5th Edition

Nutrition in Pediatrics

Basic Science • Clinical Applications

Duggan • Watkins • Koletzko • Walker

NUTRITION
IN PEDIATRICS

BASIC SCIENCE • CLINICAL APPLICATIONS

FIFTH EDITION

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DEDICATIONS

To the continued successful growth and nourishment of Michael, Brendan, and Emily Duggan and in gratitude for many teachers and students in the field of pediatric nutrition.

—Christopher Duggan, MD, MPH

To the children, parents, and staff of the growth and nutrition program whose shared knowledge, caring, and expertise enriches us all and to our grandchildren: Mariposa, Charlotte, Lillie, Gwen, and their “Pinkhouse” partners in “Friendship.”

—John B. Watkins, MD

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—Berthold Koletzko, MD, PhD

To my youngest grandchild William McDonald Walker (Mac), the paradigm of healthy nutrition in children.

—W. Allan Walker, MD

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PREFACE

This fifth edition of *Nutrition in Pediatrics: Basic Science and Clinical Applications* is our continuing effort to establish a comprehensive and accessible approach to pediatric nutrition for a wide range of clinicians, scientists, and—most importantly—trainees. An important addition to the textbook has been the inclusion of Professor Berthold Koletzko to our Editorial Board. As Professor of Pediatrics at the University of Munich and Head of the Division of Metabolic and Nutritional Medicine at Hauner Children's Hospital, Dr. Koletzko brings a wealth of clinical and research expertise to this text. In addition, his global collaborations have allowed us to substantially broaden our team of authors, making this version of the text a truly international one.

The fifth edition builds on the foundations of the several previous versions, with updated chapters on the broad themes of General Concepts, Physiology and Pathophysiology, Perinatal Nutrition, Obesity, Nutritional Aspects of Specific Disease States, and Approach to Nutritional Support. Owing to the recognition that nutritional issues overwhelmingly affect children living in resource-poor countries, we have also added a new section entitled "Nutrition in Low- and Middle-Income Populations." Expert authors in this field have contributed reviews on the topics of the nutrition transition, complementary feeding, economic development, HIV disease, and the occurrence of obesity in developing economies.

Although all of our contributions are excellent, notable additions to this 5th edition include an outstanding leadoff chapter on the role of nutrition for health, disease prevention, and development; new contributions on macronutrients, epigenetics, and the microbiome; and several significantly revised and updated classic chapters. As in past editions, comprehensive appendices are included that serve the reader by collating important tools for nutritional assessment, nutritional requirements, and enteral products.

The editors are grateful to Ms. Linda Mehta for her many efforts in the publication of this textbook.

Finally, we sincerely thank the dozens of authors who contributed countless hours of writing and research for the completion of this text. Their expertise and labors constitute the heart of this book.

—Christopher Duggan,
for the editors
Berthold Koletzko
John B. Watkins
W. Allan Walker

Nutrition: The Driving Force for Health, Disease Prevention, and Development

1

Robert D. Baker, MD, PhD and Susan S. Baker, MD, PhD

A SWEEPING LOOK AT NUTRITION

Nutrition is the underpinning of life itself. Good nutrition has consequences for health, societal well-being, economic stability, and advancements. Poor nutrition has a direct and measurable impact on all aspects of human functioning. Nutrition is the driving force for much of human and societal evolution. This fundamental role of nutrition has been recognized since ancient times. More recently, evolutionary biologists have recorded the importance of nutrition on evolution, and the basic requirements for the human organism have been identified.

This book deals with the scientific and clinical practice of pediatric nutrition. That it is now into its fifth edition implies that readers and users of this book are convinced of the importance of nutrition to the growing and developing child. In this first chapter, we invite “devotees” of pediatric nutrition to take a very broad look at the importance of food and to consider food as a driving force for the evolution of the human race, as a major part of our culture, as an economic force, and as a means toward future change.

From prehistory forward, food and the search for food have been

central to human evolution. In examining the expansion of humans from their African origins throughout the Middle East, Europe, Asia, the Far East including the Pacific Islands, across the bridge to North America, and south through Central America to include all of South America, one of the most striking aspects of this amazing migration is the rapidity with which it took place. After existing in Africa for 5–6 million years, the great migration started about 1 million years ago and was essentially complete about 20,000 years ago.[1] The migration was not a single sweep, but occurred in waves and fits and starts. The reasons for man's moving were undoubtedly multifactorial, but prominent among these factors had to be food availability. The move from "gathers" to "hunter-gathers" required the acquisition of tools, weapons, and necessitated cooperation, but also ushered in conflict. The beginning of agriculture, in the fertile crescent, not only provided a more stable source of nutrition but also allowed humans to establish settlements, which required rules and patterns of behavior far different from the behavior of hunter-gathers. Among many other results of "settlements" was the possibility of specialization; most would be farmers but there were also warriors, carpenters, builders, teachers, and eventually philosophers and scientists.[1] The move toward agriculture was gradual. Man first learned that by tending plants that bore fruit, the yield could be increased. Some tribes in New Guinea still practice this early form of agriculture. They clear completing plants from food-bearing plants and then leave returning months later to harvest the enhanced fruit production.[1] Wheat and other grains were the first food plants to be domesticated. The cultivation of pulses in addition to grains allowed both protein and carbohydrate needs to be largely supplied through plants. Domesticated animals became a readily available and dependable source of protein. Initially in the Middle East but then spreading, communities began domesticating animals; first sheep and then goats and finally cattle.

LACTOSE INTOLERANCE

About 7000–8000 years ago, these Middle Eastern farmers began consuming milk.[2] This created a genetic dilemma for humans. Lactose is the disaccharide in most mammalian milk, including human milk.[3] Human infants, to survive, must be able to digest and use lactose. Before the introduction of dairy products into the human food chain, there was no advantage of being able to digest lactose beyond the age of weaning. So, for most of the human race, the gene that codes for lactase becomes progressively less active during childhood. However, with the introduction

of milk into the human diet, an evolutionary pressure for persistent lactase activity was created. Humans dealt with this dilemma in two ways. The lifelong use of dairy products spread from the Middle East north to Europe and Scandinavia where the persistence of the lactase gene was common. An added advantage for human at northern latitudes was lactose's positive effect on calcium absorption, partially making up for decreased vitamin D due to lack of exposure to sunlight. Dairy as a food source also spread from the Middle East into Eastern Europe and Asia. Here, the gene of persistence of lactase was less common, but man developed a system to decrease the lactose by fermenting milk to make yogurts and cheeses.[2]

THE POTATO FAMINE

The results of agriculture have not always been beneficial. The potato was first domesticated 7000 years ago in the Andes, where thousands of varieties are still grown.[4] Potatoes were introduced to Europe after the Spanish conquest of South America in the 1500s. After an initial slow start in Europe, it became a staple food and is estimated to be responsible for 25% of the European population growth between 1700 and 1900. The limited varieties of potatoes grown in Europe created a setup for disease. The Great Irish Potato Famine began in 1845 when a fungus, *Phytophthora infestans,* caused potato harvest failure.[5] In Ireland, where a third of the population was entirely dependent on potatoes for food, over a million people died and a million emigrated.[6] This diaspora forever changed the history of Ireland, Great Britain, and the United States. In Ireland, so great was the suffering and death that the famine has entered in the folk psyche of the people. It triggered the growth of Irish nationalism and soured the Irish–English relationship. It furthered the split between the Catholic and Protestant islanders. Great Britain is still dealing with the aftermath of the famine and the sense among the Irish that they were abandoned. In the United States, one need only look at surnames on the ballot in any election to verify to what extent the Irish have entered into our national heritage.

THE DUST BOWL

The Great Plains were originally known as the "Great American Desert," because this region received an average of less than 10 inches of precipitation a year and was considered unacceptable for agriculture. However, a combination of huge pressure to settle in the West and a string

of unusually wet years induced farmers, mostly immigrants, into this area.[7] Poor farming techniques such as deep plowing of virgin top soil, no cover crops, no crop rotation, and lack of wind breaks created a few very profitable years followed by a collapse of the agriculture when the wet years gave way to more normal rainfall. The result was soil erosion on a vast scale leading to huge dust storms called “black rollers.”Dust from the Great Plains reached East Coast cities. Hundreds of thousands of people were displaced. Hunger became so severe that tumble weed (an invasive species inadvertently introduced from the Ukrainian steppes) was used for feeding cattle and even for human consumption.[7]

THE GREEN REVOLUTION

The green revolution refers to the widespread application of modern farming techniques, improved seeds, fertilizers, and pesticides, to areas where traditional, small-scale farming was practiced. This movement began in the 1940s in Mexico, but became vitally important in the 1960s in India. In 1961, India faced a huge food shortage. The prospect of massive food shortages and famine frightened the Indian government and the world. The Indian government adopted the green revolution methods, in particular, use of a variety of rice developed at the International Rice Research Institute along with fertilizers and pesticides. Yields were up to 10 times that of traditionally grown rice crops. Some say that over a billion people, worldwide, have been saved from starvation because of the green revolution.[8] Green revolution techniques have gained widespread use. Famine, suffering, and death have been avoided. But the green revolution is not without its critics. The green revolution is heavily dependent on herbicides, pesticides, fertilizers, and monoculture. Hence, reliance on petrochemical products necessarily increased. While the crop yield dramatically increased so did the energy input needed to produce crops. In addition, the world population continues to increase, leading some to propose the Malthusian argument that we have merely postponed starvation and famine that will surely come. The green revolution has led to widespread deforestation and dramatic loss of biodiversity. So the verdict on the green revolution is not yet in.[9]

GENETICALLY MODIFIED FOODS

Genetically modified (GM) foods have been genetically engineered via DNA modification. Currently, there are many examples of GM foods on

the market. There is a general consensus that GM foods do not add risk to the consumer. The DNA of GM foods is largely broken down and inactivated in the gastrointestinal (GI) tract. To date, there have been no reports of allergy induced by conformational changes within the structure of GM foods. Likewise, there have been no reports of toxicity. However, there are concerns. Could GM crops become locally invasive? The evidence is against this as almost always the GM crop is less "fit" than its non-GM counterpart, so although it can escape the field, it rarely survives in the wild. To date, the major aim of developing a GM crop is to increase the yield. Examples of this are Bt. In this case, a gene from the bacteria, *Bacillus thuringiensis*, is introduced into the plant genome. This gene codes for a toxin that attacks the Lepidoptera larvae, allowing for naturally occurring bacteria to infect and kill the larva. In the case of corn, the initial target was the European Corn Borer.[10] Since first introduced, Bt crops have been further modified to include other insect pests. The modified varieties have become significantly more sophisticated than the original Bt varieties. Another aim of GM technology has been to improve the quality of the crop. An example of this is "golden rice," a variety of rice genetically modified to contain beta-carotene and thus serves as a tool to fight vitamin A deficiency.[11] As with the Green revolution, there has been substantial opposition to genetically altering the food chain. The opposition mainly centers around fears of unintended environmental consequences and fear that a few large multinational corporation will control all access to seeds.

FOOD USED FOR GOOD AND EVIL

In writing about Ethiopian refugees in 1986, Nevin Scrimshaw wrote: "In Ethiopia today as in Biafra in 1969 and frequently throughout history, enforced hunger has been a weapon to crush political resistance."[12] A US policy of using food as political weapon could not have been more clearly stated than it was by Henry Kissinger in a memo written in 1974, where he stated that food aid could be withheld from third world countries that did not implement birth control as demanded by the US government.[13] Recently, we have witnessed an example of food as a political weapon when the Obama administration stopped food shipments to North Korea in response to the launch of a missile into space by North Korea.[14] One can argue the propriety of such a use of food; one can question the effectiveness in achieving the desired results, but it is clear that food is a weapon in world politics.

Food is also a means to achieve laudable ends. Treating vitamin A deficiency with “golden rice” is a desirable goal. Fortifying fish sauce with iron in Vietnam has greatly reduced the prevalence of iron-deficiency anemia.[15] Salt in the United States has been fortified with iodine since 1924. Adding iodine to salt virtually eliminated goiter resulting from iodine deficiency in the United States.[16] The addition of folate to wheat has reduced the occurrence of neural tube defects.[17]

The wide distribution and relative lack of safety measures (most of the regulations are adhered to and monitored by the producer and thus largely voluntary) in our food supply have opened the way to accidental contamination, but also to allow an opening to those who would like to harm large numbers of people. A challenge for the future is to devise safety measure that will ensure that health-promoting, uncontaminated food is delivered from the point of origin to the table.

FOOD BECOMES A SCIENCE

As discussed earlier, knowledge of food and how it relates to mammalian health was accumulating throughout history and was a driving force for health and development. However, nutritional sciences as currently understood probably began with the advances made during the mid-18th century in France.[18] Studies conducted during this time focused on understanding macronutrients and how they were incorporated into human tissue, that is, how ingested plant or animal products, or air, as it was known to contain nitrogen, were transformed into body parts. The first observations that dietary carbohydrate could be converted to fat were made, and it was established that animals generated heat and that this heat could be quantified. During the early 1900s, proteins were observed to hydrolyze into amino acids and short-order proteolytic enzymes were discovered, setting the stage for understanding the essentiality of specific amino acids.

Atwater, known as the father of nutritional sciences, initially focused on protein nutrition and also built the first calorimeter and was able to show that the heat produced by an individual is the same as that produced by the combustion of the same quantities of nutrients. He also established the estimates of metabolizable energy from protein, carbohydrate, and fat in mixed diets as 4, 4, and 9 kcal/g, respectively. These values retain their validity today.

For several decades, the focus of nutritional sciences was on the requirements for protein and energy, how they were related, and how

disease or trauma would alter them.[19,20] The essentiality of specific nutrients and deficiency states caused due to their absence from the diet were established. The list of essential nutrients is long, but vitamins, minerals, lipids, and specific amino acids were identified and synthesized. Products were developed that could be consumed to prevent or treat deficiency states.

During the late 20th century, the life-saving option of parenteral nutrition, delivery of nutrients that bypassed an absent or nonfunctional GI tract to sustain life and promote growth and development, was discovered and used clinically.[21–23] However, as the dangers of this option became apparent and the importance of directly nourishing the GI epithelial cells was discovered, parenteral nutrition as a common therapy for moderately ill patients or as a preparation for surgery in patients with an intact GI tract lost favor. Currently, parenteral nutrition is used only when the GI tract cannot deliver the required nutrition. Technical strides permitted the development of appliances, formulas, and experience, so enteral nutrition became the preferred route to deliver nutrients, even when the GI tract was compromised, to support ill children and promote health. The enteral route of nutrition support acknowledged the importance of the GI tract as a modulator of nutrition and immune function. Most recently, the complicated and dynamic interaction of nutrients, metabolism, and the GI microbiome has received attention.[24,25]

CHANGING VIEW OF NUTRIENTS

As these concepts were incorporated into the practice of nutrition, additional observations suggested that diets could provide therapeutic options and nutrients might play a role in treating disease. For example, the relative content of dietary fat and carbohydrate can have a desirable effect on the respiratory quotient and assist those with pulmonary disease.[26,27] Some nutrients, specifically, omega-3 polyunsaturated fatty acids, nucleotides, vitamin D, and specific amino acids singly or in combination have been shown to modulate the immune system within defined disease states or specific situations.[18,28–34] This has led to the concept of nutrients as pharmacological agents. Indeed, enteral nutrition support can have a positive effect on the induction and maintenance of remission in inflammatory bowel disease; however, no specific nutrient or combination of nutrients that can treat inflammatory bowel disease has been identified. To date, except for deficiency states, no single nutrient has withstood the scrutiny demanded of pharmaceutical agents to demonstrate

the efficacy for treatment of a specific condition or disease.

OVERNUTRITION

Although nutrition prescribed "correctly" can have a positive effect on health, it can also cause harm. Recent observations have brought to light the concept of overnutrition as a disease state.

According to the Centers for Disease Control, overweight and obesity are labels for ranges of weight that are greater than what is generally considered healthy for a given height. The terms also identify ranges of weight that have been shown to increase the likelihood of certain diseases and other health problems.

Growth charts for children and adolescents aged 2–19 years are used to determine the body mass index (BMI), weight/height^2, for age and sex percentile. Overweight is defined as a BMI at or above the 85th percentile and lower than the 95th percentile for children of the same age and sex.[35] Obesity is defined as a BMI at or above the 95th percentile for children of the same age and sex.[35]

The concern for obese and overweight children and the focus of resources on this disease state by health and government agencies developed because of observations that childhood obesity is associated with risk factors for chronic diseases that include cardiovascular disease, insulin resistance and type 2 diabetes, sleep apnea, fatty liver disease, joint and musculoskeletal problems, and a greater risk of social and psychological problems than nonobese children. These observations are magnified by the fact that obese children are likely to become obese adults and adult obesity is associated with serious, chronic health conditions.[36]

OVERVIEW OF THIS BOOK

The next chapters in this book address the current body of knowledge in nutrition for children. The basic biochemistry and metabolism of the science of nutrition is presented in a manner that makes this information clinically useful. Specifically, the book addresses nutritional strategies to support the sickest of children, to provide for normal growth and development for normal infants and children and those born with metabolic errors, to prevent diseases, both in childhood and later in adulthood, and to support normal growth and development for children who have specific disease states. The knowledge contained in this volume will be directly applicable to the practice of medicine to the primary care

physician, those who work in intensive care units and serve nutrition support services.

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Clinical Assessment of Nutritional Status

2

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The clinical assessment of nutritional status is an integral part of patient care because nutritional status affects the body's response to illness. Attention to this is especially important in pediatric patients because the nutritional requirements to support normal growth and maturation are combined with those of coexisting medical illness. This combination creates for clinicians the unique challenge of estimating and meeting the nutritional needs of pediatric patients in the clinical setting as discussed throughout this chapter and book.

The assessment should allow for the early detection of both nutrient deficiencies and excesses. There is no single nutrition measurement that is optimal; therefore, a combination of different measures is required. Growth is an important indicator of health and nutritional status of a child and requires a growth chart for interpretation; a variety of growth charts are currently available and will be reviewed in this chapter. Each growth measurement performed needs to be accurate and obtained at age-appropriate intervals in order to identify at-risk patients or monitor a patient's clinical response to nutritional therapy.

During infancy, childhood, and adolescence, profound changes in growth and body composition occur. Therefore, clinicians must understand normal growth to recognize abnormal patterns and the nutritional changes that occur with acute and chronic disease. With the epidemic of pediatric

obesity, the proper identification of the overweight or obese patient is also important. A brief nutritional screening assessment may be used to identify patients in need of an in-depth assessment. A typical nutritional screening includes a brief medical and dietary history (including feeding ability), anthropometric measurements (e.g., weight, stature), and possibly laboratory data. A full nutritional assessment includes more detailed medical and dietary histories (including a measure of dietary intake), a complete physical examination, further anthropometric and body composition measurements, sexual and skeletal maturation, laboratory data, and the estimation of nutritional requirements. In addition to the clinician's global assessment of the child based on these objective data, his/her clinical judgment is important in determining the nutritional status.[1]

MEDICAL HISTORY

Medical history is a central component of the nutritional assessment. Past and present medical information, including the duration of the current illness, relevant symptoms, diagnostic tests and therapies (e.g., chemotherapy, radiation), and medications, is documented. Because nutritional abnormalities are often associated with certain disease states, it is essential to identify underlying medical conditions and the concomitant medication history. Medications can cause nutritional deficiencies (e.g., methotrexate as a competitive antagonist of folic acid metabolism) and drug–nutrient interactions (e.g., phenytoin and tube feedings; Table 2-1). Drug–nutrient interactions may occur between drugs (prescription and nonprescription) and foods, beverages, and dietary and vitamin/mineral supplements. Alterations in drug metabolism and absorption by food or pharmacologic interactions may be clinically significant.[2] Past medical history includes previous acute and chronic illness, hospitalizations, and surgical procedures. The history of past growth patterns (with previous growth charts, as possible), onset of puberty (for the child and other family members), and a developmental history (including feeding abilities) may also be included. Family history should include a medical history and the family's social and cultural background, especially as related to diet therapy and the use of alternative and complementary medicine. The review of systems includes oral motor function, dental development, and gastrointestinal symptoms such as vomiting, gastroesophageal reflux, diarrhea, and constipation.

TABLE 2-1 Examples of Some Common Drug–Nutrient Interactions

Drug	Nutrient
Amphotericin B	Hypokalemia, hypomagnesemia
Antacids	Vitamin D and iron deficiency, hypophosphatemia
Phenobarbital	Vitamin D deficiency
Cholestyramine	Vitamin A, D, E, and K malabsorption
Cyclosporin	Elevated triglycerides, hypokalemia, hypomagnesemia
H2 blockers	Iron deficiency
Methotrexate	Folate deficiency
Phenytoin	Folate deficiency
Corticosteroids	Hyperglycemia, hypophosphatemia
Sucralfate	Hypophosphatemia
Sulfasalazine	Folate deficiency
Trimethoprim	Folate deficiency
6-Mercaptopurine	Purine metabolism (DNA synthesis/repair)

PHYSICAL EXAMINATION

Physical examination includes anthropometrics (see later), including weight, length or stature, head circumference, and upper arm measures. The frequency of measurements of well children follows the recommendations of the American Academy of Pediatrics (AAP).[3] For the preterm infant, weight should be measured daily, and length and head circumference weekly. For newborns, weight, length, and head circumference should be measured at birth and again at 3–5 days of age. For healthy children up to 2 months of age, all three measures should be obtained monthly, then every two months from 2–6 months of age, and every 3 months from 6–24 months of age. For children aged 24–36 months, weight and length/height should be assessed every 6 months and annually thereafter. The pattern of measurement for hospitalized patients depends on the age of the patient, illness, and the degree of nutritional intervention. Nutritional assessments for patients with complex chronic disease states should be conducted every one to two months and less often in those with milder disease (every 6–12 months). The general physical examination includes an assessment of the patient's general condition and close examination of skin, hair, and teeth (see Appendix Table I-8). This includes an assessment for pallor, clinical assessment of body fat stores,

wasting of muscle mass, edema, rash, thinning of hair, and evidence of specific nutritional deficiencies. Examples of specific signs include the flag sign or the loss of hair color associated with a period of malnutrition followed by recovery with a return of normal hair color and texture. Examination of specific organ systems and obtaining medical record information is helpful in assessing the severity of the underlying disease process. It is also important to consider the clinician's clinical judgment in the assessment of nutritional status.[1] Documenting sexual development by Tanner staging (Appendix I) is a routine part of the nutritional assessment of adolescents (see later). For a summary of signs and symptoms of specific nutritional abnormalities, see Appendix Table I-8.

DIETARY HISTORY

The dietary history is an essential component of the nutritional assessment. The dietary history provides information not only on the amount and quality of the food consumed but also on the eating patterns and behaviors of the family. This part of the nutritional assessment should detail the number of meals, snacks, and beverages consumed; special foods eaten by the child and family; vitamin and mineral supplements ingested regularly; food allergies; intolerances; and unusual feeding behaviors. The child and family are asked about psychosocial factors that impact on food selection and intake, including family history, socioeconomic status, and use of the Special Supplemental Nutrition Program for Women, Infants, and Children and supplemental food programs, parent/caretaker's perception of the child's nutritional status, and religious and cultural considerations. Food-related factors may affect dietary intake and include food allergies, intolerances, self-imposed and prescribed diets, and feeding skills. These factors are also noted in the assessment.

The assessment of dietary intake of breastfed infants is more difficult because the volume of milk consumed cannot be directly measured. An estimate is obtained by weighing the infant before and after feeds and using a conversion factor of 1 mL volume of breast milk consumed for each gram of weight gained. In formula-fed infants, the clinician should inquire about both the amount and type of formula consumed and the details of the method of preparation (concentrates, powders, modular additives).

The quantity and quality of dietary intake are assessed by prospective food records (with weighed or estimated food portions), retrospective 24-hour recalls (previous 24 hours or of a "typical" 24-hour period), or food

frequency questionnaires.[3] The prospective food records are usually carried out for three to seven days (including a combination of weekend and weekdays) and provide the most accurate assessment of actual intake. However, food records are used most often in the research setting because they are labor intensive and time consuming. As available, these records are analyzed and compared to the dietary reference intakes (DRIs) (see later) using a computerized nutrient analysis program. A limitation of food records is that parents tend to forget to record all foods eaten or modify feeding practices to be more healthy, which may lead to incorrect estimates of intake.[4] The retrospective 24-hour diet recall provides a quicker assessment of dietary intake. For a 24-hour recall, the child/parent is asked to recall what and how much the child ate and drank over the past 24 hours. Recall accuracy depends on the child/parent's memory and their ability to estimate portion sizes. Also, because this is only one day of intake, it may not be representative of the usual intake. When the child's intake is affected by acute illness, a 24-hour recall of a "typical day" is more useful to estimate usual intake. The 24-hour recall tends to underestimate usual energy intake yet may overreport the intake of infants and toddlers.[5]

Another way of assessing dietary intake is the food frequency questionnaire method. These questionnaires collect information on both the frequency and the amount consumed of specific foods and are useful in the clinical setting to identify usual eating patterns. A limitation of the food frequency questionnaires is that the amounts of food and thus intake of energy and some nutrients are often overreported.[5] All of these methods of dietary assessment are somewhat limited owing to gaps in the nutrient databases, which lack information about bioavailability, presence of inhibitors and enhancers of absorption, and nutrient availability of specific nutrients of interest.[6]

The most commonly used method of dietary assessment in hospitalized patients is the calorie count. This is a variation of the prospective food records as the amount of food consumed from a known quantity of food (as specified by a menu or list) is recorded. The accuracy of the calorie count assessments is limited by the number of individuals required for the completion of these forms throughout a 24-hour period (e.g., the dietitian, the nurse for each shift, the child's family, the child). However, calorie counts are a useful part of nutritional assessment follow-up because these provide a rough assessment of the patient's appetite, intake, and compliance with nutrition recommendations.

ANTHROPOMETRICS AND BODY COMPOSITION

At a minimum, nutritional assessment of a child includes a measured weight, length or height, and head circumference (birth to 3 years of age), and these measurements are followed up over time to assess short- and long-term growth and nutritional status. For children with chronic disease, a mid-upper arm circumference (MUAC) and triceps skinfold (TSF) thickness are also part of the assessment to determine body fat and protein stores. In addition, a dual energy x-ray absorptiometry (DXA) scan may be added to more thoroughly assess body composition (percent fat, lean body, and fat mass) and bone mineral density (BMD) (see Chapter 4).

Accurate and reliable anthropometric and body composition measurements require proper equipment and techniques. Training and practice in anthropometric technique cannot be overemphasized. For all growth measures, three independent measures should be obtained. The current convention is to use the average of three measurements. The clinician's assessment for a child depends on the quality of these data. Equipment requirements for each measure are discussed below.

Weight

Weight is a measure of overall nutritional status. Optimal interpretation requires additional information regarding the age, sex, and height/length of the child. Weight is determined using a digital or beam balance scale. Until the child is approximately 24 months or can cooperate and stand independently, a pan version of the scale is used. Weight should be measured in light or no clothing and without a diaper for infants. It is important that the scale is zeroed prior to each measurement and is calibrated using known weights at least monthly or on movement of the scale.[3] Weights are recorded to the nearest 0.01 kg in infants and 0.1 kg in older children.

Stature: Length or Height

A measure of stature is important for monitoring long-term nutritional status. Recumbent length is measured using a length board for children from birth to 2 years. The measurement of length requires two individuals. The first person positions the infant straight on the board so that the infant's head is against the headboard and positioned with the Frankfort plane parallel to the headboard.[3] The Frankfort plane is the alignment from the lower margin of the orbit to the upper margin of the auditory meatus as

shown in Figure 2-1. The second person extends the infant's legs with the knees flattened and adjusts the moveable footboard such that the heels lie flat against the movable footboard.[3] For children aged 2 years and older who are able to stand independently and cooperate, height is measured using a stadiometer, with a moveable headboard at a fixed 90-degree angle to the back of the stadiometer. The child is measured barefoot or in thin socks and in minimal clothing to allow the observer to check for correct positioning. For the measurement, the child stands erect, with feet close together, heels, buttocks, and back of head touching the stadiometer, and looking ahead with the Frankfort plane parallel to the floor.[3] Asking the child to inhale deeply just prior to obtaining the measurement assists in attaining fully erect posture. Because length overestimates the height by 0.7 cm,[7] it is essential to record the method of measurement during the transition from recumbent length to standing height. The change to standing height is also accompanied by the transition to pediatric (2–18 years) growth charts (see later). Both length and height measurements are recorded to the nearest 0.1 cm.

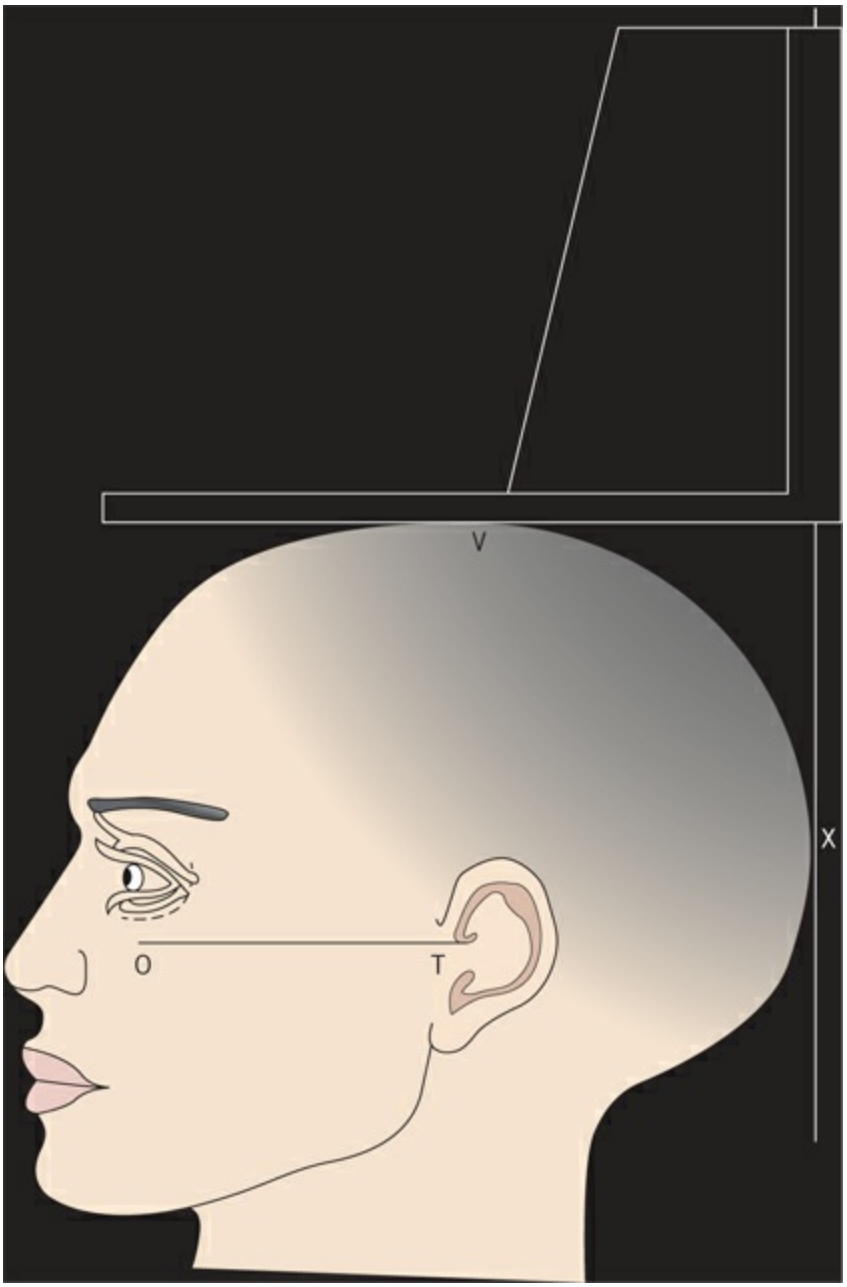

Figure 2-1 The Frankfort plane is the horizontal line extending from the auditory meatus (T) to the lower margin of the orbit (O). Reprinted with permission from Anthropometry Illustrated, Roww WD, Carr RV, and Carter JEL, Turnpike Electronic Publications, Inc.

Among children for whom the stature measurements are not possible owing to physical constraints (e.g., contractures, nonambulatory), alternative measures are available. Upper arm and lower leg lengths provide reliable and valid indexes of stature in children.[8,9] These

measurements are conducted using sliding calipers. All measurements are recorded to the nearest 0.1 cm.

The shoulder to elbow length is used for the upper arm measurement in infants and young children (birth to 24 months).[8,9] This measurement is obtained with the arm bent to a 90-degree angle, and the measurement is taken from the superior lateral surface of the acromion to the inferior surface of the elbow. For older children (2–18 years), the arm should hang in a relaxed position at the side, and the distance between the superior lateral surface of the acromion and the proximal tip of the radius is measured. The lower leg length is measured as the knee-to-heel length for infants and young children (0–24 months) and as a tibia length in older children (2–18 years). For infants and young children, the superior surface of the knee to the heel is measured while the leg is bent at a right angle at the hip, knee, and ankle. In older children, the tibia length is measured from the proximal medial border of the tibia plateau to the medial malleolus; ideally, the leg being measured is crossed over the opposite knee.[3] Alternatively, knee-to-heel length can be measured in older children and used to predict stature.[10,11] The right-side extremity should be measured for these alternative stature estimates.[3] If there are asymmetric extremity abnormalities, the measurement should be taken on the least affected side and the side of measurement noted in the chart.

Head Circumference

Head growth, primarily owing to brain development, is most rapid during the first 3 years of life. Routine measurement of head circumference (the frontal occipital circumference) is a component of the nutritional assessment in children up to age 3 and longer in children who are at high nutritional risk. Head circumference is a less-sensitive indicator of short-term nutritional status than weight and height because brain growth is generally preserved in cases of nutritional stress. Head circumference is not a helpful nutritional status measure in children with hydrocephalus, microcephaly, or macrocephaly.

Head circumference is measured using a flexible, nonstretch tape measure. The circumference should be taken at the maximum distance around the head, which is found by placing the measuring tape above the supraorbital ridge and extending around the occiput.[3] Care should be taken to keep the tape measure flat against the head and parallel on both sides. The measurements should be recorded to the nearest 0.1 cm.

GROWTH CHARTS AND TABLES

Serial measurements are essential for the optimal assessment of short- and long-term growth and nutritional status. A number of growth charts and tables are available for the comparison of weight, stature, and head circumference with reference populations by age and sex. Weight is also assessed relative to a child's stature using growth charts that evaluate weight for length/height, weight/height[2] (body mass index [BMI]) for age, or weight/length[3] (ponderal index) for age; these measures assess "relative weight" or weight independent of stature. The types of charts and tables available for clinical assessment in infants and children are reviewed. Several of these charts are included in Appendix I.

Premature Infant Growth Charts

Several types of charts are available for growth assessment of premature infants in the neonatal intensive care unit (NICU). Intrauterine growth charts[12–15] are preferred over postnatal growth charts[16–19] as the pattern and rate of normal intrauterine growth are the standard for growth of premature infants.[20] Postnatal growth charts are based on actual, not ideal, growth of premature infants over time so that these can serve as a useful adjunct curve in a nutritional assessment. Growth measurements are plotted using corrected gestational age of 12–36 months, depending on the child's size and growth.

The three most widely used intrauterine growth charts in US NICUs include the Lubchenco,[12,13] Fenton,[15] and Olsen[14] charts. All include weight-, length-, and head circumference-for-age curves. The newest and first gender-specific set of charts from Olsen et al.[14] are becoming a clinical standard of care as these were based on more recent data (1998–2006) and a large sample of birth data that represents the racial distribution of US births. The Fenton unisex growth charts[15] have a popular "hybrid" curve presentation that joined intrauterine data with postnatal data and span from 22–50 weeks gestational age. However, the intrauterine portions of these curves were created from mixed sources of non-US data: Canadian data[21] were used for weight-for-age, and a combination of Swedish data[22] and Australian data[23] were used for the length- and head circumference-for-age curves. The postnatal portion of the Fenton curves used the Centers for Disease Control and Prevention (CDC) 2000 data[24] and later the World Health Organization (WHO) data.[25] Finally, the Lubchenco growth charts,[12,13] while historically a NICU standard of care,

are now less representative of the growth of infants in the US NICUs. However, this set of charts has the advantage of including a measure of relative weight (ponderal index-for-age) that may be helpful in the growth assessment of premature infants (see "Weight-for-Length/Height" section).

The Olsen curves define new cutoffs for the classification of infants as small-for-gestational age (or <10th percentile) or large-for-gestational age (>90th percentile), and the cutoffs vary from existing curves used in NICUs. For example, the Olsen curves tend to have a lower average size than the Lubchenco curves at younger gestational ages and a higher average size at the older gestational ages; differences from the Fenton curves vary based on age, gender, and growth measurement.[14] The relationship between these newly defined high-risk groups and health outcomes is under investigation.

Once a preterm infant reaches 40 weeks corrected gestational age, their growth should be monitored on the WHO growth charts[25] until 2 years of age and then switched to the CDC 2000 growth charts[24] for 2–20 years of age as recommended by the CDC for infants born at full term. Former premature infants are plotted on these charts based on their corrected gestational age (as mentioned earlier). Although all premature infants may not achieve "good" placement on these growth charts, these charts provide an appropriate goal for growth. Also available as adjunct assessment tools are two series of postnatal growth charts: the Infant Health and Development Program charts for low-birth-weight (LBW, 1501–2500 g) and very low-birth-weight (VLBW, <1500 g) premature infants for boys[16,17] and girls[18,19] and the National Institute of Child Health and Human Development Neonatal Research Network Growth Observational Study[26] projected growth charts and tables for VLBW infants (available online at http://neonatal.rti.org). These charts provide a comparison of how a LBW or VLBW premature infant grows relative to two reference populations of similar infants. Although these postnatal growth charts are based on older data, more recent charts do not exist. As noted earlier, postnatal charts represent actual, not ideal, patterns of growth for former premature infants and may be used in conjunction with but not in place of the WHO growth charts.

CDC, NCHS, and WHO Growth Charts

2000 CDC Growth Charts

In 2000, the CDC and National Center for Health Statistics (NCHS) released an updated set of growth charts called the CDC growth charts (see

Appendix I, Figures I-9 to I-18).[24] These charts are available for boys and girls aged 0–36 months for weight, length, and head circumference by age and weight for length, and aged 2–20 years for weight, height, and BMI for age and weight for height. Further details on the CDC growth charts, including data exclusions, are reviewed in the 2000 CDC report.[24] The CDC growth charts are available on the Internet (www.cdc.gov/growthcharts).

2006 WHO Growth Charts

The WHO undertook the multicenter growth reference study to generate international growth reference standards based on a large healthy sample of infants and children. Data were gathered from Brazil, Ghana, India, Norway, Oman, and the United States. The sample was selected to reflect healthy children living under conditions (breastfed, nonsmoking environments) favorable for fully achieving growth according to their growth potential. The data combined a longitudinal follow-up from birth to 24 months as well as a cross-sectional survey of the children between birth and 71 months. The growth standards derived are prescriptive rather than descriptive; that is, they represent how children should grow as opposed to how they grew at a particular time and place, thereby underscoring that the new growth charts are consistent with growth outcomes occurring under the best health practices. The 2006 WHO reference standards include weight for age, length/height for age, weight for length/height, and BMI by age for children from birth to 60 months.[3] The CDC recommends the use of these charts to monitor the growth of infants and children (breast and bottle, or infant formula fed), birth to 2 years of age, and the use of the CDC 2000 growth charts for children aged 2–20 years.[27]

When comparing the 2000 CDC growth charts to the 2006 WHO growth charts, several differences are notable. The CDC growth charts used a population-based sample that included all children regardless of health status or feeding mode. On average, the CDC sample was heavier and shorter children than that of the WHO growth study. For this reason, the 5th–95th percentile is considered as the normal range. In contrast, the WHO growth charts are based upon a healthy population of breastfed infants, and two standard deviations above and below the median is considered as the normal range. Generally, the recommended cutoffs for these two respective growth charts, the WHO (two standard deviations from the mean for age, or the 2.3rd percentile) and CDC cutoff values (5th and 95th percentiles), are fairly similar when screening for shortness and overweight in the first two years of life,[28] although some age-specific

differences occur. For example, the use of the WHO growth charts results in a higher prevalence of underweight during the first 6 months of life and a lower prevalence thereafter.[29] Another difference between the charts is that the WHO weight for length curves span from 45 to 110 cm, whereas the CDC weight for length curves span from 45 to 103 cm. The extended range for length in the WHO weight for length curves facilitates the assessment of tall children who are unable to stand (for whatever reason). As a consequence of these differences in study design, selection of the sample, and resulting growth curves, slightly fewer US children will be identified as underweight using the WHO charts, and the slower growth among breastfed infants during ages 3–18 months will appear within the normal range. Finally, gaining weight more rapidly than indicated on the WHO charts might signal early development of overweight.[27]

In summary, there are age-specific differences in the WHO and CDC growth charts owing to differences in the study design and the samples used to generate the reference ranges.[29] Accordingly, the cutoffs used to identify children at risk of nutritional complications are different for these two sets of growth charts. The WHO charts are recommended for growth assessment up to the age of 2 years, and the CDC 2000 charts are recommended for children aged 2–20 years. These growth curves are included in Appendix I and Figures I-1–I-18.

Incremental Growth Velocity

Reference data are also available for incremental growth velocity for boys and girls for weight, stature, and head circumference from 0 to 18 years (see Appendix I and Tables I-4 and I-5).[30–35] These data are presented according to the time interval between measurements (1, 3, or 6 months) and are used to evaluate growth velocity percentile (3rd–97th or 5th–95th percentiles). New incremental growth standards for breastfed infants from the WHO are available for weight, length, and head circumference.[35] These detailed tables offer weight increments (grams) and velocity (grams per day) by birth weight group for the first 60 days of life, weight increments (grams) in 1-, 2-, 3-, 4-, and 6-month time intervals, and length (centimeters) and head circumference (centimeters) increments over 2-, 3-, 4-, and 6-month intervals up to 24 months of age. Because of the rapidly changing rate of growth during the first 2 years of life, the presentation by time intervals between measurements allows for more accurate and convenient assessment. Calculating growth velocity and comparing it to standards based on a larger or smaller measurement interval can yield

inaccurate assessment. Downloadable tables can be found at http://www.who.int/childgrowth/standards/en/.

In clinical practice, the incremental tables for weight, length, and head circumference[30,33–34] are helpful in the assessment of former premature infants and other children with growth failure from any cause. The growth increments are easily divided into daily, weekly, or monthly weight gain goals. Assessment of incremental growth is more sensitive in detecting growth faltering or catch-up growth than the use of growth charts that assess static growth status at one point in time based on cross-sectional data. However, incremental growth measurements are extremely sensitive to measurement error, so attention to measurement technique is required.

Growth charts for the assessment of height and height velocity in relation to the stage of sexual maturity based on US reference data are also available (see Appendix I and Figures I-23 and I-24).[36] These charts provide height growth for early, middle, and late maturers by sex and age at which peak height velocity was reached and explain some of the variation in growth related to different stages of puberty. The height velocity charts are often used in the care of children with poor growth and chronic illnesses.

Special Growth Charts

Although the WHO and CDC growth charts are recommended for the growth and nutritional assessment of all children, a number of disease-specific charts have been published (e.g., achondroplasia, Brachmann-de Lange syndrome, cerebral palsy, Down syndrome, Marfan syndrome, myelomeningocele, Noonan's syndrome, Prader–Willi syndrome, sickle cell disease, Silver–Russell syndrome, Turner's syndrome, Williams syndrome; see Appendix I and Table I-7). The weight-for-age and height-for-age growth charts for boys and girls with Down syndrome of ages 0–36 months and 2–18 years were published in the 1980s.[37,38] However, due to improvements in care of children with Down syndrome, these charts no longer represent the growth of contemporary children. Until new growth charts become available, the AAP recommends using the growth charts for typical children to monitor growth in children with Down syndrome.[39] Many other disease- or syndrome-specific growth charts are based on small samples of children and include children with suboptimal nutritional status. Disease-specific charts may be helpful to use in conjunction with the WHO or CDC growth charts for comparison to "peers."

A set of growth charts is also available for the assessment of alternate

stature measures,[8,9] including upper arm length (infants, 0–24 months; girls, 3–16 years; boys 3–18 years) and lower leg length (infants, 0–24 months; girls, 3–16 years; boys, 3–18 years). Similar to other measures of stature, these linear growth measures are used along with weight to help determine a child's nutritional status.

ASSESSMENT OF ANTHROPOMETRICS

Nutritional status indices are essential for the clinical interpretation of growth measurements. Every nutritional assessment requires one or more of the following indices for interpretation.

Percentiles for Age and Sex

When each growth measure is plotted on a growth chart, a percentile or rank of the individual compared to the reference population is determined. For example, the 25th percentile weight for age means that the individual weighs the same or more than 25% of the reference population of the same age and sex, and the 75th percentile weight for age means that the individual weighs the same or more than 75% of the reference population of the same age and sex.[40] Percentiles are easily interpreted and used clinically. Available growth charts provide reference growth of children ranging from the 5th to 95th percentiles or the 3rd to 97th percentiles, depending on the chart. In clinical practice, the WHO and CDC recommended cutoffs should be used for screening and follow-up of healthy children. Weight-for-age and height-for-age percentiles are also used to screen for malnutrition using published classifications (see Appendix I and Table I-6). BMI percentiles are used to identify patients at risk for under- or overnutrition; however, the Waterlow criteria are still used by many practitioners. Height-for-age is an indicator of long-term nutritional status, with low height-for-age reflecting stunting. Height-for-age is generally interpreted as short (<5th percentile), normal (5th–95th percentile), and tall (>95th percentile) for children aged 2–20.

Genetic Growth Potential: Midparental Height

In the assessment of a child's stature, it is helpful to estimate the genetic potential for stature as determined by the biologic parents' adult height.[41] This is important to distinguish whether the child is achieving their genetic potential for growth based on family genetic background or whether disease and/or poor nutrition might be affecting their growth. An

adjustment for parental height is used for a child's length (0–36 months) or height (3–18 years) and is based on the mean of the height of both biological parents. This allows adjustments to the child's stature for tall or short parents. The corrections are based on the Fels Institute and older NCHS data.[42] Parental height adjustment is appropriate for use with most of the parents and children in the United States; however, it should not be used when the parents do not meet their genetic potential for height (e.g., in situations of poor health and/or nutritional status during the parental childhood or adolescence).[41]

Weight for Length/Height

Weight relative to length/height provides information on growth and nutritional status that is different from weight-for-age or length/height-for-age alone; it helps to determine and classify nutritional status in the individual patient.[43] Although there is no routinely used measure of relative weight in preterm infants, there is evidence to suggest that there should be.[44] For children aged 0–2 years, the CDC recommends that weight-for-height is assessed by determining a percentile on the WHO growth charts.[25] Weight-for-height is generally interpreted as underweight (<5th percentile using the CDC charts; <3rd percentile using the WHO charts), within normal variation (5th–95th percentile using the CDC charts; 3rd–97th percentile using the WHO charts), and overweight (>95th percentile using the CDC charts; >97th percentile using the WHO charts) and is used in screening healthy children. Weight-for-height measures are also used for screening classification of protein–calorie malnutrition (see Appendix I and Table I-6).

BMI is another measure of weight relative to height. The CDC growth charts provide BMI for age and sex from age 2 to 20 years[24,45] and is the recommended assessment tool for children aged 2 years and older. The WHO growth charts also include infant BMI graphs; however, these are not widely used; the WHO BMI-for-age curves range from birth to 2 years of age and 2–5 years of age. Because both weight and height in children change over time, there is no fixed BMI value for the diagnosis of obesity in children as there is for adults (e.g., BMI ≥ 30). The BMI percentile for age must be used for interpretation. In the United States, the 85th and 95th BMI percentiles for age and sex are used to define "overweight" and "obesity" in children.[3] A comparison of BMI-for-age and weight-for-height to predict underweight and overweight in children and adolescents (2–19 years) showed good agreement, especially in young children (2–5

years of age), but BMI had the greatest sensitivity to detect overweight and obesity across the entire age range.[46] From the International Obesity Task Force, cutoff points for BMI to define overweight and obesity in children based on cross-sectional growth studies from six countries (Brazil, Great Britain, Hong Kong, the Netherlands, Singapore, the United States) are also available.[47]

Differences in BMI at the lower percentiles of the reference range largely reflect lean mass, whereas at upper percentiles of BMI, differences are largely due to fat mass.[48] BMI is not a perfect measure of adiposity, since height is not fully independent of weight in children. Stature has been postulated to affect BMI, and in populations with taller stature, BMI may overestimate the prevalence of obesity.[49] One study comparing techniques to evaluate adiposity (BMI, isotopic dilution, skinfold equations) in stunted and nonstunted children concluded that BMI predicted percent body fat in both groups of children.[50] An additional study showed that the relationship between BMI and adiposity varied across different populations.[51] BMI should be interpreted with caution in certain clinical conditions including edema, pregnancy, in individuals with a high tumor burden, and in individuals with increased lean body mass such as in well-developed athletes. BMI is a screening tool to identify children and adolescents at risk for overweight or obesity, and further assessments to determine adiposity should be considered as clinically indicated.

Percent Ideal Body Weight

Historically, percent of ideal body weight (IBW) was used to classify the degree of over- or undernutrition into clinical classification: >120% IBW as obese; 110%–120% IBW as overweight; 90%–110% IBW as normal range; 80%–90% IBW as mild wasting; 70%–80% IBW as moderate wasting; and <70% IBW as severe wasting. IBW is also used as a clinical weight goal in the nutritional rehabilitation of a child.

Percent IBW should be used with caution. A recent study[52] compared the use of BMI percentiles and percent IBW to screen for malnutrition in children with cystic fibrosis using data from the cystic fibrosis patient registry. Among children with stature between 25th and 75th percentiles, both percent IBW and BMI yielded similar estimates of ideal weights, and in the classification of malnutrition. However, compared with the BMI, percent IBW underestimated the severity of malnutrition in children with short stature (height <25th percentile), whereas the opposite trend was

found for the subjects with tall stature (height >75th percentile). These findings support the use of BMI in lieu of percent IBW for the classification of pediatric malnutrition, especially for children aged 2 years and older. Currently, BMI charts are preferred in the classification of overweight and obesity. The use of the BMI charts for classification of degrees undernutrition is not as well established. The WHO uses weight-for-height cutoffs of <–2SD for moderate undernutrition and <–3SD for severe undernutrition[53] and has proved to be an effective screen for identifying children at risk of nutrition-related morbidity and mortality.[54]

Percent Weight Loss

The percent of usual body weight loss is an important clinical indicator of nutritional status and nutritional risk. Percent weight loss is calculated as [(previous weight – current weight)/previous weight × 100]. A 5% or greater weight loss in one month may be considered an indicator of nutritional risk in children. However, it is important to also look at the absolute weight loss as opposed to the percent weight loss alone, as this may be additionally informative and clinically meaningful. For obese children, change in BMI is recommended for monitoring weight management.[55]

Growth Velocity

Growth velocity (change in the growth parameter over time) is useful to detect a change in nutritional status and to monitor the effectiveness of nutritional and medical therapy. As discussed earlier, age- and sex-specific charts and tables are available for the evaluation of weight, stature, and head circumference growth over time.[7,30–34,36]

Body Composition

In children with many acute and chronic diseases, the nutritional assessment requires measurement of body composition (body fat and protein stores) in addition to weight, stature, and head circumference (see Chapter 4) for a detailed discussion of this topic). The measures described below also are useful to perform in critically ill children for whom weight and length/height measurements cannot be performed easily, and in those conditions with significant fluid shifts and fluid retention.

Mid-Upper Arm Circumference

MUAC can be used as a measurement of growth, an index of energy and

protein stores and can provide information on fat patterning.[3] The measurement is taken at the midpoint of the upper arm, located halfway between the lateral tip of the acromion and the olecranon when the arm is flexed at a 90-degree angle (measured and marked). For the MUAC measurement, the child should be upright with the arm relaxed by the side. A flexible, nonstretchable measuring tape is placed perpendicular to the long axis of the arm. The measuring tape should encircle the arm without compressing the soft tissue, and MUAC should be recorded to the nearest 0.1 cm.[3] This measurement should be taken in triplicate and used as an average.

Triceps Skinfold Thickness

The TSF thickness is an indicator of subcutaneous fat (energy) stores and total body fat and provides information on fat patterning.[3] For the TSF measurement, the child should be upright with the arm relaxed at the side. The TSF thickness is measured at the midpoint of the upper arm (defined earlier) over the center of the triceps muscle on the back of the arm (measured and marked beforehand). The anthropometrist lifts the skinfold with the thumb and index finger, approximately 1 cm above the marked midpoint, and places the calipers at the marked point. Two to three seconds after the handles of the calipers are released, the measurement is taken and the calipers are removed. This measurement should be taken in triplicate, used as an average, and recorded to the nearest 0.1 cm.[3]

Reference data (age and sex specific) are available for the assessment of mid-upper arm circumference (MAC) and TSF thickness[56] (see Appendix I, Figures I-34, I-35, I-38, and I-39, and Tables I-1 and I-2). The MAC and TSF measurements are used to calculate upper arm muscle area and fat area.[56,57] These are clinical indicators of total body stores of muscle and fat.

$$\text{Upper arm muscle area (cm}^2\text{)} = [\text{MUAC (cm)} - (\text{TSF (cm)} \times \pi)]^2/(4 \times \pi),$$
where $\pi = 3.14$.

$$\text{Upper arm fat area (cm}^2\text{)} = \text{upper arm area (cm}^2\text{)} - \text{upper arm muscle area (cm}^2\text{)},$$
where upper arm area $(\text{cm}^2) = \text{MUAC}^2/(4 \times \pi)$.

Dual Energy X-Ray Absorptiometry

DXA is a noninvasive, rapid, indirect, low-radiation measurement that is used to assess BMD. Bone fragility is of a concern in a variety of pediatric disorders associated with altered bone mineral acquisition or increased fracture risk. A small number of pediatric disorders involve primary bone diseases, such as osteogenesis imperfecta or idiopathic juvenile osteoporosis, where the disorder directly targets bone formation. Secondary bone disorders involve diseases that affect the skeleton through other disease mechanisms such as inflammation, malabsorption, low physical activity, endocrine disturbances, hematological disorders, and poor dietary intake, or disease treatments such as glucocorticoid therapy.[58]

DXA scans can be performed on the lumbar spine, proximal and distal femur, forearm, and whole body. The recommended sites for children and adolescents are the lumbar spine and whole body; when these measurement sites are not feasible, the distal forearm and proximal femur should be considered. For older adolescents, the proximal femur may be a useful measure to obtain for long-term follow-up, since the lumbar spine and proximal femur are the preferred sites in adults.[59] DXA scans provide information on bone mineral content (BMC) in grams per centimeter or areal BMD (aBMD) in grams per square centimeter in different skeletal regions or the whole body. Although primarily used for the assessment of bone health, whole-body scans also provide body composition measures of fat-free mass, fat mass, and percent body fat.[60] Smoothed percentiles for percent body fat assessed by DXA are now available for children aged 8–19 years.[61]

As with other growth-related outcomes, BMC and aBMD values used to assess bone health must be compared with the reference data in healthy age- and sex-matched children and adolescents to interpret bone health status. The results for BMC and aBMD are expressed as a Z-score (standard deviation score), determined by the comparison of an individual child's BMC or aBMD with the reference database. A Z-score of 0 is the median (similar to the 50th percentile on a growth chart) for the reference data, with +1, +2, –1, and –2 representing plus and minus 1 and 2 standard deviations from the reference median. The International Society of Clinical Densitometry[62] defines low BMC or aBMD as a Z-score ≤ −2, adjusted for age, sex, and body size, as appropriate. Osteoporosis in children cannot be made solely on the basis of low BMC or aBMD. Osteoporosis is defined as low BMC or aBMD in the presence of a clinically significant fracture history. A "clinically significant fracture history" consists of a long bone fracture of the lower extremities, a vertebral compression fracture, or two

or more long bone fractures of the upper extremities.[62]

Recently, the ability to assess bone health in children aged 5–20 years has been improved by the availability of reference ranges based on a large multicenter, multiethnic sample in the United States from the National Institutes of Health Bone Mineral Density in Childhood Study.[63] Sex- and age-specific reference ranges are provided for African American and non-African American for BMC and aBMD of the total body, total body less head, lumbar spine, proximal femur, femoral neck, and radius. African American children and adults have higher bone density than other ethnic groups.[64,65] Age, sex, and ancestry group reference ranges for the lateral distal femur are also available[66]; this measurement is particularly helpful for children with metal implants or contractures for whom traditional measurement sites are not feasible. The use of ancestry group-specific reference ranges (African American vs. non-African American) is used as an indicator of whether a child is reaching their genetic potential for BMC or aBMD. As recommended by the International Society for Clinical Densitometry, adjustment of BMC/aBMD values for growth in children is preferred since DXA measurements are influenced by growth status. Several techniques have been proposed.[67,68] The least biased technique requires the calculation of height-for-age Z-score, and the BMC/aBMD adjustment is based on whether a child is tall for age or short for age.[69]

The advantages of the DXA are the low radiation exposure, fast scan time, and noninvasive nature. The precision of the instrument is excellent. The radiation dose is small (<1 mrem, Hologic Delphi Clinical Bone Densitometer product specifications) or less than that received during a standard airline flight across the United States.[70] A limitation of DXA in the assessment of body composition is that it provides a two-dimensional assessment of three-dimensional structures and is unable to distinguish between cortical and trabecular bone. However, it is the most widely used clinical technique for bone health assessment. The timing of initial DXA scans and frequency of follow-up measurements depends on the clinical needs, particularly the risk factors for poor bone acquisition, disease-specific patterns of bone loss, and medical therapies.[58] Patients with poor BMD measurements are rarely measured less than six months after the baseline assessment. Bone health in children and adults is altered by weight-bearing physical activity and intake/absorption of calcium and vitamin D. Other nutrients such as protein, vitamin K, magnesium, and zinc[71–73] have also been implicated in bone health.

Cortical and trabecular bone can be measured using quantitative

computed tomography (QCT). This technique describes volumetric BMD (grams per cubic centimeter) and also differentiates between cortical and trabecular bone. Specialized peripheral QCT and high-resolution peripheral QCT scanners have been developed to decrease radiation exposure for the peripheral skeleton, and the measure derived indices of bone structure and strength for the research setting.[74] Although peripheral quantitative computed tomography (pQCT) has provided insights into the nature of bone deficits in the children with chronic disease, lack of standardization of measurement sites and inadequate pediatric reference data limit the use of these techniques in clinical care.[75]

Air Displacement Plethysmography

Air displacement plethysmography method of body composition assessment is safe, noninvasive, and fast. There are two commercially available plethysmographs from Life Measurement, Inc. (Concord, CA): the BOD POD® for use in children and adults[76] and the PEA POD® for use in infants up to 6 months of age.[77,78] A pediatric option for the BOD POD now permits assessment of children aged 2–5 years.[79] The method requires the subject to sit (BOD POD) or lie (PEA POD) within a closed chamber in minimal, close fitting, or no clothing. The subject's total body volume is estimated indirectly by measuring the volume of air that he/she displaces inside an enclosed chamber.[76] This volume is used to compute body density (body mass or weight/body volume) and in turn fat mass (kilogram), fat-free mass (kilogram), and percent body fat. Overall, the BOD POD[76,79] and PEA POD[77] provide reliable and valid estimates of body composition; however, neither device is widely available in the clinical setting at this time.

Sexual and Skeletal Maturation

The tempo of growth and body composition changes are influenced by sexual/pubertal and skeletal maturation. Many factors, such as genetics and disease processes, can affect sexual and skeletal maturation. Overnutrition and undernutrition can also affect the tempo of maturation and are therefore important in the nutritional assessment of an individual patient and their growth potential. The physically immature child with likely growth delay has the potential to catch up to the size of his/her peers once maturity advances.

Sexual maturity is assessed using the Tanner staging system by the clinician physical examination[80] or as a pubertal self-assessment form

completed by the child/parent.[81–84] Pubic hair in both males and females should be assessed using the Tanner Pubic Hair stages 1–5. Breast development in girls and genital development or testes size in boys are also categorized into stage 1–5 based on the classifications of Tanner (see Appendix I and Figures I-19 to I-22).

Skeletal maturation (or bone age) is the second method for the assessment of physical maturity. Bone age is assessed by a left hand-wrist radiograph and scored using the standards developed by Greulich and Pyle[3] or the newly revised TW3 method developed by Tanner and colleagues[3] Bone age provides a measure of "how far a given individual has progressed along his or her road to full maturity"[3] regardless of chronologic age. Sexual and skeletal maturity provide a measure of physical maturity and are valuable in formulating the nutritional assessment of children and adolescents.

Laboratory Tests

Laboratory testing is a helpful but less essential part of a nutritional assessment in most children and is presented in detail in Chapter 3. Nutritional information can be obtained from plasma, serum, urine, stool, hair, and nail samples. The latter two are rarely used clinically. Depending on the underlying medical condition and related nutritional problems from the history and physical examination, a focused laboratory assessment may be obtained. Serum albumin and prealbumin reflect the adequacy of protein and calorie intake. Because the half-life of albumin is approximately 20 days, it also reflects long-term protein stores. The shorter half-life of prealbumin (two to three days) is a better short-term indicator of calorie and protein intake. However, the usefulness of prealbumin in the hospitalized patient may be limited by the fact that it is decreased in the setting of stress, sepsis, and acute illness. Checking a C-reactive protein level may help identify when the low prealbumin level is related to stress. Anemia can be attributable to multiple nutritional deficiencies (e.g., iron, vitamin B12, folate, vitamin C, protein, and vitamin E), and a careful analysis of the red blood cell indices and peripheral blood smear will help to determine what further nutritional laboratory tests should be obtained (e.g., iron studies, vitamin levels). In premature infants, nutritional anemias can be attributable to iron, vitamin E, and copper deficiencies. Nutritional tests to check for bone health may include serum, calcium, phosphorus, alkaline phosphatase, magnesium, and 25-hydroxyvitamin D. Additional information on bone health may be

obtained from a parathormone level, radiography, and DXA scan. Specific vitamin and mineral levels can be checked when deficiency or excess states are suspected. A urine analysis, along with serum electrolytes, is useful in assessing the hydration status of the patient. See Appendix Table I-8 for a list of selected clinical findings related to nutritional inadequacies and Chapter 3 for a more in-depth look at laboratory assessment of nutritional status.

NUTRITIONAL REQUIREMENTS

The estimation of nutritional requirements is the last step in a nutritional assessment. Recommendations for energy and protein intake, as well as specific vitamins and minerals, are needed for patient care (see Chapters 8–10). The history (medical and dietary), physical examination, and anthropometric and laboratory data obtained are used to help estimate these nutritional requirements. These provide a starting point for nutritional therapy and are modified over time based on the patient's ongoing health status and response to nutritional therapy. The adequacy of the nutritional therapy provided should be vigilantly monitored in children with failure to thrive and obesity and in those patients with conditions requiring enteral or parenteral nutrition.

The DRIs[85] provide updated protein recommendations (see Appendix II; also see Chapter 6). Adequate intakes (AIs) for protein in infants 0–6 months are based on the mean protein intake of healthy breastfed infants.[3] Nitrogen intake, nitrogen balance (the minimum protein intake necessary to maintain nitrogen balance), rates of protein deposition, and efficiency of protein use all influence protein requirements. For individuals 7 months through 18 years of age, the protein recommendations are based on a combination of these factors, plus a safety factor to account for individual variation.[85] The DRIs provide protein recommendations (grams per kilogram per day) by age from birth to 8 years and by age and sex starting from 9 years. Individualized needs can be estimated by multiplying the age/sex appropriate grams of protein per kilogram per day by the body weight (in kilograms). As previously noted, DRIs may be further individualized based on the child's nutritional, medical, and growth needs and should be adjusted over time based on clinical status and response to nutritional intervention.

There are a number of methods to estimate energy needs of children in the clinical setting, including the DRIs for estimates of total energy needs,[85] the WHO[86] and Schofield[87] prediction equations for estimates of

resting energy expenditure (REE), and a direct measurement of REE (see below). The DRIs include estimated average requirements, AIs, and tolerable upper intake levels for most nutrients; see Chapter 11 for details.[3] The DRIs are used in Canada and the United States, and nutrient intakes at the suggested levels promote nutrient function, biological and physical well-being, and disease prevention. DRIs are available for vitamins, minerals (see Chapters 8–10), energy, and macronutrient recommendations (see Chapters 5–7). Generally, the DRIs provide for the nutritional needs of the healthy individual and population. Therefore, DRIs may require adjustments in the clinical setting because they do not address energy or nutrient requirements for individuals who are malnourished or have acute/chronic disease.

Both the Food and Nutrition Board DRI and the Food and Agricultural Organization of the WHO recommendations for energy requirements in children 0–2 years are estimated from total energy expenditure (TEE) measurements (by the double-labeled water methods) and estimated energy needs for tissue deposition for growth "at rates consistent with good health."[85,86] For children at this young age, estimated energy requirements (EERs) vary based on weight. The EERs for children aged 3–8 years and 9–18 years are also from TEE and energy deposition costs (20 and 25 kcal/day, respectively) and are based on age, weight, height, and level of physical activity (see Appendix II). The important role of moderate physical activity in achieving and maintaining the appropriate energy balance for optimal health is emphasized in these new recommendations. Levels of physical activity are categorized into four levels: sedentary, low active, active, and very active.[3] EER equations are also available for use in children aged 3 years and above who are at "risk of overweight" defined as a BMI >85th percentile and "overweight" as a BMI >95th percentile.[3] DRIs provide an estimate of total energy needs in kilocalories per day and may be adjusted based on nutritional, medical, and growth needs of the individual patient.

The WHO and Schofield REE prediction equations offer another method to estimate energy requirements. These equations are based on the evaluation of several thousand children and are clinically useful. The WHO equations (see Appendix II and Table II-15) estimate REE by sex, age, and weight groups and approximate the basal metabolic rate.[88] Total daily energy needs are then estimated by multiplying the estimated REE by a factor to adjust for physical activity, medical status, and/or the need for catch-up growth. The Schofield equations (see Appendix II and Table II-13) use sex, age, weight, and height of the child and may more

accurately predict REE in children with altered growth and body composition (i.e., failure to thrive and obesity).[89] Schofield REE estimates are also adjusted for the patient's activity, stress, and growth needs (see Table 2-2) to approximate total daily energy needs.

The current DRI for EER provides additional guidance beyond the 1985 FAO/WHO/UNU report for energy requirements with respect to catch-up growth in undernourished or stunted children[90] based on limited data. Similarly, the 2001 FAO/WHO/UNU report on Human Energy Requirements does not specifically address energy requirements for children recovering from moderate or severe malnutrition or chronic illnesses.[91] Direction with respect to energy replacement to allow for twice the normal growth rate for children aged 6–24 months is provided. Similar to the new WHO growth charts, the emphasis in the WHO report is prescriptive as opposed to descriptive. Thus, it indicates how individuals should grow in response to appropriate energy intake in optimal conditions rather than reflect how they were observed to grow with inadequate energy intake or excess.

TABLE 2-2 Disease and Physical Activity Factors for Adjustment of Resting Energy Expenditure (REE)

REE Factor	Disease and Activity Factors
×1.0–1.1	Well-nourished children, sedated on ventilator, extracorporeal membrane oxygenation; minimal stress
×1.3	Well-nourished children with decreased activity, minor surgery, mild-to-moderate sedation; minimal stress
×1.5	Ambulatory child with mild-to-moderate stress Inactive child with sepsis, cancer, trauma, extensive surgery Minimally active child with malnutrition and catch-up growth requirements
×1.7	Active child with catch-up growth requirements Active child with severe stress

Source: Adapted from Mascarenhas MR, Tershakovec AM, Stallings VA. Parenteral and enteral nutrition. In: Wyllie R, Hyams JS, eds. *Pediatric Gastrointestinal Disease*. Philadelphia: WB Saunders; 1999:741–757.

Resting Energy Expenditure and Indirect Calorimetry

Prediction equations to estimated energy needs in children are not designed to address the special needs of children with complex health

conditions. The indications for performing indirect calorimetry for REE measurements are to determine energy requirements for medically and nutritionally complex patients. These studies can be performed in critically ill and intubated patients, provided cuffed endotracheal tubes are used to measure gas exchange precisely.

The REE approximates basal metabolic rate and can be determined by indirect calorimetry. This technique measures gas exchange, specifically, the oxygen consumed and carbon dioxide produced as a product of the oxidation of a dietary substrate. The amount of heat or energy produced from the oxidation of a specific dietary substrate is determined by the ratio of carbon dioxide exhaled to the oxygen inhaled and is referred to as the respiratory quotient (RQ). Complete oxidation of pure glucose or carbohydrate will yield equal amounts of carbon dioxide produced for oxygen consumed, resulting in an RQ of 1. For fats and mixed meals, the RQ is less than 1, since they are oxidized less than a carbohydrate only meal.

Following consumption of a mixed meal for dinner in which the macronutrient proportions are known, an age appropriate overnight fast precedes the measurements of REE. Studies are performed early in the morning in a rested, awake state, with minimal preceding physical activity/exertion. For children who are unable to cooperate or limit their movement, the test is sometimes performed in a sedated state. For infants, REE is usually measured while sleeping after a feed. The study subject lies still on a bed and gas exchange is measured usually via a ventilated hood device. The studies typically take 30–60 minutes to complete. The REE values obtained are then compared to the WHO/Schofield equations[87,88] to calculate a REE as a percent of predicted values based on age, sex, and body size. The EER can also be calculated using a physical activity level (PAL) to estimate the needs for physical activity.

Table 2-2 provides an example of PAL adapted to estimate energy requirements in children with different types of illnesses and corresponding expected physical activity. Further research is required regarding REE adjustment factors for disease states and PAL needed, and their ability to determine the energy needs of children with difference severities of malnutrition and in the context of acute and chronic illnesses.

In summary, for the estimation of energy needs in the clinical setting, an REE based on indirect calorimetry is preferred for children with complex medical and nutritional needs. If an REE measurement cannot be obtained, then the WHO or Schofield equations are recommended. These estimates of REE are then adjusted based on activity, stress, and growth

for an estimate of total daily energy needs for the individualized patient. As mentioned earlier, the new DRIs for total energy recommendations may replace these estimates in the clinical setting. However, these estimates of TEE are not as reliable as those values obtained by more accurate research methods (e.g., doubly labeled water).[92] Finally, it should be remembered that all estimates are guidelines for the initiation of nutritional therapy. Adjustments in the nutritional regimen are made over time based on objective measures, such as weight gain, laboratory data, and medical condition.

CONCLUSION

In pediatric care, adequate nutrition must support both usual nutrient requirements and nutrients needed for optimal growth and development. However, nutritional status depends in part on current and past illnesses, and a child's response to illness is affected by his/her nutritional status. Thus, understanding and addressing the nutritional status of a hospitalized child are important components of clinical care. No single measure provides an adequate assessment of nutrition status. A nutritional assessment often includes the input of many members of the health care team. This chapter provides the factors to be considered in the nutritional assessment and monitoring of a hospitalized child. Initial nutritional goals are adjusted over time as the child's medical and nutrition status change to provide optimal care.

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3

Laboratory Assessment of Nutritional Status

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Nutritional assessment in pediatrics is primarily a clinical process, based on analysis of recent dietary intake and anthropometric measurement methods (as outlined in Chapter 2: Clinical Assessment of Nutritional Status). Laboratory assessment of nutritional status plays a complementary role that may be critical in specific situations, including:

- identification of suboptimal micronutrient status;
- objective and quantitative confirmation of nutritional deficiencies suggested by clinical assessment;
- provision of baseline and serial data with which to monitor response to nutritional interventions, particularly important in prevention of the refeeding syndrome (see Chapter 13: Protein–energy malnutrition);
- provision of clues to the underlying cause of growth failure, which may be related to undernutrition (e.g., malabsorption) or have alternative explanations (e.g., endocrine disorders, chronic kidney disease);
- epidemiological studies, which seek to identify associations

between disease and nutritional biomarkers.

Table 3-1 indicates the range of tests involved in assessing nutritional status. Table 3-2 lists age- and gender-based reference ranges for Exactly which supporting laboratory tests are used, when repeated and how often, will depend on the clinical status of the patient and whether monitoring or evaluation of nutritional support is also indicated.[2]

Effective use of the laboratory service demands an awareness of nonnutritional factors that can influence results. After a discussion of potentially confounding factors in the interpretation of laboratory data, we review laboratory assessment of protein and energy status, micronutrient status, and hematological and immunological testing relevant to nutrition, before finishing with a look at technologies that are likely to dominate nutritional testing in the laboratory in the foreseeable future.

POTENTIAL CONFOUNDERS OF INTERPRETATION

Interpretation of laboratory tests must take account of the range of biological and analytical factors that can influence results.[3] Some examples of relevance to nutritional assessment are given to illustrate these factors.

Biological Variation

Interindividual variation refers to differences in true concentrations of any nutrient between individuals. These may be dependent on several parameters unrelated to diet, including physiological, pathological, genetic, and environmental influences. Analytes that are significantly influenced by factors that cannot be controlled will often be unreliable indicators of intake. Examples include:

TABLE 3-1 Components of Assessment of Nutritional Status in Clinical Pediatrics

Clinical assessment	• Clinical history • Subjective global assessment[1] • Physical examination
Anthropometric assessment	• Height for age percentiles/Z-scores • Weight for age percentiles/Z-scores • Body mass index percentiles/Z-scores

	• Triceps skinfold and mid-arm circumference percentiles
Dietary assessment	• 24-hr recall • 72-hr diary • Semiquantitative food frequency questionnaire
Laboratory assessment	• CBC (Hb, hematocrit, total and differential WCC) • Albumin (or prealbumin if available)[a] + CRP; total protein • Renal function/hydrational status: BUN, creatinine, sodium • Potassium, phosphate, magnesium[a] • Liver function tests[a] • Fasting lipids[a] • Glucose[a] • Calcium, alk phos, vitamin D • Iron studies, vitamin B_{12} and folate • Selenium, zinc, copper • Prothrombin time • Other vitamins, other minerals • Nitrogen balance studies

Abbreviations: CBC, complete blood count; CRP, C-reactive protein; WCC, white cell count.

[a]Tests of particular relevance to monitoring in nutritional support

TABLE 3-2 Reference Ranges of Select Nutritional Laboratory Values

Nutrient	Age	Males	Either	Females
Albumin (g/dL)	< 5 d (<2.5kg)		2.0–3.6	
	< 5 d (>2.5kg)		2.6–3.6	
	1–3 y		3.4–4.2	
	4–6 y		3.5–5.2	
	>6 y		3.7–5.6	
Alkaline phosphatase (U/L)	1–30 d	75–316		48–406
	31–365 d	82–383		124–341
	1–3 y	104–345		108–317
	4–6 y	93–309		96–297
	7–9 y	86–315		69–325

	10–12 y	42–362		51–332
	13–15 y	74–390		50–162
	16–18 y	52–171		47–119
Calcium (mg/dL)	1–30 d	8.5–10.6		8.4–10.6
	31–365 d	8.7–10.5		8.9–10.5
	1–3 y	8.8–10.6		8.5–10.4
	4–6 y	8.8–10.6		8.5–10.6
	7–9 y	8.7–10.3		8.5–10.3
	10–12 y	8.7–10.2		8.6–10.2
	13–15 y	8.5–10.2		8.4–10.0
	16–18 y	8.4–10.3		8.6–9.8
Calcium, ionized (mg/dL)	0–1 mo		3.9–6.0	
Whole blood	1–6 mo		3.7–5.9	
	1–17 y		4.9–5.5	
Carnitine, total, fasting	1–12 mo		15–39	
(µmol/L)	1–7 y		18–37	
	7–15 y		31–43	
Cerulosplasmin (mg/L)	1–30 d	77–253		33–275
	31–365 d	154–484		154–429
	1–3 y	253–561		286–539
	4–6 y	286–561		264–539
	7–9 y	253–517		231–484
	10–12 y	209–506		209–484
	13–15 y	198–495		209–462
	16–18 y	198–451		220–495
Cholesterol (mg/dL)	1–30 d	54–151		62–155
	31–182 d	81–147		62–141

	183–365 d	76–179		76–216
	1–3 y	85–182		108–193
	4–6 y	110–217		106–193
	7–9 y	110–211		104–210
	10–12 y	105–223		105–218
	13–15 y	91–204		108–205
	16–18 y	82–192		92–234
Copper (µg/dL)	0–6 mo		38–104	
	6–12 mo		24–152	
	1–2 y		76–193	
	2–4 y		87–187	
	4–6 y		56–191	
	6–10 y		117–181	
	10–14 y		87–182	
	14–18 y		75–187	
Ferritin (ng/mL)	1–30 d	6–400		6–515
	1–6 mo	6–410		6–340
	7–12 mo	6–80		6–45
	1–5 y	6–60		6–60
	6–19 y	6–320		6–70
Folic acid (nmol/L)	0–1 y	16.3–50.8		14.3–51.5
	2–3 y	5.7–34.0		3.9–35.6
	4–6 y	1.1–29.4		6.1–31.9
	7–9 y	5.2–27.0		5.4–30.4
	10–12 y	3.4–24.5		2.3–23.1
	13–18 y	2.7–19.9		1.7–16.3
Glucose (mg/dL)	Outside neonatal period		70–126	
Glutathione peroxidase activity, U/L (serum)	Newborn (term)		180–890	
	1–5 y		554–985	