing countries:
    - High rates of infections/infections
    - Double burden of under/over-nutrition
    - Physically active younger populations
    - Nutrient deficiencies is still the main problem, i.e. issue of nutrient needs

- Possible differences in micronutrient needs?
Increasing nutrient requirements for infections: Developed countries vs. Developing countries (2)

- Can developing country populations meet higher nutrient requirements?
  - diet often lack diversity
  - many nutrient-rich foods are seasonal
  - supplementation/fortification often do not reach vulnerable populations.
    - Eg. Ca requirement difficult to meet when intakes of milk/milk products are low.

- What would be goal – criterion for adequacy?
Conclusions

- Systematic review to inform recommendations
- Research on quantitative effect of infestations
  - Especially sub-clinical infections
- Develop appropriate strategies to combat infections/infestation.
- Consider a set of recommendations for developing countries, with allowance for infections