Exocrine Pancreatic Insufficiency
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Dual Function of the Pancreas
- 85% Exocrine (acinar and duct tissue)\(^1\): Secretes digestive enzymes, water, and \(\text{NaHCO}_3\) into the duodenum
- 2% Endocrine (islets of Langerhans)\(^2\): secretes hormones including insulin and glucagon into the bloodstream

References:

Anatomy and Physiology of the Endocrine and Exocrine Pancreas are Linked
- Anatomy of the pancreas
  - Islet and acinar cells are not separated by a capsule or basement membrane\(^1\)
  - Exocrine pancreas receives a large part of its blood supply via the islets (insulo-acinar portal system)\(^1\)
- Physiology of the pancreas
  - Islet hormones function in the regulation of exocrine pancreas\(^1\)
    - Insulin stimulates acinar protein, RNA, and DNA synthesis
    - Glucagon, somatostatin, and pancreatic polypeptide (PP) inhibit pancreatic exocrine secretion

References:
The Exocrine Pancreas Produces 3 Main Types of Enzymes

- Lipase
  - Breaks down fats into fatty acids
- Protease
  - Breaks down proteins into amino acids
- Amylase
  - Breaks down carbohydrates into simple sugars


Normal Digestion of Carbohydrates and Proteins

- Carbohydrate digestion begins with salivary amylase
- Protein digestion begins with gastric acid and pepsin
- Carbohydrates and proteins are further digested by pancreatic and small bowel enzymes in duodenum


Normal Digestion of Fats

- Intragastric breakdown accounts for approximately 10% of total lipid digestion
- Fat digestion begins in the stomach with lingual and gastric lipases
- Triglycerides are for the most part unchanged until they reach the small intestine

Pancreatic Enzyme Activity

- Normal pancreatic enzyme secretion is integral for digestion and absorption of nutrients
- Normal digestion also depends on postprandial synchrony between delivery of nutrients to the duodenum and discharge of pancreatic enzymes

References:

Neural and Hormonal Mechanisms Regulate Pancreatic Exocrine Secretion

- The hormones responsible for regulation are secretin and cholecystokinin (CCK)
  - Secretin is secreted in response to acid in the duodenum, causing duct cells to release water and bicarbonate
  - In response to protein and fat in the small intestine, CCK is released and stimulates acinar cells to release pancreatic enzymes

Reference:

Exocrine Pancreatic Insufficiency (EPI)

- EPI occurs when the pancreas does not provide sufficient amounts of pancreatic enzymes
- EPI results in inability to digest food properly (maldigestion)
- Maldigestion of fat is more profound than maldigestion of protein or carbohydrate
  - Pancreatic lipase accounts for up to 90% of fat digestion

Reference:
EPI and Maldigestion

- Steatorrhea, the classic clinical sign of EPI, may not occur until the disease is advanced\(^1,2\).
- Steatorrhea occurs when <10% of pancreatic exocrine function remains.
- There may be significant maldigestion and malabsorption without steatorrhea.


EPI can Have Different Underlying Causes\(^1\)

- Cystic fibrosis
- Chronic pancreatitis
- Pancreatic tumor
  - Obstructs the main pancreatic duct
- Pancreatic resection
  - Loss of pancreatic parenchyma


Many Factors can Interfere with Pancreatic Luminal Digestion\(^1,3\)

- Loss of pancreatic parenchyma
  - Chronic pancreatitis, severe acute pancreatitis, pancreaticectomy
- Ductal obstruction
  - Pancreatic cancer, main duct intraductal papillary mucinous neoplasm, strictures/stones
- Diminished stimulation
  - Refractory celiac disease, duodenectomy
- Decreased activation of enzymes (loss of enterokinase)
  - Celiac disease, Crohn's disease
Many Factors can Interfere with Pancreatic Luminal Digestion1-3 Cont’d

- Premature destruction of enzymes
- Zollinger-Ellison syndrome
- Mismatch of secretion with food passage
  - Dumping syndrome, antrectomy, gastric bypass, gastroparesis
- Duct dysfunction
  - Cystic fibrosis, pancreatic divisum, common channel syndrome
- Pancreatic trauma


Malabsorption with EPI

- Fat malabsorption precedes malabsorption of other macronutrients1
  - Protein (azotorrhea) and starch (amyorrhea) malabsorption may occur later in the course of disease2
- Undigested fat, rather than being absorbed, is excreted in the feces3
- Malabsorption of fat-soluble vitamins A, D, E, and K may accompany EPI3


Symptoms of Fat Malabsorption

- Symptoms may include the following1,2:
  - Foul-smelling, greasy stools (steatorrhea)
  - Does not occur until disease is advanced
  - Unexplained weight loss
  - Frequent diarrhea
  - Abdominal pain
  - Bloating and gas

Symptoms of Protein Malabsorption

- Symptoms of protein malabsorption (azotorrhea) may include the following:
  - Weight loss
  - Diarrhea
  - Edema (anywhere throughout the body)
  - Hair loss
  - Dry, scaly skin
  - Muscle atrophy

References:

Tests May Confirm an EPI Diagnosis

- Invasive measures
  - Direct measures of pancreatic function such as the secretin-pancreozymin stimulation test are performed at specialized centers.
- Non-invasive measures
  - Quantitative fecal fat
  - Standard for fat maldigestion
  - Qualitative fecal fat
  - Screening test only
  - Fecal elastase concentration (FEC)
  - Fat soluble vitamin

References:

Comprehensive EPI Management Plan

- Pancreatic enzyme replacement therapy
  - PERTs are the basis of therapy for treatment of EPI
- Lifestyle modifications
  - Avoid or limit alcohol intake
  - Eat a well-balanced diet
  - Smoking cessation
- Vitamin supplements
  - Consider vitamin supplementation, including fat-soluble vitamins A, D, E, and K
PERTs are the Standard of Care for EPI

- Pancreatic enzyme replacement therapy (PERT) should:
  - Replace enzymes not secreted in patients with EPI
  - Contain lipase, amylase, and protease
  - Deliver lipase within the duodenum
  - By improving maldigestion, PERTs can help the correction of steatorrhea


Surgery May Result in EPI Depending Upon the Type and Extent of Resection

- Distal pancreatectomy
- Pancreatoduodenectomy (Whipple procedure)
- Total pancreatectomy (Chronic Pain/Transplant)
- Peptic, Malignant or Bariatric Resections


Strategies for Diagnosing and Treating EPI

- Consider EPI in your differential diagnosis of GI symptoms
- Prescribe appropriate treatment for diagnosed patients
  - PERT
  - Dietary and lifestyle recommendations
- Ensure patients work with a registered dietitian to meet dietary needs

EPI Presents Many Challenges

- EPI is an under-recognized condition¹
- Look for signs and symptoms, as EPI is largely a clinical diagnosis²
- EPI signs and symptoms overlap with those of other GI conditions¹
- Many patients on a pancreatic enzyme replacement therapy (PERT) are underdosed²

References: