REVIEW ARTICLE

NUTRITION IN MEDICINE
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Malnutrition in Adults

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Malnutrition is an imbalance between the growth and breakdown of body tissues and nutrient stores, resulting in loss of muscle and organ mass, diminished physical and mental functioning, and impaired clinical outcomes. Over the past 50 years, malnutrition has been increasingly recognized as a deleterious consequence of chronic and acute disease. On the basis of the cause of malnutrition, three subtypes are recognized: disease-related malnutrition in the absence of underlying inflammation, disease-related malnutrition with underlying inflammation, and starvation due to inadequate access to food (i.e., food insecurity) (Fig. 1).[1,2]

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N Engl J Med 2024;391:155-65.
DOI: 10.1056/NEJMra2212159

PATHOPHYSIOLOGY

The concept of two major pathophysiological pathways of malnutrition is well established. The inflammation-related pathway results from anorexia and increased tissue breakdown, and the deficiency-related pathway is initiated by decreased intake or absorption of food and nutrients (Fig. 2).[1,2]

ENERGY AND NUTRIENT DEFICIENCIES

Inadequate intake or absorption of energy and nutrients is the classic scenario of malnutrition. Dysphagia after stroke and short bowel syndrome are examples of this noninflammatory pathway. Under such conditions, human metabolism adapts by decreasing resting energy expenditure, heart rate, body temperature, and spontaneous physical activity. Glycogen stores in the liver and muscles are depleted within 1 to 2 days and replaced by body fat as the main energy source. Protein stores are partially protected, but muscle is still depleted to ensure a supply of amino acids for protein synthesis and oxidation for energy. This adaptation contributes to the ability to survive starvation. Historical observations indicate that survival for up to 60 days in a state of complete starvation is possible if fluids are available.[3]

INFLAMMATION-DRIVEN DISEASE-RELATED MALNUTRITION

When the underlying disease is accompanied or driven by inflammation that is mediated by inflammatory cytokines and prostaglandins, as in cancers, infections, end-stage organ disease, or critical illness, metabolism becomes more complex and maladaptive.[4,5] In contrast to energy expenditure with pure food deprivation, resting energy expenditure increases with food deprivation and inflammation. The resting heart rate and body temperature increase. Protein breakdown in skeletal muscle increases.[6] Amino acids from muscle are used as fuel for the production of glucose through gluconeogenesis and for the synthesis of proteins such as acute-phase reactants. During inflammation, protein turnover is not regulated by nutri-

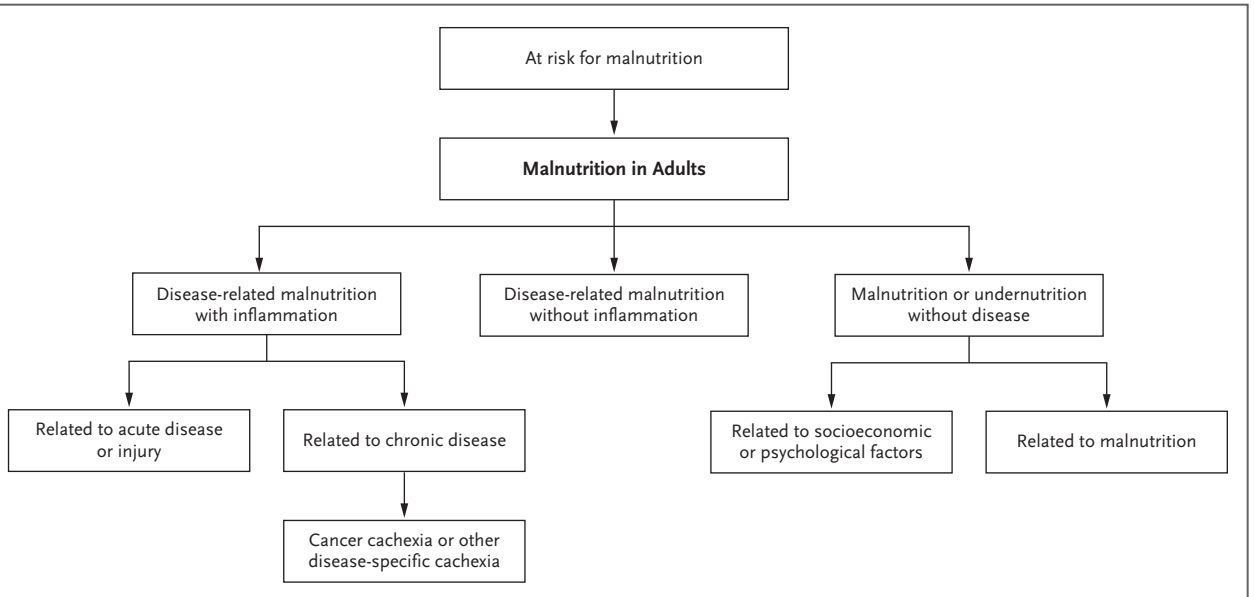

Figure 1. Diagnostic Overview of Malnutrition in Adults and Malnutrition Subcategories.

Malnutrition in adults is confirmed according to phenotypic and etiologic criteria in persons who are identified through screening as being at risk for possible malnutrition. The three subtypes of malnutrition in adults are classified according to their underlying cause: disease-related malnutrition in the absence of underlying inflammation, disease-related malnutrition with underlying inflammation, and starvation due to inadequate access to food (i.e., food insecurity).

ent requirements but continues even when sufficient energy and protein are supplied. The result is loss of muscle mass. Nutritional intake in acutely ill older patients is substantially reduced when the concentration of C-reactive protein (CRP) exceeds 30 mg per liter.[7] Many chronic diseases are associated with low-grade inflammation, such as chronic obstructive pulmonary disease (COPD), Crohn's disease, kidney failure, chronic pancreatitis, and various cancers in which CRP concentrations are just above the upper limit of the normal range. Slow, continuous tissue erosion and blunted responses to nutritional treatments are well-known consequences of such long-term exposure.[8]

EPIDEMIOLOGY OF MALNUTRITION

As expected, the prevalence of malnutrition varies according to age, the underlying disease, and the setting.[9] In the population of persons who are older than 65 years of age, malnutrition is found in 5 to 10% of community-dwelling persons, 20 to 40% of hospitalized patients, and up to 50% of nursing home residents.[10] Among patients with cancer, the prevalence varies widely according to the type and stage.[11] Cancers of the upper gastrointestinal tract lead to malnutrition early, whereas in breast, lung, and renal cancers, malnutrition occurs with more advanced disease. Severe trauma, burns, and acute infections trigger excessive inflammation, which rapidly degrades fat, muscle, and organ tissue. In patients with Crohn's disease or celiac disease, malabsorption with weight loss and malnutrition are the main manifestations of the disease.

In most end-stage chronic diseases of major organ systems, inflammation-driven malnutrition eventually occurs. Malnutrition develops in 20 to 50% of patients with COPD,[12] congestive heart failure,[13] liver cirrhosis,[14] or chronic kidney failure.[15] Patients with certain neurologic disorders (e.g., dysphagia after stroke or Parkinson's disease) and those with psychiatric or cognitive disorders have a similar risk of malnutrition, which is mainly related to reduced food intake for noninflammatory reasons. Alzheimer's disease is associated with malnutrition from various causes in 20 to 30% of cases.[16] In addition, half of patients with major depressive disorder lose weight.[17]

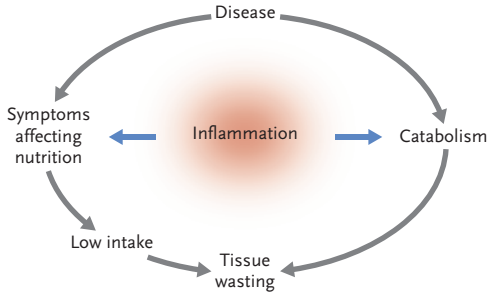

Figure 2. Two Pathways of Disease-Related Malnutrition.
Malnutrition with underlying disease develops through two parallel and partly intertwined pathways. In the absence of inflammation, symptoms affecting nutrition (e.g., appetite loss, dysphagia, and malabsorption) result in low food intake and reduced assimilation. With inflammation, muscle and fat breakdown increases and results in tissue loss. Inflammation also often induces loss of appetite that may decrease intake as well.

CONSEQUENCES OF MALNUTRITION

Decreased muscle strength and mass (i.e., sarcopenia) is a major disabling complication of disease-related malnutrition, with subsequent mobility limitations, falls, and fractures.[18] In older people, frailty is increased.[19] Immunodeficiencies and resulting infections occur early in the course of malnutrition. The rapid turnover of immune cells requires high energy and nutrient supplies. T-cell dysfunction resembles that seen in human immunodeficiency virus infection and acquired immunodeficiency syndrome. B-cell dysfunction attenuates humoral antibody production. Such effects are likely to have contributed to the high incidence of death from coronavirus disease 2019 (Covid-19) among older persons residing in nursing homes.[20] Micronutrient deficiencies, including deficiencies in vitamins B_1, B_6, B_{12}, and D, folic acid, and essential n–3 and n–6 fatty acids, have specific deleterious effects.[21] Depression was an unexpected observation in young men voluntarily exposed to semistarvation in the Minnesota Starvation Experiment of the mid-1940s.[22]

In addition to the humanitarian costs, malnutrition has high societal costs.[23] In recent years, awareness of the harmful effects of malnutrition and the often unmet nutritional needs of patients and older adults has led to a plea to consider clinical nutrition a human right.[24]

RECOGNIZING MALNUTRITION

SCREENING FOR MALNUTRITION RISK

Screening for possible malnutrition is recommended within the first 24 to 48 hours after admission to a hospital or nursing home. A number of screening tools are available[35] that typically classify persons as at risk or malnourished on the basis of two or three criteria (Table 1). For hospitalized patients, the Nutritional Risk Screening 2002 tool,[27] the Malnutrition Universal Screening Tool,[26] the Short Nutritional Assessment Questionnaire,[26] and the Malnutrition Screening Tool[25] provide rapid assessment of nutritional risk. The Mini Nutritional Assessment–Short Form[30] is adapted to assess the risk of malnutrition among older persons. The distinction between the risk of malnutrition (e.g., weight loss or underweight) and risk factors for malnutrition (e.g., loss of appetite or illness) is gaining new attention.[36]

For patients in the intensive care unit, who typically require immediate nutritional care, conventional screening tools are usually not applicable. Still, the Nutrition Risk in the Critically Ill score has been shown to have prognostic value.[37]

ASSESSMENT FOR DIAGNOSIS

Other diagnostic approaches, not necessarily called screening tools, are generally more complex and combine more measures[15,28,29,31-33,38] (Table 1). Examples are the Subjective Global Assessment (SGA)[28]; the Patient-Generated SGA, which is mainly for patients with cancer[29]; and the Academy of Nutrition and Dietetics–American Society for Parenteral and Enteral Nutrition Indicators to Diagnose Malnutrition approach.[38] All methods use a mixture of similar phenotypic and etiologic criteria, with criteria combinations and cutoff variations leading to differences in prevalence estimates.[39]

GLOBAL LEADERSHIP INITIATIVE ON MALNUTRITION

In 2019, four major international clinical nutrition societies unveiled the Global Leadership Initiative on Malnutrition (GLIM) criteria to bring together existing tools for diagnosing malnutrition,[34] with the goal of establishing a consensual diagnostic process for global use. The two-step procedure involves initial use of a sensitive screening tool to identify persons at

Table 1. Major Screening, Assessment, and Diagnostic Tools for Malnutrition in Adults.*

Tools (Year)	Phenotypic Variables				Cause		
	Weight Loss	Appetite Loss	Low BMI	Low Muscle Mass	Low Food Intake	Disease Burden or Inflammation	Other
Screening							
MST[25] (1999)	>2 lb (1 kg)	Yes	—	—	—	—	
MUST[26] (2000)	>5% in the past 3–6 mo	—	<20	—	Yes	Yes	
NRS[27] (2002)	>5%	—	<20.5	—	Yes	Yes	
SNAQ[26] (2005)	>3 kg in the past 1 mo or >6 kg in the past 6 mo	Yes	—	—	—	—	
Assessment and diagnosis							
SGA[28] (1987)	>5% in the past 6 mo	Yes	—	Yes	Yes	Yes	Reduced function
Patient-Generated SGA[29] (1995)	>2% in the past 1 mo	Yes	—	Yes	Yes	Yes	Reduced function
MNA[30] (1999)	>1 kg in the past 3 mo	Yes	<23	—	Yes	Yes	
MNA–Short Form[30] (2001)	>1 kg in the past 3 mo	Yes	<23	—	Yes	Yes	
Definition of cachexia[31] (2008)	>5% in the past 1 yr	Yes	<20	Yes	—	Yes	Elevated serum CRP
Definition of protein energy wasting[15] (2008)	>5% in the past 3 mo or >10% in the past 6 mo	—	<23	Yes	Yes	CKD	Low serum albumin, low body fat
Definition of cancer cachexia[32] (2011)	>5% in the past 6 mo or >2% if low BMI	—	<20	Yes	—	Cancer	
AAIM[38] (2012)	>1–2% in the past 1 wk or >5% in the past 1 mo	—	—	Yes	Yes	Yes	Fluid retention, reduced function
ESPEN[33] (2015)	>5% in the past <3 mo or >10% in the past >3 mo	—	<20/22†	Yes	—	—	
GLIM[34] (2019)	>5% in the past <6 mo or >10% in the past >6 mo	—	<22/20/18.5†	Yes	Yes	Yes	

* AAIM denotes Academy of Nutrition Dietetics (AND)–American Society for Parenteral and Enteral Nutrition (ASPEN) Indicators to Diagnose Malnutrition, BMI body-mass index (the weight in kilograms divided by the square of the height in meters), CKD chronic kidney disease, CRP C-reactive protein, ESPEN European Society for Clinical Nutrition and Metabolism, GLIM Global Leadership Initiative on Malnutrition, MNA Mini Nutritional Assessment, MST Malnutrition Screening Tool, MUST Malnutrition Universal Screening Tool, NRS Nutritional Risk Screening, SGA Subjective Global Assessment, and SNAQ Short Nutrition Assessment Questionnaire.

† According to ESPEN and GLIM, the BMI cutoff is 22 for persons 70 years of age or older and 20 for persons younger than 70 years of age. GLIM also adjusts its BMI cutoffs for differences in ethnic group (i.e., for Asian persons, the BMI cutoffs for persons in those age groups are <20 and <18.5, respectively).

risk for malnutrition, followed by confirmation of the diagnosis in persons with apparent malnutrition. GLIM recommends mandatory assessment of three phenotypic criteria — weight loss, low body-mass index (BMI), and low muscle mass — and two etiologic criteria — decreased food intake or food assimilation and a high disease burden, as indicated by the presence of persistent or recurrent inflammation (Fig. 3). Simultaneous fulfillment of at least one phenotypic and one etiologic criterion confirms the diagnosis. The malnutrition is classified as moderate or severe, depending on the degree of aberration in the phenotypic criteria. Finally, malnutrition can be categorized according to cause: disease-related malnutrition with inflammation, disease-related malnutrition without perceived inflammation, or malnutrition in the absence of disease (i.e., starvation) (Fig. 1).

The GLIM criteria combine nutrition-related variables, including BMI, that are validated separately on the basis of their prognostic value. The current obesity pandemic may limit the use of BMI in regions with a high prevalence of overweight and obesity.[40,41] In addition, thresholds for underweight are lower in Asian persons than in other populations.

Initially, GLIM was criticized as a new concept that was introduced without solid validation. Approximately 4 years after the introduction of the criteria, PubMed listed more than 300 observational and validation studies of varying quality and more than 10 systematic reviews and meta-analyses. Criterion validity, tested mainly with the SGA as the comparator, appears to be satisfactory,[42] and predictive validity is good, with overall survival being the most common outcome assessed.[43] Nevertheless, continuous improvement of the method is needed. Guidance on the use of the muscle mass and inflammation criteria has recently been provided.[44] Because technical devices for measuring body composition are not usually available, measurement of calf circumference and trained physical examination are approved methods for estimating muscle mass. It has also been suggested that clinical judgment about disease burden and inflammation does not always require laboratory confirmation.[34] The fact that the choice of screening method leads to unjustified variations in the prevalence of malnutrition warrants thorough consideration.[36]

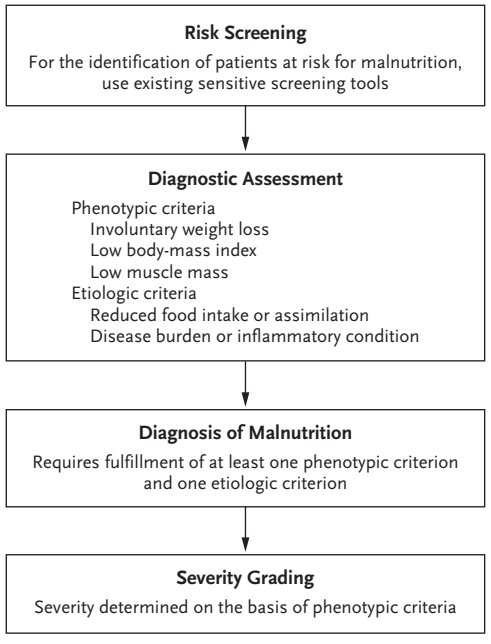

Figure 3. Global Leadership Initiative on Malnutrition (GLIM) Approach to Screening, Diagnosis, and Grading of Malnutrition.

After risk screening, persons identified as being at risk for malnutrition should undergo diagnostic evaluation according to three phenotypic and two etiologic criteria. If one of each is fulfilled, the diagnosis is confirmed.

INTERNATIONAL DIAGNOSTIC CLASSIFICATION

The *International Classification of Diseases, 11th Revision* (ICD-11), currently lacks a clinically relevant diagnostic code for malnutrition in adults. More than 40 national clinical nutrition societies with global reach, together with the Swedish National Board of Health and Welfare, submitted a proposal to the World Health Organization in 2020 to fill this gap.[45] The proposal is based on the consensus in the clinical nutrition community that malnutrition in adults is diagnosed by means of a combination of phenotypic and etiologic criteria.

TREATMENT OF MALNUTRITION

ASSESSMENT FOR NUTRITIONAL TREATMENT

A thorough nutritional assessment is recommended to facilitate an individualized nutritional treatment program.[46] This assessment should include the medical history (coexisting conditions),

social and psychological history (living conditions and factors such as loneliness and depression), and nutritional history (dental status and factors such as difficulty chewing and dysphagia), if the appropriate sources of information are available. Meal observations, as well as records and recall of food intake, should be considered. Physical examination should include an estimate of muscle mass[44] and fat mass. Coexisting sarcopenia,[18] sarcopenic obesity,[40] or frailty[19] should be noted. Laboratory measurements that are usually performed for other reasons and may provide nutritional information include hemoglobin, liver function, lipids (e.g., serum cholesterol levels, which are usually decreased with inflammation and malnutrition), and CRP (the preferred biomarker of inflammatory activity). Visceral proteins such as serum albumin are negative acute-phase reactants and should not be used as indicators of nutritional status.[47] Serum insulin-like growth factor 1 may indicate anabolic activity. The serum creatinine level may reflect muscle mass if renal function is intact.[48]

GENERAL ASPECTS OF NUTRITIONAL THERAPY

A regular oral diet or medical nutrition is used to compensate for inadequate energy and nutrient intake.[1,2] Medical nutrition consists of modified therapeutic diets, such as fortified foods and oral nutritional supplements; enteral nutrition (tube feeding); and parenteral nutrition.[1,2] The effect of nutritional therapy depends on the mechanism underlying malnutrition. When food intake is inadequate, the supply of energy and nutrients usually restores nutritional status,

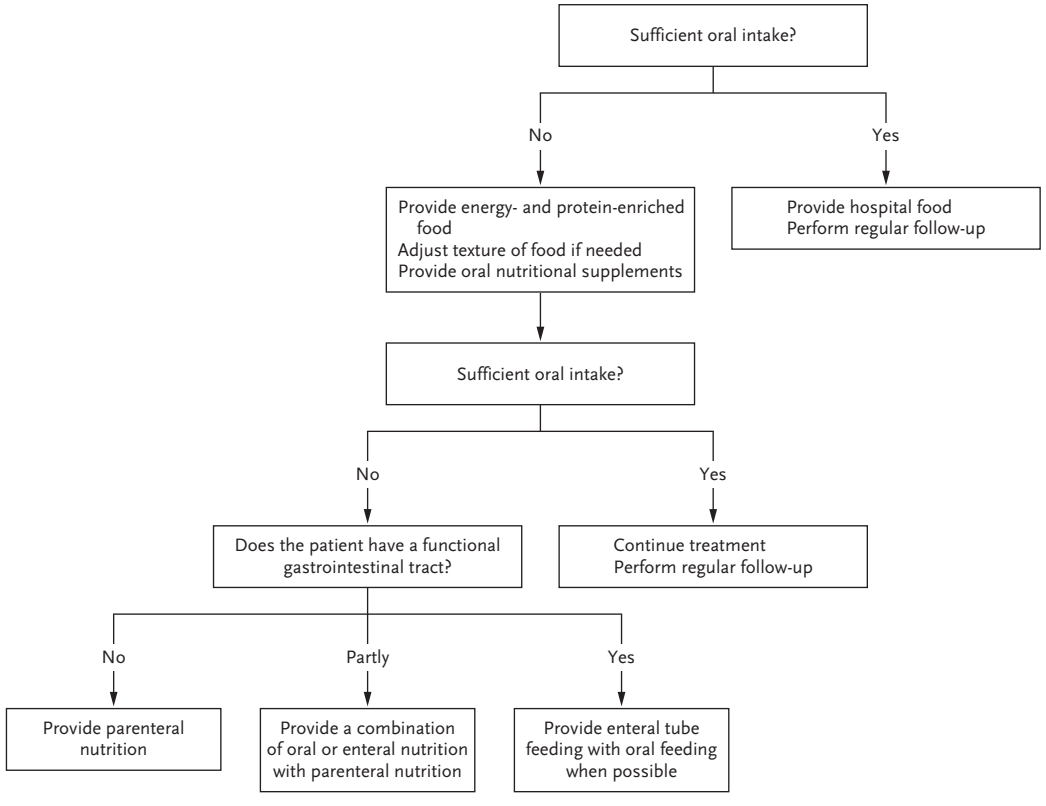

Figure 4. Algorithm for Nutritional Support.

First-line therapy for insufficient oral intake is the provision of nutritional counseling, modified food, oral nutritional supplements, or all three. If first-line therapy is insufficient or not feasible, enteral or parenteral nutrition is provided.

whereas the anabolic response is limited when inflammatory mechanisms predominate.[8]

The general indication for enteral or parenteral nutrition is inadequate nutrient intake for a week or more, whereas in critical care, nutritional needs must be met promptly. In general, the preferred choice is enteral nutrition[49] (Fig. 4), which requires a functioning gut. Enteral nutrition improves gut barrier functions, and it is associated with fewer infectious and metabolic complications than parenteral nutrition. A small proportion of patients require total parenteral nutrition.

EVIDENCE BASE FOR NUTRITIONAL TREATMENT

Numerous studies of nutritional therapy have been conducted. Complex patient populations, lack of consensus on outcome variables, blinding difficulties, inadequate funding, and other factors make it challenging to conduct high-quality randomized, controlled trials according to the requirements for pharmacologic trials. Nutritional therapy trials are usually conducted in the context of underlying diseases, which further complicates the interpretation of results. As a consequence, the evidence base for nutritional therapies has been inconsistent.[50] Recently, however, it has been strengthened by major studies and meta-analyses (discussed below).

ENERGY AND PROTEIN REQUIREMENTS

Patients with malnutrition who are not critically ill often have functional impairments that reduce energy expenditure, whereas other nutrient requirements are generally unchanged.[51,52] Indirect calorimetry, a preferred method for measuring energy requirements,[53] is usually not available outside intensive care units. On the basis of expert consensus, the estimated energy requirement is 30 kcal per kilogram of body weight per day in mobile persons with limited physical activity and 25 kcal per kilogram per day in bedridden patients.[51,52] For hospitalized and critically ill patients, the expert consensus–based recommendation is 70 to 75% of calculated energy requirements (i.e., 18 to 20 kcal per kilogram per day), especially in the first phase of treatment.[51,52,54-56]

Protein requirements are the subject of considerable debate in the nutrition community.[57] Until recently, young and old people were considered to have the same requirement — 0.8 g of protein per kilogram per day — on the basis of short-term nitrogen balance studies.[58] With a new understanding of age-related changes in metabolism, immunity, hormone synthesis, and progressive frailty with age, protein requirements of 0.8 to 1.2 g per kilogram per day in healthy adults, 1.2 to 1.5 g per kilogram per day in acutely ill patients or well-nourished patients after surgery, and 1.5 to 2.0 g per kilogram per day or even higher in patients with burns or multiple trauma are now widely recommended but remain controversial.[51,52,54-57,59] In patients with impaired protein utilization, such as those with hepatic or renal insufficiency (estimated glomerular filtration rate, <30 to 40 ml per minute per 1.73 m^2 of body-surface area), the recommendations are lower.[60]

ORAL TREATMENT

Food intake is facilitated by nutritional counseling (preferably provided by dietitians); assistance with eating for disabled persons; modification of texture, especially for those with dysphagia; and food fortification with energy (preferably nontropical vegetable oils) and protein for "small eaters." The volume of food taken orally should be adjusted to accommodate the amount of nutrients needed.[61]

Energy and protein can also be provided in fortified oral nutritional supplements: the typical amounts are 200 to 300 kcal and 10 to 20 g of protein per 100 ml.[61] Even in light of the difficulties in conducting flawless randomized, controlled trials of nutrition interventions, the EFFORT[62] and NOURISH[63] trials provide solid evidence of the positive clinical effects of oral nutritional supplements. The EFFORT trial randomly assigned more than 2000 medical inpatients to individualized nutritional counseling and support or standard hospital food. Energy and protein intakes were increased in the intervention group as compared with the control group, and at 30 days, functional capacity was improved, and readmission rates and mortality were reduced. Subgroup analyses indicated that patients with cancers also benefit from the intervention.[64]

The NOURISH trial, which involved 600 dis-

charged patients with various diseases who were malnourished, showed that a 3-month course of oral nutritional supplements was associated with almost a 50% reduction in mortality.[63] The average intake was 1 to 2 packages per day, with 350 kcal and 20 g of protein plus vitamin D and hydroxymethylbutyrate (HMB) contained in each package. Similar results were also observed in a subgroup analysis of data from patients with COPD.[65] Moreover, early nutritional intake reduced complications and mortality among patients hospitalized for acute heart failure.[66]

Systematic reviews and meta-analyses support the conclusions from these two trials.[67-69] The more recent and well-conducted studies appear to offer the best evidence.[69] Questions for further investigation are whether some of the essential amino acids (e.g., leucine and HMB) have specific anabolic effects and whether marine n–3 fatty acids have immunomodulatory as well as growth-promoting effects.

ENTERAL NUTRITION

Enteral nutrition is provided with a tube inserted orally through a nostril into the stomach or proximal small intestine (for use for up to a few weeks) or placed directly into the gastrointestinal tract as a nutritive stoma by means of percutaneous endoscopic gastrostomy or surgery.[70] Patients who are conscious often find the discomfort associated with a nasogastric tube unacceptable. Once the correct position of the tube has been confirmed, enteral nutrition is usually administered in intermittent doses (boluses) of 500 ml.[71] Especially in acute care settings, continuous flow with pump control for 20 to 24 hours per day is an option. Conversion to postpyloric feeding is recommended if gastric feeding is not acceptable to the patient.[54]

A slow infusion rate at the beginning of therapy may prevent gastrointestinal and metabolic symptoms. If nausea and vomiting occur, feeding should be reduced or discontinued to lower the risk of pulmonary aspiration. Prokinetic medications may be considered. Diarrhea is the most common complication. Metabolic complications of enteral nutrition include fluid imbalances, hyperglycemia, electrolyte abnormalities, and occasionally, refeeding syndrome (discussed below).

PARENTERAL NUTRITION

Parenteral nutrition provided through a peripheral or central venous catheter is indicated when gastrointestinal function is insufficient to ensure adequate absorption of nutrients and fluids.[54-56,72] A central venous catheter is preferred for higher osmotic loads to prevent phlebitis and when parenteral nutrition is required for longer than a few weeks. Central access carries the risk of bloodstream infection and thrombosis. For long-term use, such as in patients with chronic intestinal failure, a central venous catheter is tunneled subcutaneously from the venous access point to the skin exit.

Parenteral solutions meet basic glucose needs, provide adequate energy, and provide amino acids for protein synthesis. Approximately 125 g of glucose per day is sufficient, but up to 200 g per day may be protein-sparing. At the beginning of nutritional treatment, a reduced dextrose load can be administered to assess whether parenteral nutrition is associated with unacceptable side effects. Glucose monitoring is required to ensure appropriate insulin coverage. Essential fatty acid requirements can be met with approximately 200 g of lipid emulsion per week, but usually up to half the nonprotein energy is provided by lipids. The first lipid emulsions were based on soybean oil, which is rich in n–6 fatty acids. In recent years, lipid preparations based on monounsaturated oleic acid and n–3 polyunsaturated fatty acids have been introduced, since high soybean oil concentrations may cause hepatobiliary complications. Moreover, a lower ratio of n–6 to n–3 polyunsaturated fatty acids may modulate the inflammatory response. Amino acid solutions should provide 0.10 to 0.15 g of nitrogen per kilogram per day as a basal replacement. In inflammatory and hypermetabolic states, 0.15 to 0.20 g of nitrogen per kilogram per day is required. Fat- and water-soluble vitamins and trace elements should be added to complete parenteral nutrition.

Complications of parenteral nutrition include mainly catheter-related thrombosis and bloodstream infections but also local infections at the exit site. Metabolic complications are usually related to the rate of infusion. Elevated blood glucose levels, changes in blood electrolyte levels, azotemia, and hypertriglyceridemia are common. Hepatic dysfunction, often with cholestasis or hepatic

steatosis, may complicate long-term parenteral nutrition. Maintaining some level of oral or enteral intake or using alternative lipid emulsions is likely to reduce hepatobiliary risks. For patients receiving enteral or parenteral nutrition at home, outpatient nutritional counseling is critical for clinical outcomes, including survival.[73,74]

REFEEDING SYNDROME

Refeeding syndrome may develop, especially in severely malnourished patients, at the beginning of nutritional therapy.[75] Cautious initial caloric and fluid provision and careful monitoring are warranted to prevent this syndrome.

When supplied glucose increases insulin levels, phosphate, potassium, and magnesium shift intracellularly in the blood, and serum concentrations are decreased. This shift can lead to hypophosphatemia, edema, and cardiac and respiratory failure (tachycardia and tachypnea, in particular) and should be carefully monitored. Thiamine requirements increase during the transition from starvation to feeding. Wernicke's encephalopathy, characterized by confusion, delirium, ataxia, and ophthalmoplegia, may occur. Thiamine supplementation is generally given to prevent this life-threatening complication.

Treatment and prevention of refeeding syndrome consist of reducing caloric and fluid delivery, correcting low blood levels of phosphate and other electrolytes and nutrients (thiamine), and slowly increasing nutrients and fluids to recommended levels within 4 to 7 days.[75]

POSSIBLE FUTURE DEVELOPMENTS

Pharmacologic treatments to improve appetite (e.g., megestrol acetate and ghrelin agonists) or anabolism (e.g., myostatin decoy receptors and selective androgen receptor modulators) have been tested over the years, but without major breakthroughs. Nevertheless, ongoing research is likely to improve the understanding and treatment of malnutrition. Examples of the topics of such research include interactions between the gut microbiome and malnutrition, genomic and metabolomic profiling for precision nutritional treatments, the anorexia of aging and the potential development of pharmacologic appetite stimulants, and potential stroma-cell infusions. The development of options for treatment that are environmentally sustainable is a contemporary challenge.

SUMMARY

Malnutrition in adults follows two major pathological pathways — nutrient deprivation and inflammation-induced anorexia with tissue catabolism — and can be divided into disease-related malnutrition with inflammation, disease-related malnutrition without perceived inflammation, and non–disease-related malnutrition. Loss of muscle mass and weakness contribute to sarcopenia and amplify frailty in older adults. Increased susceptibility to infection and dysfunction of major organ systems are the main negative consequences.

Malnutrition occurs in up to 10% of community-dwelling older people and in 20 to 50% of hospitalized or institutionalized older people and is an imminent threat for critically ill patients with a high inflammatory burden. Adults admitted to hospitals or long-term care facilities should be screened for the risk of malnutrition, and a diagnosis of malnutrition should be documented. The recently introduced GLIM approach, which includes weight loss, underweight, and low muscle mass as phenotypic criteria and decreased food intake or assimilation and an inflammatory disease burden as etiologic criteria, is promising for a future consensus approach to the diagnosis of malnutrition.

Persons with malnutrition should receive nutritional counseling and oral, enteral, or parenteral nutrition as appropriate. Electrolyte, cardiac, and respiratory monitoring are essential for preventing refeeding syndrome. Precision nutrition will allow for personalized treatment. In general, daily energy and protein requirements are 20 to 30 kcal per kilogram and 0.8 to 1.5 g of protein per kilogram. In recent years, large-scale randomized, controlled trials have shown the beneficial effects of individualized nutritional counseling combined with energy- and protein-fortified oral nutritional supplements. Interventions may still not reverse the condition because of the inflammatory nature of the underlying disease. Future directions for research include a refinement of the techniques for detecting malnutrition and a better understanding of catabolic metabolism and anorectic mechanisms, leading to improved treatment.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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