Pediatric GI problems in Primary care

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Celiac disease

Screen children with increased risk:

- first degree relatives with celiac
- T21
- Turner syndrome
- William syndrome
- IgA deficiency
- Autoimmune diseases (diabetes, thyroid disease, Addison's)

Gastrointestinal	Chronic or intermittent diarrhea*
	Chronic constipation not responding to usual treatment
	Chronic abdominal pain
	Distended abdomen*
	Recurrent nausea, recurrent vomiting
Extraintestinal symptoms	Weight loss, failure-to-thrive*, stunted growth/ short stature*
	Delayed puberty, amenorrhea
	Irritability, chronic fatigue
	Neuropathy
	Arthritis/arthralgia
	Chronic iron-deficiency anaemia
	Decreased bone mineralization (osteopenia/osteoporosis), repetitive fractures
	Recurrent aphthous stomatitis,
	Dermatitis herpetiformis–type rash
	Dental enamel defects
	Abnormal liver biochemistry
Specific conditions	First-degree relatives with CD
	Autoimmune conditions: T1DM, thyroid disease, liver disease
	Down syndrome, Turner syndrome
	Williams-Beuren syndrome
	IgA deficiency

Celiac disease

- Screening labs: Total IgA and tissue transglutaminase IgA (TTG IgA)
  - Need to make sure there is no IgA deficiency that would lead a false negative TTG IgA
  - No need for celiac panel
  - If IgA deficiency (level <7), then screen with TTG IgG or deamidated gliadin IgG
  - Pls don't refer to GI for isolated IgA deficiency

Celiac disease

- Elevated TTG IgA --> refer to ped GI and advise to continue gluten in diet (equivalent to 1 slice of bread/day)
  - potential false negative or unclear diagnosis on endoscopy if patient goes on GFD

- N. American guidelines differ from European guidelines but both agree that if TTG is < 10 x ULN, endoscopy is needed
  - TTG >10 x ULN --> could make a non-biopsy diagnosis if +endomysial antibody (Europe)
  - TTG >10 xULN --> scope to confirm (North America)

- Lactose intolerance common (lactase located at tip of villi)

HLA testing

- Positive celiac risk alleles HLA DQ2 or HLADQ8
  - Negative HLA DQ2 and DQ8 --> risk of celiac is very low (essentially rules out)
  - Positive HLA DQ2 and DQ8 --> does not confirm the diagnosis
- For some at-risk groups eg Type 1 diabetes, HLA testing may not be cost-effective due to high % of HLA positives
- May be more beneficial in other groups eg 1st degree relatives or in Down syndrome

Siblings

- Screen in genetically at-risk children every 2-3 years beginning at age 3 (if they have a diagnosed sibling)
- Consider doing HLA testing if available

CMA, CMPA, MPA, CMPI, FPIAP

- Cow's milk allergy
  - Hypersensitivity reaction to cow’s milk
  - 3 categories: IgE-mediated, non-IgE-mediated and mixed
- Diagnosis challenging d/t non-specific symptoms also common in healthy infants
  - May be overdiagnosed
  - Risks of misdiagnosis: allergic/nutritional risk, diminished quality of life for infant/caregiver, financial burden

Symptoms

- Non-IgE mediated allergy: delayed symptom onset 6-72h

TABLE 1. Signs and symptoms associated with cow's milk allergy*

	IgE†	Non-IgE†
General	Anaphylaxis	Colic, irritability Failure to thrive Iron deficiency anaemia
Gastro-intestinal‡	Regurgitation, vomiting Diarrhoea	Food refusal Dysphagia Regurgitation, vomiting‡ Diarrhoea‡ Constipation Anal fissures Perianal rash Blood loss
Respiratory‡	Rhinitis and/or conjunctivitis Asthma Mild dysphonia	Rhinitis Wheezing Chronic cough
Skin	Eczema (atopic dermatitis) Acute urticaria‡ Angio-oedema Oral allergy syndrome	Eczema (atopic dermatitis)

Food protein induced allergic proctocolitis

- Manifestation of CMA
- Hematochezia and persistent mucous diarrhea in otherwise healthy young infant
  - Inflammation of the distal colon in response to 1 or more food proteins through non-IgE mechanism
- Generally benign and self limited
- Debatable whether this needs to be treated
  - OK to monitor for a month without dietary changes

An ESPGHAN Position Paper on the Diagnosis, Management, and Prevention of Cow's Milk Allergy

Cow's milk allergy (CMA) is frequently misdiagnosed (especially overdiagnosed) and inadequately treated in infants and young children

This study provides updates and recommendations based on the European Society of Paediatric Gastroenteology, Hepatology, and Nutrition (ESPGHAN) guidelines for CMA

Best practice for confirming CMA diagnosis upon suspicion

Breastfed baby

Continue breastfeeding; mother should be on a CM-free diet and calcium for 2–4 weeks

Symptoms improve or disappear

- **No** → **Good compliance** — Not CMA
- **No** → **Doubtful compliance** — Refer patient to dietitian or nutritionist for reevaluation
- **Yes** → Reintroduction/challenge CM
  - No symptoms → Not CMA
  - Symptoms → CMA

Formula-fed baby — Mild to moderate symptoms

May require extensively hydrolysed formula (eHF) or hydrolysed rice formula (HRF) for 2–4 weeks

Symptoms improve or disappear

- **eHF/HRF: Yes** → Reintroduction/challenge CM
  - No symptoms → Not CMA
  - Symptoms → CMA
- **eHF: No** → May not be CMA → Consider switching to other regimens to confirm
- **HRF: No** → Not CMA

Formula-fed baby — Severe symptoms/anaphylaxis

Amino acid (based) formula (AAF) for 2–4 weeks

Symptoms improve or disappear

- **No** → Not CMA
- **Yes** → CMA

Long-term management

- Eliminate all CM sources (refer to dietitian/nutritionist)
- Consider breast milk or eHF/HRF/AAF (depending on tolerance) for 6 months or until 9 to 12 months of age
- Monitor tolerance development

To confirm the diagnosis of CMA and avoid overdiagnosis, an oral food challenge is recommended after a short diagnostic elimination diet

Description unavailable

An ESPGHAN Position Paper on the Diagnosis, Management, and Prevention of Cow's Milk Allergy

Vandenplas et al. (2023)

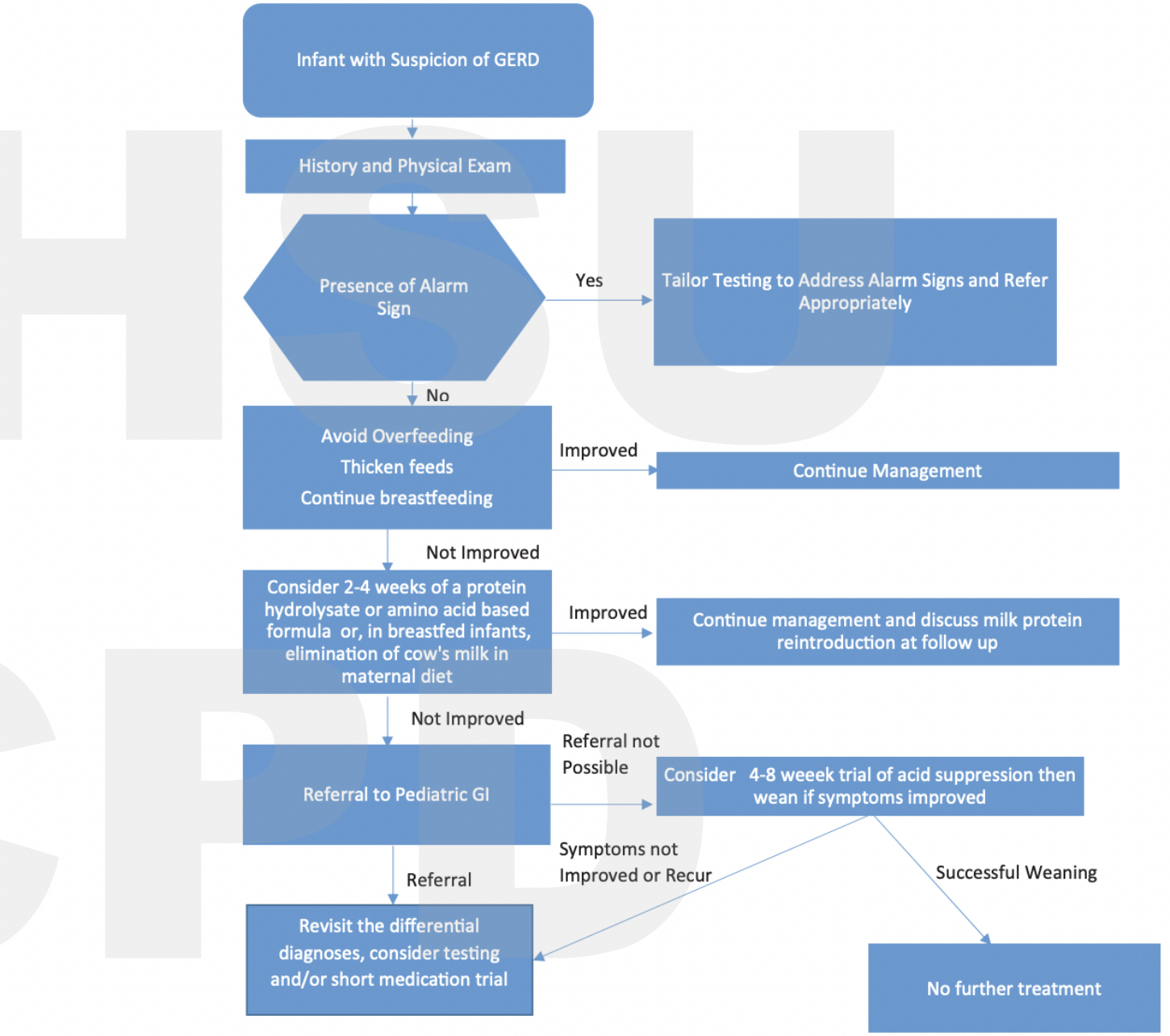
JPGN Journal of Pediatric Gastroenterology and Nutrition

Reflux

- GER- Passage of gastric contents into the esophagus with or without regurgitation and/or vomiting

- GERD - when the reflux leads to troublesome symptoms and/or complications, such as esophagitis or stricturing
  - Symptoms non specific and vary widely by age
  - proving that reflux events cause one or multiple symptoms is often difficult
  - Infant GERD may include excessive crying, back arching, regurgitation and irritability (also occurs in babies without GERD!)
  - Older children >8yo and teens - more typical symptoms eg heartburn and regurgitation similar to adults
  - More common in children with underlying medical conditions eg prematurity, neurologic impairment, pulmonary problems eg CF
- Refractory GERD - not responding to optimal treatment after 8 weeks

Infant GERD



ALGORITHM 1. Management of the symptomatic infant.

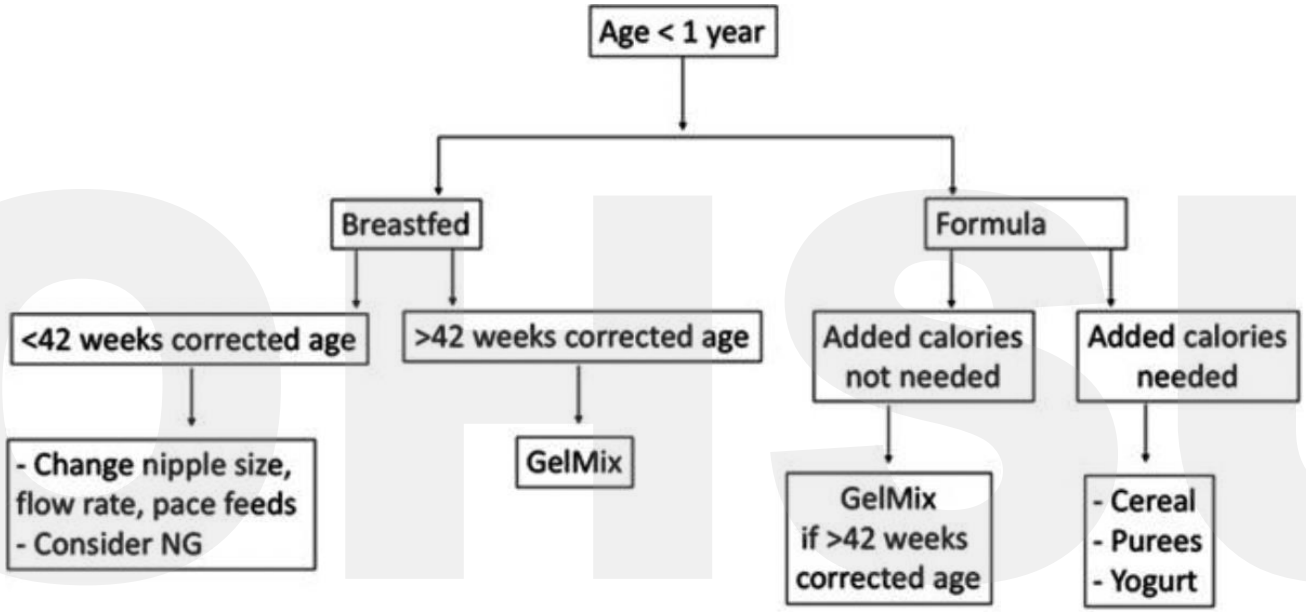
Management – non pharmacologic (minimum 2 week trial)

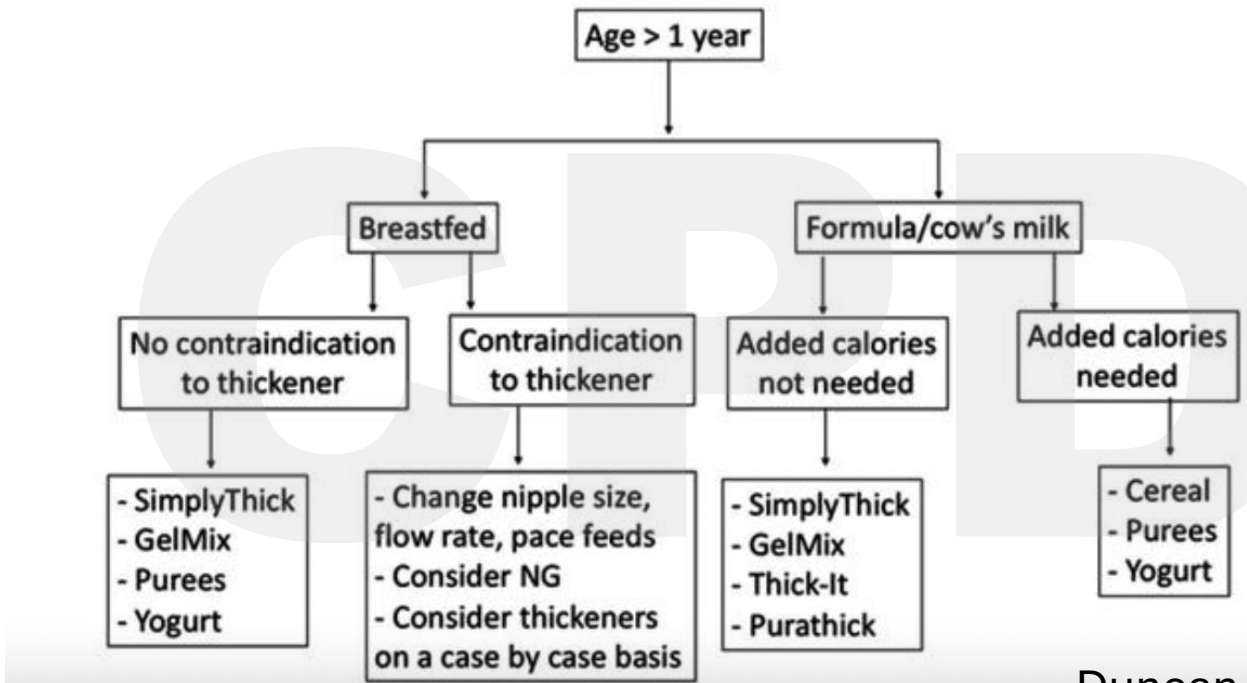
- **Smaller volumes, more frequent feeds**
- **Trial dairy free**
- **Despite potential benefit of sleeping on side or at an incline, sleep positions outside of supine are not recommended due to risk of SIDS**
- **Thickeners** (Horvath et al. 2008)
  - reduced vomiting and visible regurgitations per day
  - increased the number of days without regurgitation
  - reduced symptoms such as crying and irritability

Thickeners

- Cereal based
  - Concerns about arsenic level in rice cereals (can use oatmeal cereal instead)
  - Not effective to thicken breastmilk (digested by amylase in breastmilk)
  - Can cause constipation or excessive weight gain
  - May clog nipple

- Commercial thickeners
  - Gelmix (Carob bean)- use for breastmilk, approved for infants >42 weeks corrected age and >6lbs (NEC risk)
  - Thick-it (corn starch) – use for formula (12mo corrected age)
  - Simply thick (Xanthan gum) – approved for infants >12 months (NEC risk)





Duncan et al. Curr Gastroenterol Rep 2019

Thickener recipes

- GelMix works with breastmilk or formula
- Thick it will NOT work with breastmilk

- **GelMix:**
  - Slightly thick: 2 scoops per 4-6 oz
  - Mildly thick: 2 scoops per 3-4 oz
- **Thick-It**
  - Slightly thick: 4 tsp (or 1 TBSP 1 TSP) per 4 oz
  - Mildly thick: 4 tsp (or 1 TBSP 1 TSP) per 4 oz
- **Oatmeal cereal**
  - 1 tsp to 1oz of formula

Management – pharmacologic

TABLE 4. Dosages of most frequently used drugs for the treatment of gastroesophageal reflux disease

Drugs	Recommended pediatric dosages	Maximum dosages (based upon adult dosage)
Histamine-2 Receptor Antagonists (H2RAs)		
~~Ranitidine~~	5–10 mg/kg/day	300 mg
~~Cimetidine~~	30–40 mg/kg/day	800 mg
~~Nizatidine~~	10–20 mg/kg/day	300 mg
Famotidine	1 mg/kg/day	40 mg
Proton Pump Inhibitors (PPIs)		
Omeprazole	1–4 mg/kg/day	40 mg
Lansoprazole	2 mg/kg/day for infants	30 mg
Esomeprazole	10 mg/day (weight <20kg) or 20 mg/day (weight >20kg)	40 mg
Pantoprazole	1–2 mg/kg/day	40 mg
Prokinetics		
Metoclopramide	0.4-0.9 mg/kg/day	60 mg
Domperidone	0.8–0.9 mg/kg/day	30 mg
Baclofen	0.5 mg/kg/day	80 mg
Antacids		
Mg alginate plus simethicone	2.5 ml 3×/day (weight < 5kg) or 5 ml 3×/day (weight >5 kg)	NA
Sodium alginate	225 mg sodium alginate and magnesium alginate 87.5 mg) in a total 0.65 g One sachet/day (weight <4.54 kg) or Two sachet/day (weight >4.54 kg)	NA

No effect of PPIs on crying and irritability

- Gieruszczak-Bialek et al. Journal of Pediatr 2015
  - Systematic review (5 RCTs)
  - Found that PPIs not effective for crying/irritability in infants

- Davidson et al 2013
  - 52 infants aged <1 y with GERD randomly assigned to receive esomeprazole 0.5 mg/kg or placebo once daily for up to 14 d
  - Timing / duration of irritability/crying/fussing assessed using 8-h video monitoring session
  - No significant difference at the end of treatment

- Orenstein et al 2009
  - 162 infants <12 mo of age with symptomatic GERD remained symptomatic with crying, fussing, or irritability during or within 1 h after feeding despite at least 1 wk of nonpharmacologic management
  - Subjects randomized to receive lansoprazole or identically appearing placebo for 4 wk
  - No differences found

PPI and infections

- French study Lasalle et al. 2023
  - Cohort study of >1 million children (unexposed, <6mo, 7-12mo, >12mo)
  - Increased risks of serious infections (requiring hospitalization) overall regardless of duration of PPI exposure
    - digestive tract, ENT, lower respiratory tract, kidneys or urinary tract, and nervous system infections and both bacterial and viral infections
  - Median time interval between PPI withdrawal and first occurrence of serious infection was 9.7months
  - Risk gradually decreased with increasing time elapsed since PPI withdrawal
  - Possible mechanism of action
    - Alterations in microbiota
    - Direct action on immune system (Fisher et al Clin Drug Investig 2017)

PPI and atopic conditions

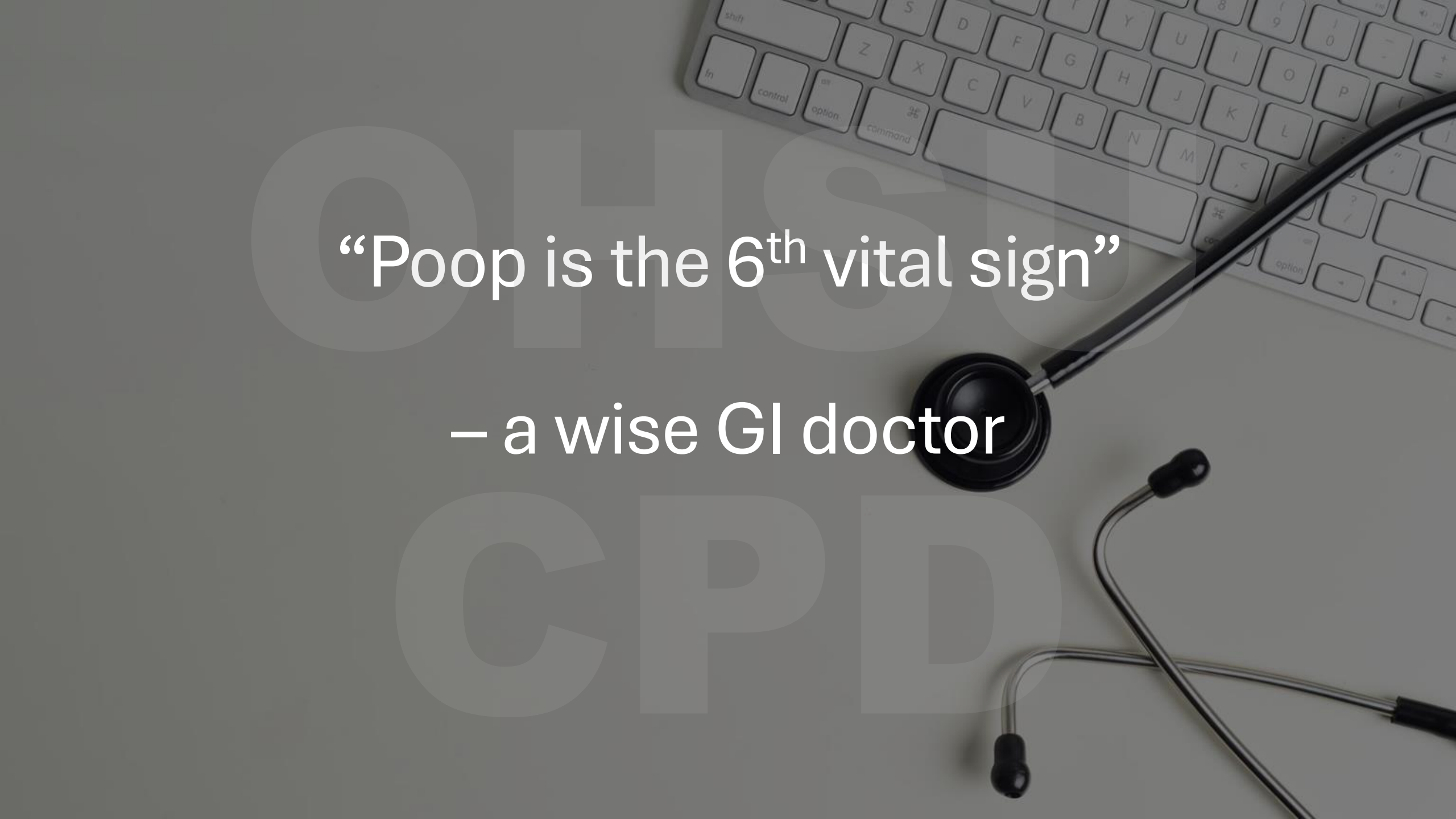
- 2009 - first association was described between prenatal exposure to PPIs and H2 blockers and increased risk for asthma in childhood
  - Confirmed with 2 meta-analyses for PPIs
- Large cohort study Mitre et al 2018, found that children prescribed PPIs during first 6 months of life had increased risk of multiple atopic conditions incl asthma
  - Similar findings in Sweden Wang et al 2021

- Less known about association between PPI and IgE mediated food allergy but there are some studies to support
  - Small cross-sectional study 2013 DeMuth et al
    - increased risk for food allergy after childhood exposure to PPI and all other acid suppressants
  - Small case control study 2018 Jensen et al
    - Increased risk of EoE development in pts exposed to acid suppressant in infancy

EoE

- Chronic inflammatory disease of esophagus characterized by esophageal dysfunction and eosinophils infiltration in esophageal epithelium
- When to suspect?
  - Solid food dysphagia – meat, bread, needing lots of water to gets food down, eating very slowly
  - Food impaction
  - History of atopy – asthma, eczema, food allergies
  - Poor weight gain
  - Male
  - Relative with EoE
  - Younger children – more non specific symptoms eg vomiting, food refusal

- Treatment: 6 food elimination diet (difficult to adhere), step-up (eg start with 1 or 2 food elimination), amino acid formula, swallowed viscous budesonide or swallowed flovent, PPI, dupixent


“Poop is the 6th vital sign”
– a wise GI doctor

Constipation: Differential diagnoses

- **<u>Non-organic</u>**
- Functional Constipation
  - **responsible for >95% of cases in healthy children**
- Situational
  - Toilet training
  - Toilet phobia
  - School bathroom avoidance
  - Sexual abuse
- Constitutional
  - Colonic inertia
- Reduced stool volume and dryness
  - Low fiber in diet
  - Dehydration
  - Underfeeding or malnutrition

<u>Organic</u> (responsible for <5% in children w/constipation)

- Abnormalities of the colon & rectum
- Spinal cord lesions
- Neuropathic lesions
- Metabolic conditions
- Systemic disorders

Naspghan guideline

Rome IV Criteria for the Diagnosis of Functional Constipation in Children

Infants and toddlers <4 yrs old

At least 2 of the following present for at least 1 month:

- ≤ 2 BMs per week
- Hx of excessive stool retention
- Hx of painful or hard BMs
- Hx of large-diameter stools

In toilet-trained children, the following additional criteria may be used:

- ≥ 1 episode/wk of incontinence
- Hx of large-diameter stools that may obstruct the toilet

Children and adolescents ≥ 4 yrs old

At least 2 of the following present at least once per week for at least 1 month:

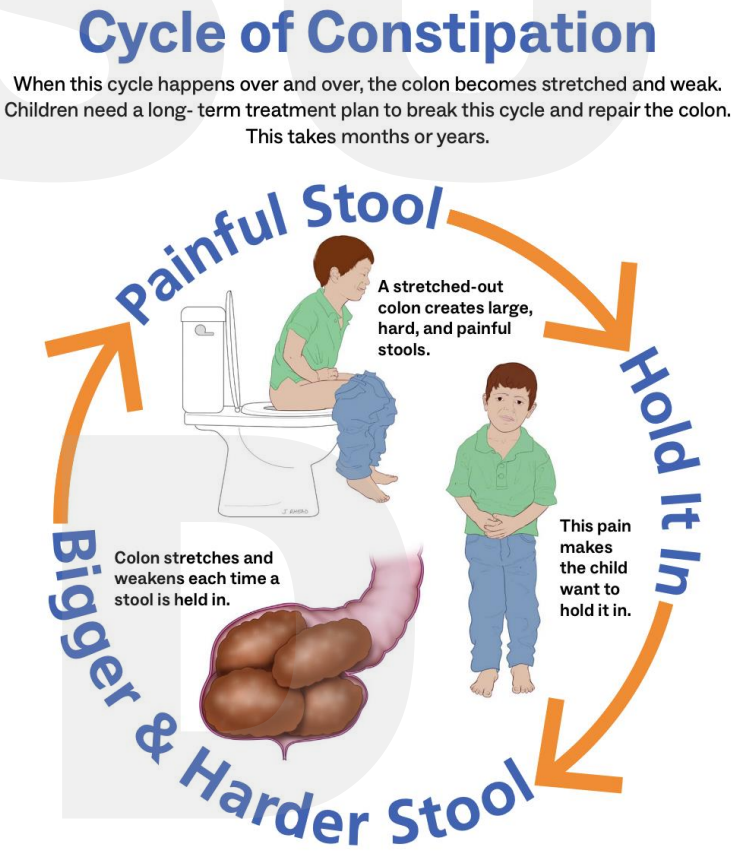
- ≤ 2 BM in toilet per wk
- ≥ 1 fecal incontinence per wk
- Hx of retentive posturing or volitional stool retention
- Hx of painful or hard BMs
- Presence of a large fecal mass in the rectum
- Hx of large-diameter stools that may obstruct the toilet

The symptoms cannot be fully explained by another condition

Chronic constipation management

- Parental Education
  - The poo in you (Youtube)
  - Treatment can take a long time!

https://www.youtube.com/watch?v=SgBj7Mc_4sc



https://intermountainhealthcare.org/ckr-ext/Dcmnt?ncid=520408179

Chronic constipation management

- Disimpaction/Clean out (per oral or rectum)
- Maintenance
  - stool softener and/or stimulant
  - Stimulant if stools are infrequent
- Lifestyle modifications: Hydration, dietary fiber, exercise, toilet hygiene (toilet sits after meal, squatty potty, blow pinwheel, reward system)
- Psychology support: encopresis, withholding, med adherence
- Follow up frequently (at least every 6 weeks at the beginning)

Disimpaction

- Impaction: hard mass in lower abdomen palpable during PE, dilated rectum filled with large amount of hard stool on rectal exam, excessive stool in colon/rectum on KUB
- Disimpaction (oral, rectal, combo, manual)
- Recommended if the child has:
  - Fecal soiling/encopresis
  - Rectal bleeding/fissure
  - Large stool burden palpated on exam
- Use lots of Miralax!
  - UpToDate will tell you 1-1.5g/kg/d for up to 6 days
  - What we really do – way more! (see next slide)
  - Stimulant – senna/bisacodyl
- May need to use enemas to get things going from below
  - Mineral oil, Sodium phosphate, saline enemas

Bowel Cleanout

Check dosing with your child's healthcare provider

Time of day	Age 2 to 4 years (22 to 44 pounds)	Age 5 to 10 years (45 to 88 pounds)	Older than 10 years (more than 88 pounds)
Morning	Take 1 chocolate laxative square	Take 1 + ½ chocolate laxative squares	Take 2 chocolate laxative squares
During the day	Mix 4 capfuls of PEG 3350 powder in 20 ounces of fluid. Drink it over 8 hours.	Mix 7 capfuls of PEG 3350 powder in 32 ounces of fluid. Drink it over 8 hours.	Mix 14 capfuls of PEG 3350 powder in 64 ounces of fluid. Drink it over 8 hours.
Evening	Take 1 more chocolate laxative square	Take 1 + ½ more chocolate laxative squares	Take 2 more chocolate laxative squares

https://intermountainhealthcare.org/ckr-ext/Dcmnt?ncid=520408179

Maintenance Therapy

Evaluation and Treatment of Constipation in Infants and Children: Recommendations of NASPGHAN. JPGN. 2006.

Osmotic	Dose
Lactulose (70% solution)	1-3 ml/kg/day
Sorbitol (70% solution)	1-3 ml/kg/day
Magnesium hydroxide	0.5-3 ml/kg/day
Magnesium citrate.	1-3 ml/kg/d (>6yo: 150ml/d)
Polyethylene glycol	1-1.5 g/kg/day

Lubricant

Mineral oil	1-3 ml/kg/day

Stimulant

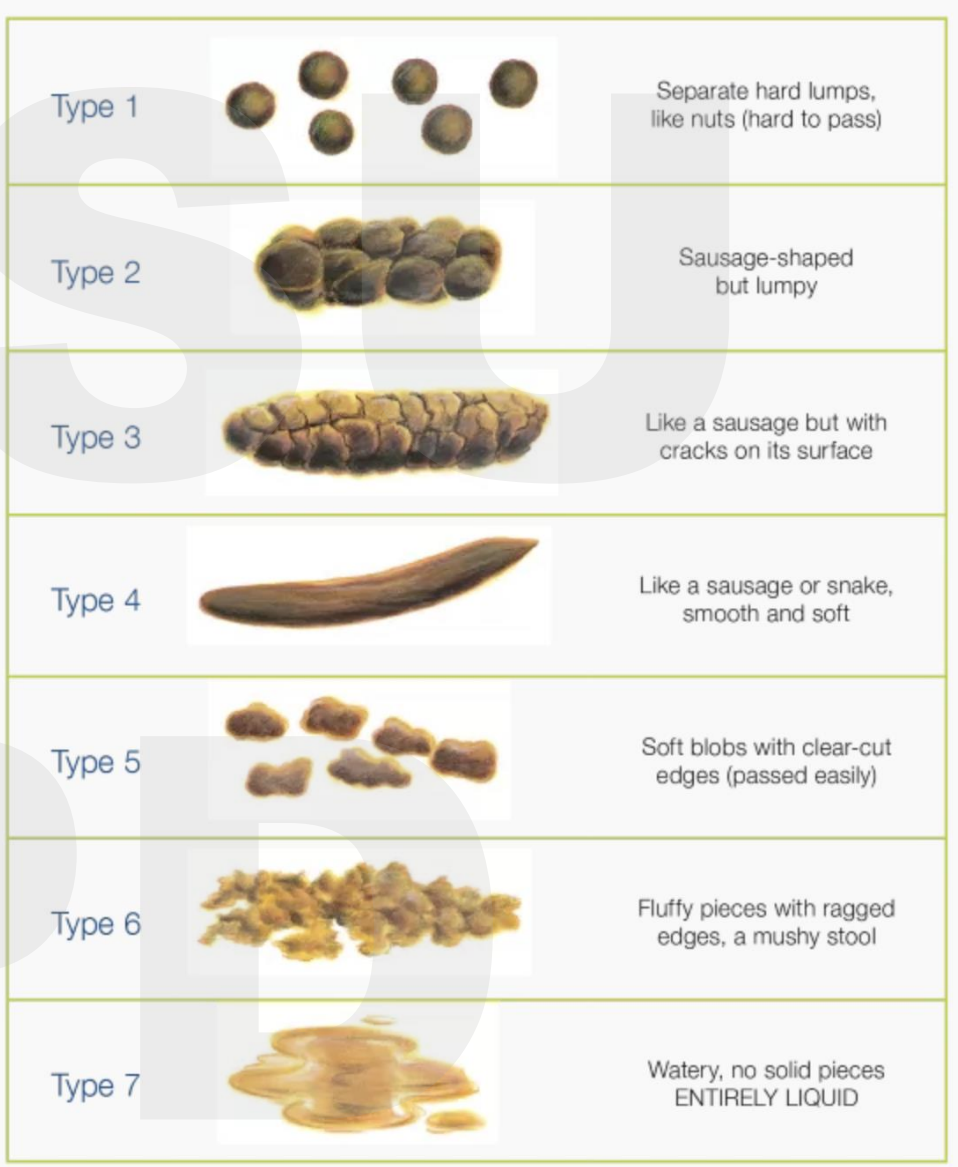
Senna	2.5-7.5 ml/d (2-6 yo)
Bisacodyl	5-10 mg/d
Glycerin suppository	---

Don't worry about staying in this dosing range!

- Start at 1 cap in 8oz clear liquid daily
  - Not milk or carbonated beverages
- Then titrate up or down to achieve daily, soft, frozen yogurt/peanut butter consistency stool.
  - Can titrate by quarter caps
  - Can divide doses 2-3 times/d
  - **~4 teaspoons in 1 capful**
- You can't overdose! You will just cause diarrhea…which is ok!
- No, it doesn't cause autism!

Goals of treatment

- 1-2 soft (Bristol 3-5) stools per day or every other day
- Resolution of soiling/accidents
- Return of rectal sensation
- Empowerment of child and parent
- Positive experience



Practical Guidelines

- Stool hard put passes daily or every other day?
  - Start Miralax
- Stools soft but stooling once a week?
  - Start senna (5mL = 8.8mg) = ~1 tablet
- Stools hard and infrequent?
  - Combo miralax + senna
- Do not start or change during toilet training

- **Follow up frequently!**
- **Refer for refractory constipation or persistent encopresis**

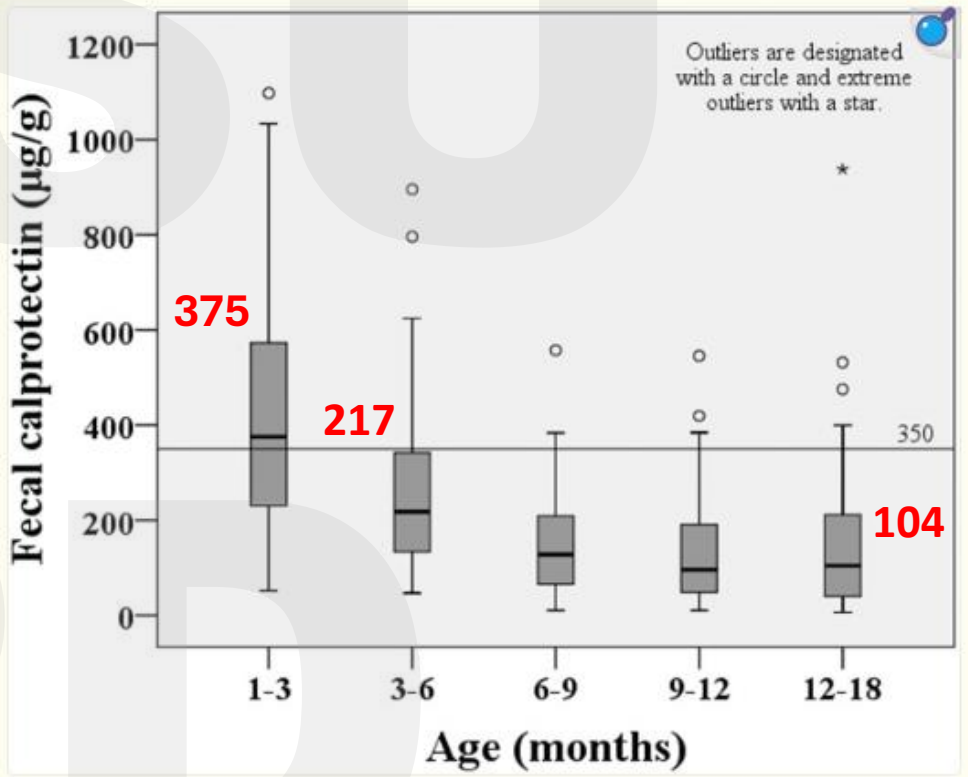
IBD

- When to suspect? Chronic abdominal pain, chronic diarrhea, bloody stools, **nocturnal stools,** high frequency of stools, weight loss
- **Height plateau or poor growth velocity** (crossing percentiles)
- Labs: CBC, CMP, CRP, ESR
  - Microcytic anemia (blood/iron loss)
  - hypoalbuminemia (GI protein loss)
  - Elevated inflammatory markers (CRP, ESR, platelets)
- Stool studies: **fecal calprotectin**, GI bacterial and viral PCR (or stool culture), C diff

Fecal calprotectin

- Biomarker of gut inflammation (neutrophil migration marker)
- Levels are high in healthy infants, IBD, infection, polyps
- Not recommended to obtain in infants
- Conflicting data regarding calprotectin in FPIAP (just don't order it)

Fig 1. Fecal calprotectin concentrations in six age groups of healthy children.



Li et al. PlosOne 2015

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