Carol Rees Parrish, R.D., MS, Series Editor

Nutrition Issues in Cystic Fibrosis

Barbara Goodin

Of the 22,300 individuals currently identified with cystic fibrosis (CF), nearly 4% were identified after the age of 18 (4). Health care clinicians should be aware of symptoms of CF that warrant testing for CF in order to provide interventions in a timely manner. A sweat test result >60 mmol/L chloride on two separate occasions confirms the diagnosis (3). However adult patients may present with symptoms that are not phenotypic of the disease, with borderline sweat test results. Medical management of CF is multifaceted. The role of nutrition in improving mortality has been established. Early identification of nutrition issues with appropriate intervention plays a vital role in pulmonary health, which is key to longevity. This article provides an overview of nutrition issues encountered with this population, offering guidelines for nutrition management. Pancreatic function testing, enzyme dosing, and vitamin supplementation, as well as interventions that are helpful when patients are in nutrition failure are also reviewed.

INTRODUCTION

Cystic fibrosis (CF), a multisystem progressive disease, is characterized by exocrine pancreatic insufficiency, chronic lung disease, excessive loss of sweat electrolytes, and malnutrition. The defect in the CF gene leads to abnormal transport of sodium, chloride, and water across the cell membrane causing the formation of thick, sticky secretions in airways that provide a rich medium for bacterial growth. Pulmonary infections, which increase resting metabolic rate, are the major cause of the downward spiral of weight loss, weakened lung tissue, and malnutrition. The individual with CF must work diligently to consume adequate energy in order to meet increased needs caused by the increased work of breathing and altered digestive absorption. Since pulmonary function is strongly linked with adequate nutrition and weight gain, monitoring weight and pulmonary function every three months is considered the standard of care for patients with CF.

Barbara Goodin, M.S., R.D., Nutrition Specialist Inborn Errors of Metabolism, Cystic Fibrosis and Pediatric Diabetes, University of Virginia Health Systems, Department of Pediatrics, Division of Medical Genetics, Charlottesville, Virginia.

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DIAGNOSING CYSTIC FIBROSIS

Cystic fibrosis occurs in 1 in 3,200 births among the Caucasian population (1). In the US, 85% of those diagnosed with CF are identified before age one year (2). However, it is increasingly being identified in adults. Approximately 2% of patients identified present with an atypical phenotype consisting of chronic sino-pulmonary disease, pancreatic sufficiency, and either a borderline (40–60 mmol/L) or normal (<40 mmol/L) sweat test (3). Testing for CF should be performed on anyone with a family history of CF, as well as those with one or more symptoms set out in Table 1. The diagnosis of CF is confirmed with a sweat test result of >60 mmol/L chloride concentration. It is important that the test is interpreted in the context of the patient's age and clinical picture by a physician knowledgeable about CF. For detailed information regarding diagnostic procedure, please refer to the CFF Consensus Statement (3). Two positive sweat test results performed at separate occasions are recommended to confirm the diagnosis (3).

Adults with late diagnosed CF are usually pancreatic sufficient with inconclusive sweat test results. Mutation analysis is recommended to identify adults with CF who are pancreatic sufficient and have borderline sweat test results. The 2000 CFF Patient Registry reported that of the 22,301 patients enrolled, 831 (3.7%) were diagnosed at or after the age of 18, with chronic respiratory problems being the most common presentation (4). A strong link has been established between nutritional status, lung function, and survival in children and adults with CF (5–7). Predicted age of survival is currently 32.9 years of age (8). Research has also found a strong link between pulmonary function and nutritional status (9). Achieving and maintaining adequate nutrition status is an essential component of survival.

Table 1
Symptoms That Warrant Sweat Testing

- Acute or persistent respiratory symptoms
- Meconium ileus / distal intestinal obstruction syndrome (DIOS)
- Rectal prolapse
- Steatorrhea or abnormal stools
- Failure to thrive or malnutrition
- Family history
- Recurrent Pancreatitis
- Chronic sinopulmonary disease / nasal polyps
- Hepatobiliary disease
- Digital clubbing
- Salt loss syndrome with acute salt depletion
- Male urogenital abnormalities (obstructive azospermia)

Orenstein, David M. Cystic Fibrosis: A Guide for Patient and Family, 2d ed. Yankaskas, James R. Cystic Fibrosis Adult Care: Consensus Conference Report, 2004

WHY IS NUTRITION A RISK FACTOR

In adults with CF, wasting associated with decreased lung function has been a predictor of mortality, but more recently, wasting has been found to be an independent predictor (5). In children, studies have indicated that the degree to which a CF child is underweight was an independent factor which adversely affected survival and more recently short stature has been identified as an independent risk factor of survival (10, 11). Treatment goals aim to prevent the cascade of wasting precipitated by reduced lung function, increased energy expenditure, decreased intake due to poor appetite and increased losses due to malabsorption. The expectation that individuals with CF will be short and thin is no longer acceptable. Early identification of nutrition risk is necessary in order to intervene at a time when interventions can make a positive impact on outcome. Once ideal body weight falls below 75%, nocturnal feeds via g-tube while beneficial, may never achieve the desired outcome of bringing weight back up to 90% of ideal or greater. Striving to improve outcomes with early education regarding supportive therapies, early identification of patients at nutrition risk, and institution of supportive therapies before the downward spiral begins has become the standard of care at the University of Virginia Health Systems CF Center.

ASSESSMENT OF NUTRITION STATUS

Early assessment of failing nutritional status is an essential component of care for individuals with cystic

Table 2
Definitions of Nutrition Status in Patients with Cystic Fibrosis (13)

Age Group	*At Risk*	*Nutritional Failure*
0–2 years old	Weight for length 10%–25%	Height Percentile <5%, or weight for length <10% or IBW <90%
2–20 years	BMI percentile 10th–25th	BMI percentile <10% or IBW <90%
Adults	BMI 19–20	BMI <19 or percent IBW <90%

fibrosis. Among the most powerful tools to assess nutritional status are Body Mass Index (BMI) and percent ideal body weight (% IBW) (12). Height for age and weight for length are the recommended parameters for children less than 2 years. For adults, IBW range as estimated by the Metropolitan Life Insurance Company height and weight tables for individuals of small frame is a useful tool in both assessing and educating adults with CF as to their nutritional status (13). These tables are available as hard copy and on compact disc from Axcan Scandipharm (see Table 6 for contact information). The Clinical Practice Guidelines for Cystic Fibrosis of the CF Foundation contains guidelines for nutrition classification (14). Patients who are >90% IBW are considered well nourished, 85%–89% IBW underweight, 80%–84% IBW mildly malnourished, 75%–79% IBW moderately malnourished, and <75% IBW severely malnourished. More recently the CF Foundation has established protocols by which to classify the nutrition status of the CF patient that can be used to quantify the need for more frequent follow-up and earlier interventions (Table 2) (15). Patients who are found to be at nutrition risk will need closer follow-up with guidance from a nutritionist experienced with CF. Patients classified as "nutrition failure" may require enteral nutrition support in order to facilitate improvement in nutrition status.

GASTROINTESTINAL INVOLVEMENT

Eighty-five to ninety percent of patients with CF are exocrine pancreatic insufficient (PI) (16). Patients who are pancreatic insufficient are more likely to have more severe lung disease, malnutrition and liver involvement while those who are pancreatic sufficient are at higher risk of developing pancreatitis (17). The gold standard test for determining exocrine function has been the 72-hour fecal fat test, which requires collection of stool for 72 hours while at the same time keeping accurate diet records of all food intake or consuming a fixed amount of fat. Fecal fat excretion [(grams of fat)/fat ingested × 100%] can be calculated from that data. Percent fecal fat excretion >7% of the dietary fat ingested indicates malabsorption (18). Recently Fecal Elastase-1 (FE-1) has been recognized as a valid tool for determining pancreatic exocrine function in the CF population (19–21). A FE-1 value of >200 µg/g stool indicates pancreatic sufficiency (18). FE-1 is used to establish pancreatic exocrine function and is not affected by pancreatic enzyme replacement therapy (19). Fecal fat studies are currently the only tool reliable enough to quantify the effectiveness of enzyme dosing for individuals who are PI. In clinical practice symptoms are often the strongest predictors of malabsorption. If the clinical picture suggests malabsorption, a trial of pancreatic enzymes is given. If patient response is the reduction of symptoms and/or improved weight gain, enzyme therapy is deemed effective, and therefore continued.

Table 3
Symptoms of Malabsorption

GI Symptoms
- Abdominal pain, cramping, bloating and flatus
- Loose and frequent stools
- Steatorrhea (visible oil, foul odor)

Other indicators
- Fat soluble vitamin deficiency
- Poor weight for height

Table 4
Dosing Pancreatic Enzymes (24)

Age Group	*Dose*	*Adjusting Dose*
Infants	2000–4000 Units lipase/120 ml formula or with each nursing OR 450–900 units lipase/gram of fat	Increase by 2000–2500 Units lipase per feed as volume increases or if symptoms of malabsorption return
Children <4 years	1,000–2,000 Units lipase/kg/meal OR 500–4,000 Units lipase/gm fat	Snacks: 1/2 meal dose Compare U lipase per fat gram when weight dose appears above range.
Adults and children >4	500–2000 Units lipase/kg/meal OR 500–4,000 Units lipase/gm fat	Snacks: 1/2 meal dose Compare U lipase per fat gram when weight dose appears above range.

Note:
- Doses of lipase greater than 2500 units/kg/meal (10,000 units/kg/d) are not recommended (23).
- >6,000 units lipase/kg/meal has been associated with colonic strictures in children <12 years (23, 24).

It is then necessary to find the optimal dose to minimize symptoms. Refer to Table 3 for symptoms of malabsorption.

Abdominal pain occurs with frequency among the CF population (22). Sorting out the cause of the discomfort can be a challenge. Of the many causes of abdominal pain, only distal intestinal obstructive syndrome (DIOS) and fibrosing colonopathy are unique to cystic fibrosis (4). The term DIOS has replaced the previous term of *meconium ileus equivalent* because the obstruction can occur within the right colon as well as the terminal ileus. Typical symptoms include decreased stool output, colicky periumbilical and /or right-lower-quadrant pain, abdominal distension, nausea and vomiting. The goal of management is to institute treatment early to avoid the need for surgical intervention. The reader is referred to the CF Adult Care Consensus Conference Report for a review of approaches to diagnosing and managing abdominal pain in the CF patient (4).

USE OF PANCREATIC ENZYMES

Pancreatic enzymes are dosed by units of lipase/kg/meal, or units of lipase/gram fat ingested. Dosing lipase based on estimated fat intake while biologically more accurate, is not always feasible. Therefore, a weight-based method has been developed as a practical way to determine the dose of enzymes per meal. Recommendations for dosing enzymes are set out in Table 4. Newly diagnosed adults should start with 500 Units lipase/kg/meal and half that for snacks. If fat malabsorption is quickly corrected, then attempts should be made to reduce the dose to the minimum effective dose. If symptoms continue, increase the lipase dose by 150–250 Units lipase/kg/meal until symptoms improve, up to a maximum dose of 2500 Units lipase/kg/meal or 4000 Units lipase/gm fat/meal (24).

In the mid 1990's fibrosing colonopathy prompted the CF community to review enzyme dosing practices. Very high enzyme doses of >6,000 Units lipase/kg/meal, or 10,000 Units lipase/kg/day were associated with fibrosing colonopathy (23). When enzyme dose approaches this level, it is helpful to determine fat intake. When calculating enzyme dose based on fat grams consumed, lipase usually falls within the guideline of 500–4000 Units lipase per gram of fat. Comparing Units lipase/gm fat ingested becomes a helpful tool to evaluate the need for continuation of what appears to be a dose that is higher than that which is considered safe.

Pancreatic enzymes are enteric coated which protects the enzyme from the acidic environment of gas-

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Table 5.
Name-Brand Enzymes Currently Available

Enzyme Manufacturer	*Units Lipase*	*Units Protease*	*Units Amylase*	*Bead size*	*How Supplied*	*Cost/1000 Units lipase/capsule*[1]
Solvay						
Creon 5	5,000	18,750	16,600	Minimicrospheres*	100 & 250	.09
Creon 10	10,000	37,500	33,220	Minimicrospheres*	100 & 250	.088
Creon 20	20,000	75,000	66,400	Minimicrospheres*	100 & 250	.086
Axcan Scandipharm						
Ultrase	4500	25,000	20,000	Microspheres*	100	.106
UltraseMT12	12,000	39,000	39,000	Minitablets	100	.082
UltraseMT18	18,000	58,500	58,500	Minitablets	100	.085
UltraseMT20	20,000	65,000	65,000	Minitablets	100	.085
McNeil						
Pancrease	4500	25,000	20,000	Microspheres*	100 & 250	.10
PancreaseMT4	4000	12,000	12,000	Microtablets	100	.10
PancreaseMT10	10,000	30,000	30,000	Microtablets	100	.10
PancreaseMT16	16,000	48,000	48,000	Microtablets	100	.10
PancreaseMT20	20,000	44,000	56,000	Microtablets	100	.10
Digestive Care, Inc.						
Pancreacarb MS4	4000	25,000	25,000	Microspheres* w/ bicarbonate buffer	100	.17
Pancreacarb MS8	8000	45,000	40,000	Microspheres* w/ bicarbonate buffer	100	.15
Pancreacarb MS16	16,000	52,000	52,000	Microspheres w/ bicarbonate buffer	100	.13

[1]Prices from CF Services Pharmacy pricing 2005
*Indicates smallest beads

tric juices. Capsules are filled with microencapsulated enzyme beads or microspheres that mix with the stomach contents, and enter the duodenum. As the pH approaches 6, the enteric coating dissolves, releasing enzyme in the small intestine where nutrient breakdown is meant to occur. However, individuals with CF often have increased gastric acid secretion, and inadequate or deficient bicarbonate secretion. This combination reduces the effectiveness of pancreatic enzymes in the upper GI tract. It may be necessary to use adjunctive therapies to improve efficacy of enzyme dose. Use of proton pump inhibitors (PPI's) and histamine-2 blockers in conjunction with pancreatic enzymes may improve digestion in cases where enzyme dosing is at the upper limit, but symptoms of malabsorption persist. Abnormal gastric and intestinal motility, reduction of bile acids, precipitation of bile acids, and thick intestinal mucous lining may also contribute to fat malabsorption (25).

It is important that enzyme beads are not broken prior to swallowing as this will expose the enzyme to gastric acid causing degradation. If capsules cannot be swallowed whole, sprinkle the contents onto a pureed acid-based food such as applesauce or other pureed fruit and feed with a spoon, being careful to prevent

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Table 6.
Incentive programs

Program Name	*Sponsor*
Cystic Fibrosis Services Pharmacy, Inc. Registration: by calling 800-541-4959 or on line at www.CFServicesPharmacy.com To order refills: refills@cfserv.com	Cystic Fibrosis Foundation 6931 Arlington Road, 2nd floor Bethesda, MD 20814
Comprehensive Care Program for CF P.O. Box 52065 Phoenix, AZ 85072-9152 Enrollment No: (866) 292-2679 Care First for CF P.O. Box 52065 Phoenix, AZ 85072-9152 Enrollment No: (866) 292-2679 Assist Program Enrollment No.: (866) 292-2679	Axcan Scandipharm, Inc. 22 Inverness Center Parkway Birmingham, AL 35242 Customer service (877) 657-6737 www.axcan.com
Wee Care (Administered through CF Services Pharmacy) O.N.E. Program Customer Service 1-800-241-1643 Extra Helpings (Administered through CF Services Pharmacy)	Solvay Pharmaceuticals, Inc. 901 Sawyer Road Marietta, GA 30062-9987 Customer Service 1-800-241-1643
Source Points Helping Hands Program	Source CF 6705 Odyssey Drive Huntsville, AL 35806 www.sourcecf.com (256) 319-1416 (888) 419-8357

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Description	*Restrictions*
A full service pharmacy to provide ease of access and availability to CF medications as well as assistance with insurance issues. Provides pharmacy services, patient advocacy service, patient education materials, pancreatic enzymes, pulmonary medications, inhalers, antibiotics, diabetes medications and supplies, nutritional items and other over-the-counter items.	None Mail Rx to: 7472 South Tucson Way, #100 Centennial, CO 80112. or fax: 800-263-0251
Patients using Ultrase enzymes can receive 24 Scandishakes or two Scandical canisters and ADEK vitamins with proof-of-purchase of Ultrase enzymes. Also provide a certificate to obtain a Flutter mucus clearance device and *Cystic Fibrosis: A Guide for Patient and Family* by David Orenstein, MD	Must purchase Ultrase Enzymes
Free Ultrase Microspheres, Ultrase MT12 or Viokase Powder ADEK Pediatric Drops Copy of *Cystic Fibrisos: A Guide for Patient and Family* by David Orenstein, MD	CF patients under 2 years
Free Ultrase enzymes, Viokase powder enzyme, or URSO for one year for patients who qualify after completing enrollment application. Initial 30-day presumptive eligibility is done over telephone.	Must have total annual income below Federal Poverty Level with limited prescription drug coverage and living in the US.
Free pancreatic enzyme (Creon Minimicrospheres) and Vitamax liquid pediatric drops multivitamins	CF patients under 2 years of age
Provides 12 cans of Nestle Instant Breakfast Plus, or Nutren 1.0 per month with proof-of-purchase of Creon pancreatic enzymes. Fax: enrollment form and proof of purchase to 1-770-578-5901	CF patients 2 years and older
Free Vitamax Pediatric Drops or Chewable Tablets with proof-of-purchase of 30-day supply of Creon enzymes.	For patients who do not qualify for federal medical assistance
A program to help reduce the out-of-pocket expenses for patients to acquire a variety of Source CF products that insurance would not cover such as, vitamins, nebulizers or aerosol masks	For individuals who have obtained the Med Pulse vest and not eligible for federal medical assistance.
Provides free Source CF vitamins Soft Gels with use of X-Gen Pharmaceuticals brand of colistimethate. 1 bottle monthly	Use X-Gen Colistimethate; not receiving federal medical assistance.

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chewing prior to swallowing. In instances where gastric emptying time is increased, and GI transit is rapid, the addition of small amounts of non-enteric coated enzyme (Viokase powder) may improve fat digestion (25). When using this enzyme, it is important to avoid inhaling the enzyme powder, which will irritate the mucosal lining of the nasal passages, and to be careful that all enzyme powder has cleared the oral cavity.

The Cystic Fibrosis Foundation has discouraged the use of generic enzymes. Generic enzymes, while containing a comparable dose of lipase, may not be biologically equivalent because of varied enteric coatings used by different manufacturers, which may delay dissolution. Individual response will vary from one enzyme to another (24). Refer to Table 5 for a listing of the name-brand enzymes currently prescribed.

One enzyme manufacturer has combined a bicarbonate buffer with enzyme within the microsphere beads that improves the pH of the gastric environment and thus enzyme activation. Combining the bicarbonate-buffered enzyme with the established enzyme has proven effective in facilitating weight gain in children who were not experiencing symptoms of malabsorption, but were not gaining as expected. This practice has the added benefit of allowing patients to continue participating in incentives offered by one enzyme manufacturer while improving digestion with the addition of a second enzyme. Lipase dosing is maintained within the recommended guidelines with the combined therapy. The combination of enzymes with different dissolution rates may also improve absorption by providing better enzyme coverage at various sites in the small intestine (23).

Table 7
Factors that affect enzyme efficacy

- Outdated prescription
- Improper storage of enzymes (exposure to heat)
- Generic enzymes that are not bioequivalent
- Chewed or crushed enzyme beads
- Prolonged exposure of beads to alkaline foods or fluids
- Excess acidity of gastric juices
- Slow gastric emptying time
- Timing of enzyme administration
- Diet content is high fat or contains tomato-based foods

Incentive programs are provided by various companies to assist the CF patient in obtaining nutrition supplements, vitamins, or free enzymes when the patient uses their product. They are either administered through the CF Services Pharmacy, or the company providing the incentive. A simple telephone call by the patient or health care provider to enroll is often all it takes to start the program. There may be a monthly proof-of-purchase required, as well as age or income requirements. See Table 6 for detailed information regarding incentive programs currently available to the CF patient.

EFFICACY OF ENZYMES

Factors that affect efficacy are enzyme bead size, diet content, acidity of gastric juices, GI transit time and timing of enzyme dosing. Symonds, et al studied lipase activity in relation to gastric emptying time (25). They found that those CF children between 5 and 18 years old with slow gastric emptying time had reduced pancreatic lipase activity. It is difficult to assess gastric emptying time, however, if enzyme dosing appears adequate, an adjustment in the timing of when enzymes are taken may improve lipase activity. Enzymes must be taken with all foods containing fat. When regular meals and snacks are not scheduled, and "grazing" occurs, it is difficult to adequately cover all food consumed with enzymes. Beverages that contain fat, such as milk, liquid supplements, and shakes must be thought of as "foods" that require enzymes. With foods that are tomato-based (i.e. pizza, spaghetti, lasagna), an extra enzyme capsule may be needed to improve digestion. Fast foods, which are high in fat content, may also require an increased enzyme dose.

Symptoms of malabsorption that continue with what appears to be an adequate lipase dose should trigger questions regarding enzyme use and storage (see Table 7). Patients need to check expiration dates and store their enzymes in a cool, dry environment. Efficacy may be affected if enzymes are stored in a vehicle glove compartment during the heat of summer. Enzymes need to be taken no earlier than 30 minutes before, or no later than 30 minutes after, a meal. Ask-

Table 8
Vitamin Recommendations for Cystic Fibrosis (4,15)

*Age**	*Vit A (IU)*	*Vit E (IU)*[1]	*Vit D (IU)*	*Vit K (mcg)*
>8 years	5,000–10,000	200–400	400–800[2]	300–500
>18 years	10,000	400–800	400–800[2]	300–500
To correct deficiencies	10,000–20,000	400–12,000	800–1600[2] 2–4 mg/kg/d[3]	5–10 mg/week or daily[4]

[1] d-α-tocopherol
[2] D_2 or D_3
[3] Calcifediol (25-OHD)
[4] Frequency of supplementation is dependent on response to therapy.

Biochemical Testing:
Vitamin E—Serum α tocopherol
Vitamin D—Serum 25-OHD
Vitamin A—Serum retinol, retinol binding protein
• Monitor serum retinyl esters – elevation indicates toxicity
Vitamin K - PIVKA-II level or prothrombin time

*Refer to reference 15 for vitamin recommendations for children <8 years.

ing when enzymes are consumed in relation to meals may reveal enzymes are taken outside of the 30 minute window of meals rather than with the meal. In this case, the enzyme beads may not be adequately mixed with the gastric content as it enters the duodenum. Spreading the enzymes throughout a meal may further improve bead distribution and therefore absorption of nutrients.

VITAMIN SUPPLEMENTATION

In addition to the normal doses of water soluble vitamins, it is recommended that individuals with CF receive supplementation of fat soluble vitamins. There are several vitamin supplements manufactured specifically for the CF population (Table 9). These vitamins contain the recommended dose of water soluble and fat soluble vitamins. Vitamin supplements should be taken with food and enzymes in order to enhance absorption. See Table 8 for CFF vitamin supplementation recommendations and guidelines for biochemical testing. Vitamin levels should be checked annually, and one to two months after any change in vitamin dosing (4).

There has been recent concern that, due to poor absorption and increased endogenous fecal zinc losses, some children with CF may experience zinc deficiency (26). Zinc deficiency can affect vitamin A status, making zinc supplementation a reasonable therapy for CF patients with suboptimal vitamin A status who have not responded to supplementation (28). For non-CF children the zinc supplement recommendation is 1 mg elemental zinc/kg/d up to 10–15 mg/day (27). There are no specific dosing recommendations for cystic fibrosis. Taking multivitamins with pancreatic enzymes will enhance absorption of zinc as well as fat soluble vitamins (26). Water-miscible forms of the fat soluble vitamins are not essential to correct deficiency when administered correctly with meals and enzymes (29).

APPETITE STIMULANTS

The effect of appetite stimulants on nutritional status of CF patients in nutrition failure has been reported in the literature. Megestrol acetate (MA) has been used in several controlled studies. MA seems to facilitate significant weight gain in treatment subjects, but is not

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Table 9.
Vitamin Products Specific to Cystic Fibrosis

Product	*Vitamin A IU*	*Vitamin D IU*	*Vitamin E IU*	*Vitamin K (mcg)*	*Availability*	*Cost (CF Services Pharmacy) (800) 541-4959*
CF Foundation Recommendations	5,000–10,000	400–800	200–800	300–500		
ADEK Chewables	9,000	400	150	150	Rx CF Services Pharmacy Local pharmacies	$21.95/60
Vitamax Chewables	5,000	400	200	150	Rx CF Services Pharmacy Local pharmacies	$12.95/90
ABDEK Soft Gel Capsules	9,000	400 800/chewable tablet	200	500 600/chewable tablet	Rx CF Services Local pharmacies	$18.95/90 gelcaps $29.95/90 chewables

without side effects (31,32,33). It has been successfully used in patients with CF who have failed conventional nutrition interventions. Appetite improvement is reported with significant weight gain consisting of both fat mass and lean body mass. In all studies where MA was successfully used, there was also a trend toward improved pulmonary function and decreased clinical exacerbations. Studies indicated that weight gain was maintained after the treatment period (31–33). Reported side effects include glucosuria, increased insulin levels, insomnia, hyperactivity and irritability. One anecdotal report of testicular failure and adrenal insufficiency in an adult CF male is reported. Symptoms reversed when MA was discontinued (34). Side effects with MA therapy seem to be fewer among younger CF patients (33).

A more recent study has reported success with appetite improvement and weight gain using cyproheptadine hydrochloride (Periactin), a first-generation

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Table 10
Commonly Utilized Oral Nutrition Supplements/Calorie Boosters

Product Name	*Manufacturer*	*Calorie Density*	*Cost**	*Availability*
Instant Breakfast Powder packets	Carnation or store brand	130/packet	Check Local Grocer	Grocery Store
Ensure Plus	Ross	1.5 cal/ml	$40/case	Drug/Grocery store
Scandishake Powder	Axcan Scandipharm	450/packet	$66/30 packets	CF Services, Axcan Select Grocery Stores
Scandical powder	Axcan Scandipharm	32/Tbsp.	$7/8 oz can	CF Services, Axcan
Duocal powder	Scientific Hospital Supplies (SHS) (800) 365-7354	42/Tbsp	$21.88/30 oz. can	CF Services, SHS

*CF Services Pharmacy prices

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Table 11
Clinical Symptoms of Diabetes in Cystic Fibrosis (37)

- Unexplained polyuria or polydipsia
- Failure to gain weight despite nutrition intervention
- Poor growth velocity
- Delayed progression of puberty
- Unexplained chronic decline in pulmonary function

antihistamine and serotonin antagonist. Among the treatment group, benefits included improved nutritional status as measured by % IBW, skin fold measures, and body mass index. The percent of lean body mass vs. fat mass was comparable to MA in this small study. The only reported side effect was drowsiness, which resolved after several days (35).

There is a need for further study of appetite stimulant use with the CF population. They provide an alternative to nocturnal tube feedings, which some patients refuse. CF patients who have poor pulmonary function may not respond to nocturnal feedings because of poor compliance, and anorexia associated with advanced pulmonary disease.

ENTERAL SUPPORT

Patients who maintain nutrition failure, despite the use of high calorie oral nutrition supplements (Table 10), and with normal glucose tolerance, should be evaluated for placement of gastrostomy tube to receive nocturnal feedings. This procedure is well tolerated and will allow the provision of needed calories. Non-elemental formulas are tolerated and absorbed as well as elemental formulas when enzymes are provided (36). The goal of dosing enzymes during nocturnal feeding is to expose all formula to the enteric coated beads in the duodenum.

There are several ways to dose pancreatic enzymes for nocturnal feedings. One method is to provide a meal dose of enzyme capsules at the beginning of the feeding period and half-a-meal dose at the end of the feeding. Depending on the flow rate, it might be difficult to achieve complete absorption using oral enzyme replacement. We have had success using Viokase powder, dosing at 2,000 Units of lipase/gm fat. Viokase powder is not enteric coated and will predigest the formula. It can be added directly to the formula bag and does not

Table 12.
Criteria for Diagnosis of Cystic Fibrosis Related Diabetes (37)

1. 2-hr Plasma Glucose ≥200 mg/dl during a 75 gram OGTT
2. Fasting Blood Glucose ≥126 mg/dl on two or more occasions
3. Fasting Blood Glucose ≥126 mg/dl plus casual glucose level >200 mg/dl
4. Casual glucose levels ≥200 mg/dl on two or more occasions with symptoms

Table 13
Categories of Oral Glucose Tolerance in Cystic Fibrosis (37)

Category	*FBG mg/dl (mM)*	*2-h Plasma Glucose mg/dl (mM)*
Normal Glucose Tolerance (NGT)	<126 (7.0)	<140 (7.8)
Impaired Glucose Tolerance (IGT)	<126 (7.0)	140–190 (7.8-11.1)
CFRD Without Fasting Hyperglycemia	<126 (7.0)	≥200 (11.1)
CFRD With Fasting Hyperglycemia	≥126 (7.0)	OGTT not necessary

Note: OGTT is performed by giving 1.75 gm/kg body weight up to 75 grams oral glucose load to a fasting patient. FBG and 2-h plasma glucose are measured. The patient should have consumed at least 150 grams of carbohydrates per day for the three days prior to testing. Most CF patients consume much more carbohydrates than 150 grams on a daily basis.

Table 14
Nutrition Management of Cystic Fibrosis Related Diabetes

1. Maintain high calorie intake with both simple and complex carbohydrates
2. Cover all simple carbohydrates with insulin
3. Maintain high fat diet (40%) for weight maintenance
4. Restrict sugary beverages unless they are counted as part of the carbohydrates and covered appropriately with insulin

require dilution. After addition to the formula, shaking the bag will distribute the enzyme and facilitate breakdown. When a 2 calorie/mL formula is used, this method might cause tubing to clog over time. Shaking the bag periodically will redistribute the solids and prevent clogging. It is also possible to combine Viokase powder and oral enzymes to fine-tune enzyme coverage. Dosing should not exceed 4,000 Units lipase/gm fat.

CYSTIC FIBROSIS RELATED DIABETES (CFRD)

Diabetes occurs in 5%–6% of the CF population, with incidents increasing as the population ages. It is a separate clinical entity from Type 1 and Type 2 diabetes, and requires a slightly different management approach. CFRD is caused by insulin deficiency and may or may not be associated with fasting hyperglycemia. For this reason, it is recommended that CF patients with symptoms of diabetes (Table 11), or casual glucose levels ≥126 mg/dL, undergo oral glucose tolerance testing (OGTT). Diabetes is diagnosed when any one of the criteria listed in Table 12 are present. Diagnosis of CFRD should be identified as either "with fasting hyperglycemia" or "without fasting hyperglycemia" (37). Categories of OGTT in CF are found in Table 13.

CFRD is treated with insulin. It differs from Type 1 diabetes in that ketoacidosis is rare, although a small percent of patients produce ketones without acidosis (37). CFRD is not associated with the same macrovascular disease that is associated with Type 1 diabetes; therefore the fat content of the diet should not be restricted and may need to be as high as 40% to meet energy requirements. Simple carbohydrates are not restricted, but are covered with the appropriate amount of insulin. See Table 14 for dietary guidelines of CFRD. Please refer to the CFF Consensus Conference on diagnosis, management and treatment of CFRD for more detailed information regarding medical management (37). Table 15 provides suggestions for nutrition counseling of the CF patient. It is not specific to CFRD, but is applicable to all patients with cystic fibrosis.

Table 15
Cystic Fibrosis Nutrition Counselling Guidelines

- Is patient aware of connection between nutrition, weight and pulmonary function?
- Check calorie content of diet
- Check dosing of enzymes with fat content
- Are nutritional supplements available?
  - Check incentive programs (see Table 6
- Is patient aware of ways to boost calories?
  - Provide list of high calorie foods to compliment diet
- Are snacks available, and if so, are enzymes taken?
- Is work/school schedule interfering with eating?
  - Brainstorm with patient ways to adjust
- Are psychosocial issues at work?
  - Appropriate referral made
- Feeding/behavioral issues? (parent/child)
- Is stress at meals interfering with appetite?
- How often are enzymes missed with meals/snacks?
- Are vitamins taken as prescribed?
- Is patient using alternative nutrition therapies?

CONCLUSION

The challenge of caring for the CF patient is one that should be addressed by a team of health professionals knowledgeable in the multifaceted characteristics of the disease. It is the desire of the Cystic Fibrosis Foundation and health professionals who work with the CF population that medical management treats all systems of involvement. Early detection of nutrition failure is necessary in order to have a positive impact on mortality. As our medical therapies improve, so must the manner in which we respond to small changes in lung function and nutrition status. Until a cure is found, this is the best hope for our patients with cystic fibrosis. ■

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