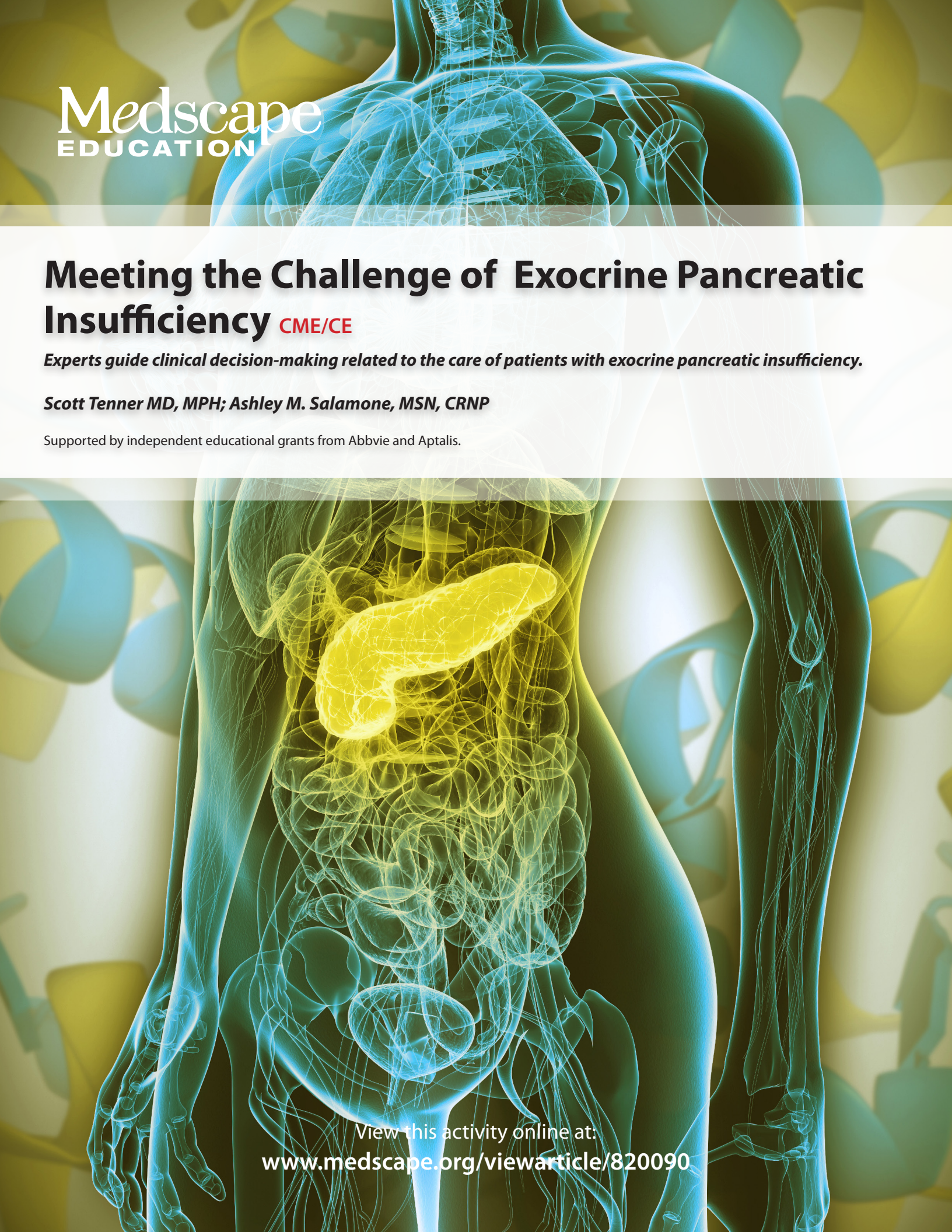

Medscape EDUCATION

Meeting the Challenge of Exocrine Pancreatic Insufficiency CME/CE

Experts guide clinical decision-making related to the care of patients with exocrine pancreatic insufficiency.

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Supported by independent educational grants from Abbvie and Aptalis.

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Target Audience
This activity is intended for gastroenterologists and nurses who care for patients who have exocrine pancreatic insufficiency (EPI).

Goal
The goal of this activity is to engage clinicians in decision making for patients who have conditions that can cause EPI.

Learning Objectives
Upon completion of this activity, participants will be able to:

1. Describe appropriate noninvasive tests to diagnose and assess the status of EPI

2. Recognize common complications associated with EPI

3. Summarize appropriate treatment of EPI and followup

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Overview

The Medscape Practice Challenge is a case-based activity that incorporates consequence-based feedback and guidance from expert faculty as it challenges you with practice-based **clinical decision questions.** Making an incorrect decision results in feedback as to why that decision was incorrect and the clinical consequences of that decision; you will then be given the opportunity to return to the clinical decision point to make a more informed choice. By observing the potential patient outcomes in a case-based learning environment, you can objectively analyze the success and/or consequences of your clinical decisions.

In addition to clinical decision questions, each case also includes questions that **test your knowledge.** After selecting your answer choice for these questions, you will see the correct answer choice, how your peers answered the same question, and an explanation supporting the correct answer.

The Medscape Practice Challenge is designed to support future knowledge retrieval in real-world circumstances, which is the foundation for improving your clinical competence and performance.

Case 1: Roger

Roger is a 55-year old high school teacher who was recently divorced and now lives alone. He was treated by your colleague for acute pancreatitis 2 months ago, at which time he was hospitalized. During today's follow-up visit to your office, he complains of foul-smelling diarrhea and stools that appear fatty and float in the toilet water.

During Roger's hospital admission, contrast-enhanced computed tomography (CT) demonstrated fulminant pancreatic necrosis, and he spent 2 weeks in the intensive care unit, where his care included enteral feeding. Insulin was started due to the development of endocrine pancreatic insufficiency. After a month in the hospital, he resumed a normal diet and was discharged on long-acting insulin.

Today, Roger complains of diarrhea 6 to 8 times per day but reports no abdominal pain and his temperature is normal. Although over-the-counter antidiarrheal agents such as Pepto-Bismol® have been somewhat helpful, his symptoms have persisted. He describes some bloating and increased flatulence. You note that he has lost 10 lb since his discharge from the hospital. No melena or hematochezia are found and Roger is taking no medications other than insulin. Blood pressure is 110/70 mm Hg, pulse is 95 beats/min, respirations are 13/min, and he is afebrile. Physical examination reveals slight dehydration, sunken eyes, and dry oral mucosa; the examination is otherwise unremarkable.

What is the most appropriate next step in the approach to Roger's situation?

- Perform a 24-hour fecal fat test to establish malabsorption as the cause of diarrhea
- Initiate a trial of pancreatic enzyme replacement therapy (PERT)
- Obtain magnetic resonance imaging (MRI) with cholangiopancreatography
- Initiate empiric metronidazole for *Clostridium difficile* infection

See next page for answer and explanation

Correct Answer

- Perform a 24-hour fecal fat test to establish malabsorption as the cause of diarrhea
- Initiate a trial of pancreatic enzyme replacement therapy (PERT)
- Obtain magnetic resonance imaging (MRI) with cholangiopancreatography
- Initiate empiric metronidazole for *Clostridium difficile* infection

Consequence: You Initiate a trial of PERT and the effect confirms the diagnosis and addresses the malabsorption, but does not delay treatment while C *difficile* infection is being ruled out.

Correct Answer Explanation: A trial of PERT should be initiated when the clinical presentation is strongly suggestive of exocrine pancreatic insufficiency (EPI).[1,2] EPI should be suspected in this patient with a history of fulminant pancreatic necrosis as well as *endocrine* pancreatic insufficiency. The clinical manifestation of EPI is fat malabsorption manifested as steatorrhea, which develops in patients who have decreased luminal pancreatic enzyme activity below approximately 10% of the normal capacity of the pancreas. Steatorrhea can be thought of as a syndrome that consists of fecal excretion >6 g/d of fat, weight loss, abdominal discomfort, and abdominal swelling (from gas). The stool in steatorrhea is characterized as loose, malodorous, and greasy (oil droplets) and may be difficult to flush. As Roger's imaging has already established fulminant pancreatic necrosis, PERT should be initiated. PERT is indicated in patients with steatorrhea and weight loss, and at a sufficiently high dosage to resolve the steatorrhea.

Perform a 24-hour fecal fat test to establish malabsorption as the cause of the diarrhea

Consequence: You order a 24-hour fecal fat test, but the results provide no useful information and delay the initiation of treatment.

Explanation: The test will provide no useful information.

Obtain an MRI with magnetic resonance cholangiopancreatography

Consequence: You obtain this test and subject the patient to unnecessary testing.

Explanation: Both MRI and CT studies done during Roger's recent hospitalization demonstrated fulminant pancreatic necrosis, which is irreversible, so further testing is unnecessary.

Initiate empiric metronidazole for *Clostridium difficile* infection

Consequence: You begin metronidazole, which delays appropriate treatment and exposes Roger to unnecessary antibiotic use.

Explanation: Although C *difficile* infection is an important cause of diarrhea and must be identified in a patient recently discharged from the hospital, Roger's clinical picture and history point to EPI.

Because EPI has multiple possible causes and is not usually recorded as a medical statistic, its prevalence and demographics cannot be established with certainty. Studies have shown that EPI may be present in approximately 20% of patients with diabetes mellitus, although it may not be severe enough to require treatment.[16,17] Table 1 includes tests for assessing malabsorption and direct and indirect tests of pancreatic function.

Table 1. Tests to Assess Malabsorption and Pancreatic Function

72-hour fecal fat test	Quantitative measurement of fat absorption. Patients are instructed to consume a normal amount (80-100 g/d) of fat before and during the collection. On the basis of this level of intake, fecal fat excretion in healthy individuals should be less than 7 g/d. The coefficient of fat absorption (CFA) is the percentage of absorbed fat in the diet. Normal CFA is approximately 90%. The various diseases that can give rise to EPI will produce different degrees of pancreatic insufficiency and, hence, different CFAs.
Hydrogen breath test	A sensitive test for carbohydrate malabsorption. Patients are administered an oral solution of lactose. In cases of lactase deficiency, colonic organisms digest the unabsorbed lactose, which results in elevated hydrogen content in the expired breath.
Bile salt breath test	Can determine the integrity of bile salt metabolism. In interrupted enterohepatic circulation (eg, from bacterial overgrowth, ileal resection, or disease), a radioactively labeled elevated breath carbon dioxide level will be noted.
Schilling test	May help differentiate malabsorption of vitamin B_{12} as a consequence of an intrinsic factor deficiency, pancreatic insufficiency, bacterial overgrowth, ileal resection, or disease.
^{13}C-D-xylose breath test	Although this breath test may be used to verify treatment success, this approach is rarely feasible in clinical practice.
Direct Tests of Pancreatic Function	
Secretin test	Measures the ability of the ductal cells to secrete bicarbonate. Porcine or human synthetic secretin is given in doses ranging from 0.5 to 5 clinical units (CU)/kg. A bicarbonate concentration lower than 80 mEq/L in all 4 aliquots represents exocrine insufficiency. A peak bicarbonate concentration lower than 50 mEq/L is indicative of severe exocrine insufficiency.
Cholecystokinin (CCK) test	Measures the ability of the acinar cells to secrete digestive enzymes. An accurate determination is made of enzyme concentration, enzyme output, and fluid volume on the basis of recovery of the polyethylene glycol marker.
Secretin-CCK test	The combined secretin-CCK test allows simultaneous assessment of ductal and acinar secretory capacity.
Indirect Tests of Pancreatic Function	
Qualitative fecal fat analysis via microscopic examination of random stool samples	Screening test only.
Fecal elastase and fecal chymotrypsin levels	Sensitivity is limited to moderate or severe disease, and the result can be falsely positive as a result of dilution by watery stools.

Which enzyme contained in pancreatic enzyme products plays the dominant role in therapy for exocrine pancreatic insufficiency?

- Lipase
- Protease
- Amylase
- Esterase

See next page for answer and explanation

Correct Answer

- (●) Lipase
- ( ) Protease
- ( ) Amylase
- ( ) Esterase

Explanation:
Lipase plays the dominant role in therapy for EPI. Because pancreatic lipase accounts for up to 90% of fat digestion, maldigestion of fat is more profound in EPI than is maldigestion of proteins and carbohydrates. To restore nutrient digestion in patients who have EPI, enzymes must be delivered into the duodenal lumen in sufficient quantities and synchronized with meals. Intraluminal lipase activity requires a minimum of 40 to 60 U lipase/min in postprandial chyme throughout the digestive period.[3]

You decide to initiate a trial of PERT consisting of 8000 U of lipase, 30,000 U of amylase, and 30,000 U of protease per meal and advise Roger to use half that dose when eating snacks, depending on the size and fat content of the snacks. For example, no PERT is needed with a midnight snack of an Italian ice, but a dish of ice cream will require a dose.

You explain to Roger that pancreatic enzymes should be taken at the first bite of a meal (not before or after the meal) and advise him not to crush or chew the capsule because doing so could dissolve the enteric coating, diminishing the enzymatic activity and irritating his throat. You also tell him he should not hold tablets in his mouth to avoid exposure of his oral mucosa to the enzymes. You also explain that if for some reason he has difficulty swallowing capsules, he can open them and sprinkle the contents on soft food with a pH level of 4.5 or lower, such as applesauce.

Within 1 week of initiating PERT, Roger reports that the diarrhea has improved. Over the course of 1 month he gains 4 lb and reports he is doing well. Six months after initiating PERT, however, Roger's symptoms gradually recur: first he experiences bloating, followed one month later by diarrhea. A fecal fat test is positive. Stool cultures for ova and parasites are normal.

You ask Roger to describe his use of PERT and are satisfied that he has been using it correctly. He reports that he found it helpful over the last few days to reduce the amount of fat he was consuming and he is starting to lose weight. You order a CT scan, which demonstrates walled-off pancreatic necrosis (WOPN) with the entire pancreas replaced by liquefied pancreatic parenchyma (Figure 1).

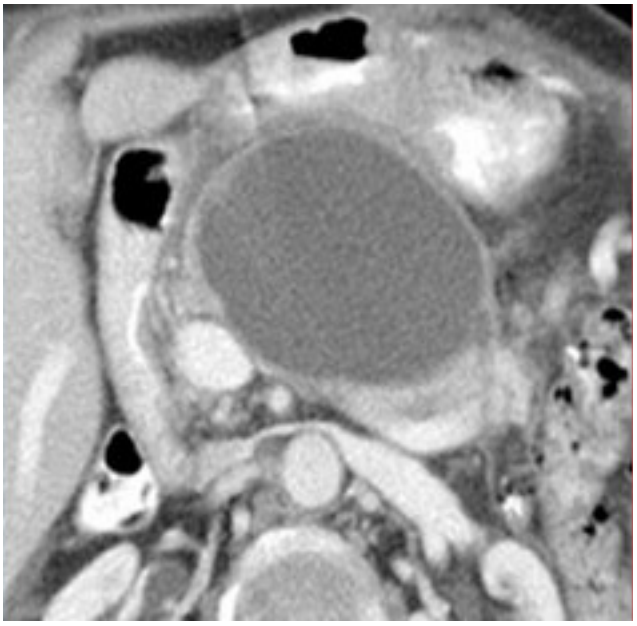

Figure 1. CT scan demonstrating organization of the necrosis. No pancreatic parenchyma is identified

What is the best approach for the management of Roger's WOPN?

- Laproscopic surgical resection of necrotic tissue
- Initiate an antibiotic to prevent infection of the necrotic tissue
- Endoscopic resection of the necrotic tissue
- Conservative management with no drainage or antibiotic therapy

See next page for answer and explanation

Correct Answer

- ○ Laproscopic surgical resection of necrotic tissue
- ○ Initiate an antibiotic to prevent infection of the necrotic tissue
- ○ Endoscopic resection of the necrotic tissue
- ◉ Conservative management with no drainage or antibiotic therapy

Consequence: You manage Roger's condition conservatively.

Correct Answer Explanation: The presence of infected necrotic tissue often necessitates surgical debridement but is not necessary in asymptomatic patients with sterile necrosis. Similar to pseudocysts, regardless of size and location, asymptomatic WOPN is treated conservatively.

Laproscopic surgical resection of necrotic tissue

Consequence: You refer Roger for laparoscopic surgery to resect the necrotic tissue. Surgery subjects Roger to unnecessary risk and expense.

Explanation: Roger does not have infected necrosis.

Initiate an antibiotic to prevent infection of the necrotic tissue

Consequence: You begin antibiotic therapy unnecessarily.

Explanation: Antibiotic prophylaxis has no role in sterile necrosis. Antibiotic therapy should be reserved for patients found to have an infection, biliary sepsis, or both.

Endoscopic resection of the necrotic tissue

Consequence: You perform endoscopic surgery to resect the necrotic tissue. Surgery subjects Roger to unnecessary risk and expense.

Explanation: Surgical intervention, although necessary in infected necrosis, increases morbidity and mortality in patients with acute pancreatitis. The timing of debridement is controversial and under intense study. Cases should be considered individually; most patients with sterile necrosis and some patients with infected necrosis will not require surgical debridement.

Which of the following is true regarding PERT (8000 U of lipase, 30,000 U of amylase, and 30,000 U of protease per meal) in an adult with EPI?

- The initial dosage of lipase is too low
- The dosage of all 3 enzymes are correct initial therapy
- The dosage of amylase is too low
- The dosage of protease is too low

See next page for answer and explanation

Correct Answer

- (●) The initial dosage of lipase is too low
- ( ) The dosage of all 3 enzymes are correct initial therapy
- ( ) The dosage of amylase is too low
- ( ) The dosage of protease is too low

Explanation:
Approximately 25,000 to 50,000 U lipase per meal are recommended, but a higher dose may be needed, especially in the setting of necrotizing pancreatitis. The optimal dose of PERT in patients with necrotizing pancreatitis has not been systematically investigated, although investigators recommend a higher dosage of lipase (70,000-80,000 U) to be given with the main meal.[4,5]

Based on Roger's new symptoms, current treatment, and history, what is the most appropriate next step?

- Add a proton pump inhibitor (PPI), such as omeprazole, daily
- Obtain a fecal elastase test
- Perform an upper gastrointestinal endoscopy with biopsies of the duodenum to rule out celiac disease and *Giardia lamblia*
- Increase the dosage of lipase to 70,000-80,000 U per meal

See next page for answer and explanation

Correct Answer

- ○ Add a proton pump inhibitor (PPI), such as omeprazole, daily
- ○ Obtain a fecal elastase test
- ○ Perform an upper gastrointestinal endoscopy with biopsies of the duodenum to rule out celiac disease and Giardia *lamblia*
- ◉ Increase the dosage of lipase to 70,000-80,000 U per meal

Consequence: You increase the dose of lipase and Roger's symptoms improve.

Correct Answer Explanation: The purpose of treating EPI with pancreatic enzymes is to induce a lipolytic capacity that corresponds to the amount of ingested fat at every meal. A higher dose of lipase is necessary for large, high-fat meals and a lower dose is sufficient for snacks and lean meals. Approximately 25,000 to 50,000 U lipase per meal are recommended, but a higher dose may be required. Although the optimal dose of pancreatic enzyme needed in patients with necrotizing pancreatitis has not been systematically investigated, investigators recommend a high dosage of lipase (70,000 to 80,000 U) per main meal.

Add a proton pump inhibitor (PPI) such as omeprazole daily

Consequence: You prescribe a PPI for Roger and his symptoms do not improve.

Explanation: The rationale for adjuvant treatment with PPIs is that insufficient buffering of gastric chyme when it enters the small bowel may compromise the effect of PERT. Lipase degrades rapidly at a low pH, and enzyme release from microspheres is pH dependent.

Obtain a fecal elastase test

Consequence: You order a fecal elastase test, which delays initiation of appropriate treatment.

Explanation: Fecal elastase test is an inaccurate measure of exocrine pancreatic insufficiency. Sensitivity is unacceptably low (eg, 64% for severe disease and 40% for mild to moderate disease)[6] and specificity is poor.

Perform an upper endoscopy with biopsies of the duodenum to rule out celiac disease and *Giardia lamblia*

Consequence: Roger undergoes an upper gastrointestinal endoscopy, which unnecessarily exposes him to an invasive procedure.

Explanation: Although *G lamblia* infection and celiac disease can present with similar symptoms, it is unlikely that Roger has either condition, given his history.[7,8]

Conclusion

You adjust the dosage of enzymes to 2 enteric-coated capsules containing 36,000 U lipase with each meal. Depending on the fat content, Roger may need to use 1 capsule for snacks such as ice cream, a doughnut, or a muffin. The goal in treating Roger long-term is not only to decrease the symptoms of EPI but also correct the malabsorption.

Roger returns in 3 months feeling well on the increased dosage. He has gained weight and feels productive at work. Physical examination and review of systems suggests that his EPI is well controlled on the current dosage of PERT. You remind Roger to call you if he experiences any abdominal symptoms or unexplained weight loss, and schedule the next follow-up visit.

Case 2: Diedre

Diedre is a 56-year-old freelance writer seeing you now for a complaint of fatigue and a 10-lb weight loss over the last year. She now weighs 110 lb on a 5′ 3″ frame. In addition to the weight loss, she has also been experiencing loose stools and bloating.

After the death of her child in a car accident 20 years ago, Diedre began drinking a bottle of vodka daily. She has been sober for 5 years and has remained healthy and has no history of abdominal pain. Based on her age, weight loss, and 15-year history of chronic alcohol abuse, you order an abdominal CT scan, laboratory tests, colonoscopy with biopsies, and stool analysis.

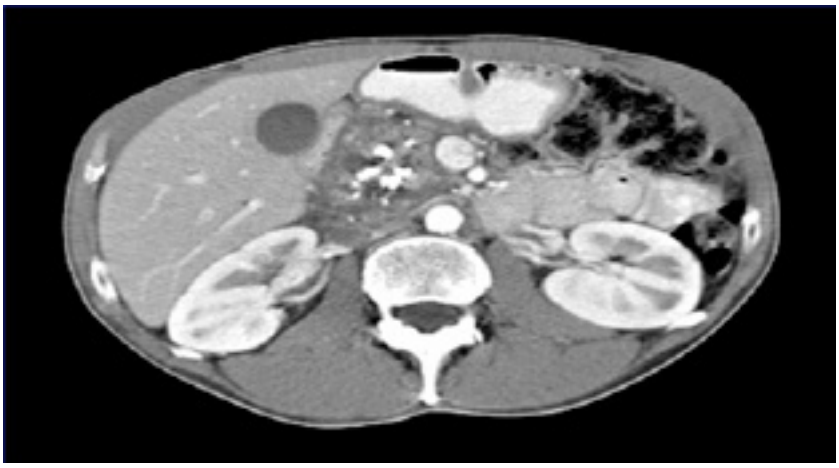

Figure 2. CT scan demonstrates calcific chronic pancreatitis

The CT scan demonstrates calcific chronic pancreatitis (Figure 2). Colonoscopy with random biopsies to exclude microscopic colitis is negative. Stool analysis, including *Giardia* antigen, is negative. Sudan stain is positive for fecal fat. Thyroid-stimulating hormone level is normal and tissue transglutaminase antibody is negative. Serum amylase and lipase levels are 2 times the upper limit of normal.

What is most likely the cause of Diedre's symptoms?

- New-onset celiac disease
- Acute pancreatitis
- EPI
- Bacterial overgrowth

See next page for answer and explanation

Correct Answer

- New-onset celiac disease
- Acute pancreatitis
- EPI
- Bacterial overgrowth

Consequence: You initiate PERT for EPI.

Correct Answer Explanation: Given Diedre's history, imaging findings, and laboratory results, it is likely that chronic pancreatitis has progressed to EPI. Chronic pancreatitis is most often caused by alcohol use such as in Diedre's case, although genetic, autoimmune, and environmental factors may contribute.[9] Development of irreversible fibrosis of the pancreatic parenchyma typically leads to changes in the pancreatic ducts that later in the course of the disease are easily identified on imaging. The disease is often difficult to diagnose early. Diedre has advanced disease, with CT demonstrating chronic changes and calcification of the pancreas consistent with chronic pancreatitis, likely leading to EPI.

New-onset celiac disease

Consequence: You investigate further for celiac disease, delaying initiation of appropriate treatment.

Explanation: The history, imaging findings, and lab results do not support a diagnosis of celiac disease.

Acute pancreatitis

Consequence: You order additional testing to assess for acute pancreatitis, subjecting Diedre to additional unnecessary testing.

First Explanation: Diedre's symptoms and history of chronic pancreatitis do not fit with acute pancreatitis (usually associated with acute abdominal pain).

Bacterial overgrowth

Consequence: You initiate antibiotic treatment for bacterial overgrowth.

Explanation: A diagnosis of bacterial overgrowth is not suggested by the laboratory results and initiating antibiotic treatment is inappropriate.

Which of the following tests is regarded as the gold standard for detection of EPI?

- Fecal elastase
- Secretin-cerulein test
- Bentiromide test
- 72-hour fecal fat study

See next page for answer and explanation

Correct Answer

- Fecal elastase
- Secretin-cerulein test
- Bentiromide test
- 72-hour fecal fat study

Explanation:
The secretin-cerulein test depends on the fact that EPI can be established by demonstrating a decrease in bicarbonate secretion after secretin is administered intravenously (IV). The test requires multiple measurements of duodenal bicarbonate from the pancreas responding to high-dose IV secretin. The test is time consuming and uncomfortable for the patient. Less-invasive alternative tests that indirectly suggest EPI include fecal elastase, lipase, or chymotrypsin; pancreolauryl test; bentiromide test; and breath tests using radiolabeled pancreatic substrates such as triolein. Both fecal elastase and the 72-hour fecal fat study can identify steatorrhea, but not specifically EPI.

Based on Ct, colonoscopy, stool studies, and laboratory tests, you are confident that EPI arising from longstanding chronic pancreatiis is likely the cause of Diedre's symptoms. Elevated serum amylase and lipase levels do not predict acute or chronic pancreatitis, pancreatic cancer, or pancreatic insufficiency.

What is the most appropriate next step in Diedre's care?

- Prescribe 20,000 to 40,000 U of lipase per meal and 10,000 to 20,000 U of lipase per snack
- Perform an endoscopic retrograde cholangiopancreatograph (ERCP) with possible stone extraction from the pancreatic duct
- Prescribe 5,000 to 10,000 U of lipase per meal

See next page for answer and explanation

Correct Answer

- (●) Prescribe 20,000 to 40,000 U of lipase per meal and 10,000 to 20,000 U of lipase per snack
- ( ) Perform an endoscopic retrograde cholangiopancreatograph (ERCP) with possible stone extraction from the pancreatic duct
- ( ) Prescribe 5,000 to 10,000 U of lipase per meal

Consequence: You initiate PERT at a starting dosage that based on her weight should be high enough to resolve her symptoms.

Correct Answer Explanation: Starting at a high dosage of lipase (greater than 30,000 U per meal) is preferable to starting at a lower dosage and waiting to gauge therapeutic effect. A significant effect may not be noticed for 1 week.

Perform an endoscopic retrograde cholangiopancreatograph (ERCP) with possible stone extraction from the pancreatic duct

Consequence: You order an ERCP and subject Diedre to an unnecessary procedure.

Explanation: No further testing is needed as the diagnosis of chronic pancreatitis is established by the presence of calcifications within the pancreas and Diedre's clinical history of alcohol abuse.

Prescribe 5,000 to 10,000 U of lipase per meal

Consequence: You start Diedre at too low a dosage of lipase to have any therapeutic effect and she continues to have symptoms.

Explanation: The dosage is too low to have a desired therapeutic benefit.

Based on Diedre's weight and the dietitian's assessment of usual fat grams consumed, you prescribe an initial dosage of 20,000 to 40,000 U of lipase per meal and 10,000 to 20,000 U of lipase per snack in an enteric-coated capsule (Table 2). You explain to Diedre exactly how and when the enzymes should be taken. You provide a patient handout with details on how to use the enzymes, ask if she has any questions, and schedule a follow-up appointment with Diedre in 2 weeks.

Table 2. Lipase Content of Currently Available Pancreatic Enzyme Products

Pancreatic Enzyme Product	Lipase Content, U	Comment
Creon® 1203	3000	Capsule can be opened for patients unable to swallow
Creon 1206	6000	
Creon 1212	12,000	
Creon 1224	24,000	
Zenpep® EURAND 3	3000	Capsule can be opened for patients unable to swallow
Zenpep EURAND 5	5000	
Zenpep EURAND 10	10,000	
Zenpep EURAND 15	15,000	
Zenpep EURAND 20	20,000	
Zenpep EURAND 25	25,000	
Pancreaze® MT 4	4200	Capsule can be opened for patients unable to swallow
Pancreaze MT 10	10,500	
Pancreaze MT 16	16,800	
Pancreaze MT 24	21,000	
Ultresa® 13800UL	13,800	Capsule can be opened for patients unable to swallow
Ultresa 20700UL	20,700	
Ultresa 23000UL	23,000	
Viokace® 9111	10,440	Tablet must be taken whole, not crushed. Proton pump inhibitor should be given daily with the medication unless another reason for acid suppression exists
Viokace 9116	20,880	
Pertzye® 8	8000	Capsule can be opened for patients unable to swallow
Pertzye 16	16,000	

What is an appropriate adjunctive therapy in a patient who is taking lipase at a dosage of 100,000 U per meal in a nonenteric coated product?

- Add a PPI
- Increase the dosage of amylase and protease in addition to the lipase
- Add an H_2 blocker
- Switch to an enteric-coated product

See next page for answer and explanation

Correct Answer

- (●) Add a PPI
- ( ) Increase the dosage of amylase and protease in addition to the lipase
- ( ) Add an H_2 blocker
- ( ) Switch to an enteric-coated product

Explanation:
Acid suppression should be considered when high doses of a nonenteric-coated formulation of a pancreatic enzyme product are used. The rationale for adjuvant treatment with PPIs is that bicarbonate secretion is impaired in chronic pancreatitis, resulting in insufficient buffering of the gastric chyme when it enters the small bowel. This phenomenon may in turn compromise the effect of PERT because lipase is rapidly degraded at a low pH and because enzyme release from microspheres is pH dependent. PPIs are preferred over H_2 blockers to protect the degradation of lipase.

Diedre returns 2 weeks after beginning 20,000 to 40,000 U of lipase per meal and 10,000 to 20,000 U of lipase per snack in an enteric-coated capsule. Although her weight has stabilized, she has not regained the lost weight. She has noticed only a slight improvement in bloating and continues to have diarrhea 3 or 4 times daily. She has no abdominal pain.

What is the most appropriate next step in Diedre's care?

- Switch to a different brand with the same amount of lipase
- Add a PPI
- Advise the patient to decrease her fat intake
- Verify that Diedre is taking the PERT correctly

See next page for answer and explanation

Correct Answer

- ○ Switch to a different brand with the same amount of lipase
- ○ Add a PPI
- ○ Advise the patient to decrease her fat intake
- ◉ Verify that Diedre is taking the PERT correctly

Consequence: You ask Diedre to describe in detail her use of enzymes and it becomes clear to you that she has been taking them incorrectly -- after she completes her meal -- and she sometimes forgets to take them with snacks. You reinforce the importance of taking the enzymes with the first bite of a meal and with certain snacks.

Correct Answer Explanation: It is important to confirm that the patient is taking the enzymes correctly before making any adjustments to the enzyme regimen.

Switch to a different brand with the same amount of lipase

Consequence: You prescribe a different brand of enzyme formulation with the same amount of lipase and see no improvement in Diedre's symptoms.

Explanation: Pancreatic enzyme formulations are not interchangeable due to pharmacokinetics, dosage, and delivery.

Add a PPI

Consequence: You prescribe a PPI. Diedre has no improvement in symptoms.

Explanation: Acid suppression is needed when using a nonenteric-coated formulation such as Viokase, unless the patient is an infant or has another reason to have a nonacidic gastric pH. The enzymes in these formulations are rapidly inactivated by acid in the stomach.[12]

Advise the patient to decrease intake of fat

Consequence: You advise Diedre to reduce her fat intake. She complies, but continues to lose weight.

Explanation: The goal is not to reduce the symptoms by reducing the intake of nutrients or fat, but to maximize absorption through PERT. Decreasing fat intake rarely is successful and often leads to further weight loss.

At the 1-month follow-up visit, Diedre reports that she feels fine and her bowel habits have returned to normal. She has gained 3 lb since her last visit.

Knowing that she must use PERT long term, Diedre is concerned about the safety of these agents and she has reviewed information on the Internet to supplement the information you have given her about EPI and the use of enzymes. Her research on the Internet has suggested that PERT can put her at risk for fibrosing colonopathy.

You explain to Diedre that she is not at risk for fibrosing colonopathy because its occurrence in association with use of PERT has been limited to children who had EPI related to cystic fibrosis, and these children were on very high doses of enzymes. You explain that in adults, porcine-derived pancreatic enzyme products contain purines that may increase blood uric acid levels, but because she has no history of gout, renal impairment, or hyperuricemia, this is not a concern.

Conclusion

Three months later, Diedre has gained 10 lb. She continues to feel good and she has confidently taken on a new writing assignment that requires travel and interviews.

Nursing Perspective on Care: Exocrine Pancreatic Insufficiency

For patients with a chronic condition such as exocrine pancreatic insufficiency (EPI), the systematic approach to nursing -- assessment, diagnosis, planning, implementation, and evaluation -- is especially important in providing comprehensive, education-oriented and individualized treatment to improve patient care, outcomes, and quality of life.

EPI is the inadequate pancreatic enzyme activity due to insufficient enzyme production or activation, or early enzyme degradation. EPI can be a consequence of a number of conditions, including pancreatic diseases leading to a loss of pancreatic parenchyma (such as in chronic pancreatitis and cystic fibrosis), obstruction of the main pancreatic duct (ampullary and pancreatic tumors), decreased pancreatic stimulation (such as in celiac disease), acid-mediated inactivation of pancreatic enzymes (such as in Zollinger-Ellison syndrome), and gastrointestinal resection.[13,14] What does this mean for nurses and how can nurses best care for patients with EPI? What should nurses look for, and what kind of education should we provide our patients?

Case Study

It has been 6 years since Mrs P, 56 years of age, was given a diagnosis of chronic pancreatitis secondary to alcohol abuse and smoking. She has been sober and tobacco-free for the past 10 years and is otherwise generally healthy. Today's visit is a follow-up to a visit 1 week earlier for new gastrointestinal problems and to review the results of a CT scan and blood work. You ask how she is doing and review her problems and concerns. Her chief complaint is unintentional weight loss, and she hesitatingly states that she has had a change in bowel habits. You encourage her to describe the change, and Mrs P reveals that she has been troubled for 6 months with frequent, oily, foul-smelling stools. She also describes nonspecific symptoms of abdominal bloating, discomfort, and postprandial nausea. No family members have similar symptoms.

You weigh Mrs P and note that she has lost 15 lb over the past 6 months. She denies fever, chills, vomiting, jaundice, or other symptoms. The CT scan was reported as normal and results of complete blood cell count and complete metabolic panel lab work were within normal limits. None of the over-the-counter medications she tried (multivitamin, loperamide antidiarrheal agents, and ginger and peppermint herbal supplements) were helpful. She reports no new prescription medications and no change in her diet or exercise regimen. Her daily stress is well managed and her family is in good health. Her symptoms have started to interfere with her daily life and limit her ability to socialize with friends and family. She has a steady job with prescription coverage with her health insurance. She wants to know what is wrong with her and asks for help.

Is it EPI?

This case study with Mrs P is an example of a patient who demonstrates undiagnosed EPI. To appreciate EPI and the role of the nurse in its diagnosis, it is important to understand how EPI manifests.

EPI is a relatively common -- and often unrecognized -- condition of an impaired ability to produce sufficient pancreatic enzymes required for digestion. Short- and long-term effects of EPI can lead to serious complications related to malabsorption.[15] Steatorrhea is among the main symptoms of EPI. In a patient such as Mrs P, EPI should be suspected in the setting of steatorrhea and history of chronic pancreatitis. As a nurse, you alert the primary care physician to your suspicion of EPI. The primary care physician reviews the information, assesses Mrs P, and refers her to a nutritionist. Mrs P is started on a trial of pancreatic enzyme replacement therapy (PERT). The physician asks you to ensure Mrs P fills this prescription and understands the dosing instructions. She will return in 4 weeks for follow-up.

EPI is a common concomitant problem with disease processes that affect the pancreas, such as cystic fibrosis and chronic pancreatitis. EPI can also be present with other conditions such as celiac disease, inflammatory bowel disease, stomach ulcer, autoimmune disease, and pancreatic cancer. Patients who undergo gastrointestinal and pancreatic surgery also are predisposed to EPI.[13-15] Studies have shown that EPI may be present in approximately 20% of patients with diabetes mellitus, although it may not be severe enough to require treatment.[16,17]

Asking about specific stool characteristics is important to distinguish steatorrhea from what the patient may describe as diarrhea. Understanding how patients describe the distinguishing features of steatorrhea is important in recognizing this clue to EPI. A patient may complain of pale stools that float in the toilet bowel; have a loose, oily consistency; and have a very foul odor. These alterations develop as a result of fat that is not absorbed in the small intestine.[15] Other important clues to malabsorption in EPI include unexplained weight loss, poor appetite, abdominal bloating, nonspecific abdominal pain, and signs and symptoms of vitamin deficiencies.

Diagnosis of EPI is usually based on a patient's medical history and presenting symptoms. Diagnostic tests include indirect and direct measures of pancreatic enzyme concentration via stool analysis or duodenal aspirate. Fecal elastase is an adequate test used to detect steatorrhea as a sign of moderate to severe EPI but does not allow for monitoring of enzyme therapy response. Due to their cumbersome nature, 72-hour fecal fat studies in an outpatient setting have been limited in use. Dietary modification and pancreatic enzyme supplements are the cornerstones of EPI treatment.

Assessment

When you suspect EPI, ask the patient specific questions about any changes or difficulties in bowel habits, signs and symptoms of malabsorption, or gastrointestinal symptoms such as abdominal bloating and nonspecific pain. Your careful attention to the details of these answers is key. Patients are often uncomfortable or unfamiliar with speaking about their bowel habits; explaining your line of questioning can help put the patient at ease. Helpful to investigating a concern for malabsorption is a review of systems and targeted questions pertaining to symptoms of deficiency in fat-soluble vitamins, such as joint pain, muscle aches and weakness, easy bruising, dermatologic changes, and night blindness.

Diagnosis and Planning

Nurses can play a pivotal role for a patient struggling with signs and symptoms of undiagnosed EPI. A nurse who suspects EPI should speak with the patient's provider about investigating this common condition. Ensuring that the patient understands the importance of the workup associated with EPI can be an instrumental step in reaching a diagnosis. Once a diagnosis is established, the patient may meet with a nutritionist to assess caloric and nutrient intake, and to learn about the effect of dietary modification on EPI, such as the effect on symptoms of eating smaller, frequent meals to evenly distribute fat intake throughout the day. Current US dietary guidelines recommend 20% to 35% of daily caloric intake from fat and avoidance of high-fat foods.[15]

Pancreatic enzyme products are generally recommended when dietary modification alone is ineffective. These oral supplements are the mainstay of treatment for malabsorption secondary to EPI, and counseling the patient about the timing and dosage of pancreatic enzyme administration is crucial in the planning process. Enzymes are taken with every meal and with certain snacks to aid digestion and improve vitamin deficiencies, as well as to promote weight gain. As a result, they are effective in reducing steatorrhea.[13] A recent study demonstrated a statistically significant weight gain and reduced stool frequency with use of pancrelipase in patients who had EPI due to CP or pancreatic surgery.[18] However, adequate dosing can be a challenge for patients.[14]

Implementation and Evaluation

A patient initiating dietary modification and/or pancreatic enzyme supplementation should be monitored for improvement or resolution of symptoms and the development of new problems. The patient's weight should be documented at each visit, as trends in weight change indicate response to therapy. A thorough medication history is vital, as is questioning to determine exactly how and when patients use the enzymes to gauge adherence to medication. Inadequate dosing and improper ingestion of pancreatic enzymes are among the most common reasons for ongoing steatorrhea. A medication conversation should always be conducted when a patient continues to have signs and symptoms of EPI after having been given a prescription for pancreatic enzyme product. It is imperative to ensure patients are educated on their use. Although 13C-labeled mixed triglyceride (C-MTG) breath test may be used to verify treatment success, this approach is rarely feasible in clinical practice. Most guidelines recommend a reevaluation of symptoms and weight and a reevaluation of serum tests of malnutrition.[1,2]

Nurses are in an ideal position to conduct this ongoing assessment and to identify any barriers to patient adherence, such as frequency of dosing and the cost of the pancreatic enzyme product. Investigating perceived barriers with the patient is often fruitful. For example, some insurance prescription plans cover only a portion of the cost of the pancreatic enzyme product, which may cause a patient to eat less or underdose their enzymes to cut costs. Many pharmaceutical companies offer financial assistance programs to help patients who may not be able to afford these necessary replacements. Staying current about these programs provides an opportunity to better serve patients.

Summary

The case of Mrs P demonstrates an opportunity for nurses to have a positive effect on patient quality of life. Nurses have the ability to understand EPI and identify those individuals who may be at risk for it and are well positioned to work collaboratively with healthcare professionals. Nurses are patient advocates who have been taught to use the nursing process to improve patient outcomes.

References

1. Frulloni L, Falconi M, Gabbrielli A, et al. Italian consensus guidelines for chronic pancreatitis. *Dig Liver Dis.* 2010;4(Suppl 6):S381-S406.
2. Toouli J, Biankin AV, Oliver MR, et al. Management of pancreatic exocrine insufficiency: Australasian Pancreatic Club recommendations. *Med J Aust.* 2010;193:461-467.
3. Dominguez-Munoz JE, Iglesias-Garcia J, Iglesias-Rey M, et al. Effect of the administration schedule on the therapeutic efficacy of oral pancreatic enzyme supplements in patients with exocrine pancreatic insufficiency: a randomized, three way crossover study. *Aliment Pharmacol Ther.* 2005;21:993-1000.
4. Whitcomb DC, Lehman GA, Vasileva G, et al. Pancrelipase delayed-release capsules (CREON) for exocrine pancreatic insufficiency due to chronic pancreatitis or pancreatic surgery: a double-blind randomized trial. *Am J Gastroenterol.* 2010;105:2276-2286.
5. Thorat V, Reddy N, Bhatia S, et al. Randomised clinical trial: the efficacy and safety of pancreatin enteric-coated minimicrospheres (Creon 40000 MMS) in patients with pancreatic exocrine insufficiency due to chronic pancreatitis -- a double-blind, placebo-controlled study. *Aliment Pharmacol Ther.* 2012;36:426-436.
6. Hahn JU, Bochnig S, Kerner W, et al. A new fecal elastase 1 test using polyclonal antibodies for the detection of exocrine pancreatic insufficiency. *Pancreas.* 2005;30:189-191.
7. Rubio-Tapia A, Hill ID, Kelly CP, et al; American College of Gastroenterology. ACG clinical guidelines: diagnosis and management of celiac disease. *Am J Gastroenterol.* 2013;108:656-676.
8. Minak J, Kabir M, Mahmud I, et al. Evaluation of rapid antigen point-of-care tests for detection of Giardia and Cryptosporidium species in human fecal specimens. *J Clin Microbiol.* 2012;50:154-156.
9. Chari ST, Singer MV. The problem of classification and staging of chronic pancreatitis. Proposals based on current knowledge of its natural history. *Scand J Gastroenterol.* 1994;29:949-960.
10. American Society for Gastrointestinal Endoscopy. Guideline: the role of endoscopy in chronic pancreatitis. *Gastrointestinal Endoscopy.* 2006;63:933-937.
11. DiMagno EP, Malagelada JR, Go VL, Moertel CG. Fate of orally ingested enzymes in pancreatic insufficiency. Comparison of two dosage schedules. N Engl J Med. 1977;296:318-322.
12. Löhr J-M, Oliver MB, Frulloni L. Synopsis of recent guidelines on pancreatic exocrine insufficiency. *United European Gastro J.* 2013;1:79-83.
13. Domínguez-Muñoz JE. Pancreatic exocrine insufficiency: diagnosis and treatment. *J Gastroenterol Hepatol.* 2011;2:12-16.
14. Fieker A, Philpott J, Armand M. Enzyme replacement therapy for pancreatic insufficiency: present and future. *Clin Experimental Gastroenterol.* 2011;4:55-73.
15. Dietary Reference Intakes: Recommended Intakes for Individuals. United States Department of Agriculture website. http://fnic.nal.usda.gov/dietary-guidance/dietary-reference-intakes/dri-tables. Accessed January 18, 2014.
16. Hardt PD, Hauenschild A, Nalop J, et al. High prevalence of exocrine pancreatic insufficiency in diabetes mellitus. A multicenter study screening fecal elastase 1 concentrations in 1,021 diabetic patients. *Pancreatology.* 2003;3:395-402.
17. Löhr M, Klöppel G. [Pathology of the pancreas in chronic type 1 diabetes mellitus: B-cell content, exocrine atrophy and angiopathy]. *Verh Dtsch Ges Pathol.* 1987;71:114-119.
18. Gubergrits N, Malecka-Panal E, Lehman GA, et al. 6-month, open-label clinical trial of pancrelipase delayed-release capsules (Creon) in patients with exocrine pancreatic insufficiency due to chronic pancreatitis or pan creatic surgery. Aliment Pharmacol Ther 2011;33:1152–1161.

Abbreviations

CT = computed tomography
EPI = exocrine pancreatic insufficiency
ERCP = endoscopic retrograde cholangiopancreatograph
IV = intravenous
MRI = magnetic resonance imaging
PERT = pancreatic enzyme replacement therapy
PPI = proton pump inhibitor
U = units
WOPN = walled-off pancreatic necrosis