

11.4 Severe malnutrition

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ESSENTIALS Severe malnutrition is the consequence of systemic deficiency of energy and nutrients over a prolonged period: in children development is stunted and the individual is at risk of fatal (often clinically 'silent') infection and other illnesses. It is a medical and societal emergency: mortality is high, despite attempts to provide appropriate care. When severe malnutrition affects several individuals in a society, it reflects a state in which basic needs and justice are not met. Severe malnutrition may also result from clinical disorders affecting a single person with gastrointestinal disease, poor appetite, or reduced food intake for other reasons.

Classification The World Health Organization has produced guidelines for facility-based care of patients suffering severe malnutrition. Prompt classification into groups of differential risk assists in the identification of those requiring the most immediate clinical care (severe acute malnutrition, defined as weight for height more than three standard deviations below the reference mean, a mid upper-arm circumference of less than 115 mm, or the presence of oedema of both feet) and in monitoring the outcomes of intervention. Low height for age indicates long-term malnutrition or poor health (stunting); low weight for height or low mid upper-arm circumference indicate recent or continuing severe weight loss (wasting); low weight for age implies stunting and/or wasting.

Prevention Malnutrition is a preventable condition and the early identification of those at risk (e.g. by regular weighing) and the implementation of interventions (e.g. advice and demonstration of best practice in child care and feeding) which correct underlying problems and prevent further deterioration is central to strategies for effective care. Childhood malnutrition is a clinical problem for the individual, but also a symptom of ineffective public health policy. Aside from feeding, important aspects are to recognize and treat infection, immunize against infection, enhance the child-rearing skills of the parents, and strengthen general hygienic practices, especially for water and sanitation.

Severe acute malnutrition Severe malnutrition results from the interaction of three distinct but related processes: (1) reductive adaptation, which is a general response to preserve essential function that takes place when the demands of the body for energy and nutrients are not adequately met; (2) inflammatory/immune responses and healing, which are impaired as a result of reductive adaptations; (3) specific nutrient deficiencies, when failure because of marginal diet to correct excessive losses of nutrients (e.g. through diarrhoea and vomiting) leads to major

imbalances. These combine to put the child at risk of the deadly triad of infection, hypothermia, and hypoglycaemia, often compounded by marked fluid and electrolyte disturbances. Sick malnourished individuals have no appetite for food, with loss of appetite being an important protective mechanism against consuming food which is likely to stress the systems of the body. Attempts (well meaning) to force feed are dangerous: the potentially fatal 'recovery syndrome' (manifest as heart failure, progressing to circulatory collapse, often with severe secretory diarrhoea) must be avoided. Aside from the provision of a sympathetic and quiet environment during treatment, key aspects of management include: (1) resuscitation—management of infection, fluid, and electrolyte imbalances, and shock, also treatment of vitamin A deficiency; (2) stabilization—give small frequent meals (every 3–4 h throughout 24 h; 100 kcal/kg per day; 1–1.5 g protein/kg per day), add specific nutrients to food to correct deficiency (potassium, magnesium, folic acid, zinc, copper, multivitamin), treat infections, transfuse for severe anaemia, treat skin lesions, exclude tuberculosis; (3) weight gain (rapid catch-up growth)—ad libitum intake, continue with micronutrient supplements, add supplemental iron. Introduction Severe malnutrition occurs in societies that are not able to meet basic needs for healthcare and survival. It is characterized by underdevelopment, poverty and deprivation, an insanitary environment, frequent infections, and food that is poor in quality or limited in availability. A series of vicious cycles operate within individuals and across generations, limiting the ability of vulnerable groups, families, 11.4 Severe malnutrition Alan A. Jackson

11.4 Severe malnutrition 1881 and individuals to cope with the harsh realities of a hostile environment, either through the exigencies of nature or a human unwillingness to share the available resources with greater equity. Across the globe, severe malnutrition is a common condition during childhood. It is most prevalent among the poorest in developing countries, but it is also found with uncomfortable frequency among the most deprived of every society, including those in Europe and North America. It is a frequent aspect of clinical medicine in patients who, for any reason, have a loss of appetite or a reduction in food intake. The same principles of management and care apply wherever the problem is found. Malnutrition at any age impairs the ability to perform and function. Children with severe malnutrition are at risk of life-threatening diseases, which require urgent attention. More insidiously, malnutrition during childhood stunts development and leaves a scar that remains for the rest of that person's life. This lost potential can express itself as an increased risk of ill health, as impaired intellectual development leading to poor school performance, or in limited physical development leading to poorer work performance. Once part of an individual's potential for development has been lost, the clinical and social implications tend to be cumulative. On a global scale, the sum total of the loss of individual capability represents a fundamental brake on aspirations for social and economic development. Most recent estimates indicate that globally, 45% of the disease burden for children under 5 years of age can be attributed directly or indirectly to malnutrition, at least 3 million deaths and 6% of total global disability-adjusted life years (DALYs). This burden is not spread evenly between different parts of the world. For the worst-affected countries, as many as 50% of children under 5 have malnutrition, which is severe enough to threaten life, with the highest prevalence in sub-Saharan Africa and the greatest numbers in Southeast Asia. This is representative of the day-to-day situation, and is not a peculiarity of special emergencies. There are at least 150 million children in the world for whom severe deprivation, indexed as stunting or survival on less than \$2/day, has limited their potential for normal physical and neurocognitive development. Notwithstanding the large number of children with severe malnutrition, over the past 20 years there has been a shift to the right of the curve

for the distribution of the height and weight of children, indicating a general success for specific interventions. Thus, change is possible, and when suitable measures are put in place sustained improvement can be achieved. However, there is absolutely no basis for complacency, as recent figures suggest a slowing down, or even a reversal, of this improvement. This may relate to an inability to control infections effectively, with tuberculosis, malaria, and diarrhoea continuing to play a major role and the HIV epidemic making a significant contribution. The world's population continues to increase, so an improvement in percentage terms does not necessarily mean a decrease in the absolute numbers of malnourished people across the globe. Severe malnutrition is a late stage in a process where an individual has had inadequate access to sufficient energy and nutrients for a period of time. During this time, the function of the body changes until a point is reached where severely malnourished children are significantly different from normal children in their response to medical treatment. This stage differentiates those who might be readily treated in a community setting from those who require more skilled care in a facility. If this group is treated in the same way as normal children, they will very likely die. Based upon best practice, mortality would be expected to be around 5 to 10%, but in many centres, case mortality has remained unchanged for 50 years, around 40 to 50%. Sometimes, this can be attributed to poor case management, with four major errors in care occurring in about 80% of centres (Table 11.4.1). However, frequently, the organization of systems of care is poor or the availability of simple, basic resources are limited or insecure. The World Health Organization (WHO) has produced guidelines for community and facility-based care with effective facility-based treatment using a 10-step approach (Fig. 11.4.1). During the early period of care, the order in which different aspects of treatment are carried out is critical for a successful outcome. A central feature is that, as a first step, the body's cellular machinery has to be repaired Table 11.4.1 The case mortality for complicated severe malnutrition has failed to improve because of four major errors of management

1. The assumption that a low plasma albumin concentration is the basis of oedema and can be effectively treated with a high-protein diet
2. The use of diuretics for the treatment of oedema
3. Early use of iron supplements to treat anaemia
4. Failing to differentiate that the acute illness should be managed before any attempts to correct weight loss

From Schofield C and Ashworth A (1996). Why have mortality rates for severe malnutrition remained so high? Bulletin of the World Health Organization, 74, 223–9.

Activity Treat or prevent: hypoglycaemia hypothermia dehydration
Treat Infection Correct electrolyte imbalance Correct micronutrient deficiencies Begin feeding Increase feeding to recover lost weight ('catch-up growth') Stimulate emotional and sensorial development Prepare for discharge Follow-up Initial treatment Rehabilitation weeks 7–26 weeks 2–6 days 3–7 days 1–2 with iron without iron

Fig. 11.4.1 WHO recommendations for the 10-step approach to the management of severe malnutrition.

SECTION 11 Nutrition 1882 if function is to be restored. Silent infections are common. There have been unusual losses of nutrients from the body, which cannot be corrected adequately on a standard diet. The damaged systems of the body are not able to cope with excess energy or further stress. Effective treatment requires the ordered correction of the underlying problems before any attempts are made to correct the tissue deficits. Clinical syndromes Severe malnutrition can present with an array of clinical symptoms and signs, which depend upon the duration of the illness, the extent of coinfection, the particular pattern of nutrient deficiencies and metabolic disturbances, and other associated complications such as diarrhoea and vomiting with attendant disturbances in fluid and electrolytes (Table 11.4.2). All descriptions of the condition emphasize one or other feature of the presentation. The archetypal descriptive terms for childhood

malnutrition—kwashiorkor, marasmus, or marasmic kwashiorkor—were originally used to characterize clinical syndromes. The first description of the kwashiorkor syndrome emphasized the development, location, and timing of the skin lesion, with progression from friable hyperpigmented skin, which stripped to reveal hypopigmented skin, which ulcerated easily to provide a ready portal for infection—lesions distinct from pellagra. Other features such as abnormal affect and hepatomegaly were noted, but were less remarkable. Placing emphasis upon variability in clinical presentation has made comparison difficult and encouraged the idea that the underlying pathophysiology, and hence its treatment, differs in important ways between locations. This has diverted attention from similarities in the fundamental changes that take place across the range of clinical presentations. The function of the body is controlled through the integration of many systems. A fault in any one has implications for the function of all the others. Thus, there is the need for adequate amounts of energy, energy-generating nutrients (carbohydrate, lipid, and protein), minerals, and a range of micronutrients for the body to function effectively in a harmonized way. Lack of any one component, or an imbalance, leads to deranged handling of other components. By adopting an agreed classification, relevant comparisons have been drawn, and it is clear that the range of clinical features represent varying manifestations of a clinical disorder with the interaction of qualitative and quantitative factors. The quantitative change results from an inadequate intake of food and leads to a wasting syndrome, classically marasmus, with the progressive loss of tissue, especially marked for subcutaneous fat and muscle. The result is a thin appearance, with pinched features, thin arms and legs, and a scaphoid abdomen. Qualitative changes are usually associated with unusual losses of nutrients from the body, for example, through diarrhoea or infection, reordered metabolism to deal with metabolic stress, or the toxic effects of a range of noxious exposures. The end result of this process is likely to be the loss of cellular integrity and control, leading to oedema.

Classification An effective classification differentiates those at greatest risk, guides suitable interventions, and helps determine the extent to which interventions have successfully corrected the problem. The more severely malnourished an individual, the greater the risk of complications, and the risk of an adverse outcome is related to the severity of the weight deficit or the extent to which normal function is deranged. The term ‘severe acute malnutrition’ (SAM) has been introduced to differentiate those who are in need of immediate clinical care associated with wasting, from the more chronic problems associated with stunting. These changes can all be marked either quantitatively or qualitatively. SAM is defined as severe wasting (a score of less than -3 standard deviations weight for height, or on screening a mid upper-arm circumference of less than 115 mm), or the presence of oedema of both feet, or clinical signs of severe malnutrition (Table 11.4.3). Recently, WHO/UNICEF introduced guidance on the identification of severe malnutrition and the use in practice of the new WHO growth standards for infants and children from 6 months to 5 years of age. Quantitative measures indicate the extent to which the expected pattern of growth in height and weight has not been achieved: low height for age, low weight for height, and low weight for age. Low height for age (shortness or stunting) is indicative of longer-term malnutrition or poor health. Low weight for height (thinness or wasting) implies recent or continuing current severe weight loss. Low weight for age (insufficient weight relative to age) implies stunting and/or wasting. Weight is more easily measured than height, and assessing weight for age is the simplest way of excluding severe malnutrition in the absence of oedema. Weight for age is influenced by both height for age and weight for height. Where deprivation is common, there is a high prevalence of low height for age. Weight for age is more strongly influenced by stunting than by wasting, and requires broader public health approaches for its alleviation, being unlikely to respond in the short term to aggressive

Table 11.4.2 Important

clinical features to enable immediate clinical decisions for emergency management of severe malnutrition

Feature Details/relevance

Anthropometry Stunting, wasting, presence of pitting oedema

Gastrointestinal History of anorexia, poor appetite, vomiting, diarrhoea. Appearance of mouth. Distended or scaphoid abdomen, with succussion splash

Liver Degree of enlargement, jaundice, petechiae

Cardiovascular Circulatory collapse, anaemia, shock (depleted intravascular volume, cold hands and feet, weak radial pulse, diminished consciousness) $\pm$ signs of 'dehydration' (sunken eyes, sunken fontanelle, decreased skin turgor)

Infection Hypothermia, fever, localizing signs (respiratory distress, broken skin, mouth, ears)

Specific deficiencies Eye signs of xerophthalmia, vitamin A

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1883 clinical intervention. Around one-third of stunting is present at birth, but the prevalence starts to increase at around 3 months of age, and the progression of stunting slows down at around 3 years of age, after which mean heights run below but parallel to the reference. Weight for height has the advantage that it can be used when age is not known reliably and suggests recent severe weight loss, indicating those children who are most likely to benefit from immediate aggressive nutritional intervention and support. The rate at which weight improves is used to assess progress during recovery, and success of care is indicated by the achievement of a weight that is appropriate for the individual's height. The measurement of mid upper-arm circumference provides simple, robust indication of the degree of wasting in this age group and is recommended in screening for SAM. In places where SAM is common there is the need to differentiate those who can be effectively and reliably managed by supervised care in the community, and those who require the level of care that can only be provided in a facility. This differentiation is made using qualitative criteria on the basis of appetite, the presence of oedema, or other identifiable serious comorbidity. Qualitative criteria are more difficult, because of their variability and uncertainty about whether they mark any particular pathophysiological process. It has been agreed that the presence of pitting oedema is the archetype of qualitative change, identified as kwashiorkor in the Wellcome classification and now called oedematous malnutrition. In milder forms, oedema might be restricted to the limbs, but in more severe forms it embraces the entire body. Obtaining a reliable measure of body weight is difficult in the presence of oedema, because of the uncertain contribution of oedematous fluid. The overall appearance might be of a child who superficially appears full, but has evident wasting below the oedema when examined carefully with the clothes removed. The extent of poor appetite or anorexia may be elicited by history, but a formal appetite test should be carried out if there is any uncertainty. Multiple infection is common and often silent, so that specific sites of infection may be difficult to identify or localize. A high index of suspicion is required for the presence of silent infections, which should be presumed to be present. Infection is not part of the diagnostic criteria. Natural history and clinical presentation

Inadequate nutrition slows the pace of growth and development and the greater the severity of the limitation or insult, or the longer its duration, the greater the difference between the achieved development and that expected. The stress of an insult of greater severity evokes a metabolic response that is associated with a loss of body weight and a reordering of function, so that resources and effort devoted to growth and development are diverted to maintain the integrity of the individual. The nutritional health of the infant is critically determined by how well prepared the mother was to carry the pregnancy, and the effectiveness with which breastfeeding is established and maintained. During pregnancy and for the first months of life, the infant is totally dependent upon the mother for its nutrient supply. During early pregnancy, there is the elaboration of structure in the embryo and maturation of function in the fetus. The last trimester is of critical

importance as it is when the fetus accumulates effective reserves of nutrients, helping survival and facilitating development during the first year of life. The fetus accumulates reserves of energy, as subcutaneous lipid, and of minerals and vitamins, such as iron, zinc, copper, vitamin A, riboflavin, and pyridoxine, in liver and muscle. At birth, the relative protection of the intrauterine environment is replaced by the many hazards of the external world. Gastrointestinal and respiratory infections are among the serious dangers to survival, and breastfeeding provides effective protection from both. Even in affluent societies, breastfeeding provides the infant with a level of protection against ill health that identifies effective breastfeeding as a singularly important feature in any rational policy in public health nutrition. There is a massive increase in the risk of ill health for infants who are not breastfed during the early months of life. This risk is magnified enormously for infants exposed to unsanitary environments with limited access to healthcare. Anything that limits the growth of the fetus, impairs its development, or causes it to be delivered early will limit its ability to cope with extrauterine life, and increase the risk of problems, infections, and malnutrition. There is enhanced mother-infant bonding and emotional development with breastfeeding, and other special benefits include the remarkable bioavailability of energy and nutrients, the presence of nonnutritional factors, protective factors, and growth factors.

Screening: Identification and prevention Malnutrition is a preventable condition, and the early identification of those at risk and the implementation of interventions that correct underlying problems and prevent further deterioration are central to strategies for effective care. Early growth failure can be detected by regular weighing, as an integral part of immunization and other health programmes. A series of plotted weights is most valuable, and intervention is required for those whose weight crosses two

Table 11.4.3 Classification of malnutrition. The diagnoses are not mutually exclusive

	Moderate malnutrition	Severe malnutrition
Symmetrical oedema	No	Yes (oedematous malnutrition) ^a
Weight for height SD score between -3 and -2 ^b (70-79%)	c SD score below -3 (<70%) (severe wasting)	d Height for age SD score between -3 and -2 (85-89%) SD score below -3 (<85%) (severe stunting)
Mid upper-arm circumference	Below 125 mm	Below 115 mm

^a This includes kwashiorkor and marasmic kwashiorkor in older classifications. To avoid confusion with the clinical syndrome of kwashiorkor, which includes other features, the term 'oedematous malnutrition' is preferred. ^b Below the WHO growth standard; the SD score is defined as the deviation of the value for the individual from the median value for the reference population, divided by the standard deviation of the reference population. ^c Percentage of the median WHO growth standard. ^d This corresponds to marasmus (without oedema) in the Wellcome clinical classification, and to grade III malnutrition in the Gomez system. To avoid confusion the term severe wasting is preferred.

SECTION 11 Nutrition 1884 growth centiles on successive measurements. If measurements are only available for a single time point, then height for age, weight for height, or mid upper-arm circumference provides an indication of any past or ongoing growth failure. Advice and demonstration of best practice in child care and feeding may be sufficient to correct a mild degree of growth failure, but persistent or more severe growth failure requires closer investigation to exclude underlying problems. Poor anthropometry, with a history of poor appetite and weight loss, should always be taken very seriously and pursued until a cause has been identified and corrected. Severe malnutrition is a medical emergency. Childhood malnutrition is a clinical problem for the individual, but is also a symptom of ineffective public health policy. Targeted interventions should address the immediate needs of the child, but should also embrace broader considerations. For the child, there is the need to effectively immunize against infection, recognize and treat infection in a timely way, and ensure an effective period of nutritional support following infection.

For the family, there is the need to enhance the child-rearing skills of the parents, create a stimulating environment, acquire and practice simple skills in hygiene and food preparation, and strengthen family dynamics and coping strategies. For the community, there is the need to improve the economic base of households, increase food purchasing power, increase food security or household food availability, and treat specific nutrient deficiencies. Sound hygienic practices have to be strengthened at the group or household level, and where necessary, the amount and quality of water and the safe and effective removal of solid waste improved. Each activity can exert a beneficial effect on growth and development. Any one might be relatively easy to introduce, but the real difficulty is to ensure that all are sustained. The need is for a fundamental change in the health culture and the creation of a framework of behaviour in which development activities become rooted and take place as a matter of course. A failure to establish and maintain an effective system of healthcare leads to a progressive deterioration in the clinical state of the most vulnerable infants, leading eventually to severe malnutrition. The World Bank has identified the severe limitation this places on national development, and the need to have effective interventions before 2 years of age if this critical potential is not to be lost.

Aetiology and pathophysiology Children may become malnourished simply because there is not enough food available. Community-based interventions place emphasis on providing adequate amounts of food of high nutritional value, if necessary as ready-to-use therapeutic foods, but sick malnourished individuals have no appetite for food. It seems paradoxical that a child who has obviously lost weight and needs to eat may refuse food even when it is readily available. If food is forced, there is the possibility that the child will become worse, or even die. In managing severe malnutrition, appetite is one of the most important symptoms. A loss of appetite is an important protective mechanism against consuming food, which is likely to stress the systems of the body. In experimental studies, there are two major biological reasons why appetite is lost: a deficiency of a specific nutrient and infection. Severe malnutrition is a disorder that results from the interaction of three distinct but related processes, each of which appears to be related directly to the food consumed, but none of which can be easily understood simply by a consideration of food:

- reductive adaptation
- inflammatory and immune responses
- specific nutrient deficiencies

Food helps meet the many needs for normal function, growth, and development in childhood, but also the ability to cope with environmental challenge. A diet that is adequate, but marginal under normal circumstances, is inadequate for the increased demands during recovery from frequent intercurrent illness with the double burden of the need to catch-up growth and to make good the unusual losses of nutrients during the infective episode itself. The time available for successful convalescence before the next bout of infection is too short to adequately make up the deficit.

Reductive adaptation: Failure to meet the body's usual demands for macronutrients Reductive adaptation takes place when the demands of the body for energy and nutrients are not adequately met by the dietary intake. The general features are similar, regardless of the basis for the inadequate intake. It is a general response to preserve essential function, but carries a cost. Normal metabolism takes place within a highly regulated environment, through the control and integration of exchange and turnover among cells and tissues. For the cellular machinery of the body to remain functionally intact and operationally effective, it requires a constant supply of energy and other nutrients. An estimated one-third of resting energy expenditure may be consumed through the synthesis and degradation of macromolecules such as protein, and a further one-third is associated with the movement of material across membranes (e.g. through the pumping activity of the sodium/potassium pump, $\text{Na}^+/\text{K}^+-\text{ATPase}$). These processes represent the internal work of the body at cellular level and underlie the functioning of all the organs and

tissues. They take place continuously, and the total activity can be measured as energy expenditure. As food consumption is intermittent, the processes are independent of the immediate food intake. However, a sustained lack of food leads to progressive impairment of the cellular machinery as damage due to the wear and tear of normal use can no longer be replaced effectively. Structure When food consumption is significantly reduced, metabolic processes continue to enable the body to function, and the energy to support these processes is derived from reserves within the body. The body is in negative energy balance, and tissue mass cannot be maintained, leading to loss in weight. The losses are uneven between tissues, with major losses in subcutaneous fat and muscle, and relative preservation of the metabolically more active visceral tissues. One important consequence is that heat generated by muscle is reduced, and at the same time, insulation in the skin is impaired leading to greater heat loss. The altered body composition underlies all anthropometric methods that are used to assess nutritional status. In addition to the changes in mass, efficiencies in the utilization of energy have to be found. Function Efficiencies are achieved by reducing the amount of work carried out by the body. External work is reduced by decreasing physical

11.4 Severe malnutrition 1885 activity. Internal work is reduced by decreasing cellular metabolic activity, with subsequent effects upon tissue function. Significant efficiencies might be achieved for the major energy-consuming processes such as membrane pumping, protein turnover, and cellular replication. The relative distribution of potassium in the intracellular space and sodium in the extracellular space is fundamental to maintaining the chemical environment of cells. As potassium tends to leak out of the cell and sodium tends to leak into the cell, for the cell membrane to maintain the effective partitioning of electrolytes requires that sodium is pumped out of the cell in exchange for potassium, consuming ATP. The cell membrane tends to become more 'leaky' in malnutrition as its lipid composition changes, and the Na^+, K^+ -ATPase is down-regulated as one way in which to reduce energy expenditure. Therefore, compared with normal, all people with malnutrition have reduced intracellular potassium and increased intracellular sodium, hence decreased total body potassium and increased total body sodium, which is not necessarily identified on standard biochemical tests. The ability to maintain protein synthesis is fundamental but energetically expensive; energetic efficiency requires a reduction in protein synthesis, which is not divided equally among tissues. Liver normally accounts for about 25% of protein synthesis, with the synthesis of nutrient transport proteins playing a critical role in the delivery of lipid, minerals, and vitamins to the other tissues. Reduced synthesis of nutrient transport proteins may save energy, but at the cost of reduced delivery to peripheral tissues (e.g. limited synthesis of apolipoproteins limits the delivery of lipid to peripheral tissues and enhances the accumulation of lipid in liver). Cellular replication is energetically demanding, requiring the ready availability of all nutrients. A reduction in cellular replication provides efficiencies in energy and nutrient use but impairs the function of systems critically dependent upon cellular replication: the skin, gastrointestinal tract, respiratory tract, and immune system. Functional and metabolic cost of reductive adaptation The function of the cells in all tissues is affected by reductive adaptation. With relative protection of more vital functions, the cost is a reduction in those functions that are not immediately vital, but which provide the functional reserve capability that enables the metabolic flexibility to respond to a changed internal environment or a challenge from the external environment. As a consequence, changes that would be readily managed in the normal state present a metabolic stress in the reductively adapted state. What would normally be a modest challenge can induce a major metabolic perturbation. Reductive adaptation represents the loss of

reserve capacity, which leads to increased metabolic brittleness and vulnerability. The cellular machinery is no longer capable of responding effectively to the usual challenges. There is a change in the function of all systems.

Gastrointestinal tract There is loss of mucosa and submucosal tissues, loss of gastric acidity, and a reduced capacity for digestion and absorption. This leads to impaired bioavailability of nutrients from food, decreased transit time, and predisposition to small bowel bacterial overgrowth. An impaired ability to repair and maintain the integrity of the endothelium predisposes to bacterial translocation and overexposure to endotoxins.

Skin The skin wastes, loses its ability to retain heat, and readily becomes breached and infected.

Immune system There is increased exposure to pathogens and a decreased capacity to respond (inflammation and immune response—see following paragraphs).

Liver There is downregulation of synthetic and excretory processes. The reduced functional reserve makes it more difficult to maintain glucose homeostasis in the face of increased bacterial exposure. Intermediary metabolism is impaired, and transport proteins for the delivery of lipid, vitamins, and minerals to other parts of the body are reduced. The formation of clotting factors is impaired. Reduced bile and bile salt formation affect digestion. Metabolism and clearance of drugs, toxins, and xenobiotics is also reduced.

Cardiovascular system A reduction in the functional reserve of the heart, slower pulse, and increased circulation time make heart failure more likely if excess fluid is given intravenously. There is poor circulatory control, with a tendency to reduced intravascular volume with an expanded interstitial fluid space. Iron is an integral part of haemoglobin in red blood cells, involved in the transport of oxygen from the lungs to the tissues. The mass of red cells is related to the amount of oxygen that has to be transported, which, in turn, relates to the mass of active lean tissue. As part of reductive adaptation, there is a decrease in the lean tissue of the body with an associated decrease in the red cell mass. The iron that is released from haemoglobin is not required immediately for the formation of more red cells. The level of iron in the body is controlled by the rate at which it is absorbed from the gastrointestinal tract, as, once in the body, there are no recognized mechanisms through which iron can be lost. The iron released from red cells therefore cannot be excreted and is placed into storage. Free iron is highly reactive and acts as a focus for uncontrolled excess generation of free radicals, thereby damaging other cellular components. Excess iron is stored in the liver, bound to ferritin. A demand for ferritin synthesis is energetically expensive and diverts amino acids from the formation of other proteins. As part of reductive adaptation, the ability to effectively sequester iron in a chemically quiescent state is impaired.

Renal There is decreased functional capacity of the kidney, with an impaired ability to concentrate, dilute, or acidify urine.

Muscle Muscle mass is reduced, and muscle function impaired by reduced potassium, which together lead to reduced generation of heat.

Brain Brain function is relatively well preserved. Nevertheless, there is blunting of higher functions with decreased mentation, apathy, and depression, and impaired control of hormonal and integrative responses. There is a decrease in activity, poor work performance, and

SECTION 11 Nutrition 1886 a decrease in discretionary activities, which together contribute to a slowing of learning.

Infection: The inflammatory and immune responses

Survival in a potentially hostile world requires effective nonspecific and specific defence mechanisms. Nonspecific physical barriers (skin and mucous membranes) and chemical protection (gastric acidity, secretions such as tears and mucins) depend upon cellular replication, which is less well maintained during reductive adaptation, and even minor damage leads to a breach that is not repaired. Local damage with bacterial invasion usually elicits local inflammation, a systemic or acute-phase response, and a specific immune response. The mounting, coordination, and regulation of an effective response

require energy, increased cellular replication, and protein synthesis. The changes in hormones and cytokines associated with reductive adaptation impair the establishment and control of normal inflammatory and immune responses. The localized signs of tissue damage or infection—enlarged lymph nodes, enlargement of the spleen or liver, and the normal features of the acute-phase response (fever, rapid pulse, and respiration)—are blunted or lost in malnutrition, making diagnosis more difficult. Loss of appetite is a central feature of a more severe acute-phase response, as the body raids its own tissues for the nutrients it requires to satisfy this unusual demand. There is a shift from the usual pattern of protein synthesis, with less emphasis on growth. As muscle wastes, the amino acids are made available for the synthesis of proteins for the immune system, and the liver shifts from synthesizing large amounts of nutrient transport proteins to the formation of acute-phase response proteins, which limit cell damage and help repair. Intravascular albumin is redistributed to the third space, leading to a reduced plasma albumin concentration. A low plasma albumin is frequently seen in malnourished people and is indicative of ongoing infection rather than a dietary deficiency of protein. Correcting the problem requires that the underlying infection be effectively treated, not that dietary protein be increased. The cells of the inflammatory and immune systems increase their utilization of glucose, with increased gluconeogenesis from amino acids. A feature of the acute-phase response is a profound change in the handling of micronutrients. There is a block in the absorption of iron. Net tissue breakdown releases components for which there is no immediate use. The circulating concentrations may be reduced (iron and zinc, which are sequestered in the liver), or increased (copper), and there may be increased losses from the body in urine or stools (zinc and vitamin A). In childhood, diarrhoea is a frequent accompaniment of infection, which adds an excessive loss of nutrients from the body, especially potassium, magnesium, zinc, and vitamin A. Specific nutrient deficiencies

Deficiency of specific nutrients is the most difficult aspect of severe malnutrition to manage effectively. Whereas in classical deficiency states, inadequate dietary intake is usually the major underlying cause, in severe malnutrition, it is the failure to correct excessive losses of nutrients, which leads to major imbalances. Major losses of intracellular nutrients can be difficult to identify reliably, for three reasons:

- Losses of intracellular content may not be readily identified using standard biochemical tests on blood (e.g. potassium).
- Bone acts as a very effective buffer for many nutrients and therefore severe total body depletion can develop without obvious biochemical change or loss of function (e.g. magnesium).
- During an inflammatory response, redistribution of nutrients within the body makes standard tests for nutrient deficiency very difficult to interpret (e.g. vitamin A, zinc, or iron).

Infection causes an unbalanced loss of nutrients, which may be obvious in association with diarrhoea and vomiting, or may be more subtle as in the increased urinary losses of vitamin A and zinc which are an integral feature of the acute-phase response. For an individual consuming a diet that is marginal in one or other nutrient, increased losses may make the critical difference to achieving balance, which cannot be restored unless additional nutrients are provided during the convalescent period. All cellular functions are likely to be affected to a greater or lesser degree by specific deficiencies, but one process that is of special importance is the ability to cope with free radicals or oxidation-induced cell damage. Antioxidant protection

In severe malnutrition, there is a major imbalance between the potential for damage induced by free radicals and protective antioxidant systems. Infection, oxidative burst, and free iron all contribute to an increased potential for damage. Mortality is greatest in those with an obvious impairment of the antioxidant defences. Children with oedematous malnutrition have severely reduced concentrations of glutathione in blood, and mortality is highest in those with impaired activity of glutathione peroxidase. Although the pattern varies with location, deficiencies of micronutrients are common

and result in impaired cell function and membrane damage. The many layers of antioxidant protection, which are specific for each compartment of the cell, provide a measure of safety. However, the system is potentially vulnerable to deficiencies or limitations in multiple micronutrients (e.g. niacin, folate, thiamine, riboflavin, cobalamin, ascorbic acid, carotenoids, tocopherol, selenium, zinc, copper, magnesium). A deficiency might not be readily identifiable, either clinically or biochemically, and a high index of suspicion is required. Oedema reflects an inability to maintain the correct distribution of fluid in the intracellular space, the vascular space, and the interstitial space, and is a final common pathway representing a loss of metabolic control. Incorrect approaches to the management of oedema—the use of diuretics or of high-protein diets—are among the commonest reasons for increased mortality. The rationale behind the incorrect approach to management presumes that oedema is simply the consequence of hypoalbuminaemia, itself the result of inadequate dietary protein. There are profound perturbations of protein metabolism in kwashiorkor, but these are due to concurrent infection, loss of appetite, and increased losses of nitrogen in stools rather than a diet deficient in protein. A low plasma albumin usually indicates an acute-phase response to an unrecognized infection. Treatment with a high-protein diet or infusions of albumin does not correct the oedema, but does increase mortality. A low plasma concentration of albumin might contribute to formation of oedema, but is seldom the sole or primary cause. Although diuretics exert a direct effect on cell membranes, giving a diuretic is less likely to be effective if the intravascular space is reduced. Diuretics that lead to increased

11.4 Severe malnutrition 1887 urinary losses of potassium make the underlying problem of a deficiency of body potassium even worse. The normal distribution of water between the different body compartments is tightly controlled through several interlinked factors. Disruption of one or more of these factors may lead to the development of oedema, and will need to be corrected for the oedema to be effectively cleared (Table 11.4.4). Potassium deficiency leads to retention of sodium. Altered membrane structure and reduced activity of Na^+/K^+ -ATPase allows intracellular potassium to fall and intracellular sodium to rise. All malnourished individuals should be presumed to be deficient in potassium and to have excess intracellular sodium, regardless of the composition of the plasma measured on routine biochemistry. Indeed, plasma sodium concentrations might be low and it is tempting to give extra sodium, which is absolutely the wrong thing to do. There is more than enough sodium in the body, but it is in the wrong place. A direct approach that seeks to correct the disordered biochemistry is less likely to succeed than an approach which recognizes that the fundamental problem is disordered cellular function. Similar factors lead to cellular damage in any severely undernourished person, and by treating the malnutrition and repairing the metabolic machinery of the cells of the body, oedema will be effectively treated. What is required are generous supplements of potassium and correction of the underlying membrane dysfunction, which enables fluid and electrolyte balance to be restored. There is a close metabolic interdependence of potassium and magnesium, both of which are readily lost from the body in diarrhoea. It is extremely difficult to correct potassium deficiency in the presence of an associated magnesium deficiency, or to correct a magnesium deficiency in the face of a potassium deficiency. They have to be corrected together. Principles of facility-based care Phases of treatment: The 10 steps (See Fig. 11.4.1 and Table 11.4.5.) One of the important reasons why mortality from malnutrition has not been reduced in many centres is because the primary objective of treatment has been to try to correct the obvious weight deficit. In attempting to replace the lost tissue as soon as possible, generous intakes of food have been provided, encouraged, and even forced. If

appetite is poor, or anorexia is a feature, then generous force-feeding by nasogastric tube has been used. This can be very dangerous. The 10-step approach to treating malnutrition clearly identifies that treatment must be divided into different phases: the cellular machinery has to be repaired before it can be used to enable tissue growth. Two clinical features that are directly related to specific nutrient deficiencies and are particularly difficult to manage are oedema and persistent diarrhoea. Any specific nutrient deficiency impairs cellular function and increases the risk of infection. Infection increases nutrient losses through tissue wasting as an intrinsic feature of the acute-phase reaction and as vomitus or diarrhoea. Increased generation of free radicals is part of the body's attempts to deal with infecting organisms, and deficiencies of specific micronutrients directly impair the ability to cope with free-radical generation. Even if an individual recovers from an infection, nutrients which have been

Table 11.4.4 Major factors that contribute to the development of pitting oedema in severe malnutrition

Hypoalbuminaemia	Associated with impaired protein metabolism, infection or stress, impaired hepatic function, toxic damage
Salt and water retention	Potassium deficiency, phosphate deficiency, acid-base imbalance, impaired renal function
Impaired membrane function	Altered composition (phospholipid composition and fatty acid profile). Impaired or downregulation of Na ⁺ K ⁺ -ATPase.

Table 11.4.5 Outline clinical management of severe malnutrition

1. Resuscitate Manage infection, fluid and electrolyte imbalance and shock: oxygen, glucose, reduce heat loss, give antibiotics, maintain circulation, treat vitamin A deficiency
2. Stabilize Control energy and protein intake at maintenance: 400 kJ/kg/day (100 kcal/kg/day), 1–1.5 g protein/kg/day Small frequent meals: eight meals every 3 h, or six meals every 4 h, throughout 24 h Correct deficiencies of specific nutrients by addition to food: potassium (4 mmol/kg/day), magnesium (0.4 mmol/kg/day), folic acid (1 mg/day), zinc (2 mg/kg/day), copper (0.3 mg/kg/day), multivitamin supplement Treat bacterial infection: broad spectrum antibiotics, cotrimoxazole or ampicillin with gentamycin Treat small bowel overgrowth with metronidazole Treat helminth infections with mebendazole Transfuse for severe anaemia Topical treatment and care for skin lesions Exclude tuberculosis and HIV Give sensory stimulation and emotional support
3. Weight gain (rapid catch-up growth) Ad libitum intake to achieve at least 600 kJ/kg/day (150 kcal/kg/day), 4 g protein/kg/day Continue with micronutrient supplements Add supplemental iron Give sensory stimulation and emotional support

SECTION 11 Nutrition 1888 depleted from the body are not easily replaced. This has two important effects. First, the individual is deficient in a specific nutrient and carries the specific and general features of the deficiency, importantly loss of appetite. Secondly, if the deficiency is severe it may be very difficult for it to be corrected by consuming a normal diet without the addition of specific nutrient supplements. Under this circumstance, poor appetite, persistent reductive adaptation, and continued risk of further infection are maintained. If energy is provided in excess of the requirements for maintenance, there are few ways in which it can be excreted or handled metabolically. Any significant excess is deposited as new tissue, either as cells or as cells filled with fat. There is a considerable underlying drive to form new cells, but in addition to energy this requires the availability of all the nutrients contained within the cell structure. When specific deficiencies have not been corrected individual nutrients are limiting for cell formation and it is not possible to handle the excess energy through the formation of new tissue. The excess energy creates a very serious metabolic upset (see 'Recovery syndrome', later). Therefore, during the

period when nutrient deficiencies are being corrected and infections treated, it is important to give sufficient energy to cover the needs of the body, but not so much that the body is forced to make new tissue. This is the basis for identifying the different phases of treatment: first to repair the machinery and gain control of metabolism by providing only enough energy to satisfy the needs for maintenance, but not enough to drive growth. Managing reductive adaptation, specific nutrient deficiencies, infection, and free-radical-induced membrane and cellular damage lie at the heart of the problems associated with immediate care during the resuscitation period. A loss of appetite is an important protective mechanism limiting food consumption, which is likely to stress the systems of the body. Hence the loss of appetite is a cardinal sign of an underlying metabolic problem that is ongoing. If the problem is identified and corrected, then appetite is restored very quickly. Severely malnourished children may have a profound loss of appetite due to a combination of infection and deficiencies of specific nutrients, which interact to make the problem worse. Correcting the loss of appetite is central to effective care. The restoration of appetite marks the restoration of metabolic control and is a key component of therapy and a marker of progress. Once the emergency treatment required to resuscitate the child has been completed, the emphasis of care is to treat the underlying problems that are associated with a loss of appetite.

Resuscitation

Severely malnourished children present a medical emergency because of two sets of problems: the deadly triad of infection, hypothermia, and hypoglycaemia, and marked fluid and electrolyte disturbances (Table 11.4.5). The deadly triad: Hypoglycaemia, hypothermia, and infection

Brain cells are absolutely dependent upon a regular supply of glucose and oxygen to maintain the availability of ATP. Death occurs within 5 min if the supply of either is impaired, through poor circulation, reduced respiration, or low blood glucose. The glucose required is either made in the liver or taken in the diet. Reductive adaptation limits the capacity for glucose formation and delivery, and a regular dietary supply is required if blood concentrations are to be maintained. The availability of glucose for the brain can be impaired if there is competition from other tissues or functions (e.g. in order to maintain body temperature or to deal with infection). Malnourished individuals generate less heat and have reduced thermal insulation and therefore cool rapidly when exposed. Any attempt to generate more heat consumes glucose and other energy-providing fuels. A normal effective response to infection is a burst of activity in white blood cells, which places heavy demands on available glucose, competing with the brain and leading to hypoglycaemia, and increasing the rate of heat loss leading to hypothermia. Therefore, the triad of hypoglycaemia, hypothermia, and infection indicates a very serious situation in which the body is no longer able to adequately maintain the supply of glucose to support essential functions. The treatment is to increase the supply by giving oral or intravenous glucose, reducing competing demands through decreasing the amount of heat lost, and by effectively treating infections. To deliver glucose and oxygen to the brain effectively requires an adequate circulation, which is compromised by intravascular dehydration. The correction of dehydration is closely associated with the correction of electrolyte imbalances, with energy homeostasis, and with normal cellular function. Care has to be taken to ensure that each is corrected in concert with the other to ensure that imbalances do not arise. All malnourished individuals are deficient in potassium and carry excess sodium. Specific micronutrients: Vitamin A, zinc, and iron

Iron is highly reactive chemically, and fulfils many important functions related to the generation of energy for normal cellular function. High reactivity, if not adequately controlled, carries the potential for cell damage. Red cell mass reduces in malnutrition as the lean body mass decreases. The iron is not used for further haemoglobin formation and cannot be excreted, so has to be stored innocuously, as any unbound iron is liable to increase oxidative cell damage. In severe malnutrition, there is increased stored

iron and free iron. The available iron is not used for haemoglobin formation, and giving iron supplements to treat anaemia simply adds to the load, stresses the system further, and increases mortality, especially in the presence of infection such as malaria. Initially, it is more important to repair and restore the capacity to cope with free radicals by improving vitamin and trace element status. Later, when the acute problems have been resolved, the iron will be removed from storage and used to form new tissue. As stored iron is used up, supplemental iron will have to be provided to keep pace with the rate of tissue demand. Blindness and other eye signs of overt vitamin A deficiency are common in many parts of the world. Less obvious changes lead to impaired integrity of mucosal surfaces in the gastrointestinal and respiratory tracts, lowering resistance to gastroenteritis and respiratory infections. During infection, vitamin A is lost from the body, severe deficiency may develop rapidly, and the eye signs often deteriorate during early treatment. In areas where vitamin A deficiency is common, a large dose of vitamin A given very early in the treatment is an urgent necessity. Zinc is required for the function of a wide range of enzymes, and a deficiency has widespread effects. A shortage of zinc impairs the replication of cells such as the gut mucosa, leading to further mucosal damage and increased diarrhoea. Zinc deficiency leads to diarrhoea, and diarrhoea leads to zinc deficiency. Similar changes take place in damaged skin leading to ulcerated skin which is readily damaged with mild trauma.

11.4 Severe malnutrition **1889 Persistent diarrhoea** Many malnourished children have diarrhoea, which can take time to settle. The diarrhoea may be infective in origin or have an infective component, due to viruses, bacteria, fungi, or helminths. However, diarrhoea that has persisted for any time will also have an element due to specific nutrient deficiencies (zinc and vitamin A) or chemical injury (bile salt deconjugation). With continued diarrhoea, there are ongoing losses of nutrients. Few bacteria exist in the healthy small intestine, but small bowel overgrowth develops readily in malnutrition, due to a combination of gastric achlorhydria, reduced motility (potassium and magnesium deficiency), leading to bile salt deconjugation, damaged mucosa, and bacterial translocation. For the bowel to repair and re-establish its resistance requires adequate nutrients, especially zinc, vitamin A, and folates. Thus, the effective treatment of chronic diarrhoea requires a three-pronged approach: correction of potassium deficiency, treatment of bacterial overgrowth (with metronidazole), and effective repletion of specific nutrient deficiencies (such as zinc, vitamin A, and folate). **Management** The objectives of the resuscitation phase are to stabilize vital functions, by giving oxygen, supporting respiratory and cardiac functions, and correcting fluid imbalance, to ensure that adequate amounts of glucose are delivered to the brain. Body temperature must be maintained by maintaining glucose supply to the system, limiting heat loss through the skin, and starting to control infection. As the capacity for the body to carry out metabolic functions is impaired, external support has to be supplied regularly on a 24-h cycle. The regular intake of small amounts over 24 h (especially at night) is a very effective way of achieving this (Table 11.4.5). All infections must be treated. Specific nutrient deficiencies must be corrected, but no iron or extra sodium should be provided. The metabolic state must be controlled by limiting the intake of energy and protein to that required to maintain body weight, and ensuring that there is no excess (see following paragraphs). These steps will enable the repair of the metabolic machinery and allow cellular function to move towards normal. The response to a successful intervention will be a return of appetite; the patient will feel better, and smile. **Recovery syndrome** Limited availability of one or more nutrients leads to competition between all cells for the little available. Some nutrients become relatively more deficient, upsetting the balanced function between tissues, and the clinical signs of a deficiency become more obvious. There is a similar

explanation for why the clinical signs of a deficiency are not always apparent, even though the body might be particularly deficient. During reductive adaptation, the demand for nutrients is decreased, and the signs of a deficiency are masked. Signs of deficiency become exposed in rapidly dividing tissues, when the demand for nutrients is greatest. Vitamin A and zinc are examples, but the same principles apply to many other nutrients, especially the B vitamins. The recovery or refeeding syndrome develops when individuals who have undergone reductive adaptation are suddenly provided with a relative excess of food. Excess energy drives metabolism while specific nutrient deficiencies are inadequately corrected, and the metabolic machinery is still compromised. The syndrome may vary in its details, but consists of left- and right-sided heart failure associated with an overloaded circulation. This may progress to vascular collapse with abdominal distension as the circulating vascular volume is poured into the bowel as profound secretory diarrhoea. The first sign of the onset of the recovery syndrome is an increase in pulse and respiratory rate. If food continues to be consumed at the same rate, the load on the heart will progress to heart failure. This is a medical emergency, and it is vitally important that the food intake is reduced or stopped. If the changes are identified early and are relatively mild, then food intake should be reduced. If the condition has advanced and is severe, then it may be necessary to stop all food for 12 to 24 h. The problem will then resolve. Replacing lost weight The ultimate objective of treatment is to replace the lost tissue. Cellular hypertrophy and hyperplasia are critically dependent upon and limited by the available energy and nutrients. For tissue of average composition, the formation of 1 g tissue requires 20 kJ of energy. A normal 1-year-old infant gains 1 g/kg body weight per day, but for catch-up weight gain during recovery from malnutrition, it is possible to form tissue at up to 20 g/kg per day, by consuming an additional 400 kJ/kg per day. Achieving this requires an energy-dense diet, which is consumed throughout the 24 h of the day. Energy is necessary but not sufficient for new tissue formation. The nutrients needed for the formation of cell membranes and protoplasm are required in adequate amounts and suitable proportions. As the lean body mass grows it has an increased need for oxygen, and the red blood cell mass increases. Iron is taken out of storage to form new red cells, and eventually these stores are depleted with the need to add supplemental iron to the diet. There is an increased demand for amino acids to meet the needs of new tissue formation. It is safe to allow quite large intakes of protein. As the amino acids are deposited in tissue and do not accumulate in the free form, there is no risk of toxicity. However, meeting the pattern of amino acids required by the body will require the endogenous biosynthesis of relatively large amounts of the 'nonessential' amino acids in the body, which in itself will require the generous availability of minerals and vitamins. Important general aspects of care The physical care that is provided to correct the biochemical, metabolic, and infective problems is critical for success. However, there is also a need to address the broader needs of the child for healthy development. In part, this is provided by creating a warm, caring environment; in part, by suitably structured activities that provide an appropriate level of stimulation to encourage brain function to recover and develop. All aspects of care need skill and sympathy. The severely malnourished child is desperately sick and must be nursed as a critically ill child with minimum physical disturbance. With correct treatment, progress can be very rapid, and it is desirable to involve the parents and siblings, to encourage and demonstrate preferred childcare practices. This will facilitate the transfer between hospital and home, and make it more likely that the practices become embedded. Less seriously ill children can be effectively managed as outpatients, using the same principles and approach to the management decisions.

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Revision #1

Created 2026-01-22 16:37:22 UTC by Omar Ayman

Updated 2026-01-22 16:37:22 UTC by Omar Ayman