Focus Area 2: Unresolved Issues Of Nutrition In The Lifecycle

Key Nutrition Science Knowledge Gaps

Focus on the mother and child, with linkage to the wider themes of women's health in general; and particular attention to be paid to double burden contexts.

Theme 1. Preconception to early childhood (First 1000 Days and Beyond)

According to information from the WHO (2011), more than 13 million low-birth weight babies are born each year. These babies are often affected by severe short and long-term health and developmental consequences. Poor nutritional status and nutrient intake for women before, during and after pregnancy not only impact a woman's health status and productivity, but may also have detrimental effects on birth weight, nutritional status and early childhood development. Despite the critical role of maternal nutrition, few nutritional interventions for mothers have assessed a wide range of outcomes at sufficient scale.

Fetal and early postnatal life is a period of rapid growth and development and especially vulnerable to nutritional perturbations. Here, we have identified gaps in nutrition knowledge during the first thousand days from pregnancy through age two. This period provides a crucial window of opportunity for reducing malnutrition and its adverse effects.

An integrated systems biology approach is used to move towards understanding the influence of nutrition on the physiological balance of homeostasis during pregnancy and the physical growth and cognitive/motor/social-emotional development of the neonate.

GAPS IN KNOWLEDGE RELATED TO FUNDAMENTAL BIOLOGY

GAP AREA 1

Role of nutrition in Developmental Origins of Health and Disease (DOHaD)

» What is the role of nutrition during fetal growth and development, including the role of maternal nutrition (particularly maternal obesity) and the maternal-fetal interface?
» What are the dietary requirements to support growth and optimize health during early life and later? What is the role of catch-up growth and rapid weight gain? When can it be considered beneficial during early life?
» What are the mechanisms for and potential causes of stunting and malnutrition during early life? Research is especially needed to determine the influence of parental nutritional factors and the long-term effects of multi-generational nutrition/malnutrition.
» How does nutrition influence the development of metabolic systems (healthy "microbiome", immunity, etc)?

GAP AREA 2

Characterizing normal growth during early life

» What mechanisms are responsible for the normal flux of nutrients in utero between mother and infant? What are some appropriate markers that reflect functional changes consequent to that flux?
» How should adequate state-specific intake regulation for both the mother (during pre-conception, pregnancy, lactation and post-partum) and the child (in-utero, during neonatal life, infancy and early childhood) be determined?
» How should fetal malnutrition be characterized and assessed?
» Are current state-of-the art measurements for assessment of "normal" appropriate? This wouldinclude revisiting definitions and criteria for measuring and assessing childhood growth (growth standards, definitions for preterm, stunting, catch-up growth, moderate and severe acute malnutrition (SAM)).

GAP AREA 3

Characterizing and assessing optimal growth and development during early life

» How can the contribution of optimal nutrition to growth and cognitive/physical development be separated and measured?
» Do appropriate developmental markers (subjective and functional) exist to assess "normal" child development? More specifically, can enhancement of function be detected within a normal range (subtleties in cognition/behavior beyond gross deficits)?
» How can we predict the optimal timing for nutrition interventions if we do not know how, when and for how long this should be addressed? Particular gaps include recommendations for treatment and prevention of SAM (Severe Acute Malnutrition) during 0-6 months.

GAP AREA 4

Gaps in knowledge related to describing and understanding contextual factors

» What are the risk factors and causes of adverse birth outcomes (Pre-term Birth, Low Birth Weight (LBW), and Small for Gestational Age (SGA)) and how are they related to maternal nutrition, health, and environment?
» What is the relationship between maternal nutrition, maternal mental health, maternal empowerment, and their combined effects on care-giving? Related to this, how can maternal "empowerment" be better defined and measured related to maternal and child health, nutrition and development outcomes?
» Have current nutrition requirements been adapted appropriately for vulnerable populations (e.g. for pre-term infants, specific disease states, and orphaned infants/children)? If not, what type of research can provide evidence for development of better recommendations?

Theme 2. Moving from single nutrients to a systems biology food-based approach

Traditionally, human nutrition research has largely focused on evaluating one nutrient at a time. Demonstrating the health impact of nutrients such as Vitamin A, folic acid, iron and iodine has helped shape nutrition interventions and policy in both developing and developed countries. While it is critical to understand the role of these individual nutrients in improving health outcomes, there is also a need to use a more comprehensive approach that examines the effects of whole foods, suites of nutrients, and entire diets to complement our current scientific knowledge on single nutrients or isolated compounds.

Food -based, systems biology approaches can be effective tools to address the full spectrum of malnutrition in populations globally. Using an integrated view of food systems and human metabolism will help our understanding of how foods interact with the human biological system. This approach considers entire suites of essential nutrients and other components in food that together have an influence on functional outcomes, including immune function, reproductive health, cognitive development, adult chronic disease and others.

A food-based approach can also help identify strategies to improve functional outcomes during critical phases of human development, in particular pregnancy and early childhood. This type of approach can improve the general quality of the diet (for example, by increasing fruit, vegetable and animal product intake), while providing additional benefits by reducing consumption of less nutritious carbohydrates and fats, and increasing other micronutrients such as essential fatty acids and phytonutrients. This strategy is consistent with the need to lower the global risk of chronic disease and overweight that is exacerbated by consumption of poor quality diets.

GAPS IN KNOWLEDGE RELATED TO FUNDAMENTAL BIOLOGY

GAP AREA 5

Creating a food-based systems biology of nutrition and human health in mother and child

» Understanding bioavailability of nutrients and micronutrients in whole foods (most importantly: human milk, animal products, and staple foods).
» Research on suites of nutrients including fatty acids in developing countries, nutrients associated with growth (phosphorus, potassium, magnesium), and some B vitamins (choline).

» How can food-based dietary guidelines be better linked to effects on human biology? Research is needed on integrating knowledge on molecular mechanisms, human metabolism, nutrition requirements and behavior to further nutrient-based recommendations and develop food-based dietary guidelines for the entire life course.
» Can food-based approaches improve micronutrient status and do they require complementary interventions to ensure adequate intake?
» Developing food-based interventions to modify diet quality and diversity and address the double burden of malnutrition

GAP AREA 6

Gaps in knowledge related to describing and understanding contextual factors

» How to describe and understand biomarkers to reflect exposure, status and functions (individuals and population across the lifecycle), and biomarkers for evaluating response to food-based interventions, biofortification, and other dietary interventions.
» How to understand genetic variation among individuals and populations related to nutritional status and nutrient adequacy/deficiency.
» How to develop the entire food system to meet the health needs of the population, from food production and agriculture to consumers and issues affecting availability and access of food products, including economics of food choice. Can food systems realistically support healthy diets for the whole population?

Theme 3. Malnutrition, infection, developmental and functional outcomes and their interaction with nutrition interventions

Promising interventions have targeted maternal macronutrient and micronutrient intake (The Lancet 2008), but research is needed to better assess long-term impacts on maternal and child health. Trials examining multiple micronutrients have yielded inconclusive results. Some findings indicate that there may be combined effects of food and multiple micronutrient supplementations on growth and development of the offspring. Additionally, information on the optimal timing of food supplementation to malnourished pregnant women and complementary feeding during infancy is lacking.

Frequent illness can impair nutritional status as energy and essential nutrients are diverted away from growth and conversely poor nutrition can increase the risk of infection. Infections are common in the first two years of life and an integrated view of human metabolism and diet/food systems is critical to understanding the influence of nutrition on the balance of homeostasis during health and wellness. As we begin to understand the immune response and the intestinal microbiota, the pathways through which an infection may modify the impact of nutrition interventions on child growth or mechanisms through which improved nutrition may reduce the impact of infection on child growth remain unclear.

Collectively, there is a need to better understand the impact of infection & sub-clinical conditions on nutrition and child growth/development (including birth outcome), and the interactions between nutrition, infection, and non-communicable diseases (NCDs).

<u>GAPS IN KNOWLEDGE RELATED TO FUNDAMENTAL BIOLOGY</u>

GAP AREA 7

The relationship between markers of malnutrition (e.g. stunting in children, low height or BMI in women) and functional outcomes

» How do nutrition and infection interact to influence the process of stunting in both mothers and children and what are the molecular mechanisms responsible for it?
» What are the effects of environmental enteropathy and malabsorption on nutritional interventions and early growth/development?
» Nutrition/pharmacology: How do exposure to toxins in the environment and drugs of abuse interact with malnutrition? What is the impact of scaling up preventive treatments for control of infections in malnourished individuals/populations, or those at risk of becoming malnourished?

GAP AREA 8

Gaps in knowledge related to describing and understanding contextual factors

» Definition of what aspects of 'context' are most salient to describe and understand relative to health, wellness and nutrition.
» How to develop our understanding of genetic variation among individuals and populations related to nutrition and response to illness (ex. microbiome reaction/development during infection, infection during pregnancy).

Theme 4. Methodological challenges related to these research gaps

The benefits of food-based approaches may include nutritional improvement, food security, cost-effectiveness, sustainability, and human productivity. At the same time, nutrition science is also influenced by economic and environmental policies and these approaches pose their own challenges, requiring additional inputs, including nutrition education and behavior change, and strong inter-sectoral linkages with agricultural planning to supply populations with diets to meet desired health goals. Potential obstacles to studying or addressing the above research themes related to maternal and child health are outlined below.

GAP AREA 9

Understanding and driving basic science related to the systems biology approach of nutrition

» Integrating mechanisms of action studies and biomedical models prior to clinical interventions and preventative treatments (development and emergency settings).
» How to test the effects of combining nutrition with early stimulation (in a broad sense), and determine appropriate indicators/measures of success?
» How to determine criteria and types of evidence needed to evaluate and interpret the impact of economic growth (especially for the dual burden of malnutrition and nutrition transition) and other contextual parameters?
» How to deal with unexpected heterogeneity in studies involving various population groups?