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Nutritional Management of the Adult with Cystic Fibrosis – Part I

Christie L. Rogers

Medical advances, research discoveries, and an interdisciplinary healthcare environment have led to a dramatic improvement in the life expectancy and quality of life for individuals with cystic fibrosis (CF). Advanced age with CF can lead to complications, such bone disease and liver disease. This unique patient population requires a multidisciplinary healthcare team that specializes in adult CF care. This is part I of a two part series which serves to present the nutritional challenges of adults with CF and to provide tools to prevent or manage these major nutritional concerns. Part I will address weight maintenance, pancreatic insufficiency and sufficiency, vitamin supplementation, gastrointestinal issues beyond the pancreas, and bone disease. Part II will cover cystic fibrosis related diabetes, fertility, and pregnancy with cystic fibrosis.

INTRODUCTION

Cystic fibrosis (CF) is a genetic disorder most commonly seen in the Caucasian population that affects 70,000 children and adults worldwide and 30,000 children and adults in the United States.[1] The inherited mutation results in a defective protein known as Cystic Fibrosis conductance Transmembrane Regulator (CFTR). This protein controls sodium and chloride channels found in the cells that line many different organ systems, most notably the lungs, pancreas, and reproductive organs. The defective channels produce a sticky mucous which clogs the lungs and the pancreatic ducts resulting in chronic respiratory infections and nutrient malabsorption from exocrine pancreatic insufficiency.

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In the 1950s, a child diagnosed with CF was not expected to live to attend elementary school, but now more than 45 percent of those diagnosed with CF in the United States are 18 years or older.[1] Continued medical advancements as well as optimization of nutritional status have led to an aging CF population and the current median predicted age of survival for those with CF is 38.3.[1,2] This unique population requires the coordinated care of physicians, dietitians, respiratory therapists, physical therapists, nurses and social workers with an understanding of the complex management of the adult CF patient. In addition to recurrent pulmonary and sinus infections, adults with CF may also develop diabetes, liver disease, or bone disease. Despite living with chronic illness, individuals with CF often have full and productive lives. They may want to have a career, get married, and start a family. Maintaining

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optimal nutrition status throughout all phases of life with CF can be a challenge, but it is vital to achieve optimal outcomes.

Weight Beyond the Growth Curve

As a child with CF, weight and height are tracked along standard growth curves in an effort to maintain adequate growth and development and to reach appropriate height potential. As an adult, these growth curves are no longer necessary, but the importance of weight for height does not diminish. Positive correlation between body mass index (BMI), calculated as kg/m^2, and forced expiratory volume in one second (FEV_1) has been demonstrated in adult males and females with CF. FEV_1 is a spirometry measure used to evaluate lung function and FEV_1 percent predicted compares the raw FEV_1 number to those predicted from a group with similar characteristics, such as age and height. Data from the CF patient registry demonstrates that males with a BMI of at least 23 kg/m^2 and females with a BMI of at least 22 kg/m^2 have better lung function.

More than 90% of patients with CF have pancreatic exocrine insufficiency resulting in chronic nutrient malabsorption.[1] This malabsorption, in combination with increased energy requirements due to work of breathing and frequent infections, means an increased caloric and protein requirement for CF patients. A broad recommendation for energy requirements of CF patients is 120-150% of requirements for the general population. Actual caloric requirements vary from patient to patient and may increase with infection or general disease progression. Weight should be closely monitored and the CF dietitian should routinely assess caloric intake. Calorie boosting throughout the day can be accomplished by increasing meal and snack frequency, consuming oral supplements with or between meals, or by providing tips to increase caloric content of frequently consumed foods and beverages.

Enteral Feeding

Even the most motivated and compliant CF patient may have trouble consuming sufficient calories each day to maintain a healthy weight due to recurrent infection, increased work of breathing, and abdominal issues. For these patients, supplemental tube feeding can be of great benefit. Discussions regarding tube feeding to provide extra calories typically begin with parents during infancy for CF patients, so the idea of a feeding tube is often not new to the adult patient. Options for tube feeding

Table 1: Pancreatic Enzyme Dosage [11]

Units lipase/kg/meal	**Units lipase/grams of fat**
- Start with 500 units lipase/kg/meal	- Start with 500 units lipase/gram fat
- Increase to max of 2,500 units lipase/kg/meal	- Increase to max of 4,000 units lipase/gram fat
- Provide ½ meal dose with snacks	

Caution with doses > 2,500 units lipase/kg/meal or > 4,000 units lipase/gram fat

Administration of pancreatic enzymes with enteral feeding

- Determine total dosage of enzymes based on grams of fat in enteral prescription
- By mouth: Take ¾ of total dose at the start of enteral feeding and ¼ of total dose near the end of delivery
- Enteric-coated enzymes mixed in formula: Open enzyme capsule and add microspheres to a sodium bicarbonate solution.[1] Let spheres dissolve for 15 minutes. Add mixture to enteral formula and ensure adequate mixing.
- Non-enteric coated enzymes mixed in formula: Crush the total dose of enzymes and add to formula bag. Ensure adequate mixing. When crushing, take caution to avoid accidental inhalation or contact with eyes.

[1]Detailed instructions regarding sodium bicarbonate solution recipes can be found at www.ginutrition.virginia.edu

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delivery include nasogastric tube, gastrostomy tube, gastrostomy tube with jejunal extension, or jejunostomy tube. Percutaneous endoscopic gastrostomy (PEG) tube is the most common delivery option, although some patients do choose to routinely place small bore nasogastric tubes themselves to avoid a permanent feeding tube. Jejunal feeding is sometimes necessary for patients with significant gastroesophageal reflux. Typically, supplemental enteral feeding is delivered continuously overnight via enteral pump feeding and this can provide an additional six to eight hours of calorie provision.

There is often concern regarding feeding tube placement in the setting of poor lung function. Clinicians worry that pain control post-procedure will be a challenge and that abdominal pain will limit the patient's ability to achieve a productive cough or to use their chest vest for physiotherapy; thus mucous clearance is decreased, increasing risk for respiratory infection. In 1998, a retrospective study of 21 pediatric CF patients with gastrostomy tubes determined that those with a predicted FEV_1 greater than 40% at the time of feeding tube placement had improved weight velocity independent of lung function over a 2-year time period.[3] In 2004, Oliver et al[4] published a retrospective study of 37 children who had received a gastrostomy feeding tube from 1989 to 1997. Of the 37 who received a feeding tube, 11 died during the 2-year follow-up and the authors found that those with a predicted FEV_1 less than 50% had significantly increased mortality. In 2006, Efrati et al [5] also conducted a retrospective analysis of 21 pediatric CF patients with gastrostomy tubes. They found that percent predicted FEV_1 declined during the first year after feeding tube insertion, but subsequently improved during the second year while weight, height, and BMI z-scores all significantly improved after feeding tube placement. Mean percent predicted FEV_1 prior to feeding tube placement was 44.2% with pre-placement FEV_1 ranging from 25 to 77%. Limitations to these studies include the retrospective nature and small sample sizes of only pediatric patients and that in the 2004 study, the overall mortality was high indicating advanced disease of participants. However, it appears that placing a gastrostomy tube before significant lung function decline may result in better outcomes. Indicating that supplemental tube feeding should be initiated as a means to maintain adequate nutrition and lung function rather than as a rescue tool when all else fails.

Pancreas: Insufficient or Sufficient?

Individuals with CF are classified as being pancreatic insufficient (PI) or pancreatic sufficient (PS) and more than 90% of patients with CF are PI.[1] There appears to be a correlation between genotype and phenotype in regard to the exocrine function of the pancreas.[6] There are over

Table 2: Factors that may decrease response to Pancreatic Enzyme Replacement Therapy[11]

- Compliance
- Outdated prescription
- Storing enzymes in a hot environment (ex: in the car, in a clothing pocket)
- Not taking enzymes with milk products or with snacks
- "Grazing" eating behaviors (and not taking enzymes)
- Excessively high fat foods
- Foods with increased acidity (tomato based)
- Acidic gastric environment
- Slow gastric emptying
- Taking enzymes at the completion of the meal instead of at the start
- Chewing enzymes
- Pouring enzyme beads onto non-acidic food

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Table 3: Food and Drug Administration Approved Enzymes

Product Name / Manufacturer	Lipase Units	Amylase Units	Protease Units	Details
Creon (Abbott) www.creon.com 800-633-9110				
Creon 3,000	3,000	15,000	9,500	Delayed release capsule
Creon 6,000	6,000	30,000	19,000	Delayed release capsule
Creon 12,000	12,000	60,000	38,000	Delayed release capsule
Creon 24,000	24,000	120,000	76,000	Delayed release capsule
Pancreaze (Janssen Pharmaceuticals) www.pancreaze.net 855-TEAM-PST				
Pancreaze 4,200	4,200	17,500	10,000	Delayed release capsule
Pancreaze 10,500	10,500	43,750	25,000	Delayed release capsule
Pancreaze 16,800	16,800	70,000	40,000	Delayed release capsule
Pancreaze 21,000	21,000	61,000	37,000	Delayed release capsule
Pertzye (Digestive Care, Inc) www.digestivecare.com 877-882-5950				
Pertzye 8,000	8,000	30,250	28,750	Bicarbonate buffered
Pertzye 16,000	16,000	60,500	57,500	Bicarbonate buffered
Ultresa (Aptalis Pharma) www.aptalispharma.com 800-950-8085				
Ultresa 13,800	13,800	27,600	27,600	Delayed release capsule
Ultresa 20,700	20,700	41,400	41,400	Delayed release capsule
Ultresa 23,000	23,000	46,000	46,000	Delayed release capsule
Viokace (Aptalis Pharma) www.viokace.com 800-950-8085				
Viokace 10,440	10,440	39,150	39,150	Non enteric coated
Viokace 22,880	22,880	78,300	78,300	Non enteric coated
Zenpep (Aptalis Pharma) www.zenpep.com 800-950-8085				
Zenpep 3,000	3,000	16,000	10,000	Delayed release capsule
Zenpep 5,000	5,000	27,000	17,000	Delayed release capsule
Zenpep 10,000	10,000	55,000	34,000	Delayed release capsule
Zenpep 15,000	15,000	82,000	51,000	Delayed release capsule
Zenpep 20,000	20,000	109,000	68,000	Delayed release capsule
Zenpep 25,000	25,000	136,000	85,000	Delayed release capsule

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1,800 mutations associated with the CF diagnosis and those with two "severe alleles" are nearly always PI while those with one "mild mutation" are more likely PS.[2,6] With advanced age, pancreas function can decline and those who are PS may eventually become PI as adults. Consequently, PS adults should routinely be asked about the frequency and composition of their stools so that malabsorption can be addressed early in presentation. PI should be suspected in any patient who is clearly getting adequate calories, but weight is dropping regardless of GI symptoms. Pancreatic exocrine function can be assessed by a 72-hour fecal fat study or by measuring fecal elastase-1 levels in a stool sample. The 72-hour fecal fat test is the gold standard, but the fecal elastase-1 assay is easier to collect, does not require interpretation of fat intake, and is not affected by exogenous pancreatic enzymes.[6]

Those who are PI must take pancreatic enzyme replacement therapy (PERT) with all meals and snacks in order to properly absorb carbohydrate, protein, and most importantly fat. Most PERT are enteric coated, preventing the enzymes from being degraded by the acidic environment of the stomach.[7] The enteric coating subsequently dissolves once the pH exceeds 5 to 5.5, which ideally occurs within the duodenum.[8] However, CFTR plays a role in both pancreatic and duodenal bicarbonate secretion meaning that many patients with CF do not produce enough bicarbonate to neutralize the gastric acid entering the duodenum.[7] This means that the enteric coating may not dissolve until the PERT reaches the distal jejunum, having bypassed the major absorptive surface area of the duodenum and proximal jejunum.[7] CF patients are often placed on proton pump inhibitors (PPIs) or H_2-receptor antagonists in an effort to decrease gastric acid secretion and therefore increase the duodenal pH. There are limited studies to support one therapy over another. Often the sample size in these studies is small and the majority of subjects are pediatric. One random cross-over trial of fifteen pediatric patients demonstrated decreased fat malabsorption when taking omeprazole versus placebo.[9]

Dosing guidelines for PERT are based on the North American CF Foundation consensus statement and the Consensus Conference on Enzyme Therapy and Fibrosing Colonopathy.[10] General recommendations for initiation and advancement of PERT therapy can be found in Table 1. Although it is ideal to base dosage on units of lipase per gram of fat consumed, this information is often not known at each meal so most recommendations are based on units of lipase per kilogram of body weight. Before increasing PERT dosage based on subjective symptoms of malabsorption, i.e. diarrhea, abdominal pain, or steatorrhea, it is important to review the list of factors that may contribute to poor response to PERT (Table 2). Excessive administration of PERT can cause fibrosing colonopathy which may lead to colonic strictures requiring surgical intervention.[11] Therefore, finding the appropriate dose of PERT is imperative for maintaining nutritional status but without causing long-term complications.

Although in regular use for many years, PERT originally did not require Food and Drug Administration (FDA) approval. In 2004, the FDA mandated that all PERT gain new drug application approval by April 2008.[12] This deadline was later extended to April 2010 and there are currently six FDA approved enzyme brands (Table 3).[12] Of the six, four products come in delayed-release capsules. One product is non-enteric coated, meaning that it should be taken with a PPI when taken orally. One product is bicarbonate buffered.

Vitamin Supplementation

Fat Soluble Vitamins

Individuals with CF, especially those with pancreatic insufficiency, are at risk for fat-soluble vitamin deficiency. Through all stages of life, CF patients are prescribed vitamins that contain water-miscible versions of the fat-soluble vitamins: A, D, E, and K. Over the last several years, there has been a shift in the discussion of vitamin status, pushing the focus away from defining patients as "deficient" to appreciating broader terms with ranges such as "deficient, suboptimal, adequate, and optimal."[13] General dosing guidelines for CF patients for all fat-soluble vitamins can be found in Table 4.[14] Check fat-soluble vitamins levels annually for all adult CF patients. If levels are low, requiring repletion, recheck levels every one to three months until optimal levels are reached.

Vitamin A

Vitamin A and carotenoids are important for adequate vision, bone health, cell differentiation, and immunity. The human diet provides vitamin A in multiple forms including preformed vitamin A, which is metabolized to retinol, and carotenoids, such as beta-carotene. The majority of carotenoids are converted to retinol prior

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to absorption, providing a means of regulation and potentially decreasing the risk of hypervitaminosis A.[13] However, CF specific vitamins contain retinol, which is not subject to this regulatory control and may increase the risk of vitamin A toxicity. Current guidelines recommend 10,000 IU of vitamin A daily.

Retinol esters are bound to retinol binding protein (RBP) and transthyretin (TTR) in a 1:1:1 ratio and then transported from the liver to tissues.[13] TTR is also known as prealbumin. Serum retinol levels are one indicator of vitamin A status, but in healthy individuals this serum concentration does not drop until liver reserves are significantly depleted.[15] Additionally, RBP is a negative acute phase protein, meaning that concentrations of RBP, and subsequently retinol, will decrease during times of inflammation and infection. Evaluating serum vitamin A while taking into account RBP and TTR levels may provide a more accurate reflection of vitamin A stores. A study of surgical patients who underwent liver biopsy and therefore had known hepatic vitamin A stores, found that a cutoff of ≤ 0.36 for RBP:TTR was associated with marginal vitamin A deficiency.[15,16]

Zinc deficiency can occur in states of malabsorption, such as CF. Adequate zinc status is necessary for the hepatic synthesis of RBP, meaning that those with zinc deficiency may not be able to mobilize retinol from the liver.[17] A 2008 case report of a 23 year old female with CF reported that clinical vitamin A deficiency (night blindness) was resolved by correcting zinc deficiency with 220 mg of zinc sulfate daily for one week.[18] Subsequently, those with vitamin A deficiency that are not responsive to increased vitamin A supplementation may actually be zinc deficient and require additional zinc supplementation.

Vitamin D

It is widely accepted that suboptimal vitamin D status is frequently present in the general population and this is especially true in the CF population. Both vitamin D and calcium are known to be important for the development and maintenance of healthy bones. The impact of vitamin D on immune function and inflammation is still being explored.[13] The CF Foundation produced guidelines for vitamin D supplementation in 2002 and again in 2005, but several studies of pediatric and adult patients indicated that these recommendations were not sufficient.[19-22] In September 2010, the CF Foundation assembled a committee to develop new guidelines for the screening, diagnosis, supplementation, and treatment of vitamin D insufficiency.[19]

The inactive version of vitamin D comes in two forms: vitamin D_2 (ergocalciferol) and vitamin D_3 (cholecalciferol). Only vitamin D_3 is produced by the skin after sun exposure while diet and supplements can provide both vitamin D_2 and D_3.[23] Both vitamin D_2 and vitamin D_3 are then transported to the liver where they are converted to 25-hydroxyvitamin D (25OHD).[23] Vitamin D status is best assessed by measuring circulating levels of 25OHD. The goal is to maintain serum levels of at least 30 ng/ml.[19] Since vitamin D levels can vary from season to season, it is ideal to check patient's levels at the end of winter, therefore catching their nadir level to determine if their supplementation is adequate to maintain optimal levels year round.[19]

Studies evaluating the use of cholecalciferol versus ergocalciferol for vitamin D repletion are limited, especially in the adult CF population. Furthermore, most of the trials evaluating osteoporosis and vitamin D use only cholecalciferol, limiting the data linking ergocalciferol to bone health. One randomized controlled trial of 28 adult CF patients given either 50,000 IU of cholecalciferol or ergocalciferol weekly to correct low vitamin D levels demonstrated that both forms significantly raised 25OHD levels, but the response was greater for those receiving cholecalciferol (D3).[24] Given the results of this study and that cholecalciferol is the endogenously produced version of vitamin D, the CF Foundation recommends that patients with suboptimal vitamin D status be treated with cholecalciferol.[19] The repletion dose can be given weekly, or the weekly dose can be divided into a daily dose equivalent. Patients who fail to respond to high dose vitamin D therapy should be referred to an endocrinologist who specializes in vitamin D therapy. A stepwise approach was published in the current guidelines to treat vitamin D deficiency.[19] The Endocrine Society considers individuals with CF to be at risk for vitamin D deficiency and therefore recommends a daily vitamin D requirement of 1500 to 2000 IU, with an upper limit of 10,000 IU daily for those greater than 18 years of age. Those with a 25OHD level ≥ 20 ng/mL, but < 30 ng/mL should increase their daily dose by 1600 to 6000 IU of D3. Those with a 25OHD level < 20 ng/mL should increase their daily dose to the maximum of 10,000 IU per day of D3. After three months of repletion doses, recheck the 25OHD level and treat accordingly.[10] Additional studies are required to determine if these dosing guidelines will

be sufficient for repletion and maintenance of adequate vitamin D levels for CF adults. It is important to note that once serum levels are replete, those patients will most likely require ongoing vitamin D supplementation with 800 to 2000 IU per day of D3 to prevent them from returning to suboptimal levels.

Vitamin E

Vitamin E refers to a group of compounds including tocopherols and tocotrienols which all contain antioxidant properties. Signs of vitamin E deficiency include hemolytic anemia, ataxia, muscle weakness, visual defects, dementia, and cardiac arrhythmias.[25] Adults with CF should take 200-400 IU of vitamin E daily. Vitamin E status is generally measured via serum α-tocopherol and normal levels are >0.7 ml/dl.[26] However, since vitamin E is correlated with plasma lipid levels, low or high serum α-tocopherol levels may need to be viewed in the context of lipid status. The ideal, but difficult to obtain, method for assessing vitamin E status is the ratio of α-tocopherol:total lipid (cholesterol, triacyglcerol, and phospholipid) in which a level <0.8 ml/dl indicates deficiency.[13,26] An easier, but less ideal method is the ratio of α-tocopherol:cholesterol where a level of <2.47 mg/g indicates deficiency.[26]

Vitamin K

Vitamin K is an important cofactor for the conversion of glutamyl residues to prothrombin and osteocalcin making it imperative for adequate blood coagulation and bone formation.[13] Despite the production of vitamin K by bacterial flora in the intestine, patients with CF present with vitamin K deficiency without routine supplementation.[10, 27] Although the CF Foundation guidelines recommend 300-500 mcg per day of vitamin K, a recent study of children and young adults found that only those taking ≥ 1,000 mcg / day achieved optimal vitamin K status.[27] Elevated prothrombin time (PT) is an easy was to assess vitamin K status. However, this is a late marker of vitamin K deficiency, so even marginally high levels indicate the need for additional supplementation. Protein-Induced in Vitamin K Absence or Antagonist (PIVKA-II) is an early and sensitive marker of vitamin K status, but it is often an expensive lab that can only be evaluated at certain laboratories. If PT is not correcting with vitamin K repletion, PIVKA-II should be checked.

Gastrointestinal Issues Beyond Pancreatic Insufficiency

Cystic Fibrosis Related Liver Disease

Fortunately, only about one third of CF patients develop cystic fibrosis related liver disease (CFLD).[28] As an early complication of CF, the majority of cases are diagnosed by midadolescence.[7, 28] Pathogenesis of CFLD again leads back to a cellular defect. CFTR is not expressed in hepatocytes, but in the epithelial cells of the cholangiocytes and the gallbladder, causing a disruption in the fluid and electrolyte content of bile.[28]

Table 4: General Vitamin Dosing Guidelines for Adults[14]

Dosing	Vitamin A	Vitamin D	Vitamin E	Vitamin K
Daily	10,000 IU	800-2000 IU	200-400 IU	300-500 mcg
Repletion[1]	20,000 IU	1600-10000 IU	800-12,000 IU	5-10 mg/week

Multivitamins with Water-Miscible Versions of Fat-Soluble Vitamins[2]

- SourceCF (Aptalis) www.sourceCF.com 888-419-8357
- AquADEK (Aptalis) www.aptalispharma.com 800-950-8085
- VITAMAX (Shear/Kershman Laboratories) www.cfservicespharmacy.com 800-541-4959

1. Recheck levels after 1 to 3 months of elevated dosage
2. CF specific multivitamins contain water miscible versions of fat-soluble vitamins in addition to a full complement of the water-soluble vitamins plus zinc

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Increased bile viscosity creates mucous filled bile ducts and subsequent cholestasis.[28] Bile acid retention may cause secondary hepatocyte injury, but the progression from cholestasis to multilobular cirrhosis is often slow, taking decades to develop.[28] Unfortunately, those who develop cirrhosis often quickly develop portal hypertension.[28]

Diagnosis of CFLD is often based on clinical examination in combination with ultrasonography. Liver biochemistry should be done annually and those with abnormal laboratory results and/or physical examination findings should have an ultrasound. Those with CFLD are started on oral bile acid therapy, urosodiol or ursodeoxycholic acid, to improve bile viscosity and hopefully delay hepatocyte damage.[28] Nutritional consequences of CFLD include increased fat malabsorption and alterations in resting energy expenditure. Patients with CFLD are at increased risk for fat-soluble vitamin deficiency and may require aggressive supplementation to maintain normal levels. Since there is no bile acid replacer, a lower fat diet may be helpful in this setting if the patient has a functional bile salt deficiency.

Small Bowel Bacterial Overgrowth

Adults with CF are predisposed to small bowel bacterial overgrowth (SBBO) for a variety of reasons. Frequent use of antibiotics, chronic acid suppression with PPIs, and decreased gastrointestinal motility can increase the incidence of SBBO. Symptoms of SBBO are similar to those of malabsorption; gas, bloating, diarrhea, steatorrhea, and abdominal pain. Similar to the general population, diagnosis of SBBO in CF patients is difficult. Small bowel aspiration can be used to detect SBBO, but the test is invasive and results are limited to the specific area tested. Hydrogen breath tests have been used as a surrogate to diagnose SBBO as well, but can result in false-positives. SBBO is often empirically treated with enteral antibiotics that cover both aerobic and anaerobic bacteria.[29]

Pancreatitis

CF patients who are pancreatic sufficient are 900 times more likely than the general population to develop recurrent acute pancreatitis.[30] Treatment of pancreatitis with CF is similar to that of the general population and those who experience recurrent episodes should be counseled to contact their CF team when symptoms arise. Patients will require adequate pain management and likely intravenous fluids to maintain hydration. Jejunal tube feeding may be used for those who require long-term pancreatic rest and subsequently must remain *nil per os* (NPO or nothing by mouth) for an extended period of time. Although patients may be technically

Table 5: Risk Factors and Prevention of Distal Intestinal Obstruction Syndrome

Risk Factors

- Dehydration
- Immobility
- SBBO
- Previous GI surgery
- Inadequate PERT
- Narcotic use
- Respiratory infection
- Binge eating or grazing

Prevention

- Ensure adequate hydration, especially during exercise, warm weather, and with respiratory infections
- Encourage regular physical activity
- Avoid inadequate or excessive pancreatic enzyme administration
- Discourage binge eating or frequent grazing which may limit PERT effectiveness
- Stool softeners or osmotic laxatives (milk of magnesia, polyethylene glycol)

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pancreatic sufficient, recurrent episodes of pancreatitis may induce fat malabsorption indicating the use of pancreatic enzymes.

Distal Intestinal Obstruction Syndrome

Distal intestinal obstruction syndrome (DIOS) is a complication unique to CF individuals and typically occurs in adults or older children.[7] The intestinal obstruction is often incomplete and occurs in the ileo-cecal region of the small bowel extending into the colon.[7, 30] Slower transit time and a disrupted fluid environment in the small intestine can lead to accumulated stool and a subsequent obstruction. There are a number of factors that may contribute to DIOS and several dietary and lifestyle changes that can decrease the incidence (Table 5).

Gastroesophageal Reflex

Adult patients with CF experience symptoms consistent with gastroesophageal reflux (GER) and in a survey of 201 adult CF patients, 24% experienced symptoms at least weekly.[31] Additionally, females and those with weight loss had significantly more symptoms and even those on acid suppression continued to report symptoms of GER.[31] Patients with weight loss should be evaluated for GER and if present encouraged to eat small frequent meals, eat slowly, and avoid lying flat after eating.

Bone Disease

Prevalence of bone disease among adult CF patients varies from study to study, but it appears to increase with malnutrition and the severity of lung disease.[32] In 2004, a consensus statement was published regarding bone health and CF.[32] Since the pathogenesis of low bone mineral density (BMD) among CF patients is uncertain, the committee used the term CF bone disease, rather than osteoporosis, throughout the report.[32] Bone histomorphometry studies in patients with CF and low BMD reveal low bone volume due to low bone formation at tissue and cellular levels as well as decreased osteoblastic and increased osteoclastic activity.[32-34] Multiple factors contribute to the development of bone disease in CF including, inadequate nutritional status, suboptimal vitamin D levels, physical inactivity, glucocorticoid therapy, delayed puberty, and early hypogonadism.[32, 35] Chronic pulmonary inflammation also increases serum cytokine levels, which may increase bone resorption and decrease bone formation.[32, 35] One study of adult CF patients found that low BMD scores at the spine, femoral neck, and total hip significantly correlated with BMI values less than 19 kg/m^2. Studies have failed to consistently demonstrate a correlation between serum 25-hydroxyvitamin D (25OHD) levels and BMD in CF, but this may be because BMD is a reflection of lifetime bone health, whereas 25OHD levels vary throughout the year.[32] Low BMD is most often seen in adults with CF, but children can also be affected, especially those who are malnourished and frequently ill.[32] A protocol for screening and treatment of bone disease in CF was published in the consensus statement, but recommendations stem from varying degrees of evidence and additional research is needed, especially in the area of vitamin supplementation and use of bisphosphonates.[32] Adults should receive a baseline dual x-ray absorptiometry (DXA) scan, and if normal, repeat every five years.[32]

CONCLUSION

Although previously viewed as a pediatric disorder, cystic fibrosis is now managed well into adulthood. This complex disease coupled with the complications that arise with advanced age requires the coordination of a multidisciplinary healthcare team that specializes in the adult CF patient. Adequate nutrition is imperative through all life stages with CF and the adult CF dietitian must work with clients to assure weight maintenance, sufficient vitamin and mineral levels, and minimal complications.■

References

1. Cystic Fibrosis Foundation. About cystic fibrosis. http://www.cff.org/AboutCF. Updated 2011. Accessed June 30, 2012.
2. Cystic Fibrosis Foundation. Cystic Fibrosis Foundation Patient Data Registry 2010 Annual Report. Bethesda, Maryland: Cystic Fibrosis Foundation; 2010.
3. Walker SA, Gozal D. Pulmonary function correlates in the prediction of long-term weight gain in cystic fibrosis patients with gastrostomy tube feedings. J Pediatr Gastroenterol Nutr. 1998;27(1):53-56.
4. Oliver MR, Heine RG, Ng CH, Volders E, Olinsky A. Factors affecting clinical outcome in gastrostomy-fed children with cystic fibrosis. Pediatr Pulmonol. 2004;37(4):324-329.
5. Efrati O, Mei-Zahav M, Rivlin J, et al. Long term nutritional rehabilitation by gastrostomy in Israeli patients with cystic fibrosis: clinical outcome in advanced pulmonary disease. J Pediatr Gastroenterol Nutr. 2006;42(2):222-228.
6. Schibli S, Durie PR, Tullis ED. Proper usage of pancreatic enzymes. Curr Opin Pulm Med. 2002;8(6):542-546.
7. Borowitz D, Durie PR, Clarke LL, et al. Gastrointestinal outcomes and confounders in cystic fibrosis. J Pediatr Gastroenterol Nutr. 2005;41(3):273-285.
8. Fieker A, Philpott J, Armand M. Enzyme replacement therapy for pancreatic insufficiency: present and future. Clin Exp Gastroenterol. 2011;4:55-73.

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9. Proesmans M, De Boeck K. Omeprazole, a proton pump inhibitor, improves residual steatorrhoea in cystic fibrosis patients treated with high dose pancreatic enzymes. Eur J Pediatr. 2003;162(11):760-763.
10. Borowitz D, Baker RD, Stallings V. Consensus report on nutrition for pediatric patients with cystic fibrosis. J Pediatr Gastroenterol Nutr. 2002;35(3):246-259.
11. Borowitz DS, Grand RJ, Durie PR. Use of pancreatic enzyme supplements for patients with cystic fibrosis in the context of fibrosing colonopathy. Consensus Committee. J Pediatr. 1995;127(5):681-684.
12. Giuliano CA, Dehoorne-Smith ML, Kale-Pradhan PB. Pancreatic enzyme products: digesting the changes. Ann Pharmacother. 2011;45(5):658-666.
13. Maqbool A, Stallings VA. Update on fat-soluble vitamins in cystic fibrosis. Curr Opin Pulm Med. 2008;14(6):574-581.
14. Goodin B. Nutrition Issues in Cystic Fibrosis. Pract Gastroenterol. 2005;25:76-94.
15. Tanumihardjo SA. Assessing vitamin A status: past, present and future. J Nutr. 2004;134(1):290S-293S.
16. Rosales FJ, Chau KK, Haskell MH, et al. Determination of a cut-off value for the molar ratio of retinol-binding protein to transthyretin (RBP:TTR) in Bangladeshi patients with low hepatic vitamin A stores. J Nutr. 2002;132(12):3687-3692.
17. Christian P, West KP,Jr. Interactions between zinc and vitamin A: an update. Am J Clin Nutr. 1998;68(2 Suppl):435S-441S.
18. Tinley CG, Withers NJ, Sheldon CD, et al. Zinc therapy for night blindness in cystic fibrosis. J Cyst Fibros. 2008;7(4):333-335.
19. Tangpricha V, Kelly A, Stephenson A, et al. An update on the screening, diagnosis, management, and treatment of vitamin D deficiency in individuals with cystic fibrosis: evidence-based recommendations from the Cystic Fibrosis Foundation. J Clin Endocrinol Metab. 2012;97(4):1082-1093.
20. Boyle MP, Noschese ML, Watts SL, et al. Failure of high-dose ergocalciferol to correct vitamin D deficiency in adults with cystic fibrosis. Am J Respir Crit Care Med. 2005;172(2):212-217.
21. Green D, Carson K, Leonard A, et al. Current treatment recommendations for correcting vitamin D deficiency in pediatric patients with cystic fibrosis are inadequate. J Pediatr. 2008;153(4):554-559.
22. Rovner AJ, Stallings VA, Schall JI, et al. Vitamin D insufficiency in children, adolescents, and young adults with cystic fibrosis despite routine oral supplementation. Am J Clin Nutr. 2007;86(6):1694-1699.
23. Mailhot G. Vitamin D bioavailability in cystic fibrosis: a cause for concern? Nutr Rev. 2012;70(5):280-293.
24. Khazai NB, Judd SE, Jeng L, et al. Treatment and prevention of vitamin D insufficiency in cystic fibrosis patients: comparative efficacy of ergocalciferol, cholecalciferol, and UV light. J Clin Endocrinol Metab. 2009;94(6):2037-2043.
25. Sathe MN, Patel AS. Update in pediatrics: focus on fat-soluble vitamins. Nutr Clin Pract. 2010;25(4):340-346.
26. Matel JL. Nutritional management of cystic fibrosis. JPEN J Parenter Enteral Nutr. 2012;36(1 Suppl):60S-7S.
27. Dougherty KA, Schall JI, Stallings VA. Suboptimal vitamin K status despite supplementation in children and young adults with cystic fibrosis. Am J Clin Nutr. 2010;92(3):660-667.
28. Colombo C. Liver disease in cystic fibrosis. Curr Opin Pulm Med. 2007;13(6):529-536.
29. DiBaise JK. Small Intestinal Bacterial Overgrowth: Nutritional Consequences and Patients At Risk. Practical Gastroenterology 2008;32:15-28.
30. Mascarenhas MR. Treatment of Gastrointestinal Problems in Cystic Fibrosis. Curr Treat Options Gastroenterol. 2003;6(5):427-441.
31. Sabati AA, Kempainen RR, Milla CE, et al. Characteristics of gastroesophageal reflux in adults with cystic fibrosis. J Cyst Fibros. 2010;9(5):365-370.
32. Aris RM, Merkel PA, Bachrach LK, et al. Guide to bone health and disease in cystic fibrosis. J Clin Endocrinol Metab. 2005;90(3):1888-1896.
33. Elkin SL, Vedi S, Bord S, et al. Histomorphometric analysis of bone biopsies from the iliac crest of adults with cystic fibrosis. Am J Respir Crit Care Med. 2002;166(11):1470-1474.
34. Haworth CS, Webb AK, Egan JJ, et al. Bone histomorphometry in adult patients with cystic fibrosis. Chest. 2000;118(2):434-439.
35. Legroux-Gerot I, Leroy S, Prudhomme C, et al. Bone loss in adults with cystic fibrosis: prevalence, associated factors, and usefulness of biological markers. Joint Bone Spine. 2012;79(1):73-77.