Nutrition Issues in Cystic Fibrosis

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.

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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.

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

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**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 sinonasal disease / nasal polyps
- Hepatobiliary disease
- Digital clubbing
- Salt loss syndrome with acute salt depletion
- Male urogenital abnormalities (obstructive azospermia)

Nutrition Issues in Cystic Fibrosis

Among the most powerful tools to assess nutritional status are Body Mass Index (BMI) and percent ideal body weight (% IBW). 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. 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. 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). 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). 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. 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. Recently Fecal Elastase-1 (FE-1) has been recognized as a valid tool for determining pancreatic exocrine function in the CF population. A FE-1 value of >200 µg/g stool indicates pancreatic sufficiency. FE-1 is used to establish pancreatic exocrine function and is not affected by pancreatic enzyme replacement therapy. 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 2
**Definitions of Nutrition Status in Patients with Cystic Fibrosis**

<table>
<thead>
<tr>
<th>Age Group</th>
<th>At Risk</th>
<th>Nutritional Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–2 years old</td>
<td>Weight for length 10%–25%</td>
<td>Height Percentile &lt;5%, or weight for length &lt;10% or IBW &lt;90%</td>
</tr>
<tr>
<td>2–20 years</td>
<td>BMI percentile 10th–25th</td>
<td>BMI percentile &lt;10% or IBW &lt;90%</td>
</tr>
<tr>
<td>Adults</td>
<td>BMI 19–20</td>
<td>BMI &lt;19 or percent IBW &lt;90%</td>
</tr>
</tbody>
</table>

### 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
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 gastro-

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**Table 4**

Dosing Pancreatic Enzymes (24)

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

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).
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

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

<table>
<thead>
<tr>
<th>Description</th>
<th>Restrictions</th>
</tr>
</thead>
<tbody>
<tr>
<td>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.</td>
<td>None</td>
</tr>
<tr>
<td>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</td>
<td>Must purchase Ultrase Enzymes</td>
</tr>
<tr>
<td>Free Ultrase Microspheres, Ultrase MT12 or Viokase Powder ADEK Pediatric Drops</td>
<td>CF patients under 2 years</td>
</tr>
<tr>
<td>Copy of Cystic Fibrosis: A Guide for Patient and Family by David Orenstein, MD</td>
<td>CF patients under 2 years</td>
</tr>
<tr>
<td>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.</td>
<td>Must have total annual income below Federal Poverty Level with limited prescription drug coverage and living in the US.</td>
</tr>
<tr>
<td>Free pancreatic enzyme (Creon Minimicrospheres) and Vitamax liquid pediatric drops multivitamins</td>
<td>CF patients under 2 years of age</td>
</tr>
<tr>
<td>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</td>
<td>CF patients 2 years and older</td>
</tr>
<tr>
<td>Free Vitamax Pediatric Drops or Chewable Tablets with proof-of-purchase of 30-day supply of Creon enzymes.</td>
<td>For patients who do not qualify for federal medical assistance</td>
</tr>
<tr>
<td>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</td>
<td>For individuals who have obtained the Med Pulse vest and not eligible for federal medical assistance.</td>
</tr>
<tr>
<td>Provides free Source CF vitamins Soft Gels with use of X-Gen Pharmaceuticals brand of colistimethate. 1 bottle monthly</td>
<td>Use X-Gen Colistimethate; not receiving federal medical assistance.</td>
</tr>
</tbody>
</table>
chewing prior to swallowing. In instances where gas-
tric 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 coat-
ings 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 bicar-
bonate buffer with enzyme within the microsphere
beads that improves the pH of the gastric environment
and thus enzyme activation. Combining the bicarbon-
ate-buffered enzyme with the established enzyme has
proven effective in facilitating weight gain in children
who were not experiencing symptoms of malabsorp-
tion, 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 addi-
tion 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 pro-
viding better enzyme coverage at various sites in the
small intestine (23).

Incentive programs are provided by various com-
panies to assist the CF patient in obtaining nutrition
supplements, vitamins, or free enzymes when the
patient uses their product. They are either adminis-
tered 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 pan-
creatic 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 trig-
ger questions regarding enzyme use and storage (see
Table 7). Patients need to check expiration dates and
store their enzymes in a cool, dry environment. Effi-
cacy may be affected if enzymes are stored in a vehi-
cle 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 7**
<table>
<thead>
<tr>
<th>Factors that affect enzyme efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Outdated prescription</td>
</tr>
<tr>
<td>• Improper storage of enzymes (exposure to heat)</td>
</tr>
<tr>
<td>• Generic enzymes that are not bioequivalent</td>
</tr>
<tr>
<td>• Chewed or crushed enzyme beads</td>
</tr>
<tr>
<td>• Prolonged exposure of beads to alkaline foods or fluids</td>
</tr>
<tr>
<td>• Excess acidity of gastric juices</td>
</tr>
<tr>
<td>• Slow gastric emptying time</td>
</tr>
<tr>
<td>• Timing of enzyme administration</td>
</tr>
<tr>
<td>• Diet content is high fat or contains tomato-based foods</td>
</tr>
</tbody>
</table>
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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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...
Nutrition Issues in Cystic Fibrosis

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

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)

<table>
<thead>
<tr>
<th>Category</th>
<th>FBG mg/dl (mM)</th>
<th>2-h Plasma Glucose mg/dl (mM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Glucose Tolerance (NGT)</td>
<td>&lt;126 (7.0)</td>
<td>&lt;140 (7.8)</td>
</tr>
<tr>
<td>Impaired Glucose Tolerance (IGT)</td>
<td>&lt;126 (7.0)</td>
<td>140–190 (7.8-11.1)</td>
</tr>
<tr>
<td>CFRD Without Fasting Hyperglycemia</td>
<td>&lt;126 (7.0)</td>
<td>≥200 (11.1)</td>
</tr>
<tr>
<td>CFRD With Fasting Hyperglycemia</td>
<td>≥126 (7.0)</td>
<td>OGTT not necessary</td>
</tr>
</tbody>
</table>

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.

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...
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.

**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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**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

**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 complement 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?
References


