Pulmonary Diseases

Erin Redding and Shannon Despino

Promoting optimal growth and development is important for any child, but it is especially important for the child with chronic pulmonary disease. In this chapter, the nutritional management of cystic fibrosis (CF), bronchopulmonary dysplasia (BPD), and asthma is discussed. Adequate nutrition in the care of the child with CF or BPD plays an important prognostic role in the outcome of these diseases. A discussion on asthma is included because it is one of the most common chronic diseases of childhood, and nutrition may play an important role in its management.

Cystic Fibrosis

CF, a genetic disorder characterized by widespread dysfunction of the exocrine glands, is the most common lethal hereditary disease of the Caucasian race.[1] The disease is characterized by an abnormality in the CF transmembrane conductance regulator (CFTR) protein, causing an increased sodium reabsorption and a decreased chloride secretion. The result is the production of abnormally thick and viscous mucus, which affects various organs of the body. In the lungs, the thick mucus clogs the airways; causing obstruction, subsequent bacterial infections, and progressive lung disease. In the pancreas, the thick mucus prevents the release of pancreatic enzymes into the small intestine for the digestion of foods. Blockage of ducts eventually causes pancreatic fibrosis and cyst formation. About 90% of CF patients have pancreatic insufficiency (PI),[2] exhibited by such gastrointestinal symptoms as frequent, foul-smelling stools; increased flatus; and abdominal cramping. In a small percentage of patients, 8% according to the 2008 CF Foundation Patient Registry,[3] the ducts and tubules of the liver are obstructed by mucus, resulting in liver disease that may progress to cirrhosis. Common complications in the older CF population include CF-related diabetes (CFRD) and bone disease. A unique characteristic of CF is an increased loss of sodium and chloride in the sweat. Sterility in males and decreased fertility in females is also seen.

The life expectancy of CF patients has greatly improved since the disease was first described as a distinct clinical entity by Andersen in 1938.[4] During the 1930s to 1950s, CF patients usually died at an early age, secondary to malabsorption and malnutrition. Pancreatic enzyme therapy, antibiotic therapy, nutrition therapy, and earlier diagnosis have been major contributory factors to the improvement in the prognosis for patients with CF. The CF Foundation currently reports the median age of survival to be 37.4 years.[3]

Genetics/Incidence

CF is transmitted as an autosomal recessive trait. Both parents are carriers of the defective gene but exhibit no symptoms of the disease themselves. Each offspring of two carriers of the defective gene has a 25% chance of having the disease, a 50% chance of being a carrier of the defective gene, and a 25% chance of neither having the disease nor being a carrier.

The CF gene was discovered in 1989 on the long arm of chromosome 7.[5] The CF gene product is a protein called the CFTR, which is a cyclic adenosine monophosphate (cAMP)-regulated chloride channel and regulator of secondary chloride and sodium channels normally present in epithelial cells.[6–11] The most common mutation is called DF508, and it accounts for the majority of CF alleles among the Caucasian population worldwide.[12] However, over 1500 mutations of the CFTR gene have been identified,[13] which accounts for the variability of disease symptoms and severity that is seen among patients with CF. It is hoped that these genetic discoveries will lead to improved treatment, including gene therapy and ultimately a cure for the disease.

Approximately 26,000 children and adults in the United States have CF. The incidence of CF is 1 in 3500 births each year. CF is most common in Caucasians, which account for about 95% of the affected population; however, CF can be diagnosed in all racial and ethnic groups.[3]

Manifestations/Diagnosis

Manifestations of the disease are numerous and vary greatly from patient to patient, due in part to the large numbers of mutations of the defective gene. A summary of common pulmonary and gastrointestinal manifestations of CF is depicted in **Table 11-1**. Any child who repeatedly exhibits any of these symptoms should be tested for CF. In addition, CF should be considered when a child tastes salty when kissed or experiences heat prostration. Other manifestations of CF include the bilateral absence of the vas deferens in males and decreased fertility in females.

According to the consensus statement on the diagnosis of CF published by the CF Foundation,[13] the diagnosis of CF should be based on the presence of one or more characteristic features of the disease:

- Evidence of chronic sinopulmonary disease
- Evidence of gastrointestinal (GI) and nutritional abnormalities
- Evidence of salt-loss syndromes
- Evidence of obstructive azoospermia in males
- Family history of the disease
- A positive newborn screening test result plus an elevated sweat chloride test

Sweat chloride is measured by a quantitative pilocarpine iontophoresis sweat test. A sweat chloride concentration greater than 60 mmol/L is indicative of the diagnosis of CF. Patients with an intermediate sweat chloride concentration (30–59 mmol/L for infants under 6 months of age and 40–59 mmol/L for individuals over 6 months of age) should undergo CFTR mutation analysis to rule out CF. The diagnosis can also be made with the identification of CF mutations on both alleles of the CFTR gene, which is sometimes even seen in patients who have a negative sweat test (< 39 mmol/L).[13]

TABLE 11-1 Manifestations of Cystic Fibrosis

Pulmonary	Gastrointestinal
Chronic cough	Failure to thrive
Repeated bronchial infections	Steatorrhea
Increased work of breathing	Hypoalbuminemia
Digital clubbing	Rectal prolapse
Bronchospasm	Frequent, foul-smelling stools
Cyanosis	Abdominal cramping
Chronic pneumonia	Voracious appetite
Nasal polyps	Anemia
Chronic sinusitis	Intussusception of the small and large bowel
	Vitamin deficiencies

The CF Foundation recommends that all states routinely conduct newborn screening for CF. Research has revealed that earlier diagnosis of CF is linked with improved growth and lung function, reduced hospital stays, and increased life expectancy. This is largely in part to more prompt medical treatment and nutrition intervention. A positive CF newborn screen does not always mean that the patient has CF, so further medical testing such as a sweat test must be done to confirm the diagnosis. With all states conducting routine newborn screening for CF, it is expected that the median age of survival will continue to increase combined with an increased quality of life.[13]

Management

Rigorous daily management is required to control the symptoms of the disease. Daily chest percussion therapy and postural drainage, along with aerosolized medications, help to clear the airways of mucus, improve existing lung compromise, and retard future deterioration. Aerosolized, oral, or intravenous antibiotics are used to control pulmonary infections. Pancreatic enzyme replacement therapy is a crucial part of the management of the GI symptoms in patients who exhibit PI. These patients are required to take pancreatic enzymes prior to each meal and snack containing fat, protein, and/or complex carbohydrates. Dosage of pancreatic enzymes is individualized, depending on factors such as the extent of pancreatic involvement, dietary intake, and the weight and age of the patient. Vitamin, mineral, and salt supplementation are also recommended and are discussed in detail in the nutrition management section of this chapter. Providing adequate nutrition for normal growth and development is one of the primary goals of disease management in CF, and the CF Foundation recommends that every patient with CF be assessed by a registered dietitian at least once a year. The complex and multifaceted nature of the disease requires an interdisciplinary team approach with patient and family involvement in decision making to optimize disease management and improve health outcomes.

Effects of CF on Nutritional Status

CF is a disease with many nutrition implications. The following section will further explain the nutritional manifestations of this disease and how and why it is important to monitor the nutritional status of patients with CF.

Chronic Energy Deficit

Many aspects of CF stress the nutritional status of the patient directly or indirectly by affecting the patient's appetite and subsequent intake. Aspects of pulmonary and GI involvement affecting nutritional status are summarized in **Table 11-2**. CFRD and liver disease also impact nutritional status. Bile salts and bile acid losses contribute to fat malabsorption.

TABLE 11-2 Aspects of Cystic Fibrosis that Affect Nutritional Status

Pulmonary	Gastrointestinal
Increased work of breathing	Malabsorption of fat
Chronic cough	Loss of fat-soluble vitamins
Cough-emesis cycle	Loss of essential fatty acids
Chronic antibiotic therapy	Malabsorption of protein
Fatigue, anxiety	Anorexia
Decreased tolerance for exercise	Gastroesophageal reflux/ esophagitis
Repeated pulmonary infections	Bile salts and bile acid loss
	Distal intestinal obstructive syndrome (DIOS)
	Fibrosing colonopathy

Gastrointestinal losses occur in spite of pancreatic enzyme replacement therapy. Also, the catch-up growth that is often needed after diagnosis requires additional calories. The energy metabolism of CF patients has been studied and generally an increase in resting energy expenditure has been found, as compared with controls and/or predicted resting energy expenditure.[14–18] It is estimated that energy requirements for patients with CF range from 110–200% of the calories recommended for healthy individuals of the same age, gender, and size.[19,20] All of these factors can contribute to a chronic energy deficit which, if left untreated, can lead to a marasmic type of malnutrition. The primary goal of nutritional therapy is to overcome this energy deficit and to promote normal growth and development for CF patients in an effort to optimize lung function and increase longevity.

Appetite

Many references have been made to the voracious appetites of CF patients. This may be true of undiagnosed and untreated patients, particularly infants. In practice, however, dietetics professionals often deal with patients with CF who have very poor appetites and early satiety. As previously mentioned, Table 11-2 delineates some aspects of CF that can contribute to poor appetite and failure to thrive. Psychosocial issues that the patient may be dealing with may cause depression, anxiety, fatigue, and anorexia that will also impact appetite and nutritional status. Behavioral issues related to eating and ineffective parenting strategies may play a role in a child's poor appetite and intake as well. Studies of the use of medications for appetite stimulation, such as megestrol acetate, as part of therapy for CF have been conducted with positive short-term results.[21] However, more study is needed to determine the long-term effects of megestrol acetate on growth, pulmonary function, and clinical stability in CF.[21]

Growth

The expectation of the CF Foundation is that children with cystic fibrosis should grow and develop like their peers without CF. In addition, adults are expected to maintain a nutrition status similar to healthy individuals of the same age. In 2005, the CF Foundation established the following updated age-specific goals for patients with CF:[19]

- *Infants and toddlers 2 years or younger:* Achieve weight for length at the 50th percentile by 2 years
- *Children and adolescents 2 years old to 20 years old:* Achieve or exceed the 50th percentile for body mass index (BMI) for age and gender
- *Females 20 years or older:* Achieve or exceed a BMI of 22
- *Males 20 years or older:* Achieve or exceed a BMI of 23

Growth studies in the past have found CF patients to be smaller and lighter than their age- and sex-matched peers. For example, in 1964 Sproul and Huang[22] found the 50th percentile for CF patients from infancy to adolescence for height and weight to be between the 3rd and 10th percentiles on the growth charts for healthy children. These same investigators noted an absence of the adolescent growth spurt in the CF population. Growth deficiencies significantly correlated with the severity of respiratory disease but did not correlate with PI.[22]

More recent reports are revealing improved growth and weight gain in people with CF. According to the 2008 CF Foundation Patient Registry,[3] the median BMI percentile for patients 2–20 years old was 48%, and the median BMI for patients 21 years or older was 21%. These improvements are likely multifactorial, but largely can be attributed to increased nutrition intervention and a more widespread understanding of the correlation between nutrition status and lung function.

Nutrition as a Prognostic Indicator

More and more studies are indicating that nutritional status is an important prognostic indicator in the outcome of CF. For example, Konstan and associates[23] evaluated the 1990s data from the Epidemiologic Study of Cystic Fibrosis (ESCF) and found that better growth parameters at age 3 years were associated with better pulmonary function at age 6 years. Furthermore, patients whose growth parameters improved between the ages of 3 and 6 years had better pulmonary function at age 6 years.[23] Peterson and colleagues[24] found that children who weighed more and who steadily gained weight at an appropriate and uninterrupted rate had better pulmonary function as measured by forced expiratory volume at 1 second (FEV_1) than did those children with CF who experienced periodic weight losses. Data from the German CF quality assurance project found a positive association of weight-for-height with lung function.[25] Patients with

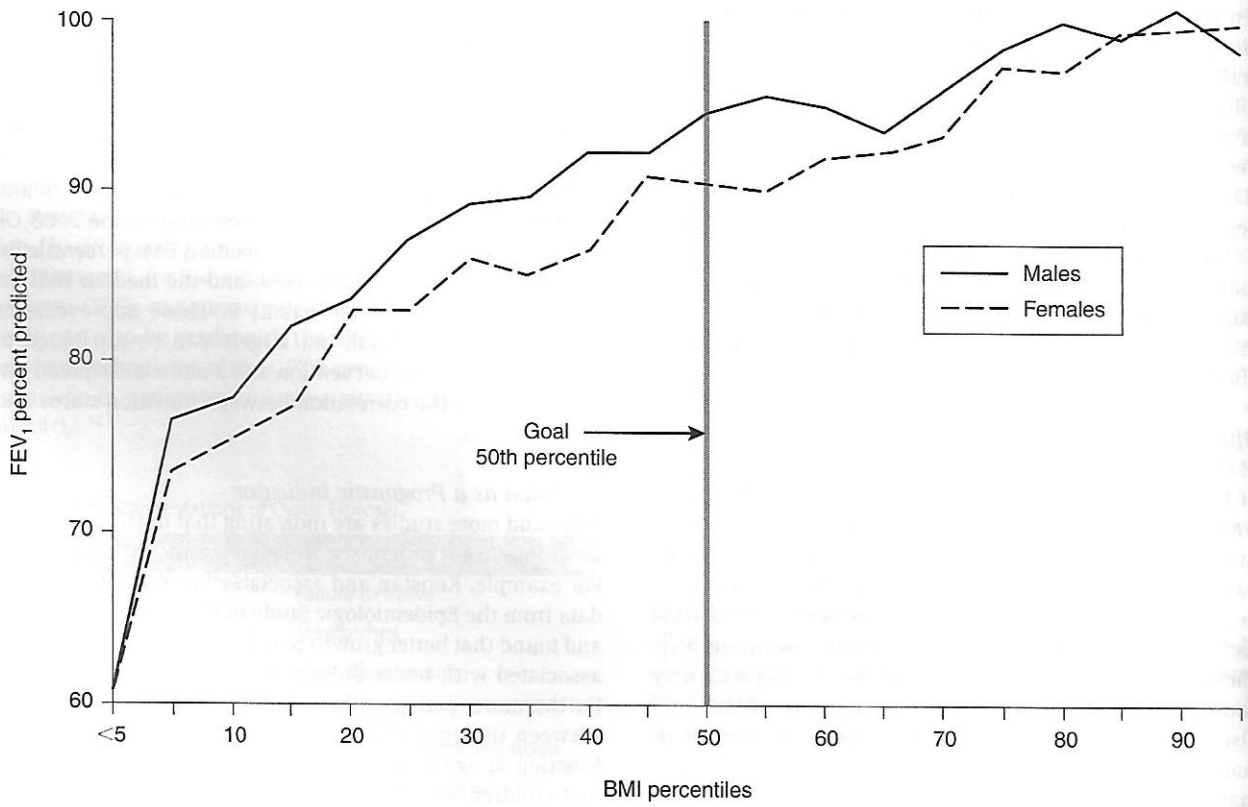
CF who had weight-for-height less than 90% of predicted had significantly lower values on pulmonary function tests than those patients with normal weight-for-height.[25] Beker and colleagues[26] found height to be an important prognostic indicator of survival for both male and female patients with CF. Refer to **Figure 11-1** for a graph demonstrating the relationship between FEV_1 and BMI percentiles. It is clear that there is an association between growth parameters and lung function. Due to the fact that progressive lung disease is usually what causes the morbidity and mortality of CF, the CF Foundation recognizes the importance of nutrition intervention to optimize growth and help improve lung function.

Nutritional Screening and Assessment

Because nutrition plays such an important role in the treatment of CF, routine nutritional screenings and thorough assessments are very important. The CF Foundation recommends that every patient with CF should be assessed by a registered dietitian annually. Some patients who are at increased nutrition risk may benefit from meeting with a registered dietitian more frequently. In this section, anthropometric, biochemical, clinical, dietary, and drug–nutrient interaction evaluations will be discussed. The CF Foundation has published a consensus report on pediatric nutrition for patients with CF as well as the *Clinical Practice Guidelines for Cystic Fibrosis*, which includes nutrition management information.[27–29] Refer to **Exhibit 11-1** for the CF Foundation's recommendations for nutritional status assessment.

Anthropometric

Monitoring growth parameters is an important component of the screening, assessment, and follow-up of CF patients. As with any child, CF patients should be weighed and measured routinely by trained individuals using appropriate techniques and equipment, such as those described by Fomon[30] and the CF Foundation.[27,28] For children less than 36 months of age, weight-for-age, recumbent length-for-age, weight-for-height, and head circumference-for-age should



FEV_1 percent predicted is positively correlated with BMI percentiles for patients 6 to 20 years of age (correlation > 0.95, $p < 0.0001$).

FIGURE 11-1 FEV_1 Percent Predicted vs. BMI Percentiles in Patients 6 to 20 Years

Source: Used with permission of the Cystic Fibrosis Foundation. Cystic Fibrosis Foundation Patient Registry, 2008 Annual Report. Bethesda, MD: Cystic Fibrosis Foundation, 2009.

EXHIBIT 11-1 Nutritional Assessment in Routine CF Center Care

	At Diagnosis	Every 3 Months Birth to 24 Months	Every 3 Months	Annually
Head circumference	x[a]	x		
Weight (to 0.1 kg)	x	x	x	
Length (to 0.1 kg)	x	x		
Height (to 0.1 cm)	x		x	
Mid-arm circumference (MAC) (to 0.1 cm)	x			x
Triceps skinfold (TSF) (to 1.0 mm)	x[b]			x
Mid-arm muscle area, mm^2 (calculated from MAC and TSF)	x[b]			x
Mid-arm fat area, mm^2 (calculated from MAC and TSF)	x[b]			x
Biological parents' heights[c]	x			
Pubertal status, female				x[d]
Pubertal status, male				x[e]
24-hour diet recall				x
Nutritional supplement intake[f]				x
Anticipatory dietary and feeding behavior guidance		x	x[g]	x

[a]If younger than 24 months of age at diagnosis.

[b]Only in patients older than 1 year of age.

[c]Record in cm and gender-specific height percentile; note patient's target height percentile on all growth charts.

[d]Starting at age 9 years, annual pubertal self-assessment form (patient or parent and patient) or physician examination for breast and pubic hair Tanner-stage determination; annual question as to menarchal status. Record month and year of menarche on all growth charts.

[e]Starting at age 12 years, annual pubertal self-assessment form (patient or parent and patient) or physician examination for genital development and pubic hair Tanner-stage determination.

[f]A review of enzymes, vitamins, minerals, oral and enteral formulas, herbal, botanical, and other CAM products.

[g]Routine surveillance may be done informally by other team members, but the annual assessment and every 3 month visits in the first 2 years of life and quarterly visits for patients at nutritional risk should be done by the center's registered dietitian.

Source: Borowitz D, Baker R, Stallings V. Consensus report on nutrition for pediatric patients with cystic fibrosis. *J. Pediatric Gastroenterology & Nutrition.* 2002;35(3):247.

be accurately measured and plotted on the National Center for Health Statistics (NCHS) growth curves at each clinic visit or hospitalization.[22] For children 2 years of age or older who are measured standing, weight-for-age, height-for-age, and BMI-for-age should be measured, plotted, and calculated. (See Appendix B for growth charts and Chapter 3 for additional information.)

Historically, % Ideal Body Weight (IBW) has been used as a method to classify nutrition risk status in children with CF. BMI percentile has been shown to be more sensitive to changes in percent predicted FEV_1 and has stronger association to percent predicted FEV_1 than %IBW. Therefore, the CF Foundation recommends that an age-appropriate BMI method be used to assess weight and height, instead of the %IBW method of assessment.[31]

According to the CF Foundation, anthropometric measurements, including mid-arm circumference and triceps skinfold thickness, should be obtained according to standard procedures by a registered dietitian at least once a year on all patients greater than 1 year of age.[27–29,32] From these measurements, mid-arm muscle circumference, mid-arm muscle area (mm^2) and mid-arm fat area (mm^2) should be calculated and compared with gender- and age-specific normative data.[33] (See Appendix D.) Measurements provide information about fat and somatic protein stores and are particularly beneficial when monitoring the

effects of nutrition intervention over time. They are also useful in monitoring the nutrition status of CF patients with liver disease and ascites, in which case weight may not be a good indicator of nutrition status.

It is important to determine whether patients with CF are achieving their full genetic potential in terms of height growth. One method is to determine mid-parental height, plot this height on the growth chart at age 20, and use this percentile as the target for the individual patient. The CF Foundation suggests calculating target height as follows: Add 13 centimeters to the mother's height if the patient is a boy, or subtract 13 centimeters from the father's height if the patient is a girl. Obtain the average of the two parents' adjusted heights. To calculate the patient's target height range, adjust +/− 10 cm for a boy and +/− 9 cm for a girl.[27,28]

Biochemical

Laboratory monitoring of nutritional status as recommended by the CF Foundation at diagnosis and annually is outlined in **Exhibit 11-2**.

Protein Status

Undiagnosed infants, particularly those who are breast-fed, often present with hypoalbuminemia and subsequent edema. The malabsorption that occurs in undiagnosed CF causes inadequate absorption of protein. The low protein content of breast milk as compared with modified cow's milk formulas further compromises the infant's protein status. Upon diagnosis of CF and the initiation of pancreatic enzyme therapy, hypoalbuminemia is usually corrected because the infant is no longer malabsorbing protein. It is wise to check a serum albumin level in newly diagnosed infants.

EXHIBIT 11-2 Laboratory Monitoring of Nutritional Status

	How Often to Monitor			
	At Diagnosis	Annually	Other	Tests
Beta Carotene			At physician's discretion	Serum levels
Vitamin A	x[1]	x		Vitamin A (retinol)
Vitamin D	x[1]	x		25-OH-D
Vitamin E	x[1]	x		α-tocopherol
Vitamin K	x[1]		If patient has hemoptysis or hematemesis; in patients with liver disease	PIVKA-II (preferably) or prothrombin time
Essential Fatty Acids			Consider checking in infants or those with FTT	Triene; tetraene
Calcium/Bone Status			> age 8 years if risk factors are present	Calcium, phosphorus, ionized PTH, DEXA scan
Iron	x	x	Consider in-depth evaluation for patients with poor appetite	Hemoglobin, hematocrit
Zinc			Consider 6-month supplementation trial and follow growth	No acceptable measurement
Sodium			Consider checking if exposed to heat stress and becomes dehydrated	Serum sodium; spot urine sodium if total body sodium depletion suspected
Protein Stores	x	x	Check in patients with nutritional failure or those at risk	Albumin

[1]Patients diagnosed by neonatal screening do not need these measured.

Abbreviations: FTT, failure to thrive; PTH, parathyroid hormone; DEXA, dual energy x-ray absorptiometry; PIVKA, protein induced by vitamin K antagonistism or absence.

Source: Borowitz D, Baker R, Stallings V. Consensus report on nutrition for pediatric patients with cystic fibrosis. *J. Pediatric Gastroenterology & Nutrition.* 2002;35(3):252.

Any time an inadequate protein intake is suspected, it may be beneficial to assess the albumin or prealbumin level. However, it is important to remember that other potential causes of an abnormal albumin value include infection and other physiologic stress, fluid overload, congestive heart failure, and severe hepatic insufficiency.[34] CF patients, who chronically have inadequate calorie intakes, usually have a marasmic type of malnutrition. Their visceral protein levels are usually in the normal range, whereas somatic protein stores are low.[34]

Iron Status

Hemoglobin and hematocrit are checked annually. If there is evidence of anemia, further iron studies should be obtained, including serum iron, iron-binding capacity, ferritin, transferrin, and reticulocyte count.[29] A trial of iron therapy will help determine if the anemia is caused by iron deficiency or anemia of chronic disease.

Fat-Soluble Vitamins

Even patients who are adequately treated with pancreatic enzymes may continue to malabsorb fat and consequently fat-soluble vitamins, so it is important that fat-soluble vitamin levels are checked annually. Vitamin A levels should not be drawn during an acute illness because vitamin A is a negative acute phase reactant and will be decreased with acute illness and inflammation.[27,28] Many CF patients, especially those in northern latitudes, among certain cultures, or with limited sun exposure, may not be exposed to enough sunlight to meet vitamin D needs. Measuring 25-hydroxyvitamin D and parathyroid hormone (PTH) annually in the late fall is recommended for monitoring bone disease (see the bone health section later in this chapter).[27,28] Reports of low vitamin E levels and symptomatic deficiency states have been reported.[27,28]

The long-term antibiotic therapy commonly used in the treatment of CF alters the gut flora. Because an important source of vitamin K is microbiologic synthesis in the gut, vitamin K status is often negatively affected. For this reason, it is important to monitor serum vitamin K levels. It is preferable to monitor proteins induced by vitamin K absence or antagonism (PIVKA-II), but this measurement is not always available. Prothrombin time (PT) is an indirect measurement of vitamin K status and is more widely utilized. PT may also be a useful measure of hepatic synthetic function in patients with nutritional failure or biliary cirrhosis.[27,28]

Essential Fatty Acids

Patients with CF are also at risk of essential fatty acid (EFA) deficiency. The etiology of EFA deficiency can be multifactorial, including fat malabsorption and abnormal fatty acid oxidation. It also has been associated with certain CF genotypes and pancreatic status. Some of the clinical manifestations of EFA deficiency include scaly rash, poor growth, and alopecia. EFA deficiency is also correlated with an increased inflammatory response in patients with CF. Checking a triene to tetraene ratio has often been the common way to assess for EFA deficiency in patients exhibiting poor growth; however, more recent studies have shown serum linoleic acid status to be associated with improved growth and pulmonary status.[35] The goal of nutrition care is to prevent EFA deficiency. A minimum of 3–5% of total calories should come from EFAs.[36] Some sources of EFAs include soybean oil, canola oil, walnuts, fatty fish, and flaxseed.

CF-Related Diabetes Screening

With the increased life expectancy of CF patients, the frequency of glucose intolerance in this population has increased.[37] One study estimated that up to 75% of adults with CF have some form of glucose intolerance and 15% have CFRD.[38] CFRD is a distinct clinical entity because it has features of both type 1 and type 2 diabetes.[37,38] Clinical symptoms of CFRD include polydipsia, polyuria, fatigue, unintentional weight loss, and decreased lung function. **Table 11-3** outlines how CFRD is diagnosed.

CFRD can be classified as CFRD with fasting hyperglycemia or CFRD without fasting hyperglycemia. CFRD with fasting hyperglycemia is characterized by a fasting blood glucose (FBG) equal to or greater than 126 mg/dL. CFRD without fasting hyperglycemia is characterized with a normal FBG but an oral glucose tolerance test (OGTT) equal to or greater than 200 mg/dL. The type of CFRD a patient is diagnosed with may affect their treatment plan.[37]

Pancreatic Function/Malabsorption

PI is often inferred based on a patient presenting with symptoms of malabsorption. Stool fecal elastase-I is considered a highly sensitive and specific way to measure pancreatic function and is generally tested at the time of diagnosis. Patients who are initially pancreatic sufficient can become pancreatic insufficient over time. This is especially true of those who have an identified mutation that is associated with PI. These patients should have their pancreatic function evaluated annually by checking a stool fecal elastase-I.[27,28]

When a patient is pancreatic insufficient and on pancreatic enzyme therapy, it is important to evaluate the appropriateness of their enzyme regimen at regular intervals. In some instances, a 72-hour fecal fat test is used to assess fat absorption. This test is conducted as follows:[36]

1. Patient's stool is collected for 72 hours and frozen.
2. An accurate food record must be kept for a minimum of the 3 days that stool is being collected. In addition,

TABLE 11-3 Diagnosis of Cystic Fibrosis Related Diabetes

Test	Time	Blood Glucose Level	Diagnosis	Action
Casual blood glucose	Done at any time regardless of eating	< 100 mg/dL (< 5.6 mmol/L)	CFRD is not likely	Do blood glucose levels every year or earlier if CFRD symptoms occur.
		100–199 mg/dL (5.6–1.0 mmol/L)	Gray zone	Do a fasting blood glucose test or an OGTT.
		≥ 200 mg/dL (≥ 11.1 mmol/L)	CFRD likely	Do a fasting blood glucose test or an OGTT.
Fasting blood glucose	Done in the morning before breakfast	< 100 mg/dL (< 5.6 mmol/L)	Normal	Do blood glucose levels every year or unless CFRD symptoms occur.
		100–125 mg/dL (5.6–6.9 mmol/L)	Impaired fasting glucose	Make sure the level was fasting. If so, an OGTT should be done.
		≥ 126 mg/dL (≥ 7.0 mmol/L)	CFRD with fasting hyperglycemia	Make sure the level was fasting. More testing may be done to confirm CFRD diagnosis unless patient has symptoms. Other tests may be another fasting glucose test or an OGTT. If the patient has CFRD, he or she will learn to manage it with insulin.
OGTT (with normal fasting glucose)	2 hours after glucose load	< 140 mg/dL (< 7.8 mmol/L)	Normal glucose tolerance	Do blood glucose levels every year or earlier if CFRD symptoms occur.
		140–199 mg/dL (7.8–11.0 mmol/L)	Impaired glucose tolerance	Do an OGTT every year or earlier if CFRD symptoms occur.
		≥ 200 mg/dL (≥ 11.1 mmol/L)	CFRD without fasting hyperglycemia	High risk of getting CFRD with fasting hyperglycemia. Patients will learn to use a blood sugar meter and how to count carbohydrates in the food they eat. The doctor may give insulin if the patient has symptoms, is ill, or is taking steroids.

Abbreviations: CFRD, cystic fibrosis related diabetes; OGTT, oral glucose tolerance test.

Source: Courtesy of Hardin D, Brunzell C, Schissel K, Schindler T, Moran A. *Managing Cystic Fibrosis Related Diabetes (CFRD): An Instruction Guide for Patients and Families*, 4th ed. Bethesda, MD: Cystic Fibrosis Foundation, 2008.

sometimes it may be useful to keep a food record 1–2 days prior to the stool collection to ensure the patient is consuming adequate fat for the test results to be accurate (goal: 2–3 g fat/kg/day). Using the food diary, the average fat intake per day is calculated in grams.

3. The coefficient of fat absorption (COA) is calculated:

$$(\text{grams of fat consumed} - \text{grams of fat excreted}) / \text{grams of fat consumed} \times 100\% = \text{COA}$$

The normal COA for premature infants is 60–75%, for full-term newborns 80–85%, for age 10 months to 3 years 85–95%, and for age > 3 years 95%.[36] Any CF patient who demonstrates a percentage less than is deemed normal in correlation with their age may require an increased dosage of pancreatic enzymes or the initiation of pancreatic enzymes if not already prescribed. Although 72-hour fecal fat tests are an accurate way of assessing fat absorption, the steps that must be completed are cumbersome for patients and families. In addition, older patients are uncomfortable or embarrassed collecting their stools. For these reasons, it can be difficult to complete a 72-hour fecal fat test, and adjustments are often made to pancreatic enzyme dosages based on reported symptoms of malabsorption or poor weight gain in the setting of adequate caloric intake.

Clinical

An assessment of the patient's overall health status should be obtained. Questions about activity and energy levels should be asked. Any missed school or work days should be noted. A general review of systems should be performed

by the physician and a description of the patient's Tanner stage should be noted.[27–29] (See Appendix E, Progression of Sexual Development.) Co-morbid medical conditions such as active pulmonary or sinus disease, gastroesophageal reflux disease (GERD), CFRD, hepatobiliary disease, or history of gut resection should be noted.[27–29] These conditions will also have a direct impact on the patient's nutritional status by affecting appetite, intake, and disease state. Questions about the patient's use of alternative/complementary medicine therapies should be asked in addition to questions about the use of routine medications.

Stool Pattern

Information about the patient's stool pattern should be monitored carefully at each clinic visit because this is a good indication of the adequacy of the enzyme therapy. Questions to be asked during a nutrition screening and assessment should include the following:

- Number of stools per day
- Consistency of stools
- Presence of oily discharge
- Rectal prolapse
- Foul-smelling, floating stools and/or flatus
- Abdominal cramping
- Protruding abdomen

Increased frequency or volume of stool output, notable oil in stools or in toilet water, extremely malodorous stools, increased gassiness and abdominal distention, and/or stools that float instead of sinking to the bottom of the toilet are all signs that a patient may be experiencing malabsorption. Some patients with persistent malabsorptive symptoms should also be evaluated for nonpancreatic causes of malabsorption such as lactose intolerance, bacterial overgrowth of the small intestine, giardia or other parasites, celiac disease, or inflammatory bowel disease.[27,28] It is also important to ask about constipation. Constipation can be a symptom of distal intestinal obstructive syndrome (DIOS), which is also a complication of PI.

Enzyme Therapy

Important aspects of enzyme replacement therapy that need to be checked during every clinic visit and hospitalization are:

- Type of enzymes
- Brand
- Amount taken
- When taken
- Method of administration
- Timing with meals
- Calculation of units of lipase/kilogram body weight/meal and total units of lipase/kilogram body weight/day
- Compliance
- Where enzymes are being stored

Enzymes should be stored at room temperature because they may be deactivated by extreme heat or cold. The expiration date should be monitored closely because enzymes become less potent when expired.

Other Medications

It is important to note other medications the patient may be taking at each clinic visit, including antibiotics, bronchodilators, H_2 blockers, antacids, prokinetic agents, steroids, diuretics, cardiac medications, appetite stimulants, probiotics, vitamins, and minerals.

Pulmonary Status

The pulmonary status of the patient will directly influence the patient's nutritional status. The dietetics professional should note the presence of an acute pulmonary exacerbation and chronic disease. CF patients older than about 6 years of age will be able to perform pulmonary function tests to assess the extent of their pulmonary involvement.

Bone Health Indices

Patients with CF are at risk for developing osteopenia and osteoporosis. The origin of bone disease in CF appears to be multifactorial (**Figure 11-2**). Important contributing factors include malabsorption of vitamins D and K, failure to thrive, delayed puberty, physical inactivity, and use of corticosteroid medications. The prevalence of bone disease appears to increase with severity of lung disease and malnutrition.[39] Several studies have demonstrated a positive correlation between bone mineral density (BMD) Z-scores, FEV_1, and BMI.[40–43] Patients with severe pulmonary disease ($FEV_1 < 30\%$) often have severe bone disease with a high rate of kyphosis and fractures of long bones, vertebrae, and ribs.[41,44]

According to the 2004 *Guide to Bone Health and Disease in CF: A Consensus Statement*, patients older than 8 years of age should have a dual energy x-ray absorptiometry (DXA) as a measure of bone mineral density if $< 90\%$ ideal body weight, $FEV_1 < 50\%$ predicted, glucocorticoids ≥ 5 mg/day for ≥ 90 days/yr, delayed puberty, or history of fractures.[39] In addition to the DXA, children at risk for poor bone health should have annual tests for serum calcium, phosphorus, intact parathyroid hormone, and 25-hydroxyvitamin D level.[45] Normative data are not available for children younger than 8 years of age. All patients should have DXA scans by age 18 years if the scans have not been previously obtained for other reasons.

Dietary

As part of the nutritional assessment, dietary analysis provides important information about what, where, and how

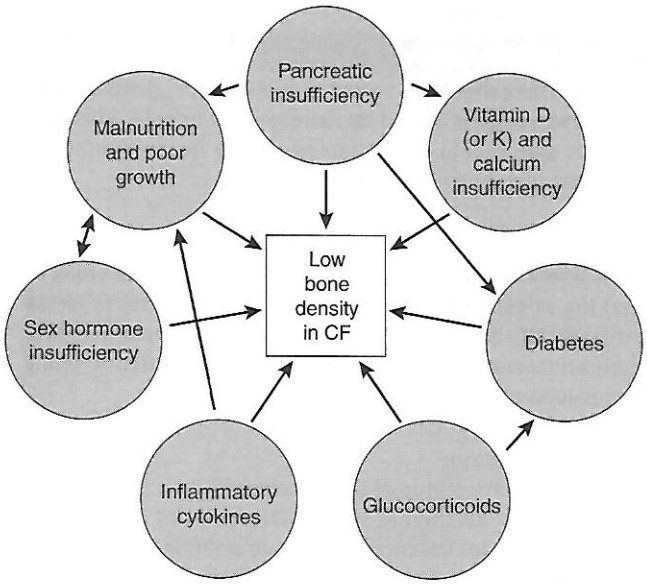


FIGURE 11-2 Pathogenesis of Bone Disease in CF

Source: Courtesy of Aris RM, Merkel PA, Bachrach LK, et al. Consensus statement: guide to bone health and disease in cystic fibrosis. *J Clin Endocrinol Metab.* 2005;90:1888–1896.

much the CF patient is eating. Several methods of gathering the data can be utilized, including a 24-hour dietary recall, a 3- to 5-day food record, and a food frequency questionnaire. The dietetics professional should analyze the diet's adequacy in terms of energy, protein, and other key nutrients such as calcium and iron by looking for a variety of foods in adequate amounts. During this interview, information about the patient's appetite, eating patterns, consumption of sweetened beverages, and behavioral issues related to feeding should be noted.[27–29] The Behavioral Pediatrics Feeding Assessment Scale, which is a self-report measure of meal-time problems, may be administered to identify and evaluate behavioral issues related to eating.[27,28,46]

Drug–Nutrient Interactions

It is important to consider drug–nutrient interactions when assessing any patient, and CF patients are often on a long list of medications. A dietitian or other healthcare provider should take into account how these medications may impact the patient's appetite, if there are dietary restrictions related to any of the patient's medications, and/or what biochemical data may need to be evaluated with the use of certain medications. For example, prolonged antibiotic therapy can alter the gut flora and subsequently influence vitamin K status. In addition, some of the intravenous antibiotics can cause nausea in a number of patients. CF patients with an asthma component of their disease may be on steroids periodically. As the CF patient's pulmonary disease progresses, issues with fluid status may develop. If diuretics are prescribed, fluid and electrolyte status need to be carefully monitored.

Nutritional Management

The overall goal of nutrition management is to promote normal growth and development for the patient with CF. The main components of nutrition management in CF are the provision of adequate energy, protein, and nutrients; pancreatic enzyme therapy; and vitamin and mineral supplementation.

Adequate Diet for Normal Growth and Development

In the past, the GI symptoms of the disease, such as increased number of bulky, foul-smelling stools; increased flatus; and abdominal cramping, were treated with a low-fat diet. Today, with the advent of better enzyme replacement therapy, fat restriction is no longer routinely imposed on all patients. Health professionals now appreciate the tremendous energy demands of the disease, and there is good evidence to support that higher energy intake results in improved weight gain.[31] Estimated energy recommendations to support age-appropriate growth in children with CF over the age of 2 years range from 110% to 200% of energy needs for the healthy population of similar age, gender, and size.[31] This can be accomplished by increasing both the amount and caloric density of foods consumed. To achieve this energy goal, patients with CF often require a greater amount of dietary fat, 35–40% of total energy.[28] It is appropriate to encourage the use of polyunsaturated fats that are good sources of the EFAs, linoleic acid and alpha-linolenic acid, rather than saturated fats. Vegetable oils such as flax, canola, and soy and cold-water marine fish are high in calories and a good source of these fats.[27,28] Limited information is available describing specific dietary protein recommendations for children with CF;[35] however, protein intake is correlated with overall calorie intake and, in general, patients with CF who consume adequate calories also consume adequate protein.[47,48] Defining energy needs in patients with CF can be a challenge due to many individual variables. It is suggested that formulas be used as a starting point, but gain in weight and height, velocity of weight and height gain, and fat stores may provide a more objective measure of energy balance.[35]

Age-specific considerations in the nutritional management of CF are summarized in **Exhibit 11-3**. Infants with CF may be successfully breastfed, as long as pancreatic enzymes are administered prior to each feeding. Standard iron-fortified infant formulas are alternatives to breast milk but also require the administration of pancreatic enzymes prior to each feeding. A study of newly diagnosed infants

EXHIBIT 11-3 Nutritional Management of CF Patients

1. Infant
   - Breast milk or standard iron-fortified infant formula should be recommended. Special formulas such as Alimentum (Abbott Laboratories) and Pregestimil (Mead Johnson Nutritionals), protein hydrolysate formulas containing medium-chain triglycerides, can be recommended for infants in special situations, such as gut resection or increased fat malabsorption.
   - Pancreatic enzymes should be given prior to feedings.
   - Vitamin supplements and a source of fluoride should be given.
   - Introduction of solid foods and advancement of diet should proceed as recommended by the American Academy of Pediatrics (AAP). The RD should guide parents toward foods that will enhance weight gain. Meat, a good source of iron and zinc, may be recommended as a first food for infants consuming human milk.
   - Salt should be added to breast milk or infant formula, particularly in hot weather. When solid foods are added to the infant's diet, salt should be added to these foods.
   - Referrals should be made to community programs such as the WIC program.
2. Toddler
   - Toddlers' diets should be based on a normal healthy diet for age with a variety of foods.
   - Parents should be forewarned of the normal decrease in growth and appetite during this age.
   - Regular meal and snack times should be encouraged.
   - Constant snacking or "grazing" should be discouraged.
   - Drinking of sweetened beverages should be discouraged.
   - Pancreatic enzymes and vitamins are continued.
   - Continue communication with community programs such as the WIC program.
3. Preschool and school age
   - A normal healthy diet with a variety of foods should continue to form the basis of the diet.
   - Limit sweetened beverages.
   - Parents lose control of what child eats away from home at preschool, child care, and school.
   - Arrangements need to be made for child to take enzymes during the school day.
   - Vitamin therapy is continued.
   - Diet prescriptions for a high-calorie, high-protein, high-salt diet can be sent to the school.
4. Adolescent
   - Patients are exercising more independence in food choices.
   - Parents can provide appropriate food environment at home.
   - Patients can be taught to include quick-to-prepare high-calorie foods in daily diet.
   - Snack and fast foods can add a significant amount of calories to the diet and should not be discouraged.
   - Limit sweetened beverages.
   - Health professionals should emphasize the importance of high-calorie intake and enzyme and vitamin therapy directly to the patient and not via the parents.
   - Nutrition needs increase prior to and during adolescent growth spurt.

with CF compared nutrition and growth parameters of those infants fed standard infant formula with those fed a protein hydrolysate formula.[49] There was no significant difference in growth parameters between the two groups of infants. Therefore, standard infant formulas should be used for the routine care of newly diagnosed infants with CF, rather than expensive hydrolyzed formulas.[49]

To close the gap between energy needs and the amount of calories the patient is able to consume, energy-dense foods can be added to the patient's diet. For example, butter, cheese, sour cream, and peanut butter can easily be added to the patient's favorite foods, as tolerated. **Exhibit 11-4** depicts one approach to increasing calories and protein.

A meta-analysis of the literature has been conducted on the various treatment approaches to the nutrition management of CF patients including oral supplementation, enteral nutrition, parenteral nutrition, and behavioral intervention, and their effectiveness on weight gain. Weight gain was produced in CF patients with all interventions. The behavioral

EXHIBIT 11-4 Instructional Handout on Increasing Calories

Calorie-Protein Boosters

—Some ways to hide extra calories and protein—

Powdered milk (33 cal/tbsp, 3 g pro/tbsp)
Add 2–4 tbsp to 1 cup milk. Mix into puddings, potatoes, soups, ground meats, vegetables, and cooked cereal.

Eggs (80 cal/egg, 7 g pro/tbsp)
Add to casseroles, meat loaf, mashed potatoes, cooked cereal, and macaroni & cheese. Add extra to pancake batter and french toast. (Do not use raw eggs in uncooked items.)

Butter or margarine (45 cal/tsp)
Add to puddings, casseroles, sandwiches, vegetables, and cooked cereal.

Cheeses (100 cal/oz, 7 g pro/oz)
Give as snacks or in sandwiches. Add melted to casseroles, potatoes, vegetables, and soup.

Wheat germ (25 cal/tbsp)
Add a tablespoon or two to cereal. Mix into meat dishes, cookie batter, casseroles, etc.

Mayonnaise or salad dressings (45 cal/tsp)
Use liberally on sandwiches, on salads, as a dip for raw vegetables, or as a sauce on cooked vegetables.

Evaporated milk (25 cal/tbsp, 1 g pro/tbsp)
Use in place of whole milk, in desserts, baked goods, meat dishes, and cooked cereals.

Sour cream (26 cal/tbsp)
Add to potatoes, casseroles, dips; use in sauces, baked goods, etc.

Sweetened condensed milk (60 cal/tbsp, 1 g pro/tbsp)
Add to pies, puddings, milkshakes. Mix 1–2 tbsp with peanut butter and spread on toast.

Peanut butter (95 cal/tbsp, 4 g pro/tbsp)
Serve on toast, crackers, bananas, apples, and celery.

Carnation Instant Breakfast (130 cal/pckt, 7 g pro/pckt)
Add to milk and milkshakes.

Gravies (40 cal/tbsp)
Use liberally on mashed potatoes and meats.

High Protein Foods

- MEATS—Beef, Chicken, Fish, Turkey, Lamb
- MILK & CHEESE—Yogurt, Cottage Cheese, Cream Cheese
- EGGS
- PEANUT BUTTER (with Bread or Crackers)
- DRIED BEANS & PEAS (with Bread, Cornbread, Rice)

Source: Courtesy of Pediatric Pulmonary Center, ©1990, University of Alabama at Birmingham, Birmingham, Alabama.

interventions were found to be as effective as more invasive medical procedures.[50] The best choice of intervention for a CF patient needs to be made on an individual basis.

Pregnancy

With the increased life expectancy of patients with CF, more women with the disease are becoming pregnant. In addition to the usual nutrient recommendations of CF, the increased energy needs of pregnancy must be taken into consideration. Emphasis needs to be put on proper weight gain. The woman's weight before and during pregnancy has a tremendous impact on the outcome for both mother and infant.[51] A pregnant woman with CF must add between 340 and 1000 kcal/day to her usual diet, depending on her weight at conception, degree of malabsorption, and level of pulmonary function and infection.[51] A diet sufficient in iron and calcium should be emphasized, and salt intake should not be restricted except for medical reasons.[45]

Intake of vitamins and minerals should be monitored and blood levels of fat-soluble vitamins should be obtained before and during pregnancy to determine the correct vitamin dose.[45] Mothers with CF have successfully breastfed their infants.[52] Breastfeeding further increases the energy demands on the patient with CF and needs to be considered on an individual basis.

CF-Related Diabetes

As with any patient with CF, the treatment goal for CFRD is to provide a diet that promotes optimal growth and development in children and adolescents, achievement and maintenance of normal weight in adults, and optimal nutritional status.[37,53] Other treatment goals include controlling hyperglycemia to reduce diabetes complications, avoiding severe hypoglycemia, and assisting the patient in adapting to another chronic illness from a psychological standpoint.[37] The patient with CFRD should be allowed as much flexibility as possible in the nutrition management of these two diseases.[37] The primary goal remains meeting the patient's energy needs.[37] Foods with carbohydrates have the greatest impact on blood sugar. Simple sugars can be included in the diet plan, but regular sodas and other sweetened beverages should be discouraged. The patient needs to learn how to recognize the carbohydrate content of foods, such as with the carbohydrate counting method, which is used when taking rapid acting insulin to cover meals.[37,53] For those on a fixed insulin regimen, blood sugars can be better managed by eating a consistent amount of carbohydrate at each of the three meals and three snacks in addition to eating at the same time each day.[38] Eating protein and fat-containing foods along with simple sugars slows the absorption of the simple sugars from the intestinal tract. Fat should continue to contribute about 40% of total calories, and protein intake should provide about 20% of total calories.[37]

Patient/Family Education

Patient and family education on nutrition management and its importance in the patient's overall health care is an integral component of the individual patient's care plan. A qualified, registered dietitian should be available to the patient and family to assist them in meeting the nutritional needs of the patient in the least invasive way possible. Information about the nutrient content of foods and suggestions for increasing the patient's caloric intake should be available.

Luder and Gilbride[54] studied the effects of nutrition counseling that was provided quarterly for a 4-year period, based on self-management skills in a group of patients with CF. These patients had significant increases in their energy intakes as well as in their body mass index values, without decline in pulmonary function over this time period.[54] Considerable emphasis should be placed on anticipatory guidance as an integral part of nutrition management.[27–29]

Feeding issues are prominent in this patient population, and the health professional needs to provide anticipatory guidance to the parents/caretakers of these patients to try and avoid battles over eating.[55,56] The importance of behavioral programs in the nutritional care of CF patients is receiving more and more recognition.[56]

For children with CF ages 1–12 years with or at risk of growth deficits, the CF Foundation recommends that intensive treatment with behavioral intervention in conjunction with nutrition counseling be used to promote weight gain.[19] Some strategies include complimenting children for appropriate feeding behaviors (e.g., trying a new food, taking consecutive bites), paying minimal attention to behaviors not compatible with eating (e.g., refusing food), and limiting mealtimes to 15 minutes specifically for toddlers.[57]

Supplemental Nutrition

Milkshakes and other high-calorie drinks can be used to supplement oral intake. Commercial oral beverages (such as Ensure or Boost) can also be used to boost calories, but they require additional expense.

Oftentimes, in spite of vigorous efforts by the patient, the patient's family, and dietetics professionals, it is very difficult to meet the patient's energy needs by the oral route alone. The CF Consensus Conference on pediatric nutrition for patients with CF suggests that the use of supplemental tube feedings be considered when optimization of feeding behaviors and addition of oral supplements have not achieved adequate weight gain or growth parameters. The patient and family need to be given the facts about available adjunct therapies in a positive way and be involved in the decision making.[27,28] CF centers have reported using various forms of tube feedings, including nasogastric, gastrostomy, and jejunostomy feedings. Tube feedings are often administered on a continuous basis while the patient is asleep. There are a variety of formulas available, some with fairly high concentrations of MCT oil, which can be helpful with fat absorption issues. Intact formulas of various caloric concentrations can be used. Hydrolyzed or elemental formulas can be used when appropriate and may reduce the amount of pancreatic enzyme replacement therapy needed; however, they are more costly than intact formulas. Both types of formulas have been associated with successful nutrition repletion.[45] Pancreatic enzyme administration with overnight tube feeds will be discussed briefly in the "Pancreatic Enzyme Replacement Therapy" section of this chapter.

Vitamin and Mineral Supplementation

Vitamins

Recommendations of the CF Consensus Conference for pediatric nutrition for patients with CF regarding vitamin supplementation can be found in **Exhibit 11-5**.[27,28] CF-specific multivitamin preparations are available on the market that contain high amounts of the fat-soluble vitamins A, D, E, and K in a water-miscible form to meet the needs of patients with CF. **Table 11-4** compares the amounts of fat-soluble vitamins in different CF-specific vitamins to a standard multivitamin. The use of the CF-specific multivitamins simplifies patients' vitamin regimen and helps to improve patient compliance.[30] Not all of the commercially available products contain the recommended level of vitamin K, so vitamin K status needs to be monitored carefully. Often additional vitamin K is given to patients as a prophylactic measure to prevent vitamin K deficiency, especially given the frequent usage of antibiotics.[24,25]

Vitamin D deficiency is common in CF and is found in infants diagnosed by newborn screening and in children and young adults.[35] The CF Foundation has specific recommendations in regard to treating a 25-OH vitamin D level that is less than 30 ng/mL.[53] The recommendation is to treat with Ergocalciferol for 8 weeks according to the following dosing schedule: 12,000 IU weekly for patients less than 5 years of age and 50,000 IU weekly for patients over 5 years of age. If 25-OH vitamin D levels remain less than 30 ng/mL 2–4 weeks after completion of treatment, then the vitamin D dose is increased to twice per week for 8 weeks. When repleting vitamin D levels it is always important to make sure the patient is also getting adequate calcium. If after this additional treatment, the levels are still less than 30 ng/mL, then phototherapy or increased sunlight exposure should be considered or a referral to endocrinology for consideration of use of more polar vitamin D supplements, which may be better absorbed.[53]

Vitamin D treatment recommendations as outlined by the CF Foundation Bone Consensus report may not correct low vitamin D levels.[58] A study by Green and colleagues at the Johns Hopkins Medical Institutions demonstrated the success of treatment with 50,000 IU of ergocalciferol once, twice, or three times weekly as 33%, 26%, and 43%,

EXHIBIT 11-5 Recommendations for Vitamin Supplementation

In addition to a standard, age-appropriate dose of nonfat-soluble multivitamins, the following should be given:

	Individual Vitamin Daily Supplementation			
	Vitamin A (IU)	Vitamin E (IU)	Vitamin D (IU)	Vitamin K (mg)
0–12 months	1500	40–50	400	
1–3 years	5000	80–150	400–800	
4–8 years	5000–10000	100–200	400–800	At least 0.3 mg*
> 8 years	10000	200–400	400–800	

*Currently, commercially available products do not have ideal doses for supplementation. In a recent review, no adverse effects have been reported at any dosage level of vitamin K. Clinicians should try to follow these recommendations as closely as possible until better dosage forms are available. Prothrombin time or, ideally, PIVKA-II levels should be checked in patients with liver disease, and vitamin K dose titrated as indicated.

Source: Borowitz D, Baker R, Stallings V. Consensus report on nutrition for pediatric patients with cystic fibrosis. *J. Pediatric Gastroenterology & Nutrition*. 2002;35(3):251.

respectively. This institution has since changed its practice to treating vitamin D deficiency with 50,000 IU daily for 4 weeks in both adult and pediatric patients, though there is no long-term data available yet to evaluate the success of this regimen.[58] Another study by Boas and colleagues evaluated the safety and efficacy of a 2-week trial of very high dose ergocalciferol (50,000 IU/day for 14 days) for children and adults with CF and PI, all of whom had 25-OH vitamin D levels < 30 ng/mL. When post-treatment vitamin D levels were measured, 94% of the participants demonstrated a significant increase in 25-OH vitamin D levels within the therapeutic (30–50 ng/mL) or high therapeutic (50–100 ng/mL) range, without any potentially toxic vitamin D levels noted.[59]

More institutions are now developing their own vitamin D treatment protocols in CF patients; further studies are needed to determine the appropriate treatment strategies.

Minerals

Minerals such as zinc, iron, and selenium have been studied in the CF population. Additional study is needed before specific supplementation recommendations can be made. A trial of zinc supplementation for 6 months may be initiated for patients with CF who have poor growth.[27,28] All patients with CF should be encouraged to consume at least the DRIs for calcium for their age group. For example, the DRI for calcium for children older than 9 years of age is 1300 mg.[60] CF patients who are on steroids, who have decreased dietary intake of calcium, and/or who are found to have decreased bone density may benefit from calcium supplementation. These minerals as well as other macro- and micronutrients are important to the overall nutritional status of the patient with CF. Therefore, eating a variety of foods should be encouraged.

Additional salt should be added to the diet during times of increased sweating, such as

- During hot weather
- With fevers
- During strenuous physical activity
- With profuse diarrhea

The additional salt compensates for the increased losses of sodium and chloride through perspiration. In most instances, liberal use of the salt shaker and the inclusion of high-salt foods in the diet will supply the needed sodium and chloride. Salt supplements may be used in instances of very heavy sweating. Both breastfed and formula-fed infants need supplementation with sodium chloride, particularly during hot weather.[27,28] Infants without CF require 2 to 4 mEq/kg/day of sodium; infants with CF are likely to require the upper end of this normal range, even when not exposed to heat stress.[27,28] In practice, 1/8 teaspoon per day of table salt is recommended for infants less than 6 months of age, and ¼ teaspoon per day is recommended for infants greater than 6 months of age. The table salt is typically added to the infant's formula throughout the day.[35]

Pancreatic Enzyme Replacement Therapy

Types of Available Enzymes

In an effort to confirm safety and efficacy of pancreatic enzymes, a new rule was issued in 2004 requiring makers of pancreatic enzyme products to obtain approval by the U.S.

TABLE 11-4 Comparison of Cystic Fibrosis–Specific Vitamin and Mineral Supplements in United States to Non–Cystic-Fibrosis–Specific Products[a]

Age	SourceCF[b,c] Drops, Chewables, and Softgels	ADEK Chewables[b,d]	AquADEKs[b,e] Drops and Softgels	Vitamax[b,f] Drops and Chewables	Poly-Vi-Sol Drops[g] and Centrum Chewables and Tablet
Vitamin A (IU): Retinol and Beta Carotene					
0–12 mo	4627 (1 mL) 75% BC[h]	—	5751 (1 mL) 87% BC	3170 (1 mL) 0% BC	1500 (1 mL) 0% BC
1–3 y	9254 (2 mL) 75% BC	—	11502 (2 mL) 87% BC	6340 (2 mL) 0% BC	3000 (2 mL) 0% BC
4–8 y	16,000/chewable 88% BC	9000/chewable 60% BC	Ages 4–10 y: 18,167/1 softgel 92% BC	5000/chewable 50% BC	3500/chewable 29% BC
> 9 y	32,000/2 softgels 88% BC	18,000/2 chewables 60% BC	Ages 10 and up: 36,334/2 softgels 92% BC	10,000/2 chewables 50% BC	7000/2 tablets 29% BC
Vitamin E (IU)[i]					
0–12 mo	50 (1 mL)	—	50 (1 mL)[i]	50 (1 mL)	5 (1 mL)
1–3 y	100 (2 mL)	—	100 (2 mL)[i]	100 (2 mL)	10 (2 mL)
4–8 y	200/chewable	150/chewable	Ages 4–10 y: 150/1 softgel[i]	200/chewable	30/chewable
> 9 y	400/2 softgels	300/2 chewables	Ages 10 and up: 300/2 softgels[j]	400/2 chewables	60/2 tablets
Vitamin D (IU)					
0–12 mo	500 (1 mL)	—	400 (1 mL)	400 (1 mL)	400 (1 mL)
1–3 y	1000 (2 mL)	—	800 (2 mL)	800 (2 mL)	800 (2 mL)
4–8 y	1000/chewable	400/chewable	Ages 4–10 y: 800/1 softgel	400/chewable	400/chewable
> 9 y	2000/2 softgels	800/2 chewables	Ages 10 and up: 1600/2 softgels	800/2 chewables	800/2 tablets
Vitamin K (μg)					
0–12 mo	400 (1 mL)	—	400 (1 mL)	300 (1 mL)	0
1–3 y	800 (2 mL)	—	800 (2 mL)	600 (2 mL)	0
4–8 y	800/chewable	150/chewable	Ages 4–10 y: 700/1 softgel	200/chewable	10/chewable
> 9 y	1600/2 softgels	300/2 chewables	Ages 10 and up: 1400/2 softgels	400/2 chewables	50/2 tablets
Zinc (mg)					
0–12 mo	5 (1 mL)	—	5 (1 mL)	7.5 (1 mL)	0
1–3 y	10 (2 mL)	—	10 (2 mL)	15 (2 mL)	0
4–8 y	15/chewable	7.5/chewable	Ages 4–10 y: 10/softgel	7.5/chewable	15/chewable
> 9 y	30/2 softgels	15/2 chewables	Ages 10 and up: 20/2 softgels	15/2 chewables	22/2 tablets

[a] The content of this table was confirmed December 2008. Products also contain a full range of water-soluble vitamins; see SourceCF.com for content.

[b] CF-specific products.

[c] SourceCF Liquid, Chewables, and Softgels are registered trademarks of SourceCF Inc., a subsidiary of Eurand Pharmaceuticals, Inc.

[d] ADEK Chewables is a registered trademark of Axcan Pharma, Inc.

[e] AquADEKs Liquid and Softgels are registered trademarks of Yasoo Health Inc.

[f] Vitamax Drops and Chewables are registered trademarks of Shear/Kershman Labs, Inc.

[g] Poly-Vi-Sol Drops is a registered trademark of Mead Johnson and Company. Centrum Chewables and Tablets are registered trademarks of Wyeth Consumer Care.

[h] Beta carotene.

[i] ∝-Tocopherol.

[j] Contains mixed tocopherols.

Abbreviation: BC, beta carotene.

Source: Reprinted from Pediatric Clinics of North America, Vol. 56, Michel S, Maqbool A, Hanna M, Mascarenhas M. Nutrition management of pediatric patients who have cystic fibrosis. *Pediatric Clin N Am.* 2009;56:1123–1141. Copyright 2009, with permission from Elsevier.

Food and Drug Administration (FDA) by April 28, 2010. There are 3 brands which received FDA approval (**Table 11-5**), and they contain varying amounts of lipase, which breaks down fat; protease, which breaks down protein; and amylase, which breaks down carbohydrate.

The nonproprietary name of these products is pancrelipase. The products are available in capsule form and feature an enteric coating that protects the enzymes from inactivation in the acid environment of the stomach. The enzymes become activated in the alkaline pH of the duodenum.

Dosage/Administration

There is a CF consensus statement on the use of pancreatic enzyme supplements.[61,62] Extremely high doses of pancreatic enzymes have been associated with fibrosing colonopathy or strictures in the colon in CF patients.[63,64] A recommended starting dose for infants is 2000 to 5000 units of lipase per 4 oz feeding, though this may be less in newborns who take less volume at each feeding.[57] Another proposed weight-based enzyme dosing schedule is starting with 1000 units of lipase/kg body weight/meal for children younger than 4 years of age and 500 units of lipase/kilogram body weight/meal for those over age 4.[61,62] The usual enzyme dose for snacks is one-half of the mealtime dose. It is recommended not to exceed 2500 units of lipase/kg body weight/meal, with a maximum daily dose of 10,000 units lipase/kg body weight. Calculating units of lipase/kilogram body weight/meal has become an integral component of routine care. For example, a 10-year-old child weighing 35.7 kg who takes a mealtime dose of three capsules of a pancreatic enzyme preparation containing 20,000 units of lipase per capsule will receive 1681 units of lipase/kg body weight/meal (60,000 units of lipase divided by 35.7 kg = 1681 units of lipase/kg body weight/meal). Careful monitoring of the patient's growth, stool pattern, and the absence or presence of gastrointestinal symptoms is necessary to determine the adequacy of therapy. Monitoring and adjusting the dosage as needed should be continued throughout the patient's treatment. If the patient with CF is still exhibiting symptoms of malabsorption after reaching a maximum enzyme dose, it may be because the stomach contents are too acidic when reaching the small intestine and are inactivating the enzymes. In these cases, the addition of bicarbonate or other drugs that inhibit gastric acidity may be helpful.[61,62] Nonpancreatic reasons for malabsorption should also be considered.

Enzymes should be taken immediately prior to meals and snacks that contain fat, protein, and complex carbohydrate. The enterically coated enzymes should not be chewed or crushed. For infants and small children who are unable to swallow a capsule, the capsule can be opened and the contents mixed with a soft, acidic food such as applesauce. Enzymes mixed with food should be used within 30 minutes of mixing. When the enterically coated enzymes are mixed with a higher pH food such as pudding or milk, the enzymes will become activated and begin breaking down the food. Older patients swallow their enzymes whole prior to eating a meal or snack.

There is currently no consensus on enzyme dosing for gastrostomy tube feedings, and often it can be difficult to dose enzymes appropriately. The CF Foundation recommends that

TABLE 11-5 Examples of Pancreatic Enzymes

Enzyme	Form*	Lipase USP Units	Protease USP Units	Amylase USP Units
Creon 6[1]	Delayed release capsules	6000	19,000	30,000
Creon 12[1]	Delayed release capsules	12,000	38,000	60,000
Creon 24[1]	Delayed release capsules	24,000	76,000	120,000
Pancreaze MT4[2]	Delayed release capsules	4200	10,000	17,500
Pancreaze MT10[2]	Delayed release capsules	10,500	25,000	43,750
Pancreaze MT16[2]	Delayed release capsules	16,800	40,000	70,000
Pancreaze MT20[2]	Delayed release capsules	21,000	37,000	61,000
ZENPEP 5[3]	Delayed release capsules	5000	17,000	27,000
ZENPEP 10[3]	Delayed release capsules	10,000	34,000	55,000
ZENPEP 15[3]	Delayed release capsules	15,000	51,000	82,000
ZENPEP 20[3]	Delayed release capsules	20,000	68,000	109,000

*Form as described by respective company

[1]Solvay Pharmaceuticals: http://www.creon-us.com/default.htm

[2]Ortho-McNeil-Janssen Pharmaceuticals: http://www.pancreaze.net

[3]Eurand: http://www.zenpep.com/pdfs/zenpep_PI_09.pdf

patients take their usual meal dose of pancreatic enzymes by mouth prior to the initiation of the feeding.[27,28] If receiving continuous overnight tube feeds, some patients may need to take additional enzymes during the middle of the night or at the end of their feeding.[27,28] Giving enterically coated microspheres or microtablets via the feeding tube as a med during a feed or prior to a feed is another option but may result in clogging of the feeding tube. Unfortunately, there is currently no optimal way to dose enzymes during continuous tube feeds. A patient's tolerance to their tube feeds, as well as if the patient will be able to comply with the enzyme regimen at home need to be assessed. It is important to tailor the enzyme regimen to the individual needs of each patient.

Patient Compliance

Administering enzymes to an extremely young infant can be a frustrating endeavor for the parent or caretaker, primarily because of the young infant's natural extrusion reflex. After a few months of age, taking enzymes becomes part of a patient's daily routine. Parents of toddlers should be warned against allowing the child to "graze" throughout the day because this makes enzyme dosing difficult. In the preadolescent and adolescent age groups, patient compliance with enzyme administration can become a big issue. Some schools require the child to come to the school office for medications, and this may be a source of embarrassment and alienation from peers for the child with CF. The lack of compliance needs to be discussed with the child and a solution must be found that is agreeable to the child, parents, and school authorities.

Pancreatic enzyme therapy is very expensive and contributes significantly to the overall cost of the disease management. Enzymes are often covered by third-party payers and some state programs for children with special healthcare needs.

Referral to Food/Nutrition and Other Resources

Referral to food and nutrition resources such as the USDA's Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) program and the Food Stamp Program should be made based on the individual's needs. In some states, referrals can be made to the state program for children with special healthcare needs for aid in obtaining supplemental feedings, enzymes, and vitamins. Children who participate in the Child Nutrition Program at their school will need diet prescriptions for high-calorie, high-protein diets sent to their schools.

CF has a tremendous impact on patients and their families emotionally, physically, and financially. Most CF centers provide an interdisciplinary team approach to the care of these children and their families to better help them meet their many needs.

Alternative/Complementary Medicine

As with other chronic diseases, the use of alternative/complementary medicine in CF care has sparked the interest of patients with CF, their families, and health professionals. To date, little published science-based research exists in the area of alternative and complementary medicine in CF care. More and more CF centers are surveying their patients to ascertain the extent of alternative medicine practices. Currently, patients with CF are obtaining a lot of their information from the Internet, with many CF Internet sites having links to alternative medicine sites. CF centers need to study alternative medicine practices further so that CF caregivers can advise patients and their families as to the safety and efficacy of various therapies.

Patients at three CF centers participated in a survey regarding the use of nonmedical treatment.[65] Nonmedical treatment was used by 66% of the population; 57% of the population used at least one religious treatment; 27% used at least one nonreligious treatment.[65] Group prayer (48%) was the most common nonmedical therapy, and 92% of those participating in group prayer perceived benefit. Chiropractors were consulted by 14%, with 69% of these patients perceiving benefit. Nutrition modalities other than those prescribed by the CF caretakers were employed by 11% of the population; 78% of these patients used these treatments frequently (more than five times); 87% perceived benefit. Meditation was used by 5%, with 94% reporting perceived benefit.

It is important that CF caregivers ask questions about alternative/complementary medicine practices when interviewing patients with CF and their family members, especially in regard to ingested substances. This is especially important information to obtain from patients who may be participating in studies with experimental drugs because the possibility exists that substances such as unregulated botanical products may confound the study results.

Identification of Areas Needing Further Research

There are many unanswered questions about CF in general and, more specifically, in regard to nutrition. Additional research is needed to determine specific nutrient requirements of patients with CF in regard to energy, protein, vitamins, minerals, and EFAs. The most appropriate method for delivering these nutrients must be determined. Further study on the psychosocial and emotional benefits and drawbacks of invasive nutritional therapy and the effect of improved nutritional status on body composition and the progression of the pulmonary disease would be beneficial. More study is needed on the role of anabolic agents such as insulin and growth hormone and on appetite stimulants, such as megastrol acetate, to determine the cost/benefits of these adjunct therapies. With lung transplantation becoming more

available to CF patients, appropriate nutrition management pre- and posttransplantation will need further study.

CF is a complicated disease, affecting many organs of the body, and the disease process is highly variable. Proper nutritional care is an integral part of its therapy. Therefore, every patient and family deserves individualized treatment and support from an interdisciplinary team of health professionals, including a qualified dietetics professional, trained in the care of patients with CF.

Bronchopulmonary Dysplasia

Bronchopulmonary dysplasia (BPD) was first described by Northway and colleagues[66] in 1967 as a form of chronic lung disease seen in infants with severe hyaline membrane disease who required mechanical ventilation and high concentrations of oxygen for prolonged periods of time. Since that time, improvements in neonatal intensive care and changing epidemiology or prematurity have resulted in changes in both the definitions of BPD and the pathology of the lung disease. Most recently, clinical practice has advanced, resulting in a decrease in lung injury in larger (greater than 1200 gram birth weight) and more mature infants. At the same time, more and more premature infants are surviving at earlier gestational ages and lower birth weights. The National Institute of Child Health and Human Development/National Heart, Lung and Blood Institute refined the definition of BPD to reflect differing criteria for infants born at less than or greater than 32 weeks gestation.[67] The expanded definition includes different diagnostic criteria for mild, moderate, and severe forms of the disease.[67] For example, the definition of severe BPD for an infant with a gestational age of less than 32 weeks is the need for 30% oxygen or more and/or positive pressure at 36 weeks postmenstrual age or discharge, whichever comes first.[67]

Today's definition of BPD includes infants who have had an acute lung injury with minimal clinical and radiographic findings, as well as those with major radiographic abnormalities. BPD represents a continuum of lung disease. The pathogenesis of BPD is multifactorial but includes primarily arrested lung development due to the necessary accelerated maturation of the lungs due to premature birth. Severe, diffuse, acute lung injury and an early inflammatory response exacerbate the abnormal lung development due to primary injury and inadequate immature repair mechanisms. The lungs may be damaged by the barotrauma from the use of intermittent positive pressure ventilation (IPPV) and by oxygen toxicity from the high concentrations of oxygen required by these infants early in life.[68,69] Infection may play a role in the pathogenesis of BPD.[68] Other factors that may contribute to the development of the disease include increased fluids contributing to pulmonary edema[70] and inadequate early nutrition impeding lung reparative processes.[71,72]

Today, younger and smaller preterm infants are surviving with the aid of mechanical ventilation. Consequently, BPD has become one of the most common sequelae of newborn intensive care unit stays. BPD has become rare in premature infants weighing 1500 grams or more with uncomplicated respiratory distress syndrome. This is due to the use of antenatal steroids, surfactant replacement therapy, gentler ventilation that reduces barotrauma, better nutrition, and careful use of supplemental oxygen.[73] However, the incidence of BPD is about 30% of infants with birth weight under 1000 grams and is higher in lower birth weight infants. As BPD patients are followed over time, chronic lung disease remains a major clinical problem for many of these patients into late childhood and early adolescence.[68,74]

Signs of respiratory distress, such as chest retractions, tachypnea, crackles, and wheezing, characterize BPD. Supplemental oxygen therapy may be required, and there may be changes on the patient's chest radiograph. Pulmonary complications of BPD may include recurrent atelectasis, pulmonary infections, and respiratory failure requiring mechanical ventilation. Other complications of BPD include pulmonary edema, cor pulmonale, poor growth, neurodevelopmental delays including delayed feeding skills, and cardiovascular problems.

The primary goal of BPD management is to provide the patient with the necessary pulmonary support during the acute and chronic phases of the disease to minimize lung damage and to maintain optimal oxygen saturation. This may include mechanical ventilation, supplemental oxygen, anti-inflammatory and β-adrenergic aerosols, and diuretic therapy. Of equal importance is the provision of adequate nutrition, not only for growth and development, but also to compensate for the demands of the disease. Growth of new lung tissue can occur in humans until about 8 years of age. Theoretically, a BPD patient can "outgrow" the disease if adequate pulmonary and nutritional support can be provided.

Increased Nutrient Requirements

Adequate nutrition is important for patients with BPD but can often be a challenge for parents and health providers. The following section will further explore the nutrition implications of BPD.

Effects of Prematurity

Most babies who develop BPD are premature infants, so it is easy to see that these infants have little fat, glycogen, or other nutrients in reserve, particularly iron, calcium, and phosphorus. Faced with the demands of prematurity and the stress of BPD, the infant can quickly develop a state of negative nutrient balance.

Effects of Bronchopulmonary Dysplasia

Several factors increase the energy and nutrient requirements of BPD patients, including the following: