Patients with pancreatic disease can develop severe malnutrition. Many factors contribute to the malnutrition seen in this patient population, one of the most problematic being pancreatic exocrine insufficiency (PEI) with resultant malabsorption. Pancreatic enzyme replacement therapies (PERT) are predominantly designed for oral administration, but this can be challenging in patients requiring enteral nutrition (EN). This review explores the use of PERT in complex patients who are on EN. Case studies will be utilized to demonstrate different methods available in order to provide practical guidance on administration, both in the United States (U.S.) and the United Kingdom (U.K.).

**INTRODUCTION**

Patients with pancreatic disease, pancreatic resection, and cystic fibrosis often develop significant malnutrition as a result of the numerous gastrointestinal (GI) complications preventing adequate oral intake. Malabsorption, as well as side effects of medications such as antibiotics and opiates, adds an additional challenge to meeting nutritional requirements. In patients requiring EN, standard elemental formulas may not be tolerated or absorbed. Semi-elemental (or peptide-based) formulas are often utilized, providing less long-chain triglycerides and more medium-chain triglycerides, thereby decreasing the dependence of pancreatic lipase for absorption. However, some patients will continue to malabsorb, even with semi-elemental products, worsening the malnutrition present.

Traditional signs and symptoms of malabsorption include the presence of pale stools (often described as yellow or clay colored), floating or oily stools, stools with an unusually foul and offensive odor, abdominal bloating, cramping or gas, urgency and/or frequent stools. The use of gut slowing medications, such as opiates, or the use...
of low fat enteral feedings may result in reduction of obvious clinical signs and mask ongoing malabsorption. In these patients, constipated or infrequent stools (vs. diarrhea) may be reported, as well as abnormal color, unusually large volume stools, abnormal cramping and/or gas etc. The addition of antibiotics or prokinetics, can further confuse the clinical picture. Hence, sometimes it is the presence of more subtle signs of malnutrition such as difficulty with wound healing, worsening functional status, ongoing weight loss, or recurrent hypoglycemia/reduction in insulin requirement despite adequate caloric intake, that should trigger the consideration to consider an empiric trial of PERT.\textsuperscript{2,3}

EN and PERT products vary internationally. The aim of this paper is to provide a guide in the management of this complex patient group, combining the experience of dietitians specializing in patients with PEI, both in the U.S. and the U.K. We will also provide practical guidance in implementing the various modalities that can be utilized when it is determined that a patient is malabsorbing on their current EN regimen, as direction provided in the literature is sparse.\textsuperscript{4-10}

**CASE #1**

A 62 year old female with pancreatic cancer and poorly controlled diabetes (HbA1c = 8.3\%) completed a neo-adjuvant course of chemo-radiation prior to surgery. She reported a recent reduction in her insulin dose due to multiple episodes of severe hypoglycemia. Her oncologist also recently started her on enteric coated PERT due to reported yellow, oily stools and continued weight loss. She underwent a classic Whipple procedure, combined with a percutaneous gastro-jejunostomy (PEG-J) tube placement. Semi-elemental EN (Perative \textsuperscript{®}, Abbott, U.S.) was chosen due to the presence of malabsorption preoperatively. Her recovery was complicated by delayed gastric emptying requiring NPO (nil per os) status, and she was treated with a prokinetic and high dose proton pump inhibitor (PPI) given via her J-port. Her gastric port was vented as needed for gastric decompression. She was experiencing diarrhea, but was receiving enteral electrolyte replacement therapy (including magnesium oxide) and a prokinetic. On discharge, she was tolerating G-tube clamping around the clock. She transitioned to a nocturnal feeding regimen that met her nutritional needs and was kept NPO.

Once home, her diarrhea increased. Her prokinetic dose was successfully weaned, with no worsening of her nausea. The patient reported improvement in her diarrhea, yet, eventually frequent loose stools associated with cramps and urgency were again reported. Her glycemic control was erratic; she began holding her long acting insulin due to episodes of hypoglycemia.

Two weeks post discharge her weight was down 5 pounds (2.25 kg), and an area of her midline wound opened, which required packing. At this time, it was determined an EN change was required. The elemental formula Vivonex \textsuperscript{®} (Nestle, U.S.) was considered for its very low fat profile, however the patient was quite volume sensitive and would not have tolerated the rate increase needed. She was to be tried on a non-enteric coated PERT (Viokace \textsuperscript{®}; Aptalis Pharma, U.S.), that could be crushed and added directly to her EN, but her insurance denied coverage for this product. We were hesitant to attempt enteric coated granules to mix with EN (described elsewhere\textsuperscript{6,7}) for fear of tube clogging, as the patient was completely dependent on her jejunal EN.

Fortunately, she advanced to oral intake. Full liquids were tolerated and she was able to take medications by mouth. She began to take herenteric coated PERT (2 capsules of Zenpep \textsuperscript{®} 25,000 USP; Aptalis Pharma, U.S.) by mouth at the start of feedings, ~3 hours into her feeding cycle, and again before turning her EN off in the morning. Her stools firmed and improved; however, she still reported urgency and pale stools in the middle of the night. We increased her oral PERT administration to four times during her nocturnal cycle (she reported being awake and ambulatory at night, and agreeable to medication at this time), with one loperamide at the start of EN. This finally resulted in normalization of stooling and weight maintenance. She also resumed her intermediate acting insulin due to rising blood glucose with improved absorption; her blood glucose now remaining in the 80-200mg/dL range. Over the next 2 months she increased her weight by 12 pounds (5.5 kg) and her abdominal wound began to heal.
# Pancreatic Exocrine Insufficiency and Enteral Feeding

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## Table 1. Clinical Parameters Pre- and Post-PERT

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Case 1</th>
<th>Case 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diagnosis</strong></td>
<td>Pancreatic cancer, Post Whipple (classic)</td>
<td>Cystic fibrosis related PEI, no anatomic abnormalities</td>
</tr>
<tr>
<td>IBW</td>
<td>52.3 kg/ 115 lbs</td>
<td>75 kg/ 166 lbs</td>
</tr>
<tr>
<td>Goal wt</td>
<td>62.7 kg/ 138 lbs</td>
<td>72 kg/ 160 lbs</td>
</tr>
<tr>
<td><strong>EN Access</strong></td>
<td>PEG-J</td>
<td>Low profile G-tube</td>
</tr>
<tr>
<td><strong>Timing</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PERT</td>
<td>N/A</td>
<td>3 Zenpep® 25,000 USP units. Taken orally at start of EN, mid-EN x 2, end of EN. Alternatively, crush and add 1-2 tablets, 10,440 USP units of Viokace® to EN.</td>
</tr>
<tr>
<td>Weight</td>
<td>62.7 kg/138 lbs</td>
<td>70 kg/154 lbs</td>
</tr>
<tr>
<td><strong>Stool Output</strong></td>
<td>Constant loose stools w/ EN; clay colored</td>
<td>Color normalization, formed, decreased frequency</td>
</tr>
<tr>
<td><strong>EN</strong></td>
<td>Perative®</td>
<td>Perative®</td>
</tr>
<tr>
<td><strong>Glycemic Control</strong></td>
<td>Poor; insulin requirement variable, glucose labile</td>
<td>Increased insulin requirement with stabilization of glucoses</td>
</tr>
<tr>
<td><strong>Additional Changes</strong></td>
<td>Wound breakdown, weight loss</td>
<td>Wound healing, weight increase</td>
</tr>
</tbody>
</table>
Pancreatic Exocrine Insufficiency and Enteral Feeding

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
<th>Case 4</th>
<th>Case 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
<td>Pancreatic cancer, gastric outlet obstruction</td>
<td>Post Whipple (classic)</td>
<td>Cystic fibrosis related PEI, no anatomic abnormalities</td>
<td>Total gastrectomy, total colectomy; severe chronic pancreatitis</td>
<td>Total pancreatectomy; duodenectomy, hepatico-jejunostomy on roux loop</td>
</tr>
<tr>
<td>IBW</td>
<td>52.3 kg/115 lbs</td>
<td>75 kg/166 lbs</td>
<td>64.5 kg/142 lbs</td>
<td>UK does not use</td>
<td>64.5 kg/142 lbs</td>
</tr>
<tr>
<td>Goal wt</td>
<td>62.7 kg/138 lbs</td>
<td>72 kg/160 lbs</td>
<td>65 kg/143 lbs</td>
<td>UK does not use</td>
<td>64.5 kg/142 lbs</td>
</tr>
<tr>
<td>EN Access</td>
<td>Low profile G-tube</td>
<td>Jejunostomy</td>
<td>PEG-J</td>
<td>PEG-J</td>
<td>Naso-jejunal</td>
</tr>
<tr>
<td>Timing</td>
<td>Pre-PERT</td>
<td>Post-PERT</td>
<td>Pre-PERT</td>
<td>Post-PERT</td>
<td>Pre-PERT</td>
</tr>
<tr>
<td>PERT</td>
<td>N/A</td>
<td>Creon® 24,000 USP units; 2 capsules/can of EN; opened and mixed with Nabicarb tabs and 60mL water for 30 minutes; flush via tube q 4 hours during EN infusion</td>
<td>N/A</td>
<td>Not applicable</td>
<td>Pancrex V® powder 4g (100,000 units)/400mL EN</td>
</tr>
<tr>
<td>Weight</td>
<td>52 kg/114 lbs</td>
<td>57 kg/125 lbs</td>
<td>59.1 kg/130 lbs</td>
<td>64.5 kg/142 lbs</td>
<td>84 kg/185 lbs</td>
</tr>
<tr>
<td>Fluid overloaded</td>
<td>64.5 kg/142 lbs</td>
<td>84 kg/185 lbs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High volume stoma output &gt;2000mL/day</td>
<td>Stoma output &lt;600mL/day</td>
<td>Frequent, yellow, oily; alternating w/ constipation d/t use of opiates</td>
<td>Constipated, requiring miralax</td>
<td>Brown formed stool every 1-2 days</td>
<td>Brown formed stool every 1-2 days</td>
</tr>
<tr>
<td>Peptisorb®, Peptamen HN®, Peptamen®</td>
<td>Vital 1.5®</td>
<td>Vital 1.5®</td>
<td>Vital 1.5®</td>
<td>Peptisorb®</td>
<td>Vital 1.5®</td>
</tr>
<tr>
<td>Normal</td>
<td>Normal</td>
<td>Well-controlled, HbA1C= 6.3</td>
<td>Well-controlled</td>
<td>2-32mmol/L (36 – 576 mg/dL)</td>
<td>5-11mmol/L (90-198mg/dL)</td>
</tr>
<tr>
<td>Weight stabilization with use of supplemental PN</td>
<td>Improved functional status, d/c PN</td>
<td>Inability to gain weight</td>
<td>Weight regain, improved strength</td>
<td>Wound breakdown, recurrent hypoglycemia, peripheral edema, poor functional status</td>
<td>Wound healing, improved functional status, glucose stabilization with no further incidence of hypoglycemia</td>
</tr>
</tbody>
</table>

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Table 2. Advantages and Disadvantages of Diagnostic Tests for PEI

<table>
<thead>
<tr>
<th>Test</th>
<th>Advantages</th>
<th>Limitations</th>
</tr>
</thead>
</table>
| Quantitative Fecal Fat (24, 48, 72 hour collection) | • Demonstrates extent of malabsorption, comparing fat intake vs. output.  
• Traditionally 100g fat diet prescribed, but results can still be used if less fat consumed when careful record of how much fat patient consumes for comparison with output.  
• Can demonstrate adequacy of therapy for patients already on PERT or semi-elemental EN. | • May require stopping PERT.  
• Unpleasant for patients.  
• Requires 100g daily fat ingestion.  
• Cumbersome, requiring stool collection from 1-3 days.  
• Any stool loss during the collection can skew results.  
• Careful monitoring of fat intake essential for result interpretation.  
• Not available in the UK. |
| Qualitative Fecal Fat or Sudan Stain (“spot check”) | • Easy, only requires one small stool sample.  
• Positive result showing fat in the stool indicates malabsorption.  
• Must ingest fat; no particular amount. | • Positive result is unable to inform the extent of malabsorption.  
• Negative result does not definitively rule out malabsorption (based on one sample at one time, may not catch what would be in the next stool sample).  
• Not available in the UK. |
| Fecal Elastase (FE-1)  
fecal elastase <200 µg/g = pancreatic insufficiency;  
< 100 µg/g = severe pancreatic insufficiency | • Easy, only requires one small stool sample.  
• Do not have to stop PERT for test.*  
• No special diet required. | • Reduced accuracy if used post-pancreatic resection.  
• Watery stools cause falsely low result due to dilution.  
• Unable to evaluate for continued malabsorption on current PERT. |

* Though the manufacturer of the polyclonal fecal elastase test issued a disclaimer to discontinue PERT prior to the test, evidence reveals that the antibodies in the ELISA are to human elastase and are unaffected by the porcine elastase found in PERT.15

CASE #2
A 26 year old male with cystic fibrosis (CF) related PEI was struggling to gain weight and adhere to his EN regimen. He had been taking oral enteric coated PERT with his meals since being diagnosed with PEI at a young age, and was automatically started on PERT with a polymeric EN formula via G-tube. His original EN regimen consisted of a 2.0 kcal/mL formula (TwoCalHN®, Abbott, U.S.) with enteric coated PERT taken by mouth at the beginning and end of an 8-hour nocturnal EN schedule. He continually endorsed abdominal discomfort and stool urgency in the middle of the night during his EN. Though taking oral enzymes at the beginning and end of an EN cycle tends to be the easiest regimen for CF patients, this

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method does not provide enzymatic coverage for the entire duration of nocturnal EN. Due to continued malabsorptive symptoms and failure to gain weight, a non-enteric coated PERT product (Viokace®) was crushed and mixed with his EN prior to administration. This helped relieve some of the abdominal discomfort, but he continued to have difficulty consuming breakfast due to post-feeding appetite suppression. This patient also struggled with EN adherence due to the reported burden of effort to crush and mix PERT into the EN formula. Furthermore, the patient did not have a consistent living situation and did not always have EN supplies with him. We then trialed an in-line digestive enzyme cartridge (Relizorb®, Alcresta, U.S.), as this would greatly reduce the burden of EN preparation, and discontinued Viokace®. Due to poor fat hydrolysis data of TwoCal HN® using Relizorb®, his EN was changed to the highest caloric density compatible formula available at our facility (Osmolite 1.5®, Abbott, U.S.). The patient had a dramatic improvement in tolerance and adherence to his EN regimen. His abdominal discomfort was much improved and he was able to consume a large breakfast due to reduced post-EN appetite suppression (consistent with results of a recent study10). He gained 10 pounds (4.5 kg) in the first three months after this therapy change, but was not able to maintain the rate of weight gain. In order to increase caloric provision, his outpatient EN was changed to Nutren 2.0® (Nestle, U.S.). He continued to tolerate the new EN regimen with 2 cartridges of Relizorb® nightly and gained 22 pounds (10 kg; 17.5% body weight) over the following year. It should be noted that the patient’s appetite and oral intake also improved, contributing to weight gain.

CASE #3
A 54 year old male with chronic pancreatitis suffered a splenic bleed which resulted in extensive ischaemia of the bowel. A total gastrectomy, hemihepatectomy, total colectomy with end ileostomy, and feeding jejunostomy was performed; high stool output followed. The oesophagus was left disconnected (with a drain in situ, or “spit fistula”) for 18 months prior to reconstruction.

Short bowel syndrome was presumed, as there had been concern over the perfusion of his small bowel, and we utilized a full range of trials with peptide-based EN. In addition, loperamide up to 16mg QID and 60mg of codeine TID was administered. An electrolyte mix was used to flush his jejunostomy instead of water. Additional sodium (50mL 30%NaCl solution which provides 50mmol sodium, increasing the total sodium to 90-100mmol/l) was added to the EN to optimize water absorption. His stoma output remained >2000mL per day, and he continued to require supplemental parenteral nutrition (PN) to prevent weight loss. As this management was ineffective, his ongoing high stoma output was presumed to be not only due to loss of compensatory mechanisms (saliva and gastric secretions; colonic fermentation of malabsorbed carbohydrate, intestinal hurry), but also to severe PEI.

PERT was administered as 2g Pancrex V® powder (Essential Pharmaceuticals, U.K.) dissolved in 50mL sterile water and flushed by the nursing staff every 2 hours through his 24 hour EN. No benefit was observed and the decision was made to administer PERT to the EN directly. The 4 g Pancrex V® powder (100,000 units lipase) was added directly to 400 mL of Vital 1.5® (Abbott, U.K.), the mixture was shaken well and run at 100mL/hr over 4 hours. UK guidelines limit hang time for EN with any additives to 4 hours.11 This was repeated 4 times during the day, and provided a total of 2400 calories. His stoma output reduced to less than 600mL per day, and he was weaned off PN and began to gain weight. This method of EN was continued until he underwent reconstructive surgery and was able to recommence oral intake.

CASE #4
A 64 year old man status post chemotherapy, radiation, and distal pancreatectomy/splenectomy for pancreatic cancer suffered many post-operative complications including a chyle leak, GI bleed, recurrent abscesses, bacteremia, and delayed gastric emptying requiring placement of a PEG-J. He required multiple readmissions and continued to struggle with nausea, vomiting, abdominal pain and weight loss. He eventually requested a second opinion and was admitted to our facility. His esophagogastroduodenoscopy (EGD), upper

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GI series and computed tomography (CT) scan showed gastric stenosis that would require surgical revision. Due to his malnourished state, nutritional optimization prior to surgery was necessary. He came to us receiving 6 cans of Vital 1.5® (Abbott, U.S.). Each can of Vital 1.5 was mixed with 2 capsules of Creon 24,000® (AbbVie, U.S.), which were opened and mixed with 2 tabs of sodium bicarbonate (650 mg) crushed and mixed with 60mL of water and sat as a slurry for 30 minutes prior to administration. This slurry was flushed via his feeding tube every 4 hours. He had lost 21% of his usual body weight over the last year, and presented to us with a weight of 130 pounds (59 kg). He was 5 feet, 6 inches (168cm); preoperative weight goal was 140-145 pounds (63-65 kg). He was switched to 8 cans of Vivonex® allowing him to stop the PERT slurry flushes. However, after 2-3 weeks, he had not gained any weight. His EN regimen was then changed to a mixture of 1 can of Vital 1.5® mixed with 3 cans of Vivonex® twice daily for a total of 8 cans per day. This provided increased calories while keeping fat content low, avoiding the use of enzymes. However, his lack of weight gain persisted and the patient reported a decline in quality of life due to the continuous EN infusion regimen. At this time his EN was adjusted to 7 cans of Vital 1.5®, and PERT slurries were restarted every 4 hours. Over the next 4 weeks EN was increased to 8 cans, then 9 cans of Vital 1.5®. One month after his 9th can was added, he reached his goal weight of 142 pounds (64.5 kg) and was able to undergo a surgical gastro-jejunostomy with eventual progression to an oral diet.

CASE #5

A 68 year old male underwent a pancreaticoduodenectomy for adenocarcinoma of the pancreas with subsequent completion pancreatectomy following the development of a high volume pancreatic fistula. A nasojejunal (NJ) feeding tube was placed and the patient was started on a regimen of Vital 1.5® and Creon 24,000® (AbbVie, U.S.) mixed with sodium bicarbonate (650 mg) crushed and mixed with water and sat as a slurry for 30 minutes prior to administration. This slurry was flushed via his feeding tube every 4 hours. After 2-3 weeks, he had gained 15 pounds (6.8 kg) and his weight was stable. The patient was then switched to Vivonex®, allowing him to stop the PERT slurry flushes. However, after 2-3 weeks, he had not gained any weight. His EN regimen was then changed to a mixture of 1 can of Vital 1.5® mixed with 3 cans of Vivonex® twice daily for a total of 8 cans per day. This provided increased calories while keeping fat content low, avoiding the use of enzymes. However, his lack of weight gain persisted and the patient reported a decline in quality of life due to the continuous EN infusion regimen. At this time his EN was adjusted to 7 cans of Vital 1.5®, and PERT slurries were restarted every 4 hours. Over the next 4 weeks EN was increased to 8 cans, then 9 cans of Vital 1.5®. One month after his 9th can was added, he reached his goal weight of 142 pounds (64.5 kg) and was able to undergo a surgical gastro-jejunostomy with eventual progression to an oral diet.

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was inserted intra-operatively and he was initially fed with a semi-elemental EN (Peptisorb®, Nutricia Clinical Care, U.K.). He had a protracted length of stay and ongoing delayed gastric emptying, thus he remained dependent on NJ feedings for his nutrition. He had normal bowel function, yet continued to lose weight, developed a hospital acquired pneumonia and an abdominal wound breakdown requiring the use of a vacuum wound management system.

His glycemic control was erratic despite continuous EN, with frequent episodes of hypoglycemia. Given his complete pancreatectomy, malabsorption was presumed, and 4g of Pancrex V® powder (100,000 units lipase) was added to each bottle of his peptide EN, which was changed to a 1.5kcal/mL product (400mL Vital 1.5®) to allow a rest period for physiotherapy. This was repeated 4 times a day, to provide 2400 calories. Within a week, his insulin requirements increased and he no longer experienced hypoglycemic episodes. Over the next few weeks his grip strength and weight started to increase. There was no change in his bowel habits, and he continued with brown formed stools every 24-36 hours. His wound began to heal, and he began to eat and drink. On day 92 he discontinued NJ feedings and was discharged home on day 94 on an oral diet, PERT and insulin. Table 1 provides an overview of all 5 cases including nutritional parameters, PERT, and outcomes.

Not Everyone Needs PERT
The cases above highlight the need to identify patients with PEI who would benefit from the use of PERT. However, it is worth noting that not all patients with pancreatic disease and frequent stooling require PERT. The use of antibiotics, prokinetics, diagnosis of Clostridium difficile, and occurrence of dumping syndrome among other

Table 4. Medicare Coverage for PERT 2018

Pancreatic enzymes are a Tier II drug, covered under Medicare Part D. Initially the patient will pay-out-of-pocket for PERT until they reach their deductible (currently, no Medicare plan deductible can exceed $405). After the deductible is met, the patient will pay a copayment or coinsurance for the drug (copay depends on particular plan). Once total expenses (the amount the patient pays for the medication PLUS what Medicare pays for the medication) reaches $3750.00, the patient lands in the “coverage gap” or “donut hole”. Once there, the patient will pay 35% of name brand drug cost until total costs (the 35% patient paid PLUS 50% manufacturer discount payment, which will get the patient past the coverage gap faster) of drug payments exceed $5000.00. Once this amount is met, “catastrophic coverage” begins and the patient only pays a small flat co-pay for the remainder of the year. The plan the patient chooses at enrollment will determine this co-pay amount. Plans are available to help with the “donut hole” coverage that can be signed up for during Medicare’s open enrollment. However, these plans will have a higher out of pocket monthly cost. Additionally, there is the “Extra Help” program Medicare offers, which is income based and further helps drug costs (to qualify, double income has to be less than $24,960 with less than $28,150 in countable resources).

At the time this article was written, the authors found the average cost was $7-11 per 25,000 USP units of an enteric coated PERT. Therefore, if a patient consumes 8 pills in a day, the out of pocket cost of PERT could be $56- $88 per day or $1680- $2640 per month.

Relizorb® cartridges are classified by the FDA as a device and not a medication, which can affect coverage. It is currently covered by Medicaid and various private insurance plans, but not Medicare.

Of note, most PERT companies have financial assistance available for patients with commercial insurance or no insurance, but not for those on governmental assistance programs such as Medicaid/Medicare.
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causative factors should be considered prior to adjusting EN or initiating PERT for suspected malabsorption from PEI.

A 76 year old patient post Whipple procedure for ampullary adenocarcinoma was readmitted with severe diarrhea, nausea, vomiting, dehydrated and failure to thrive. He was also on a prokinetic due to symptoms of delayed gastric emptying, and receiving enteral electrolytes, both of which could potentially affect stool output. In attempts to rule out malabsorption, the surgical team ordered a fecal elastase, which came back low; the watery stool sample as well as recent pancreatic surgery invalidated the low result. A fecal fat check (qualitative) was obtained, however, he had little to no enteral nutrition (hence fat) for days. As a result, the fecal fat came back negative, adding little to the clinical assessment. His CT scan showed colitis (stool sample was negative for Clostridium difficile). The team ordered PERT, with no change in stool output. Eventually the enzymes were stopped. Ultimately, the patient required a PEG-J, tolerating standard EN, and his stools improved over time as his colitis resolved based on his repeat CT scan.

**DISCUSSION**

Assessment of nutritional adequacy and feeding tolerance is complex in patients who have pancreatic disease. There are no standard guidelines in the administration of PERT with EN, and clinical practice differs internationally as a result of the differences in EN and PERT products. Consequently, methods for adding PERT to EN also differ.

The use of a fecal fat stool collection or fecal elastase may help to support the diagnosis of ongoing malabsorption in certain circumstances; however, limitations exist (see Table 2). Assessment of residual pancreatic function, signs and symptoms, in concert with clinical judgment, is needed to establish if the patient is malabsorbing. Ongoing reassessment to ensure adequate response to therapy is also important (see Table 3).

In the U.K., peptide/semi-elemental formulas are used as first line EN in patients with pancreatic disease as per European Society for Enteral and Parenteral Nutrition (E.S.P.E.N) guidelines; it is also standard practice to use PERT routinely in patients after pancreatic head resection

Figure 1. Enteral Nutrition and Pancreatic Enzyme Replacement Therapy Options in Pancreatic Enzyme Insufficiency

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Of note, enzyme dosing guidelines suggest: 500-4000 lipase units per gram of fat

Powdered or crushed non-enteric coated PERT:
- **Powered enzymes:**
  - *Not available in the US*
  - *Pancrex V Powder in U.K.*

- **Non-enteric coated enzymes, crushed:**
  - *Viozilac*
  - *Use pill crusher/Silent Knight; use gloves/mask to avoid handling or inhaling enzymes*

- 2 ways to administer:
  - *Dissolve in 60ml water, flush via FT every 2-4 hours during continuous feeding or*
  - *Add directly to EN. Manipulate bag or shake formula to mix.*
  - *Maximum suggested hang time: Pancrex V: 4 hours Crushed Viozilac: 8 hours*

PERT Cartridges:
- *Not available in the UK*
- *Reizorb is a FDA approved device to hydrolyze fats in enteral formulas.*
- *Cartridge is a small clear plastic/vial containing white beads (immobilized lipase), which is directly connected to the EN pump feeding line and hydrolyzes fat as EN infuses through the cartridge*
- *One cartridge per 500ml of formula; maximum of 2 cartridges every 24 hours. Of note, some patients can tolerate higher volumes of EN per cartridge*
- *Maximum flow rate = 120ml/hr.*
- *Not compatible with EN formulas containing soluble fiber.*
- *Also shown to have poor fat hydrolysis using TwoCal HN.*

**EN only options (no enzymes):**
- *Mix semi-elemental EN 1:1 with strict elemental EN*
- *Elemental only formula (not available in the UK). Possible issues of this method include cost, 1.0 cal/ml requiring increased volume, increased carbohydrate (and less fat)/moderate protein profile may require additional insulin in some and use of protein modulators.*

**Oral Administration of PERT:**
- *Gastric/Reflux: Swallow capsule(s) with each bolus feeding*
- *Jejunum:* Best to give every 2-3 hours during EN infusion. If not feasible, instead try to give at the start of EN, 3-4 hours into cycle (near bedtime), again just prior to stopping EN.
- *In patients where delivery of PERT via J-tube is not feasible, this method can be tried; although imperfect, it may be the next best alternative.*
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inoperable pancreatic cancer. In the U.S. practices vary, but at UVA, we consider standard EN as first line therapy when initiating EN and readjust as signs or symptoms of malabsorption develop or PEI is confirmed. If a patient fails on standard EN, a semi-elemental feeding will be tried, followed by a strict elemental product or initiation of PERT. Initiation of PERT is carefully considered on an individual basis as circumstances dictate. If a clinician determines PERT with EN is the best approach, they then must also decide on the best method of administration. Figure 1 provides methods that may be employed when providing PERT with EN.

In the U.S., another major hurdle when utilizing PERT with EN (or orally) is obtaining insurance coverage. Certain enzyme formulations may not be covered, or the patient may not have met their out-of-pocket premiums for their particular insurance plan (see Table 4 for an overview of Medicare Part D drug coverage).

CONCLUSION

Patients with pancreatic disease are often complex and present many nutritional challenges. There are significant variations in absorptive capacity between patients with cystic fibrosis, acute and chronic pancreatitis, pancreatic resection, pancreatic cancer, and other conditions that may lead to PEI. Therefore, it is crucial that clinicians have a range of management options to optimize the nutritional care of these vulnerable patients. This is a ‘how to’ guide for the addition of PERT to EN, and highlights the variation in practice and patient management internationally.

References

14. NICE. Pancreatic Cancer in Adults: Diagnosis and Management (NG 85) 2018