Discussion on Micronutrient Requirements

Setting the Terms of Discussion for the Workshop

The 70th Workshop of the Nestlé Nutrition Institute was entitled ‘Micronutrient Requirements for Health and Development’. Two distinguished scientists with experience in developing countries with important micronutrient deficiencies: Dr. Zulfiqar Bhutta and Dr. Mary Penny took part in this workshop. The interaction of nutrition, growth and child survival are prominent public health issues in both the South Asian subcontinent and the Andean region, providing ample opportunity for the two speakers in the inaugural session to gain experience and synthesize their reflections.

One of the important terms of reference in the Workshop title is that of ‘micronutrient requirements’. For the introductory talks, and throughout the Workshop, however, randomized trials with single or multiple micronutrients formed the evidence for a discussion of a requirements theme. Most often, levels of nutrients well above the ‘requirement’ (daily recommended intake) amounts are delivered in such experimental settings. The variance in health and developmental outcomes that can derive from improving the micronutrient offering from dietary interventions with high-quality foods and beverages was only rarely alluded to. Such a perspective would have been more consonant with the explicit terms of reference in the title of the Workshop. To her credit, Dr. Penny was one of the speakers who used the prism of dietary variation, although the title and message of her presentation dealt with treatment – of stunting and of severe malnutrition.

Another term of reference is health. Impaired health is associated with altered nutrient requirements, usually a selective increase in the needs for macro- and micronutrients. Dr. Penny’s discussion of prescription of nutrients to assist what is called in the title as ‘moderate malnutrition’ (underweight), derives from her years of experience in defining the safe and effective rescue, recovery and rehabilitation of children with clinical syndromes of undernutrition. An opportunity was missed in this session, and the subsequent program, to examine the term ‘health’ in terms of nutrient requirements. What are established as reference intakes by bodies such as the UN Systems Food and Agricultural Organization and World Health
Organization or by the Food and Nutrition Board of the Institute of Medicine in the USA are explicitly applicable to 'healthy populations'. Children in low-income settings are more often than not infested by protozoan and helminthic parasites and beset by recurrent communicable diseases affecting the respiratory and gastrointestinal tracts. These alter intermediary metabolism and can interfere with nutrient intake and provoke excessive nutrient wastage. Are the environmental and epidemiological correlates of living in disadvantaged circumstance a motive for adjusting the recommendations to compensate for the ambient stress?

The nutrients most associated with growth and survival, as mentioned in this session, were vitamin A, iron, zinc and iodine. Severe deficiency of all four nutrients is, indeed, associated with decreased survival, and even marginal vitamin A deficiency increases mortality from common childhood infections. Where both Dr. Bhutta and Dr. Penny produced a potential disconnect across the title topic was in the arena of what degree of recovery of linear growth we should expect from nutrient exposures across the full panorama of intervention possibilities. Almost any nutrient at severe enough restriction will cause livestock, poultry or laboratory rodents to falter in their growth; this is the basis for the classical demonstration of specific food factors as essential nutrients. Profound effects on linear growth in free-living populations can only be related to zinc and iodine, with vitamin A and iron producing limited growth faltering. In places like Afghanistan, Angola, and the Horn of Africa, and in my region of Guatemala, the accumulated deficit in height at 5 years of age reaches 10 cm or more. However, when it comes to preservation in linear growth, effect sizes of only a few cm are the maximal outcomes even in the most successful single and multiple micronutrient interventions on record. It may not be the dosage or combination of micronutrients that limit this effect, but rather the intrinsic biological nature of short stature. Evidence can be mobilized from livestock management and experimental science that inflammation and the stress of living in an unsanitary environment are important determinants of growth faltering, and will not be overcome by any amount of additional nutrient exposures.

Salient Points of the Session's Presentations
The titular theme of Dr. Bhutta's presentation involved 'global micronutrient deficiencies'; using maps, he illustrated the estimated prevalence of vitamin A, zinc and iodine deficiency. Not surprisingly, the concentration of micronutrient deficiency problems aligned with the poorest nations of Latin America, Africa and Asia. He accompanied this geography lesson with a narrative on the impacts on health and development of the deficiency of these micronutrients in early life, pointing out that vitamin A and zinc deficiency is associated with an estimated 1 million child deaths and 9% of global childhood disability-adjusted life years. In this respect, he harkened to the 50-year-old paradigm of the interaction of nutrition and infection introduced by Nevin Scrimshaw, noting that child health is an outcome as well as a risk factor.
He reinforced the relevance of the period from conception to 24 months of life, the so-called 1,000 days’ window of opportunity, involving maternal health in pregnancy and the adequacy of complementary feeding. He also mentioned that other nutrients beyond the primary three, namely iron, was also associated with limitations of human development, especially with an onset in infancy. The opportunity to mention vitamin D deficiency as an impending public health problem was missed both in this session, and throughout the Workshop.

On repeated opportunities in the presentation, the pediatrician from Pakistan cited the challenge as being ‘to implement intervention strategies that combine appropriate infant and young child feeding with micronutrient interventions at scale’. There is a sense of detachment or dissociation of the appropriate feeding and the interventions. One wonders if the concentration on what are appropriate estimates for required intakes of nutrients from young-child diets in low-income societies would not obviate the need for large-scale interventions with micronutrient supplements.

The treatment of moderate undernutrition involves correction of inappropriate weight deficit. Although energy and protein are the primary nutritional considerations when repleting body tissue mass, the British pediatrician in Peru, Dr. Penny, pointed out how micronutrients could not be ignored in this therapy. The broad consideration of micronutrients, beyond those of primary public health interest, is exemplified in the comprehensive therapeutic approach to moderate malnutrition. In fact, this led to a discussion of multiple micronutrients administered in combination. Surprisingly, again in light of the title of the Workshop, if we take the whole program and its 14 invited presentations into perspective, only Dr. Penny’s piece in the Introduction, the two presentations in the pregnancy session (Dr. Darnton-Hill; Dr. Bhutta), and the fortified food topic of Dr. Allen put the emphasis on multiple micronutrients in combination. The other 11 are monotonic for single nutrients.

The treatment of stunting or short stature is also addressed by Dr. Penny, and she invokes both single-nutrient and multi-nutrient formats. To her credit, she provides a balanced review of the literature, and shows the mixed – and not overwhelming – evidence for efficacy of reversing linear growth faltering with single or combined nutrients in stunted populations. The most interesting insight into the biology of stunting is that the length of the head, neck and torso of stunted children is equivalent to that of a normally grown peer. The growth faltering is largely the result from the failure of elongation of the long bones of the legs. This could point to some disruption of the hormonal cascade that supports bone growth at the epiphyses.

Summary of the Question and Answer Participation
In the question and answer discussion period, Dr. Bhutta was challenged on several points. Since both issues of bodyweight (underweight) and diverse micronutrient deficiencies seem to predict and predispose to under-five mortality,
how does one parse and separate out the specific impact of the different deficiency conditions, and how does one translate that into effective programmatic actions. The discussion moved to the inconsistencies related to the impact of zinc interventions in achieving improvements in survival, disease resistance and other functional benefits. One factor is the (as yet imperfect) approaches to assessing the existence of zinc deficiency due to lack of a specific biomarker of deficiency. Regarding the query of why vitamin D deficiency has yet to be incorporated into the global micronutrient deficiency agenda, it was admitted that the so-called ‘sunshine vitamin’ can be deficient in populations of the tropics. Insofar as this realization is of recent origins, we are only at the incipient level of inquiry into vitamin D deficiency, beyond overt rickets, in the global statistics of mortality, morbidity and intrauterine growth failure.

Dr. Penny extended her discussion of animal protein food in meeting requirements from dietary sources in response to questions as to whether milk was also in this category. Two characteristics of milk that could produce positive trophic effects in children were identified. The first is that bovine milk has been found to contain insulin-like growth factor-I, which may be absorbed intact and function as a hormone in the milk consumer. Another thought was that of surreptitious and serendipitous correction of an unrecognized iodine deficit by milk. Due to the iodine-containing antiseptic solutions used to disinfect the cows’ udders prior to industrial milking, residual iodine remains in the dairy items derived. By repleting iodine status, milk consumption might positively impact those short children with prior iodine deficiency. Rounding out the discussion on nutrients from actual foods was a focus on the limitations to obtaining adequate micronutrient nutrition during the critical 6–12 months of life covering transition from exclusive breastfeeding to mixed feeding. In this period, the critical quest is getting complementary foods with a high enough nutrient density to provide the residual needs of vitamins and minerals with a low allotment for additional calories. This is where animal protein foods are indispensible because of their generally more nutrient dense composition.

The remainder of the discussion centered on deriving useful insight on the Workshop topic from published trials. The question of how the various study designs included together in a review of intervention studies are casting light on micronutrients and growth was raised. Obvious issues such as the nutrient dosages, the mixtures of nutrients, the duration of the trial, the age and status of the children, and the degree of preexisting stunting in the trial populations are all features that could influence the findings of benefits. The issues of nutrient–nutrient interactions in multiple nutrient interventions were raised within this context. That interactions might be responsible for the variability of results from trial to trial was raised. Most of the interest centered on the competitive interaction of iron and zinc. The possibility of certain interactions having the effect of accentuating the actions of the nutrients was also raised as a theoretical possibility when multinutrient combinations are at play.
The status of parasitosis with protozoan and helminthic pathogens in the various intervention trials was advanced as another issue of potential relevance to the interpretation of the findings. Parasite loads vary from setting to setting depending upon residual infections in the population and ecological factors supporting parasite transmission and propagation. One commentator opinion was that multicellular pathogens are much more common as agents of severe gastroenteritis episodes and malabsorption than has been previously recognized. Finally, an interesting suggestion on transgenerational effects, i.e. that attention to micronutrients in the mother will have beneficial effects for her daughters and her granddaughters, was raised in the discussion.

Conclusion of the Discussant

The issue of micronutrient requirements from the connotation of diet has become divorced from the thrust of the field research on nutrient supplementation conducted over past quarter of a century. These years have allowed for the proliferation and collation of well-conducted and statistically powerful field trials, now coalesced into systematic reviews and meta-analyses. By their very design and nature, they allow for pharmacological actions of high-dose nutrients to be misinterpreted as nutritional functions of the nutrients and produce imbalances that can distort the normal metabolism of nutrients taken in from the diet itself. For all of their citation by the lead-off speakers and by the majority of presentations to follow, their capacity to inform us regarding ‘micronutrient requirements’ should be viewed with healthy skepticism. Aside from the question of the long-term sustainability of intervention programs as public policy, their limitations in eradicating the survival, growth, health and developmental issues may derive from the simple reality that other, nutrient-independent environmental assaults are influencing or even determining the outcomes. An alternative view might be to let the best quality diet do what diet can do, and address the collateral causes of poor health and development with a comprehensive array of complementary actions directed at the residual ecological origins.

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