Chapter 46

Nutrition, Food Security, and Health

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MALNUTRITION AS THE INTERSECTION OF FOOD INSECURITY AND HEALTH INSECURITY

Undernutrition is usually an outcome of 3 factors, often in combination: household food supply, child-caring practices, and access to health and water/sanitation services. In famine and emergency settings, food shortage is the foremost factor, but in many countries with widespread undernutrition, food production or access to food might not be the most limiting factor. More important causes might be repeated childhood infections, especially diarrheal diseases linked with an unsafe environment and lack of exclusive breastfeeding, or inadequate complementary feeding practices, or the lack of time families have available for appropriate infant or maternal care. Figure 46-1 shows some of the many causal factors on the pathway to undernutrition and how they extend from household and community levels to national/international levels. Inequitable distribution of resources because of political, economic, and agricultural policies often denies families their right to adequate land, water, food, healthcare, education, and a safe environment, all of which can influence nutritional status.

Families with few economic resources who know how to care for their children and are enabled to do so can often use available food and health services to produce well-nourished children. If food resources and health services are not available in a community, or not utilized, or not accessible to some families, children might become undernourished. Undernutrition is not confined to low-income countries. It has been noted in chronically ill patients in neonatal and pediatric intensive care units in high-income countries and among patients with burns, HIV, tuberculosis, cystic fibrosis, chronic diarrhea syndromes, malignancies, bone marrow transplantation, and inborn errors of metabolism. Severe malnutrition has been reported in affluent communities in infants whose families believe in fad diets, and in infants with food allergies fed nutritionally inadequate foods such as rice "milk," which has a very low protein and micronutrient content (Fig. 46-2).

FOOD SECURITY

Food security exists "when all people, at all times, have access to sufficient, safe, nutritious food to maintain a healthy and active life." Four main dimensions of food security can be identified: **availability**, **access**, **utilization,** and **stability**. *Availability* refers to the supply of food (reflecting the level of food production, food stocks, and net trade). *Access* is at the household level, reflecting purchasing power, household food production, and food/cash transfers received through social safety net programs. The *utilization* dimension recognizes that even when a household has access to food it is not necessarily shared equitably within a household. *Stability* refers to being food secure at all times: Examples of situations that affect stability are the "lean seasons" before a harvest, natural disasters, political unrest, and rising food prices. To be food secure, all 4 dimensions must be met simultaneously.

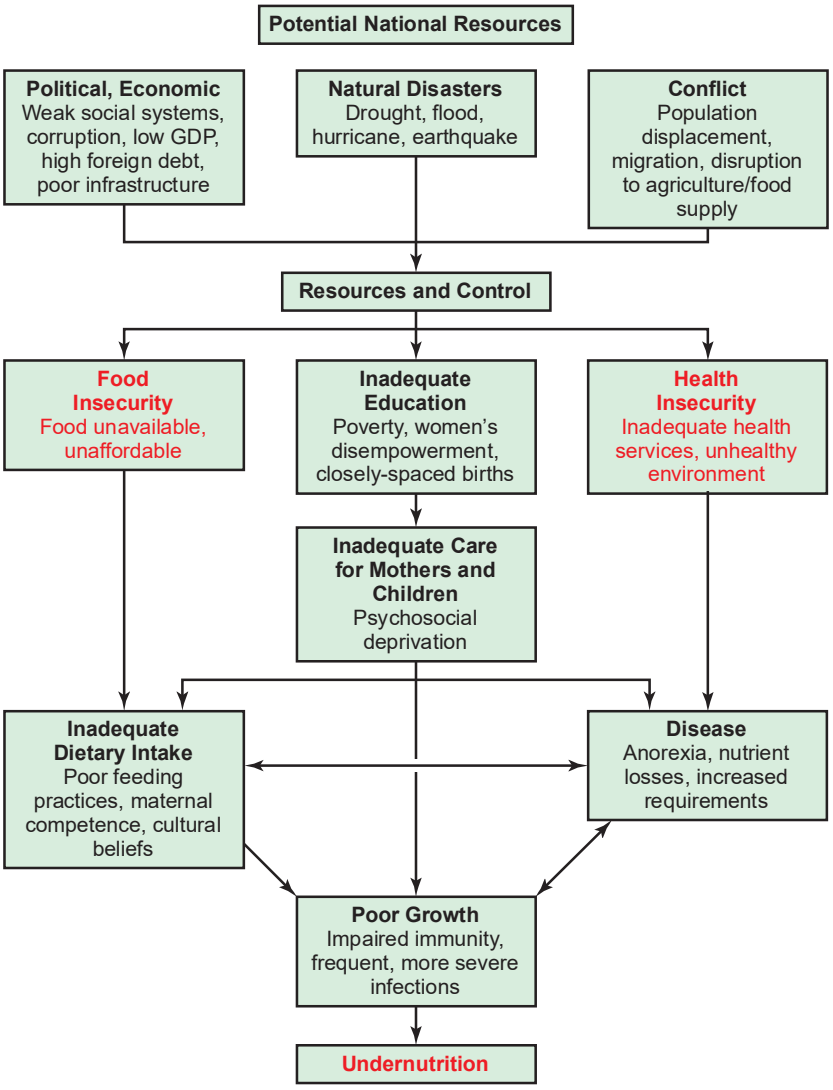

Figure 46-1 Basic, underlying, and immediate causes of undernutrition.

Measuring Food Insecurity

The most commonly used measurement of food insecurity is "undernourishment" (chronic hunger), and is the proportion of the population who are unable to meet daily energy requirements for light activities. It is an estimate calculated by the Food and Agriculture Organization (FAO) based on country-level Food Balance Sheets. It does not take nutrient adequacy into account, but has the advantage of being available for almost all countries annually (although with a time-lag) and assists in monitoring global trends. In addition, FAO measures food access by asking individuals about their experiences over the last 12 mo, such as whether they ran out of food, or skipped meals. The responses are graded from mild to severe food insecurity.

In 2011-2013, FAO estimated that about 842 million people, or 12% of the world's population, were undernourished, 98% of whom were in developing countries. The majority are rural poor subsisting on small plots of land or hired as laborers, and urban poor who lack the means to grow or buy food. Alongside the 0.84 billion people who are underfed, there are 1.5 billion who are overfed reflecting global inequalities, and the "double burden of malnutrition" in low- and middle-income countries.

Nutrition, Food Security, and Poverty

Household food security tracks income closely. With rising incomes, very poor households first increase their dietary energy intake to avert hunger. If incomes rise further there is a shift to more expensive staple foods and then to a more varied diet with a greater proportion of energy from animal sources, fruits and vegetables, fats and sugars, and less from cereals, roots and tubers. National economic growth tends to be accompanied by reductions in stunting, but economic growth can pass by the poor if they work in unaffected sectors, or are unable to take advantage of new opportunities because of lack of education, access to credit, or transportation, or if governments do not channel resources accruing from economic growth to healthcare, education, social protection, and other public services and infrastructure. There is good evidence that economic growth reduces poverty, but does not necessarily reduce undernutrition.

Food Security and Nutrition Targets

World leaders collectively agreed to 8 Millennium Development Goals (MDGs) in 2000. MDG 1 aimed to eradicate extreme poverty and hunger. The target to halve the proportion of people whose income is less than $1 per day was reached at the global level 5 yr ahead of the 2015 target. This was greatly helped by the progress made by China and India. Sub-Saharan Africa is unlikely to reach the target. The reductions in hunger are broadly consistent with those of poverty reduction, and rates of undernourishment in developing regions fell from 23.2% in 1990 to 14.3% in 2011-2013. Sub-Saharan Africa is the region least likely to achieve the target of halving undernourishment by 2015. The prevalence of underweight children (another MDG indicator of "hunger") fell from 29% in 1990 to 17% in 2012 for the

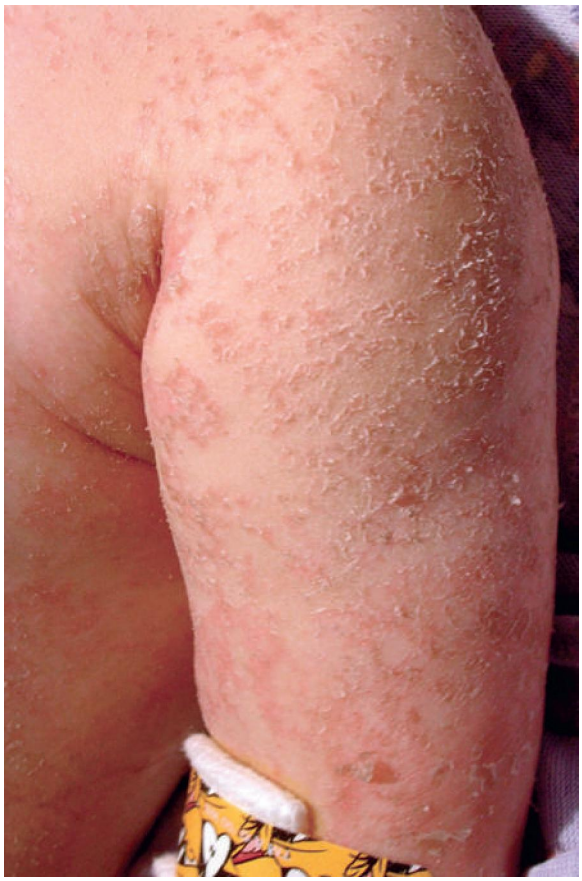

Figure 46-2 A 14 mo old girl with a "flaky paint" dermatitis. *(From Katz KA, Mahlberg MH, Honig PJ, et al: Rice nightmare: kwashiorkor in 2 Philadelphia-area infants fed Rice Dream beverage,* J Am Acad Dermatol *52(5 Suppl 1):S69–S72, 2005.)*

developing regions combined, but the rate of decline is thought insufficient to reach the global target by 2015. Rural children are almost twice as likely to be underweight as urban children, and the poorest quintile is almost 3 times as likely to be underweight as the richest quintile.

Sustainable Development Goals are expected to follow on from the MDGs. In addition, in 2012 the World Health Assembly agreed to 6 global nutrition targets to be reached by 2025, measured against a 2010 baseline, and the United Nations Secretary-General launched the Zero Hunger Challenge with 5 objectives that "would boost economic growth, reduce poverty and safeguard the environment" and "would foster peace and stability" (Table 46-1).

Table 46-1 Global Food Security and Nutrition Targets

ZERO HUNGER CHALLENGE OBJECTIVES	WORLD HEALTH ASSEMBLY GLOBAL NUTRITION TARGETS FOR 2025
• Access to an adequate and stable food supply for all • Elimination of stunting in children <2 yr and no malnutrition in pregnancy and early childhood • Sustainable food systems • Doubling of smallholder productivity and income, particularly for women • No loss or waste of food, and responsible consumption	• A 40% reduction in the number of stunted children <5 yr • A 50% reduction in anemia in women of reproductive age • A 30% reduction in low birthweight • No increase in childhood overweightness • Increase exclusive breastfeeding rates to at least 50% in the first 6 months • Reduce and maintain childhood wasting to less than 5%

Future Food Security

Between now and 2050 the world's population is expected to rise to around 9 billion, and an increase in food supply of 70-100% will be needed to feed this larger, more urban, and more affluent populace. Over this same period, the world's food supply is expected to diminish unless action is taken. Accelerating the decline in fertility rates and reducing overconsumption are basic, but difficult, actions to bridge the gap between increasing demand and diminishing supply. Equally challenging actions include limiting climate disruption, increasing the efficiency of food production, reducing waste, and reducing the demand for meat and dairy foods.

- *Limit climate disruption:* Drought, floods, and other extreme weather events are becoming more prevalent and destroy crops and livestock, often on a huge scale. Rising sea levels will lead to loss of productive land through inundation and salinization. Acidification of oceans will reduce marine harvests. Curbing greenhouse gas emissions is essential to minimize climate disruption, hence the aim to (a) cut fossil fuel use by at least half of present levels by 2050 so as to reduce CO_2 emissions and (b) change livestock husbandry and agronomic practices to reduce methane and nitrous oxide emissions.
- *Increase efficiency of food production*: Expanding the area of agricultural land to any large extent (e.g., by deforestation) is not a sustainable option because of adverse consequences on ecosystems and biodiversity, although some expansion of food production could be achieved by switching good quality land away from first-generation biofuels. For example, 40% of the U.S. corn harvest in 2010 went to biofuels. Efforts to increase the intensity of production need to be environmentally sustainable. These include optimizing yields by soil and water conservation, removal of technical and financial constraints faced by farmers, and breeding resource-efficient crops and livestock that are also climate-resilient and pest/disease-resistant.
- *Reduce waste*: Some 30-40% of food is wasted, either between harvesting and the market, or during retail, at home, and in the food service industry. Better transport and storage facilities in developing countries, less stringent sell-by dates, lower cosmetic standards for fruits and vegetables, and ending supersized portions would help reduce waste.
- *Change diets:* As wealth increases, so does the demand for processed foods, meat, dairy products, and fish. About one-third of global cereal production is fed to animals, so reducing consumption of meat from grain-fed livestock and increasing the proportion derived from the most efficient sources (pigs and poultry) would allow more people to be fed from the same amount of land.

UNDERNUTRITION

The greatest risk of undernutrition (underweight, stunting, wasting, and micronutrient deficiencies) occurs in the first 1000 days, from conception to 24 mo of age, and this early damage to growth and development can have adverse consequences in later life on health, intellectual ability, school achievement, work productivity, and earnings. Governments and agencies are therefore advised to focus interventions on this critical window of opportunity. For folate deficiency, which increases the risk of birth defects, this particular window of opportunity is before conception.

Measurement of Undernutrition

The term ***malnutrition*** encompasses both ends of the nutrition spectrum, from undernutrition to overweight. Many poor nutritional outcomes begin *in utero* and are manifest as low birthweight (LBW, <2,500 g). Preterm delivery and fetal growth restriction are the 2 main

nguyên nhân sinh nhẹ cân hàng đầu:
-nước phát triển: sinh non
-nước đang phát triển: chậm phát triển trong tử cung

Table 46-2 Classification of Undernutrition

CLASSIFICATION	INDEX	GRADING
Gomez (underweight)	90-75% of median weight-for-age	Grade 1 (mild)
	75-60%	Grade 2 (moderate)
	<60%	Grade 3 (severe)
Waterlow (wasting)	90-80% of median weight-for-height	Mild
	<70%	Severe
Waterlow (stunting)	95-90% of median height-for-age	Mild
	90-85%	Moderate
	<85%	Severe
WHO (wasting)	<–2 to >–3 SD weight-for-height	Moderate
	<–3	Severe
WHO (stunting)	<–2 to >–3 SD height-for-age	Moderate
	<–3	Severe
WHO (wasting) (for age group 6-59 mo)	115-125 mm mid-upper arm circumference	Moderate
	<115 mm	Severe

Figure 46-3 Measuring mid-upper arm circumference. *(Image courtesy of Nyani Quarmyne/Panos Pictures.)*

causes of LBW, with prematurity relatively more common in richer countries and fetal growth restriction relatively more common in poorer countries.

Nutritional status is often assessed in terms of anthropometry (Table 46-2). International standards of normal child growth under optimum conditions from birth to 5 yr have been established by the World Health Organization (WHO). To compile the standards, longitudinal data from birth to 24 mo of healthy, breastfed, term infants were combined with cross-sectional measurements of children ages 18-71 mo. The standards allow normalization of anthropometric measures in terms of *z* scores (standard deviation scores). A z-score is the child's height (weight) minus the median height (weight) for the age and sex of the child divided by the relevant standard deviation. The standards are applicable to all children everywhere, having been derived from a large multicountry study reflecting diverse ethnic backgrounds and cultural settings.

Height-for-age (or length-for-age for children <2 yr) is a measure of linear growth, and a deficit represents the cumulative impact of adverse events, usually in the first 1,000 days from conception, that result in *stunting*, or chronic malnutrition. A low height-for-age typically reflects socioeconomic disadvantage. A low **weight-for-height**, or *wasting*, usually indicates acute malnutrition. Conversely, a high weight-for-height indicates *overweight*. **Weight-for-age** is the most commonly used index of nutritional status, although a low value has limited clinical significance as it does not differentiate between wasting and stunting. Weight-for-age has the advantage of being somewhat easier to measure than indices that require height measurements. In humanitarian emergencies and some field settings, **mid-upper arm circumference** is used for screening wasted children (Fig. 46-3).

Body mass index (BMI) is calculated by dividing weight in kilograms by the square of height in meters. For children, BMI is age- and gender-specific. BMI-for-age can be used from birth to 20 yr and is a screening tool for thinness (<–2 SD), overweight (between +1 SD and +2 SD), and obesity (>+2 SD). To diagnose obesity, additional measures of adiposity are desirable as a high BMI can result from high muscularity, and not only from excess subcutaneous fat.

Micronutrient deficiencies are another dimension of undernutrition. Those of particular public health significance are vitamin A, iodine, iron, and zinc.

Vitamin A deficiency is caused by a low intake of retinol (in animal foods) or its carotenoid precursors, mainly beta-carotene (in orange-colored fruits and vegetables and dark green leaves) (see Chapter 48). The prevalence of clinical deficiency is assessed from symptoms and signs of xerophthalmia (principally night blindness and Bitot spots). Subclinical deficiency is defined as serum retinol concentration <0.70 μmol/L. Vitamin A deficiency is the leading cause of preventable blindness in children. It is also associated with a higher morbidity and mortality among young children.

Iodine deficiency is the main cause of preventable mental impairment (see Chapter 54). An enlarged thyroid (goiter) is a sign of deficiency. Severe deficiency in pregnancy causes fetal loss and permanent damage to the brain and central nervous system in surviving offspring (cretinism). It can be prevented by iodine supplementation before conception or during the first trimester of pregnancy. Postnatal iodine deficiency is associated with impaired mental function and growth retardation. The median urinary iodine concentration in children ages 6-12 yr is used to assess the prevalence of deficiency in the general population, and a median of <100 μg/L indicates insufficient iodine intake.

Iron-deficiency anemia is common in childhood either from low iron intakes or poor absorption, or as a result of illness or parasite infestation (see Chapter 54). Women also have relatively high rates of anemia as a result of menstrual blood loss, pregnancy, low iron intakes, poor absorption, and illness. Hemoglobin cutoffs to define anemia are 110 g/L for children 6-59 mo, 115 g/L for children 5-11 yr, and 120 g/L for children 12-14 yr. Cutoffs to define anemia for nonpregnant women are 120 g/L, 110 g/L for pregnant women, and 130 g/L for men.

Zinc deficiency increases the risk of morbidity and mortality from diarrhea, pneumonia, and possibly other infectious diseases (see Chapter 54). Zinc deficiency also has an adverse effect on linear growth. Deficiency at the population level is assessed from dietary zinc intakes.

Prevalence of Undernutrition

It is estimated that approximately 15% of births in low- and middle-income countries in 2010 were LBW. Rates of LBW are highest (26%) in southern Asia, and are twice those of sub-Saharan Africa. India accounts for approximately 40% of the world's low-weight births. Globally, in 2011 16% of children <5 yr of age were *underweight* (weight-for-age <–2 SD). The global prevalence of *stunting* (height-for-age <–2 SD) has declined from an estimated 40% to 26% over the last 20 yr, with the greatest reductions having taken place in Asia. Stunting prevalence is now highest in the African region (36% prevalence). *Wasting* (weight-for-height <–2 SD) affects 8% of children <5 yr, the prevalence having changed little over the past 2 decades. These figures represent 101 million underweight children, 165 million stunted children, and 52 million wasted children.

Asia carries 69% of the global burden of underweight children, 58% of the global burden of stunted children, and 70% of the global burden

< 5 tuổi:
- thiếu Vt A: 33%
- thiếu Iod: 29%
- thiếu kẽm: 17%
- thiếu sắt: 18%
=> Vt A thiếu nhiều nhất

of wasted children because of the combination of large population size and high prevalence. Africa carries most of the remaining global burden. For children <5 yr, the global prevalence is estimated to be 33% for *vitamin A deficiency*, 29% for *iodine deficiency*, 17% for *zinc deficiency*, and 18% for *iron-deficiency anemia*. Prevalence of micronutrient deficiencies tends to be highest in Africa. For pregnant women, the estimated prevalence of vitamin A deficiency is 15% and for iron-deficiency anemia 19%.

Rates of clinical deficiency of vitamin A in children <5 yr have been declining, probably as a result of high-dose vitamin A supplementation programs and measles vaccination (as measles leads to sizeable urinary loss of vitamin A), but subclinical deficiency remains widespread (more than 90 million children). Large-scale availability of iodized salt has reduced rates of iodine deficiency substantially, and iodized salt now reaches an estimated 70% of households. In contrast, progress in reducing rates of iron-deficiency anemia is slow, and rates remain largely static.

Consequences of Undernutrition

The most profound consequence of undernutrition is premature death (Table 46-3). Fetal growth restriction together with suboptimal breastfeeding in the first month of life contribute to 19% of all deaths in children <5 yr (1.3 million deaths/yr). When the effects of stunting, wasting and deficiencies of vitamin A and zinc are also considered, these 6 items jointly contribute to 45% of global child deaths (3.1 million deaths/yr), and many more are disabled or stunted for life. Anemia contributes to over one-quarter of maternal deaths.

The risk of child death from infectious diseases increases even with mild undernutrition, and as the severity of undernutrition increases, the risk increases exponentially (Table 46-4). Undernutrition impairs immune function and other host defenses, consequently childhood infections are more severe and longer lasting in undernourished children and more likely to be fatal compared with the same illnesses in well-nourished children. Also, infections can adversely affect nutritional status, and young children can quickly enter a cycle of repeated infections and ever-worsening malnutrition. Even for the survivors, physical and cognitive damage as a result of undernutrition can impact their future health and economic well-being. For girls, the cycle of undernutrition is passed on to the next generation when undernourished women give birth to LBW babies.

Fetal growth restriction and early childhood undernutrition also have consequences for adult chronic illness. LBW is associated with an increased risk of hypertension, stroke, and type 2 diabetes in adults. The increased risk is thought to reflect "fetal programming," a process by which fetal undernutrition leads to permanent changes in the structure and metabolism of organs and systems that manifest as disease in later life. The risk is exacerbated by low weight gain during the first 2 yr of life. The increased risk of adult chronic disease emanating from undernutrition in early life is a particular challenge to low-income countries with rapid economic growth.

Stunting before the age of 3 yr is associated with poorer motor and cognitive development and altered behavior in later years. The effect is

Table 46-3 Global Deaths in Children <5 yr Attributed to Nutritional Conditions

CONDITION	ATTRIBUTABLE DEATHS	% OF TOTAL DEATHS <5 YR
(a) Fetal growth restriction (<1 mo)	817,000	11.8
(b) Stunting (1-59 mo)	1,017,000	14.7
(c) Wasting (1-59 mo)	875,000	12.6
(d) Zinc deficiency (12-59 mo)	116,000	1.7
(e) Vitamin A deficiency (6-59 mo)	157,000	2.3
(f) Suboptimal breastfeeding (0-23 mo)	804,000	11.6
Joint effects of (a) + (f)	1,348,000	19.4
Joint effects of all 6 factors	3,097,000	44.7

From Black RE, Victora CG, Walker SP, et al. Maternal and child undernutrition and overweight in low- and middle-income countries, Lancet *382:427–451, 2013.*

Table 46-4 Hazard Ratios for All-Cause and Cause-Specific Deaths Associated with Stunting, Wasting, and Underweight in Children <5 yr

	DEATHS				
SD Score	All	Pneumonia	Diarrhea	Measles	Other Infections
Height/length-for-age					
<–3	5.5	6.4	6.3	6.0	3.0
–3 to <–2	2.3	2.2	2.4	2.8	1.9
–2 to <–1	1.5	1.6	1.7	1.3	0.9
≥–1	1.0	1.0	1.0	1.0	1.0
Weight-for-length					
<–3	11.6	9.7	12.3	9.6	11.2
–3 to <–2	3.4	4.7	3.4	2.6	2.7
–2 to <–1	1.6	1.9	1.6	1.0	1.7
≥–1	1.0	1.0	1.0	1.0	1.0
Weight-for-age					
<–3	9.4	10.1	11.6	7.7	8.3
–3 to <–2	2.6	3.1	2.9	3.1	1.6
–2 to <–1	1.5	1.9	1.7	1.0	1.5
≥–1	1.0	1.0	1.0	1.0	1.0

From Black RE, Victora CG, Walker SP, et al. Maternal and child undernutrition and overweight in low- and middle-income countries, Lancet *382:427–451, 2013.*

6-13 DQ (developmental quotient) points. Iodine and iron deficiencies also lead to loss of cognitive potential. Indications are that children living in areas of chronic iodine deficiency have an average reduction in IQ of 12-13.5 points compared with children in iodine-sufficient areas. Iron deficiency has a detrimental effect on the motor development of children <4 yr and on cognition of school-age children. The estimated deficit is 1.73 IQ points for each 10 g/L decrease in hemoglobin concentration.

Undernutrition can have substantial economic consequences for survivors and their families. The consequences can be quantified in 5 categories: increased costs of healthcare, either neonatal care for LBW babies or treatment of illness for infants and young children; productivity losses (and hence reduced earnings) associated with smaller stature and muscle mass; productivity losses from reduced cognitive ability and poorer school performance; increased costs of chronic diseases associated with fetal and early child malnutrition; and consequences of maternal undernutrition on future generations. The impact of nutrition on earnings appears to be independent of the effects of childhood deprivation.

Key Interventions

Interventions to address child undernutrition can be divided into those that address immediate causes (*nutrition-specific interventions*) and those that address underlying causes (*nutrition-sensitive interventions*) (Table 46-5). In the short-term, nutrition-specific interventions (e.g., salt iodization) can have substantial impacts even in the absence of economic growth, and micronutrient interventions (supplementation and fortification) are consistently ranked by economists of the Copenhagen Consensus Center as the most cost-effective investment. Increased attention is being given to nutrition-sensitive interventions as the best means of sustainably eliminating malnutrition, and to multisectoral policies that harness the synergism between the 2 types of intervention. Cross-sectoral linkages between agriculture, nutrition, and health are 1 example.

To reduce the adverse consequences of undernutrition on mortality, morbidity, and cognitive development, interventions must encompass both fetal and postnatal periods. Preventing LBW is essential, with emphasis on prevention of low maternal BMI and anemia, and in the longer term, prevention of low maternal stature. Other measures include smoking cessation, birth spacing, delaying pregnancy until after 18 yr of age, and intermittent preventive treatment of malaria. In the postnatal period, promotion and support of exclusive breastfeeding is a high priority. Although the Baby Friendly Hospital Initiative has a marked benefit on rates of exclusive breastfeeding in hospital, postnatal counseling from community workers or volunteers is needed to facilitate continuation of exclusive breastfeeding at home for 6 mo. Most studies show a lower risk of HIV transmission with exclusive breastfeeding than with mixed breastfeeding. The risk of transmission of HIV by breastfeeding is approximately 5-20% depending on duration, but can be reduced to <2% with antiretroviral drugs. Even without antiretroviral drugs, exclusively breastfed children of HIV-infected mothers in low-income countries have lower mortality than non-breastfed children, as the latter are at increased risk of death from diarrhea and pneumonia.

Interventions to improve infant feeding must be designed for the local setting and thus require careful formative research during their development. Messages should be few in number, feasible, and culturally appropriate. For complementary feeding, nutrient-rich, energy-dense mixtures of foods, and responsive feeding, are often emphasized. Where adequate complementary feeding is difficult to achieve and subclinical deficiencies are common, high-dose vitamin A supplementation every 6 mo in children <5 yr of age can reduce child mortality by 5-15% and zinc supplementation can reduce 1-4 yr mortality by 18%, diarrhea incidence by 13%, and pneumonia incidence by 19%. Monitoring of child growth provides an early alert to a nutrition or health problem but is only worthwhile if accompanied by good counseling and growth promotion activities. The impact of growth monitoring and promotion will be related to coverage, intensity of contact, health worker performance and communications skills, adequacy of resources, and the motivation and ability of families to follow agreed actions.

Table 46-5 Examples of Nutrition-Specific and Nutrition-Sensitive Interventions

NUTRITION-SPECIFIC INTERVENTIONS	NUTRITION-SENSITIVE INTERVENTIONS
• Promotion and support for exclusive breastfeeding for 6 mo, and continued breastfeeding for at least 2 yr • Promotion of adequate, timely, and safe complementary feeding from 6 mo • Increased micronutrient intake through dietary diversity • Micronutrient supplements for pregnant women (iron/folate) and young children (vitamin A, iron, zinc) in deficient areas • Zinc supplements to children during and after diarrhea (10-20 mg/day for 2 wk) • Prevention and treatment of severe acute malnutrition • Crop biofortification, food fortification, salt iodization • Reduced heavy physical activity in pregnancy	• Increased access to affordable, nutritious food; smallholder agriculture; credit and microfinance • Postharvest food processing and preservation • Vaccination against neonatal and childhood illness; access to healthcare • Improved water/sanitation and hygiene (e.g., handwashing with soap) • Education; women's empowerment; gender equality • Social protection (e.g., cash transfers) • Malaria prevention (vector control/bednets); intermittent preventive treatment during pregnancy and in children 3-59 mo • Birth spacing; delaying pregnancy until after 18 yr of age

Clinical Manifestations and Treatment of Undernutrition

Treatment of vitamin and mineral deficiencies is discussed in Chapters 48-54. Treatment of low birthweight and intrauterine growth restriction are discussed respectively in Chapter 97.

SEVERE ACUTE MALNUTRITION

Severe acute malnutrition is defined as severe wasting and/or bilateral edema.

Severe wasting is extreme thinness diagnosed by a weight-for-length (or height) below −3 SD of the WHO Child Growth Standards. In children ages 6-59 mo, a mid-upper arm circumference <115 mm also denotes extreme thinness: a color-banded tape (see Fig. 46-3) is a convenient way of screening children in need of treatment.

Bilateral edema is diagnosed by grasping both feet, placing a thumb on top of each, and pressing gently but firmly for 10 seconds. A pit (dent) remaining under each thumb indicates bilateral edema.

This definition of severe acute malnutrition distinguishes wasted/edematous children from those who are stunted, as the latter (although underweight) are not a priority for acute clinical care as their deficits in height and weight cannot be corrected in the short term. The previous name *protein-energy malnutrition* is avoided, as it oversimplifies the complex multideficiency etiology. Other terms are *marasmus* (severe wasting), *kwashiorkor* (characterized by edema), and *marasmic-kwashiorkor* (severe wasting + edema).

Children with severe acute malnutrition have had a diet insufficient in energy and nutrients relative to their needs. The magnitude of the deficits will differ depending on the duration of inadequacy, quantity and diversity of food consumed, presence of antinutrients (such as phytate), individual variation in requirements, and number and severity of coexisting infections and their duration. Infections can lead to profound nutrient deficits and imbalances: For example, amino acids are diverted to form acute-phase proteins and there are losses through diarrhea of potassium, magnesium, vitamin A, and zinc, and of glycine and taurine linked to small bowel bacterial overgrowth. Deficits can

also arise from increased nutrient utilization in response to noxae (e.g., cysteine and methionine to detoxify dietary cyanogens). Heterogeneity in the extent and nature of the deficits and imbalances, reflecting the diverse pathways to severe acute malnutrition, helps explain why affected children differ in their clinical presentation and degree of metabolic disturbance. Children who develop edematous malnutrition are more likely than nonedematous children to have been exposed to noxae that generate oxidative stress and/or to have greater deficits in free radical-scavenging antioxidants (glutathione, vitamins A, C, and E, and essential fatty acids) or cofactors (zinc, copper, selenium).

Clinical Manifestations of Severe Acute Malnutrition (Table 46-6)

Severe wasting (Fig. 46-4) is most visible on the thighs, buttocks, and upper arms, and over the ribs and scapulae where loss of fat and skeletal muscle is greatest. Wasting is preceded by failure to gain weight and then by weight loss. The skin loses turgor and becomes loose as subcutaneous tissues are broken down to provide energy. The face may retain a relatively normal appearance, but eventually becomes wasted and wizened. The eyes may be sunken from loss of retroorbital fat, and lachrymal and salivary glands may atrophy leading to lack of tears and a dry mouth. Weakened abdominal muscles and gas from bacterial overgrowth of the upper gut may lead to a distended abdomen. Severely wasted children are often fretful and irritable.

In *edematous malnutrition*, the edema is most likely to appear first in the feet and then in the lower legs. It can quickly develop into generalized edema affecting also the hands, arms, and face (Fig. 46-5). Skin changes commonly occur over the swollen limbs and include dark, crackled peeling patches (flaky paint dermatosis) with pale skin underneath that is easily infected. The hair is sparse and easily pulled out and may lose its curl. In dark-haired children, the hair may turn pale or reddish. The liver is often enlarged with fat. Children with edema are miserable and apathetic, and often refuse to eat.

Table 46-6 Clinical Signs of Malnutrition

SITE	SIGNS
Face	Moon face (kwashiorkor), simian facies (marasmus)
Eye	Dry eyes, pale conjunctiva, Bitot spots (vitamin A), periorbital edema
Mouth	Angular stomatitis, cheilitis, glossitis, spongy bleeding gums (vitamin C), parotid enlargement
Teeth	Enamel mottling, delayed eruption
Hair	Dull, sparse, brittle hair, hypopigmentation, flag sign (alternating bands of light and normal color), broomstick eyelashes, alopecia
Skin	Loose and wrinkled (marasmus), shiny and edematous (kwashiorkor), dry, follicular hyperkeratosis, patchy hyper- and hypopigmentation (crazy paving or flaky paint dermatoses), erosions, poor wound healing
Nails	Koilonychia, thin and soft nail plates, fissures, or ridges
Musculature	Muscle wasting, particularly buttocks and thighs; Chvostek or Trousseau sign (hypocalcemia)
Skeletal	Deformities, usually as a result of calcium, vitamin D, or vitamin C deficiencies
Abdomen	Distended: hepatomegaly with fatty liver; ascites may be present
Cardiovascular	Bradycardia, hypotension, reduced cardiac output, small vessel vasculopathy
Neurologic	Global developmental delay, loss of knee and ankle reflexes, impaired memory
Hematologic	Pallor, petechiae, bleeding diathesis
Behavior	Lethargic, apathetic, irritable on handling

From Grover Z, Ee LC: Protein energy malnutrition, Pediatr Clin N Am *56:1055–1068, 2009.*

Pathophysiology

When a child's intake is insufficient to meet daily needs, physiologic and metabolic changes take place in an orderly progression to conserve energy and prolong life. This process is called *reductive adaptation*. Fat stores are mobilized to provide energy. Later protein in muscle, skin, and the gastrointestinal tract is mobilized. Energy is conserved by reducing physical activity and growth, reducing basal metabolism and the functional reserve of organs and by reducing inflammatory and immune responses. These changes have important consequences:

- The liver makes glucose less readily, making the child more prone to hypoglycemia. It produces less albumin, transferrin, and other transport proteins. It is less able to cope with excess dietary protein and to excrete toxins.
- Heat production is less, making the child more vulnerable to hypothermia.
- The kidneys are less able to excrete excess fluid and sodium, and fluid easily accumulates in the circulation, increasing the risk of fluid overload.
- The heart is smaller and weaker and has a reduced output, and fluid overload readily leads to death from cardiac failure.
- Sodium builds up inside cells due to leaky cell membranes and reduced activity of the sodium/potassium pump, leading to excess body sodium, fluid retention, and edema.
- Potassium leaks out of cells and is excreted in urine, contributing to electrolyte imbalance, fluid retention, edema, and anorexia.
- Loss of muscle protein is accompanied by loss of potassium, magnesium, zinc, and copper.

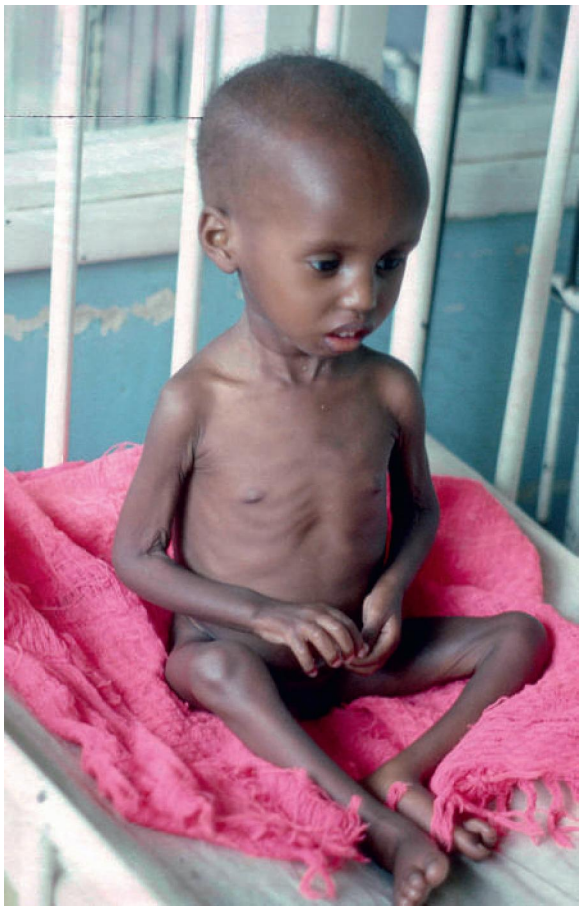

Figure 46-4 Child with severe wasting.

- The gut produces less gastric acid and enzymes. Motility is reduced, and bacteria may colonize the stomach and small intestine, damaging the mucosa and deconjugating bile salts. Digestion and absorption are impaired.
- Cell replication and repair are reduced, increasing the risk of bacterial translocation through the gut mucosa.
- Immune function is impaired, especially cell-mediated immunity. The usual responses to infection may be absent, even in severe illness, increasing the risk of undiagnosed infection.

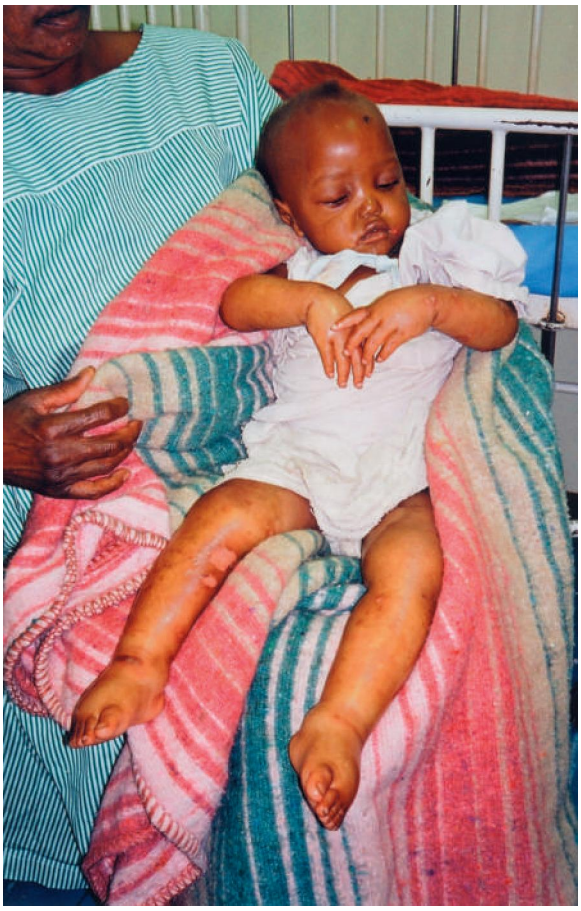

Figure 46-5 Child with generalized edema.

- Red cell mass is reduced, releasing iron which requires glucose and amino acids to be converted to ferritin, increasing the risk of hypoglycemia and amino acid imbalances. If conversion to ferritin is incomplete, unbound iron promotes pathogen growth and formation of free radicals.
- Micronutrient deficiencies limit the body's ability to deactivate free radicals, which cause cell damage. Edema and hair/skin changes are outward signs of cell damage.

When prescribing treatment it is essential to take these changes in function into account, otherwise organs and systems will be overwhelmed and death will rapidly ensue.

Principles of Treatment

Figure 46-6 shows the 10 steps of treatment, which are separated into 2 phases referred to as stabilization and rehabilitation. These steps apply to all clinical forms and all geographic locations, including North America and Europe. The aim of the stabilization phase is to repair cellular function, correct fluid and electrolyte imbalance, restore homeostasis, and prevent death from the interlinked triad of hypoglycemia, hypothermia, and infection. The aim of the rehabilitation phase is to restore wasted tissues (i.e., catch-up growth). It is essential that treatment proceeds in an ordered progression and that the metabolic machinery is repaired before any attempt is made to promote weight gain. Pushing ahead too quickly risks inducing the potentially fatal "refeeding syndrome."

Caregivers bring children to health facilities because of illness, rarely because of their malnutrition. A common mistake among healthcare providers is to focus on the illness and treat as for a well-nourished child. This approach ignores the deranged metabolism in malnourished children and can be fatal. Such children should be considered as severely malnourished with a complication, and treatment should follow the 10 steps. Two other potentially fatal mistakes are to treat edema with a diuretic and to give a high-protein diet in the early phase of treatment.

- ***Emergency treatment***: Table 46-7 summarizes the therapeutic directives for malnourished children with shock and other emergency conditions. Note that treatment of shock in these children is different (less rapid, smaller volume, different fluid) from treatment of shock in well-nourished children. This difference is because shock from dehydration and sepsis often coexist and are difficult to differentiate on clinical grounds. Thus one has to be guided by the response to treatment: children with dehydration respond to IV fluid whereas those with septic shock will not respond. Since severely malnourished children can quickly succumb to fluid overload, they must be monitored closely.
- ***Stabilization:*** Table 46-8 summarizes the therapeutic directives for stabilization steps 1-7. Giving broad-spectrum antibiotics (Table 46-9) and feeding frequent small amounts of F75 (a specially formulated low-lactose milk with 75 kcal and 0.9 g protein per

	Stabilization		Rehabilitation
	Day 1–2	Day 3–7	Week 2–6
1. Prevent/treat hypoglycemia	→		
2. Prevent/treat hypothermia	→		
3. Treat/prevent dehydration	→		
4. Correct imbalance of electrolytes	→	→	→
5. Treat infections	→	→	
6. Correct deficiencies of micronutrients	no iron →		with iron →
7. Start cautious feeding	→	→	
8. Rebuild wasted tissue (catch-up growth)		→	→
9. Provide loving care and play	→	→	→
10. Prepare for follow-up		→	→

Figure 46-6 The 10 steps of treatment for severe acute malnutrition and their approximate time frames.

Table 46-7 Emergency Treatment in Severe Malnutrition

CONDITION	IMMEDIATE ACTION
Shock • lethargic or unconscious and • cold hands Plus either: • slow capillary refill (longer than 3 sec) or • weak fast pulse	1. Give oxygen 2. Give sterile 10% glucose (5 mL/kg) by IV 3. Give IV fluid at 15 mL/kg over 1 hr, using: • Ringers lactate with 5% dextrose or • half-normal saline with 5% dextrose or • half-strength Darrow solution with 5% dextrose • if all of the above are unavailable, Ringer lactate 4. Measure and record pulse and respirations at the start and every 10 minutes If there are signs of improvement (pulse and respiration rates fall) repeat IV 15 mL/kg for 1 more hr. Then switch to oral or nasogastric rehydration with ReSoMal, 5-10 mL/kg in alternate hr (see Table 46-8 step 3) If there are no signs of improvement assume septic shock and: 1. Give maintenance fluid IV (4 mL/kg/hr) while waiting for blood 2. Order 10 mL/kg fresh whole blood and transfuse slowly over 3 hr. If signs of heart failure, give 5-7 mL/kg packed cells rather than whole blood 3. Give furosemide 1 mL/kg IV at the start of the transfusion
Hypoglycemia Blood glucose less than 3 mmol/L	See Table 46-8 step 1 for treatment
Severe dehydration	Do *not* give IV fluids except in shock See Table 46-8 step 3 for treatment
Very severe anemia Hb less than 4 g/dL	If very severe anemia (or Hb 4-6 g/dL AND respiratory distress): 1. Give whole blood 10 mL/kg slowly over 3 hr. If signs of heart failure, give 5-7 mL/kg packed cells rather than whole blood 2. Give furosemide 1 mL/kg IV at the start of the transfusion
Emergency eye care Corneal ulceration	If corneal ulceration: 1. Give vitamin A immediately (age <6 mo 50,000 IU, 6-12 mo 100,000 IU, >12 mo 200,000 IU) 2. Instill 1 drop atropine (1%) into affected eye to relax the eye and prevent the lens from pushing out

Table 46-8 Therapeutic Directives for Stabilization

STEP	PREVENTION	TREATMENT
1. Prevent/treat hypoglycemia blood glucose <3 mmol/L	Avoid long gaps without food and minimize need for glucose: 1. Feed immediately 2. Feed every 3 hr day and night (2 hr if ill) 3. Feed on time 4. Keep warm 5. Treat infections (they compete for glucose) *Note:* Hypoglycemia and hypothermia often coexist, and are signs of severe infection	If conscious: 1. 10% glucose (50 mL), or a feed (see step 7), or 1 teaspoon sugar under the tongue-whichever is quickest 2. Feed every 2 hr for at least the first day. Initially give ¼ of feed every 30 min 3. Keep warm 4. Start broad-spectrum antibiotics If unconscious: 1. Immediately give sterile 10% glucose (5 mL/kg) by IV 2. Feed every 2 hr for at least first day. Initially give ¼ of feed every 30 min. Use nasogastric (NG) tube if unable to drink 3. Keep warm. 4. Start broad-spectrum antibiotics
2. Prevent/treat hypothermia axillary <35°C (95°F); rectal <35.5°C (95.9°F)	Keep warm and dry and feed frequently 1. Avoid exposure 2. Dress warmly, including head and cover with blanket 3. Keep room hot; avoid draughts 4. Change wet clothes and bedding 5. Do not bathe if very ill 6. Feed frequently day and night 7. Treat infections	Actively rewarm 1. Feed 2. Skin-to-skin contact with carer ("kangaroo technique") or dress in warmed clothes, cover head, wrap in warmed blanket and provide indirect heat (e.g. heater; transwarmer mattress; incandescent lamp) 3. Monitor temperature hourly (or every 30 min if using heater) 4. Stop rewarming when rectal temperature is 36.5°C (97.7°F)
3. Prevent/treat dehydration	Replace stool losses 1. Give ReSoMal after each watery stool. ReSoMal (37.5 mmol Na/L) is a low-sodium rehydration solution for malnutrition	Do *not* give IV fluids unless the child is in shock 1. Give ReSoMal 5 mL/kg every 30 min for first 2 hr orally or NG tube 2. Then give 5-10 mL/kg in alternate hours for up to 10 hr. Amount depends on stool loss and eagerness to drink. Feed in the other alternate hour 3. Monitor hourly and stop if signs of overload develop (pulse rate increases by 25 beats/min and respiratory rate by 5 breaths/min; increasing edema; engorged jugular veins) 4. Stop when rehydrated (3 or more signs of hydration: less thirsty, passing urine, skin pinch less slow, eyes less sunken, moist mouth, tears, less lethargic, improved pulse and respiratory rate).

Continued

Table 46-8 Therapeutic Directives for Stabilization—cont'd

STEP	PREVENTION	TREATMENT
4. Correct electrolyte imbalance—deficit of potassium and magnesium, excess sodium		1. Give extra potassium (4 mmol/kg/day) and magnesium (0.6 mmol/kg/day) for at least 2 wk (see Table 46-12) *Note:* Potassium and magnesium are already added in Nutriset F75 and F100 packets
5. Prevent/treat infections	Minimize risk of cross-infection 1. Avoid overcrowding 2. Wash hands 3. Give measles vaccine to unimmunized children age >6 mo	Infections are often silent. Starting on the first day, give broad-spectrum antibiotics to all children. 1. For antibiotic choices/schedule see Table 46-9 2. Ensure all doses are given, and given on time 3. Cover skin lesions so they do not become infected *Note:* Avoid steroids as they depress immune function
6. Correct micronutrient deficiencies	*Note:* Folic acid, multivitamins, zinc, copper, and other trace minerals are already added in Nutriset F75 and F100 packets	Do *not* give iron in the stabilization phase 1. Give vitamin A on day 1 (under 6 mo 50,000 units; 6-12 mo 100,000 units; >12 mo 200,000 units) if child has any eye signs of vitamin A deficiency or has had recent measles. Repeat this dose on days 2 and 14 2. Folic acid 1 mg (5 mg on day 1) 3. Zinc (2 mg/kg/day) and copper (0.3 mg/kg/day).These are in the electrolyte/mineral solution and Combined Mineral Vitamin mix (CMV) and can be added to feeds and ReSoMal 4. Multivitamin syrup or CMV
7. Start cautious feeding		1. Give 8-12 small feeds of F75 to provide 130 mL/kg/day,100 kcal/kg/day and 1-1.5 g protein/kg/day 2. If gross edema, reduce volume to 100 ml/kg/day 3. Keep a 24-hr intake chart. Measure feeds carefully. Record leftovers 4. If child has poor appetite, coax and encourage to finish the feed. If unfinished, reoffer later. Use NG tube if eating 80% or less of the amount offered 5. If breastfed, encourage continued breastfeeding but also give F75 6. Transfer to F100 when appetite returns (usually within 1 wk) and edema has been lost or is reduced 7. Weigh daily and plot weight.

Table 46-9 Recommended Antibiotics*

	GIVE
If no complications	Amoxicillin oral 25 mg/kg twice daily for 5 days
If complications (shock, hypoglycemia, hypothermia, skin lesions, respiratory or urinary tract infections, or lethargy/sickly)	Gentamicin (7.5 mg/kg IV or IM) once daily for 7 days *and* Ampicillin (50 mg/kg IV or IM) every 6 hr for 2 days, then oral amoxicillin (25-40 mg/kg) every 8 hr for 5 days

*Local resistance patterns may require these to be adjusted: Ensure that there is Gram-negative cover.
If specific infections are identified, add appropriate antibiotics.
For persistent diarrhea/small bowel overgrowth, add metronidazole (7.5 mg/kg oral) every 8 hr for 7 days.

100 mL to which potassium, magnesium, and micronutrients are added), will reestablish metabolic control, treat edema, and restore appetite. The parenteral route should be avoided; children who lack appetite should be fed by nasogastric tube, as nutrients delivered within the gut lumen help in its repair. Table 46-10 gives recipes for preparing the special feeds, and their nutrient composition. Two recipes for F75 are shown: one requires no cooking, the other is cereal-based and has a lower osmolality, which may benefit children with persistent diarrhea. F75 is also available commercially in which maltodextrins replace some of the sugar and to which potassium, magnesium, minerals, and vitamins are already added.

Dehydration status is easily misdiagnosed in severely wasted children, as the usual signs (such as slow skin pinch, sunken eyes) may be present even without dehydration. Rehydration must therefore be closely monitored for signs of fluid overload. Serum electrolyte levels can be misleading because of sodium leaking from the blood into cells and potassium leaking out of cells. Keeping the intake of electrolytes and nutrients constant (see Table 46-9) allows systems to stabilize more quickly than adjusting intake in response to laboratory results.

Table 46-11 gives a recipe for the special rehydration solution used in severe malnutrition (ReSoMal). Therapeutic Combined Mineral Vitamin mix (CMV) contains electrolytes, minerals, and vitamins and is added to ReSoMal and feeds. If unavailable, potassium, magnesium, zinc, and copper can be added as an electrolyte/mineral stock solution (Table 46-12 provides a recipe) and a multivitamin supplement given separately.

◆ ***Rehabilitation***: The signals for entry to this phase are reduced/minimal edema and return of appetite.

A controlled transition over 3 days is recommended to prevent the "refeeding syndrome." After the transition,

Table 46-10 Recipes for Milk Formulas F75 and F100

	F75[b] (STARTER)	F75[c] (STARTER) (CEREAL-BASED)	F100[d] (CATCH-UP)
Dried skimmed milk (g)	25	25	80
Sugar (g)	100	70	50
Cereal flour (g)	—	35	—
Vegetable oil (g)	30	30	60
Electrolyte/mineral solution (mL)[a]	20	20	20
Water: make up to (mL)	1000	1000	1000
Content/100 mL			
Energy (kcal)	75	75	100
Protein (g)	0.9	1.1	2.9
Lactose (g)	1.3	1.3	4.2
Potassium (mmol)	4.0	4.2	6.3
Sodium (mmol)	0.6	0.6	1.9
Magnesium (mmol)	0.43	0.46	0.73
Zinc (mg)	2.0	2.0	2.3
Copper (mg)	0.25	0.25	0.25
% Energy from protein	5	6	12
% Energy from fat	32	32	53
Osmolality (mOsm/L)	413	334	419

Whisk at high speed to prevent oil from separating out.
[a]See Table 46-12 for recipe, or use commercially available therapeutic Combined Mineral Vitamin mix (CMV).
[b]A comparable F75 can be made from 35 g dried whole milk, 100 g sugar, 20 g oil, 20 mL electrolyte/mineral solution, and water to 1000 mL; or from 300 mL full cream cow's milk, 100 g sugar, 20 g oil, 20 mL electrolyte/mineral solution, and water to 1000 mL.
[c]This lower-osmolality formula may be helpful for children with dysentery or persistent diarrhea. Cook for 4 min.
[d]A comparable F100 can be made from 110 g dried whole milk, 50 g sugar, 30 g oil, 20 mL electrolyte/mineral solution, and water to 1000 mL; or from 880 mL full cream cow's milk, 75 g sugar, 20 g oil, 20 mL electrolyte/mineral solution, and water to 1000 mL.

Table 46-11 Recipe for Rehydration Solution for Malnutrition (ReSoMal)

INGREDIENT	AMOUNT
Water	2 L
WHO-ORS	One 1-L sachet*
Sucrose	50 g
Electrolyte/mineral solution†	mL

ReSoMal contains 37.5 mmol sodium and 40 mmol potassium/L
*Sachet contains 2.6 g sodium chloride, 2.9 g trisodium citrate, 1.5 g potassium chloride, 13.5 g glucose.
†See Table 46-12 for recipe, or use commercially available therapeutic Combined Mineral Vitamin mix (CMV).

Table 46-12 Recipe for Concentrated Electrolyte/Mineral Solution*

INGREDIENT	g	mol/20 mL
Potassium chloride: KCl	224.0	24 mmol
Tripotassium citrate	81.0	2 mmol
Magnesium chloride: $MgCl_2$. $6H_2O$	76.0	3 mmol
Zinc acetate: Zn acetate.$2H_2O$	8.2	300 µmol
Copper sulfate: $CuSO_4$. $5H_2O$	1.4	45 µmol
Water: make up to	2500 mL	

Add 20 mL when preparing 1 L of feed or ReSoMal.
*Make fresh each month. Use cooled boiled water.

unlimited amounts should be given of a high-energy, high-protein milk formula such as F100 (100 kcal and 3 g protein per 100 mL), or ready-to-use therapeutic food (RUTF), or family foods modified to have comparable energy and protein contents.

To make the transition, for 2 days replace F75 with an equal volume of F100 and then increase each successive feed by 10 mL until some feed remains uneaten (usually at around 200 mL/kg/day).

After the transition, give 150-220 kcal/kg/day and 4-6 g protein/kg/day and continue to give potassium, magnesium, and micronutrients. Add iron (3 mg/kg/day). If breastfed, encourage continued breastfeeding.

Children with severe malnutrition have developmental delays, so loving care, structured play, and sensory stimulation during and after treatment are essential to aid recovery of brain function.

Community-based treatment: Many children with severe acute malnutrition can be identified in their communities before medical complications arise. If these children have a good appetite and are clinically well, they can be rehabilitated at home through community-based therapeutic care, which has the added benefit of reducing their exposure to nosocomial infections and providing continuity of care after

recovery. It also reduces the time caregivers spend away from home and their opportunity costs, and can be cost-effective for health services.

Figure 46-7 shows the criteria for inpatient versus outpatient care. To maximize coverage and compliance, community-based therapeutic care has 4 main elements: community mobilization and sensitization; active case-finding; therapeutic care; and follow-up after discharge.

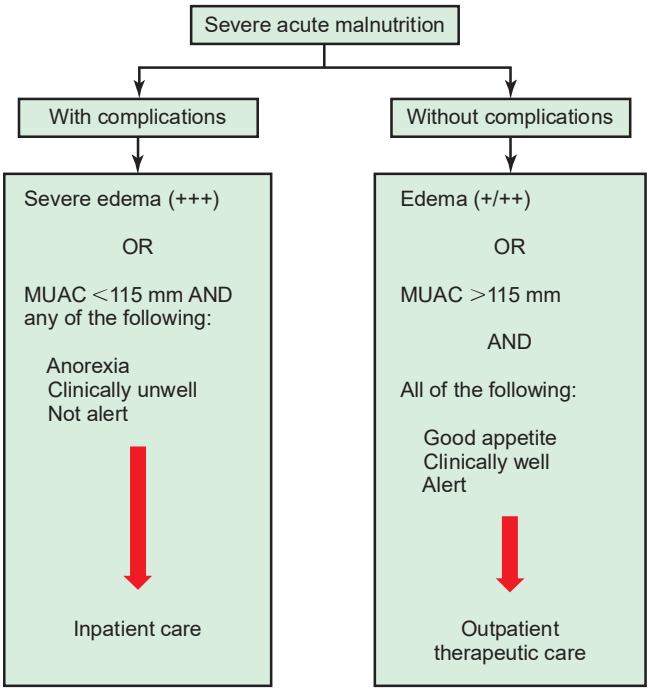

Figure 46-7 Flow diagram for inpatient and outpatient care in the child with severe acute malnutrition. MUAC, Mid upper arm circumference.

Community-based therapeutic care comprises steps 8-10, plus a broad-spectrum antibiotic (step 5). RUTF is usually provided, especially in times of food shortage. RUTF is specially designed for rehabilitating children with severe acute malnutrition at home. It is high in energy and protein and has electrolytes and micronutrients added. The most widely used RUTF is a thick paste that contains milk powder, peanuts, vegetable oil, and sugar. Pathogens cannot grow in it because of its low moisture content. Hospitalized children who have completed steps 1-7 and the transition can be transferred to community-based care for completion of their rehabilitation, thereby reducing their hospital stay to about 7-10 days.

Bibliography is available at Expert Consult.

46.1 Refeeding Syndrome

Robert M. Kliegman

Refeeding syndrome can complicate the acute nutritional rehabilitation of children who are undernourished from any cause (Table 46-13). Refeeding syndrome is rare when the WHO recommendations for the treatment of malnutrition are followed (see Chapter 46); however, it may follow overly aggressive enteral or parenteral alimentation. Malnutrition usually has normal serum electrolytes but is associated with intracellular electrolyte depletion. When excessive carbohydrates are administered, the resultant increase in serum insulin levels may produce hypokalemia, hypophosphatemia, and hypomagnesemia. The hallmark of refeeding syndrome is the development of severe hypophosphatemia after the cellular uptake of phosphate during the 1st wk of starting to reefed. Serum phosphate levels of ≤0.5 mmol/L can produce weakness, rhabdomyolysis, neutrophil dysfunction, cardiorespiratory failure, arrhythmias, seizures, altered level of consciousness, or sudden death. Phosphate levels should be monitored during refeeding, and if they are low, phosphate should be administered during refeeding to treat severe hypophosphatemia (see Chapter 55.6).

Table 46-13 Clinical Signs and Symptoms of Refeeding Syndrome

HYPOPHOSPHATEMIA	HYPOKALEMIA	HYPOMAGNESEMIA	VITAMIN/THIAMINE DEFICIENCY	SODIUM RETENTION	HYPERGLYCEMIA
Cardiac Hypotension Decreased stroke volume **Respiratory** Impaired diaphragm contractility Dyspnea Respiratory failure **Neurologic** Paresthesia Weakness Confusion Disorientation Lethargy Areflexic paralysis Seizures Coma **Hematologic** Leukocyte dysfunction Hemolysis Thrombocytopenia **Other** Death	**Cardiac** Arrhythmias **Respiratory** Failure **Neurologic** Weakness Paralysis **Gastrointestinal** Nausea Vomiting Constipation **Muscular** Rhabdomyolysis Muscle necrosis **Other** Death	**Cardiac** Arrhythmias **Neurologic** Weakness Tremor Tetany Seizures Altered mental status Coma **Gastrointestinal** Nausea Vomiting Diarrhea **Other** Refractory hypokalemia and hypocalcemia Death	Encephalopathy Lactic acidosis Death	Fluid overload Pulmonary edema Cardiac compromise	**Cardiac** Hypotension **Respiratory** Hypercapnia Failure **Other** Ketoacidosis Coma Dehydration Impaired immune function

Data from Kraft MD, Btaiche IF, Sacks GS: Review of RFS, Nutr Clin Pract *20:625–633, 2005. From Fuentebella J, Kerner JA: Refeeding syndrome,* Pediatr Clin North Am *56:1201–1210, 2009.*

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