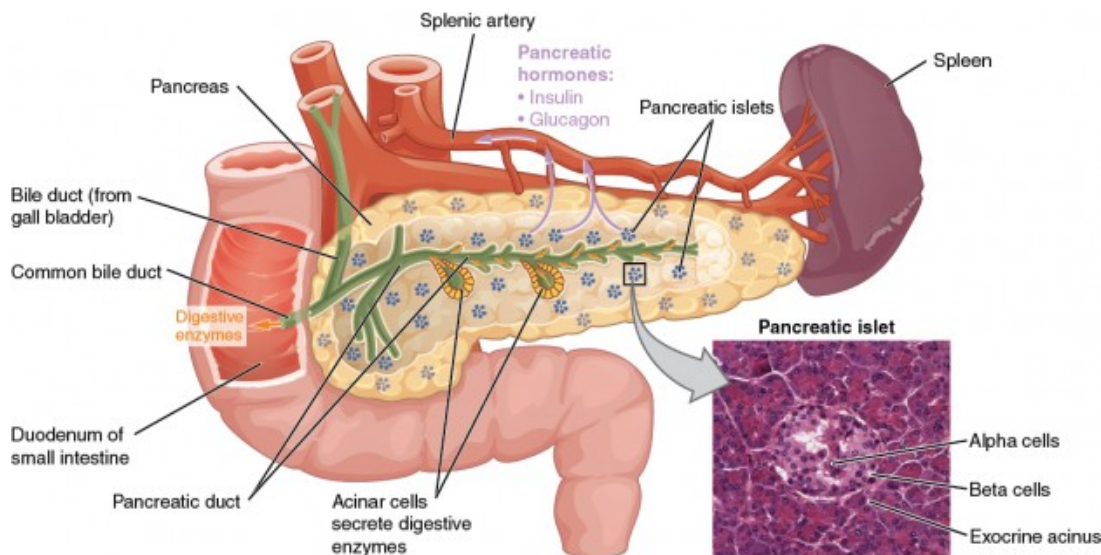


Pancreatic Enzyme Replacement Therapy

[See online here](#)

Patients with chronic pancreatic insufficiency develop improper digestion due to the lack of digestive pancreatic enzymes. Such patients might complain of diarrhea and multi-nutrient deficiencies. Children with cystic fibrosis are at an increased risk of developing pancreatic insufficiency, while adults can develop chronic pancreatitis due to gallbladder disease or alcohol consumption. Regardless of the etiology, these patients might develop an exocrine pancreatic deficiency and are at risk of developing malabsorption. Pancreatic enzyme replacement therapy is indicated in patients with malabsorption due to exocrine pancreatic insufficiency.



Definition

Pancreatic enzyme replacement therapy **implies to the administration of pancreatic enzymes in the form of supplement pill.** The supplement contains pancreatin that is a mixture of enzymes secreted by pancreas, lipase, amylase, and protease.

Normal Composition of the Pancreatic Fluid

The pancreas takes on both endocrine and exocrine function in the body. The endocrine function is primarily related to glucose control, while the exocrine part of the pancreas is involved in the secretion of different enzymes mainly responsible for lipid digestion.

The three main enzyme families secreted by the pancreas are lipases, amylases, and proteases. Lipase and amylase are secreted in their active form by the pancreas while the protease trypsinogen is secreted as a proenzyme. Once in the duodenum, trypsinogen is then converted to trypsin, the active enzyme.

Etiologies of Exocrine Pancreatic Insufficiency

Patients with chronic pancreatitis, cystic fibrosis and diabetes are at an increased risk of developing exocrine pancreatic insufficiency due to a reduction in lipase production. Patients with pancreatic duct obstruction due to tumors, strictures or pancreatic cancer might also develop exocrine pancreatic insufficiency. Finally, certain diseases, such as Celiac disease and Crohn's disease, have been associated with decreased lipase synthesis.

Pancreatic Enzyme Replacement Therapy

Pancreatic enzyme replacement therapy is **mainly indicated for the correction of lipid malabsorption**. Patients with lipid malabsorption also develop a multi-vitamin deficiency, especially of vitamins A, D, E and K because their absorption is lipid-dependent. To mimic the normal physiologic pancreatic enzymes, pancreatic enzyme supplements should be inactive in the stomach and be activated only in the duodenum. Additionally, this activation should be achieved only when food reaches the duodenum for food digestion.

Two main replacement therapies exist: Pancrelipase and Pancreatin.

Pancrelipase has more lipase, amylase and protease activity compared to Pancreatin. Thus, it is usually recommended as first-line replacement therapy. Patients should not be prescribed uncoated tablets for replacement therapy because they are activated in the acidic environment of the stomach.

Lipid digestion is considered as physiologic only in the duodenum. Instead, enteric-coated tablets should be used of either Pancreatin or Pancrelipase. Enteric-coated tablets only dissolve in the duodenum's less acidic environment where the pH ranges between 5 and 5.5. Unfortunately, the pH in the stomach is not always strongly acidic because it is also largely dependent on the acidity of the ingested food.

Non-coated tablets are usually indicated to alleviate chronic pancreatitis pain but not to correct malabsorption due to pancreatic insufficiency. Coated microspheres with or without bicarbonate buffers are superior to traditional enteric-coated tablets in terms of enzyme delivery to the duodenum.

Patients with progressive weight loss and diarrhea with high-fat content should be started on pancreatic enzyme replacement therapy.

Administration of Pancreatic Enzyme Replacement Therapy

Two dosing schedules exist for pancreatic enzyme supplements. First, it is important to note that symptomatic exocrine pancreatic insufficiency ensues only when lipase production is decreased below 90 % of normal quantities. Therefore, the initial goal should be to correct the pancreatic insufficiency only to the extent where it is no longer symptomatic before going up in the dosage to obtain a more optimal result.

Typically, one might start with 25,000 to 40,000 IU of lipase per meal. **The starting dosage per day can range from 50,000 to 150,000 IU of lipase.** Whatever dosage system you choose, you should remember that patients who are receiving more lipase usually report better clinical outcomes such as a resolution of steatorrhea. Enzyme

replacement therapy should be ideally administered with the meal or after finishing the meal.

Efficacy of Pancreatic Enzyme Replacement Therapy

Patients receiving a minimum daily dosage of 150,000 IU of lipase usually report a significant improvement in abdominal pain, flatulence, and steatorrhea. A small number of prospective studies showed that despite a symptomatic improvement in steatorrhea, patients did not add any significant weight and remained largely underweight. Additionally, despite reducing stool fat content, micro-nutrient deficiencies were not corrected in a large set of patients.

Additionally, a significant number of patients report treatment failure. Pancreatic enzyme replacement therapy might fail because of poor compliance or due to secondary causes of diarrhea, which are misinterpreted by the patient as steatorrhea.

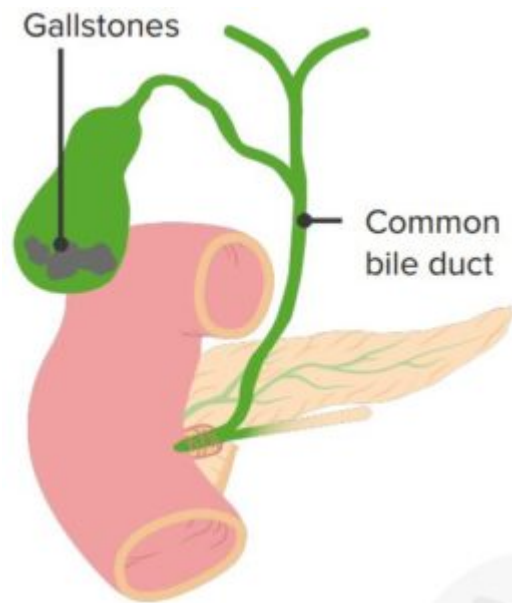
Patients might not be compliant with the medication, might take too many snacks (which should be accounted for while designing the dosing schedule) and might take the medication before the meal—which was found to be inferior to taking the enzyme replacement during the meal or after. **If noncompliance is suspected, fecal chymotrypsin tests might be used which show whether the patient is taking their pancreatic enzyme replacement therapy as indicated or not.** In case of poor compliance, education about the benefits and the importance of adherence to the administration schedule should be emphasized.

Patients taking too much lipase might develop diarrhea as a side effect, which can be misinterpreted as ongoing steatorrhea. Additionally, patients should be educated to limit their fat content in the diet, should reduce their fiber and should avoid alcohol intake and antacids. **Patients might have other causes of their diarrhea that can be related to bacterial overgrowth, infections such as in giardiasis, or might have malabsorption due to another etiology such as celiac disease, which is also associated with pancreatic insufficiency.**

Future lipases are being investigated. They are extracted from microbial sources such as fungi and bacteria. These lipases are superior to the currently available swine formulations Pancreatin and Pancrelipase because they work in a wider pH range, 3 to 10, and they are resistant to acidic destruction in the stomach.

On the other hand, Pancreatin and Pancrelipase are also undergoing extensive research to develop novel delivery mechanisms that would only allow the activation of lipase in the duodenum while protecting it in the stomach's acidic environment. **A recent microbial pancreatic enzyme replacement combination therapy, Liprotamase, has passed clinical trials with very promising results.** Liprotamase contains bacterial lipase, fungal protease, and fungal amylase. The drug was mainly studied in cystic fibrosis cases, and the results were at least as good as for swine-based lipases.

Gallstone Prevention and Pancreatic Deficiency



"Gallstone Prevention" Image created by Lecturio

One of the common causes of acute pancreatitis is gallstone disease. Prevention of gallstones has become possible after the introduction of Ursodeoxycholic acid. Patients undergoing intense weight loss programs, i.e., bariatric surgery or very-low-calorie diets, are at risk of developing cholesterol gallstones and are good candidates for receiving Ursodeoxycholic acid treatment for prevention of gallstones' formation.

Contraindications

There are certain disease conditions where pancreatic enzyme replacement therapy is contraindicated, such as:

- Gout
- Gastrointestinal surgery
- Crohn's disease
- Gastrointestinal blockage like in intestinal obstruction, fibrosis.
- Short colon

References

Fieker A, Philpott J, Armand M. Enzyme replacement therapy for pancreatic insufficiency: present and future. *Clin Exp Gastroenterol.* 2011;4:55-73. doi:10.2147/CEG.S17634.

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