

Malnutrition and health in developing countries

Olaf Müller, Michael Krawinkel

Abstract

MALNUTRITION, WITH ITS 2 CONSTITUENTS of protein–energy malnutrition and micronutrient deficiencies, continues to be a major health burden in developing countries. It is globally the most important risk factor for illness and death, with hundreds of millions of pregnant women and young children particularly affected. Apart from marasmus and kwashiorkor (the 2 forms of protein–energy malnutrition), deficiencies in iron, iodine, vitamin A and zinc are the main manifestations of malnutrition in developing countries. In these communities, a high prevalence of poor diet and infectious disease regularly unites into a vicious circle. Although treatment protocols for severe malnutrition have in recent years become more efficient, most patients (especially in rural areas) have little or no access to formal health services and are never seen in such settings. Interventions to prevent protein–energy malnutrition range from promoting breast-feeding to food supplementation schemes, whereas micronutrient deficiencies would best be addressed through food-based strategies such as dietary diversification through home gardens and small livestock. The fortification of salt with iodine has been a global success story, but other micronutrient supplementation schemes have yet to reach vulnerable populations sufficiently. To be effective, all such interventions require accompanying nutrition-education campaigns and health interventions. To achieve the hunger- and malnutrition-related Millennium Development Goals, we need to address poverty, which is clearly associated with the insecure supply of food and nutrition.

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Malnutrition continues to be a major public health problem throughout the developing world, particularly in southern Asia and sub-Saharan Africa.^{1–5} Diets in populations there are frequently deficient in macronutrients (protein, carbohydrates and fat, leading to protein–energy malnutrition), micronutrients (electrolytes, minerals and vitamins, leading to specific micronutrient deficiencies) or both.^{3,6–8}

The high prevalence of bacterial and parasitic diseases in developing countries contributes greatly to malnutrition there.^{3,5,9–11} Similarly, malnutrition increases one's susceptibility to and severity of infections, and is thus a major component of illness and death from disease.^{3,5,12–14} Malnutrition is consequently the most important risk factor for the burden of disease in developing countries.^{12,15} It is the direct cause of about 300 000 deaths per year and is indirectly responsible for about half of all deaths in young children (Fig. 1).^{5,15–17} The risk of death is directly correlated with the degree of malnutrition.^{17–22}

Poverty is the main underlying cause of malnutrition and its determinants (Fig. 2).^{23,24} The degree and distribution of protein–energy malnutrition and micronutrient deficiencies in a given population depends on many factors: the political and economic situation, the level of education and sanitation, the season and climate conditions, food production, cultural and religious food customs, breast-feeding habits, prevalence of infectious diseases, the existence and effectiveness of nutrition programs and the availability and quality of health services.^{3,5–7,25–27}

Here we provide an overview on the epidemiology, pathophysiology, clinical features, management and control of protein–energy malnutrition and micronutrient deficiencies in developing countries.

Protein–energy malnutrition

Epidemiology

Worldwide, an estimated 852 million people were undernourished in 2000–2002, with most (815 million) living in developing countries.⁵ The absolute number of cases has changed little over the last decade. However,

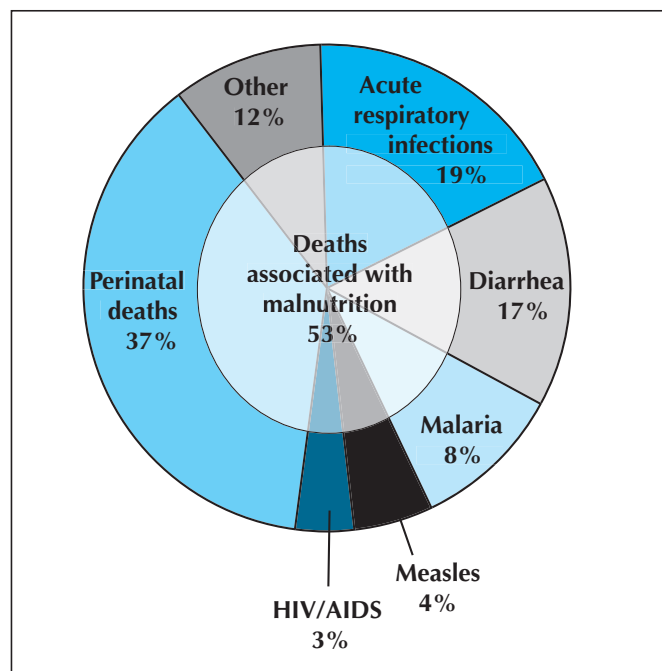


Fig. 1: Causes of death among children under 5 years of age, 2000–2003, worldwide.

while China had major reductions in its number of cases of protein–energy malnutrition during this period, this was balanced by a corresponding increase in the rest of the developing world.⁵

In children, protein–energy malnutrition is defined by measurements that fall below 2 standard deviations under the normal weight for age (underweight), height for age (stunting) and weight for height (wasting).⁶ Wasting indicates recent weight loss, whereas stunting usually results from chronic weight loss. Of all children under the age of 5 years in developing countries, about 31% are underweight, 38% have stunted growth and 9% show wasting.³ Protein–energy malnutrition usually manifests early, in children between 6 months and 2 years of age and is associated with early weaning, delayed introduction of complementary foods, a low-protein diet and severe or frequent infections.^{13,16,28} Table 1 shows the geographic distribution of protein–energy malnutrition among young children in developing countries.⁵

Severe malnutrition, typified by wasting, edema or both, occurs almost exclusively in children.³ Marasmus is defined as severe wasting; marasmic kwashiorkor, as severe wasting in the presence of edema; and kwashiorkor, as malnutrition with edema.^{3,29} The word kwashiorkor originates from the Ga language in Ghana; it implies “the disease that the

young child developed when displaced from his mother by another child or pregnancy.” Early marasmus, occurring in the first year of life, is frequently associated with contaminated bottle-feeding in urban areas.⁶

Pathophysiology and clinical features

After insufficient supply of protein, carbohydrates and fat, the next major cause of protein–energy malnutrition is severe and chronic infections — particularly those producing diarrhea, but also other diseases such as helminthic infections. The underlying mechanisms include decreased food intake because of anorexia, decreased nutrient absorption, increased metabolic requirements and direct nutrient losses.^{6,30}

The term protein–energy malnutrition describes the cause (i.e., the imbalance between nutrient supplies and requirements) more than the pathogenesis of starvation.³¹ The pathologic changes include immunologic deficiency in the humoral and cellular subsystem from protein deficiency and lack of immune mediators (e.g., tumour necrosis factor). Metabolic disturbances also play a role in impaired intercellular degradation of fatty acids because of carbohydrate deficiency. Synthesis of pigments in the hair and skin fails (e.g., hair colour may change and skin become hyperpigmented) because of a lack of substrate (e.g., tyrosin) and coenzymes.³²

Marasmus is diagnosed when subcutaneous fat and muscle are lost because of endogenous mobilization of all available energy and nutrients. Clinical aspects typically include a triangular face, primary or secondary amenorrhea, extended abdomen (from muscular hypotonia) and anal or rectal prolapse (from loss of perianal fat).³³

Kwashiorkor usually manifests with edema, changes to hair and skin colour, anemia, hepatomegaly, lethargy, severe immune deficiency and early death. Despite decades of debate, sometimes quite intense, the pathologic features of kwashiorkor are still not fully understood.³ The role of aflatoxins and insufficient protein intake has been stressed because the presence of edema and ascites seems related to reduced osmolarity in the blood, which is thought to be caused mostly by severe anemia.³⁴ It is puzzling that total protein concentrations in the plasma do not differ between children with marasmus and those with kwashiorkor.³⁵

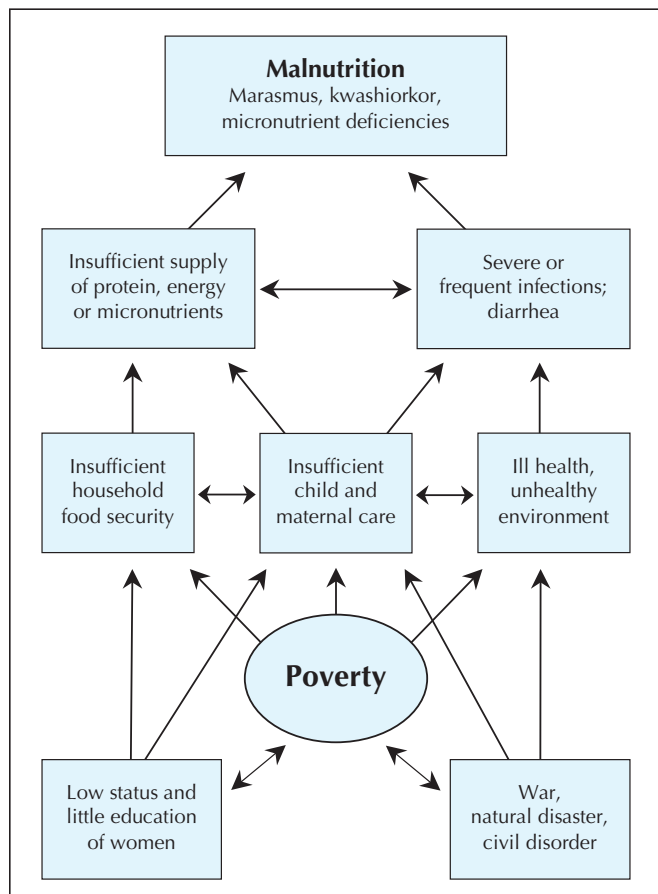


Fig. 2: Direct and indirect causes of malnutrition.

Table 1: Prevalences of protein–energy malnutrition among children under 5 years of age in developing countries, 1995

Region	Stunting, %	Underweight, %	Wasting, %
Africa	39	28	8
Asia	41	35	10
Latin America and Caribbean	18	10	3
Oceania	31	23	5

More recently, a role for free radicals in the etiology of kwashiorkor has been considered,³⁶⁻⁴³ but the findings of initial intervention studies have not been up to expectations. This may possibly be the result of inappropriate experimental design.^{44,45}

One essential aspect of severe protein-energy malnutrition is the fatty degeneration of such diverse organs as the liver and heart. This degeneration is not just a sign of severe malnutrition; it causes subclinical or overt cardiac insufficiency, especially when malnutrition is accompanied by edema.⁴⁶ If the myocardial insufficiency is not corrected, iatrogenic fluid and sodium overload quickly escalate it into cardiac failure. A second injurious aspect is the loss of subcutaneous fat, which markedly reduces the body's capacity for temperature regulation and water storage.⁴⁷⁻⁴⁹ As a consequence, malnourished children become dehydrated, hypothermic and hypoglycemic more quickly and severely than others. Finally, severe protein-energy malnutrition is associated with atrophy of the mucosa of the small bowel, leading to a loss of absorption as well as of digestion capacity.⁴⁸

Severe malnutrition is furthermore associated with chronic hypovolemia, which leads to secondary hyperaldosteronism, and further complicates fluid and electrolyte balance. Because the development of muscular dystrophy mobilizes much of the body's potassium, which is then lost through urinary excretion, affected children do not show signs of hyperkalemia.⁵⁰

Most children with severe protein-energy malnutrition have asymptomatic infections because their immune system fails to respond with chemotaxis, opsonization and phagocytosis of bacteria, viruses or fungi. So depressed is the system that the body cannot produce even the fever that is typical of inflammation.³³

Malnutrition is diagnosed by anthropometric measurements and physical examination. Where available, some laboratory investigations are helpful (Table 2).

Table 2: Laboratory features of severe malnutrition

Blood or plasma variables	The information derived
Hemoglobin, hematocrit, erythrocyte count, mean corpuscular volume	Degree of dehydration and anemia; type of anemia (iron/folate and vitamin B ₁₂ deficiency, hemolysis, malaria)
Glucose	Hypoglycemia
Electrolytes and alkalinity	
Sodium	Hyponatremia, type of dehydration
Potassium	Hypokalemia
Chloride, pH, bicarbonate	Metabolic alkalosis or acidosis
Total protein, transferrin, (pre-)albumin	Degree of protein deficiency
Creatinine	Renal function
C-reactive protein, lymphocyte count, serology, thick and thin blood films	Presence of bacterial or viral infection or malaria
Stool examination	Presence of parasites

Management and control

Despite the manifold dietary approaches to severe malnutrition that have been tried,^{51,52} patients with kwashiorkor (including marasmic kwashiorkor) continue to die much more frequently than those with marasmus alone.^{1,53,54} In sub-Saharan Africa and, increasingly, India, an additional concern is that many patients with severe malnutrition are also infected with HIV.⁵⁵

The high mortality indicates a need for a systematic approach to the severely malnourished patient that goes beyond an appropriate diet. To reduce mortality, a complex management scheme is pivotal.⁵⁶ Essential steps include a reduced intake of volume, protein and sodium during the first phase while emergency measures are taken to reduce the risk of hypoglycemia, hypothermia and dehydration.⁵⁷⁻⁵⁹ Oral, enteral and parenteral volume loads must be checked carefully to avoid imminent heart failure; continuous monitoring of central venous blood pressure is very desirable. In this early phase of rehabilitation, a protein intake exceeding 1 g/kg body weight in combination with impaired liver function (with breakdown of the urea cycle) and little urine excretion (a result of dehydration) easily exceeds the malnourished child's metabolic capacity to rid him- or herself of excess ammonia.

Although the effectiveness of the World Health Organization (WHO) 10-step scheme (shown in Table 3) is proven, there are still pitfalls for certain patients, such as those with extreme anemia and those who are close to cardiac failure.⁶⁰ The need for transfusions must be weighed against the risk of heart failure; combining transfusions with diuresis or applying exchange transfusion can resolve the dilemma. The WHO is currently revising its protocol to address 3 difficulties: the specific nutritional problems of

Table 3: Elements in the management of severe protein-energy malnutrition⁶⁰

Problem	Management
Hypothermia	Warm patient up; maintain and monitor body temperature
Hypoglycemia	Monitor blood glucose; provide oral (or intravenous) glucose
Dehydration	Rehydrate carefully with oral solution containing less sodium and more potassium than standard mix
Micronutrients	Provide copper, zinc, iron, folate, multivitamins
Infections	Administer antibiotic and antimalarial therapy, even in the absence of typical symptoms
Electrolytes	Supply plenty of potassium and magnesium
Starter nutrition	Keep protein and volume load low
Tissue-building nutrition	Furnish a rich diet dense in energy, protein and all essential nutrients that is easy to swallow and digest
Stimulation	Prevent permanent psychosocial effects of starvation with psychomotor stimulation
Prevention of relapse	Start early to identify causes of protein-energy malnutrition in each case; involve the family and the community in prevention

children with HIV infection or AIDS; different dietary regimens, particularly for infants younger than 6 months; and the limited availability of potassium–magnesium–zinc–copper preparations.⁶¹

The need to reduce the high sodium content (90 mEq/L) of common oral rehydration solutions for starving children has led to the production of ReSoMal (a 45-mEq/L rehydration solution for the malnourished). Now that a 75-mEq/L oral rehydration solution has become a standard treatment for nonsecretory diarrhea,^{62,63} there is less need for a special sodium-reduced rehydration preparation. Nevertheless, modification of the standard oral rehydration solution is recommended, with dilution to reduce the sodium concentration and enrichment with potassium, magnesium, zinc, copper and selenium.^{48,50,64} Finally, the severely malnourished child should always be given an effective broad-spectrum antibiotic, even in the absence of any signs of infection.^{65,66}

People's diets can benefit from preventive interventions ranging from income generation and nutritional education to maternal support, food supplementation and food prize subsidies. High immunization coverage and early and correct management of cases of infectious disease play major roles in the prevention and treatment of protein–energy malnutrition.¹³ In poor communities, the treatment of helminth infections 3 times per year improved child growth and development.¹⁵

Protein–energy malnutrition and diarrhea typically interact in a vicious cycle, but the control of diarrhea depends on more than medical help.^{30,67} Although growth monitoring is considered potentially important in child health clinics, there is often a lack of appropriate follow-up action.^{6,68–70} As much as functional health services may need to be made available, in order to address infectious diseases as a cause

of protein–energy malnutrition it is likewise important to promote breast-feeding, improve the water supply and sanitation, and educate people about hygiene.^{7,15,71–74} The multifaceted horizontal approach of the WHO-supported Integrated Management of Childhood Illness initiative has recently been shown to be an effective strategy.^{75,76}

Micronutrient deficiencies

Epidemiology

Deficiencies in iron, iodine, vitamin A and zinc are still major public health problems in developing countries, but vitamin C, D and B deficiencies have declined considerably in recent decades.^{7,77} Micronutrient deficiencies affect at least 2 billion people worldwide.⁵ As there are often no reliable biochemical indices of marginal micronutrient status, randomized controlled trials of supplementation are the best method to study the relation between micronutrient deficiencies and health parameters in human populations.⁷⁸

Globally, 740 million people are deficient in iodine, including up to 300 million with goitre and 20 million with brain damage from maternal iodine deficiency during their fetal development.^{7,79–81} About 2 billion people are deficient in zinc; 1 billion have iron-deficiency anemia. Vitamin A deficiency affects some 250 million, mainly young children and pregnant women in developing countries.^{14,82–102} The main causes worldwide of these 4 major micronutrient deficiencies are shown in Table 4.

Pathophysiology and clinical features

Not only do protein–energy malnutrition and micronutrient deficiencies overlap, but a lack of 1 micronutrient

Table 4: Causes, manifestations, management and prevention of the major micronutrient deficiencies

Nutrient	Essential for the production or function of	Causes of deficiency	Manifestations of isolated deficiency	Management and prevention
Iron	Hemoglobin Various enzymes Myoglobin	Poor diet Elevated needs (e.g., while pregnant, in early childhood) Chronic loss from parasite infections (e.g., hookworms, schistosomiasis, whipworm)	Anemia and fatigue Impaired cognitive development Reduced growth and physical strength	Foods richer in iron and with fewer absorption inhibitors Iron-fortified weaning foods Low-dose supplements in childhood and pregnancy Cooking in iron pots
Iodine	Thyroid hormone	Except where seafood or salt fortified with iodine is readily available, most diets, worldwide, are deficient	Goitre, hypothyroidism, constipation Growth retardation Endemic cretinism	Iodine supplement Fortified salt Seafood
Vitamin A	Eyes Immune system	Diets poor in vegetables and animal products	Night blindness, xerophthalmia Immune deficiency Increased childhood illness, early death Contributes to development of anemia	More dark green leafy vegetables, animal products Fortification of oils and fats Regular supplementation*
Zinc	Many enzymes Immune system	Diets poor in animal products Diets based on refined cereals (e.g., white bread, pasta, polished rice)	Immune deficiency Acrodermatitis Increased childhood illness, early death Complications in pregnancy, childbirth	Zinc treatment for diarrhea and severe malnutrition Improved diet

*Regular vitamin A supplementation is sometimes a part of immunization programs.

is typically associated with deficiencies of other micronutrients. The pathophysiology and manifestations of the main deficiencies are summarized in Table 4.

Iron is an essential part of hemoglobin, myoglobin and various enzymes. Its deficiency thus leads mainly to anemia, but also to several other adverse effects.^{7,15,23,83}

Lack of iodine reduces the production of thyroid hormone and increases that of thyroid-stimulating hormone. As a result, the thyroid gland becomes hyperplastic and goitrous, and hypothyroidism develops.^{3,7}

Vitamin A deficiency contributes to anemia by immobilizing iron in the reticuloendothelial system, reducing hemopoiesis and increasing susceptibility to infections. Vitamin A is essential for the functioning of the eyes as well as the immune system.^{83,103} Although diarrhea and related mortality has clearly been shown to be associated with vitamin A deficiency, the evidence for associations with acute infections of the lower respiratory tract and with malaria is much weaker.^{96,104,105}

Zinc is essential for the functioning of many enzymes and is thus involved in a large number of metabolic processes, including RNA and DNA synthesis.^{78,100} Consequently, zinc deficiency interferes with a variety of biological functions, such as gene expression, protein synthesis, skeletal growth, gonad development, appetite and immunity. Zinc plays a central role in the function of cells mediating unspecific immunity, such as neutrophils and natural killer cells, and is needed for specific immune processes, such as balancing T helper cell functions.¹⁰⁰ Zinc deficiency is a major determinant for diarrhea and pneumonia, but evidence about its role in malaria and growth retardation is conflicting.^{78,106–110}

Management and control

Foods with a high content of absorbable micronutrients are considered the best means for preventing micronutrient deficiencies.^{111–113} In communities where supplies of such foods are unavailable, specific preventive and curative interventions are needed.^{92,114}

There is growing consensus on the importance of multiple micronutrient interventions in populations with a high prevalence of malnutrition.^{112,115} However, synergistic and antagonistic interactions between micronutrients have to be taken into consideration during the development of appropriate formulations.^{115–125} A special kind of intervention is the provision of fat-based spreads (e.g., peanut butter) and “sprinkles” containing multiple micronutrients to be mixed with food.¹⁵ A principle limitation of all these interventions (except dietary diversification, of course) is their orientation toward single nutrients rather than plant ingredients (e.g., phytosterols and fibre), despite the desirability of plant ingredients for the prevention of cancer and cardiovascular diseases.

Micronutrient supplementation is usually provided through the existing health services and can be taken orally

or (more rarely) by injection. Priority should be given to vulnerable populations, such as pregnant women and children.¹²⁶ Supplementation is mandated in cases of a specific deficiency when other approaches are too slow. Although some micronutrients must be taken daily or weekly (e.g., iron and zinc), others can be stored in the body and need only be taken at intervals of months to years (e.g., vitamin A and iodine).^{7,127} However, modes of delivery, patient compliance and potential toxicity all need to be considered.^{7,15} Table 4 describes the principles of management and prevention of the 4 most common isolated micronutrient deficiencies.

Diet-based strategies are probably the most promising approach for a sustainable control of micronutrient deficiencies. Increasing dietary diversification through consumption of a broad variety of foods, preferably from home gardens and small livestock production, is effective.^{15,112} Households should be educated and supported to increase production of dark-green leafy vegetables, yellow and orange fruits, poultry, eggs, fish and milk.

A possible future strategy to prevent micronutrient deficiencies is to breed micronutrient-rich crops, through either conventional breeding techniques or genetic modification of existing crops. So far, however, the micronutrient concentrations achieved are very low. For vitamin A, nobody knows if β -carotene from the new “golden rice” variety is bioavailable and how much rice must be consumed to meet an individual’s needs, and iron concentrations in bio-engineered rice are no higher than those in natural varieties such as basmati or jasmine rice.¹²⁸

Conclusions and outlook

Because malnutrition has many causes, only multiple and synergistic interventions embedded in true multi-sectoral programs can be effective.¹²⁹ A variety of actions are needed, including agricultural and micronutrient interventions and the provision of safe drinking water and sanitation, education about and support for better diets, special attention to gender issues and vulnerable groups such as pregnant women and young children, and quality health services.^{15,130} Nutrition education about locally available protein- and micronutrient-rich plants is particularly effective and sustainable.^{131,132}

During the United Nations Millennium Summit in 2000, 147 heads of state adopted 8 development goals. The goal specifically about hunger is to reduce extreme poverty and hunger by the year 2015 by half relative to 1990 figures,¹³³ but progress toward the other 7 goals (universal primary education; empowerment of women; improved maternal health; decreased child mortality; advances in the prevention and management of HIV/AIDS, malaria and other diseases; environmental protection; and global partnerships for development) would directly or indirectly contribute to major reductions of malnutrition in developing countries.

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From the Department of Tropical Hygiene and Public Health, Ruprecht-Karls-University Heidelberg (Müller), and the Institute of Nutritional Sciences and Department of Pediatrics, Justus-Liebig-University Giessen (Krawinkel), Germany

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Correspondence to: Dr. Olaf Müller, Department of Tropical Hygiene and Public Health, INF 324, 69120 Heidelberg, Ruprecht-Karls-University Heidelberg, Germany; olaf.mueller@urz.uni-heidelberg.de