CF Pancreatic Disease: Exocrine Pancreatic Insufficiency (EPI)

Diagnosis:

- **Definition:** Inadequate exocrine pancreatic function, which requires >90% loss of functional exocrine pancreatic tissue, resulting from destruction of acinar and ductal tissue, where digestive enzymes are produced for fat, protein, and carbohydrates
  - Diagnosis can be made with increased IRT level on newborn screen, elevated chloride test (≥60 mmol/L), and genetic testing

- **Differential Diagnosis:** cystic fibrosis, chronic pancreatitis, Schwachman-Diamond syndrome, Johanson-Blizzard Syndrome, pancreatic agenesis, congenital pancreatic hypoplasia, gastro-intestinal disease (i.e. celiac disease), Zollinger-Ellison syndrome

Key History to Review:

- History of pancreatitis, celiac disease, any other GI disease, fat soluble vitamin deficiencies (A, D, E, K); symptoms including steatorrhea, abdominal pain, weight loss/poor weight gain, bloating, rickets, easy bruising/bleeding, night blindness
- Family history of pancreatitis, cystic fibrosis, celiac disease, autoimmune disease

Key Physical Exam Components:

- Features of malnutrition: wasting, stunting, underweight, micronutrient deficiencies
- Abdomen: abdominal distension, +/- abdominal tenderness (may be diffuse/generalized)
- Signs of fat-soluble vitamin deficiencies, i.e. bruising, jaundice, abnormal skeletal exam, abnormal neurologic exam

Key Labs/Imaging:

- **Blood testing:** CBC, CMP, direct bilirubin, GGT, vitamin A, vitamin E, vitamin D-25, INR; consider genetic testing for *CFTR* if not already completed, OGTT test starting from age 10.
- **Stool:** fecal elastase (FE-1; 72-hour fecal fat is regarded as being more cumbersome)
  - Indirect way to detect EPI, 99% negative predictive value with cut off >100 mcg/g of stool
    - Note: loose stool/diarrhea can cause FE-1 to be falsely low. FE-1 is not impacted by PERT
- **Imaging:** MRCP with secretin (to look for any structural pancreatic changes and pancreatic function)

Management Considerations:

- Monitor growth and symptoms/signs of malabsorption
- Screen for EPI at time of CF diagnosis regardless of age
  - Infants with normal FE-1: retest at age 1 and annually or if develop EPI symptoms
  - May test more often if severe genotype
- If clinical signs of EPI or 2 severe CFTR mutations, then start PERT while awaiting results
- Test for fat soluble vitamin deficiencies at EPI diagnosis and at least annually
- **PERT dosing:**
  - Porcine-derived pancrelipase containing lipase, protease, and amylase
  - Dosing for Infants:

Primary Author(s): Christina Chadwick, MD
NASPGHAN Pancreas Committee
November 2024

        - 450-900 lipase units/g of fat or 2,000-4,000 lipase units per 120 ml of formula or when breastfeeding
    - Older children and adults:
        - 500-4,000 lipase units/g of fat (mean, 1,800 lipase units/g) or 500-2,500 lipase units/kg/meal (250-1,250 lipase units/kg/snack)
        - Do not exceed 10,000 units/kg per day if possible

Additional Notes/References:

doi.org/10.1067/mpd.2002.124829
doi.org/10.1016/j.jcf.2017.06.011
CFF.org