



Hyperinsulinism and the GI tract



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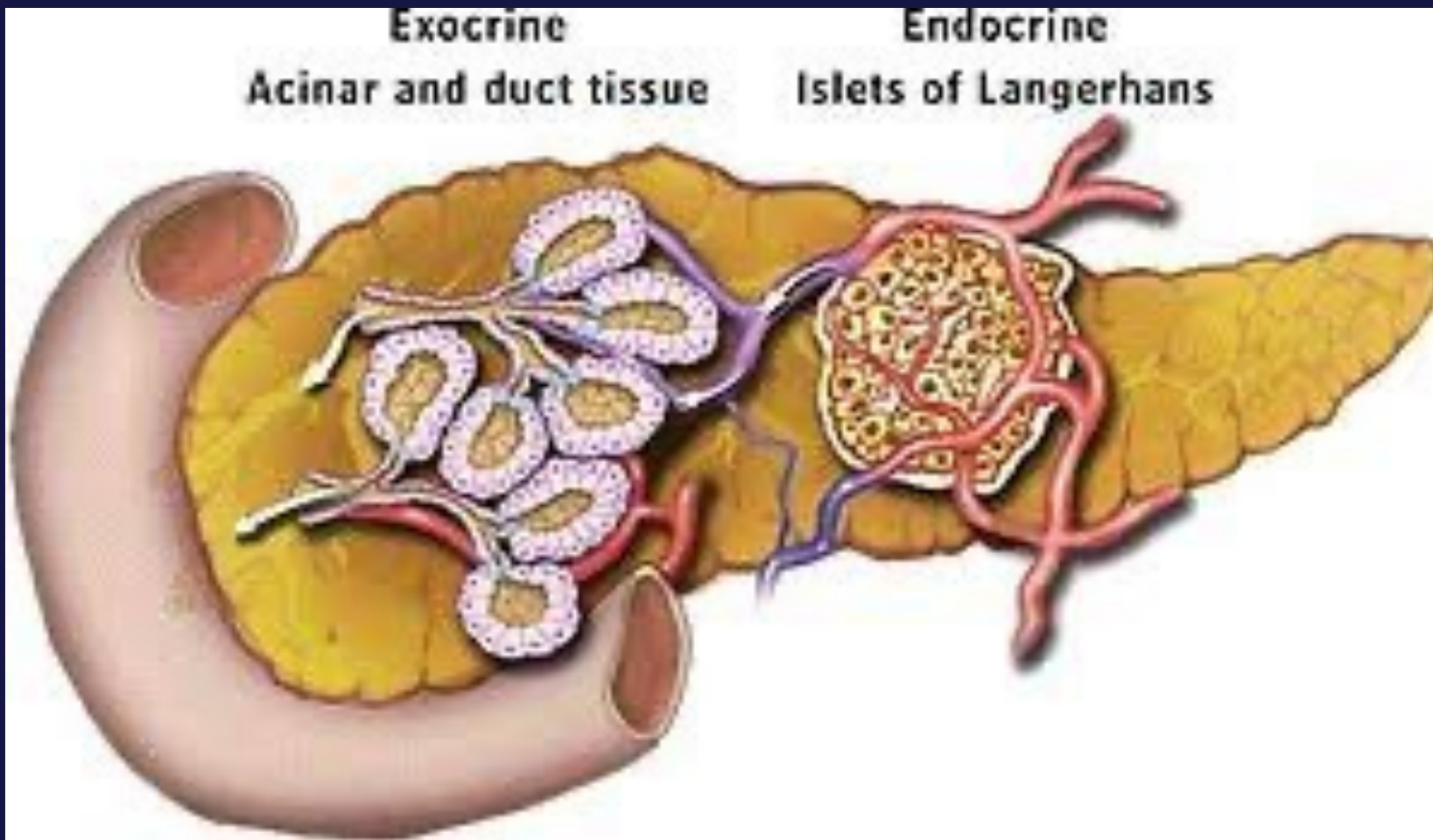
Disclosures

- LYM-X-SORB™



To understand:

- the role the pancreas plays in normal digestion
- Causes of digestive/exocrine pancreatic insufficiency (EPI) in patients with hyperinsulinism
- clinical manifestations of EPI
- diagnostic approaches to EPI
- management of EPI

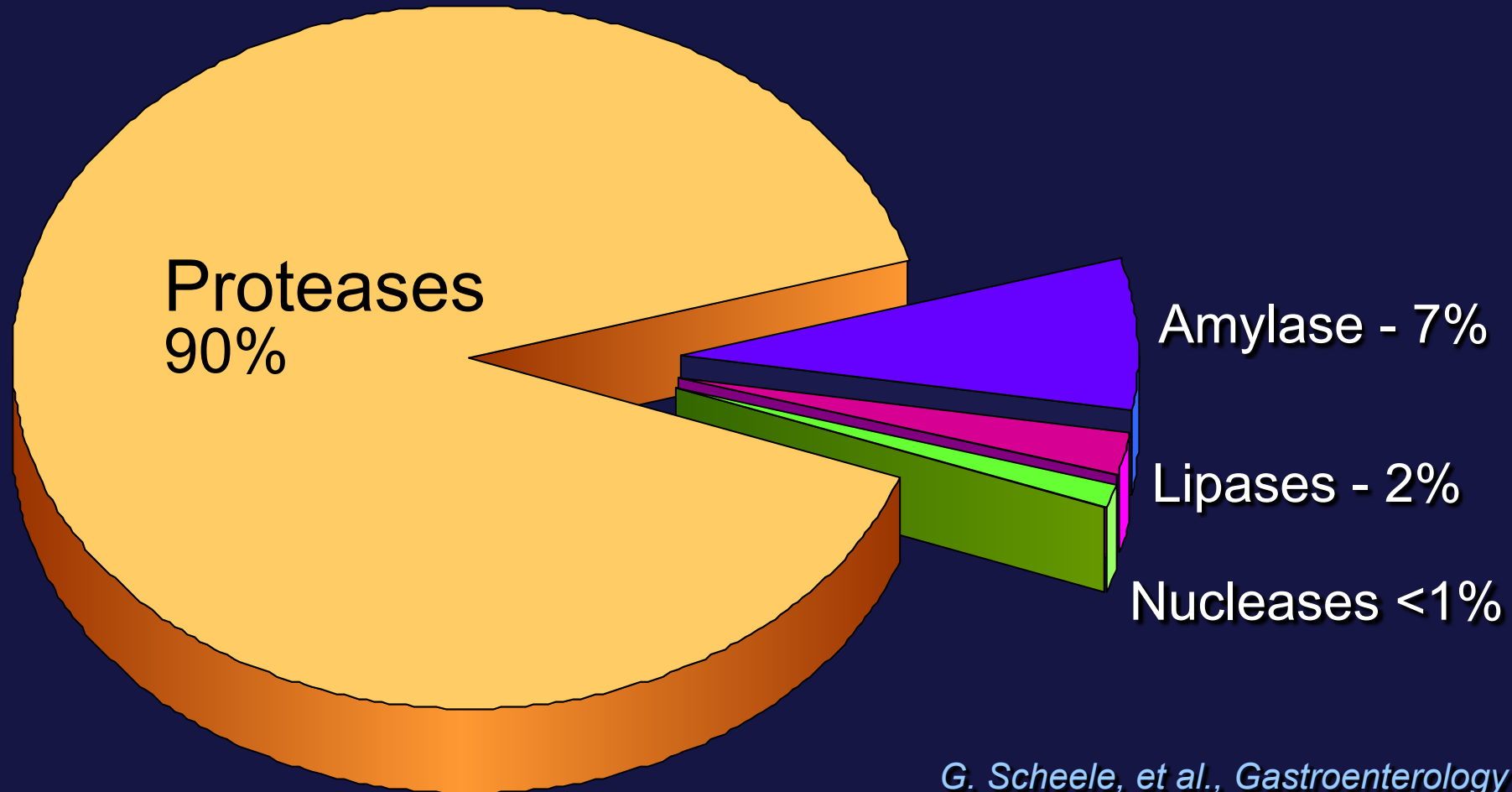




Causes of EPI in patients with Hyperinsulinism:

- Surgery
- Medications: somatostatins -Octreotide and Lanreotide

Classes of Pancreatic Enzymes



G. Scheele, et al., Gastroenterology 1981; 80:461



General

- Change in stools
 - Greasy, malodorous
- Gas
 - Flatulence
 - Bloating
- Abdominal pain
- MOST OF THE TIME THIS IS SUBLE and SUBCLINICAL!
- Potentially consequential

Nutrient specific

- Energy losses
 - weight loss, suboptimal growth
- Fat soluble vitamin-related
 - Vision, balance, bruising, bleeding
- B₁₂ deficiency
 - Macrocytic anemia; neurological changes
- Essential fatty acid deficiency
 - Skin issues, alopecia, growth issues

- **Steatorrhea- greasy “floaters”; foul smelling**
- **Abdominal distention**
- **Failure to thrive**
- **Skin breakdown**





Direct

- Dreiling tube
- Endoscopic pancreatic function testing
- Secretin stimulated magnetic cholangiopancreatography [s-MRCP]

Indirect / Surrogate markers

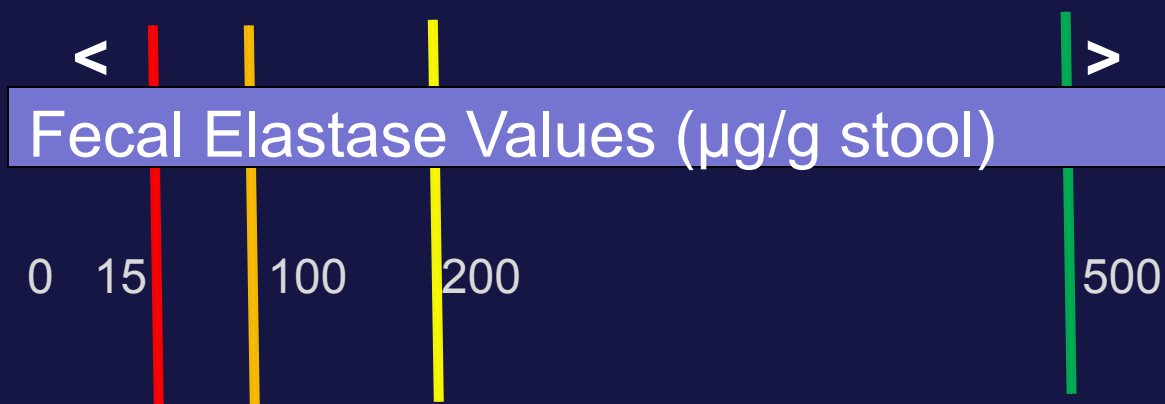
- Fat soluble vitamin status
- Stool markers
- Mixed TG breath test

Remember that EPI is not “yes or no” but a spectrum between absolutes sometimes



Fecal Elastase

- Age related reference ranges
- Validated primarily in CF
- No direct correlation with degree of impairment
- Dilution a major problem: must be performed on at least non watery and as close to solid stool
- Elastase can change over time, so can and should follow it.
 - Especially if you have EPI while on somatostatins



Maqbool and Stallings. eCF review March 2009

Stein J et al. Clin Chem. 2005; 51(6):1052-1054.

Borowitz D, Lin R, Baker SS. JPGN. 2007;44(2):219-223.

Cohen JR, Schall JI, Ittenbach RF, Zemel BS, Stallings VA. JPGN J Pediatr Gastroenterol Nutr. 2005;40(4):438-444.

Beharry S, Ellis L, Corey M, Marcon M, Durie P J Pediatr. 2002;141(1):84-90.

Walkowiak J, Nousia-Arvanitakis S, Cade A, et al. J Cyst Fibros. 2002; 1(4):260-264.

Luth S, Singer M et al. Scan J. Gastroenterol 2001. Oct;36(10):1092-9.



- **Fat soluble vitamins**
- **Vitamin B₁₂**
- **Fatty acids**
- Calcium
- Magnesium
- Iron
- Trace minerals : Zinc, Selenium
- Plasma proteins



EPI: Blood Markers

	Most common markers	Further considerations
Vitamin A	Serum retinol	Pre-albumin or RBP and albumin [1:1:1] Modified/relative dose response Stable isotope dilution Iron status
Vitamin E	Alpha tocopherol	Gamma tocopherol; Express as a function of total fasting lipids
Vitamin D	25 [OH] vitamin D	Be careful with your units ng/ml versus nmol/L
Vitamin K	PT	PIVKA II- NO LONGER AVAILABLE %undercarboxylated osteocalcin
Essential Fatty Acid	T:T	LA, ALA; Mol% versus $\mu\text{mol/L}$
B₁₂	Serum B ₁₂ and methylmalonic acid	

Serum levels do not usually drop unless/until stores are exhausted

Tanumihardjo SA. J. Nutr. 134: 290S–293S, 2004.

Huang SH, Schall JI, Zemel BS, Stallings VA. J Pediatr. 2006 Apr;148(4):556-559.

Lagerstedt et al. Molecular Genetics and Metabolism 73, 38–45 (2001).



- Nutrition
- Multivitamins
- Pancreatic enzyme replacement therapy



Pancreatic enzyme replacement therapy (PERT)

PERT dosing method	Feeding and dose considerations
Weight-based	Oral feeding <ul style="list-style-type: none">• start 500-1000 lipase units/kg/meal; dose escalation until limits reached
Fat-based	Oral/enteral feeds <ul style="list-style-type: none">• If suboptimal response to weight-based approached• 500-4000 lipase units/g fat
Volume-based	Enteral feeds (especially with continuous feeds) <ul style="list-style-type: none">• enteral in line feeding cartridge• 1 cartridge/ 500 ml;• add additional cartridge for 1000 ml of formula
Age-based	<ul style="list-style-type: none">• Infants<ul style="list-style-type: none">• 2000-4000 lipase units per 120 ml of formula or per breast feeding Children <ul style="list-style-type: none"><4 yrs = 1000-2500 lipase units/kg/meal>4 yrs = 500-2500 lipase units/kg/meal

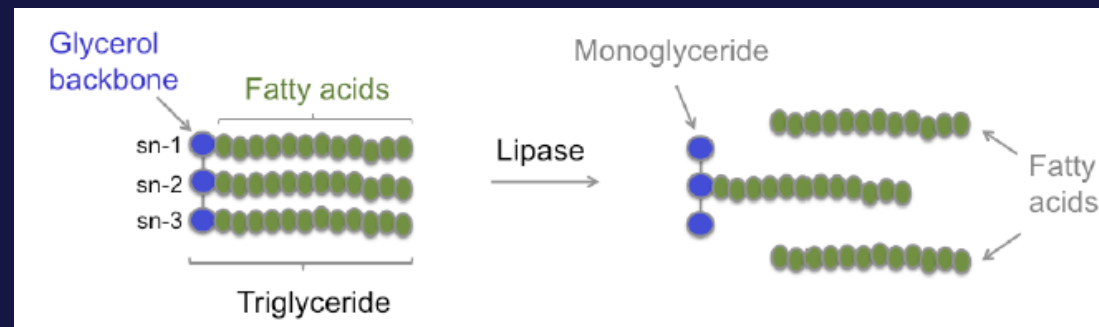
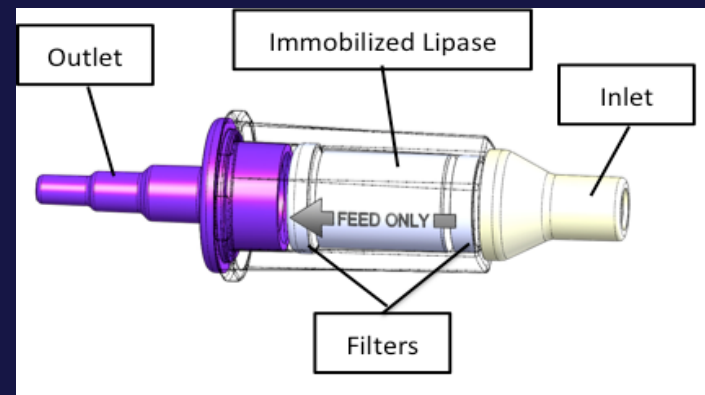
Therapeutics:

- **Lym-X-Sorb™**

- dietary fat structured lipid; bypasses chylomicron formation; delivery vehicle

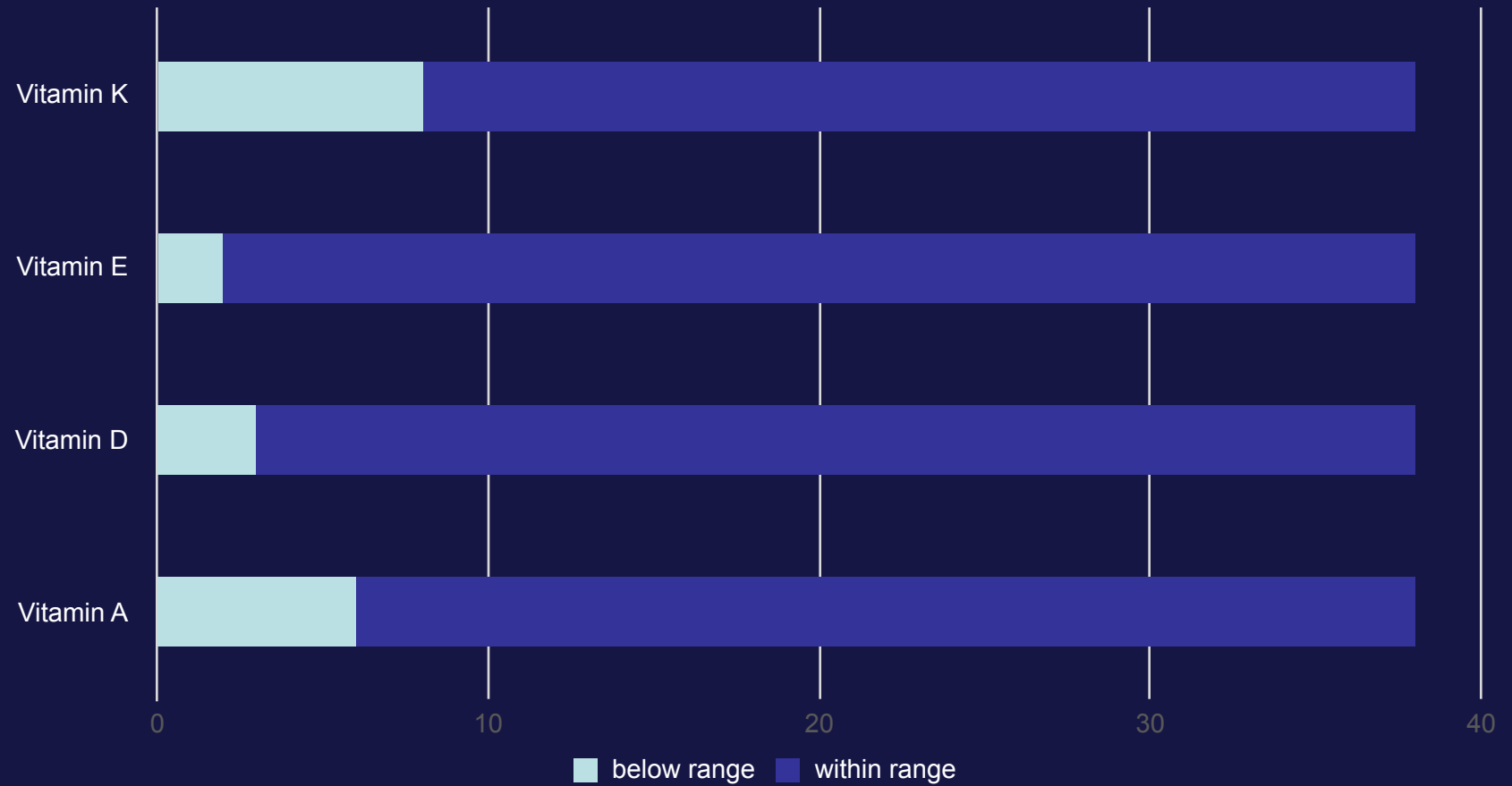
- **EFIC**

- device that hydrolyzes TG into 2 free fatty acids and monoglyceride



Fat-Soluble Vitamin Status

N=38





Characteristics	
EPI Diagnosis	29 (61.7%)
Age at EPI diagnosis in years ¹	3.39 [0.12,10.1]
EPI Symptoms	20 (42.6%)
PERT Use	26 (55.3%)
Average PERT dose, in lipase units/kg/d ¹	3339 [372,8655]

EPI defined as:

- ≥ 2 fat soluble vitamin deficiencies
- Low fecal elastase ($< 200 \mu\text{g/g}$ stool)
- On PERT
- Symptoms
- As defined by a pediatric gastroenterologist

¹median [range]



Predicting EPI in post pancreatectomy patients: variables of interest

- Age at diagnosis
- Diffuse versus focal disease
- Percent pancreatic resection
- Age at surgery
- ? Sites of resection



Additional concerns for EPI with medication use:

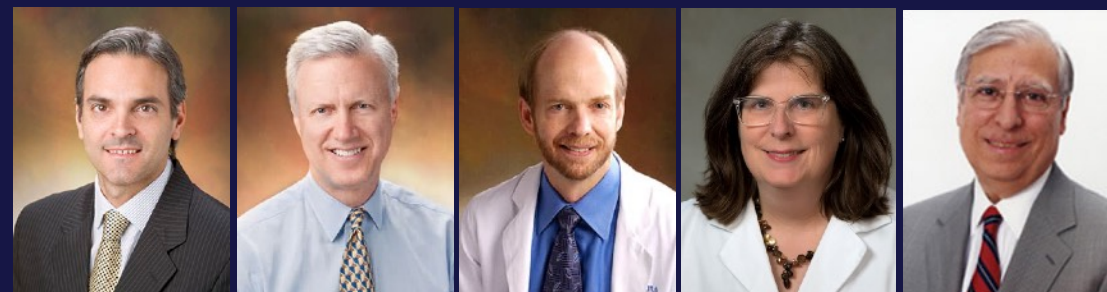
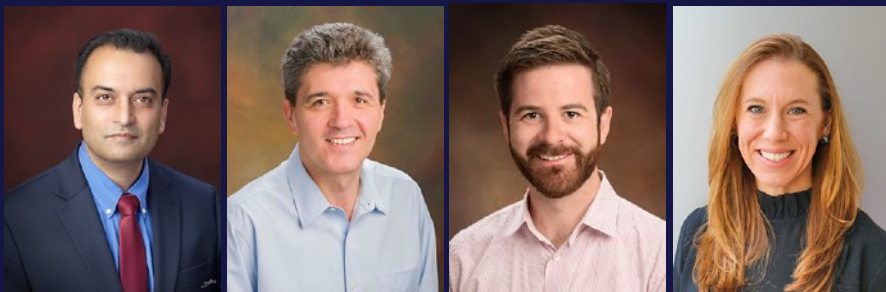
- Somatostatin/analogues:
 - Gallbladder sludge and stones
- Treatment
 - Observation, imaging, labs
 - Ursodeoxycholic acid/Ursodiol
 - Surgery to remove the gallbladder



- **The role the pancreas plays in normal digestion and facilitating absorption is for :**
 - dietary fat
 - essential fatty acids
 - fat soluble vitamins
 - vitamin B₁₂
- **Exocrine Pancreatic insufficiency can be subtle, transient or longer term, and can be consequential**
 - Maintain a high index of suspicion
 - Need to re-assess
- **Medical Management of Exocrine Pancreatic insufficiency requires:**
 - A team approach
 - Vitamin supplementation
 - Pancreatic enzyme replacement therapy
 - Surveillance!



Pancreatic Disorders Program



Multidisciplinary team with the mission to provide state-of-the art, comprehensive care to all children with pancreatic(obiliary) disorders



