Chronic Diarrhea

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Resident Education Series

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Case

- A 15 year old boy with PMH of obesity, anxiety disorder & ADHD presents with **3 months of non-bloody loose stool 5-15 times/day** and diffuse **abdominal pain** that is episodically severe

Case - History

- Wellbutrin was stopped prior to the onset of her symptoms and her Psychiatrist was weaning Cymbalta
- After stopping Cymbalta, she went to Costa Rica for a month long medical mission trip
- Started having symptoms of **abdominal pain and diarrhea** upon return from her trip.
- Ingestion of local Georgia creek water, but after her symptoms had started
- Subjective fever x 4 days

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Case - Lab work by PCP

- At onset of illness:
  - **+ occult blood in stool**
  - **+ stool calprotectin** (a measure of inflammation in the colon)
  - Negative stool WBC
  - Negative stool culture
  - Negative *C. difficile*
  - Negative ova & parasite study
  - Negative giardia antigen
  - Normal CBC with diff, Complete metabolic panel, CRP, ESR

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Case - History

- Non-bloody diarrhea and abdominal pain continues
- No relation to food
- No fevers
- No weight loss
- Normal appetite
- No night time occurrences
- No other findings on ROS
- No sick contacts

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Case – Work-up prior to visit

Labs

- Fecal occult blood, stool calprotectin, stool WBC, stool culture, stool O&P, stool giardia all **negative**
- Repeat CBC, CMP, CRP, ESR **negative**
- Skin testing for food allergies - **negative**

Imaging and Procedures

- MRI enterography (MRI of the abdomen/pelvis with special cuts to evaluate the small bowel) **normal**
- Upper GI with small bowel follow through **normal**
- Esophagogastroduodenoscopy and colonoscopy **normal**
- Video capsule endoscopy **normal**

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Case - Therapies Without Benefit

Diet modifications

- 2 week lactose free diet
- “Specific Carbohydrate Diet” with poor compliance

Medications

- Metronidazole trial for several courses
- Nitazoxanide trial (anti-protozoal)
- Loperamide trial
- Probiotics

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How to approach this case?

Definition of Chronic Diarrhea

- > 2 weeks
- Stool output > 10cc/kg/day (or >200mL/day for adults)
- **Practical definition:** increase in frequency, increased water content compared to previous pattern for individual
- Occurs in about 1 case per 5 person-years in infants and young children in US[1]

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Pathophysiology: Osmotic Diarrhea

Defect	1. Maldigestion 2. Transport defects 3. Ingestion of unabsorbable solute
Stool Exam	1. watery 2. pH < 5.5 3. + reducing substances 4. increased osmolality 5. elevated osmotic gap > 100 [stool osmolar gap: 290 – 2 x (stool Na + stool K)]
Examples	1. Lactase deficiency 2. Glucose-galactose malabsorption 3. Lactulose use 4. Laxative abuse 5. Polyethylene glycol (Miralax) use
Comments	**Stops with fasting;** increased breath hydrogen with carbohydrate malabsorption; no stool leukocytes

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Pathophysiology: Secretory Diarrhea

Defect	1. Decreased absorption 2. Increased secretion 3. Electrolyte transport
Stool Exam	1. Watery 2. normal stool osmolality 3. Stool osmotic gap < 100 [stool osmolar gap: 290 – 2 x (stool Na + stool K)]
Examples	1. Carcinoid 2. VIP 3. Neuroblastoma 4. Congenital chloride diarrhea
Comment	**Persists during fasting;** bile salt malabsorption also may increase intestinal water secretion

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Pathophysiology: Increased motility

Defect	1. Decreased transit time
Stool Exam	1. loose to normal-appearing stool 2. normal pH and osmolality 3. stimulated by gastrocolic reflex
Examples	1. Irritable bowel syndrome 2. Thyrotoxicosis
Comments	Infection also may contribute to increased motility

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Pathophysiology: Decreased motility

Defect	1. Defect in neuromuscular units 2. Stasis (bacterial overgrowth)
Stool Exam	1. Loose to normal appearing stool 2. Normal or abnormal pH and osmolality
Examples	1. Blind loop syndrome
Comment	Possible bacterial overgrowth

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Pathophysiology: Decreased surface area
(osmotic and motility)

Defect	1. Decreased functional capacity
Stool Exam	1. Watery
Examples	1. Short bowel syndrome 2. Celiac disease 3. Rotavirus enteritis
Comments	May require elemental diet plus parenteral alimentation

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Pathophysiology: Mucosal irritation

Defect	1. Inflammation 2. Decreased colonic reabsorption 3. Increased motility
Stool Exam	1. Blood and increased WBCs in stool
Examples	1. Acute bacterial enteritis 2. Inflammatory bowel disease
Comments	Mucosal *invasion??*

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Differential Diagnosis in Infants:
Milk and Soy Protein Intolerance-
not an IgE mediated illness

TWO syndromes:

- Enterocolitis - bloody diarrhea in first 3 months of life
- Protein-losing enteropathy - occult blood loss and hypoproteinemia most often seen in infants > 6 months old

Treatment:

- Protein-hydrolysate formula required (due to 20-40% cross reactivity of soy protein)

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Differential Diagnosis in Infants:
Post Infectious Enteropathy

Clinical Presentation & Evaluation

- Prolonged diarrhea after an acute illness
- More common in infants <6 months old
- Damage to small intestinal villi leads to a loss of disaccharidase activity and reduced mucosal surface
- Can document mucosal damage with endoscopy

Treatment

- First, treat with lactose free formula
- If severe, try protein hydrolysate formula
- Very compromised patients may require TPN and/or elemental formula (broken down to amino acids)
- Recovery takes at least 4 weeks, with no long term problems expected

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Differential Diagnosis in Toddlers/Children:
Chronic Nonspecific Diarrhea aka "Toddler's Diarrhea"

Clinical Presentation & Evaluation

- Mostly in 1-3 years olds
- Non-bloody stools get looser as day progresses
- Undigested vegetable matter usually seen
- Normal weight gain and diet
- Thought to be "IBS" of this age group

Treatment

- Reassurance
- Eliminate juice or other highly osmolar food from diet (fruit, popsicles, candy, etc.)
- Usually resolves by 3-4 years old

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Differential Diagnosis in Toddlers/Children: Fat Malabsorption caused by Pancreatic Insufficiency

Clinical Presentation & Evaluation

- Greasy, foul smelling stool
- Most common is Cystic Fibrosis
  - Picked up on newborn screen usually
  - sweat test is screening test for CF
- Evaluation
  - Fecal fat (72 hour fecal fat is not practical but better test)
  - Stool elastase (surrogate marker for pancreatic insufficiency)

Treatment

- Pancreatic enzyme supplementation

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Differential Diagnosis in Toddlers/Children:
Celiac Disease

Clinical Presentation & Evaluation

- Variable presentation
- Evaluation
  - Screen with Celiac serologies
    - Tissue transglutaminase
  - Confirm with upper endoscopy biopsies

Treatment

- Gluten-free diet for life
  - Adherence is a major issue
- Concerns of nutritional deficiencies, growth and pubertal delay, bone health

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Differential Diagnosis in Adolescents: Irritable Bowel Syndrome

Clinical Presentation & Evaluation

- Constellation of symptoms including abdominal pain and changes in bowel habits
- Diagnosis of exclusion although do not need to perform every test to diagnose IBS
- A positive family history is frequently seen
- Explore inciting psychological factors/stressors

Treatment

- cognitive behavioral therapy
- anti-spasmodics
- antidepressants, especially amitriptyline
- avoid “trigger” foods which can be different between patients

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Differential Diagnosis in Adolescents: Inflammatory Bowel Disease

- General Clinical Characteristics
  - Weight loss, abdominal pain, diarrhea
  - Peri-anal involvement - anal tags/fistula (Crohn's)
  - Positive Family history
- Laboratory findings
  - Anemia, Hypoalbuminemiaa, elevated CRP and ESR
- Evaluation
  - Upper endoscopy and colonoscopy for diagnosis
  - Small bowel imaging with MRI or small bowel follow through
- Treatment
  - Anti-inflammatory medication
  - Immunosuppressants
  - Biologics
  - Surgery

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Additional Differential Diagnosis in all Pediatric patients

- Giardia
- Cryptosporidiosis
- *C. difficile* colitis
- Food allergy
- Bacterial overgrowth
- Disaccharidase deficiency
- Overflow encopresis secondary to severe constipation
- Iatrogenic
- Factitious

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Differential Diagnosis - Rare

- **Congenital secretory etiologies** - clue will be profuse diarrhea with electrolyte derangements shortly after birth
  1. Congenital chloride diarrhea- due to mutations in a mucosal exchanger protein, excessive fecal secretion of chloride
  2. Congenital sodium diarrhea
  3. Microvillus inclusion disease- villi are formed incorrectly
  4. Tufting enteropathy- villous atrophy

- **Congenital osmotic etiologies** - clue will be severe life-threatening diarrhea when ingesting specific certain dietary components. Stops when fasting.
  1. Glucose-galactose malabsorption - cannot absorb lactose nor hydrolyzed product: glucose and galactose
  2. Sucrase-isomaltase deficiency - develop diarrhea after sucrose formulas or food introduced.

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General Treatment

- Treat the underlying cause
- Eliminate juices (sorbitol) and high fructose corn syrup
- Push hydration
- Anti-diarrheal
  - Can try loperamide (immodium) except in cases of infection

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Summary

- Practical definition: ↑ looseness & ↑ frequency of stool above "normal" for patient for > 2 weeks
- Causes in children include:
  - Functional
  - Infectious
  - inherited disorders of immune regulation, macronutrient digestion, mucosal barrier function, and transport
- High proportion are **functional** in all age groups
- Celiac disease is relatively common, especially in Caucasians, and should be considered since it can present with minimal symptoms

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Case patient

Diagnosed with Functional Abdominal Pain &
Post-infectious IBS-Diarrhea type

- Treated with levsin (anti-spasmodic)
- Metronidazole, Nitazoxanide and loperamide discontinued
- With psychiatrist's guidance, she optimized her anti-depressants and started working on biofeedback/pain coping in therapy
- No diet limitations (except healthy eating)
- Discontinue pain/diarrhea diaries
- Focus on school attendance

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References

1. Vernacchio L, Vezina RM, Mitchell AA, et al. Characteristics of persistent diarrhea in a community-based cohort of young US children. JPGN 2006; 43:52.
2. Kliegman, Robert; Greenbaum, Larry; Lye, Patricia. Practical Strategies in Pediatric Diagnosis and Therapy. Second Edition. 2004. Chapter 15. “Diarrhea” by Subra Kugathasan.
3. UpToDate. Overview of causes of chronic diarrhea in children. Last updated Oct 18, 2011.

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