Nutrition, Immunity, and Infection in Infants and Children

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Preface

This 45th Nestlé Nutrition Workshop served as an invigorating forum for scientists engaged in the fundamental and applied aspects of research in the area of nutrition, immunity, and infection in infants and children. By enhancing knowledge of the prevention and treatment of childhood malnutrition and infectious disease, one recognizes the positive impact that nutrition can have on initiatives which catalyze on disease processes. Practical clinical research initiatives, which catalyze action in the field of nutrition and health, should be undertaken with clear goals in mind. In addition, basic research, which provides fundamental and newer insights into the malnutrition/disease process, should be actively pursued. A working plan armed with practical action for achieving substantial change in the field is necessary as our infants and children enter the new millennium.

At the outset, the workshop reviewed the global burden of malnutrition and infectious diseases in children as evidenced from the not only alarming associated morbidity and mortality, but also from the ever-present threats to children’s well being. Low birth weight (LBW) and nutritional deficiencies, in particular, have adverse effects on child survival and development, and serve as an important risk factor for a number of adult diseases. Childhood malnutrition leads to growth deficiency in adult life, resulting in reduced work output and a decrease in the individual’s, and therefore society’s, development and productivity. The pathophysiology of malnutrition in the young child leads to changes in the malnourished child, many of which are reversible, except for those related to mental development. It is well established that there are strong influences of early malnutrition on subsequent mental development.

Malnutrition also affects susceptibility to infection, with documented evidence that cellular immunity, humoral immunity, and the complement system are markedly impaired in malnourished children. These changes, fortunately, are reversed with improved nutrient intake. The pathologic effect of infection on the development of an appropriate immune response, including the acute phase response, is well established. The clinical balance between microbes and the host defence system in malnourished children needs to be more clearly defined. Ultimately, nutrition modulated events in host-pathogen interactions are vital to understanding where exactly nutrition fits in. In particular, the role of micronutrients is important not only in the therapy but in the prevention and control of malnutrition.

The methodologies for evaluating the impact of nutrition on function includes identifying phenotype abnormalities, molecular defects, gene defects, and errors in gene transcription that occur in the malnourished host. There is clearly a need to use immunological tools available in the differential diagnosis of primary and secondary immune abnormalities. Under the subject of molecular and immunologic evaluation of nutritionally at-risk hosts, the mutual influences of nutrition on the immune re-
response and the effect of immunity on infection merit attention. A practical testing structure that includes a three-tiered system needs to be developed to obtain immunological information in different nutritional states. Relationships between body weight and immunity, the impact of the immune response on nutrient requirements and more specifically, the dietary management of immune incompetence are further areas of study.

The presentations then focused on various aspects of nutrition and immunity. Recent literature is emerging on “immune enhancing” formulas for feeding, a field which needs further research. The definition of adverse nutritional outcome, the immune assessment of botanicals and the development of diets to improve immune systems are subjects for further exploration. Expansion, quantification, and application of standardized immunologic tests become imperative, especially for human populations to understand the “host response” in realistic field situations. Development of specific bio-markers is required to enable translation of immunologic indices into specific benefits and outcomes. This has valuable implications in refining methodologies for assessing the immune system in states of malnutrition as well as disease. A public health approach must be adopted to address the multifactorial factors affecting the nutritional status of the host.

With respect to nutritional concerns such as low birth weight and its consequences on susceptibility to infection and immunity, the future research agenda calls for specific measures of immune function in this population of children at risk. Methodologies need further improvement, disaggregation of stunting and wasting and the development of practical and sustainable nutrition intervention for LBW infants are urgent priorities. The interrelationships of LBW and the immune deficiency response, and specifically, the impact of trace element merits further exploration of supplementation. The effects of varying types and levels of dietary lipids, specifically oils, were presented as areas for future research and practice. The alteration of host defence by specific fatty acids such as fish oil need to be resolved in humans in view of the marked nutritional benefits demonstrated in animal models. The manifestation of essential fatty acid deficiency is well known to impair the development of the immune system. Additional areas of exploration include the impact of a reduction of fat in human diets to enhance lymphocyte proliferation. Immune competence must be appreciated and understood in the context of endocrine reorganization of metabolism in PEM. Exercise, stress, and nutrition in the context of the immune response needs to be more clearly defined.

Micronutrient malnutrition in its broadest sense alters the immune system; the most affected responses include cell-mediated immunity, phagocyte function, the complement system, mucosal immunity, and the humoral immune response. The complexity and interdependence of the immune response and the sensitive and functional effects of nutrient intake and nutritional status on the immune response and susceptibility to infection was reviewed. Deficiencies of vitamins E and A have been shown to impair both the humoral and the cell-mediated responses in animal models, while in humans, indirect evidence indicates an increased susceptibility to infection. Serum vitamin E levels in children with AIDS reportedly are lower than those of HIV
controls. Lower serum tocopherol levels have also been reported to be associated with persistent human papillomavirus infection and pulmonary tuberculosis. Beneficial effects of vitamin A supplementation in reducing morbidity and mortality from measles in children with low vitamin A status exist. However, the benefits in infants as well as in the timing of the administration of the vitamin and the co-administration with childhood vaccines remain controversial. It has recently been shown to adversely affect antibody production and limit the protection afforded by vaccination. Vitamin A supplementation is beneficial in reducing the severity of diarrheal diseases, while the evidence for its impact on malarial infection is equivocal and needs further investigation. An update was also presented relating immunocompetent cells and cytokines, which are involved in the evolution and alterations of nutritional status to eating disorders and infectious diseases.

A new understanding has emerged into the mechanisms involved in the development of allergic sensitization. IgE antibodies are the host components responsible for triggering the allergic reaction. Allergic reactions can occur at any age, though regulation of the immune response is modified with maturation of the immune system through gradual changes of fetal and newborn responses. Infections, vaccines, and exposure to allergens influence the development of allergies. There is a need to develop suitable allergy prevention programs. In addition, there is a need to understand more closely who is at risk for developing allergies, what is the allergic risk, and what is the relationship between the history of allergy and skin test results. Demonstration among large-scale populations is required. Prevention of allergy and infectious disease in general populations is crucial over the long term.

The presentation of nutrition and infection reiterated that while much of the impact of infectious disease is reflected in the prevalence of malnutrition, the effects on nutritional status of chronic sub-clinical or “inapparent” infections have recently been appreciated. The metabolic effects of infection, which are mediated through cytokine activation and the ensuing amplification of host defense mechanisms, favor partitioning and redistribution of dietary and endogenous nutrients away from the maintenance of host nutritional status, body composition and growth toward support of the immune system and the acute phase response.

Infection confounds clinical assessment of nutritional status, blurs the distinction between dietary and infectious etiologies of impaired nutritional status, and thus complicates intervention. There is a need to learn more about the extent to which low-grade subclinical infections cause a re-orientation of amino acid metabolism, to the extent that growth and/or micronutrient status, are altered. While the relationship between infection, undernutrition, and growth retardation in infants and young children is well-established, there is a need to know whether growth retardation relates solely to anorexia and reduced food intake or whether there is an independent effect of infection/inflammation on growth and development. Mechanisms by which pro-inflammatory cytokines generate during infection and the mechanism by which inflammation impairs growth and development were summarized.

Gastrointestinal illnesses have a higher probability of occurring in children with pre-existing nutritional deficits. Episodes in malnourished children are more likely to
be of longer duration, greater severity and to lead to increased mortality in malnourished children. Results of community-based supplementation trials using zinc, vitamin A, or iron were described. Populations at high risk of zinc deficiency are likely to have a reduced incidence of diarrheal disease upon receiving supplemental zinc. Vitamin A may also confer similar benefits with regard to diarrhea, especially in populations with vitamin A deficiency. The possibility of iron supplementation increasing the risk of diarrhea, however, is uncertain.

Interactions of acute respiratory infections, measles, and nutritional status failed to show consistent beneficial impacts of vitamin A supplementation on the incidence, prevalence, or mortality from acute lower respiratory infections in children between the ages of 6 months and 5 years. While low plasma zinc appears to be associated with lower respiratory tract infections, zinc supplementation does not reduce childhood mortality. Malnutrition was clearly shown to affect HIV transmission and progression. Energy balance, food intake, nutrient malabsorption, cytokines, hormonal changes, and metabolic alterations all play a role in the etiology of malnutrition during HIV infection. Parasitic infections have also been shown to severely affect host nutrition as a result of the blood loss associated with malaria or hookworm infections and the enteropathy associated with gastrointestinal infections and its effects upon digestion and absorption.

All presentations were followed by fruitful discussions, which supported the viewpoint of the experts. This volume, which documents most of the issues and discussions of the workshop, is intended to provide valuable reference material for practitioners and researchers in the field of clinical nutrition. We hope that this will pave the way for newer and exciting research for translation at the field level so that childhood nutrition and health can be improved in countries throughout the world.

My co-chairman, Dr. Robert Suskind, and I thank all the participants for their enlightening contributions to this meeting. We are grateful to Prof. Ferdinand Haschke and Dr. Anne-Lise Carrié-Faessler, Nestec Ltd., Vevey, Switzerland, Mr. Giorgio Albertini, Nestlé Italiana S.p.A., Milano, Italy, and Mr. Thomas Coley, Nestlé (Thailand) Ltd., for their strong support of our endeavors towards making this workshop a meaningful one.

Prof. Kraisid Tontisirin, Thailand
Prof. Robert M. Suskind, USA
Foreword

Primary protein-energy malnutrition is still common in developing countries, and physicians and healthworkers throughout the world are becoming increasingly aware of malnutrition secondary to diseases such as AIDS. More than 50% of the world’s children who suffer from malnutrition live in Southeast Asia. It was, therefore, important to organize the 45th Nestlé Nutrition Workshop in Thailand, where clinical research in this field was coordinated by the World Health Organization (WHO) collaborating center at Mahidol University, Bangkok.

Substantial recent advances have increased our ability to understand and evaluate the immune system of children in health and disease. Clinical immunology has increased the ability to recognize immunological abnormalities and now permits better diagnosis and treatment of many immunological abnormalities due to infections with HIV or malnutrition.

The participants of the meeting proposed to establish international project platforms for further coordination of research in the field of nutrition and immunology. Among the priority projects were the development of a standardized questionnaire to evaluate diseases in relation to nutrition and immunology, as well as the standardization of field studies and animal work.

I thank the two Chairmen, Prof. Kraisid Tontisirin and Prof. Robert Suskind, for putting the program together and inviting experts to present their opinions on selected topics in the field of nutrition and immunity. The invited scientists from 32 countries substantially contributed to the discussions that are published in the book. Mr. Tom Coley’s team from Nestlé Thailand provided all logistical support and all participants enjoyed a taste of Thai hospitality. Dr. Carrié-Faessler from the Nutrition Division in Vevey, Switzerland was responsible for the scientific coordination. Her excellent cooperation with the Chairmen was fundamental to the success of this Workshop.

Professor Ferdinand Haschke, M.D.
Vice-President
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Children living in poor and unsanitary environments, younger children, and those sick, stunted, wasted, or consuming diets low in vitamin A were at a significantly higher risk of dying. In general, cell-mediated and nonspecific immunity are more sensitive than humoral immunity. Zinc-deficient infants showed a reduced risk of incidence of acute lower respiratory infection after zinc supplementation (relative risk: 0.30; 95% CI: 0.10, 0.92); among the non-zinc-deficient infants there were no significant differences between treatment groups. Zinc-deficient Bangladeshi infants showed improvements in growth rate and a reduced incidence of acute lower respiratory infection after zinc supplementation.