NUTRITIONAL DEFICIENCY AND IMBALANCES

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Nutrition has been clearly identified as a key factor in human development, not only as a conditioning factor for health but also as a determinant of quality of life throughout the life cycle and of overall development. Starvation, total or partial, affects the function of key organ systems such as respiratory, locomotor, muscular/skeletal, gastrointestinal, immune system, and related inflammatory response.

Malnutrition affects not only mortality and morbidity figures but also physical growth and intellectual development, school performance, effectiveness of education, productivity of labor, and virtually all aspects of human and social development. It is for

these reasons that present development efforts on a global basis include measures to improve nutrition and food security as an important component of poverty alleviation.

The causes of malnutrition encompass food, health, and caring strategies. Its underlying causes are divided into three groups: lack of access to nutritionally adequate food and diet, inadequate care for mothers and children, and other poor-health-related factors. The basic causes are human, economic, and organizational resource and control, current economic structures, and education policies.

Protein-energy malnutrition is quite widespread, especially in developing countries. Although the number of deaths that are directly attributable to protein-energy malnutrition in developing countries is small, the condition is an underlying cause of most death due to infections. The incidence and case-fatality rates of viral and bacterial infections are greatly increased by malnutrition. This is due to the altered host defense mechanism of the malnourished host and the increased nutritional requirements imposed by infection. The interaction between infection and nutrition is the major factor determining the high infant and childhood mortality rates throughout the developing world.

A concerted effort to address both the basic and underlying causes of malnutrition is necessary to end or significantly reduce malnutrition. Unfortunately, treating hundreds or thousands of affected people will not solve malnutrition. Unless society at large confronts this issue on a broader basis, the problem will continue. Access to adequate quality foods in the right quantities is a basic human right and a necessary precondition for health. Nutritionists should not be passive bystanders but rather be activists in this process. In the industrialized countries health workers need to be aware of secondary malnutrition as a conditioning factor delaying recovery from illness and as a major determinant of the quality of life of children, in particular, with chronic illness.

How can we get more nutrition action? We can learn from successful experiences of countries that have made significant progress in eradicating malnutrition. Components of success include: a) community awareness about the social and economic cost of malnutrition so that food and nutrition security gain a high priority in the political agenda of the country, b) technical consensus establishing that malnutrition is unacceptable to society, which should lead to a political base for action, c) establishment of adequate food, nutrition, and health as basic human rights that should be fulfilled for all, d) institutions for research and training that will train and form the human resources necessary for action. This includes community leaders, field workers, implementers of community level activities, trainers and researchers, and policy decisionmakers.

1. Introduction

Nutrition has been clearly identified as a key factor in human development, not only as a conditioning factor for health but also as a determinant of quality of life throughout the life cycle and in overall development. Starvation, total or partial, affects the function of key organ systems such as respiratory, locomotor, muscular/skeletal, gastrointestinal, immune system, and related inflammatory response

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The causes of malnutrition encompass food, health, and caring strategies. Its underlying causes are divided into three groups: lack of access to nutritionally adequate food and diet, inadequate care for mothers and children, and other poor-health-related factors. The basic causes are human, economic, and organizational resources and control, current economic structures, and education policies.

2. Protein-Energy Malnutrition (PEM)

Protein-energy malnutrition (PEM) is a problem affecting children and adults throughout the world. It is an important underlying cause of death and disability in developing countries. Protein deficiency affects the transport of many essential nutrients that are normally bound to protein carriers in the plasma, and thus correction of protein synthesis improves the apparent deficiency of specific nutrients.

An imbalance between dietary protein and energy intake is associated with relatively high insulin and low plasma cortisol levels, which impede mobilization of muscle protein from the peripheral to the visceral compartments. The resulting protein deficit primarily compromises protein synthesis in the liver. The related low levels of serum proteins, specifically albumin (edema), ferritin (anemia), ceruloplasmin (hair depigmentation), retinol-binding protein (xerophthalmia), and lipoproteins (fatty infiltration of the liver) may explain the clinical features of kwashiorkor best. Despite this florid symptomatology, which might suggest multiple specific nutrient deficiencies, kwashiorkor responds well to protein supplementation of the diet.

The protein deficiency affects the transport of many essential nutrients that are normally bound to protein carried in the plasma, and thus correction of protein synthesis improves the apparent deficiency of specific nutrients. Failure of antioxidant systems that depend on sulfur amino acid supply have also been implicated in the pathogenesis of kwashiorkor.
The number of deaths that are directly attributable to PEM in developing countries underestimates the significance of PEM . Malnutrition also contributes to prolonging illness and hospitalization and influences the final outcome of many specific disease processes by interfering with T-cell immune function and other host defense mechanisms. Liver metabolism, ventilatory function (as a result of muscle wasting), central nervous system function, cardiac contractility, and intestinal absorption also are adversely affected.

The consequences of malnutrition for growth and development depend on the timing, severity, and duration of the nutritional deficits. Children under six years of age are most susceptible because of their fast growth rate and increased vulnerability to diarrhea and other infectious diseases (see *Nutrition and Human Life Stages*).

2.1. Malnutrition and Growth of Children and their Survival Around the World

Malnutrition is a major determinant of growth for children around the world. The effect of malnutrition on growth depends on timing, severity, and duration of the nutritional deficits. Children under one year of age are most susceptible because of their fast growth rate and increased vulnerability to diarrhea and other infectious diseases, especially if they were weaned early from the breast and fed cow's milk-based formula (see *Nutrition and Human Life Stages*). The diagnosis of malnutrition is usually based on anthropometric criteria that document poor growth. The specific combination of environmental and host factors that are responsible for malnutrition in any one individual depends on the ecologic setting (see *Economic Development, Food, and Nutrition*).

PEM produces two classic clinical syndromes (marasmus and kwashiorkor) that represent the extremes of a wide spectrum of signs and symptoms. Marasmus is a severe form of malnutrition in infants who were weaned early from the breast or were not breastfed at all and who are offered formula that is inadequate to meet their nutritional needs and/or is contaminated with infectious agents. It most commonly occurs in urban poverty. The diagnosis of marasmus is usually based on anthropometric criteria that document poor growth. Marasmus usually occurs in the early years of life after bouts of diarrhea and inadequate food intake. Kwashiorkor occurs most commonly after the first year in children who have been breastfed or received adequate nutrition early in life, but later were fed low protein starchy diets. On a global basis, marasmus is the more prevalent form of PEM, although in some rural areas, especially in Africa, kwashiorkor may be commonly seen.

Mixed forms, or marasmic kwashiorkor, also occur and can be precipitated by severe infections in an already marasmic infant. The diagnosis is often made solely on the basis of clinical examination, but early forms of kwashiorkor can only be identified by laboratory measurements of serum proteins. Table 1 summarizes the principal features of both forms of protein-energy malnutrition. Marasmus, if severe, can be diagnosed by its physical findings. The most common signs are decreased body fat and skeletal muscle, and an appearance of "skin and bones" because of decreased adipose tissue. Typically an infant or child will look older than its chronologic age and will have a wasted face, decreased body weight and mass for length, and decreased muscle strength and tone. The milder forms of marasmus cannot be diagnosed by inspection alone and depend on physical measurements such as weight and height.

	Marasmus	Kwashiorkor
Frequency	• More frequent	• Seen mainly in rural areas
Cause	• Severe deprivation of both calories and protein	• Acute protein loss or deprivation
Clinical features	• Growth retardation • Weight loss • Muscular atrophy • Loss of subcutaneous tissue	• Edema • Skin lessions • Hair changes • Apathy, anorexia • Enlarged fatty liver • Decreased serum total proteins
Age	• Younger (since first months of life)	• Usually after one year of age

Recovery	• Slow recovery	• Rapid recovery with a high-protein diet

Table 1. Principal features of marasmus and kwashiorkor.

In a clinical setting marasmus occurs in most chronic diseases of childhood or where malabsorption is present, while kwashiorkor is often seen in patients after catabolic stress such as surgery or sepsis, especially when parenteral glucose is used as the sole source of nutritional support. In industrialized societies, it occurs mainly because of pathologic factors that interfere with nutrient absorption and utilization, rather than because of food scarcity. Clinical management of illness may sometimes preclude normal modes of feeding or appropriate nutritional support, despite the recognition that increased metabolic demands are usually present. Endogenous body stores may be utilized effectively for a period of days without overt body wasting in patients who were previously well nourished and not chronically ill. Preexisting undernutrition from any cause shortens this period of endogenous supply, however, and the risk of significant body mass wasting, even during initial management, is increased.

Marasmus is the end result of the body's response to inadequate energy and protein supply. The basic model is one of semistarvation. The adaptation to energy-protein deficit includes a series of steps to assure survival, maintaining the function of key organs while sacrificing the functions of organs less essential for life. Thus, body energy reserves in terms of glycogen, fat, and muscle are used as fuel. The depletion of liver glycogen occurs in less than a day of starvation. Fat from adipose tissue is utilized as a supply of energy while muscle protein serves as a source of amino acids to preserve visceral protein synthesis. Marasmus is considered by many a successful adaptation to decreased food intake. The marasmic lives at the expense of his or her tissues, while children with kwashiorkor are unable to mobilize their stores and therefore are considered maladapted. Loss of muscle in marasmus is not without cost. Weakness and poor muscle tone accompany it, and this may include ventilatory function. In severe forms of marasmus, immune function is also affected proportionately to the loss of body mass.

The most practical approach to the diagnosis of PEM is one based on a combination of weight and height. These serve to define acute weight for height deficit (wasting), and height for age loss as an index of chronic sequelae from early PEM (stunting). Table 2 presents an example of a functional classification. Additional methods to diagnose marasmus include measures of body composition such as skinfolds, total body potassium, body impedance, urinary creatinine excretion, and densitometry. These methods serve to confirm the decrease in body fat and muscle tissue. Kwashiorkor can be recognized by the presence of edema or better by the measurement of plasma proteins such as albumin or retinol-binding protein.

Stunting (Height for age) –2 SD or < 90% ---	Wasting (weight for age) –2 SD or < 80%	
	Over	Under
Over	Normal	Wasting

Under	Stunting	Stunting and wasting

Table 2. Functional classification of PEM (adaptation from Waterlow, Bull, WHO, 1977; 55:489–498)

The incidence and case-fatality rates of viral and bacterial infections are greatly increased by malnutrition. This is due to the altered host defense mechanism of the malnourished host and the increased nutritional requirements imposed by infection. The interaction between infection and nutrition is a major factor in determining infant and childhood mortality rates throughout the world.

Estimates based on increase mortality of children who are moderately or severely malnourished indicate that on average 56% of deaths in children less than five years old are related to malnutrition. Mortality risks are higher for those severely malnourished as measured by weight for age and also by weight for height, and the effect is more pronounced in those with low socioeconomic status. On a population basis since there are more moderately malnourished infants than severely malnourished, and the population-attributable risk of death is greater for moderate malnutrition.

2.2. Activity Level and Somatic Growth in Children

In children, activity level and somatic growth are the first signs of compromise from protein energy deficit. Because it is extremely difficult to evaluate changes in activity level, we rely on growth and body composition measures to detect early forms of PEM. During the first six months of life, growth may represent up to 30% of energy needs, but after 12 months it is only 5%. Reducing growth rate is only part of the effect of PEM; the decrease in activity level may be more significant.

If malnutrition occurs before 18 months of age, it will affect length as well as weight gain, which is recuperable with feeding, but length lost may not be recovered under most conditions. Length increments are mainly related to hyperplastic growth. Linear growth will be severely restricted if protein is absent from the diet during critical periods or if overall nutrition (including protein and energy) is insufficient. Catchup linear growth after malnutrition may not lead to full recovery in length, since arrests in cell division (hyperplastic growth) may not be reversible if the nutritional deprivation has been severe, prolonged, and has occurred early in life.

Weight gain during the first 12 months of life is dependent on both hyperplastic and hypertrophic growth; later on, hypertrophy is the main determinant of weight gain. Weight gain will be mainly affected by energy supply. Catchup recovery from weight loss is usually complete and fully reversible. Thus, stunting is a good marker of malnutrition in early life, moreover because linear growth during this stage of life is dependent on cell replication, other tissues that are undergoing cell division concurrently such as brain and muscle may also be affected. The relationship between poor linear growth (stunting) and mental development has been characterized by multiple studies. This association should not be construed as causal but indicative of concomitant damage.

Based on the information available from epidemiological studies and from controlled community-based studies the biological and social consequences of linear growth retardation can be summarized as follows:

- higher risk of death in childhood if environmental conditions are poor, higher risk of death from chronic disease in adults
- lower scores in cognitive tests and in school performance, higher rate of school failure
- decreased lean body mass, lower aerobic capacity affecting physical work and economic productivity
- higher risk of labor complications and of fetal growth retardation in short mothers, which phenomenon may explain the transgenerational effect.

These associations should not be considered as causally related, because both short stature and a specific consequence may be explained by common factor.

2.3. Adult Slimness—A New Form of Malnutrition

A new form of malnutrition has been recognized by nutritionists and public health specialists and has become a new priority in international policies (see *Malnutrition: Hunger and Satiety, Obesity and Anorexia*). Adult slimness used to be thought of as a useful form of adaptation to a modest diet and physical demands. However, new FAO analyses reveal a progressive reduction in physical capacity, with increased rates of sickness and premature mortality, as body weight declines below the lowest normal range of body weight, i.e. a height-adjusted index of weight (the body mass index or BMI) of 18.5.

New analyses reveal that 30% to 50% of adults in South Asia are underweight, and that 15% to 30% of Africans are affected, particularly during scourges of drought and civil strife. There are about a billion malnourished (wasted) adults worldwide. Adult malnutrition is exacerbated by intestinal infections that induce loss of appetite, but the principal cause is the lack of readily available food in sufficient quantity to sustain both normal body weight and the physical activity needed for all the tasks of daily life. The well-documented lethargy and reduced spontaneous physical activity of poor societies is not a cultural feature, but is induced by severe nutritional deprivation: it is a reflection of inadequate access to food. Adult work productivity may be affected by low BMI in addition to the effect of iron deficiency (see *Nutritional Assessment: Methods for Selected Micronutrients and Calcium* and *Food Modification and Impact on Nutrition*).

Another disadvantage of adult malnutrition in women is the impact on the outcome of pregnancy. Fetal growth depends both on how well nourished the mother was before conception and on how much weight she gains during pregnancy (see *Nutrition and Human Life Stages*). Low maternal BMI at the start of pregnancy leads to low birth-weight babies. In general, supplementation trials have not proved successful, with supplements to pregnant women not translating into a significant weight gain for the infant. Trials with women who are genuinely at risk, with a low body weight, and who are supplemented during late pregnancy with a balanced protein/energy supplement, do, however, show improvements in birth weight. Low maternal stature, i.e. height, also

influences the likelihood of having low birth-weight babies who grow slowly, so the important intergenerational implications of maternal size need now to be recognized

2.4. The Interaction between Infection and Nutrition

The interaction between infection and nutrition is the major factor determining the high infant and childhood mortality rates throughout the developing world. Malnutrition also contributes to prolonged hospital stay. It may influence the final outcome of many specific disease processes by interfering with T-cell immune function and other host defense mechanisms. Liver metabolism, ventilatory function (as a result of muscle wasting), central nervous system function, cardiac activity, and intestinal absorption are adversely affected.

Anthropometric and biochemical parameters that help define in-hospital undernutrition indicate that nutritional depletion may affect up to 50% of the hospitalized population. Repetitive stress periods necessitating prolonged hospitalization without adequate substrate support can clearly contribute to this occurrence. The low birth-weight infant, the malnourished infant, or the chronically ill child possess diminished reserves to handle acute substrate demands and may exhaust those reserves rapidly. Consequently, the risk of an evolving substrate deficit or unnoticed relative starvation based on protein-energy malnutrition may be high even during acute management.

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Bibliography

ACC/SCN (1997). *Update on the Nutrition Situation 1996*. Geneva: ACC/SCN.

FAO (1999b). *The State of Food Insecurity in the World*. Rome: FAO.

National Research Council (1989). *Recommended Dietary Allowances*, Tenth Edition. Washington, DC. National Academy of Sciences. [This is the main accepted source on nutrient allowances for the maintenance of good health.]

Tsang R.C. and Nichols B.L. (1988). *Nutrition During Infancy*, 440 pp. Philadelphia, PA, US: Hanley and Belfus. [This is a nutrition book that is informative, readable, entertaining, and, at times, provocative.]

UNICEF (1998). *The State of World's Children 1999*. Oxford, England: Oxford University Press. [An update on children's health through the world.]

World Health Organization (1996). *Trace Elements in Human Nutrition and Health*, 343 pp. Geneva, Switzerland: WHO. [This is a review which gives recommendations for monitoring and improving trace-element-related nutritional health in world populations.]

Ziegler E.E. and Filer L.J. (1996). *Present Knowledge in Nutrition*, 684 pp. Washington, DC: ILSI Press. [This is a comprehensive and up-to-date examination of nutrition science.]

Biographical Sketches

Ricardo Uauy, M.D., Ph.D., received his Medical Doctor degree from the University of Chile in 1972, completed residency training in Pediatrics at Children's Hospital in Boston (Harvard University) and a Neonatology fellowship at Yale New-Haven Hospital (Yale University). In 1977 he obtained his Doctoral degree in Nutritional Biochemistry from the Massachusetts Institute of Technology (MIT). He joined the Institute of Nutrition and Food Technology of the University of Chile (INTA) in 1977 as an Associate Professor and in 1981 became Professor of Nutrition and Pediatrics. He has directed INTA's training programs, the Clinical Research Center, the Division of Human Nutrition and Medical Sciences, and was resident-coordinator for UN University activities at INTA. From 1985 through 1990 he was Associate Professor of Nutrition and Pediatrics at the Center for Human Nutrition University at Texas Southwestern Medical Center at Dallas. He returned to INTA in 1991 to head the Area of Human Nutrition and Medical Sciences and direct the Clinical Nutrition Unit, in 1994 he became INTA's Director, and was reappointed in 1998. He is board certified (US) in Pediatrics and in Neonatal-Perinatal Medicine. He has served as President of the Chilean Nutrition Society and has participated as an expert at WHO/FAO on Protein and Energy Requirements, 1981, Fats and Oils in Human Nutrition, 1993, Food-Based Dietary Guidelines,1987, Obesity, 1997, Nutrition in the Elderly, 1998, Human Nutritional Requirements, 1998. He was a member of the NIH (US) Nutrition Study Section and is a member of the Scientific Advisory of the Novartis Foundation. He has contributed more than 200 scientific publications on various aspects of human nutritional needs in health and disease with an emphasis on neonatal nutrition. He has coedited two books, *Protein Energy Requirements Under Conditions Prevailing in Developing Countries* (Rand, Uauy, and Scrimshaw, 1983), and *Nutritional Needs of Preterm Infants: Scientific Basis and Practical Guidelines* (Tsang, Lucas, Zlotkin, and Uauy, 1993). He is on the editorial boards for *Early Human Development*, *Nutritional Biochemistry*, the *Journal of Pediatrics*, and the *Journal of Pediatric Gastroenterology and Nutrition*. Since 1995 he is a member of the UN ACC/SCN Advisory Group in Nutrition (AGN), and he has been chairman of the AGN since 1997. He was elected a member of the IUNS council in 1997. Present research interests include: essential fatty acids and CNS development in humans, copper deficiency and toxicity, protein energy needs in health and disease. He was elected as a member of the IUNS council in 1997 and designated President Elect by the IUNS general assembly in 2001. Received the McCollum award presented by the American Society for Nutritional Sciences (USA) in 2000. Was inducted as member of the Chilean Academy of Medicine in 2002. In July 2002 he became Professor and Chair in Public Health Nutrition at the London School of Hygiene and Tropical Medicine sharing his time between the UK and Chile. In 2003 he received the Lawton Chiles International Lecturer Award from the NIH (FIC/NICHD).

Eva Hertrampf, M.D., M.Sc., has a Medical Doctor Degree from the Universidad de Chile, and a Master's Degree in Human Nutrition at the Institute of Nutrition and Food Technology (INTA), Universidad de Chile. She is an Associate Professor at INTA since 1979. Her research, which was oriented toward child nutrition, is focused on the prevention of nutritional anemias, especially iron deficiency. She is also interested in other micronutrients such as zinc, copper, and folates. Her interest in the application of scientific knowledge to combat micronutrients deficiency has led her to accept expert consultancies in Latin America and Indonesia and Pakistan when asked by PAHO/WHO, UNICEF, and the International Atomic Energy Agency (IAEA-UN). She was invited to participate in the Steering Committee of the International Nutritional Anemia Consultative Group (INACG). She is currently in charge of INTA's training courses.