Gastrointestinal Disorders (2)

Jillian Sullivan, MD MSCS
Associate Professor of Pediatrics
Larner College of Medicine at the University of Vermont

PREP The Course: St. Petersburg, FL
March 2017
• I have no relevant financial relationships with the manufacturer(s) of any commercial product(s) and/or provider of commercial services discussed in this CME activity.

• I will be discussing an unapproved/investigative use of a commercial product/device in my presentation.
  – Antibiotic use in C. difficile infections (aside from metronidazole and vancomycin)
  – Fecal microbial transplantation (FMT) in ulcerative colitis
• GI Disorders 1 and 2 cover most of the intestinal and nutritional objectives for PREP The Course
• Hepatic diseases are discussed in the concurrent GI case discussion
Objectives

• Understand differences between Ulcerative Colitis and Crohn’s Disease
• Define appropriate testing for Clostridium difficile
• Understand various types of infant formula and indications for use
• Identify criteria for Functional Abdominal Pain of Childhood
Diseases of the Colon

- Inflammatory Bowel Disease
- \textit{Clostridium difficile} infection
- Polyposis Syndromes
- Hirschsprung’s Disease
- Eosinophilic (Allergic) Proctocolitis
Inflammatory Bowel Disease (IBD)

- Chronic inflammatory disease of the intestine
- 2 major subtypes**:
  - Crohn’s Disease: transmural, granulomatous inflammation, can affect the entire GI tract (from mouth to anus), may have patchy involvement, mucosal aphthous ulcers
  - Ulcerative Colitis: superficial inflammation, limited to the colon, contiguous involvement beginning in the rectum extending proximally
Inflammatory Bowel Disease (IBD)

• Clinical features**
  – **Intestinal signs/symptoms**: chronic diarrhea, hematochezia, vomiting, weight loss, perianal disease (Crohns), chronic abdominal pain, anorexia, bowel obstruction (Crohns)
  – **Extraintestinal signs/symptoms**: rash (erythema nodosum or pyoderma gangrenosum), arthritis, ankylosing spondylitis, uveitis, nephrolithiasis, short stature (Crohns)
Inflammatory Bowel Disease (IBD)

- **Initial evaluation**: 
  - Rule out infectious causes of diarrhea (particularly *c. difficile*)
  - Laboratory evaluation
    - CBC: evaluate for anemia, may see elevated WBC and/or platelets
    - Albumin (may be decreased)
    - Inflammatory markers (ESR and CRP)—may be increased
    - **Pearl**: normal labs do NOT exclude inflammatory bowel disease
    - Serologic markers may help to differentiate between Crohn’s and UC however are not indicated for initial diagnosis
  - Urgent pediatric GI referral and endoscopy with colonoscopy
Inflammatory Bowel Disease

Ulceration in Crohn’s Disease

Ulcerative Colitis
Inflammatory Bowel Disease

• Initial Management
  – Ulcerative Colitis:
    • Severe colitis**: bowel rest, IVF/TPN, antibiotics, steroids, ?pRBCs
      – Can also consider using biologic therapy, including infliximab (anti-TNF antibody)
      – Colectomy is indicated if colitis is refractory to above treatment
    • Mild-moderate: Steroids (for induction of remission), 5-ASA (i.e. mesalamine), immunomodulators including azathioprine or 6-MP
    • Probiotics may be useful and fecal microbial transplantation (FMT) is currently being studied
Inflammatory Bowel Disease

• Initial Management
  – Crohn’s Disease:
    • Severe: Bowel rest, IVF/TPN, antibiotics, steroids
      – Likely using infliximab or adalimumab, particularly if growth failure or complicated Crohn’s (i.e. perianal disease, intestinal fistula, abscess) is present
      – Can also consider enteral therapy (90-100% of calories from formula)
    • Mild/Moderate:
      – Steroids (for induction of remission), immunomodulators (azathioprine or 6-MP), 5-ASA (for disease limited to the colon)
**Clostridium difficile** Infection

- Spore-forming, gram positive anaerobic bacillus
- Clinical presentation can range from asymptomatic carriage to severe colitis**
- Should be suspected in cases of bloody diarrhea
  - Particularly if use of antibiotics occurred recently
- Diagnosis**: positive *C. difficile* toxin (from feces)
  - Can be present in infants <12 months WITHOUT colitis/symptoms (up to 70% of infants may be colonized)

Schutze GE et al 2013
Clostridium difficile Infection

- Should not test infants <12 mo unless there are unusual risk factors (test is likely to not reflect true disease)
  - Prolonged hospital stay, bloody diarrhea, etc.
- Initial infections are usually treated with metronidazole**
  - First recurrence: repeat course with metronidazole
  - Second recurrence/refractory infections can be treated with vancomycin (PO), rifaximin, or nitazoxanide
  - Probiotics (particularly Saccharomyces boulardii) may be helpful for prevention of recurrence
  - Fecal microbial transplantation can be used to treat refractory cases
Clostridium difficile Infection

• Infection Control **:
  – Rapidly identify and isolate patients with C. difficile (or suspected C. difficile infection)
  – Wear gloves and gowns when treating patients with C. difficile (or suspected C. difficile infection)
  – Wash hands with soap and water when treating patients with (suspected) C. difficile infection
• Spores are resistant to hand sanitizer
Intestinal Polyps

• Can present with rectal bleeding, abdominal pain, or intussusception
  – Can also be found incidentally

• Solitary juvenile polyp—most common**
  – Hamartomatous polyp
  – Should be removed, even if found incidentally
  – if <5 polyps found and no family history of polyp syndromes, no further evaluation is needed
Polyposis syndromes are rare but occur
- **Pearl**: use genetics/oncology consultation to help guide diagnosis and screening
  - GeneReviews.org
- **Juvenile Polyposis Syndrome** (1:100,000)
  - > 5 polyps present
  - Premalignant condition
    - Increased risk of colorectal cancer
      - Also stomach, pancreas, small intestine (risk = 9-50%)
  - Gene mutations associated with syndrome (SMAD4, BMPR1A)
  - Screening begins at age 12-15 if mutation is detected
    - Repeat colonoscopy (+/- EGD) yearly until no more polyps are detected, then every 3 years
Intestinal Polyps: Polyposis Syndromes

- **PTEN Hamartoma Syndrome**
  - Cowden Syndrome
    - Multiple hamartoma syndrome
    - Macrocephaly, papillomatous papules, mucocutaneous lesions, acral keratosis (hamartomas on skin usually seen by 20s)
    - Increased risk of breast cancer, endometrium, thyroid cancer
      - Usually in 30s-40s
    - Recommend routine screening beginning at age 35 (colonoscopy)

- Children: yearly thyroid u/s and skin check
- Adults: yearly thyroid u/s, derm eval; mammogram and vaginal u/s at age 30
- Earlier screening may be appropriate
Intestinal Polyps: Polyposis Syndromes

- **Peutz-Jeghers Syndrome** (1:50,000-1:200,000)
  - STK11/LKB1 mutation
  - Mucocutaneous pigmentation
    - Starts in infancy (around mouth, nostrils, buccal mucosa)
  - Small bowel polyps (+ stomach and colon)
    - Risk for intussusception
  - Risk of cancer in many organs: colon, pancreas, stomach, lung, testes, breast, uterus, ovary, cervix
    - 75% chance of developing cancer by age 70
    - Specific screening guidelines for each organ
Intestinal Polyps: Polyposis Syndromes**

- **FAP (Familial Adenomatous Polyposis)**
  - APC mutations = classic FAP
  - Begins with benign adenomatous polyps in colon (teens)
    - Polyps will become malignant over time
      - Average age of colorectal CA with classic disease (without colectomy): 39 years
      - Annual colonoscopy until colectomy
  - Extracolonic: gastric/duodenal polyps, desmoid tumors, other cancers
    - Gardner syndrome = colonic polyps (FAP) + osteomas and soft tissue tumors
    - Turcot syndrome = colonic polyps (FAP) + CNS tumors
Hirschsprung’s Disease

- Occurs in 1:5000 births
- Defined as the absence of ganglion cells in the intestine
  - May be limited to rectum or can extend proximally in the intestine
- Presentation
  - Neonate:
    - Abdominal distention, bilious emesis, large bowel obstruction OR
    - Otherwise healthy infant with delayed passage of meconium
  - Infant/older child: constipation
    - Particularly children requiring rectal stimulation repeatedly to pass stool
Hirschsprung’s Disease

• Diagnosis**: 
  – If clinically suspected, referral to pedi GI/pediatric surgery is warranted
  – Supported by exam (rectal examination may demonstrate increased tone; explosive bowel movement may result after exam)
    • **Pearl:** Normal examination does not rule out Hirschsprung’s
Hirschsprung’s Disease

- KUB may demonstrate LBO
- Contrast enema demonstrates narrow distal colon and transition zone with dilated large bowel
- **Gold standard:** rectal biopsy (histology demonstrates absence of ganglion cells)
Hirschsprung’s Disease

• Treatment
  – Surgical resection of aganglionic segment
    • Colostomy followed by endorectal pullthrough at a later date
  – Complications**
    • Hirschsprung’s associated enterocolitis
      – Abdominal distention, diarrhea, fever, vomiting
      – Patients can rapidly deteriorate
      – Can look just like viral gastroenteritis initially
      – Treatment: bowel rest, IV antibiotics, rectal irrigation
    • Constipation, stricture, fecal incontinence (usually due to overflow)
Eosinophilic Proctocolitis**

- Common cause of rectal bleeding in infants
  - Blood streaked stools, diarrhea, mucousy stools
- AKA: “Cow’s milk protein allergy”
  - Common food offenders: milk and soy protein
- Usually begins <2 months of age
- Exam, growth, laboratory studies are generally normal
- Treatment: removal of milk/soy protein from infant’s diet
  - Prognosis is excellent and most infants outgrow the allergy by 1-5 years of age
Principles of Pediatric Nutrition

• Enteral nutrition
  – Infant and pediatric formula
  – Devices to administer enteral nutrition
• Parenteral nutrition
Principles of Nutritional Support

**Infant Nutrition**

- Breastmilk—ideal food for infants
  - However many instances where this is not an option
- Various types of formulas available to choose!
  - Cow’s Milk Protein
  - Modified Cow’s Milk Protein
  - Soy Protein
  - Hydrolyzed
  - Amino Acid
Infant Formula:

How do you choose??????
Infant Formula**

- 18-20 kcal/oz
- **Cow’s Milk Protein**—most commonly used
  - Many variations: low lactose, partially hydrolyzed proteins, added starch, different whey:casein ratios
- **Soy Protein**—NO lactose (can be used for galactosemia); also in some babies with CMP allergy
- **Hydrolyzed Formulas**—small peptides and some free AA
  - CMP allergy
  - Fat malabsorption/maldigestion (high MCT oil), $$
- **Amino-Acid Based (Elemental)**—100% free amino acids
  - Extreme allergy, intestinal failure; $$$
Pediatric Formula**

- Usually 30-45 kcal/oz
- Designed for PO supplementation and for tube feeding
- Polymeric (Cow’s milk protein, soy protein, clear liquid)
  - Used when bowel function is intact
  - Most taste “OK”
- Semi-Elemental (small peptides, some free amino acids)
  - Used with milk/soy allergy
  - Good for problems with fat malabsorption/maldigestion
  - Not particularly palatable!
- Elemental (free amino acids)
  - Used for severe allergy/intestinal failure; high osmotic load
Enteral Nutrition (Tube Feeding)**

- Various options
  - NG Tube (temporary but not generally used > 6 weeks)
    - Can do bolus feeds or continuous feedings
  - NJ Tube (temporary; can deliver feedings past the stomach)
    - Good for severe reflux, delayed gastric emptying; continuous feeds
    - Placed in interventional radiology
  - Gastrostomy tube
    - Requires surgical placement but is easier to manage
  - GJ tube
    - Requires endoscopy/IR for replacement; needs continuous feeds
  - Jejunostomy tube—button directly into jejunum
Enteral Nutrition

• Indications**
  – dysphagia
  – anatomic ENT abnormalities (i.e. cleft lip)
  – neurologic impairment (risk of aspiration)
  – esophageal disease (i.e. caustic ingestion)
  – FTT
  – intrinsic GI disease (intestinal failure, Crohn’s)
  – specific nutritional/medication needs (metabolic disease)
Parenteral Nutrition (PN)

- Reasons to consider parenteral nutrition**
  - Inability to deliver caloric needs enterally (i.e. intestinal failure, severe cholestasis, ileus)
  - Generally enteral feeding is desired over PN
    - PN carries significant risk of infection due to need for central line
    - Risk of line complications
    - Hepatotoxicity
- PN can be delivered centrally or peripherally
  - Centrally is generally preferred (“TPN”)
  - Peripheral PN (PPN) may be used for short term parenteral nutrition when hyperosmolar solutions are not necessary
**Parenteral Nutrition (PN)**

- Line-related complications (line infection, sepsis, thrombosis)
- Careful monitoring needed
  - Daily electrolyte monitoring when first starting
  - Once stabilized, monitoring labs 1-2x/week
    - CBC, CMP, PT/INR
  - For those on long term PN (i.e. >1 month), careful attention needs to be paid to trace element/vitamin levels
Functional Gastrointestinal Disorders

- Rome III Criteria
  - Rome IV due to be published Spring 2016
- Will highlight today:
  - Irritable Bowel Syndrome
  - Childhood Functional Abdominal Pain
  - Functional Dyspepsia
  - Abdominal Migraine
- Constipation
Irritable Bowel Syndrome**

- Criteria fulfilled at least 1x/week for at least 2 months
  - Abdominal pain associated with 2 or more (>25% of the time)
    - Improvement with defecation
    - Onset associated with a change in frequency of stool
    - Onset associated with a change in appearance of stool
  - No evidence of inflammatory, anatomic, metabolic, neoplastic process
  - Treatment:
    - Antispasmodics, peppermint oil, tricyclic antidepressants, probiotics, FODMAP diet (adults), Cognitive Behavioral Therapy
    - Lactose may not be a big player**
Childhood Functional Abdominal Pain**

- Criteria fulfilled at least once per week for 2 months
  - Episodic or continuous abdominal pain
  - No evidence of an inflammatory, anatomic, metabolic, or neoplastic process
  - Treatment:
    - Antispasmodics, peppermint oil, tricyclic antidepressants, probiotics, FODMAP diet (adults), Cognitive Behavioral Therapy
Functional Dyspepsia**

- Criteria fulfilled at least once per week for at least 2 months
  - Persistent/recurrent pain or discomfort centered above the umbilicus
  - Not relieved by defecation (i.e. not IBS)
  - No evidence of an inflammatory, anatomic, metabolic, or neoplastic process
- Treatment may be similar to other functional GI disorders
Abdominal Migraine

- Criteria fulfilled 2+ times in the last 12 months
- Intense, periumbilical pain that lasts for >1 hour
- Well being in between episodes
- Pain interferes with normal activities
- Associated with at least 2: anorexia, nausea, vomiting, headache, photophobia, pallor
- No evidence of other cause of symptoms
- Treatment: similar to classic migraines
Constipation

• A very common problem!
• In most children, there is no underlying medical disease
• Differential diagnosis
  – Infants: Hirschsprung’s, allergic proctitis, anorectal malformation, hypothyroidism, CF, spinal cord abnormalities
  – Older children: Hirschsprung’s, celiac disease, hypothyroidism, still need to consider anatomic abnormalities!
• Initial treatment: PEG as first line therapy; can also consider lactulose, milk of magnesia, stimulant laxatives
Constipation

• In addition to medication, provide behavioral therapy to promote a positive toileting experience!
• Maintenance medications should continue for >2 months and should not be stopped unless symptoms have been resolved for >1 month
• During toilet training, medications should continue until toilet training is well-established.
Encopresis

- Encopresis is most commonly related to “overflow” and the presence of constipation
  - Stool withholding allows a child to accumulate a large mass of stool in the rectum
  - Liquid stool can then seep around the mass of stool and is unable to be controlled
  - Treatment is aimed at the underlying constipation (i.e. using stool softeners)
    - Timed sitting after meals and in the afternoon in conjunction with oral laxative use
    - Parental education about encopresis (i.e. the child is not “lazy”)
    - Rewards for following instructions (sitting, meds)
Good mechanics are important!!
Changes You May Wish to Make in Practice

• Refer early to pediatric GI if IBD is suspected.
• Children with >5 polyps should be evaluated for polyposis syndromes and additional screening for cancers (aside from GI cancers) may be warranted.
• Model positive reinforcement to parents of children with and encopresis.