NUTRITION AND THE PANCREAS: WHAT THE PRACTICING CLINICIAN SHOULD KNOW

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DISCLOSURES

- I, Kevin Walton, am involved in a research project funded by Alcresta Therapeutics. Alcresta Therapeutics has not contributed any funds or payment to the development for this session.

SESSION OUTLINE

- Review of basic digestion and absorption in the GI tract
- Review basic anatomy and physiology of the pancreas
- Complications of pancreatic dysfunction
  - Endo and exocrine dysfunction
  - Common medical complications and surgical procedures
- Medical nutrition therapy considerations including enteral and parenteral nutrition
- Case study

BASIC OVERVIEW OF DIGESTION AND ABSORPTION

Upper GI Tract

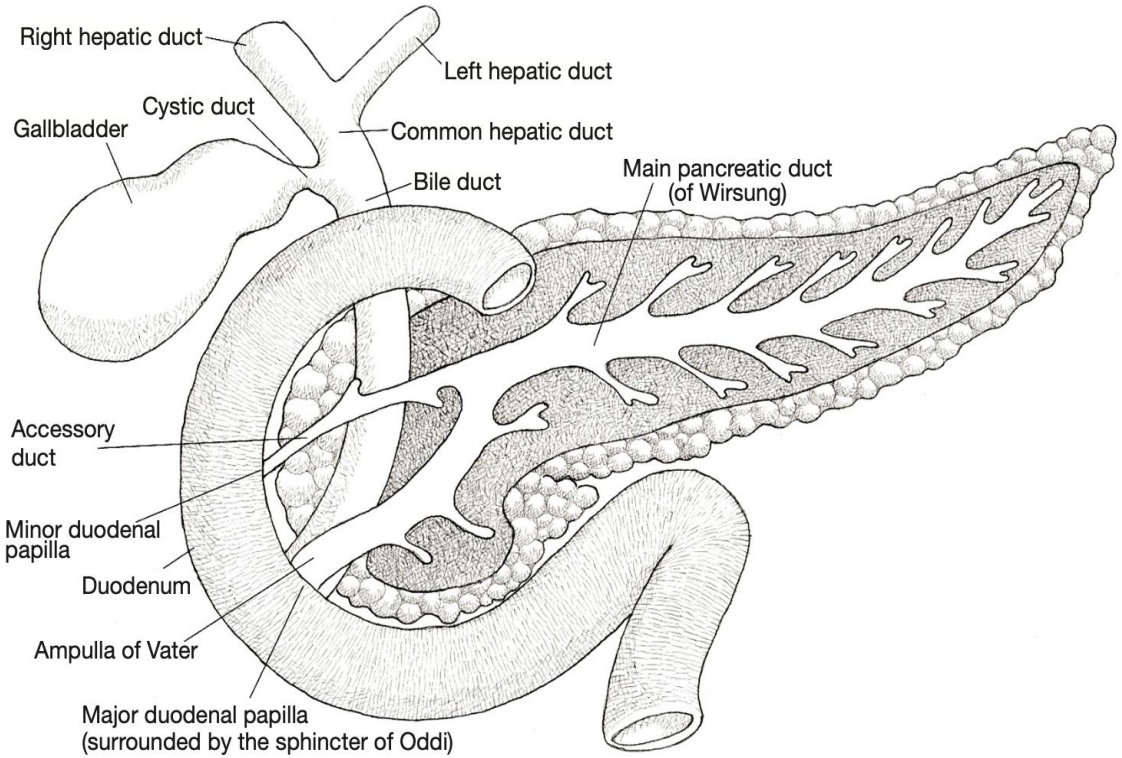
- Mouth: mastication, lingual lipase, and salivary amylase for preliminary digestion
- Esophagus: connects the mouth to the stomach
- Stomach: secretion of strong acids, mixing/churning into chyme. Intrinsic factor, gastrin, gastric lipases, and pepsin.
- Small intestine
  - Duodenum: relatively short only about 1 foot in length, mixing chyme with bile, pancreatic enzymes, and bicarbonate. Start of **mineral** and vitamin absorption.

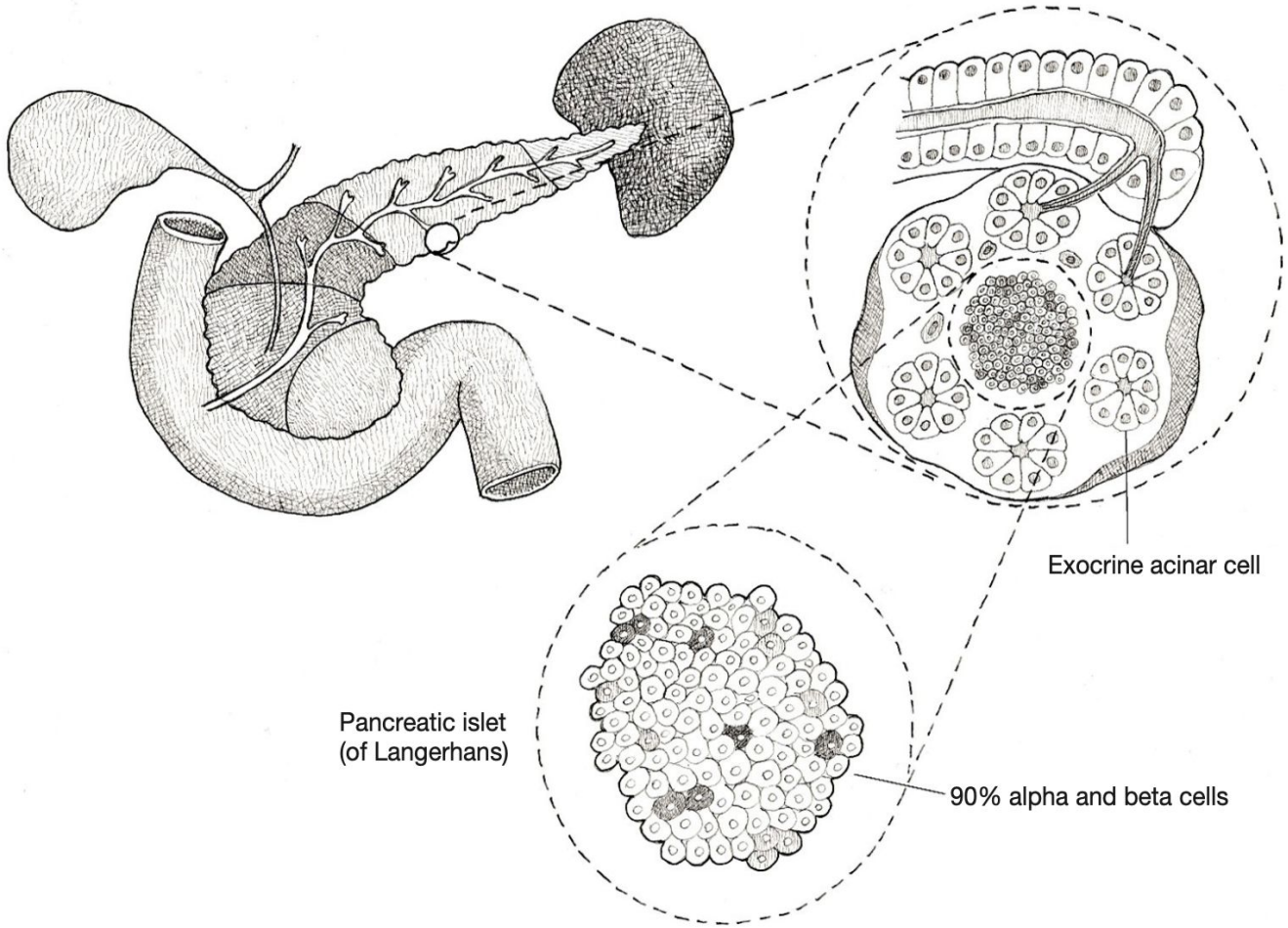
Lower GI Tract

- Small intestine
  - Jejunum: about 8 feet long, a major site of nutrient absorption for vitamins, minerals, **lipids (free fatty acids and micelles), amino acids, and monosaccharides.**
  - Ileum: about 10 feet long, with some absorption of vitamins like B12, minerals, and **bile salts.**
- Large intestine: about 5 feet long. Reabsorption of water, electrolytes, and production of short-chain fatty acids by fermenting fiber.

-Jackson et al, 2009. Surgery (oxford), 276(6), 231-236
-Goodman, 2010. Advances in physiology education.
-Basile et al, 2023, Physiology, Nutrient Absorption.

BASIC ANATOMY OF THE PANCREAS





-Russell et al, 2022. Art of Surgery, 6.

BASIC FUNCTIONS OF THE PANCREAS

Endocrine Function

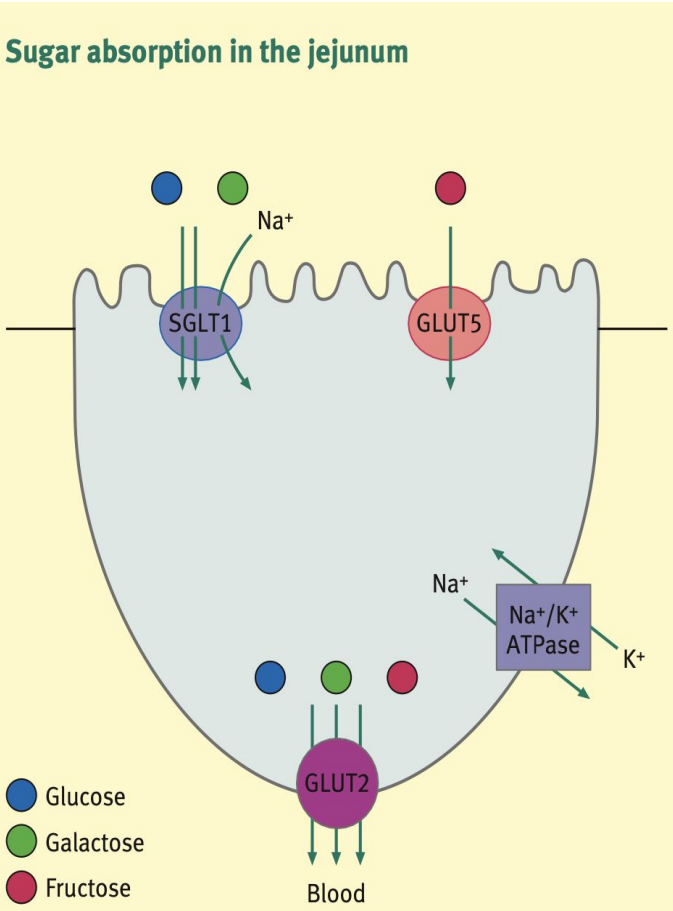
- Islets of Langerhans
  - Alpha cells: glucagon
  - Beta cells: insulin
  - Delta cells: ghrelin, glutamine, urocortin-3, and somatostatin. "Regulator cell"

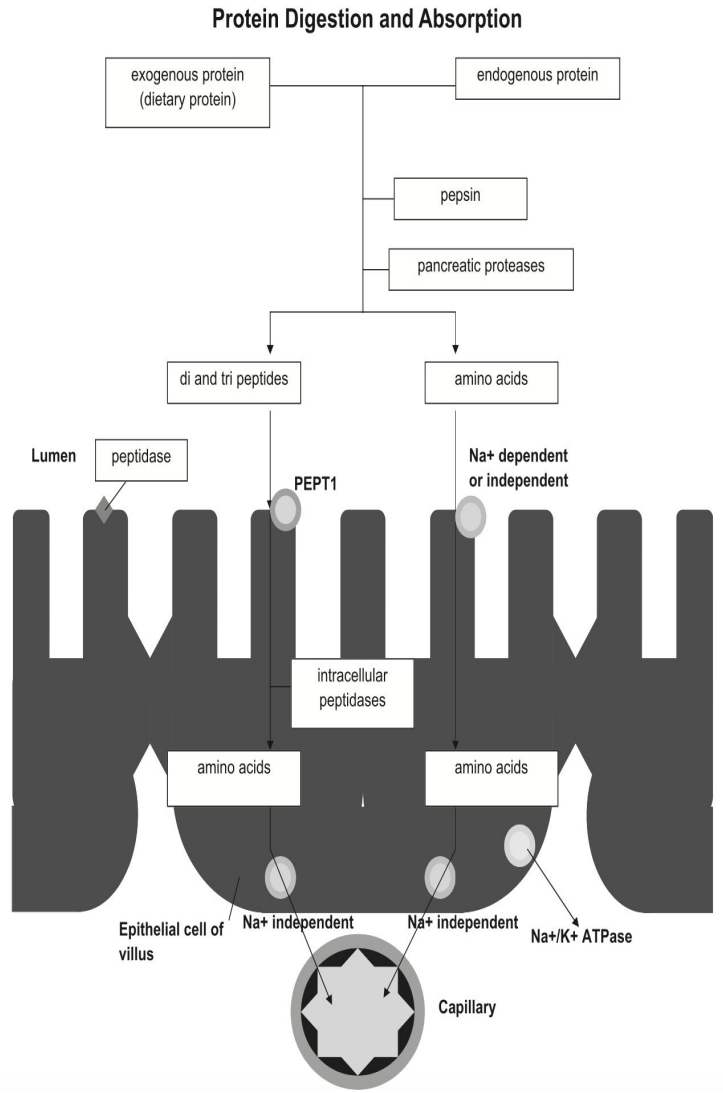
Exocrine function

- Creation and secretion of pancreatic juices via acinar and ductal cells.
  - Proteases: chymotrypsin, trypsin, trypsinogen, elastase, carboxypeptidase.
  - Lipase: responsible for ~70% of hydrolysis of dietary fat that is typically in the form of triglycerides.
    - Co-lipase: activated by trypsin, prevents inactivation of lipase from bile salts.
  - Amylase
  - **Bicarbonate** to neutralize gastric acidity of chyme.
    - Correct pH is important in digestive effectiveness

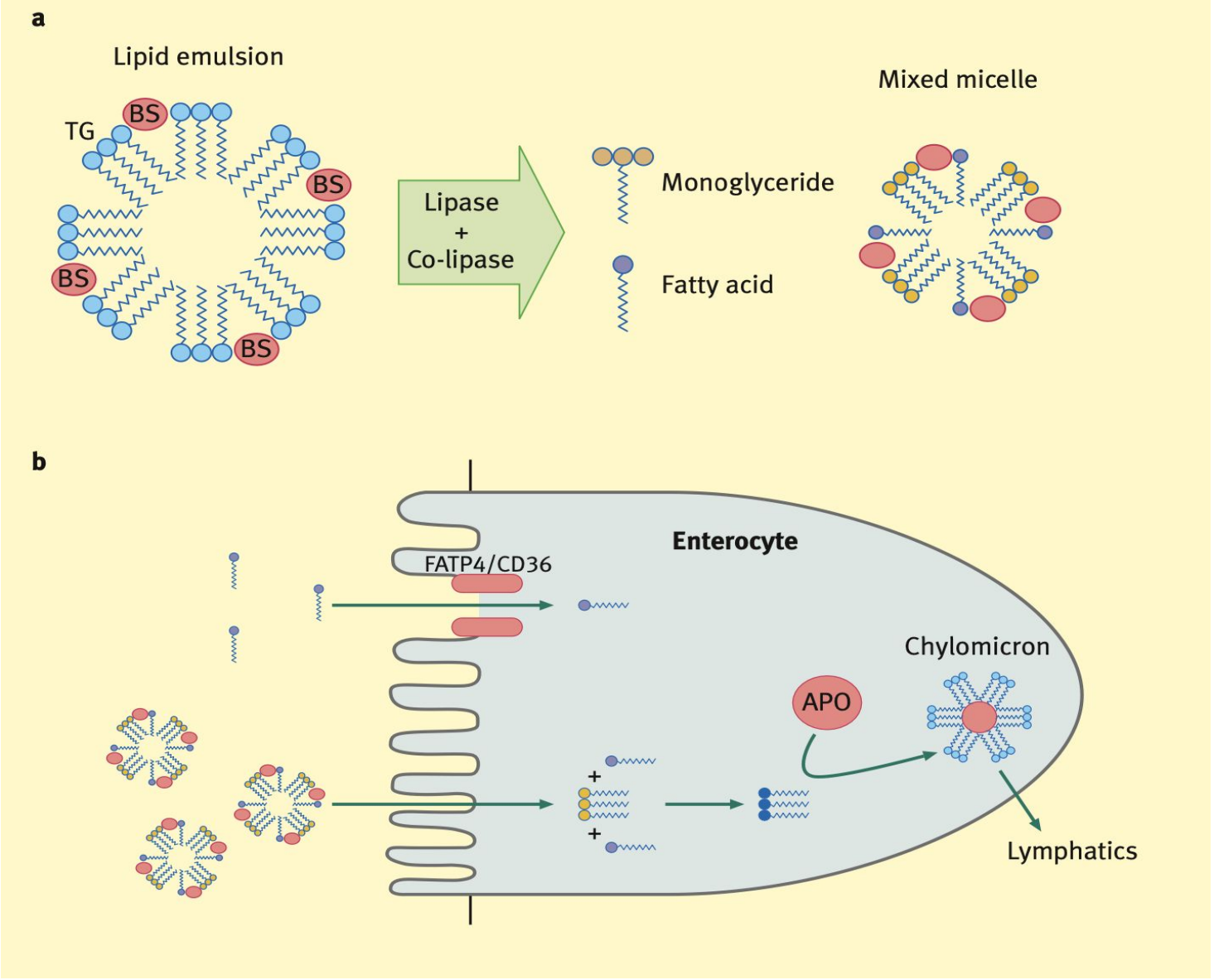
-Russell et al, 2022. Art of Surgery, 6.
-Jackson et al, 2009. Surgery (oxford), 276(6), 231-236
-Goodman, 2010. Advances in physiology education.

CARBOHYDRATE AND PROTEIN ABSORPTION





-Jackson et al, 2009. Surgery (oxford), 276(6), 231-236
-Goodman, 2010. Advances in physiology education.



LIPID DIGESTION AND ABSORPTION

- Bile is made by the liver, stored, concentrated, and secreted by the gallbladder to help emulsify fat.
  - Bile contains bile acids
- Pancreatic lipase is responsible for ~70% hydrolysis of dietary fat, which is primarily in the form of triglycerides.

-Jackson et al, 2009. Surgery (oxford), 276(6), 231-236
-Berry 2014, Nutrition in Clinical Practice, 29(3), 312-321.

EXOCRINE DYSFUNCTION

- Exocrine pancreatic insufficiency (EPI)
  - Insufficient enzymatic production from injury or a blockage that results in maldigestion.
    - Typically occurs when production and/or secretion falls below 10% of normal function
  - Dietary fat is typically the most impacted macronutrient while micronutrient disturbances can also occur if chronic and untreated
  - Common signs and symptoms of EPI include post-prandial bloating, foul-smelling diarrhea, floating, greasy/oily appearance, unintentional weight loss, and abdominal pain.
  - 72 fecal fat vs fecal pancreatic elastase vs treatment response.
    - Maldigestion vs malabsorption
    - Small intestine bacterial overgrowth (SIBO)

-Arvanitakis et al, (2024), Clinical Nutrition, 43(2), 395-412.
-Ramanathan, et al, (2019), Nutrition in Clinical Practice, 34, S7-S12.
-O'Brien, et al, (2019), Nutrition in Clinical Practice, 34, S13-S26.

Table 2. Tests Used to Evaluate Pancreatic Exocrine Insufficiency.

Test	Details	Advantages	Limitations
Fecal fat quantitation	Collection of all stool samples in a 3-day period to quantitate fecal fat, and the coefficient of fat absorption	Accurate quantitation of fat absorption	3-day test Requires patient adherence to strict diet Handling of large volumes of feces by laboratory personnel
Fecal elastase 1	Quantitative measurement of elastase-1 in single stool sample	Noninvasive Single stool sample required	Inaccurate with large-volume diarrhea Inaccurate in mild to moderate exocrine insufficiency
^{13}C-mixed triglycerides breath test	Measurement of $^{13}CO_2/^{12}CO_2$ in serial exhaled breath samples following ingestion of ^{13}C-mixed triglycerides in a standardized meal ^{13}C-mixed triglycerides are degraded to fatty acids and metabolized. Exhaled $^{13}CO_2$ can be measured in exhaled breath samples	Measurement of fat absorption and metabolism	Variation in protocols between institutions Long test (6 hours)
Secretin-cholecystokinin stimulation test	Gastroduodenal tube is inserted. Gastric limb collects gastric secretions. Basal pancreatic secretions are collected in the duodenal tube Intravenous secretin is administered over 2 hours, and cholecystokinin is administered over the second hour. Pancreatic secretions are collected from the duodenal limb every 15 minutes Quantitation of the fluid volume, bicarbonate, and pancreatic enzymes is performed	Direct measurement of pancreatic secretions Allows measurement of pancreatic ductal and acinar cells	Poorly tolerated by patients Relatively long test Invasive Requires specialized endoscopy and fluoroscopy services

.-O'Brien, et al, (2019), Nutrition in Clinical Practice, 34, S13-S26.

PANCREATIC ENZYME REPLACEMENT THERAPY (PERT)

- Medications containing protease, amylase, and/or lipase.
- To be taken concurrently with meals
- Typically, dosed by weight or by total lipase units/meal
  - 500-2500 lipase units/kg/meal, maximum of 10,000 units/kg/d **or** 25,000-80,000 lipase units/kg/meal, 50% dose w/ snacks. Rarely dosed by lipase-units/g-fat per meal but an option. Up-titrate per symptoms.
- Enteric and non-enteric coated: pancreatic enzymes degrade in low pH like the stomach.
  - Enteric-coated capsules are coated in a casing that only degrades in a high pH environment like the duodenum. Creon®, Zenpep®, Pancreaze®.
  - Non-enteric-coated PERT activates immediately and degrades in an acidic environment. Viokace®\
  - Proton Pump Inhibitor / H2 blocker
  - Very high (insoluble) fiber diets discouraged

-Berry, (2014) Nutrition in Clinical Practice. 29(3), 312-321
-Whitcomb et al, (2023), Gastro Hep Advances, 2(3), 395-411
-Arvanitakis et al, (2024), Clinical Nutrition, 43(2), 395-412..
-O'Brien, et al, (2019), Nutrition in Clinical Practice, 34, S13-S26

ENDOCRINE DYSFUNCTION & DIABETES MELLITUS (DM)

Type 1 DM

- An autoimmune disorder that results in β-cell destruction.
  - Typically occurs early on in life resulting in insulin deficiency

Type 2 DM

- Progressive secretory defect + insulin resistance
  - In late stages, β-cell damage can result in insulin deficiency

Type 3c DM

- Damage to the pancreatic tissue from inflammation or fibrosis
  - In early stages, decreased β-cell function and decreased insulin production
  - In late stages, α-cell damage results in decreased glucagon production
- Often labeled as "brittle" diabetics

Gestational DM

- Typically, a result of chronic insulin resistance + β-cell dysfunction.
  - Typically present before pregnancy but insulin resistance is exacerbated and becomes prevalent in later stages of pregnancy

-Blair, 2016. Urologic nursing. 36 (1)
-Bhattamisra et al. 2019. Current diabetes review, 15(5), 382-394.

TYPES OF INSULIN AND ORAL MEDICATIONS

Insulin

- Rapid-acting: Lispro (Humalog®) or Aspart (NovoLog®)
  - Onset of 10-30min, peaks in 30min-3hrs w/ a 3-5hr duration. Should eat within ~5 or so min.
- Short-acting: "regular" insulin (Humulin® or Novolin®R)
  - Onset of 30min-1hr, peaks in 2-4hr w/ a 5-8hr duration. Eat within 30min
- Intermediate-acting: NPH (Novolin®N)
  - Onset of 1-3hr, peaks in 6-8hr w/ a 12-18hr duration.
- Long acting: Glargine (Lantus®) or Detmir (Levemir®)
  - Onset of 1-4hr, does not "peak" w/ a 24-26hr duration

Oral Medications

- Biguinides: Metformin (Glucophage®)
  - Decreases the liver's production of glucose + increases the sensitivity of muscles to insulin
- Sulfonyureas: Glipizide (Gucotrol®) Chlorpropamide (Diabenase®)
  - Stimulates beta cells to produce/release more insulin
- SGLT-2 inhibitors: Canagliflozin (Invokana®) Dapagliflozin (Farxiga®)
  - Causes excess glucose to be excreted in urine
- GLP-1 Agonist: Dulagluitide (Trulicity®) Semaglutide Injection (Ozempic®), Liraglutide (Victoza®)
  - Stimulates insulin production, slows appetite, gastric emptying, and glucagon secretion

-Blair, 2016. Urologic nursing. 36 (1)
-Bhattamisra et al. 2019. Current diabetes review, 15(5), 382-394.

COMMON MEDICAL COMPLICATIONS OF THE PANCREAS

- Pancreatitis: Etiologies include gallstone, alcohol, smoking, medication, injury, genetics, cancer, autoimmune, or endoscopic retrograde cholangiopancreatography (ERCP).
  - Acute: One of the most common GI-related reasons for hospital admission. Can be mild, moderate, or severe. Acute inflammation and activation of acinar cell enzymes that can result in some degree of autodigestion. Potential cascade of systematic inflammatory response syndrome (SIRS) and multiorgan involvement. *Endocrine and exocrine dysfunction may be impacted pending the degree of injury.*
  - Chronic: This may be caused by recurrent acute pancreatitis. Progressive and chronic inflammation resulting in visible changes to anatomy. Potential exocrine and endocrine dysfunction resulting in EPI or DM. Malnutrition is a significant risk.
- Pancreatic Cancers: Adenocarcinomas, squamous cell carcinomas, intraductal papillary mucinous neoplasm (IPMN), neuroendocrine tumors, etc.
- Cystic Fibrosis: Thick secretions may negatively impact the flow of pancreatic juices.

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-O'Brien, et al, (2019), Nutrition in Clinical Practice, 34, S13-S26.

COMMON SURGICAL PROCEDURES OF THE PANCREAS

- Pancreaticoduodenectomy / Whipple:
  - Classic: The distal stomach, a portion of the duodenum, and the head of the pancreas are removed
  - Pylorus sparing: The stomach and pylorus are typically left intact but this type may increase the risk for delayed gastric emptying
- Pancreatectomy
  - Distal: Resection of the tail and or portion of the body
  - Central: Resection of the central or "body" of the pancreas. May improve longevity endocrine and exocrine function
  - Total pancreatectomy: The entire pancreas is removed
    - Islet autotransplantation: The pancreas is "blended and digested" to be purified for isolation of islets that are infused into the liver. May lessen DM severity.
- Cyst-gastrostomy: Creation of an opening between pancreatic pseudocyst and stomach for internal drainage.

-Jabłońska et al, (2023), Life, 13(6), 1400
-Sutherland et al, (2012). Journal of the American College of Surgeons, 214(4), 409-424
-Saribeyoglu at el, (2008). Turkish Journal of Medical Sciences, 38(4), 311-317.

MEDICAL NUTRITION THERAPY CONSIDERATIONS

- The main goal is to identify, prevent, and treat malnutrition as it has been shown to negatively impact surgical outcomes, increase mortality and morbidity, increase LOS, hospital costs, and readmission rates.
- Consider the etiology of the problem, degree of injury or dysfunction, and patient's signs and symptoms! Collaboration is key!
  - EPI Assessment: and consideration of pancreatic enzyme replacement therapy (PERT)
    - Consider dosing, timing of administration, and habitual diet. Proton pump inhibitor (PPI) is usually recommended in conjunction as it makes up for the lack of bicarbonate that is typically produced by ductal cells for optional pH for enzymatic activity. Although controversial, usually start dosing at 500 lipase units/kg/meal, up titrate as needed with a limit of 10,000 units/kg/day.
    - Potential micronutrient involvement: Fat soluble Vit. A/D/E/K, Se, Zn, Mg, Fe-studies, B12, folate. PTH. Changes to hair, nails, skin, eyes.
  - DM: Consistent carb intake, limiting simple sugars, incorporating complex carbohydrates, endocrinology collaboration.
  - Diet modification: Low fat may not be appropriate for all, potential for fiber reduction, prioritizing protein, oral nutrition supplements. The overarching goal is to attenuate malnutrition.

-Jimenez et al. 2024 The American Journal of Clinical Nutrition, 199(3) 779-787
-La Torre et al. 2013. Journal of Surgical Oncology, 107(7) 702-708
-Mosquera et al. 2016. Journal of Surgical Research, 205(1), 95-101
-Arvanitakis et al, (2024), Clinical Nutrition, 43(2), 395-412.

NUTRITION SUPPORT AND THE PANCREAS

- If oral nutrition optimization fails, enteral nutrition (EN) should be considered:
  - Gastric vs jejunal access: Dependent on the degree of injury, dysfunction and plan of care. Consider the etiology of the issue or complication (acute vs chronic pancreatitis, Whipple, pancreatic cancer, etc).
  - Formula selection:
    - Consider polymeric formula if no significant injury or dysfunction is present.
    - Consider formula with some % of fat derived from medium chain triglycerides (MCT) if necrosis is present, severe injury/dysfunction, intolerance to polymeric formula, and history of oral PERT at baseline.
  - PERT and EN
- Consider parenteral nutrition if unable to gain enteral access, inability to feed due to ileus, GI bleed, ischemia, high output fistula, bowel obstruction, etc. Restart oral or trial enteral nutrition ASAP.
- Collaboration with providers is essential!

-Whitcomb et al,)2023), Gastro Hep Advances, 2(3), 395-411
-Arvanitakis et al, (2024), Clinical Nutrition, 43(2), 395-412.
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CASE STUDY

- 42-year-old patient, transferred from an outside hospital after a ~2 week stay for acute complicated gallstone pancreatitis w/ new concern for necrosis. No other notable PMHx. Normal BMI.
- Pt had failed PO trials and had not been eating much at all during the 2 week stay.
- They had an NGT for only 4 days and reported receiving a "tan-colored" formula. Pt reported feeling "uncomfortable" when the formula was infused so it was frequently stopped. NGT was removed before transfer as it clogged.
- Pt reported a 10% weight loss from their usual body weight over ~4 weeks. They have no appetite or interest in trying to eat again given fear of pain. Pt reported, "runny and smelly" bowel movements that they attested to "that formula".

- Nutrition service consulted for "c/f malnutrition, unsure if needs nutrition support, c/f severe acute necrotizing pancreatitis".
  - Pt is found to be severely malnourished given unintentional weight loss and lacking nutrition delivery

CASE STUDY

- Refeeding risk?
- Obtaining more details from OSH course
  - What oral intake was the pt able or unable to tolerate?
  - What formula was used and how was it administered?
  - Why no NJT if failed NGT?
- Was there any sort of assessment for EPI or a trial of PERT?
- Are we concerned about micronutrients?
- What happens if pt refuses, or is unable, to have NJT placed

QUESTIONS AND DISCUSSION