Chapter 164: Assessment of Nutrition Status and Nutrition Requirements

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CHAPTER SUMMARY FROM THE PHARMACOTHERAPY HANDBOOK

For the Chapter in the Schwinghammer Handbook, please go to Chapter 60, Nutrition Assessment and Support.

KEY CONCEPTS

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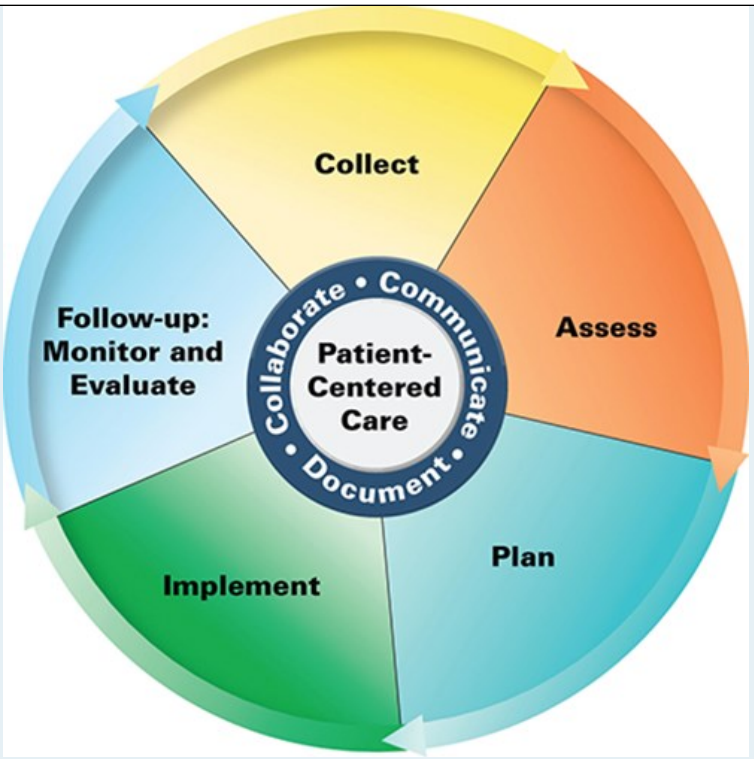
1. Malnutrition encompasses both undernutrition and overnutrition (obesity); although, the term is most often used to refer to undernutrition.
2. Nutrition screening is distinct from nutrition assessment; an effective screening process should be designed to identify quickly and consistently those with pre-existing malnutrition or those at risk for malnutrition.
3. A comprehensive medical, surgical, and dietary history; a nutrition-focused physical examination (NFPE); and anthropometric and laboratory measurements are essential components of a comprehensive nutrition assessment.
4. Anthropometrics, physical measurements of the size, weight, and proportions of the human body, are important parameters used to assess nutrition status.
5. Laboratory assessment of nutrition status must be interpreted in the context of clinical status and acute and chronic inflammation.
6. Macronutrient or micronutrient deficiencies or toxicities or risk factors for these deficiencies or toxicities can be identified by a comprehensive nutrition assessment.
7. Evidence-based patient-specific goals should be established considering the patient's clinical condition and the need for maintenance or repletion in adults and continued growth and development in children.
8. Validated predictive equations and population estimates are most often used to determine energy requirements; however, if available, indirect calorimetry is the most accurate bedside method to determine energy requirements.
9. Daily protein needs are based on age, sex, nutrition status, disease state, and clinical condition.
10. Drug–nutrient interactions can affect response to medication therapy and nutrition status.

PATIENT CARE PROCESS

Patient Care Process for Nutrition Screening and Assessment



Collect

- Patient characteristics (eg, age, sex, diagnosis)
- Patient history (eg, medical, surgical, diet, recent GI losses, environmental exposures, alcohol use; see Tables 164-1, 164-2)
- Current medications, including nutrition supplements
- Objective data
  - Body weight (current and usual)
  - Stature, body mass index (BMI), head circumference
  - Recent dietary and fluid intake
  - Nutrition-focused physical exam (see Table 164-3)
  - Labs (eg, serum electrolytes; glucose; blood urea nitrogen; serum creatinine [SCr]; albumin, prealbumin; C-reactive protein [CRP]; liver function tests; vitamin, mineral, and trace element concentrations)

Assess

- Nutrition status: presence of malnutrition, obesity (see Table 164-4)
- Risk of refeeding syndrome (eg, unintentional weight loss of more than 5% to 10% of usual body weight, prolonged period with poor caloric intake, BMI less than 18.5 kg/m^2, loss of subcutaneous fat, loss of muscle mass, electrolyte abnormalities)
- Signs and symptoms of micronutrient deficiencies or toxicities (see Tables 164-7, 164-8)
- Determine nutrition requirements based on current clinical condition (see Tables 164-9, 164-10, 164-11, 164-12, 164-13, 164-14, 164-15)

Plan*

- Conduct indirect calorimetry to estimate energy needs, if appropriate
- Develop a nutrition care plan to ensure delivery of estimated nutrition needs (energy, protein, fluid, vitamins, trace elements)
- Develop a plan to avoid or manage potential drug-nutrient interactions (see Table 164-16)
- Develop a plan to monitor nutritional recovery
- Make referrals to other providers, when appropriate (eg, dietitian, speech therapist, wound care nurse, lactation specialist)

Implement*

- Provide nutrition support using estimated goals
- Provide nutrient supplements to correct deficiencies
- Restrict nutrients to avoid toxicities
- Provide patient education regarding all elements of the nutrition care plan

Follow-up: Monitor and Evaluate

- Appropriate weight gain, loss, or maintenance
- Appropriate gains in length and head circumference in children
- Maintenance or return of function, including muscle strength
- Laboratory parameters, as indicated
- Monitor for side effects of nutrition care
- Monitor for patient adherence to nutrition care plan

* ***Collaborate with patient, caregivers, and other healthcare professionals***

BEYOND THE BOOK

BEYOND THE BOOK

Watch these videos from the American Society for Parenteral and Enteral Nutrition to enhance understanding of malnutrition, the etiology of malnutrition, and identification of malnourished patients. These videos will aid in the COLLECT and ASSESS steps in the patient care process:

- "Malnutrition Matters: A Call to Action for Providers Caring for Adult Patients" (15 minutes): https://youtu.be/JORLgsyri5U
- "GLIM Educational Series Part 1: What is GLIM?" (11 minutes): https://youtu.be/XIgB7eobGRY

INTRODUCTION

Nutrition care is an essential component of quality patient care. Nutrition screening and assessment are integral components of the nutrition care process. No single clinical or laboratory parameter is an absolute indicator of nutrition status, so information must be collected and analyzed from a

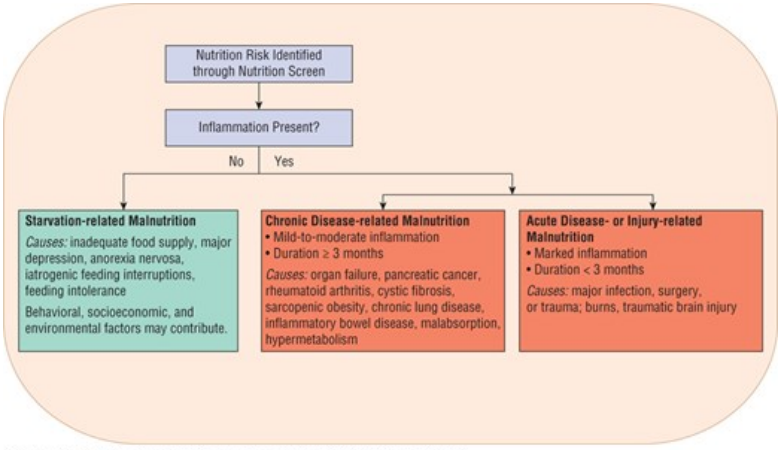
number of sources. This chapter reviews tools most commonly used for accurate, relevant, and cost-effective nutrition screening and assessment, including various methods used to determine patient-specific macro- and micronutrient requirements and potential drug–nutrient interactions (DNI).

CLASSIFICATION OF NUTRITION STATUS

1 *Malnutrition* encompasses both undernutrition and overnutrition (obesity); although, the term is most often used to refer to undernutrition. Malnutrition is a consequence of nutrient imbalance. In general, deficiency states can be classified as those involving protein, energy, or single nutrients such as individual vitamins or trace elements. Many terms have been used to define malnutrition leading international nutrition experts to propose standardization of nomenclature and diagnosis for both adults and children.[1–3] Starvation-associated malnutrition, *marasmus*, results from prolonged inadequate intake, absorption, or utilization of protein and energy. It can occur in patients with an inadequate food supply, anorexia nervosa, major depression, and malabsorption syndromes (Fig. 164-1). Somatic protein (skeletal muscle) and adipose tissue (subcutaneous fat) wasting occurs, but visceral protein (albumin [ALB] and transferrin [TFN]) production is usually preserved. Moderate weight loss of 10% of usual body weight (UBW; typical weight) over a 6-month period is prognostic of poor clinical outcomes. A severe weight loss (30% or more of UBW) is life-threatening.[4] Patients with starvation-associated malnutrition commonly have a prototypical wasted appearance. When starvation-associated malnutrition develops as a consequence of primarily inadequate protein intake as is seen in areas of famine or limited food supply, affected individuals may not appear malnourished because of relative adipose tissue sparing, especially with mild undernutrition, but visceral (and to some degree somatic) protein stores are depleted, resulting in severe hypoalbuminemia and edema in more advanced cases. In patients with starvation-related malnutrition, enhancing nutritional intake or bypassing impaired absorption with nutrition support can reverse the condition. Careful nutritional resuscitation is required to avoid complications related to refeeding.[5]

FIGURE 164-1

Etiologic basis for malnutrition diagnosis. (*Data from References* 1 and 2.)



Malnutrition (undernutrition) may also develop as the result of an acute or chronic condition or disease, especially those associated with mild-to-severe inflammation (see Fig. 164-1).[1,2,4,6] Patients with severe acute disease or injury (major infections, burns, trauma) or with chronic inflammatory diseases (Crohn's disease), organ failure, or cancer can develop disease-related malnutrition because of increased metabolic demands despite seemingly adequate nutrition intake. Individuals with pre-existing starvation-related malnutrition can develop pronounced malnutrition if they experience a severe injury or inflammatory process. In patients with disease-related, acute or chronic, malnutrition, simply providing nutrients in usual or even increased amounts may not be sufficient to reverse the nutrient imbalance due to the chronic inflammatory process. As a patient's clinical course progresses, they may change from one malnutrition classification to another.[4] Regardless of the cause, malnutrition (undernutrition and overnutrition) can result in changes in subcellular, cellular, or organ function that increase morbidity and mortality.

Nutrition screening is also used to identify overnutrition: overweight and obese individuals and those at risk of becoming overweight or obese. Obesity is a major global healthcare concern; during 2017 to 2018, the age-adjusted prevalence of obesity (defined as a BMI ≥ 30 kg/m^2) was 42.4% and severe

obesity (defined as a BMI ≥ 40 kg/m^2) was 9.2% of US adults.[7] In all states, more than 20% of adults were obese. Obesity prevalence in 2020 was 20% to 24.99% only in Colorado, Hawaii, Massachusetts, and the District of Columbia; and 35% or more in 16 states (Alabama, Arkansas, Delaware, Indiana, Iowa, Kansas, Kentucky, Louisiana, Michigan, Mississippi, Ohio, Oklahoma, South Carolina, Tennessee, Texas, and West Virginia).[8] In fact, US obesity and severe obesity prevalence has increased from 1999-2000 to 2017-2018, 30.5% to 42.4% and 4.7% to 9.2%, respectively.[8] Additionally, 19.3% (14.4 million) of all US children and adolescents, aged 2 to 19 years, were obese (BMI ≥ 95th percentile-for-age on the gender-appropriate BMI-for-age Centers for Disease Control and Prevention's [CDC] 2000 growth chart).[7,9] The prevalence of obesity in children varied by age group: 2 to 5 years, 13.4%; 6 to 11 years, 20.3%; and, 12 to 19 years, 21.2%.[7] The consequences of obesity are numerous and include type 2 diabetes mellitus, cardiovascular disease, hypertension, and stroke. Obesity contributes significantly to all-cause mortality and decreased life expectancy.[10]

Because malnutrition is associated with higher morbidity and mortality rates in many settings, an effective nutrition screening program is essential to identify patients at nutrition-related risk, alerting clinicians to perform a comprehensive nutrition assessment to accurately characterize baseline nutrition status, estimate nutrition needs, and develop a patient-specific nutrition care plan. Diligent monitoring of ongoing nutrition status can ensure that nutrition-related goals are being met and improve patient outcomes.

NUTRITION SCREENING

2 Nutrition screening is distinct from nutrition assessment; an effective screening process should be designed to identify quickly and consistently those with pre-existing malnutrition or those at risk for malnutrition.[11] It is not practical, expedient, cost-effective, nor clinically warranted to conduct a comprehensive nutrition assessment on every individual; thus, nutrition screening provides a reliable, systematic method to identify persons for whom a detailed nutrition assessment is warranted. A validated nutrition screening tool can be used to detect those who are overweight, obese, malnourished, or at risk for malnutrition; predict their health outcomes based on nutrition-related factors; and identify individuals who would benefit from nutritional intervention.[11,12]

The ideal nutrition screening tool is quick, simple, and noninvasive and can be done by lay and healthcare providers in homes, long-term care facilities, ambulatory care clinics, and hospitals. In 1995, The Joint Commission implemented a standard for accredited healthcare institutions requiring a nutrition screen be completed within 24 hours of inpatient admission on all applicable patients.[13] Because nutrition assessment has been routinely adopted in the United States, this standard was deleted in 2016. Periodic rescreening should occur at regular intervals determined by the institution and the patient population, usually every 3 to 7 days. For outpatients, nutrition screening should occur at the first visit with a new provider and thereafter as warranted by the patient's condition.

Risk factor identification is the foundation of appropriate nutrition screening. Risk factors for malnutrition include recent unintended weight loss; presence and severity of acute and chronic disease states; medications and or other treatments; socioeconomic factors that may result in a decreased nutrient intake; and, altered nutrient absorption, metabolism, or utilization. Risk factors for obesity include a family history of obesity, certain medical diagnoses (eg, polycystic ovary syndrome, Prader-Willi syndrome, Cushing's syndrome), poor dietary habits, inadequate exercise, and some medication therapies. Various rating and classification systems have been proposed to screen for nutrition risk and guide subsequent interventions.[11] In general, checklists of varying complexity are used to quantify a person's food and alcohol consumption habits; ability to buy, prepare, and eat food; weight history; diagnoses; medical and surgical procedures; medication and supplement therapies; and, history of nutrition support (enteral nutrition [EN] or parenteral nutrition [PN]). Although no tool is 100% sensitive and specific for detecting malnutrition, the Mini Nutritional Assessment – Short Form and the Malnutrition Screening Tool (MST) have high sensitivity and specificity.[12] The Mini Nutritional Assessment – Short Form is used extensively in older adults and found to be useful in several care settings.[12] The Nutrition Risk Screening 2002 (NRS 2002) and the Nutrition Risk in the Critically Ill (NUTRIC) may be used as nutrition assessment tools in critically ill adults, but supporting literature is limited.[14–16] Given the drawbacks with use of these tools, a more simple approach is to ask two simple questions: 1) Has there been a recent weight loss of at least 5% to 10%?; and 2) Has there been inadequate food intake for at least 1 to 2 weeks? If the answer to either question is *Yes*, then further assessment is warranted.[11] Nutrition screening for children generally is based on the evaluation of growth parameters against the World Health Organization (WHO; birth to 2 years of age) or CDC (2 to 19 years of age) growth charts,[9,17] the presence of medical conditions known to increase nutrition risk, and recent changes in weight or food intake. Estimates of the prevalence of in-hospital malnutrition for pediatric and adult patients are variable depending on the patient population, disease severity, and the criteria used. According to data from the 2018 Healthcare Cost and Utilization Project, 8.9% of all US nonmaternal,

nonneonatal hospital discharges included a coded diagnosis of malnutrition.[18]

In any setting, patients screened to be nutritionally-at-risk should receive a timely comprehensive nutrition assessment to verify nutrition-related risk and to formulate a complete nutrition care plan which includes monitoring parameters to ensure that desired outcomes are met. For patients who are screened to be *nutritionally-at-risk*, a comprehensive nutrition assessment ideally will be completed by a trained professional within 48 to 72 hours. Most nutrition assessments are completed by dietitians or nurses but may be completed by others including pharmacists, physicians, and physician assistants with training in nutrition support.

NUTRITION ASSESSMENT

3 A comprehensive medical, surgical, and dietary history; a nutrition-focused physical examination (NFPE); and anthropometric and laboratory measurements are essential components of a comprehensive nutrition assessment. Goals of nutrition assessment include identification of risk factors associated with malnutrition, including disorders resulting from macro- or micronutrient deficiencies (undernutrition), obesity (overnutrition), or impaired nutrient absorption, metabolism, or utilization; determination of the risk of nutrition-related complications; estimation of nutrition needs; and establishment of baseline nutrition parameters against which to measure nutrition therapy outcomes.[11]

Nutrition-Focused History and Physical Examination

The nutrition-focused medical, surgical, and dietary history serves to identify factors that predispose to malnutrition (eg, prematurity, chronic disease, gastrointestinal [GI] dysfunction, alcohol misuse, acute or chronic inflammation [eg, cancer, surgery, trauma]), and overnutrition (eg, poor dietary habits, limited exercise, chronic disease, family history) (Table 164-1). The clinician should clarify any history of weight gain or loss (intended or unintended), anorexia, vomiting, diarrhea, decreased or restrictive food intake, and EN or PN. Any conditions that suggest ongoing inflammation, including fever, hyperthermia, tachycardia, or infection should be documented (Table 164-2).[6]

TABLE 164-1

Pertinent Data from a Nutrition-Focused Medical, Surgical, and Dietary History

Nutrition Intake and Dietary Habits
Anorexia
Unusual or absent taste
Diet, including vegetarian, vegan
Specialized nutrition support (enteral or parenteral nutrition)
Supplemental vitamin, mineral, or herbal intake
Food allergies or intolerances
Underlying Pathology with Nutritional Effects
Chronic infection or inflammatory state
Cancer
Endocrine disorders
Chronic illness (lung disease, cirrhosis, kidney failure)
Hypermetabolic states (trauma, burns, sepsis)
Digestive/absorptive disease, nausea, vomiting, diarrhea, constipation
Hyperlipidemia
End-organ Effects
Weight changes
Skin or hair changes
Exercise intolerance or fatigue
Gastrointestinal tract symptoms (diarrhea, vomiting, constipation)
Gastrointestinal Surgery
Bariatric surgery
Small bowel or colon resection or diversion
Gastrectomy
Miscellaneous
Catabolic medications or therapies (corticosteroids, immunosuppressive agents, radiation, chemotherapy)
Other medications (diuretics, laxatives, antipsychotics, anabolic steroids)
Genetics (body habitus of parents, siblings, family)
Alcohol or drug misuse
Pregnancy or lactation

TABLE 164-2

Assessment of Inflammation

Laboratory Assessment	Clinical Findings	Acute/Chronic Disease States
Decreased Albumin Transferrin Prealbumin Nitrogen balance Elevated CRP Serum glucose % neutrophils Decreased or increased WBC	Fever Hyperthermia Infection Urinary tract Pneumonia Bacteremia Wound/incision Abscess	Cancer Celiac disease Cystic fibrosis Inflammatory bowel disease Organ failure (ARDS) Pancreatitis Rheumatologic disorders (RA, SLE) Trauma (burns, major surgery, TBI)

ARDS, acute respiratory distress syndrome; CRP, C-reactive protein; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; TBI, traumatic brain injury; WBC, white blood cell count.

The NFPE uses a systematic approach to assess for abnormal nutrition-related clinical and physical findings in each region of the body. Components of the NFPE include: general inspection; vital signs; skin; nails; head/hair; eyes/nose; mouth; neck/chest; abdomen; and, musculoskeletal.[15] The clinician completing a NFPE assesses for muscle and fat loss; fluid status; micronutrient deficiency/toxicity; functional status/hand grip strength; and, for children, mid-arm muscle circumference (MUMC).[19,20] Findings commonly associated with malnutrition (eg, muscle wasting, alopecia, dermatitis, glossitis, cheilosis, jaundice) are noted (Table 164-3).

TABLE 164-3

Nutrition Focused Physical Examination (NFPE) Findings Suggestive of Malnutrition

General Inspection	**Eyes/Nose**
Edema	Dull dry appearance to sclerae or inner lids
Cachexia or obesity	Dull milky appearance of cornea
Signs/symptoms of dehydration (poor skin turgor, sunken eyes, orthostasis, dry mucous membranes)	Bitot's spots[a]
Muscle wasting or loss of subcutaneous fat	Icteric sclerae
Vital Signs	Pale conjunctiva
Fever	Cracked red corners of eyes
Tachycardia	**Mouth**
Skin	Pale, red, or bleeding gums
Thin, shiny, dry, or scaly skin	Dry, cracked, red lips
Dermatitis, rash	Fissures at corners (angular stomatitis)
Decubitus ulcers, poorly healing wounds	Vertical cracks of the lips (cheilosis)
Bruising, petechiae	Magenta or beefy red tongue (glossitis)
Follicular hyperkeratosis	Atrophied papillae
Pallor, cyanosis, jaundice	Excessive dental caries
Nails	**Neck/Chest**
Spoon shape, clubbing	Enlarged thyroid
Transverse ridging/banding	Distended neck veins
Mottled, pale, poor capillary refill	Prominent bony chest, visible ribs (muscle and fat wasting)
Head/Hair	**Abdomen**
Dry, dull, brittle, sparse, easily pluckable hair	Scaphoid, concave, or protuberant abdomen
Corkscrew, coiled, or depigmented hair	Hepatomegaly, ascites
Alopecia	**Musculoskeletal**
Scaly, flaky scalp	Ataxia (poor muscle control)
Moon face	Numbness, tingling
Bilateral temporal wasting	Swollen or painful joints
	Rickets, knock knees, bowleg

[a] Bitot's spots are foamy spots on the surface of the eye.

The Subjective Global Assessment (SGA) and the tool described in the Academy of Nutrition and Dietetics (AND) and the American Society for Parenteral and Enteral Nutrition (ASPEN) consensus statement on the identification and documentation of adult malnutrition are representative examples of a relatively simple, reproducible, cost-effective, bedside approach to nutrition assessment.[1,11] The SGA assesses five aspects of the medical and dietary history: weight change in the previous 6 months, dietary changes, GI symptoms, functional capacity, and disease states known to affect nutrition status. Weight loss of less than 5% of UBW is considered a "small" loss, 5% to 10% loss is "potentially significant," and more than a 10% loss is "definitely significant." Dietary intake is characterized as normal or abnormal, and the duration and degree of abnormal intake are noted. The presence of daily GI symptoms (anorexia, nausea, vomiting, diarrhea) for longer than 2 weeks is significant. Functional capacity assesses the patient's energy level and whether the patient is active or bedridden. Finally, disease state impact on metabolic demands (no, low, moderate, or high stress) is documented. Four physical examination findings are rated as normal, mild, moderate, or severe: loss of subcutaneous fat (triceps and chest), muscle wasting (quadriceps and deltoids), edema (ankle and sacral), and ascites. The patient's nutrition status is then rated as adequately nourished, moderately malnourished or suspected of being malnourished, or severely malnourished. Critics of the SGA find it time-consuming and complex. The AND/ASPEN consensus tool assesses six characteristics: insufficient energy intake, weight loss, loss of muscle mass, loss of subcutaneous fat, localized or generalized fluid accumulation, and diminished functional status measured by hand grip strength. The presence of two or more of these

characteristics identifies malnutrition in an adult.

Given variability in diagnostic criteria for malnutrition, the Global Leadership Initiative on Malnutrition (GLIM) was convened to reach global consensus.[3] GLIM established a two-step model that includes malnutrition risk screening of at-risk individuals with a validated tool and assessment for diagnosis and severity grading. Patients who are identified at-risk undergo diagnostic assessment that incorporates phenotypic criteria (nonvolitional weight loss, low BMI, reduced muscle mass) and etiologic criteria (reduced food intake or assimilation, disease burden/inflammatory condition). Malnutrition is diagnosed in patients with at least one phenotypic and one etiologic criterion with further severity grading based on phenotypic metrics.

Anthropometric Measurements

Anthropometrics, physical measurements of the size, weight, and proportions of the human body, are important parameters used to assess nutrition status. Common measurements are weight, stature (standing height or recumbent length), waist circumference, and head circumference (occipital frontal circumference) for children younger than 3 years of age. Measurement of limb size, such as skinfold thickness, MUMC, and wrist circumference, may be useful in selected individuals. Accurate measurement of anthropometrics rather than the use of self-reported values is critical for accurate assessment. Measurement can be difficult in injured and critically ill patients but should be conducted as soon as feasible.

Bioelectrical impedance analysis (BIA) is also an anthropometric assessment tool. Body measurements can be compared with normative population standards to identify clinical concerns and may be repeated at various intervals to monitor response to a nutrition care plan. In adults, nutrition-related changes in anthropometric measurements tend to occur slowly; several weeks or more may be required before detectable changes are noted. In infants and young children, changes occur more quickly. Significant acute changes in weight and skinfold thickness usually reflect changes in hydration status, which must be considered when interpreting these parameters.

Weight, Stature, and Head Circumference

Body weight is a nonspecific measure of body cell mass, representing skeletal mass, body fat, and the energy-using component, lean body mass (LBM). Fat-free mass includes skeletal muscle, bone, connective tissue, organs, and water while fat mass includes the subcutaneous fat beneath the skin and the visceral (internal) fat. Change in weight over time, particularly in the absence of edema, ascites, or voluntary losses, is an important indicator of altered LBM. Actual body weight (ABW) interpretation should include consideration of ideal weight-for-height, referred to as ideal body weight (IBW), UBW (typical weight), fluid status, and age (Table 164-4). Both acute and chronic changes in fluid status can affect the ABW; these changes often can be detected by monitoring the patient's daily fluid intake and output. Patients who are dehydrated will have a decreased ABW but not a loss of LBM. Once rehydrated, these patients must be reweighed to establish an appropriate baseline weight for nutrition evaluation. Edema and ascites increase total body water (TBW), thus increasing ABW but not LBM. The ABW of patients with severe edema and ascites should not be used for nutrition assessment, and practitioners often use an estimated "*dry weight*" to account for this TBW increase.

TABLE 164-4

Evaluation of Body Weight and Waist Circumference

Parameter	Interpretation	NHLBI Obesity Classification	Waist Circumference	
ABW compared with IBW				
ABW <69% IBW	Severe malnutrition			
ABW 70%-79% IBW	Moderate malnutrition			
ABW 80%-89% IBW	Mild malnutrition			
ABW 90%-120% IBW	Normal			

ABW >120% IBW	Overweight			
ABW ≥150% IBW	Obese			
ABW ≥200% IBW	Morbidly obese			
ABW compared with UBW				
ABW 85%-95% UBW	Mild malnutrition			
ABW 75%-84% UBW	Moderate malnutrition			
ABW <75% UBW	Severe malnutrition			
BMI (kg/m^2)				
Adults				
<16	Severe malnutrition			
16-16.9	Moderate malnutrition			
17-18.9	Mild malnutrition			
19-24.9	Healthy		Disease risk above BMI-related risk[a]	
22-30 (Older adults)	Healthy		Women ≤89 cm (35 in) Men ≤102 cm (40 in)	Women >89 cm (35 in) Men >102 cm (40 in)
25-29.9	Overweight		Increased	High
30-40	Moderate obesity			
30-34.9		I	High	Very high
35-39.9		II	Very high	Very high
>40	Severe or morbid obesity	III	Extremely high	Extremely high
Children				
BMI for age <5th percentile	Underweight			
BMI for age 5th-84th percentile	Healthy			
BMI for age 85th-94th percentile	Overweight			
BMI for age ≥95th percentile	Obese			

[a]Increased risk for Type 2 diabetes mellitus, hypertension, and cardiovascular disease.

NHLBI, National Heart, Lung, and Blood Institute.

The IBW is a population reference standard against which the ABW can be compared. IBW-for-height reference tables are available, and IBW can be calculated using mathematical equations based on sex and height. The most commonly used equations for calculating IBW for adults are the Devine equations where IBW is calculated as follows:[21]

$$\text{Adult men: IBW} = 50\ \text{kg} + (2.3 \times \text{inches over 6 feet})$$
$$\text{Adult women: IBW} = 45.5\ \text{kg} + (2.3 \times \text{inches over 6 feet})$$

Adult men: IBW=50 kg+(2.3×inches over 6 feet)Adult women: IBW=45.5 kg+(2.3×inches over 6 feet)

Adjusted body weight (AdjBW) has been suggested as a logical means to account for the percentage of the obese weight that is LBM (22% to 38%). For obese adults, use of an AdjBW has been recommended for nutrition-related calculations, as follows:

$$\text{AdjBW} = ([\text{ABW} - \text{IBW}] \times 0.25) + \text{IBW}$$

AdjBW=([ABW−IBW]×0.25)+IBW

However, the use of AdjBW is generally not recommended; its use is not evidence-based because most of the metabolic rate equations were formulated using ABW in a mix of obese and nonobese individuals.[22]

Multiple methods are available for estimating the IBW of children.[23] The Traub equation can be used for a child younger than 18 years of age and 60 inches or shorter:

$$\text{IBW} = ([\text{height(cm)}]^2 \times 1.65)/1,000$$

IBW=([height(cm)]2×1.65)/1,000

The McLaren method uses the WHO or CDC growth chart to compare height and weight relative to the child's age. A vertical line is graphed between the child's height-for-age measurement and the corresponding 50th percentile weight-for-age to determine the IBW. This approach becomes less accurate as the child's height deviates from the 50th percentile.[23]

Change in weight over time can be calculated as a percentage of UBW. Use of UBW as a reference point provides a more accurate reflection of clinically significant weight change over time (Table 164-4). The use of UBW avoids the inherent problems with normative tables and documents comparative changes in body weight. However, unless documented in the medical record, determining UBW depends on patient or family recall, which is often inaccurate. All weight changes should be interpreted relative to time because unintentional weight loss, especially rapid weight loss (5% of UBW in 1 month or 10% of UBW in 6 months), increases the risk of nutrition-related poor clinical outcomes.[12]

Stature is determined by both genetics and nutrition. Accurate measurement of stature is critical to appropriate interpretation. In older children and adults, a standing height should be obtained. If a standing height cannot be measured using a wall-mounted stadiometer, recumbent length, knee height, and arm spam have been used. Each of these methods yields different results.[24] In infants and young children who are unable to stand, a recumbent length is measured using a *length board* which requires two people to obtain an accurate measurement.

Demispan is determined in a seated patient by measuring the distance from the sternal notch to the web between the middle and ring fingers along a horizontally outstretched arm with the wrist in neutral rotation and zero extension or flexion. Demispan may more accurately assess stature in elderly adults, especially those with kyphosis or vertebral collapse. After the demispan is measured, height is estimated using the following equations:[25]

$$\text{Women: Height (cm)} = (1.35 \times \text{demispan [cm]}) + 60.1$$
$$\text{Men: Height (cm)} = (1.4 \times \text{demispan [cm]}) + 57.8$$

Women: Height (cm)=(1.35×demispan [cm])+60.1Men: Height (cm)=(1.4×demispan [cm])+57.8

Knee height may also be used to estimate stature and is helpful in patients with limb contractures, such as patients with cerebral palsy and the elderly. Knee height is measured from just under the heel to the anterior surface of the thigh just proximal to the patella. Using the average of two measurements rounded to the nearest 0.1 cm, height can be estimated using the following equations:[12]

$$\text{Women: Height(cm)} = [1.83 \times \text{knee height(cm)}] - [0.24 \times \text{age(yr)}] + 84.8$$
$$\text{Men: Height(cm)} = [2.02 \times \text{knee height(cm)}] - [0.04 \times \text{age(yr)}] + 64.9$$

Women: Height(cm)=[1.83×knee height(cm)]−[0.24×age(yr)]+84.8Men: Height(cm)=[2.02×knee height(cm)]−[0.04×age(yr)]+64.9

Appropriate growth is predictable and the best indicator of adequate nutrition in a child. At each medical encounter, weight, stature, head circumference (until 3 years), and BMI (after 2 years) should be plotted on the WHO (younger than 2 years) or CDC gender- and age-specific growth curves.[9,17] The CDC charts were revised in 2000 from US data only and indicate how US children grow. The WHO charts developed in 2006 are preferred

in those younger than 2 years because they include data from infants from six industrialized countries including the United States who were predominantly breastfed for the first 4 months of life and who were receiving some breast milk at 12 months, conditions felt to ensure optimal growth.[17] Specialized charts are also available for assessment of growth of premature infants.[26,27] For premature infants with corrected postnatal age of 40 weeks or more, the WHO growth charts can be used; however, weight-for-age, length-for-age, and head circumference-for-age should be plotted according to corrected postnatal age until 2 years, 1.5 to 3 years, and 3 years of age, respectively.

Recommended intervals between measurements in young children are weight, 7 days; length, 4 weeks; height, 8 weeks; and head circumference, 7 days in infants and 4 weeks in children until 3 years of age. Daily weight fluctuations can occur with changes in fluid status. Growth velocity can be used to assess growth at intervals too close to plot accurately on a growth chart (Table 164-5). In newborns, average weight gain is 10 to 20 g/kg/day (24-35 g/day in term infants; 10-25 g/day in preterm infants depending on gestational age). The rate of weight gain declines considerably after 3 months of age; children 6 to 10 years of age gain about 2 to 3 kg/yr. The adolescent "growth spurt" typically begins at 9 to 10 years in girls and 11 to 12 years in boys. During the 11 to 13 year-old-interval of maximum growth in height, girls will gain about 10 kg (22 lb) while boys gain 15.5 kg (33 lb). Length increases rapidly in infancy (see Table 164-5). In children 6 to 10 years of age, height increases by 2 to 3 in/yr (approximately 5-7.5 cm/yr) and continues until about 16 to 18 years of age in girls and 18 to 20 years of age in boys. Head growth (measured by head circumference), usually 0.5 cm/wk (0.2 in/wk) during the first year of life, can be compromised during periods of critical illness or malnutrition. Rapid head growth, at a rate faster than expected, suggests hydrocephalus which may be benign but must be further evaluated.

TABLE 164-5

Expected Growth Velocities in Term Infants and Children

Age	Weight (g/day)	Height (cm/mo)[a]
0-3 mo	24-35	2.8-3.4
4-6 mo	15-21	1.7-2.4
7-12 mo	10-13	1.3-1.6
1-3 yr	5-9	0.6-1
4-6 yr	5-6	0.5-0.6
7-10 yr	7-11	0.4-0.5

Example of growth assessment
Age: 2 mo; weight: 3.2 kg; weight at 1 mo of age, 3.1 kg; time since last weight was obtained: 30 days.
Growth velocity = ([3.2 kg–3.1 kg] × 1,000 g/kg)/30 days = 3.3 g/day.
Interpretation: suboptimal growth; comprehensive nutrition assessment needed.

[a]Growth velocity of 1 cm/mo is equivalent to 0.4 in/mo.

In the International Classification of Disease-10 (ICD-10), failure-to-thrive (growth faltering) in a child is defined as *lack of expected normal physical growth*, *failure to gain weight*, or *lack of growth*. Not all children with low weight have failure-to-thrive, but it has been defined as weight-for-age, length-for-age, BMI-for-age, or weight velocity below the 2nd percentile or a weight deceleration crossing two or more major percentiles (major percentiles are defined as 97th, 95th, 90th, 75th, 50th, 25th, 10th, 5th, and 3rd), or if an infant is not gaining the expected daily weight.[28] In children, a significant weight loss is defined as: greater than 2% in 1 week; greater than 5% in 1 month; greater than 7.5% in 3 months; and, greater than 10% in 6 months. Growth faltering is best defined by using z-scores for weight-for-length, BMI-for-age, or length- or height-for age: a z-score of -1 indicates mild malnutrition; -2 moderate malnutrition; and, -3 severe malnutrition.[2] Weight-for-height evaluation is age independent and helps differentiate a

stunted child (chronic malnutrition) from a wasted child (acute malnutrition). Short stature can be associated with chronic undernutrition, but short stature in the absence of poor weight gain suggests another etiology, such as growth hormone deficiency or constitutional growth delay.[29]

Body Mass Index

BMI can be calculated as either body weight in kilograms divided by height in meters squared (kg/m^2) or body weight in pounds multiplied by 703 divided by height in inches squared (lb/in^2). The assessment of BMI is the first step but not the sole criterion to judge potential health risk.[30] A BMI of 25 kg/m^2 or higher is a risk factor for premature death and disability. Health risks increase with increasing BMI; however, individual variation, especially in very muscular persons, can lead to erroneous nutrition status classification when BMI alone is used. Thus, BMI must be interpreted based on characteristics such as sex, frame size, race/ethnicity, and age. For example, at the same BMI, a woman tends to have more body fat than a man, and an older adult will have more body fat than a younger one.

The National Institutes of Health obesity expert panel report classifies a BMI between 18.5 and 24.9 kg/m^2 as a healthy or normal weight, between 25 kg/m^2 and 29.9 kg/m^2 as overweight, between 30 kg/m^2 and 39.9 kg/m^2 as obese; and, 40 kg/m^2 or higher as extreme obesity (see Table 164-4).[31] These BMI classifications may not be appropriate for adults older than 60 to 65 years. The Centers for Medicaid and Medicare Services defines normal BMI for adults older than 65 years to be between 23 kg/m^2 and 30 kg/m^2; the National Screening Initiative defined normal BMI for this age as 22 to 27 kg/m^2. The NIH classifies a BMI of less than 18.5 kg/m^2 as undernutrition, but this relationship is not as well established.[31] BMI values below 18.5 kg/m^2 have been associated with higher mortality rates in patients with cancer.[32] Children 2 years of age and older whose BMI is at or above the 85th percentile or at or above the 95th percentile on the age- and gender-specific CDC BMI chart are classified as overweight and obese, respectively.[9,17] Use of these charts at each medical encounter helps to heighten awareness of children whose BMI and family history put them at risk for adult obesity and its associated complications.

Waist Circumference

Body fat distribution is associated with health risk. Waist circumference is a simple measurement used to assess abdominal (visceral) fat. Waist circumference is determined by measuring the distance around the waist just above the iliac crest after exhaling. Extra weight around the waist rather than peripheral (subcutaneous) fat confers a greater health risk than extra weight around the hips and thighs. The larger the waist circumference, the greater the risk of obesity-related complications, especially diabetes mellitus, cardiovascular disease, and all-cause mortality.[30,33] Men and women are considered to have abdominal obesity and at increased risk (beyond their BMI-related risk) when the waist circumference is greater than 40 inches (102 cm) and greater than 35 inches (89 cm), respectively (Table 164-4). Children have abdominal obesity if the waist circumference is at or above the 90th percentile according to CDC age- and sex-specific standards.[34]

Waist-to-Hip and Waist-to-Height Ratios

The waist-to-hip ratio is determined by dividing the waist circumference by the hip circumference (maximal posterior extension of the buttocks). In adults, a waist-to-hip ratio of greater than 0.9 in men and 0.85 in women is considered an independent risk factor for adverse health consequences.[33] Waist-to-height ratio (both measured in centimeters) has been used to evaluate children at risk for the metabolic syndrome because, unlike waist circumference, it is independent of age and sex. A child (aged 6 to 18 years) with a waist-to-height ratio of more than 0.5 is considered to have abdominal obesity and at risk for developing the metabolic syndrome. This cutoff may overestimate abdominal obesity in younger children (aged 2 to 5 years).[34]

Skinfold Thickness and Mid-Arm Muscle Circumference

More than 50% of the body's fat is subcutaneous; thus, changes in subcutaneous fat reflect changes in total body fat. Skinfold thickness measurement provides an estimate of subcutaneous fat, and MUMC, which is calculated using the skinfold thickness and mid-arm circumference, estimates skeletal muscle mass. Although simple and noninvasive, these anthropometric measurements are used most commonly in population analysis and long-term monitoring of individuals. Triceps skinfold thickness measurement is used most often, but reference standards also exist for subscapular and suprailiac measurements.[35] Consistent technique in the use of pressure-regulated calipers is essential for reproducibility and reliability in measuring skinfold thickness. Published standards do not account for variation in bone size, muscle mass, hydration, or skin compressibility, and they do not

consider obesity, ethnicity, illness, and increased age. Results should be interpreted cautiously as these parameters change slowly in adults, often requiring weeks before significant alterations from baseline can be detected. These parameters will change more rapidly in young children.

Bioelectrical Impedance

BIA is a portable, simple, quick, noninvasive, and relatively inexpensive technique used to measure body composition.[36,37] When a weak, alternating electric current is applied to two appendages (wrist and ankle or both feet), impedance (resistance) to flow is measured as it passes through the body. Different body tissues have varying amounts of water and will conduct the electrical current differently. Water and electrolyte-rich tissues such as blood and muscle are highly conductive, but fat and bone are poor conductors. Assessment of LBM, TBW, and water distribution can be determined with BIA. Increased TBW decreases impedance; thus, it is important to evaluate hydration status when performing BIA. Other potential limitations of BIA include variability with electrolyte imbalance and interference by large fat masses, environment, ethnicity, menstrual cycle phase, and underlying medical conditions.[37] Although BIA equations have high validity when used in the population in which they were developed (mostly young healthy adults), BIA calculations are subject to considerable errors if applied to other populations or when conditions are not identical (eg, electrode placement).[37] The use of BIA in clinical practice may be limited by the lack of reference standards that reflect variations in individual age, body size, and clinical conditions.[36] Due to the proprietary nature of manufacture-specific BIA regression models and inability to compare studies using different devices, current guidelines do not provide recommendations regarding the use of BIA in clinical practice.[38]

OTHER NUTRITION ASSESSMENT TOOLS

Functional status is dependent on nutrition, but the specific tools to assess it are not well defined. Muscle function is an end-organ response; thus, diminished skeletal muscle function can be a useful indicator of malnutrition. Muscle function may also recover more quickly in response to adequate nutrition support than anthropometric measurements. Simple functional assessments include the ability to perform activities of daily living, participate in physical and occupational therapy, and wean from the ventilator. Hand-grip strength (forearm muscle dynamometry), respiratory muscle strength, and muscle response to electrical stimulation also have been used. Measuring hand-grip strength is part of a NFPE and is a relatively simple, noninvasive, and inexpensive procedure that correlates well with patient outcome.[39–41] Normative standards supplied by the manufacturer of the specific dynamometer must be used for assessment. Hand grip strength is an indirect measurement of LBM making it a good parameter for assessment of undernutrition. However, some conditions will limit hand grip strength, such as rheumatoid arthritis, stroke, neuromuscular disease, dementia, and heavy sedation. Ulnar nerve stimulation causes measurable muscle contraction and is used in most intensive care units to monitor neuromuscular blockade. In malnourished patients, increased fatigue and a slowed muscle relaxation rate are noted, and these indices may return to normal with refeeding.

Other methods used to determine body composition include bioimpedance spectroscopy, dual energy x-ray absorptiometry (DXA), quantitative computed tomography (CT), air displacement plethysmography (BodPod®), three-dimensional photonic scanning, quantitative magnetic resonance imaging (MRI), ultrasonography, and positron emission tomography.[14,37,38,42] These methods are often complex and expensive to perform. DXA, best known for its use in measuring bone density, is a promising method for routine clinical practice because it can quantify mineral, fat, and LBM compartments and is available in most hospitals and many outpatient facilities. Current guidelines recommend the use of DXA for assessing fat mass in patients with a variety of disease states, but the validity for lean mass assessment is unknown.[38] A central body DXA scanner requires a fair amount of space, and the cost depends on the scanner's complexity. Portable (or peripheral) DXA devices can be used to measure bone density in peripheral bones, such as the wrist, fingers, or heel, and have also been used to assess subcutaneous fat. Portable DXA scanners are much less expensive than central scanners and can be used in community screenings. Further research is needed to determine how DXA can be used clinically in nutrition assessment. MRI and CT can measure subcutaneous, intra-abdominal, and regional fat distribution and thus also have the potential to be useful clinically. Ultrasound uses high-frequency sound waves to image soft tissue structures in an inexpensive and noninvasive manner. Current guidelines do not recommend ultrasound to assess body composition due to the lack of evidence for supporting its validity in clinical practice.[38]

Laboratory Assessment

5 Laboratory assessment of nutrition status must be interpreted in the context of clinical status and acute and chronic inflammation. Biochemically, serum visceral proteins (ALB, TFN, and prealbumin [also known as transthyretin]) have traditionally been used to assess LBM. C-reactive protein (CRP)

can be useful as a marker of inflammation.

Serum Visceral Proteins

Visceral proteins synthesized by the liver have historically been considered useful parameters for nutrition assessment, but newer literature challenges this premise.[43] It is assumed that in undernutrition states, a low serum protein concentration reflects diminished hepatic protein synthetic mass and indirectly reflects the functional protein mass of other organs (heart, lung, kidney, and intestines). However, visceral proteins are not valid proxy measures of total body mass.[43] Many factors other than nutrition can affect the serum concentrations of these proteins including age; abnormal kidney (nephrotic syndrome), GI tract (protein-losing enteropathy) or skin (burns) losses; hydration (dehydration results in hemoconcentration, overhydration in hemodilution); liver function (synthesis); and metabolic stress and inflammation (chronic disease, sepsis, trauma, surgery, infection). Thus, visceral protein concentrations must be interpreted relative to the individual's overall clinical condition and inflammatory state (Table 164-6).

TABLE 164-6

Serum Proteins Associated with Nutrition Risk

Serum Protein	Half-Life (Days)	Functions	Factors Resulting in Increased Values	Factors Resulting in Decreased Values
Albumin	18-20	Maintains plasma oncotic pressure; transports small molecules	Dehydration, anabolic steroids, insulin, infection	Fluid overload; edema; kidney dysfunction; nephrotic syndrome; poor dietary intake; impaired digestion; burns; heart failure; cirrhosis; thyroid, adrenal, or pituitary hormones; trauma; sepsis
Transferrin	8-9	Binds Fe in plasma; transports Fe to bone	Fe deficiency, pregnancy, hypoxia, chronic blood loss, estrogens	Chronic infection, cirrhosis, burns, enteropathies, nephrotic syndrome, cortisone, testosterone
Prealbumin (transthyretin)	2-3	Binds T_3 and, to a lesser extent, T_4; retinol-binding protein carrier	Impaired kidney function	Cirrhosis, hepatitis, stress, surgery, inflammation, hyperthyroidism, cystic fibrosis, burns, zinc deficiency

Fe, iron; T_3, triiodothyronine; T_4, thyroxine.

The significant influence of inflammation on visceral protein concentrations is now well established; thus, these *negative acute phase reactants* may be considered to reflect the extent of physiologic stress or inflammation rather than the presence of undernutrition (Table 164-3).[43,44] During severe acute stress (eg, trauma, burns, sepsis), these proteins are decreased because the resultant increased vascular permeability can lead to dramatic fluid shifts and the reprioritizing of liver protein synthesis increases the production of acute-phase reactants such as CRP, ferritin, fibrinogen, and haptoglobin.[11,44] CRP is a true acute-phase protein rising within 10 hours after major surgery or acute sepsis; it can be used to assess the degree of inflammation present.[44] If CRP is elevated, then inflammation is likely contributing to decreased visceral protein concentrations making visceral proteins inflammatory markers associated with nutrition risk rather than markers of malnutrition or protein and energy intake inadequacy.[43] The role of visceral protein monitoring in nutrition support remains unclear; however, normalizing values may indicate resolving stress and inflammation, decreased nutrition risk, shift to anabolism, and/or decreasing nutritional requirements.[43] Thus, assessing individual patient trends, not comparison to normative standards, may be useful in monitoring recovery.

ALB is the most abundant serum protein and is critical for the maintenance of colloid oncotic pressure and binding and transport of numerous

hormones, anions, medications, and fatty acids. As an insensitive index of protein malnutrition, ALB is not a component of currently accepted definitions for malnutrition.[43] Factors that lead to ALB insensitivity include the large amount normally in the body (4-5 g/kg of body weight), extensive distribution in the extravascular compartment (60%), and long half-life (18-20 days). As discussed, ALB is a negative acute-phase reactant, and serum concentrations decrease with inflammation, infection, trauma, stress, and burns. Serum ALB concentrations less than 2.5 g/dL (25 g/L) can be expected to exacerbate ascites and peripheral, pulmonary, and GI mucosal edema because of decreased colloid oncotic pressure. Hypoalbuminemia also affects the interpretation of serum concentrations of calcium and highly protein bound medications (eg, phenytoin, valproic acid).

TFN is a glycoprotein that binds and transports ferric iron to the liver and reticuloendothelial system for storage. TFN is also a negative acute-phase reactant, and its concentration is decreased in the presence of critical illness and inflammation.[12] Because it has a shorter half-life (8-9 days) and there is less of it in the body (less than 100 mg/kg of body weight), TFN concentration decreases in response to various factors before the serum ALB concentration. If a direct measure of serum TFN is not available, TFN concentration can be estimated indirectly from measurement of total iron-binding capacity, as follows:

$$\mathrm{TFN(mg/dL)} = (\text{total iron} - \text{binding capacity[mcg/dL]} \times 0.8) - 43$$TFN(mg/dL)=(total iron−binding capacity[mcg/dL]×0.8)−43

Alternatively, TFN (mg/dL) = 0.7 × total iron-binding capacity (mcg/dL) and TFN (g/L) = 0.039 × total iron-binding capacity (µmol/L). Iron stores affect serum TFN concentrations: in iron deficiency, hepatic TFN synthesis is increased, resulting in increased serum TFN concentrations.

Prealbumin (transthyretin) is the transport protein for thyroxine and a carrier for retinol-binding protein. While prealbumin was historically used to monitor the short-term, acute effects of nutrition support or deficits, it is now recognized as an inflammatory marker that may be associated with risk of developing malnutrition or poor clinical outcomes.[43] Prealbumin stores are low (10 mg/kg of body weight), and it has a very short half-life (2-3 days); thus, the serum prealbumin concentration will decrease rapidly with severe metabolic stress (trauma, burns, sepsis). As with ALB and TFN, prealbumin synthesis is decreased in liver disease. Prealbumin is renally excreted, so falsely elevated prealbumin concentrations may be seen in patients with kidney dysfunction.

Nitrogen Balance Study

Nitrogen is found only in protein and at a relatively constant ratio of 1 g nitrogen per 6.25 g of protein. This ratio may vary somewhat for EN and PN formulations, depending on the biologic value of the protein source. The adequacy of protein intake can be assessed clinically by a nitrogen balance study—measuring urinary nitrogen excretion and comparing it with nitrogen intake. Nitrogen balance indirectly reflects protein utilization and/or the protein catabolic rate. As the stress level increases, a concomitant increase in protein catabolism (hypercatabolism) results in an increase in urinary nitrogen excretion. The amount of urine urea nitrogen (UUN) measured in a 24-hour urine collection in healthy individuals, accounts for 80% to 90% of the total urine nitrogen (TUN) excreted. Nitrogen output (g/day) can be approximated as 24-hour UUN + 4, where 4 is a factor representing usual skin, fecal, and respiratory nitrogen losses.[12] Alternatively, nitrogen output can be estimated using the equation: 24-hour UUN + 2 + 20% of urinary urea losses.[45] At higher UUN values (30 g nitrogen or more), then the use of a factor of + 6 may yield a more accurate measure of nitrogen output.[46] Alternatively, if available, TUN can be measured and may be more accurate, especially in critically ill patients who excrete more nitrogen-containing substances such as 3-methylhistidine. If TUN is used, then the best estimate of nitrogen output is TUN + 1.05, where 1.05 is the average extraurinary nitrogen losses.[46] In patients with decreased kidney function, in which case neither UUN nor TUN accurately represents net protein degradation, nitrogen output can be approximated with equations based on urea nitrogen appearance.[47]

Immune Function Tests

Nutrition status affects immune function either directly, via actions on the lymphoid system, or indirectly by altering cellular metabolism or organs that are involved with immune system regulation. Immune function tests most often used in nutrition assessment are the total lymphocyte count and delayed cutaneous hypersensitivity (DCH) reactions. Both tests are simple, readily available, and inexpensive. A lack of specificity, however, limits the usefulness of these tests as nutrition status markers.

Total lymphocyte count reflects the number of circulating T and B lymphocytes. Tissues that generate T cells are very sensitive to malnutrition, undergoing involution resulting in decreased T-cell production and eventually lymphocytopenia. A total lymphocyte count less than 1200 cells/mm^3 (1.2×10^9 cells/L) is a nonspecific marker for nutrition depletion.[12] Total lymphocyte count is reduced in the presence of infection (eg, human immunodeficiency virus [HIV], other viruses, tuberculosis), immunosuppressive drugs (eg, corticosteroids, cyclosporine, tacrolimus, sirolimus,

chemotherapy, antilymphocyte globulin), leukemia, and lymphoma.

DCH is commonly assessed using recall antigens to which the patient was likely previously sensitized, such as mumps and *Candida albicans*. Although not specific for nutrition status, anergy is associated with severe malnutrition, and response can be restored with nutrition repletion.[12] Factors affecting DCH include fever, viral illness, recent live-virus vaccination, critical illness, irradiation, immunosuppressive drugs, diabetes mellitus, HIV, cancer, and surgery. Other immune function tests used in nutrition research include lymphocyte surface antigens (eg, CD4, CD8, CD4:CD8 ratio), T-lymphocyte responsiveness, and various serum interleukin concentrations.

Nutrients such as arginine, omega-3 fatty acids, and nucleic acids given in pharmacologic doses may improve immune function. Monitoring efficacy of a nutrition care plan that includes these potentially immune-modulating nutrients may include these immune function assessments.

NUTRIENT DEFICIENCIES AND TOXICITIES

6 Macronutrient or micronutrient deficiencies or toxicities or risk factors for these deficiencies or toxicities may be identified by a comprehensive nutrition assessment. A comprehensive nutrition assessment should include an evaluation for possible essential fatty acid deficiency (EFAD) or vitamin or trace element toxicities. Because of their key role in metabolic processes (coenzymes and cofactors), a deficiency of any of these nutrients may result in altered metabolism and cell dysfunction. An accurate history to identify symptoms and risk factors for a specific nutrient deficiency or toxicity is critical. A NFPE and biochemical assessment to confirm a suspected deficiency or toxicity should be done in all nutritionally-at-risk patients. Ideally, biochemical assessment would be based on the nutrient's function (eg, metalloenzyme activity) rather than simply measuring the serum concentration. Unfortunately, few practical methods to assess micronutrient function are available; thus, the serum concentration is most often measured (Table 164-7).

TABLE 164-7

Assessment of Trace Element Status

Trace Element	Signs of Deficiency	Signs of Toxicity	Factors Associated with Altered Plasma Concentrations	Monitoring
Chromium	Impaired glucose/protein utilization, peripheral neuropathy, weight loss, increased LDL-C, increased free fatty acid concentrations	Industrial exposure: skin or nasal septum lesions, allergic dermatitis, increased incidence of lung cancer	**Decreased**: long-term inadequate intake **Increased**: kidney failure	Serum glucose, plasma chromium (unreliable)
Copper	Menkes' syndrome: progressive mental deterioration, vomiting, diarrhea, protein-losing enteropathy, hypopigmentation, bone and hair changes Deficiency: neutropenia, hypochromic anemia, pallor, dermatitis, neurological dysfunction, osteoporosis, myopathy, thrombocytopenia, decreased bone mineralization (children)	Wilson's disease: cirrhosis, Kayser-Fleischer rings[a], kidney dysfunction, neurologic or psychiatric symptoms (tremors, slow speech, inappropriate behavior, personality changes) Mild chronic toxicity: fatigue, anemia, thrombocytopenia Acute toxicity: nausea, vomiting, diarrhea	**Decreased**: high zinc, iron, or vitamin C intake; corticosteroid use **Increased**: infection, rheumatoid arthritis, pregnancy, oral contraceptives, decreased biliary excretion	Serum copper and ceruloplasmin with CRP[b], CBC
Iodine	Hypothyroid goiter, neuromuscular impairment,	Thyrotoxicosis: nodular goiter,	**Decreased**: long-term	Serum

	deaf-mutism, increased embryonic and postnatal mortality, cognitive impairment, impaired fertility, congenital hypothyroidism (severe cases)	weight loss, tachycardia, muscle weakness, warm skin	inadequate intake	T_3,T_4,TSH
Iron	Microcytic, hypochromic anemia (weakness, pallor, fatigue), glossitis, headache, dysphasia, nail changes, gastric atrophy, paresthesia, decreased cognitive function	Cirrhosis, cardiomyopathy, pancreatic damage, skin pigmentation changes	**Increased**: blood transfusion **Decreased**: blood loss; long-term iron-free PN	Serum ferritin[c], iron, percent iron saturation, iron binding capacity; CBC
Manganese	Nausea; vomiting; dermatitis; hair color changes; hypocholesterolemia; growth retardation; defective carbohydrate, lipid, and protein metabolism	Parkinsonian-like symptoms, hyperirritability, hallucinations, libido disturbances, ataxia, mental confusion, lack of attention, memory loss, weakness, seizures, facial nerve abnormalities, headache, dizziness, dystonia, peripheral neuropathy	**Increased**: decreased biliary excretion, high iron or vitamin C intake	Whole blood manganese, brain MRI
Molybdenum	Tachycardia, tachypnea, altered mental status, visual changes, headache, nausea, vomiting	Gout-like syndrome, increased urinary copper	**Decreased**: low birth weight, excessive GI losses	Urinary hypoxanthine, xanthine, and sulfite oxidase
Selenium	Muscle weakness or pain, cardiomyopathy, skin and hair pigmentation changes, macrocytosis, alopecia and growth retardation in infants	Nausea, vomiting, hair or nail loss, tooth decay, skin lesions, irritability, fatigue, peripheral neuropathy	**Decreased**: malignancy, liver failure, pregnancy, stress, infection **Increased**: reticuloendothelial-neoplasia	Plasma, serum, or whole blood selenium: RBC glutathione peroxidase; CBC
Zinc	Dermatitis (scaly, hyperpigmented skin lesions), stomatitis, glossitis, perioral and periungual ulceration, altered taste and smell, alopecia, diarrhea, apathy, depression, growth retardation, impaired wound healing, anorexia, confusion, immunosuppression, delayed sexual maturation, hypogonadism (decreased sperm count and function)	Acute: diarrhea, vomiting, nausea, dizziness, garlic-smelling breath; death with large IV doses Chronic: immunosuppression, decreased HDL-C, copper deficiency	**Decreased**: infection, burns, stress, hypoalbuminemia, corticosteroids, pregnancy, inflammation **Increased**: tissue injury, hemolysis, contaminated collection tube	Plasma or serum zinc with albumin and CRP, stool or ostomy output, serum copper

CBC, complete blood count; CRP, C-reactive protein; GI, gastrointestinal; HDL-C, high-density-lipoprotein cholesterol; IV, intravenous; LDL-C, low-density-lipoprotein cholesterol; MRI, magnetic resonance imaging; PN, parenteral nutrition; RBC, red blood cell; RQ, respiratory quotient; T_3, triiodothyronine; T_4, thyroxine; TSH, thyroid stimulating hormone.

[a]Kayser-Fleischer rings are dark rings that appear to encircle the iris of the eye.

[b]If CRP > 4 mg/dL (40 mg/L), serum copper concentration will be falsely elevated. Ceruloplasmin increased with inflammation, pregnancy, liver disease, malignancy, and myocardial infarction.

[c]If ferritin low, iron deficiency; if high, inflammation or iron overload.

Trace Elements

Trace elements considered essential in humans (at least one important role and a range of intakes within which homeostasis is maintained) are iron, zinc, selenium, copper, chromium, manganese, molybdenum, and iodine. A complete discussion of each of these elements is beyond the scope of this chapter.[48–52] Each trace element is involved in a variety of biologic functions and is necessary for normal metabolism, acting as a coenzyme or in other roles in hormonal metabolism or erythropoiesis. Toxicities can occur with excess intake of some trace elements. With the current interest in complementary medicine, clinicians must ask patients about their use of all dietary supplements.

Iron

Iron is the most abundant trace element and is an important component of hemoglobin, myoglobin, and cytochrome enzymes; it is also involved in oxygen transport and cellular energy production. Patients with iron-deficiency anemia typically present with fatigue, weakness, and pallor. Inadequate iron intake, malabsorption, and chronic blood loss are the principal causes of iron-deficiency anemia. Iron toxicity (overload) with possible organ damage can occur when chronic iron intake exceeds requirements, such as in patients receiving multiple blood transfusions over an extended period (1 unit of packed red blood cells provides 200-250 mg elemental iron). Iron deficiency or overload is confirmed by assessment of iron stores, as reflected indirectly by measurement of hemoglobin, serum iron, total iron-binding capacity, and serum ferritin or directly by bone marrow staining or liver biopsy. Direct methods are most accurate but invasive and rarely necessary. Because indirect parameters such as ferritin are altered by acute or chronic inflammation independent of iron stores, concomitant illness must be considered in their interpretation. As with visceral protein assessment, CRP measurement simultaneously with iron assessments will help to determine the degree to which inflammation influences these parameters.[50]

Zinc

Zinc, the second-most abundant trace element, is a cofactor in many enzymatic reactions involved in protein, fat, and carbohydrate metabolism and is involved in the regulation of gene expression, immunity, growth, wound healing, and liver regeneration.[49,50,53] Most of the body's zinc (85%) is found in muscle and bone; less than 1% is found in the serum. Zinc is eliminated through the urine and the GI tract. Zinc deficiency develops with decreased intake or absorption, increased loss, or increased demand. Risk factors for zinc deficiency include bariatric surgery, anorexia/bulimia, alcohol misuse, excessive fluid losses (bile, intestinal, urine), and increased metabolic demands (sepsis, burns).[53] Urinary zinc losses are increased by thiazide diuretics, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, and hemofiltration.[51] Zinc deficiency can develop in 14 days to 3 months with insufficient intake and is characterized by skin lesions (acrodermatitis enteropathica), a moist eczematous dermatitis that is most apparent in the nasolabial folds and around orifices, and other symptoms (Table 164-7).[49] Recovery is rapid with zinc supplementation; severe dermatitis can improve in as little as 4 to 5 days. Zinc deficiency can be documented by the presence of low serum zinc concentrations. However, serum zinc concentrations decrease during acute stress states and generally remain depressed until the stress resolves. Hair zinc analysis and urinary zinc excretion can be used as biomarkers of zinc status.[53] Excess zinc intake is eliminated by the kidneys and GI tract; thus, zinc toxicity is uncommon except in overdoses or with excessive, prolonged parenteral supplementation.

Selenium

Selenium is not an antioxidant itself but an integral part of selenoproteins. There are 25 genes coding for these selenoproteins, about half of which have a defined metabolic function. Important selenoproteins include selenoprotein P (antioxidant activity), glutathione peroxidase (antioxidant activity), iodothyronine deiodinase (thyroid hormone regulation), thioredoxin reductase (vitamin C), selenoprotein V (spermatogenesis), and selenoprotein S (inflammation, immune response).[50,54] A key metabolic function of selenium is its role in the enzymatic cofactor selenocysteine, the 21st proteinogenic amino acid.[54] Selenoprotein P is the major (60%) circulating form of selenium in serum.

Prematurity, critical illness, burns, chronic GI losses, and long-term selenium-free PN are associated with low serum selenium concentrations and decreased glutathione peroxidase activity.[49] The clinical significance of reduced serum selenium concentrations is unclear, but low selenium concentrations may increase susceptibility to physiologic stressors. Low serum selenium concentrations in critically ill patients correlate with low triiodothyronine (T_3) concentrations.[55] Serum selenium concentrations reflect acute distribution between tissues rather than selenium stores. Selenium deficiency is associated with muscle pain, wasting, and weakness (see Table 164-7), but severe biochemical deficiency is not always accompanied by these symptoms. Statins inhibit 3-hydroxy-3-methylglutaryl coenzyme A reductase and can induce myopathy by interfering with synthesis of selenoproteins.[50] Fatal cardiomyopathy may occur. Although critically ill patients may require higher selenium intakes than normal, optimal intake is unknown; current recommendations range from 20 to 1,000 mcg/day.[55]

Serum, erythrocyte, and whole-blood selenium; serum selenoprotein P; and serum, platelet, and whole-blood glutathione peroxidase activity respond to changes in selenium intake, but the response is heterogeneous.[56] Decreased serum selenium concentrations may indicate selenium deficiency, but reductions have also been observed in patients with malignancies, liver failure, pregnancy, alcohol misuse, and HIV; in patients receiving statins or corticosteroids; and in patients who smoke. Selenium toxicity (selenosis) generally occurs only in those with long-term exposure to foods grown in selenium-rich soil (eg, US Great Plains area) but may occur when intake exceeds 200 mcg/day or 5 mcg/kg/day for prolonged periods.[50] Selenium toxicity results in hair and nail brittleness and loss, GI disturbance, skin rash, garlic breath odor, fatigue, irritability, nervous system abnormalities, and has been linked to type 2 diabetes mellitus.[54]

Copper

Copper is a cofactor in oxidative enzymes vital to the function of hematopoietic, vascular, and skeletal tissue, as well as structure and function of the nervous system.[47,48,57] It is a component of ceruloplasmin and key metalloenzymes involved in iron and manganese metabolism (ceruloplasmin), electron transfer and oxidation-reduction reactions (cytochrome c oxidase), connective tissue and collagen cross-linking (lysyl oxidase), dopamine conversion to norepinephrine (dopamine monooxygenase), free radical scavenging (superoxide dismutase), and many others.[49,50] Copper is absorbed in the duodenum and excreted through the bile bound to bile salts. Most copper (67%) is found in bone and muscle, and 60% to 95% of serum copper is bound to ceruloplasmin.[58] Signs and symptoms of copper deficiency are listed in Table 164-7 and include anemia, neutropenia, thrombocytopenia, and neurologic dysfunction. In severe cases, such as in Menkes' syndrome, copper deficiency is further manifested as hypothermia, hair and skin depigmentation, progressive mental deterioration, and growth retardation. Factors predisposing to copper deficiency include generalized malabsorption, protein-losing enteropathy, nephrotic syndrome, prematurity, and copper-free PN.[57–59] Long-term PN supplemented with copper may increase the risk of copper toxicity in patients who develop cholestasis; however, copper deficiency has been reported with copper-free PN after copper removal from the PN solution due to a rising direct bilirubin concentration (cholestasis).[58] Patients undergoing bariatric surgery are at risk for copper deficiency as early as 2 months after surgery. Typically 1 to 3 weeks of oral copper supplementation or 5 days of IV supplementation (1 mg/day) is sufficient to correct the deficiency.[49,57]

Copper deficiency is assessed using serum copper concentrations along with CRP and ceruloplasmin, which appear to reflect changes in copper status in both copper-depleted and copper-replete individuals.[59] While reliable indicators of severe copper deficiency, serum copper and ceruloplasmin concentrations may not detect marginal copper deficiency because serum concentrations may be altered by a variety of conditions including inflammation (Table 164-7). Copper concentrations should be monitored every 2 to 6 months in patients receiving long-term PN. The chronic ingestion of excessive copper or inadequate elimination can result in cirrhosis as seen in Wilson's disease, an autosomal-recessive genetic disorder.

Chromium

Historically, trivalent chromium was thought to be essential for insulin function and maintenance of normal blood glucose concentrations. A low-molecular-weight chromium binding substance, *the glucose tolerance factor*, that may enhance insulin receptor response has been discussed. In 2014, the European Food Safety Authority (EFSA) determined that chromium is not an essential element in humans.[60] Chromium is stored in the heart, muscle, kidney, and liver and excreted in the urine.[49,52] Chromium deficiency may occur in patients receiving long-term chromium-free PN; symptoms include hyperglycemia, weight loss, and neuropathy.[49] Urine and serum chromium concentrations reflect chromium absorption not stores.[60] Chromium toxicity varies depending on the valence; trivalent chromium used in PN solutions is generally not toxic. No chromium toxicity has been

reported in patients receiving PN, even though intake may be 30 to 60 times higher than estimated requirements through chromium contamination, primarily Dextrose 70%,; additional supplementation is rarely needed.[52] Chromium toxicity has only been reported with contaminated drinking water or industrial exposure. Chromium supplementation as an adjunct to aerobic exercise for weight loss or diabetes mellitus management is ineffective.[60,61]

Manganese

Manganese is needed as a cofactor for several metalloenzymes, including isocitrate dehydrogenase (Krebs cycle), superoxide dismutase (mitochondrial antioxidant), glutamine synthetase (astrocytes), arginase (urea cycle), pyruvate carboxylase (carbohydrate metabolism), glycosyltransferases (bone formation), and prolidase (wound healing).[50,62] Excess manganese is rapidly and efficiently eliminated in bile in the absence of significant cholestasis. Excretion may be compromised in newborns due to immature liver function. Manganese deficiency is only associated with the ingestion of chemically defined manganese-deficient oral diets. Table 164-7 lists symptoms associated with manganese deficiency.

Manganese toxicity is more concerning and has been described in industrial exposures via inhaled manganese (welding) and in patients receiving long-term manganese-supplemented PN in the setting of chronic cholestasis. Toxicity may occur in adults receiving more than 500 mcg/day and in children receiving more than 40 mcg/kg/day.[62] Manganese can accumulate in brain tissue; an intravenous dosage of 1.1 mg/day has been associated with brain deposition.[50] Because of its paramagnetic properties, manganese is detectable using MRI with increased signal intensity on T1-weighted images of the basal ganglia, especially in the striatum, globus pallidus, and substantia nigra. Manganese appears to target the dopaminergic (DAergic) neurons but may affect other neurotransmitters.[62] Whole-blood manganese concentrations are used to assess manganese status; serum concentrations do not correlate with either whole blood concentrations or MRI findings.[62] The neurodegenerative process induced by manganese is termed *manganism*. Symptoms mimicking Parkinson's disease, including psychiatric symptoms, cognitive deficits, motor impairment, extrapyramidal symptoms, headache, dizziness, rigidity, tremors, ataxia, and facial muscle spasms.[49,62] Lewy bodies, the hallmark of Parkinson's disease, are not seen in manganism.[62] Removing manganese from the PN solution results in resolution of neurologic symptoms with partial or total MRI normalization within 1 year.[62] The newborn brain may be more susceptible to the effects of manganese toxicity which has implications for manganese supplementation in premature neonates receiving PN.[62]

Molybdenum

Molybdenum is a cofactor for enzymes involved in catabolism of sulfur-containing amino acids, purines, and pyrimidines (xanthine, aldehyde, sulfite oxidases).[49,50,63] Molybdenum deficiency is uncommon, but a rare genetic defect that prevents sulfite oxidase synthesis resulting in molybdenum deficiency has been identified. A continuous supply of sulfated compounds is needed during brain development; thus, young infants are at risk if an adequate molybdenum supply is not provided.[63] Molybdenum deficiency may occur in patients receiving long-term molybdenum-free PN; although significant molybdenum contamination is present in all PN solutions. Currently, there is no IV molybdenum product marketed in the United States, and no marketed trace element combination product contains molybdenum. Molybdenum deficiency symptoms include tachycardia, tachypnea, headache, night blindness, nausea, vomiting, central scotomas, lethargy, disorientation, and coma (Table 164-7).[49,50,63] Symptoms reverse with molybdenum supplementation. Plasma and serum molybdenum are very low and difficult to measure, and plasma concentrations do not reflect molybdenum status.[52] Biochemical abnormalities expected in molybdenum deficiency include very low serum and urine uric acid concentrations (low xanthine oxidase activity) and low urine inorganic sulfate concentrations with high urine inorganic sulfite concentrations (low sulfate oxidase activity).[49,50] Molybdenum toxicity has not been described.

Iodine

Iodine, found primarily in the thyroid gland (70%-80%) incorporated into thyroid hormones, is required for normal thyroid function which affects resting energy expenditure and growth. In iodine deficiency, there is a constant release of thyroid stimulating hormone (TSH), resulting in thyroid gland hyperplasia and goiter formation. However, not everyone with an iodine-deficient diet will develop a goiter. The most serious effects of iodine deficiency are during pregnancy and in childhood, including fetal death, cretinism, abnormal growth, and mental retardation.[49] Measurement of thyroxine (T_4), T_3, and thyroid stimulating hormone (TSH) can be used to assess iodine status (Table 164-7). Iodine needs may be met by consumption

of iodized salt or cutaneous iodine absorption from povidone–iodine, a topical antiseptic, used in catheter care.[50] Use of povidone–iodine for this indication has virtually been eliminated with the increased use of chlorhexidine for catheter site care, putting patients requiring long-term PN at risk. An IV iodine product is no longer available, and no trace element combination product marketed in the United States contains iodine. Iodine excess is rarely a clinical concern when thyroid and kidney function are normal except in overdoses or too rapid correction of iodine deficiency.[50]

Vitamins

Vitamins act as both catalysts (cofactors) and substrates in essential metabolic reactions. They are needed for normal growth, metabolism, and cellular integrity. They facilitate energy-yielding chemical reactions; they do not contribute energy. A thorough review of vitamins and their complex effects on nutrition and metabolism is beyond the scope of this chapter.[50,52,64] A comprehensive nutrition-focused history and NFPE are valuable means of assessing patients for vitamin deficiency or toxicity (Table 164-8). Generalized malnutrition is often associated with multiple vitamin deficiencies or increased needs; however, single vitamin deficiencies do occur. Thiamine (B_1) deficiency can result in early symptoms (dry or wet beriberi, GI symptoms) or advanced symptoms (lactic acidosis, Wernicke's encephalopathy, polyneuropathy, ataxia, mental confusion) due to impaired oxidative and energy metabolism often leading to serious and potentially irreversible neurological damage or death.[50,65] Macrocytic anemia, peripheral neuropathy, and neuropsychiatric sequelae may be caused by vitamin B12 (cyanocobalamin) deficiency which can occur after gastric or ileal resection due to the loss of intrinsic factor or absorption sites of the intrinsic factor-B_{12} complex, respectively. Vitamin B12 deficiency has been reported with increasing frequency in older adults, especially with prolonged gastric acid suppression with proton pump inhibitors.[66] There is a high prevalence of subclinical vitamin K deficiency in patients with chronic kidney disease, including those on hemodialysis or peritoneal dialysis. Vitamin K deficiency is a modifiable risk factor for cardiovascular disease and bone fracture in this patient population.[67]

TABLE 164-8

Assessment of Vitamin Status

Vitamin	Signs of Deficiency	Laboratory Assay	Comments
Water-Soluble Vitamins			
Thiamine (B1)	Early: anorexia, fatigue, depression, impaired memory or concentration Late: paresthesia, nystagmus, GI beriberi (nausea, vomiting, abdominal pain, lactic acidosis), beriberi (heart failure, edema), Wernicke's encephalopathy, Korsakoff's psychosis, peripheral neuropathy	Whole blood or erythrocyte transketolase activation test Blood thiamine pyrophosphate Erythrocyte glutathione reductase activity coefficient	Increased need with hemo- and peritoneal dialysis, alcohol misuse, malabsorption, hypermetabolism
Riboflavin (B2)	Mucositis, dermatitis, cheilosis, glossitis, photophobia, corneal vascularization, lacrimation, decreased vision, impaired wound healing and growth, normocytic anemia	Urine riboflavin	
Pantothenic acid	Fatigue, malaise, headache, insomnia, vomiting, abdominal cramps	Serum pantothenic acid	
Niacin	Pellagra: dermatitis, dementia, glossitis, diarrhea, memory loss, headaches	Urine niacin and N1-methylnicotinamide	Flushing, nausea, and vomiting seen with hyperlipidemia treatment; increased need with

		Erythrocyte NAD and NADP concentrations to determine "niacin number"	hemo- and peritoneal dialysis
Pyridoxine (B6)	Pellagra, dermatitis, glossitis, cheilosis, distal limb numbness or paresthesia, convulsions, microcytic anemia	Plasma pyridoxal 5-phosphate Urine 4-pyridoxic acid	Sensory neuropathy and seizures with very high doses (>2 g/day)
Folic acid	Macrocytic anemia, diarrhea, glossitis, cheilosis, angular stomatitis, fatigue, difficulty concentrating, irritability, headache, palpitations, shortness of breath, heart failure, tachycardia, postural hypotension, lactic acidosis, neural tube defects, impaired cellular immunity, paranoid behavior	Serum or plasma folate (acute) Red blood cell folate (chronic) Serum homocysteine	Decreased with increased cellular/tissue turnover (pregnancy, malignancy, hemolytic anemia); masks diagnosis of vitamin B12 deficiency; decreases risks of neural tube defects
Cyanocobalamin (B12)	Pernicious (megaloblastic) anemia, glossitis, spinal cord degeneration, peripheral neuropathy, paresthesias, pancytopenia, personality changes, dementia, depression, psychosis	Serum cobalamin Plasma homocysteine Urine or plasma methylmalonic acid[a] CBC	Decreased absorption in older adults, distal ileal resection, loss of gastric intrinsic factor due to gastrectomy or long-term gastric acid suppression
Biotin	Dermatitis, depression, lassitude, somnolence	Urine biotin	
Ascorbic acid (C)	Enlargement or keratosis of hair follicles, impaired wound healing, anemia, lethargy, depression, bleeding, ecchymosis, scurvy	Plasma ascorbic acid Leukocyte ascorbate	GI disturbances, hyperoxaluria and kidney stones, excess iron absorption with excess intake; individuals who smoke need 35 mg/day more than nonsmokers; rebound scurvy with abrupt discontinuation after long-term high doses
Fat-Soluble Vitamins			
Vitamin A (includes retinol, retinal, retinoic acid, and retinyl esters)	Dermatitis, night blindness, xerophthalmia, Bitot spots[b], pruritus, follicular hyperkeratosis, excessive deposition of periosteal bone, hair changes, poor growth and wound healing, impaired resistance to infection Irreversible: punctate keratopathy, keratomalacia, corneal perforation	Serum retinol Serum retinol-binding protein Serum retinyl esters (toxicity)	Teratogenic, liver toxicity with excessive intake; alcohol use, liver disease, hyperlipidemia, and severe protein malnutrition increase susceptibility to adverse effects of high intake; β-carotene supplements recommended only for those at risk of deficiency (fat malabsorption); may reverse corticosteroid-induced poor wound healing
D	Rickets, osteomalacia, osteoporosis, muscle weakness, poor growth, hypocalcemia, immune	Serum 25-hydroxy-vitamin D (storage form);	Elevated intake causes hypercalcemia, nephrocalcinosis, azotemia, poor growth;

	dysfunction, cardiomyopathy	1,25-dihydroxyvitamin D (active form)	decreased concentration in uremia, older adults (especially in winter), and fat malabsorption
α-Tocopherol (E)	Hemolysis	Serum α-tocopherol Ratios of serum α-tocopherol to total lipids	Excess intake: hemorrhagic toxicity; increased risk of bleeding with anticoagulants; impaired leukocyte function
K	Bleeding (ecchymosis, petechiae, hematoma)	Prothrombin time INR	Anticoagulant therapy can be affected by supplements or diet

CBC, complete blood count; GI, gastrointestinal; INR, international normalized ratio; NAD, nicotinamide adenine dinucleotide; NADP, nicotinamide adenine dinucleotide phosphate.

[a]Plasma methylmalonic acid concentrations increase with vitamin B12 deficiency.

[b]Bitot spots are spots which are oval, triangular, or irregular in shape and located superficially in the conjunctiva.

Patients with steatorrhea have an increased risk of fat-soluble vitamin (A, D, E, K) deficiencies. However, the increasing prevalence of vitamin D deficiency is a worldwide concern, including all ages, genders, and racial/ethnic groups. Risk for deficiency is higher in children and older adults, pregnant women, individuals with dark skin, patients receiving long-term PN, those living in temperate and higher latitudes, and those with disabilities or who are obese.[68] Laboratory assessment can confirm the clinical suspicion of a deficiency state. Vitamin D2 (ergocalciferol from plant-based sources) and vitamin D3 (cholecalciferol from conversion of cholesterol in the skin by ultraviolet light) are quickly converted to 25(OH)D via hydroxylation in the liver. The best marker for vitamin D deficiency is the serum concentration of 25(OH)D. Reference ranges for US laboratories are typically 20-100 ng/mL (50-250 nmol/L), but the optimal range is likely above 30 ng/mL (75 nmol/L) based on the concentration associated with parathyroid hormone (PTH) stimulation and calcium absorption efficiency.[68] The first indication of a deficiency is usually a decrease in circulating serum 25(OH)D. Subsequently, there is a decrease in urinary vitamin D excretion, which is followed by diminished tissue concentrations. Because the active form of vitamin D, $1,25(OH)_2D$, is produced only when needed, not stored, and dependent on kidney function, intact PTH concentration, and calcium and phosphorus supply, it is not a useful marker of vitamin D stores but may be helpful if assessing the kidney's ability to hydroxylate to the active form.

Vitamin toxicity can occur, especially with fat-soluble vitamins, which are stored in the body. Vitamin D toxicity can cause significant hypercalcemia, hypercalciuria, and soft tissue calcifications leading to kidney and cardiovascular damage.[50] Vitamin A toxicity is associated with many signs and symptoms including effects on bone.[50] Water-soluble vitamins, except cyanocobalamin (vitamin B_{12}), are not stored; consequently, the toxicity risk is minimal unless ingested in very high doses. However, evidence suggests that even water-soluble vitamins may be associated with adverse medication reactions when taken chronically in high doses. Preconception folic acid supplementation is definitively associated with a reduction in neural tube defects.[69] Multivitamin supplementation containing folic acid does not prevent cardiovascular disease despite its effects on homocysteine concentrations.[70] With North Americans consuming large amounts of nutrition supplements, spending more than $15.5B (2020 USD) for them each year, clinicians should be alert for signs of inappropriate vitamin use and hypervitaminosis (see Table 164-8) and be prepared to discuss rational supplement use with all patients.[71]

Essential Fatty Acids

The human body can synthesize all fatty acids except the essential fatty acids, linoleic acid (an omega-6 fatty acid) and α-linolenic acid (an omega-3 fatty acid). EFAD can be prevented if approximately 5% (linoleic acid) and 0.6% (linolenic acid) of total energy is ingested as these fatty acids.[72,73] EFAD is rare in adults and children but can occur with prolonged lipid-free PN, severe fat malabsorption, very low-fat enteral feeding formulations or diets, high medium chain triglyceride-containing diets, and severe malnutrition, especially in stressed patients.[74] Although the time needed to develop EFAD

is variable, symptomatic EFAD has occurred after only 4 weeks of lipid-free PN, and biochemical evidence can occur within 1 week.[74] The brain grows rapidly during the last trimester of gestation and the first 2 years of life. Large amounts of essential fatty acids are needed for central nervous system myelin synthesis. Newborns, especially those born prematurely, who have limited to no fat stores, may develop EFAD more rapidly than adults and should generally receive a source of essential fatty acids within 72 hours after birth.[74] Symptoms reported with EFAD include dermatitis (dry, scaly skin), increased susceptibility to infection, impaired wound healing, poor growth and brain development, and immune dysfunction.[73,74]

Linoleic acid is converted to arachidonic acid (20:4ω-6; a tetraene fatty acid). When linoleic acid is unavailable, oleic acid (18:1ω-9) is the preferred substrate, resulting in production of eicosatrienoic acid (20:3ω-9; a triene fatty acid). Thus, EFAD is associated with decreased tetraene and increased triene production. Different methods to measure fatty acids have resulted in variable proposed threshold triene-to-tetraene (T:T) values to diagnose EFAD.[75] The usual T:T ratio is approximately 0.01 to 0.05 depending on the assay; thus a T:T ratio greater than 0.05 generally suggests early EFAD. The T:T ratio will be abnormal before there are overt clinical symptoms. Clinical symptoms of EFAD will be present in patients with higher T:T ratios. EFAD diagnosis is generally made based on risk assessment and/or clinical findings with confirmation by measuring serum fatty acid concentrations.

Carnitine

Carnitine is a quaternary amine required for transport of long-chain fatty acids into the mitochondria for β-oxidation and energy production. Additionally, acyl compounds that are trapped within cells due to cell membrane impermeability can be esterified with carnitine, forming acylcarnitine derivatives, which are transported out of the cell, preventing the acyl compounds from accumulating to toxic concentrations (detoxification). Carnitine is also important in the metabolism of intracellular acetyl coenzyme A.[76,77] The L isomer is the physiologic active form.

Carnitine is available from a wide variety of dietary sources (especially dairy products and meats) and can be synthesized when intake is low from lysine and methionine.[78] Carnitine is filtered by the kidney and reabsorbed in the proximal tubule.[79] Hepatic synthesis is decreased in premature infants, and low serum carnitine concentrations and overt carnitine deficiency have been documented in premature infants receiving carnitine-free PN or diets (secondary deficiency), as well as in those with primary deficiency due to carnitine inborn errors of metabolism (eg, defect in the OCTN2 transporter; biosynthetic defects).[78,79] Other predisposing factors for secondary carnitine deficiency include pregnancy, malabsorption (cystic fibrosis, short bowel syndrome), chronic disease (HIV, kidney, liver), chronic medication therapy (valproic acid, verapamil, zidovudine), and a vegetarian diet.[79,80]

The clinical presentation of carnitine deficiency varies by type but may include generalized skeletal muscle weakness, hypotonia, lethargy, gross motor delay, poor feeding, growth failure, hypoglycemia, seizures, encephalopathy, hepatomegaly, hyperammonemia, recurrent infections, cardiomyopathy, and coma.[78,79] Symptoms are typically more severe in patients with primary deficiency. In clinical practice, carnitine status is assessed by measuring the serum total and free carnitine concentrations along with acylcarnitine; although, carnitine is distributed primarily in the muscle. When only total and free concentrations are available, the free is subtracted from the total to give the acylcarnitine concentration. Serum and urine carnitine concentrations are most helpful in primary carnitine deficiency; acylcarnitine concentrations are more helpful in secondary deficiency.[79]

Daily supplementation of neonatal PN solutions with 2 to 5 mg/kg carnitine is recommended when no enteral source is provided.[52] Higher doses (100-200 mg/kg/day) may be required for treatment of primary deficiency.[77]

NUTRIENT REQUIREMENTS

7 Evidence-based patient-specific goals should be established considering the patient's clinical condition and the need for maintenance or repletion in adults and continued growth and development in children. Individual nutrient requirements vary with age, sex, size, and clinical condition. Nutrition status, physical activity, and the need for continued maintenance of adequate nutrition or repletion in those with ongoing metabolic stress or malnutrition dictate the nutrient requirements for an individual. For obese patients, usual nutrition requirements may be altered because of desired weight loss and after bariatric surgery. In children, sustaining or reestablishing normal growth and development is critical. Organ function (intestine, kidney, liver, pancreas) may affect nutrient utilization. Nutrient requirements can be estimated using various methods interpreted in the context of patient-specific factors.

Recommended Dietary Allowances

The Recommended Dietary Allowances (RDAs) were first established in 1941. In 1997, the Food and Nutrition Board introduced a new designation for nutrition reference values, the Dietary Reference Intakes (DRIs). The four DRI categories are estimated average requirements (EARs), RDAs, adequate intakes (AIs), and tolerable upper intake levels (ULs). The nutrient intake that meets the needs of half of the healthy persons in a group (EAR) can be used for planning nutrient intakes for groups. The RDA, the nutrient intake that meets the needs of almost all persons in a designated group, is approximately two standard deviations above the EAR for nutrients for which the requirement is well defined and 1.2 times the EAR for other nutrients. To evaluate an individual's daily intake, the RDA is the most appropriate comparator. The AI, defined as the average intake for the designated group that appears to sustain growth or other indicator of health, is reserved for nutrients for which no EAR or RDA has been determined. The UL is the maximum nutrient intake unlikely to pose adverse effects in almost all persons in a designated group.[81] A new DRI category, Chronic Disease Risk Reduction level (CDRR), was recently added and defined as the nutrient intake that is expected to reduce the risk of developing chronic disease.[82] This new category has been applied to sodium and potassium guidelines.[83]

Dietary reference intakes have been established for six nutrient groups: calcium, phosphorus, magnesium, vitamin D, and fluoride; folate and other B vitamins; antioxidants (eg, selenium, vitamin C, vitamin E); trace elements; macronutrients (eg, protein, fat, carbohydrates, fiber); and electrolytes and water. An online Interactive DRI for Healthcare Professionals is available to calculate DRI-based nutrition needs for a generally healthy individual.[84]

In general, healthy adults and children older than 2 year of age should consume 45% to 65% of their total calories as carbohydrates. Protein recommendations also vary by age: 2 to 3 years, 5% to 20%; 4 to 18 years, 10% to 30%; and, adults, 10% to 35% of total calories. Recommended fat intakes vary by age: 2 to 3 years, 30% to 40%; 4 to 18 years, 25% to 35%; and, adults, 20% to 35% of total calories. Infants, especially premature infants, require a higher proportion of calories from fat (approximately 40%-50% of total calories) to ensure normal neurological development.

Energy

Validated predictive equations or population estimates are most often used to determine energy requirements; however, if available, indirect calorimetry is the most accurate bedside method to determine energy requirements. The method used will be determined by a variety of factors, including illness severity, resource availability, and clinician preference.

Estimating Energy Expenditure

Daily energy expenditure consists of the basal energy expenditure (BEE), diet-induced thermogenesis (10%), and energy used for physical activity. In sick or injured patients, the BEE is increased because of stress-related hypermetabolism, but the physical activity is usually greatly reduced. Continuous infusion EN, often used in critically ill patients, results in minimal diet-induced thermogenesis (not more than 5%) unless overfeeding. Failure to account for these changes can result in overfeeding.[22]

Numerous methods for determining an individual's daily energy requirement in a variety of settings have been published. These methods use population estimates of calories per kilogram of body weight (kcal/kg), equations that estimate energy expenditure (kcal/day or kJ/day; 1 kcal is equivalent to 4.184 kJ), or indirect calorimetry. The simplest and most convenient method to determine energy requirements is to use population estimates of calories required per kilogram of body weight. This method assumes standard values for health or the energy requirements associated with various disease states or clinical conditions, as well as the additional requirements for repletion of a malnourished individual. Most do not take into consideration age- or sex-related differences in energy needs. No stress or activity modifiers are used with these equations because the effect of the clinical condition (hypermetabolism) has been captured in the calculation. Daily adult requirements by this method can be estimated as shown below:[15,16,85]

Healthy, normal nutrition status, minimal illness severity:

20-25 kcal ABW/kg/day (84-105 kJ ABW/kg/day)20-25 kcal ABW/kg/day (84-105 kJ ABW/kg/day)

Illness, metabolic stress (first 7-10 days of intensive care unit stay):

12-25 kcal ABW/kg/day (50-105 kJ ABW/kg/day)12-25 kcal ABW/kg/day (50-105 kJ ABW/kg/day)

Illness, metabolic stress (BMI < 30 kg/m^2):

25-30 kcal ABW/kg/day (105-126 kJ ABW/kg/day)25-30 kcal ABW/kg/day (105-126 kJ ABW/kg/day)

Illness, metabolic stress (BMI ≥ 30 kg/m^2):

11-14 kcal ABW/kg/day (46-59 kJ ABW/kg/day) or 22 to 25 kcal IBW/kg/day (92-105 kJ ABW/kg/day) 11-14 kcal ABW/kg/day (46-59 kJ ABW/kg/day)or22 to25 kcal IBW/kg/day (92-105 kJ ABW/kg/day)

Major burn [≥ 50% total body surface area (TBSA)]:

25 kcal/kg ABW(kg) + 40 kcal per % TBSA burned(adult) or 25-35 kcal/kg/day in non obese patients and 21 kcal/kg/day in obese patients 25 kcal/kg ABW(kg)+40 kcal per % TBSA burned(adult) or 25-35 kcal/kg/dayin non obese patients and 21 kcal/kg/day in obese patients

When using the equations for individuals with a BMI over 30 k/m^2, as the BMI increases, the number derived using ABW compared to IBW becomes quite disparate. Accuracy is improved by using the ABW recommendation for patients with BMI 30 to 50 kg/m^2 and the IBW recommendation when the BMI is greater than 50 kg/m^2. When these recommendations are used for patients with a BMI of 30 kg/m^2 or more, the calories provided allow for permissive underfeeding (provision of approximately 65% to 75% of usual estimated energy needs), which decreases infection rates and hospital lengths of stay.[22] DRIs for energy for healthy infants and children are shown in Table 164-9.[72] These maintenance energy requirements are approximately 130% to 150% of the basal metabolic rate, with the additional calories provided to support usual activity and growth. For all ages, energy requirements may increase with fever, sepsis, major surgery, trauma, burns, and long-term growth failure and in the presence of chronic conditions such as bronchopulmonary dysplasia, congenital heart disease, and cystic fibrosis.

TABLE 164-9

Dietary Reference Intakes for Energy and Protein in Healthy Children

Age (Reference age/weight)	Estimated Energy Requirement (kcal/day)[a]		Protein RDA (g/kg/day)[b]
	Boys	Girls	
0-6 mo (3 mo/6 kg)	570	520	1.52[c]
7-12 months (9 mo/9 kg)	743	676	1.5
1-2 yr (24 mo/12 kg)	1,046	992	
1-3 yr (24 mo/12 kg)			1.1
3-8 yr (6 yr/20 kg)	1,742	1,642	
4-8 yr (6 yr/20 kg)			0.95
9-13 yr (11 yr/M: 36 kg; F: 37 kg)	2,279	2,071	0.95
14-18 yr (16 yr/M: 61 kg; F: 54 kg)	3,152	2,368	0.85

F, female; M, male; RDA, recommended dietary allowance.

[a]1 kcal is equal to approximately 4.18 kJ.

[b]Protein requirements in children with moderate to severe stress increase by 50% or more.

[c]Adequate intake.

There are many equations available to estimate energy expenditure in adults and children with an accuracy of approximately 40% to 77% when compared to indirect calorimetry (Tables 164-10 and 164-11, respectively).[15,22,72,85-89] The Harris-Benedict equations, derived in 1919 from a study of

239 individuals, are still used by some clinicians for assessing energy requirements in adults. They have the advantage of incorporating the patient's age, height, weight, and sex. These equations were derived from oxygen consumption measurements made in normally nourished healthy individuals who were in a fasting and resting state. Although they are commonly referred to as the "BEE equations," they estimate resting energy expenditure (REE), the amount of energy expended at rest by a fasting, awake individual in a temperature-controlled environment performing only basal functions such as breathing, circulation, and metabolic processes.

TABLE 164-10

Equations to Estimate Energy Expenditure in Adults[a]

Healthy Adults
Harris-Benedict[b] ***Equations (kcal/day)***
Men: BEE = 66 + (13.75W + 5H [cm]) – (6.8A)
Women: BEE = 655 + (9.6W + 1.8H [cm]) – (4.7A)
DRI Equations (kcal/day)[c]
Men: EER = 662 – 9.53A + (PA × 15.91W) + 539.6H (m)
Women: EER = 354 – 6.91A + (PA × 9.36W) + 726H (m)
PA = 1 if sedentary; 1.12 if low active; 1.27 if active; and 1.45 if very active
Mifflin-St. Jeor Equations (kcal/day)
Men: 10W + 6.25H (cm) – 5A + 5
Women: 10W + 6.25H (cm) – 5A – 161
Critically Ill Adults
Penn State Equation (kcal/day): Mifflin(0.96) + Tmax(167) + Ve(31) – 6212
Penn State Equation, modified (kcal/day) for age ≥60 yr with BMI ≥30 kg/m^2: Mifflin(0.71) + Tmax(85) + Ve(64) – 3085

A, age in years; BEE, basal energy expenditure; BMI, body mass index; DRI, dietary reference intakes; EER, estimated energy requirement; H, height in centimeters or meters, as indicated; PA, physical activity factor; Tmax, maximum body temperature in the previous 24 hours in degrees centigrade; Ve, minute ventilation in L/min; W, actual body weight in kilograms; yr, years.

[a]No real consensus exists as to which formula is best in all situations. Many clinicians use more than one equation and calculate a range of acceptable intakes.

[b]The common practice of using an adjusted body weight for obesity in these calculations is not supported by the original data that used actual body weight in all cases up to a BMI of 56 kg/m^2 in men and 40 kg/m^2 in women.

[c]1 kcal is equal to approximately 4.18 kJ.

TABLE 164-11

Equations to Estimate Energy Expenditure in Children[a,b]

FAO/WHO/UNU 2001 (kcal/day)[b]
0-12 Months
Breastfed
TEE (kcal/day) = –152 + 92.8W
TEE (MJ[c]/day) = –0.635 + 0.388W
Formula fed
TEE (kcal/day) = –29 + 82.6W
TEE (MJ[c]/day) = –0.122 + 0.346W
Boys 1-17 Years
TEE (kcal/day) = 310.2 + 63.3W – 0.263W2
TEE (MJ[c]/day) = 1,298 + 0.265W – 0.0011W2
Girls 1-17 Years
TEE (kcal/day) = 263.4 + 65.3W – 0.454W2
TEE (MJ[c]/day) = 1,102 + 0.273W – 0.0019W2
DRI Equations (kcal/day)
Birth through 2 years of age
EER = (89W – 100) + GF
GF = 175 kcal if 0-3 months; 56 kcal if 4-6 months; 22 kcal if 7-12 months; 20 kcal if 13-35 months
3-18 years of age
Boys: EER = 88.5 – (61.9A) + PA (26.7W + 903H) + GF
Girls: EER = 135.3 – (30.8A) + PA (10W + 934H) + GF
GF = 20 kcal if 3-8 years; 25 kcal if 9-18 years
PA = 1 if sedentary; 1.13-1.16 if low activity; 1.26-1.31 if normal activity; and 1.42-1.56 if very active

A, age in years; DRI, dietary reference intakes; EER, estimated energy requirement; FAO/WHO/UNU, Food and Agriculture Organization/World Health Organization/United Nations University; GF, growth factor; H, height in meters; PA, physical activity factor; TEE, total energy expenditure; W, actual body weight in kilograms.

[a]No real consensus exists as to which formula is best in all situations. Many clinicians use more than one equation and calculate a range of acceptable intakes.

[b]Additional daily calories are needed for growth; about 2 kcal/g of weight gain desired.

[c]1 kcal is equivalent to approximately 4.18 kJ; 1 MJ = 1,000 kJ.

Because these equations approximate REE, the results have been modified by an activity or stress factor that adjusts for the individual's clinical condition. For example, an individual who is confined to bed may require a calorie intake that is only 20% to 30% above the REE, while a person who has sustained a severe burn injury may require 150% to 200% of the calculated REE. Multiplying the calculated REE by both a stress factor and an activity factor will overestimate needs because these equations overestimate REE by at least 6% to 15%. Stress factors used in adults and children are shown in Table 164-12 and Table 164-13, respectively.[88] ABW (up to a BMI of 56 kg/m^2 in men and 40 kg/m^2 in women), not IBW or adjusted body weight, was used to generate the original data with these equations and thus should be used for these calculations.[22,86]

TABLE 164-12

Stress Factors for Use in Adults

Condition	Factor
No Stress	
Confined to bed	1.2
Out of bed: normal activity	1.3
Mild Stress[a]	
Postoperative recovery: uncomplicated surgery	1-1.15
Trauma: mild (eg, long-bone fracture)	1.2
Moderate Stress[a]	
Sepsis (moderate)	1.2-1.4
Trauma: CNS (sedated)	1.3
Trauma: moderate to severe	1.3-1.4
Severe Stress[a]	
Sepsis (severe)	1.3
Trauma: CNS (severe)	Up to 1.3
Burns (proportionate to TBSA burned)[b]	Up to 2.0

CNS, central nervous system; TBSA, total body surface area.

[a]Assumes decreased activity during periods of stress.

[b]Formulas specifically for estimating energy needs in burned children and adults have been published and are likely to be more accurate.

TABLE 164-13

Stress Factors for Use in Children

Condition	Factor
Well-nourished child at bedrest with mild-moderate stress	REE × 1.3
Normally active child with mild-moderate stress OR inactive child with severe stress (eg, trauma, cancer) OR child with minimal activity and malnutrition requiring catch-up	REE × 1.5
Active child requiring catch-up growth OR an active child with severe stress	REE × 1.7

There is no individual method proven to accurately determine the energy needs of all critically ill patients (see Table 164-10). The Penn State equations appear to be most accurate in critically ill adults receiving mechanical ventilation. However, when compared to indirect calorimetry in mechanically ventilated patients, the accuracy of these equations has been shown to be only 34%.[90] The Penn State equations were found to have an accuracy rate of 77%, 70%, and 53% in older nonobese, younger obese (BMI ≥ 30 kg/m^2) and nonobese, and older obese patients, respectively. In older obese patients, use of the modified Penn State equation increased accuracy to 74%.[22,90] There is no consensus as to the best equation for critically ill adults who are not mechanically ventilated.

Measuring Energy Expenditure

The most accurate method to determine energy expenditure in clinical practice is to measure it using indirect calorimetry (metabolic gas monitoring), but capital and operational costs may limit its availability in many settings. Handheld calorimeters have been shown to be more accurate than predictive equations and may be a viable alternative to the more expensive equipment in both inpatient and outpatient settings.[91,92]

Indirect calorimetry methodology is based on pulmonary gas exchange: when a substrate (carbohydrate, fat, protein) is oxidized, heat is produced, oxygen is consumed, and carbon dioxide is expired in a constant amount depending on the substrate being oxidized. More carbon dioxide is produced when a gram of glucose is metabolized than either a gram of protein or a gram of fat. Indirect calorimetry is a noninvasive procedure in which oxygen consumption (VO_2, mL/min) and carbon dioxide production (VCO_2, mL/min) are measured, and the measured resting energy expenditure (MREE; kcal/day) is calculated using the modified Weir equation, as follows:[91–93]

$$\text{MREE} = ([3.94\ \text{VO}_2 + 1.11\ \text{VCO}_2] + [2.17\ \text{uN}_2]) \times 1.44$$MREE=([3.94 VO2+1.11 VCO2]+[2.17 uN2])×1.44

The urinary nitrogen component (uN_2) is often omitted when calculating energy expenditure because it accounts for less than 4% of the energy expenditure, and its omission results in an insignificant measurement error.[86,91] Excluding the nitrogen component eliminates the need for a 24-hour urine collection, which can be difficult and delay the measurement.

The MREE represents the total energy expended during the period over which the measurements were taken extrapolated to a 24-hour period to approximate daily energy requirements. MREE reflects changes in energy requirements resulting from diseases or clinical conditions, but it does not include energy required for repletion of a malnourished individual or growth. No multiplier (activity/stress factor) should be used in critically ill adults.[82] Modifiers may be used in other settings (eg, weight loss clinics). In children, the MREE should be multiplied by a factor for physical activity or stress (Table 164-13).[88]

Indirect calorimetry can be used to determine the patient's respiratory quotient (RQ), calculated as VCO_2/VO_2, which reflects substrate utilization. RQ values for nutrient substrates are fat, 0.71; carbohydrate, 1; protein, 0.82; and mixed substrate (fat, carbohydrate, and protein), 0.85. An RQ value greater than 1 denotes either lipogenesis or hyperventilation; less than 0.7 may indicate a ketogenic diet, fat gluconeogenesis, or ethanol oxidation. Values outside the physiologic range of 0.67 to 1.3 suggest an invalid test. Clinically, the RQ is used to determine if a patient is being overfed, which is

likely if the RQ value is greater than 1.[86] Increased carbon dioxide production with overfeeding leads to increased respiratory demand which can be decreased by reducing overall energy and carbohydrate administration.

Indirect calorimetry should be considered in any patient in whom uncertainty in estimating energy requirements needs to be minimized, such as adults and children who are severely malnourished (BMI < 18.5 kg/m^2) or obese (BMI ≥ 30 kg/m^2), who have unexplained high partial arterial pressure of carbon dioxide ($PaCO_2$) concentrations or minute ventilation, spinal cord injuries, who experience weight loss despite apparently receiving adequate protein and energy intakes, critically ill surgery patients receiving PN, patients with large total body surface area burns, and patients unable to be weaned from the ventilator.[20,92]

Indirect calorimetry may not be accurate in all clinical situations. Indirect calorimetry overestimates REE for patients with hyperventilation, metabolic acidosis, overfeeding, and if there is an air leak anywhere in the ventilator circuit. Underestimation of REE is likely with hypoventilation, metabolic alkalosis, underfeeding, and gluconeogenesis. Mechanically ventilated patients are technically easier to study because the indirect calorimeter can be integrated directly into the ventilator circuit. However, the patient must be at complete rest for 1 hour, must not receive bolus feedings either by enteral feeding tube or orally for 4 hours, should have no changes in substrate delivery for 12 hours, and must be on a fraction of inspired O_2 (FiO_2) of less than 0.6 with a positive end-expiratory pressure (PEEP) less than 10 cm H_2O (approximately 1.0 kPa) and peak airway pressure of less than 30 cm H_2O [2.9 kPa]) to ensure an accurate steady-state reading.[86,88] Newer indirect calorimeters may have less restrictions on ventilator settings, but many of the patients who would benefit most from indirect calorimetry often will not meet qualifications for the measurement.

Protein

9 Daily protein requirements are based on age, sex, nutrition status, disease state, and clinical condition. For adults, the RDA for protein is 0.8 g/kg/day, which is significantly less than most Americans typically consume.[72] In adults older than 60 years of age, protein needs are increased to 1.5 g/kg/day to reduce the loss of LBM that occurs with aging, and 1.5 to 2 g/kg/day or more may be needed in states of metabolic stress.[15,72,94] Protein requirements increase in pregnant and lactating women (1.1 g/kg/day or 6-10 g protein per day above the usual RDA). Table 164-9 lists the RDAs for protein for children.[72]

Protein metabolism depends on both kidney and liver function. Critical illness results in a hypercatabolic state in which there is both increased protein synthesis and degradation. The goal of protein administration is to minimize catabolism by maximizing protein synthesis. Consequently, protein requirements are increased to 1.2 to 2 g/kg/day in critically ill patients.[15,16] For obese critically ill patients, protein needs are 2 g/kg IBW if the BMI is between 30 and 40 kg/m^2 and 2.5 g/kg IBW or more if the BMI is greater than 40 kg/m^2.[15] Adults with significant burns have protein requirements of 2.5 to 3 g/kg ABW/day or more; children with burns required between 20% and 25% of their energy needs as protein.[89] Large stool or ileostomy losses increase protein requirements. Liver failure typically results in the need for protein restriction (0.5 g/kg/day) unless a hypercatabolic state is also present, which will increase requirements to 1.5 g/kg/day. Protein needs in patients with kidney failure are variable and affected by the various renal replacement therapies. The application of these protein intake guidelines requires both clinical judgment and frequent monitoring of kidney and liver function, serum chemistries, clinical condition, and nutrition outcomes.

Fat

The daily AI for men and women for α-linolenic acid is 1.6 and 1.1 g, respectively; for linoleic acid, it is 14 to 17 g/day for men and 11 to 12 g/day for women.[72] For adults, fat should represent no more than 10% to 35% of total calories, with the recommendation that saturated fatty acids, *trans* fatty acids, and dietary cholesterol intake be kept as low as possible while a nutritionally adequate diet is consumed. Fat should constitute 30% to 40% of energy in children 1 to 3 years of age and 25% to 35% of energy in children 4 to 18 years of age.[72] Fat intake in children younger than 3 years of age is critical for proper central nervous system growth and development; generally, fat-restricted diets (skim milk) should not be imposed until after the age of 2 to 3 years except under medical supervision.

Fiber

Decreased serum cholesterol, improved glycemic control in patients with metabolic syndrome and type 2 diabetes mellitus, and maintenance of

normal laxation have been attributed to dietary fiber intake, but only 5% of Americans consume the recommended amount of fiber daily.[95] Men and women 50 years of age and younger should ingest 38 g/day and 25 to 26 g/day of total fiber, respectively. For men and women older than 50 years of age, the AI is 30 g/day and 21 g/day, respectively.[72] The AI for fiber has not been set for children younger than 1 year of age. Breast milk and infant formulas are essentially fiber-free. For older children, the recommended fiber intake is 19 g/day for children 1 to 3 years of age, 24 g/day for children 4 to 8 years of age, and 26 to 31 g/day for children 9 to 13 years of age.[72]

Fluid

The daily fluid requirement for an adult depends on many factors but is generally estimated to be 30-40 mL/kg.[96] Fluid requirements per kilogram of body weight are higher for children and even higher for preterm infants because of their higher percentage of TBW and basal energy needs. Additionally, premature neonates have increased fluid requirements because of greater insensible losses and decreased concentrating ability of the kidneys. The Holliday-Segar method is a commonly used, quick, and simple method for estimating minimum daily fluid needs of children and adults. Children weighing less than 10 kg should receive at least 100 mL/kg/day. An additional 50 mL/kg/day should be provided for each kilogram of body weight between 11 kg and 20 kg and 20 mL/kg/day for each kilogram above 20 kg.[97] Thus, the minimum fluid required for a child weighing 8-kg would be 800 mL/day, a 17-kg child would need 1,350 mL/day; and a 50-kg individual would need 2,000 mL/day.

Factors that may alter fluid needs in both adults and children are listed in Table 164-14. All sources of fluid (and sodium) intake should be considered (eg, vehicles for IV medications, IV or feeding tube flushes) when determining fluid requirements. Urine output, sodium, and specific gravity as well as serum electrolytes and weight changes can be used to assess fluid status. A urine output of at least 1 mL/kg/h (in children) and approximately 0.5 mL/kg/h or 40 to 50 mL/h (in adults) is considered adequate to ensure tissue perfusion. Urine output should be higher if large fluid volumes or high renal solute loads (eg, concentrated PN or EN formulations) are being administered. Urine sodium will be low (≤30 mmol/L) if the patient has volume and/or sodium deficits. Urine specific gravity depends on the kidneys' concentrating and diluting capabilities. Concomitant diuretic therapy, resulting in increased solute or water excretion, may limit the use of urine specific gravity and sodium as assessments of fluid status.

TABLE 164-14

Factors That Alter Fluid Requirements

Increased Requirements	Decreased Requirements
Fever	Fluid overload
Radiant warmers	Heart failure
Diuretics	Decreased urine output
Vomiting	Heat shields
Nasogastric suction	Relatively high humidity
Ostomy or fistula drainage	Humidified air via endotracheal tube
Diarrhea	Kidney failure
Glycosuria	Hypoalbuminemia with starvation
Phototherapy	Syndrome of inappropriate secretion of antidiuretic hormone (SIADH)
Diabetes insipidus	
Increased ambient temperatures	
Hyperventilation	
Prematurity	
Excessive sweating	
Increased metabolism (eg, hyperthyroidism)	

Micronutrients

Requirements for micronutrients (electrolytes, minerals, trace elements, vitamins) vary with age, sex, and route of ingestion (Table 164-15).[48–52,64,98,99] Enteral and parenteral requirements vary due to bioavailability considerations. Micronutrients poorly absorbed via the GI tract usually are required in greater amounts when given by the enteral than parenteral route. However, many water-soluble micronutrients are excreted more rapidly via the kidneys when administered intravenously. In these situations, the IV dose is greater than the enteral dose. Other factors that affect micronutrient requirements include GI losses through diarrhea, vomiting, or high-output fistula or ostomies; wound healing; and hypermetabolism or hypercatabolism. Cutaneous micronutrient losses (eg, zinc, copper, selenium) also may be significant after major burn injury. Sodium, potassium, magnesium, and phosphorus excretion are particularly dependent on kidney function, and in the setting of acute kidney injury or chronic kidney disease, intake will likely need to be restricted. Calcium needs, on the other hand, may be increased in these patients. Patients with moderate-to-severe malnutrition will have increased requirements during early refeeding owing to pre-existing deficiencies and rapid intracellular uptake with anabolism. Failure to provide adequate electrolyte replacement, especially potassium and phosphorus, and vitamin supplementation (thiamine) before advancing caloric provision can result in significant morbidity and even death from refeeding syndrome.[5,100,101]

TABLE 164-15

Recommended Daily Electrolyte, Trace Element, and Vitamin Intake in Healthy Individuals[a]

Nutrient	Adult (≥19 yr of age)[b]		Pediatric (≥6 mo of age)[c]	
	Enteral	Parenteral	Enteral	Parenteral
Electrolytes and Minerals				
Acetate[d]	—	—	—	—
Calcium	1,000 mg F (> 50 yr): 1,200 mg Lactating: 1,300[e]	0-15 mEq (0-7.5 mmol)	6-11 mo: 260 mg 12-36 mo: 700 mg 4-8 yr: 1,000 mg 9-18 yr: 1,300 mg	Premature: 2-4 mEq/kg (1-2 mmol/kg) Other: 1-2.5 mEq/kg (0.5-1.25 mmol/kg)
Chloride[d]		—	—	2-6 mEq/kg (mmol/kg)
Magnesium	M: 400-420 mg F: 310-320 mg Pregnant: 350-400 mg[e] Lactating: 310-360 mg	10-20 mEq (5-10 mmol)	6-11 mo: 75 mg 12-36 mo: 80 mg 4-8 yr: 130 mg 9-13 yr: 240 mg 14-18 yr: 360-410 mg	0.25-1 mEq/kg (0.12-0.5 mmol/kg)
Phosphorus	700 mg Pregnant, lactating (14-18 yr): 1,250 mg	20-45 mmol	6-12 mo: 275 mg 12-36 mo: 460 mg	Premature: 1-2 mmol/kg Others: 0.5-1 mmol/kg

			4-8 yr: 500 mg 9-18 yr: 1,250 mg	
Potassium	M: 3,400 mg F: 2,600 mg Pregnant, lactating (14-18 yr): 2,500-2,600 mg Pregnant, lactating (>18 yr): 2,800-2,900 mg	60-100 mEq (60-100 mmol) (1-2 mEq/kg [1-2 mmol/kg])	6-12 mo: 860 mg 12-36 mo: 2,000 mg F: 4-18 yr: 2,300 mg M (4-8 yr): 2,300 M (9-13 yr): 2,500 mg M (14-18 yr): 3,000 mg	2-5 mEq/kg (mmol/kg)
Sodium	2,300 mg	60-100 mEq (60-100 mmol) (1-2 mEq/kg [1-2 mmol/kg])	6-12 mo: 370 mg 12-36 mo: 1,200 mg 4-8 yr: 1,500 mg 9-13 yr: 1,800 mg 14-18 yr: 2,300 mg	2-6 mEq/kg (mmol/kg)
Trace Elements				
Chromium (mcg)	20-45 (varies with age and sex)	10-15 0.14-0.87[f]	0-6 mo: 0.2 7-12 mo: 5.5 1-8 yr: 11-15 9-18 yr: 21-35	0-6 mo: 0.0006 mcg/kg[f] 7-12 mo: 0.012 mcg/kg[f] 1-3 yr: 0.22 mcg[f] 4-8 yr: 0.3 mcg[f] 9-13 yr: M 0.5 mcg; F 0.42 mcg[f] 14-18 yr: M 0.7 mcg; F 0.48 mcg[f]
Copper[g] (mcg)	900 1,000 (pregnancy) 1,300 (lactation)	0.3-1.5 (increased with GI loss)	0-12 mo: 200-220 1-8 yr: 340-440 9-18 yr: 700-890	20 mcg/kg (maximum, 300 mcg)
Fluoride (mg)	M: 4	NA[h]	0-6 mo: 0.01	NA[h]

	F: 3		mg 7-12 mo: 0.5 mg 1-8 yr: 0.7-1 mg 9-18 yr: 2-3 mg	
Iodine (mcg)	150 Pregnant: 220 Lactating: 290	70-140[h]	0-12 mo: 110-130 1-8 yr: 90 9-18 yr: 120-150	1 mcg/kg[h]
Iron (mg)	M: 8 F (≤50 yr): 18 F (>50 yr): 8 Pregnant: 27 Lactating: 9-10	1 1.5 (blood loss)	6-12 mo: 11 12-36 mo: 7 4-8 yr: 10 9-13 yr: 8 M (14-18 yr): 11 F (14-18 yr): 15	Varies
Manganese[g] (mg)	M: 2.3 F: 1.8 Pregnant: 2 Lactating: 6	0.15-1	0-6 mo: 0.003 7-12 mo: 0.6 1-8 yr: 1.2-1.5 9-18 yr: 1.6-2.2	1 mcg/kg (maximum, 50 mcg)
Molybdenum (mcg)	45 Pregnant, lactating: 50	100-200[h]	0-12 mo: 2-3 1-8 yr: 17-22 9-18 yr: 34-43	0.25 mcg/kg (maximum, 5 mcg)[h]
Selenium (mcg)	55 Pregnant: 60 Lactating: 70	20-60	0-12 mo: 15-20 1-8 yr: 20-30 9-18 yr: 40-55	1.5-3 mcg/kg (maximum, 30 mcg)
Zinc[i] (mg)	M: 11 F: 8 Pregnant: 11-12 Lactating: 12-13	2.5-5	6-36 mo: 3 4-8 yr: 5 9-13 yr: 8 M (14-18 yr): 11 F (14-18 yr): 8	Premature: 300-400 mcg/kg Other: 50-250 mcg/kg
Vitamins				
Ascorbic acid (mg) (vitamin C)	M: 90 F: 75 Pregnant: 80-85 Lactating: 115-120	100	6-12 mo: 50 12-36 mo: 15 4-8 yr: 25 9-13 yr: 45 M (14-18 yr): 75	80

			F (14-18 yr): 65	
Biotin (mcg)	30	60	0-12 mo: 5-6 1-8 yr: 8-12 9-18 yr: 20-25	20
Choline (mg)	M: 550 F: 425 Pregnant: 450 Lactating: 550	NA[h]	6-12 mo: 150 12-36 mo: 200 4-8 yr: 250 9-13 yr: 375 M (14-18 yr): 550 F (14-18 yr): 400	NA[h]
Cobalamin (mcg) (vitamin B12)	2.4 Pregnant: 2.6 Lactating: 2.8	5	6-12 mo: 0.5 12-36 mo: 0.9 4-8 yr: 1.2 9-13 yr: 1.8 14-18 yr: 2.4	1
Folate (mcg DFE)	400 Pregnant: 600 Lactating: 500	400	6-12 mo: 80 12-36 mo: 150 4-8 yr: 200 9-13 yr: 300 14-18 yr: 400	140
Niacin (mg)	M: 16 F: 14 Pregnant: 18 Lactating: 17	40	6-12 mo: 4 12-36 mo: 6 4-8 yr: 8 9-13 yr: 12 M (14-18 yr): 16 F (14-18 yr): 14	17
Pantothenic acid (mg)	5	15	0-12 mo: 1.7-1.8 1-8 yr: 2-3 9-18 yr: 4-5	5
Pyridoxine (mg) (vitamin B6)	1.3 M (>50 yr): 1.7 F (<50 yr): 1.5 Pregnant: 1.9 Lactating: 2	4	6-12 mo: 0.3 12-36 mo: 0.5 4-8 yr: 0.6 9-13 yr: 1 M (14-18 yr): 1.3 F (14-18 yr): 1.2	1

Riboflavin (mg)	M: 1.3 F: 1.1 Pregnant: 1.4 Lactating: 1.6	3.6	6-12 mo: 0.3 12-23 mo: 0.5 1-8 yr: 0.5-0.6 M (9-18 yr): 1.3 F (9-18 yr): 1.0	1.4
Thiamine (mg) (vitamin B1)	M: 1.2 F: 1.1 Pregnant, lactating: 1.4	3	6-12 mo: 0.3 12-36 mo: 0.5 4-8 yr: 0.6 9-13 yr: 0.9 M (14-18 yr): 1.2 F (14-18 yr): 1.0	1.2
Vitamin A (mcg RAE)[j]	M: 900 F: 700 Pregnant: 750-770 Lactating: 1200-1300	600-1,000	6-12 mo: 500 12-23 mo: 300 4-8 yr: 400 9-13 yr: 600 M (9-18 yr): 900 F (9-18 yr): 700	700
Vitamin D (IU)[k]	≤70 yr: 600 IU >70 yr: 800 IU	200 IU	6-12 mo: 400 IU 1-18 yr: 600 IU	200-400 IU
Vitamin E (mg AT)	15 Pregnant, lactating: 19	10	6-12 mo: 5 12-23 mo: 6 4-8 yr: 7 9-13 yr: 11 14-18 yr: 15	7
Vitamin K (mcg)	M: 120 F: 90	0.7-2.5 mg	6-12 mo: 2.5 12-36 mo: 30 4-8 yr: 55 9-13 yr: 60 14-18 yr: 75	200

AT, alpha-tocopherol; DFE, dietary folate equivalent; F, female; IU, international units M, male; NA, not applicable; NE, niacin equivalents; RAE, retinol activity equivalents; TE, tocopherol equivalent

[a]Data represent either the Recommended Dietary Allowance (RDA), the Adequate Intake (AI), or the CDRR (Chronic Disease Risk Reduction level) for each nutrient.

[b]Intake in nonhealthy adults must be individualized.

[c]Term newborns, low-birthweight, and very-low-birthweight infants or older infants and children may have higher or lower requirements. Intake in nonhealthy

children must be individualized.

[d]Not established; as needed to maintain acid–base balance.

[e]Pregnancy and lactation recommendations provided if different than age-specific recommendations; recommendations include pregnant or lactating females aged 14 to 50 yr unless otherwise specified.

[f]American Society for Parenteral and Enteral Nutrition recommendations

[g]May accumulate in cholestasis.

[h]No IV product available in the United States

[i]Additional intake needed with small bowel losses, which can be 12 mg zinc/L or 17 mg zinc/kg of stool or ileostomy output; an additional 2 mg/day needed for acute catabolic stress.

[j]1 mcg RAE = 3.3 international units

[k]40 international units = 1 mcg

DRUG–NUTRIENT INTERACTIONS

10 DNIs can affect response to medication therapy and nutrition status. A comprehensive discussion of DNIs is beyond the scope of this chapter.[102–105] Medication-induced nutrient deficiency, poor therapeutic response, enhanced toxicity, and failure to achieve desired nutrition outcomes can occur if either nutrition support or medication therapy is stopped because of adverse effects. Patient outcomes may be enhanced when an effective method to identify significant DNIs is coupled with a patient counseling program. An important part of the assessment process is to recognize risk factors that influence DNIs. The potential for significant DNIs is greatest in children and older adults. Other risk factors include critical illness, multiple medications, and EN.

Mineral and electrolyte serum concentrations may change because of medication therapy. For example, with loop diuretics, urine sodium, potassium, calcium, and magnesium wasting may occur, causing a reduction in their respective serum concentrations. Alternatively, calcium excretion is reduced with thiazide diuretics. Serum electrolyte concentrations also may increase as a direct result of the medication's mechanism (potassium-sparing diuretics) or because of the medication's salt form (sodium piperacillin/tazobactam). Corticosteroids and cyclosporine are known to cause hyperglycemia; other medications are prescribed to pharmacologically lower blood glucose concentrations (insulin, oral hypoglycemics).

Vitamin and trace element status also may be affected by medications (Table 164-16). For example, sulfasalazine therapy causes a decrease in folic acid, isoniazid therapy causes pyridoxine deficiency, and furosemide therapy may result in decreased thiamine concentrations. Medication therapy outcomes also may be affected by vitamin intake. For instance, the ingestion of high folic acid doses may decrease the therapeutic effect of methotrexate, and changes in an individual's usual vitamin K or vitamin E intake may cause variability in warfarin's anticoagulant effects.

TABLE 164-16

Drug–Nutrient Interactions

Medication	Effect
Angiotensin converting enzyme inhibitors	Increased urinary zinc losses
Angiotensin receptor blockers	Increased urinary zinc losses
Antacids	Thiamine deficiency

Antibiotics	Vitamin K deficiency
Aspirin	Folic acid deficiency; increased vitamin C excretion
Cathartics	Increased requirements for vitamins D, C, and B6
Cholestyramine	Vitamins A, D, E, and K and β-carotene malabsorption
Colestipol	Vitamins A, D, E, and K and β-carotene malabsorption
Corticosteroids	Decreased vitamins A, D, and C
Diuretics (loop)	Thiamine deficiency
Diuretics (thiazides)	Increased urinary zinc losses
Efavirenz	Vitamin D deficiency caused by increased metabolism of 25(OH)-vitamin D and 1,25-(OH)2-vitamin D
Histamine2 antagonists	Vitamin B12 malabsorption (reduced acid results in impaired release of B12 from food)
Isoniazid	Vitamin B6 and niacin deficiency
Isotretinoin	Vitamin A increases toxicity
Mercaptopurine	Niacin deficiency
Methotrexate	Folic acid inhibits effect
Orlistat	Vitamins A, D, E, and K malabsorption caused by fat malabsorption
Pentamidine	Folic acid deficiency
Phenobarbital	Increased vitamin D metabolism
Phenytoin	Increased vitamin D metabolism; decreased folic acid concentrations
Primidone	Folic acid deficiency
Protease inhibitors	Vitamin D deficiency (impaired renal hydroxylation)
Proton pump inhibitors	Decreased iron and vitamin B12 absorption (reduced acid results in impaired release of B12 from food)
Sulfasalazine	Folic acid malabsorption
Trimethoprim	Folic acid depletion
Warfarin	Vitamin K inhibits effect; vitamins A, C, and E may affect prothrombin time
Valproic acid	Zinc, carnitine
Zidovudine	Folic acid and B12 deficiencies increase myelosuppression

Vehicles for medication delivery also may contain nutrients. Most IV therapies (maintenance IV fluids, medications, electrolyte replacements) are delivered using solutions of either dextrose (dextrose 5% or 10% in water) or sodium (0.9% NaCl). Lipid emulsion is used as the vehicle for the anesthetic agent propofol (10% lipid) and the IV calcium channel blocker clevidipine (20% lipid), and both contribute fat calories (1.1 kcal/mL or 4.6 kJ/mL for 10% and 2.0 kcal/mL or 8.4 kJ/mL for 20%) when these medications are used. Nutrition support regimens must be adjusted to accommodate calories, sodium, and other nutrients delivered through these therapies to avoid overfeeding, sodium overload, and other complications.

PRACTICAL GUIDELINES

The value of any marker used for nutrition screening is only as good as its ability to accurately identify malnourished patients and to correlate with nutrition-related complications. The response of the various nutrition status markers to nutrition therapy and the correlation between improvement in these markers and decreased morbidity and mortality support their validity. However, when applied to an individual, most of these markers lack specificity and sensitivity, which makes the development of a clinically useful, cost-effective approach to nutrition screening challenging.

The importance of the nutrition-focused history and NFPE in both nutrition screening and assessment cannot be overemphasized. Objective data such as weight can further substantiate the clinical impression and provide a baseline for subsequent monitoring. The cost effectiveness of many biochemical parameters is unknown. The assessment of other anthropometric measures is most useful in the setting of anticipated long-term nutrition support in which these measurements will serve as longitudinal markers of response to the nutrition care plan.

Better markers of nutrition status and methods for determining patient-specific nutrition requirements are needed to allow further refinement of estimates of an individual's nutrition needs. Functional tests and simple, noninvasive tests for body composition analysis hold promise for the future. However, until better methods of assessment become available and are demonstrated to be cost effective, the currently available battery of tests will continue to be the mainstay of nutrition assessment.

Initially, nutrition requirements are determined based on assumptions made about the patient's clinical condition and the nutrition needs associated with repletion or growth, if needed. After a nutrition intervention has been initiated, periodic reassessment of nutrition status is critical to determine the accuracy of the initial estimate. Nutrition requirements are dynamic in the setting of acute or critical illness—as the patient's clinical status changes, so will protein and energy requirements, further emphasizing the need for continued reassessment.

ABBREVIATIONS

ABW	actual body weight (kg)
AdjBW	adjusted body weight (kg)
AI	Adequate Intake
ALB	albumin
AND	Academy of Nutrition and Dietetics
ASPEN	American Society for Parenteral and Enteral Nutrition
BEE	basal energy expenditure
BIA	bioelectrical impedance analysis
BMI	body mass index
CDC	Centers for Disease Control and Prevention

CDRR	Chronic Disease Reduction Risk level
CRP	C-reactive protein
CT	computed tomography
DCH	delayed cutaneous hypersensitivity
DNI	drug-nutrient interaction
DRI	Dietary Reference Intake
DXA	dual-energy x-ray absorptiometry
EAR	Estimated Average Requirement
EFAD	essential fatty acid deficiency
EN	enteral nutrition
GI	gastrointestinal
HIV	human immunodeficiency virus
IBW	ideal body weight
IV	intravenous
LBM	lean body mass
MREE	measured resting energy expenditure
MRI	magnetic resonance imaging
MST	Malnutrition Screening Tool
MUMC	mid-arm muscle circumference
NFPE	nutrition-focused physical examination
PN	parenteral nutrition
RDA	Recommended Dietary Allowance
REE	resting energy expenditure
RQ	respiratory quotient
SCr	serum creatinine
SGA	Subjective Global Assessment

TBSA	total body surface area
TBW	total body water
TFN	transferrin
TUN	total urine nitrogen
UBW	usual body weight
UL	tolerable upper intake level
UUN	urine urea nitrogen
VCO_2	carbon dioxide production
VO_2	oxygen consumption
WHO	World Health Organization

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SELF ASSESSMENT QUESTIONS

1. A 35-year-old woman (height, 168 cm [5′6″]; weight, 54.5 kg [120 lb]) with short bowel syndrome is admitted with mild dehydration and weight loss. She has lost 4.5 kg (10 lb) in the past 4 months. Which of the following would be the *most* appropriate characterization of her nutrition status?

   A. Normal, healthy

   B. Starvation-induced malnutrition

   C. Acute, disease-related malnutrition

   D. Chronic, disease-related malnutrition

2. An interdisciplinary nutrition support team is designing a nutrition screening program for their hospital. Which of the following would be a meaningful trigger to identify a patient at high risk for nutrition-related complications?

   A. Decreased oral intake for 3 days due to vomiting.

   B. Significantly decreased oral intake for the past 3 weeks due to anorexia.

   C. Planned weight loss of 4% of usual body weight (UBW) over the past 2 months.

   D. Weight loss of 5% of UBW due to acute diarrhea-induced dehydration.

3. Using ideal body weight (IBW), how would you characterize the nutrition status of a 50-year-old man whose weight is 60 kg (132 lb) and height is 183

cm (6′0″)?

A. Normal, healthy

B. Mild malnutrition

C. Moderate malnutrition

D. Severe malnutrition

4. A 69-year-old man weighs 75 kg (165 lb) and is 178 cm (5′10″). Based on his BMI, what is the *best* interpretation of his current nutrition status?

A. Normal, healthy

B. Overweight

C. Moderate obesity

D. Severe or morbid obesity

5. A patient with severe anorexia and moderate malnutrition is started on supplemental nutrition via a gastrostomy tube. Which serum visceral protein would be the most appropriate to measure the acute inflammatory response (first 7 days) in this patient?

A. Albumin

B. Transferrin

C. Prealbumin

D. C-reactive protein

6. A patient receiving long-term home parenteral nutrition (PN) has developed a tremor and aggressive behavior during the past 4 months. His PN includes a commercially marketed trace element solution which contains zinc, copper, manganese, and selenium. Routine laboratories are within reference ranges, except for elevated total and direct bilirubin and gamma glutamyl-transferase (GGT) concentrations. This patient's new onset symptoms are *most* consistent with which of the following nutrient imbalances?

A. Chromium deficiency

B. Copper toxicity

C. Zinc deficiency

D. Manganese toxicity

7. A patient with ulcerative colitis recently underwent colon resection with end ileostomy formation. His daily ostomy output has ranged from 900 mL to 2200 mL over the past 3 months. In clinic today, he states that his hair is falling out, and he has dry, cracked lips and a sore tongue. Which trace element abnormality would *best* explain his symptoms?

A. Selenium deficiency

B. Zinc deficiency

C. Chromium toxicity

D. Copper toxicity

8. An adolescent patient with cystic fibrosis is found to have an elevated serum alkaline phosphatase, but her other hepatic enzymes are within the

reference range. She has normal kidney function. Which of the following laboratory tests should be evaluated to aid in the assessment of the increased alkaline phosphatase concentration?

A. Serum 25(OH)D

B. Serum $25(OH)_2D$

C. Serum vitamin A (retinol)

D. Serum vitamin E

9. Using the kcal/kg method, which estimate of energy requirements is the *most* appropriate for a woman (weight, 90 kg [198 lb]; height, 165 cm [5′5″]) in the intensive care unit (ICU) with multiple injuries including head trauma suffered in a motor vehicle crash?

A. 1200 kcal/day (~5016 kJ/day)

B. 1800 kcal/day (~7520 kJ/day)

C. 2250 kcal/day (~9400 kJ/day)

D. 2700 kcal/day (~11,120 kJ/day)

10. A critically ill man (45 years old; weight, 145 kg [319 lb]; height, 185 cm [6′1″] is in the Surgical/Trauma ICU. Which of the following is the *most* appropriate initial assessment of this man's daily protein requirements?

A. 84 g

B. 150 g

C. 200 g

D. 290 g

11. A 9-year-old boy (weight, 23 kg [51 lb]) is admitted to the hospital and made NPO (nil per os) in preparation for surgery. He has no significant past medical history. Which of the following is the *most* appropriate rate to run his maintenance intravenous fluids?

A. 29 mL/hour

B. 38 mL/hour

C. 65 mL/hour

D. 96 mL/hour

12. A 45-year-old man (weight, 75 kg [165 lb]; height, 178 cm [5′10″]) is in the ICU after suffering several injuries in a drive-by shooting. He is receiving PN with 122 g of protein daily. A 24-hr urine was collected for a nitrogen balance study. The results are reported as total urea nitrogen (TUN) of 22 g N per 24 hr. What is this man's estimated nitrogen balance?

A. Negative 2.5 (-2.5)

B. Negative 3.5 (-3.5)

C. Negative 4.5 (-4.5)

D. Negative 6.5 (-6.5)

13. A 50-year-old man (weight, 80 kg [176 lb]; height, 178 cm [5′10″]) is receiving PN which provides a total of 2400 kcal/day (~10,000 kJ/day) and 75 g

protein/day. The non-protein calories are distributed 60% CHO:40% fat. Indirect calorimetry was conducted. The results were reported as: REE 2210 kcal/day (~9240 kJ/day); RQ 0.95. Which of the following is the *most* appropriate interpretation of the current number of calories being provided in this patient's PN?

A. An appropriate number of calories are being provided by his current PN.

B. Too many calories are being provided by the current PN.

C. Not enough calories are being provided by his current PN.

D. There is not enough information provided to determine the adequacy of his calorie intake.

14. Which of the following nutrient imbalances is *most* likely to occur because of long-term proton pump inhibitor use?

A. Vitamin B12 deficiency

B. Vitamin D deficiency

C. Thiamine deficiency

D. Zinc deficiency

15. Which one of the following is required for the transport of free fatty acids into the mitochondria for ß-oxidation?

A. Bile salts

B. Pancreatic lipase

C. Intestinal lipase

D. Carnitine

SELF-ASSESSMENT QUESTION-ANSWERS

1. **D.** This patient has malabsorption and a chronic disease state. Her weight loss was over more than 3 months which puts her into the chronic, disease-related etiological category for malnutrition.

2. **B.** A patient with decreased oral intake for more than 1 to 2 weeks would meet the criteria for being *at nutrition risk* in most of the available nutrition screens.

3. **C.** This patient's IBW is 77.6 kg (171 lb); his actual weight is 60 kg (132 lb). His actual weight is 77% of his IBW which would be classified as moderate malnutrition.

4. **A.** The patient's BMI is 23.7 kg/m^2 which would be classified as a healthy (normal) weight.

5. **C.** Prealbumin has the shortest half-life of the visceral proteins and responds most rapidly as an inflammatory marker.

6. **D.** Manganese accumulation in the basal ganglia has been associated with symptoms mimicking Parkinson's disease, similar to those being exhibited by this patient.

7. **B.** Alopecia, dermatitis, and glossitis are hallmarks of zinc deficiency. Zinc can be lost in significant quantities with high ostomy output.

8. **A.** Alkaline phosphatase is a marker of normal bone formation, elevations suggest possible vitamin D deficiency. The storage form of vitamin D, 25(OH)D, is the most appropriate to evaluate vitamin D status.

9. **A.** For a patient with a BMI of 33 kg/m^2, energy should be provided as 11 to 14 kcal/kg (46-59 kJ/kg) based on actual body weight or 22 to 25 kcal/kg

(92-105 kJ/kg) based on IBW. Intake of 1200 kcal/day (5000 kJ/d) is 13.3 kcal/kg/day (55.6 kJ/kg/d) based on actual body weight.

10. **C.** For a critically ill patient with a BMI over 40 mg/m^2, the appropriate protein intake is 2.5 g protein per kg based on IBW. This man's IBW is 79.9 kg (176 lb), so he requires at least 200 g protein daily.

11. **C.** Maintenance fluids calculated using the Holiday-Segar method would be 1000 mL for the first 10 kg plus 500 mL for the next 10 kg plus 20 mL/kg for weight above 20 kg. Thus, 1000 mL + 500 mL + (20 ml/kg × 3 kg) = 1560 mL/day ÷ 24 hr/day = 65 mL/hr.

12. **B.** When TUN is available, nitrogen losses are estimated as TUN + 1.05. Thus, nitrogen balance would be Nin (122 g ÷ 6.25 g N per g protein) – Nout (22 + 1.05) = -3.5 g.

13. **B.** The REE of 2210 kcal/day (9250 kJ/d) should not be multiplied by any factor. PN provides 2400 kcal/day (10,000 kJ/d), so the patient is receiving too many calories.

14. **A.** Due to changes in acid in the stomach, the absorption of vitamin B12 can be affected by long-term use of proton pump inhibitors, especially in older adults.

15. **D.** The absorption of enteral fat depends on bile and lipase. However, the transport of free fatty acids into the mitochondria for energy production (by ß-oxidation) is a carnitine-dependent process.