The Way Forward on Nutrition–Infection Relationships

Robert E. Black, M.D., M.P.H.
Department of International Health
Johns Hopkins Bloomberg
School of Public Health

Comments on the Nutrition-Infection Relationships

- Resolved (?) old questions
- New twists on old questions
- Unresolved old questions
- New questions

Resolved (?) Old Questions – Infectious Diseases Contribute to Undernutrition

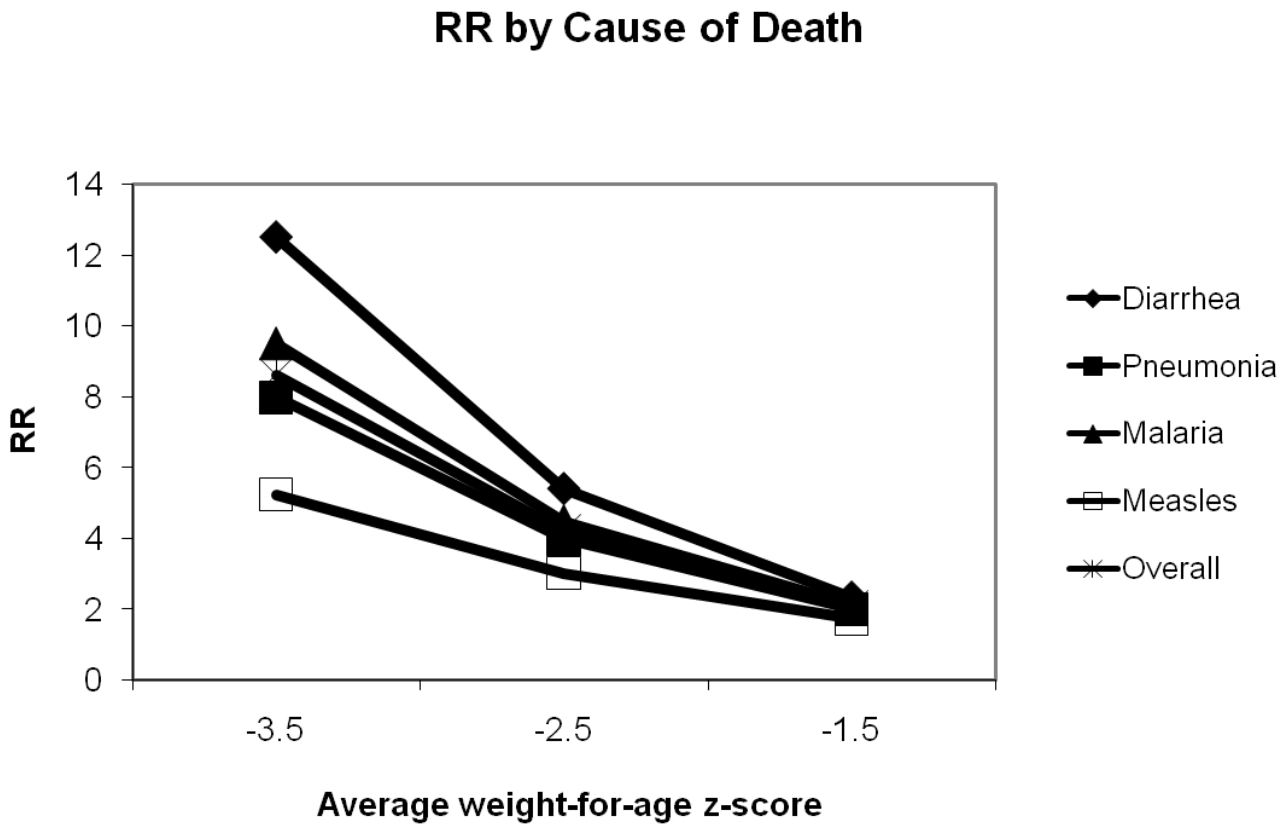
- Ample evidence that infectious diseases have a causal role in undernutrition
- Questions remain about the relative contribution of infection vs. poor diet globally and in specific settings

Resolved (?) Old Questions – Undernutrition Increases the Risk and/or Severity of Infectious Diseases

- Ample evidence of a risk relationship for some major infectious diseases i.e., diarrhea, pneumonia, malaria, measles

Resolved Old Questions – Synergy of Undernutrition and Infection in Mortality

Relative Risk (RR) of Death by Cause Due to Underweight Estimated From Random Effects Models



Caulfield L et al. Undernutrition as an underlying cause of child deaths associated with diarrhea, pneumonia, malaria and measles. Am J Clin Nutr 2004

Resolved (?) Old Questions – Undernutrition Increases the Risk and/or Severity of Infectious Diseases

- Ample evidence of a risk relationship for some major infectious diseases
- Questions remain about the relationship to the many other infectious diseases e.g., AIDS, TB
- Still unclear mechanisms i.e., effects of nutritional deficiencies on innate and adaptive immunity in humans

New Twists on Old Questions: the 1968 Monograph Revisited

- Nutritional deficiencies of importance for infection (1968)
  - Vitamin A – importance predicted
  - Vitamin D – importance uncertain
  - Zinc – importance not recognized

New Evidence on Vitamin D Deficiency

- High prevalence of vitamin D deficiency in pregnant women and children in South Asia and Africa
- Low concentrations of 25 hydroxy-vitamin D associated with risk of ALRI in India, Turkey and Bangladesh
- Role of vitamin D in immune function, e.g. endogenous synthesis of a host mucous membrane anti-microbial peptide (LL-37) by monocytes is dependent on activation of the vitamin D receptor

New Evidence on Zinc Deficiency

- High prevalence of mild to moderate zinc deficiency in low-income countries
- RCTs of zinc supplementation show:
  - 14% (2-21%) reduction in diarrhea incidence (15 trials)
  - 35% (18-48%) reduction in clinically diagnosed ALRI incidence
- Role of zinc in humoral and cellular immunity
- Zinc supplementation enhances immune response to oral vaccines

New Twists on Old Questions

- Monograph considered at length "weanling diarrhea" – complementary food contamination leading to diarrhea
- Breastfeeding and CF food hygiene still critical
- Although HIV is transmitted in breast milk, still net benefit on mortality in low-income countries for exclusive breastfeeding for first 4-6 months.

Unresolved Old Questions: Antagonism

- Monograph mentions possible antagonism, i.e., nutritional deficiencies reduce infectious diseases because of micro-organisms' requirements for nutrients, e.g. B vitamins, amino acids, iron
- May also be due to decreased immune response e.g., hepatic schistosomiasis
- Protective effect of iron deficiency for malaria and adverse effect of iron supplementation in malarious areas e.g., increased risk of hosp. or death with iron supplementation in Zanzibar

Unresolved Old Questions: Enteric Infections and Tropical Enteropathy

- Extensive description of intestinal morphologic changes in Asia and Africa in late 1960s in native children and adults, American soldiers, Peace Corps Volunteers
- Bacterial colonization of small intestine, increased permeability, microbial translocation, T-cell hyperstimulation, crypt hyperplasia, villous atrophy
- Reduced nutrient absorption, acute phase response, etc. – role in growth faltering?

New Questions (1)

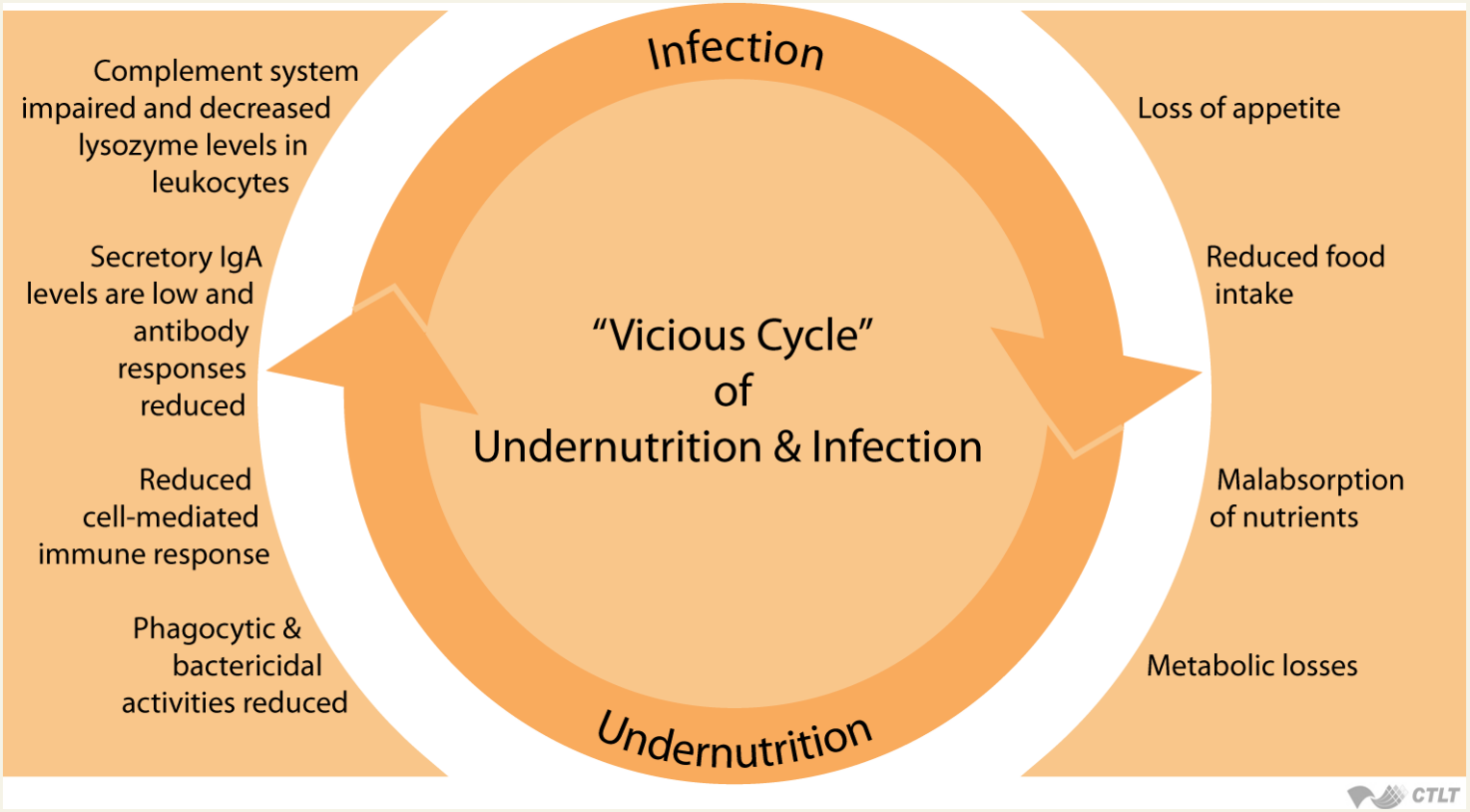
- Role of nutritional deficiencies in microbial evolution e.g., selenium deficiency selects for more virulent Coxsackie B (and influenza) viruses

- Role of the “microbiome” in human nutrition
  - Microbial cells in gut outnumber human body cells by >10-fold
  - Gut microbial community may be related to obesity and undernutrition

New Questions (2)

- Role of Helicobacter pylori gastric infection in nutritional anemia and growth faltering?
- Possible viral induction of type 2 diabetes?
- Viral infections in animal models associated with obesity-relevance for humans?
- Importance of nutrition-infection interactions in vascular disease – possible pro-inflammatory effects of viral or chlamydial infections?

Undernutrition and Infection Vicious Cycle



Still Wise Words...

- “Interactions between malnutrition and infection contribute greatly to the health of individuals and communities.” *N. Scrimshaw, C.E. Taylor, J.E. Gordon, 1968*

- “The bidirectional interrelationships between host nutrition and infectious diseases are exceedingly complex. Despite many studies conducted over the years these multifaceted associations are still incompletely understood.”

W.R. Beisel, 2003