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 and other functional GI disorders in children
Diseases of the Colon

- Inflammatory Bowel Disease
- *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

Pancolitis in 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

Rufo P et al, JPGN 2012 (Health Supervision in IBD)
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 <24 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
Intestinal Polyps: Polyposis Syndromes**

• 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)
      - Polyps can be in upper and/or lower GI tract
      - Lifetime risk of colorectal cancer is 9% (general = 4-5%); usually in 30s
    - 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** (1:200,000)
  - STK11/LKB1 mutation
  - Mucocutaneous pigmentation
    - Starts in infancy (around mouth, nostrils, buccal mucosa)
  - Small bowel polyps (+ stomach and colon)
    - Risk for intussusception
    - Hamatomatous polyps
  - 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??????

3 PACK

University Children's Hospital
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 IV Criteria—new (update from printed slides)
  – All functional disorders: “after appropriate medical evaluation, the symptoms cannot be attributed to another condition”
    • Allowance of selective (or no) testing to diagnose with functional disorder
• Will highlight today:
  – Irritable Bowel Syndrome
  – Functional Abdominal Pain-NOS
  – Functional Dyspepsia
  – Abdominal Migraine
• Constipation

Figure 1. Pathophysiology of functional abdominal pain disorders. Visceral hyperalgesia leading to disability is shown as the final outcome of sensitizing medical factors that are superimposed on a background of genetic predisposition and early life events.

Irritable Bowel Syndrome**

- Can be divided into subgroups (similar to adult criteria)
  - IBS with constipation, IBS with diarrhea, IBS with C + D, unspecified IBS
  - (subtypes may be more useful for research purposes)
- Treatment: probiotics, peppermint oil, behavioral treatments, dietary therapy

H2b. Diagnostic Criteria* for Irritable Bowel Syndrome

Must include all of the following:
1. Abdominal pain at least 4 days per month associated with one or more of the following:
   a. Related to defecation
   b. A change in frequency of stool
   c. A change in form (appearance) of stool
2. In children with constipation, the pain does not resolve with resolution of the constipation (children in whom the pain resolves have functional constipation, not irritable bowel syndrome)
3. After appropriate evaluation, the symptoms cannot be fully explained by another medical condition

*Criteria fulfilled for at least 2 months before diagnosis.

Functional Abdominal Pain-NOS**

- Must occur >4x/month and include all:
  - Episodic/continuous pain not solely occurring during physiologic events (eating, menses)
  - Does not meet criteria for IBS, functional dyspepsia, migraine
- Associated with psychological distress
  - Ability to cope with pain influences FAP outcomes
- Treatment:
  - Cognitive behavioral therapy, hypnotherapy, ?SSRI, ?antispasmodics

Functional Dyspepsia**

- **Postprandial distress syndrome**
  - Bothersome postprandial fullness or early satiation that prevents finishing a regular meal
  - Treatment: prokinetics

- **Epigastric pain syndrome**
  - Bothersome pain or burning localized to the epigastrum
  - Not relieved by defecation or passage of flatus (i.e. not IBS)
  - Treatment: PPI, tricyclic antidepressants

- Overlap may occur
Abdominal Migraine

• At least 2 episodes of the following over a 6 month period
  – Intense, acute abdominal pain lasting >1 hr
  – Episodes are separated by weeks to months
  – Incapacitating pain, interferes with normal activity
  – Similar pattern in individual patients
  – Associated with 2 +: anorexia, nausea, vomiting, headache, photophobia, pallor

• Treatment:
  – Depends on severity of events
  – May consider prophylactic therapy: amitriptyline, propranolol, cyproheptadine

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:
  – 1. Disimpact (oral/rectal) fecal impaction (if present)
  – 2. Maintenance: PEG 3350 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!
  – (“the poo in you”, youtube video from Children’s Hospital Colorado)
• 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)
**Constipation**

- Child holds in stool because of pain
- Stretched out nerves and muscle that don’t work well
- Buildup of hard stool
- Soft stool may move around hard stool and leak out

**Recovery**

- Thicker, stronger muscle that works well
- Nerves able to sense need to go
- Sphincters able to prevent leaking

Consistent emptying of colon (for months)
- Laxatives
- Toilet-sitting
Good mechanics are important!!
### Bristol Stool Chart

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Separate hard lumps, like nuts (hard to pass)</td>
</tr>
<tr>
<td>2</td>
<td>Sausage-shaped but lumpy</td>
</tr>
<tr>
<td>3</td>
<td>Like a sausage but with cracks on its surface</td>
</tr>
<tr>
<td>4</td>
<td>Like a sausage or snake, smooth and soft</td>
</tr>
<tr>
<td>5</td>
<td>Soft blobs with clear-cut edges (passed easily)</td>
</tr>
<tr>
<td>6</td>
<td>Fluffy pieces with ragged edges, a mushy stool</td>
</tr>
<tr>
<td>7</td>
<td>Watery, no solid pieces. Entirely Liquid</td>
</tr>
</tbody>
</table>
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 constipation and encopresis.