Micronutrients
and
health

Nutriview 2002/3

Contents in brief:

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Editorial:

An early start

Good nutrition is important for health at any age. There are two periods in life, however, when nutrition deficits have a greater influence: at the very beginning, during the critical stages of growth and development, and in old age, when physical, physiological and mental capacities begin to decline. It is understandable if most efforts concentrate on building a strong, healthy workforce to promote economic development in the short term. On the other hand, there are many reasons for implementing additional programs that look further ahead.

Strengthen the next generation

Improving the nutritional status of girls before they marry can help lower maternal and infant mortality, and prevent birth defects. Accumulating evidence supports the hypothesis that malnutrition during pregnancy not only impairs fetal growth, but also increases the risk for chronic diseases in the offspring later in life.

Proper nutrition during infancy is essential for the optimal development of vital organs and resistance to infection. In school children, nutritious foods help to improve school attendance and performance. This is also the best time to establish good dietary habits and a healthy lifestyle.

Prolong good health in old age

UN Secretary-General Kofi Annan told participants at this year's World Health Assembly on Aging in Madrid that the world's population of over-60-year-olds will increase over the next 50 years to almost two billion (compared to 600 million today). About 80% of them will live in Africa, Asia and Latin America. WHO Director-General Gro Harlem Brundtland warned of the resulting explosion in health costs unless the structure and priorities of current health systems are changed appropriately.

It is widely agreed that poor nutrition contributes to physiological and mental degeneration in old age, promoting the development and progression of disease. These changes can be delayed in a cost-effective way through better nutrition and a healthy lifestyle. The important thing is to make an early start, before it is too late. – *A. Bowley*

Feature:

Reducing the burden of infectious disease

Worldwide, infectious diseases are still the leading cause of death in children and young adults [1]. It is well known that poor nutritional status increases susceptibility to infections, and that micronutrient deficiencies impact adversely on immune function [2]. The vitamins A, D, E, C, B6, B12 and folate, as well as iron and zinc, play a particularly important role [3]. Most evidence supporting the immunomodulatory effects of micronutrients stems from observational and clinical data relating to undernutrition in developing countries. However, overnutrition and obesity have also been associated with impaired cellular immunity [4]. Two of the most susceptible segments of the population to both malnutrition and infection are children and elderly [5, 6]. This review therefore summarizes current knowledge about the effects of micronutrient interventions on infectious diseases in these groups.

Interventions in children

Vitamin A: Since 1993, it is known that use of high-dose vitamin A supplements in areas where vitamin A deficiency is a problem can significantly reduce mortality in children over the age of six months [7]. On the other hand, vitamin A seems to have little beneficial effect on morbidity and mortality associated with respiratory infections in children younger than 6 months [8].

Effects on frequency and severity of infections in children are inconsistent:

- In Ghana, vitamin A supplementation did not significantly affect the prevalence of diarrhea and respiratory infections, but supplemented children were less likely to need a clinic attendance or hospital admission [9].
- In Brazil, vitamin A prophylaxis reduced the number of diarrheal stools and episodes of severe diarrhea, as well as the need for hospitalization. Prevalence of pneumonia was not affected [10].
- In Tanzania, vitamin A supplementation resulted in a significant reduction (– 44%) in severe watery diarrhea during the year after discharge among children admitted to hospital with pneumonia [11].
- Reports from Indonesia and Ecuador suggested that vitamin A supplementation increases the prevalence of cough and other signs of respiratory infection [12, 13].

More research is needed to put these issues into better perspective, and to elucidate the role of vitamin A in specific infections such as malaria and shigellosis, or in the acute phase response to infection. It is also important to establish whether it would be better to use lower doses of vitamin A more frequently, either as a supplement or in fortified foods.

Iron: In iron deficiency anemia, cell-mediated immunity is impaired due to effects on iron-dependent enzymes such as myeloperoxidase and ribonucleotide reductase [14, 15]. Iron deficiency anemia in children has also been associated with low circulating levels of interleukin-2, indicating a possible role of iron in the cytokine cascade with consequences on resistance to infections [16]. However, various authors found an increased susceptibility to infection following iron supplementation [17, 18], while others

did not [19, 20]. Because the clinical significance of the association is uncertain, it is generally recommended to withhold or delay iron supplementation in the presence of severe protein energy malnutrition, in very-low-birthweight infants, and in the presence of bacterial infections [14]. Certainly, iron nutriture in relation to immune function and infection demands more intense scrutiny.

Zinc: Recent evidence indicates that poor zinc status is widespread, especially among populations with cereal-based diets [21]. Cereals contain little zinc, and its bioavailability is poor. Low plasma levels of zinc are associated with impairment of cell-mediated immunity and phagocytic function, and decreased antibody production [22]. Intervention studies among children at high risk of zinc deficiency in India [23], Peru [24] and Bangladesh [25] showed that zinc supplementation (20 mg daily) can significantly decrease the daily number of watery stools as well as the number of days with watery diarrhea. According to a pooled analysis of available data, zinc supplementation results in a significant reduction in diarrhea prevalence and severity, and a lower rate of treatment failure or death [26]. Supplements tended to be more beneficial among wasted males under 12 months of age who had low baseline levels of serum zinc.

Zinc supplements (10 mg daily) have also been associated with a significant reduction in acute lower respiratory tract infections [27], and in diarrhea, anorexia, vomiting, fever and cough [28]. Pooled analysis of seven clinical trials indicated a 50% reduction in the incidence of pneumonia [29], whereby a marked benefit was also observed in the short-term trials.

Interventions in elderly

Immunosenescence is defined as a state of immune dysfunction that contributes to an increased susceptibility of elderly individuals to infection and, possibly, to autoimmune disease [30]. It is associated with decreased delayed hypersensitivity, reduced interleukin-2 synthesis, decreased lymphocyte response to mitogens and antigens, low rates of seroconversion, and decreased antibody titre after vaccination [31]. Malnutrition, and especially deficiencies of antioxidant micronutrients, may accelerate the aging process [32, 33, 34]. The clinical significance of this still remains a subject of debate, however.

Chandra [35] investigated the effect of a multivitamin/multimineral supplement on immune function and clinical outcomes in 96 healthy elderly. Dosage was approximately one RDA for all micronutrients except vitamin E and beta carotene (administered at 4 x RDA). After one year, supplemented subjects showed an improvement in micronutrient status. This was associated with an increase in natural killer cell activity, percentage of CD4 T cells, antibody response to influenza vaccine, interleukin-2 production, and interleukin-2 receptor expression. Supplemented subjects suffered significantly fewer days of illness due to infection (23 days compared with 48 in the placebo group), and required antibiotics less often (18 days compared with 32 in the placebo group). In a second study using the same supplement over the same period of observation in 44 healthy elderly, Chandra was able to confirm these results [36]. A specially interesting finding was that the beneficial effect of supplementation on morbidity was greatest during the 7–12 month period of the trial, and that immune responses increased more in supplemented individuals who had one or more nutrient deficiencies at baseline. Jain also reported [37] that subjects who received a similar multivitamin/multimineral supplement for a year had significantly fewer days with symptoms of respiratory infection (14) than controls (29), and needed antibiotics less often (27 days compared with 58 by the control group).

While this type of study shows the benefit of supplementation in terms of defined clinical outcomes, it does not provide specificity concerning the contribution of individual nutrients. The studies by Girodon et al. on 90 [38] and 725 [39] institutionalized elderly are therefore useful in this respect. After two years of supplementation, those given a daily oral dose of 20 mg zinc and 100 µg selenium suffered fewer respiratory and symptomatic urinary tract infections, irrespective of whether they also took a supplement with vitamins C, E and beta-carotene or not. The vitamin supplement alone had no significant effect on infectious morbidity; none of the supplements improved survival. So, on the basis of current understanding, the specific contribution of individual micronutrients to clinical outcomes remains to be defined. However, accumulating evidence seems to indicate that a multivitamin supplement containing zinc and selenium may be beneficial.

Conclusion

The complex interaction between micronutrient status, immune function and infectious diseases will remain elusive and will lack adequate definition until such time that the underlying mechanisms are better understood and defined. The complexity of this interaction not only includes the role of micronutrient deficiencies on immune function itself, but also their role in enhancing microbial virulence, as best exemplified by the increased virulence of Coxsackie virus in people with selenium deficiency [40].

The available evidence supports the concept that the correction of micronutrient deficiencies can improve immune function, and can potentially provide very significant advantages in terms of disease prevention, reduced healthcare costs, and better quality of life.

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Technology:

Optimizing stability of vitamin A in fortified soybean oil

Recent surveys in Morocco established a 40% prevalence of vitamin A deficiency among preschool children. The Department of Health has therefore initiated measures, including social marketing, nutrition education, food fortification and micronutrient supplementation, to improve micronutrient intakes.

One of the measures already introduced is fortification of vegetable oil. To ensure optimal fortification levels, packaging and storage conditions, we measured the stability of retinyl palmitate added to refined, degassed soybean oil in two concentrations (33.3 and 66.6IU/g) and stored for six months under various conditions (room temperature and 42°C; daylight, fluorescent lighting and darkness). At monthly intervals, we measured changes in vitamin A concentration, as well as the acidity and oxidative status of the fortified product.

Light is critical factor

Levels of vitamin A fell continuously over the period of storage under all conditions. Results were similar in all samples stored in the dark, independent of initial vitamin concentration or storage temperature. However, much greater losses occurred in oils exposed to light. Oils stored in the dark retained more than 70% of the added vitamin A after six months; in those stored in daylight, retention was between 20% and 30%. Exposure to fluorescent lighting at high temperature resulted in an almost complete loss of vitamin A (84–90%) after only one month. Figure 1 shows the retention of vitamin A in soybean oil fortified with 66.6IU/g. Similar changes were found in the oils fortified with the lower concentration.

Oxidation status of the fortified oils stored at room temperature changed only slightly over the storage period, and was within the limits allowed by law. It was therefore not possible to determine the influence of oxidation on vitamin A degradation. Only minimal changes in acidity occurred over the six-month period (initial values: 0.06–0.12g oleic acid/100g oil; final values: 0.12–0.17).

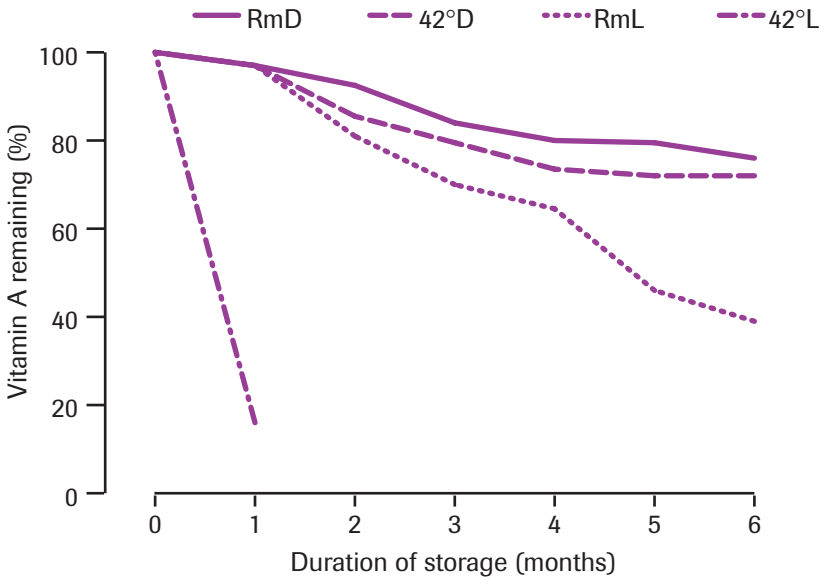
Dark storage recommended

These results show that fortification of soybean oil with vitamin A could be an appropriate way to increase vitamin A intakes by Moroccans, in addition to social marketing, nutrition education and micronutrient supplementation. It is, however, important that the fortified oil is stored in a dark place until it is used. The slightly greater vitamin losses caused by high temperatures, as might be encountered in tropical countries, could be compensated for with a 10% overage of fortificant.

Fortification of vegetable oils with vitamin A is a practical measure that should be considered by all those wishing to eliminate vitamin A deficiency. More research is needed to ensure that the containers in which these oils are sold offer optimal protection against the detrimental effects of light and air. – *Dr Mohamed Rahmani, Department of Food and Nutritional Science, Institute of Agriculture and Veterinary Science, Hassan II, Rabat (Email: m.rahmani@iav.ac.ma), Dr Hassan Aguenaou and Ms Lamyae Borghos, Faculty of Sciences, Ibn Tofail University, Kénitra, Morocco (Email: aguenaou@yahoo.com).*

A vegetable oil fortified with vitamin A (4000IU/100g) and vitamin D (400IU/100g) was recently introduced to the Moroccan market to help to increase Moroccans' intakes of these critical vitamins to adequate levels. Four tablespoons of this oil provide half of an adult's daily requirement in vitamin A and two-thirds of the requirement in vitamin D.

Fig 1: Stability of vitamin A in soybean oil (66.6IU vitamin A/g) stored for six months under various conditions (RmD: room temperature in the dark; 42°D: 42°C in the dark; RmL: room temperature in daylight; 42°L: 42°C in fluorescent light).



Technology:

World Food Programme introduces fail-safe flour fortification

The World Food Programme (WFP, the food aid agency of the United Nations) has set up its first flour mills for the production of fortified flour (*atta*) in Bangladesh. The special feature of these mills is that they can be run by the same undernourished people who benefit from them, without supervision by qualified food engineers.

What makes this possible is a special, simple, fail-safe measuring device that guarantees the correct composition of the atta. After milling, the wheat flour is mixed with a ready-made micronutrient premix (purchased, for food safety reasons, on the international market). To eliminate the risk of adding too much or too little of the premix, former WFP Country Director Pieter Dijkhuizen designed a special lid for the mixing bin. The lid is equipped with a cup measuring exactly 500 g. After the operator fills the cup with the micronutrient premix, it automatically rotates, dropping the premix into 500 kg flour, and the lid locks into place. It is now impossible to open the top of the mixer until the end of the mixing process, when the fortified flour has been transferred to the bagging machine.

In December 2001, WFP set up three of these mills as a pilot project for its Vulnerable Group Development (VGD) program. With an hourly production capacity of 1000 kg each, the mills are simple and inexpensive, and require very little maintenance—exactly what a poor country needs. Following this initial success, WFP has started an expansion scheme that will lead to a total of 40 mills over the entire country. The mills are managed by NGOs under an agreement with WFP; each plant is operated by about 20 VGD participants and NGO staff, who learn how to operate the equipment in just two weeks.

Filling the cup with micronutrient premix

As of 2002, women participants in the program receive 25 kg atta as their monthly food ration, instead of the wheat grain previously distributed since the VGD program started in the early 1980s. Locally produced atta will supply 500 000 Bangladesh women with the essential micronutrients (vitamins A and B-complex, including folate, iron and zinc) that are normally missing in their traditional diets. Through this intervention, WFP hopes to significantly reduce the 75% anemia rate and 50% vitamin A deficiency rate found among the poor women of Bangladesh.

Fortified biscuits for schoolchildren

Micronutrient premix is also the principal ingredient of the high-energy biscuits that are distributed as a mid-morning snack in Bangladesh primary schools. Each child in the program receives 75 g biscuits daily, supplying 80% of their vitamin and mineral requirements. The biscuits, produced by commercial bakeries under contract to WFP, are the first in Bangladesh to be fortified with micronutrients. In schools giving out these biscuits, attendance and enrolment rates improved immediately.

WFP has been carrying out school feeding programs for more than 40 years, and now stands as one of the world's largest providers of school meals and snacks. It began school feeding in Bangladesh as a pilot project for 225 000 schoolchildren in flood-damaged areas last year. This was later expanded into a national program, which currently reaches 825 000 schoolchildren, making it one of WFP's biggest school feeding programs. The number is expected to increase to more than 900 000 by 2004, as donor governments continue to support this project. WFP is now seeking donors to keep the program going after 2005. – *Heather Hill, Public Information Officer, World Food Programme, Asia.*

News in brief:

Information technology can advance nutrition in Africa

"The great and lightening strides made in the field of information technology (IT) could not have left the field of nutrition unaffected. As such, IT has made great inroads in nutrition not only in terms of faster, and mostly better, communication among nutrition professionals but also in education, training, research, policy formulation and implementation". With such words, Demetre Labadarios, Professor at the Dept. of Human Nutrition, University of Stellenbosch, South Africa, and Chairman of the Conference Advisory and Scientific Committee, welcomed participants to the ITANA (IT in the Advancement of Nutrition in Africa) meeting (Nairobi, Kenya, July 21–25, 2002).

ITANA 2002 was the first ever such conference on this important subject in

the African continent (initially under the auspices of the Swedish International Development Cooperation Agency, it also had the support of numerous other organizations). It brought together nutrition professionals from Africa and international experts to highlight the crucial needs for future growth of nutrition in Africa and to impart knowledge and selected take-home skills. Conference themes were: IT welcomes you to the future, e-nutrition in Africa, and information technology in practice.

The first theme included such issues as new technologies and new opportunities, communication and connectivity in Africa, e-learning, mobile technology, palm technology, connecting universities to the Web, local area networks, video conferencing, list serves and emailing, producing interactive teaching material, and creating websites. The second covered hardware, software and peopleware, where e-nutrition stands in Africa, IT and nutrition education, food composition databases, and the role of NGOs in African e-nutrition. The third presented practical applications of IT in nutritional status assessment, dietary assessment, food security, food safety, nutrition in emergency situations, nutrition advocacy, and nutrition networking.

In his closing remarks Professor Labadarios reiterated the overwhelming need to 'e-lighten' the relatively 'dark' Africa by focusing on IT connections and improving IT access. In doing so, nutrition programs and nutrition knowledge in Africa will grow and prosper. More details of the meeting can be accessed at: www.itana2002.org

Iron guidelines widely used

In May 2001, SUSTAIN issued a set of "*Guidelines for Iron Fortification of Cereal Food Staples*" to help program planners select and utilize iron fortificants appropriately. These guidelines were published in Nutriview 2001/3, posted on the websites of international nutrition organizations (Micronutrient Initiative, IDPAS, PAMM), and widely disseminated among international agencies, NGOs, donors and the private sector.

SUSTAIN has recently conducted a survey to assess how these guidelines are being implemented [1]. The responses show that the guidelines are being widely used. They have been distributed to all national offices of UNICEF, and will be included in a training package being prepared by the US Centers for Disease Control. Various countries (South Africa, Fiji, Indonesia, Brazil) and regional organizations (WHO Eastern Mediterranean Region, PanAmerican Health Organization, Asian Development Bank) have relied on the guidelines for input to establish their own fortification recommendations and regulations. Premix companies appreciate having a clear standard to communicate to customers, and are looking into supply issues.

SUSTAIN has since launched a comprehensive evaluation of iron powders currently used as fortificants. Results will be released as studies are completed. This work is being conducted with the participation of industry and the scientific community.

1. Usage report of "Guidelines for Iron Fortification of Cereal food Staples" SUSTAIN, April 2002.

Food aid compliance with fortification requirements improved

In October 2001, SUSTAIN issued a report assessing how US producers are complying with revised government requirements for fortification of food aid commodities that are distributed in developing countries under the USAID administered *Food for Peace* program (PL 480) [1]. An earlier study, the Micronutrient Assessment Project (reviewed in Nutriview 2000/3), had found shortcomings that resulted in low levels of micronutrients in many commodities.

This new review shows that major improvements have since been achieved at the production level, particularly for fortified wheat flour and bulgur. All producers now routinely test production lots for vitamin A (all fortified food products) and iron (blended foods). With few exceptions, mean vitamin A levels are now above the new minimum standards. The improvements to-date are attributed to:

1. new USDA standards and quality assurance requirements;
2. greater awareness by producers of the need to maintain adequate micronutrient levels;
3. changes made in the composition of fortification premixes;
4. improvements in premix handling during production of commodities.

While much progress has been made at the production level, there is still high variability in the micronutrient assay results between different laboratories. Another problem is how to reduce losses of highly labile micronutrients during cooking.

The report recommends a series of measures aimed at further improving the government's quality audit program, including instituting audit requirements for premix suppliers and compliance testing laboratories, and standardizing sampling and analytical testing procedures.

1. Report of "Micronutrient Compliance Review of Fortified PL 480 Commodities" SUSTAIN, October 2001. More details at <http://www.sustaintech.org/publications>

Events:

Enriching lives in West Africa, Abidjan, Côte d'Ivoire, October 15–17, 2002.

The goal of this meeting at the Novotel Plateau, Abidjan, is to engage a dialogue between private and public sectors to develop commitment and strategies to combat micronutrient malnutrition through food fortification in West Africa.

For more information, please contact Dr FZ Coulibaly, UNICEF. Tel: (225) 20 212258; Fax: (225) 20 227607; Email: fcoulibaly@unicef.org

21st IVACG Meeting, Marrakech, Morocco, February 3–7, 2003.

Tentative theme of theXXI International Vitamin A Consultative Group (IVACG) Meeting is "Improving the Vitamin A Status of Populations". It will be followed by symposia organized by the International Nutritional Anemia Consultative Group (INACG) and the International Zinc Consultative Group (IZiNCG).

For more information, please contact the IVACG/INACG Secretariat, ILSI Research Foundation, One Thomas Circle, NW, Ninth Floor, Washington, DC 20005, USA; tel: 202-659-9024; fax: 202-659-3617; e-mail: hni@ilsi.org or visit the ILSI website.

Micronutrients and infection

To protect the body against harmful bacteria, viruses, fungi and other parasites, the immune system provides mechanical, cellular and chemical barriers, and, when challenged, reacts with specialized cells and targeted reactions (Table 1).

Malnutrition impairs defences

Resistance to infection is closely linked to nutritional status (Figure 1). Individuals with nutrient deficiencies are more susceptible to infection; the infection is often more severe or prolonged, and is more likely to have a fatal outcome.

Infections can also precipitate micronutrient deficiencies in people who normally have an adequate status. During an infection, nutrient requirements increase considerably. On the other hand, nutrient intakes may be reduced, absorption impaired and excretion increased.

Table 1: Defences against infection

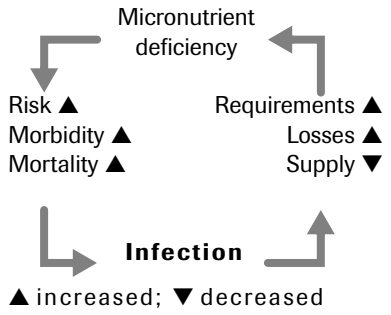
A. Nonspecific (innate)

1. Mechanical:
   - Epithelial barriers (skin, cornea, respiratory tract, gastrointestinal tract, genitourinary tract)
   - Tears, mucus, cough reflex
2. Cellular:
   - Macrophages and neutrophils in blood and tissues engulf and digest "foreign" particles (phagocytosis)
   - Lymphocytes in the blood (natural killer cells) kill "abnormal" cells
3. Chemical:
   - Acids (in sebum, stomach and inflamed tissues)
   - Enzymes (complement, lysozyme)
   - Cytokines (interleukins, interferons)
   - Free radicals
4. Thermic:
   - Febrile response

B. Acquired (adaptive)

1. Cell-mediated:
   - Antigens ("foreign" proteins) trigger production of T-lymphocytes (T-cells) in the thymus with various cytotoxic and regulatory functions.
2. Antibody-mediated:
   - Antigens activate B-lymphocytes (B-cells) to produce specific antibodies.

Fig 1: Interdependence of infection and nutrition



Effects of deficiency

Among micronutrients that play a critical role in defences against infection, those studied most extensively are zinc, selenium, copper, and the vitamins A, B_6, C and E. Some of the main effects on immune defences are shown in Table 2.

When to intervene

Groups most vulnerable to immunosuppressive effects of micronutrient deficiency are:

- infants/young children (immune system not fully developed), and
- elderly (age-related decline in immune response).

Infants and elderly are the most vulnerable (Photo Sight&Life)

Table 2: How deficiencies affect immune defences

Nutrient	Effects of deficiency
Vitamin A	Cell-mediated immunity ▼ Antibody production ▼ Barrier integrity ▼
Vitamin C	Phagocytosis ▼ Inflammatory response ▼ Barrier integrity ▼
Vitamin E	Cell-mediated immunity ▼ Antibody production ▼ NKC* activity ▼ Phagocytosis ▼ Cell membrane damage ▲
Vitamin B_6	Cell-mediated immunity ▼ Antibody production ▼ NKC activity ▼
Zinc	Cell-mediated immunity ▼ Barrier integrity ▼ NKC activity ▼ Phagocytosis ▼
Selenium	Antibody production ▼ Virus virulence ▲
Copper	Cell-mediated immunity ▼

* NKC = natural killer cell

Nutritional measures to support immune function can help reduce incidence/severity of infections, especially in the following circumstances:

- Measles (A)
- Malaria (B1, Zn, possibly A)
- Diarrhea (A, Zn)
- Respiratory infection (Zn, Se)
- Frail elderly (multivitamins).

Further reading

1. Present Knowledge in Nutrition. 8th Edition. B.A. Bowman, R.M. Russell, Eds. ILSI Press, Washington, DC. 2001.
2. Langseth L. Nutrition and Immunity in Man. ILSI Europe Concise Monograph Series. 1999.
3. Lymphatic system and immunity. Online Biology Book, Estrella Mountain Community College, Arondal, AZ. USA. <http://gened.emc.maricopa.edu/bio/BIO181/BIOBK/biobookIMMUN.htm>

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