SECTION 1

Nutritional Disorders

1 Nutrition: General Considerations

Nutrition is the science of food and its relationship to health. Nutrients are chemicals in foods that are used by the body for growth, maintenance, and energy. Nutrients that cannot be synthesized by the body and thus must be derived from the diet are considered essential. They include vitamins, minerals, some amino acids, and some fatty acids. Nutrients that the body can synthesize from other compounds, although they may also be derived from the diet, are considered nonessential. Macronutrients are required by the body in relatively large amounts; micronutrients are needed in minute amounts.

Lack of nutrients can result in deficiency syndromes (eg, kwashiorkor, pellagra) or other disorders (see p. 9). Excess intake of macronutrients can lead to obesity (see p. 56) and related disorders; excess intake of micronutrients can be toxic. Also, the balance of various types of nutrients, such as how much usaturated vs saturated fat is consumed, can influence the development of disorders.

Macronutrients

Macronutrients constitute the bulk of the diet and supply energy and many essential nutrients. Carbohydrates, proteins (including essential amino acids), fats (including essential fatty acids), macrominerals, and water are macronutrients. Carbohydrates, fats, and proteins are interchangeable as sources of energy; fats yield 9 kcal/g (37.8 kJ/g); proteins and carbohydrates yield 4 kcal/g (16.8 kJ/g).

Carbohydrates: Dietary carbohydrates are broken down into glucose and other monosaccharides. Carbohydrates increase blood glucose levels, supplying energy. Simple carbohydrates are composed of small molecules, generally monosaccharides or disaccharides, which increase blood glucose levels rapidly. Complex carbohydrates are composed of larger molecules, which are broken down into monosaccharides. Complex carbohydrates increase blood glucose levels more slowly but for a longer time. Glucose and sucrose are simple carbohydrates; starches and fiber are complex carbohydrates.

The glycemic index measures how rapidly consumption of a carbohydrate increases plasma glucose levels. Values range from 1 (the slowest increase) to 100 (the fastest increase, equivalent to pure glucose—see Table 1–1). However, the actual rate of increase also depends on what foods are consumed with the carbohydrate.

Carbohydrates with a high glycemic index may increase plasma glucose to high levels rapidly. It is hypothesized that, as a result, insulin levels increase, inducing hypoglycemia and hunger, which tends to lead to consumption of excess calories and weight gain. Carbohydrates with a low glycemic index increase plasma glucose levels slowly, resulting in lower postprandial insulin levels and less hunger, which probably makes consumption of excess calories less likely. These effects are predicted to result in a more favorable lipid profile and a decreased risk of obesity, diabetes mellitus, and complications of diabetes if present.

Proteins: Dietary proteins are broken down into peptides and amino acids. Proteins are required for tissue maintenance, replacement, function, and growth. However, if the body is not getting enough calories from dietary sources or tissue stores (particularly of fat), protein may be used for energy.

As the body uses dietary protein for tissue production, there is a net gain of protein (positive nitrogen balance). During catabolic

Table 1–1. GLYCEMIC INDEX OF SOME FOODS

CATEGORY	FOOD	INDEX*
Beans	Kidney	33
	Red lentils	27
	Soy	14
Bread	Pumpernickel	49
	White	69
	Whole wheat	72
Cereals	All bran	54
	Corn flakes	83
	Oatmeal	53
	Puffed rice	90
	Shredded wheat	70
Dairy	Milk, ice cream, yogurt	34–38
Fruit	Apple	38
	Banana	61
	Orange	43
	Orange juice	49
	Strawberries	32
Grains	Barley	22
	Brown rice	66
	White rice	72
Pasta	—	38
Potatoes	Instant mashed (white)	86
	Mashed (white)	72
	Sweet	50
Snacks	Corn chips	72
	Oatmeal cookies	57
	Potato chips	56
Sugar	Fructose	22
	Glucose	100
	Honey	91
	Refined sugar	64

*Values may vary.

states (eg, starvation, infections, burns), more protein may be used (because body tissues are broken down) than is absorbed, resulting in a net loss of protein (negative nitrogen balance). Nitrogen balance is best determined by subtracting the amount of nitrogen excreted in urine and feces from the amount of nitrogen consumed.

Of the 20 amino acids, 9 are essential amino acids (EAAs); they cannot be synthesized and must be obtained from the diet. All people require 8 EAAs; infants also require histidine.

The weight-adjusted requirement for dietary protein correlates with growth rate, which decreases from infancy until adulthood. The daily dietary protein requirement decreases from 2.2 g/kg in 3-mo-old infants to 1.2 g/kg in 5-yr-old children and to 0.8 g/kg in adults. Protein requirements correspond to EAA requirements (see Table 1–2). Adults trying to increase muscle mass need very little extra protein beyond the requirements in the table.

The amino acid composition of protein varies widely. Biological value (BV) reflects the similarity in amino acid composition of protein to that of animal tissues; thus, BV indicates what percentage of a dietary protein provides EAAs for the body. A perfect match is egg protein, with a value of 100. Animal proteins in milk and meat have a high BV (~90); proteins in cereal and vegetables have a lower BV (~40), and some derived proteins (eg, gelatin) have a BV of 0. The extent to which dietary proteins supply each other's missing amino acids (complementarity) determines the overall BV of the diet. The recommended daily allowances (RDA) for protein assumes that the average mixed diet has a BV of 70.

Fats: Fats are broken down into fatty acids and glycerol. Fats are required for tissue growth and hormone production. Saturated fatty acids, common in animal fats, tend to be solid at room temperature. Except for palm and coconut oils, fats derived from plants tend to be liquid at room temperature; these fats contain high levels of monounsaturated fatty acids or polyunsaturated fatty acids (PUFAs).

Partial hydrogenation of unsaturated fatty acids (as occurs during food manufacturing) produces trans fatty acids, which are solid or semisolid at room temperature. In the US, the main dietary source of trans fatty acids is partially hydrogenated vegetable oils, used in manufacturing certain foods (eg, cookies, crackers, chips) to prolong shelf-life. Trans fatty acids may elevate LDL cholesterol and lower HDL; they may also independently increase the risk of coronary artery disease.

Essential fatty acids (EFAs) are linoleic acid, an ω-6 (n-6) fatty acid, and linolenic acid, an ω-3 (n-3) fatty acid. Other ω-6 acids (eg, arachidonic acid) and other ω-3 fatty acids (eg, eicosapentaenoic acid, docosahexaenoic acid) are required by the body but can be synthesized from EFAs.

EFAs (see also p. 19) are needed for the formation of various eicosanoids (biologically active lipids), including prostaglandins, thromboxanes, prostacyclins, and leukotrienes. Consumption of ω-3 fatty acids may decrease the risk of coronary artery disease.

Table 1–2. ESSENTIAL AMINO ACID REQUIREMENTS IN MG/KG BODY WEIGHT

REQUIREMENT	INFANT (4–6 mo)	CHILD (10–12 yr)	ADULT
Histidine	29	—	—
Isoleucine	88	28	10
Leucine	150	44	14
Lysine	99	49	12
Methionine and cystine	72	24	13
Phenylalanine and tyrosine	120	24	14
Threonine	74	30	7
Tryptophan	19	4	3
Valine	93	28	13
Total essential amino acids (excluding histidine)	715	231	86

Requirements for EFAs vary by age. Adults require amounts of linoleic acid equal to at least 2% of total caloric needs and linolenic acid equal to at least 0.5%. Vegetable oils provide linoleic acid and linolenic acid. Oils made from safflower, sunflower, corn, soya, primrose, pumpkin, and wheat germ provide large amounts of linoleic acid. Marine fish oils and oils made from flaxseeds, pumpkin, soy, and canola provide large amounts of linolenic acid. Marine fish oils also provide some other ω-3 fatty acids in large amounts.

Macrominerals: Na, Cl, K, Ca, P, and Mg are required in relatively large amounts per day (see Tables 1–3, 1–4, and 5–2).

Water: Water is considered a macronutrient because it is required in amounts of 1 mL/kcal (0.24 mL/kJ) of energy expended, or about 2500 mL/day. Needs vary with fever, physical activity, and changes in climate and humidity.

Table 1–3. MACROMINERALS

NUTRIENT	PRINCIPAL SOURCES	FUNCTIONS
Ca	Milk and milk products, meat, fish, eggs, cereals, beans, fruits, vegetables	Bone and tooth formation, blood coagulation, neuromuscular irritability, muscle contractility, myocardial conduction
Cl	Many foods, mainly animal products but some vegetables; similar to Na	Acid-base balance, osmotic pressure, blood pH, kidney function
K	Many foods, including whole and skim milk, bananas, prunes, raisins, meats	Muscle activity, nerve transmission, intracellular acid-base balance, water retention
Mg	Green leaves, nuts, cereals, grains, seafood	Bone and tooth formation, nerve conduction, muscle contraction, enzyme activation
Na	Many foods, including beef, pork, sardines, cheese, green olives, corn bread, potato chips, sauerkraut	Acid-base balance, osmotic pressure, blood pH, muscle contractility, nerve transmission, maintenance of cell membrane gradients
P	Milk, cheese, meat, poultry, fish, cereals, nuts, legumes	Bone and tooth formation, acid-base balance, energy production

Table 1–4. RECOMMENDED DIETARY REFERENCE INTAKES* FOR SOME MACRONUTRIENTS, Food and Nutrition Board, Institute of Medicine of the National Academies

CATEGORY	AGE OR TIME FRAME (yr)	PROTEIN (g/kg)	ENERGY (kcal/kg)	CALCIUM (mg/kg)	PHOSPHORUS (mg/kg)	MAGNESIUM (mg/kg)
Infants	0.0–0.5	2.2	108.3	66.7	50.0	6.7
	0.5–1.0	1.6	94.4	66.7	55.6	6.7
Children	1–3	1.2	100.0	61.5	61.5	6.2
	4–6	1.2	90.0	40.0	40.0	6.0
	7–10	1.0	71.4	28.6	28.6	6.1
Males	11–14	1.0	55.6	26.7	26.7	6.0
	15–18	0.9	45.5	18.2	18.2	6.1
	19–24	0.8	40.3	16.7	16.7	4.9
	25–50	0.8	36.7	10.1	10.1	4.4
	51+	0.8	29.9	10.4	10.4	4.5
Females	11–14	1.0	47.8	26.1	26.1	6.1
	15–18	0.8	40.0	21.8	21.8	5.5
	19–24	0.8	37.9	20.7	20.7	4.8
	25–50	0.8	34.9	12.7	12.7	4.4
	51+	0.8	29.2	12.3	12.3	4.3
Pregnant	—	0.9	4.6	18.5	18.5	4.9
Breastfeeding	1st yr	1.0	7.9	19.0	19.0	5.4

*These amounts, expressed as average daily intakes over time, are intended to provide for individual variations among most healthy people living in the US under usual environmental stresses.

Micronutrients

Vitamins and minerals required in minute amounts (trace minerals) are micronutrients (see Chs. 4 and 5).

Water-soluble vitamins are vitamin C (ascorbic acid) and 8 members of the vitamin B complex: biotin, folate, niacin, pantothenic acid, riboflavin (vitamin B_2), thiamin (vitamin B_1), vitamin B_6 (pyridoxine), and vitamin B_{12} (cobalamin).

Fat-soluble vitamins are vitamins A (retinol), D (cholecalciferol and ergocalciferol), E (α-tocopherol), and K (phylloquinone and menaquinone).

Only vitamins A, E, and B_{12} are stored to any significant extent in the body; the other vitamins must be consumed regularly to maintain tissue health.

Essential trace minerals include chromium, copper, iodine, iron, manganese, molybdenum, selenium, and zinc. Except for chromium, each of these is incorporated into enzymes or hormones required in metabolism. Except for deficiencies of iron and zinc, micromineral deficiencies are uncommon in developed countries (see Ch. 5).

Other minerals (eg, aluminum, arsenic, boron, cobalt, fluoride, nickel, silicon, vanadium) have not been proved essential for people. Fluoride, although not essential, helps prevent tooth decay by forming a compound with Ca (CaF_2), which stabilizes the mineral matrix in teeth.

All trace minerals are toxic at high levels, and some (arsenic, nickel, and chromium) may cause cancer.

Other Dietary Substances

The daily human diet typically contains as many as 100,000 chemicals (eg, coffee contains 1000). Of these, only 300 are nutrients, only some of which are essential. However, many nonnutrients in foods are useful. For example, food additives (eg, preservatives, emulsifiers, antioxidants, stabilizers) improve the production and stability of foods. Trace components (eg, spices, flavors, odors, colors, phytochemicals, many other natural products) improve appearance and taste.

Fiber: Fiber occurs in various forms (eg, cellulose, hemicellulose, pectin, gums). It

increases GI motility, prevents constipation, and helps control diverticular disease. Fiber is thought to accelerate the elimination of cancer-causing substances produced by bacteria in the large intestine. Epidemiologic evidence suggests an association between colon cancer and low fiber intake and a beneficial effect of fiber in patients with functional bowel disorders, Crohn's disease, obesity, and hemorrhoids. Soluble fiber (present in fruits, vegetables, oats, barley, and legumes) reduces the postprandial increase in blood glucose and insulin and can reduce cholesterol levels.

The typical Western diet is low in fiber (about 12 g/day) because of a high intake of highly refined wheat flour and a low intake of fruits and vegetables. Increasing fiber intake to about 30 g/day by consuming more vegetables, fruits, and high-fiber cereals and grains is generally recommended. However, very high fiber intake may reduce absorption of certain minerals.

NUTRITIONAL REQUIREMENTS

Good nutrition aims to achieve and maintain a desirable body composition and high potential for physical and mental work. Balancing energy intake with energy expenditure is necessary for a desirable body weight. Energy expenditure depends on age, sex, weight (see Table 1–4), and metabolic and physical activity. If energy intake exceeds expenditure, weight is gained. Taking in about 100 calories/day more than needed results in a weight gain of about 4 to 5 kg in a year. If energy intake is less than expenditure, weight is lost.

Daily dietary requirements for essential nutrients also depend on age, sex, weight, and metabolic and physical activity. Every 5 yr, the Food and Nutrition Board of the National Academy of Sciences/National Research Council and the US Department of Agriculture (USDA) issues the dietary reference intakes (DRIs) for protein, energy, and some vitamins and minerals (see Tables 1–4, 4–1, and 5–2). For vitamins and minerals about which less is known, safe and adequate daily dietary intakes are estimated.

Pregnant women (see p. 2608) and infants (see p. 2703) have special nutritional needs.

The USDA publishes the Food Guide Pyramid, which specifies the number of recommended daily servings of various food groups. The recommendations are individualized based on age, sex, and physical activity (see Table 1–5). Generally, the recommended intake decreases with aging because physical activity tends to decrease, resulting in less energy expended. The new Food Guide Pyramid emphasizes the following:

- Increasing consumption of whole grains
- Increasing consumption of vegetables and fruits
- Substituting fat-free or low-fat milk products (or equivalents) for whole-fat milk products
- Reducing consumption of saturated fats and trans fatty acids
- Exercising regularly

Adequate fluid intake is also important.

Fats should constitute ≤ 30% of total calories, and saturated and trans fatty acids should constitute < 10%. Excess intake of saturated fats contributes to atherosclerosis. Substituting polyunsaturated fatty acids for saturated fats can decrease the risk of atherosclerosis. Routine use of nutritional supplements is not necessary or beneficial; some supplements can be harmful. For example, excess vitamin A can lead to hypervitaminosis A, with headaches, osteoporosis, and rash.

NUTRITION IN CLINICAL MEDICINE

Nutritional deficiencies can often worsen health outcomes (whether a disorder is present or not), and some disorders (eg, malabsorption) can cause nutritional deficiencies. Also, many patients (eg, elderly patients during acute hospitalization) have unsuspected nutritional deficiencies that require treatment. Many medical centers have multidisciplinary nutrition support teams of physicians, nurses, dietitians, and pharmacists to help the clinician prevent, diagnose, and treat occult nutritional deficiencies.

Overnutrition may contribute to chronic disorders, such as cancer, hypertension, obesity, diabetes mellitus, and coronary artery disease. Dietary restrictions are necessary in many hereditary metabolic disorders (eg, galactosemia, phenylketonuria).

Evaluation of Nutritional Status

Indications for nutritional evaluation include undesirable body weight or body composition, suspicion of specific deficiencies or toxicities

Table 1–5. RECOMMENDED DIETARY INTAKE FOR 40-YR-OLDS WITH MODERATE PHYSICAL ACTIVITY*

FOOD GROUPS	AMOUNT/DAY	
	Men	Women
Grains†	9 oz	6 oz
Vegetables‡	3.5 cups	2.5 cups
Fruits	2 cups	2 cups
Milk	3 cups	3 cups
Meat and beans	6.5 oz	5.5 oz
Oils	8 tsp	6 tsp
Sugars and fats	410 calories	265 calories
Estimated daily intake§	2600 calories	2000 calories

*About 30 to 60 min of moderate or vigorous activity (eg, brisk walking, jogging, biking, aerobic exercise, yard work) daily.
†At least half should be whole grains.
‡People should vary the vegetables they eat and include beans and peas, dark green vegetables (eg, broccoli, greens, lettuce, spinach), orange vegetables (eg, carrots, sweet potatoes, winter squash), starchy vegetables (eg, corn, potatoes), and other vegetables (eg, asparagus, cauliflower, mushrooms, tomatoes).
§Actual needed intake is determined by monitoring trends in body weight.
NOTE: Individualized recommendations can be obtained by entering the relevant information at the USDA web site (www.mypyramid.gov).

of essential nutrients, and, in infants and children, insufficient growth or development. Nutritional status should be evaluated routinely as part of the clinical examination for infants and children, the elderly, people taking several drugs, people with psychiatric disorders, and people with systemic disorders that last longer than several days.

Evaluating general nutritional status includes history, physical examination, and sometimes tests. If undernutrition is suspected, laboratory tests (eg, albumin levels) and skin tests for delayed hypersensitivity may be done (see p. 13). Body composition analysis (eg, skinfold measurements, bioelectrical impedance analysis) is used to estimate percentage of body fat and to evaluate obesity (see p. 58).

History includes questions about dietary intake, weight change, and risk factors for nutritional deficiencies and a focused review of systems (see Table 2–1 on p. 11). A dietitian can obtain a more detailed dietary history. It usually includes a list of foods eaten within the previous 24 h and a food questionnaire. A food diary may be used to record all foods eaten. The weighed ad libitum diet, in which the patient weighs and writes down all foods consumed, is the most accurate record.

A complete physical examination, including measurement of height and weight and distribution of body fat, should be done. Body mass index (BMI)—weight(kg)/height(m)^2, which adjusts weight for height (see Table 6–2 on p. 59), is more accurate than height and weight tables. There are standards for growth and weight gain in infants, children, and adolescents (see p. 2756).

Distribution of body fat is important. Disproportionate truncal obesity (ie, waist/hip ratio > 0.8) is associated with cardiovascular and cerebrovascular disorders, hypertension, and diabetes mellitus more often than fat located elsewhere. Measuring waist circumference in patients with a BMI of < 35 helps determine whether they have truncal obesity and helps predict risk of diabetes, hypertension, hypercholesterolemia, and cardiovascular disorders. Risk is increased if waist circumference is > 102 cm (> 40 in) in men or > 88 cm (> 35 in) in women.

NUTRIENT-DRUG INTERACTIONS

Nutrition can affect the body's response to drugs; conversely, drugs can affect the body's nutrition.

Foods can enhance, delay, or decrease drug absorption. Foods impair absorption of many antibiotics. They can alter metabolism of drugs; eg, high-protein diets can accelerate metabolism of certain drugs by stimulating

cytochrome P-450. Eating grapefruit can inhibit cytochrome P-450 34A, slowing metabolism of some drugs (eg, amiodarone, carbamazepine, cyclosporine, certain Ca channel blockers). Diets that alter the bacterial flora may markedly affect the overall metabolism of certain drugs. Some foods affect the body's response to drugs. For example, tyramine, a component of cheese and a potent vasoconstrictor, can cause hypertensive crisis in some patients who take monoamine oxidase inhibitors and eat cheese.

Nutritional deficiencies can affect drug absorption and metabolism. Severe energy and protein deficiencies reduce enzyme tissue concentrations and may impair the response to drugs by reducing absorption or protein binding and causing liver dysfunction. Changes in the GI tract can impair absorption and affect the response to a drug. Deficiency of Ca, Mg, or zinc may impair drug metabolism. Vitamin C deficiency decreases activity of drug-metabolizing enzymes, especially in the elderly.

Many drugs affect appetite, food absorption, and tissue metabolism (see Table 1–6). Some drugs (eg, metoclopramide) increase GI motility, decreasing food absorption. Other drugs (eg, opioids, anticholinergics) decrease GI motility. Some drugs are better tolerated if taken with food.

Certain drugs affect mineral metabolism. For example, diuretics, especially thiazides, and corticosteroids can deplete body K, increasing susceptibility to digoxin-induced cardiac arrhythmias. Repeated use of laxatives may deplete K. Cortisol, desoxycorticosterone, and aldosterone cause marked Na and water retention, at least temporarily; retention is much less with prednisone, prednisolone, and some other corticosteroid analogs. Sulfonylureas and lithium can impair the uptake or release of iodine by the thyroid. Oral contraceptives can lower blood zinc levels and increase copper levels. Certain antibiotics (eg, tetracyclines) reduce iron absorption, as can certain foods (eg, vegetables, tea, bran).

Certain drugs affect vitamin absorption or metabolism. Ethanol impairs thiamin utilization, and isoniazid interferes with niacin and pyridoxine metabolism. Ethanol and oral contraceptives inhibit folate (folic acid) absorption. Most patients receiving phenytoin, phenobarbital, primidone, or phenothiazines develop folate deficiency, probably because hepatic microsomal drug-metabolizing enzymes are affected. Folate supplements may

Table 1–6. EFFECTS OF SOME DRUGS ON NUTRITION

EFFECT	DRUGS
Increases appetite	Alcohol, antihistamines, corticosteroids, dronabinol, insulin, megestrol acetate, mirtazapine, many psychoactive drugs, sulfonylureas, thyroid hormone
Decreases appetite	Antibiotics, bulk agents (methylcellulose, guar gum), cyclophosphamide, digoxin, glucagon, indomethacin, morphine, fluoxetine
Decreases absorption of fats	Orlistat
Increases blood glucose levels	Octreotide, opioids, phenothiazines, phenytoin, probenecid, thiazide diuretics, corticosteroids, warfarin
Decreases blood glucose levels	ACE inhibitors, aspirin, barbiturates, β-blockers, insulin, monoamine oxidase inhibitors (MAOIs), oral antihyperglycemic drugs, phenacetin, phenylbutazone, sulfonamides
Decreases blood lipid levels	Aspirin and *p*-aminosalicylic acid, L-asparaginase, chlortetracycline, colchicine, dextrans, glucagon, niacin, phenindione, statins, sulfinpyrazone, trifluperidol
Increases blood lipid levels	Adrenal corticosteroids, chlorpromazine, ethanol, growth hormone, oral contraceptives (estrogen-progestin type), thiouracil, vitamin D
Decreases protein metabolism	Chloramphenicol, tetracycline

make phenytoin less effective. Anticonvulsants can cause vitamin D deficiency. Malabsorption of vitamin B_{12} can occur with use of aminosalicylic acid, slow-release K iodide, colchicine, trifluoperazine, ethanol, and oral contraceptives. Oral contraceptives with a high progestin dose can cause depression, probably because of metabolically induced tryptophan deficiency.

FOOD ADDITIVES AND CONTAMINANTS

Additives: Chemicals are often combined with foods to facilitate their processing and preservation or to enhance their desirability. Only amounts of additives shown to be safe by laboratory tests are permitted in commercially prepared foods.

Weighing the benefits of additives (eg, reduced waste, increased variety of available foods, protection against food-borne illness) against the risks is often complex. For example, nitrite, which is used in cured meats, inhibits the growth of *Clostridium botulinum* and improves flavor. However, nitrite converts to nitrosamines, which are carcinogens in animals. On the other hand, the amount of nitrite added to cured meat is small compared with the amount from naturally occurring food nitrates converted to nitrite by the salivary glands. Dietary vitamin C can reduce nitrite formation in the GI tract. Rarely, some additives (eg, sulfites) cause food hypersensitivity (allergy) reactions. Most of these reactions are caused by ordinary foods (see p. 1118).

Contaminants: Sometimes limited amounts of contaminants are allowed in foods because the contaminants cannot be completely eliminated without damaging the foods. Common contaminants are pesticides, heavy metals (lead, cadmium, mercury), nitrates (in green leafy vegetables), aflatoxins (in nuts and milk), growth-promoting hormones (in dairy products and meat), animal hairs and feces, and insect parts.

FDA-estimated safe levels are levels that have not caused illness or adverse effects in people. However, demonstrating a causal relationship between extremely low level exposures and adverse effects is difficult; long-term adverse effects, although unlikely, are still possible. Safe levels are often determined by consensus rather than by hard evidence.

2 Undernutrition

Undernutrition is a form of malnutrition. (Malnutrition also includes overnutrition—see Ch. 6). Undernutrition can result from inadequate ingestion of nutrients, malabsorption, impaired metabolism, loss of nutrients due to diarrhea, or increased nutritional requirements (as occurs in cancer or infection). Undernutrition progresses in stages; each stage usually takes considerable time to develop. First, nutrient levels in blood and tissues change, followed by intracellular changes in biochemical functions and structure. Ultimately, symptoms and signs appear.

Risk Factors

Undernutrition is associated with many disorders and circumstances, including poverty and social deprivation. Risk is also greater at certain times (ie, during infancy, early childhood, adolescence, pregnancy, breastfeeding, and old age).

Infancy and childhood: Infants and children are particularly susceptible to undernutrition because of their high demand for energy and essential nutrients. Because vitamin K does not readily cross the placenta, neonates may be deficient, so all are given a single injection of vitamin K within 1 h of birth to prevent hemorrhagic disease of the newborn, a life-threatening disorder (see pp. 46 and 2783). Infants fed only breast milk, which is typically low in vitamin D, are given supplemental vitamin D; they can develop vitamin B_{12} deficiency if the mother is a vegan. Inadequately fed infants and children are at risk of protein-energy undernutrition (PEU—previously called protein-energy malnutrition) and deficiencies of iron, folate (folic acid), vitamins A and C, copper, and zinc. During adolescence, nutritional requirements increase because the growth rate accelerates. Anorexia nervosa (see p. 1535) may affect adolescent girls in particular.

Pregnancy and breastfeeding: Requirements for nutrients increase during pregnancy and breastfeeding. Aberrations of diet, including pica (consumption of nonnutritive substances, such as clay and charcoal), may occur during

pregnancy. Anemia due to iron deficiency is common, as is anemia due to folate deficiency, especially among women who have taken oral contraceptives. Vitamin D deficiency is common during late pregnancy, predisposing the child to decreased bone mass.

Old age: Aging—even when disease or dietary deficiency is absent—leads to sarcopenia (progressive loss of lean body mass), starting after age 40 and eventually amounting to a muscle loss of about 10 kg (22 lb) in men and 5 kg (11 lb) in women. Undernutrition contributes to sarcopenia, and sarcopenia accounts for many of the complications of undernutrition (eg, decreased nitrogen balance, increased susceptibility to infections). Causes of sarcopenia include the following:

- Decreased physical activity
- Decreased food intake
- Increased levels of cytokines (particularly interleukin-6)
- Decreased levels of growth hormone and mechano growth factor (insulin-like growth factor-3)
- In men, decreasing androgen levels

Aging decreases basal metabolic rate (due mainly to decreased fat-free mass), total body weight, height, and skeletal mass; aging increases mean body fat (as a percentage of body weight) to about 30% (from 20%) in men and to 40% (from 27%) in women.

From age 20 to 80, food intake decreases, especially in men. Anorexia due to aging itself has many causes, including reduced adaptive relaxation of the stomach's fundus, increased release and activity of cholecystokinin (which produces satiation), and increased leptin (an anorectic hormone produced by fat cells). Diminished taste and smell can decrease eating pleasure but usually decrease food intake only slightly. Anorexia may have other causes (eg, loneliness, inability to shop or prepare meals, dementia, some chronic disorders, use of certain drugs). Depression is a common cause. Occasionally, anorexia nervosa (sometimes called anorexia tardive in the elderly), paranoia, or mania interferes with eating. Dental problems limit the ability to chew and subsequently to digest foods. Swallowing difficulties (eg, due to strokes, other neurologic disorders, esophageal candidiasis, or xerostomia) are common. Poverty or functional impairment limits access to nutrients.

The institutionalized elderly are at particular risk of PEU. They are often confused and may be unable to express hunger or preferences for foods. They may be physically unable to feed themselves. Chewing or swallowing may be very slow, making it tedious for another person to feed them enough food.

In the elderly, particularly the institutionalized elderly, inadequate intake and often decreased absorption or synthesis of vitamin D, increased demand for vitamin D, and inadequate exposure to sunshine contribute to osteomalacia (see p. 41).

Disorders and medical procedures: Diabetes, some chronic disorders that affect the GI tract, intestinal resection, and certain other GI surgical procedures tend to impair absorption of fat-soluble vitamins, vitamin B_{12}, Ca, and iron. Gluten enteropathy, pancreatic insufficiency, or other disorders can result in malabsorption. Decreased absorption possibly contributes to iron deficiency and osteoporosis. Liver disorders impair storage of vitamins A and B_{12} and interfere with metabolism of protein and energy sources. Renal insufficiency predisposes to protein, iron, and vitamin D deficiencies. Anorexia causes some patients with cancer or depression and many with AIDS to consume inadequate amounts of food. Infections, trauma, hyperthyroidism, extensive burns, and prolonged fever increase metabolic demands. Any condition that increases cytokines may be accompanied by muscle loss, lipolysis, low albumin levels, and anorexia.

Vegetarian diets: Iron deficiency can occur in ovo-lacto vegetarians (although such a diet can be compatible with good health). Vegans may develop vitamin B_{12} deficiency unless they consume yeast extracts or Asian-style fermented foods. Their intake of Ca, iron, and zinc also tends to be low. A fruit-only diet is not recommended because it is deficient in protein, Na, and many micronutrients.

Fad diets: Some fad diets result in vitamin, mineral, and protein deficiencies; cardiac, renal, and metabolic disorders; and sometimes death. Very low calorie diets (< 400 kcal/day) cannot sustain health for long.

Drugs and nutritional supplements: Many drugs (eg, appetite suppressants, digoxin) decrease appetite; others impair nutrient absorption or metabolism. Some drugs (eg, stimulants) have catabolic effects. Certain drugs can impair absorption of many nutrients; eg, anticonvulsants can impair absorption of vitamins.

Alcohol or drug dependency: Patients with alcohol or drug dependency may neglect their nutritional needs. Absorption and metabolism of nutrients may also be impaired. IV drug addicts typically become undernourished, as do