



# Back to Basics: GI Pediatric Pharmacology

Julie Dennison, RPh  
PICU Clinical Pharmacist

# Objectives

- Overview and discussion of pharmacological treatments for the following conditions:
  - Gastroesophageal Reflux
  - Constipation
  - Acute Gastroenteritis
  - *C. difficile*
  - Inflammatory Bowel Disease
- Overview of Probiotics and available formulations

# Gastroesophageal Reflux

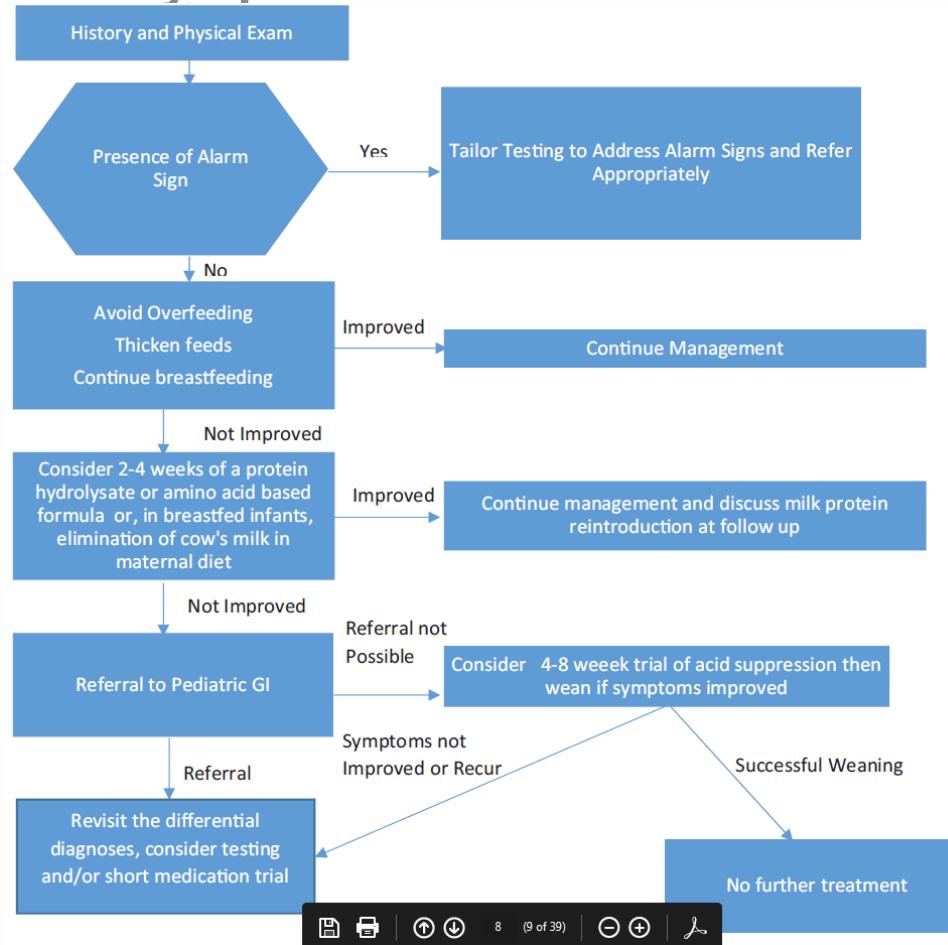
- Gastroesophageal reflux (GER) is a normal physiologic process that occurs in healthy infants and children
  - Usually does not cause symptoms or other complications
  - Conservative management
- Gastroesophageal reflux disease (GERD) occurs when the reflux is associated with complications
  - May require further evaluation and treatment
  - Common symptoms in infants:
    - Recurrent vomiting
    - Poor weight gain
    - Irritability
    - Sleep disturbance
    - Respiratory symptoms
    - Feeding refusal

# Gastroesophageal Reflux

- The frequency of reflux declines with increasing age, towards the end of the first year of life
- Symptoms and complications in children older than one year of age and adolescents
  - Abdominal pain
  - Heartburn
  - Vomiting
  - Dysphagia
  - Asthma
  - Pneumonia
  - Upper airway symptoms

# Gastroesophageal Reflux

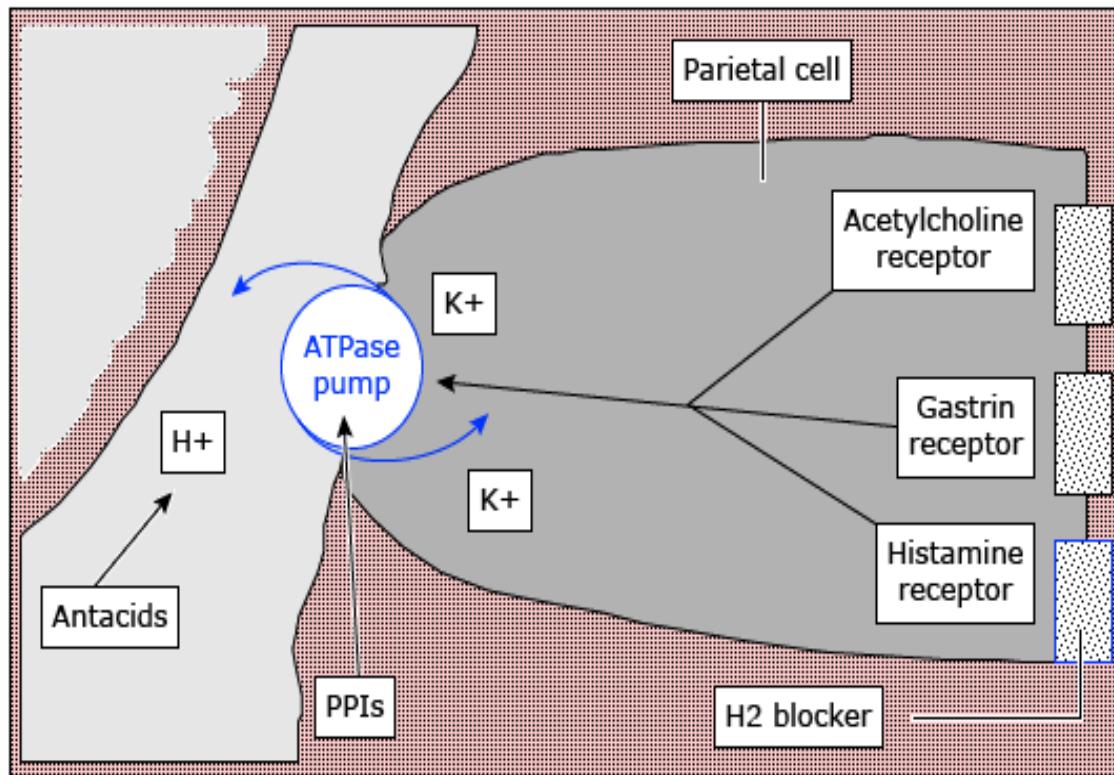
## Management of the symptomatic infant



# Gastroesophageal Reflux

- Lifestyle modifications to reduce the signs and symptoms of GERD (first-line approach)
  - Infants
    - Modifying maternal diet in breastfed infants
    - Changing formula in formula fed infants
    - Reducing feeding volume
    - Increasing feeding frequency
    - Thickening formula
    - Keeping infants in an upright position after feedings
  - Older Children
    - Losing weight (if needed)
    - Avoiding foods that may trigger symptoms
    - Chewing sugarless gum

# GERD Treatment



# Proton Pump Inhibitors (PPIs)

- To be used 1<sup>st</sup> line for the treatment of reflux-related erosive esophagitis in infants and children with GERD
- Most potent class of acid suppressants
- Superior efficacy when compared to H<sub>2</sub> antagonists
- The acid suppression ability does not diminish with chronic use
- Timing of the dose is important for maximum efficacy; 30 minutes prior to meals
- Mechanism of Action:
  - Suppresses gastric acid secretion by inhibition of the H<sup>+</sup>/K<sup>+</sup> ATPase in the gastric parietal cells
- Pediatric Considerations:
  - Associated with an increased risk for the development of acute gastroenteritis and community acquired pneumonia

# PPIs

- **Esomeprazole**

- Dosing:

- Infants, children, and adolescents: 0.7 to 3.3 mg/kg/day  
(max 40 mg/dose)

- Administration:

- Capsule: swallow, do not crush or chew. Capsule may be opened and the pellets mixed with 1 tablespoonful of applesauce and used immediately
    - Granules: mix contents of the 2.5 mg or 5 mg packet with 5 mL water or with 15 mL water for the 10 mg, 20 mg, or 40 mg packet. Mix together and leave for 2 to 3 minutes to thicken, then stir and drink within 30 minutes

- Adverse reactions:

- Abdominal pain, constipation, diarrhea, nausea, and headache

- Products:

- Capsule: 20 mg and 40 mg
    - Packet: 2.5 mg, 5 mg, 10 mg, 20 mg, and 40 mg

# PPIs

- Lansoprazole
  - Dosing
    - Infants: 1 to 2 mg/kg/day
    - Children: 0.7 to 3 mg/kg/day
  - Administration:
    - Best if taken 30 minutes prior to eating
    - Capsule:
      - Do not crush or chew. Capsules may be opened and granules sprinkled on 1 tablespoon of applesauce, pudding, cottage cheese, yogurt, or strained pears. Capsule may also be opened and mixed with 60 mL of apple, orange, or tomato juice; swallow immediately
    - ODT tablet:
      - Place on tongue and allow to disintegrate, then swallow
      - Place tablet in an oral syringe and draw up 4 mL water (15 mg) or 10 mL water (30 mg). Shake gently until dissolved and administer
  - Adverse reactions:
    - Abdominal pain, constipation, diarrhea, nausea, headache
  - Dosage Forms:
    - Capsule Delayed Release: 15 mg and 30 mg
    - Oral Disintegrating Tablet: 15 and 30 mg
    - Suspension: 3 mg/mL

# PPIs

- Omeprazole
  - Dosing:
    - Infants, children, and adolescents: 0.7 to 3.3 mg/kg/day (Max 20 mg/day)
  - Administration:
    - Best if taken 30 minutes before a meal
    - Capsule:
      - Do not crush or chew. Contents of capsule may be added to 1 tablespoon of applesauce
    - Powder for oral suspension:
      - Empty contents of packet into water, 2.5 mg (5 mL) or 10 mg (15 mL). Stir and let thicken for 2 to 3 minutes
  - Adverse reactions:
    - Rash, abdominal pain, constipation, diarrhea, nausea, headache
  - Dosage Forms:
    - Capsule Delayed Release: 10 mg, 20 mg, and 40 mg
    - Packet for Suspension: 2.5 mg or 10 mg
    - Suspension: 2 mg/mL

# PPIs

- Rabeprazole
  - Dosing:
    - Children  $\geq$  12 years and adolescents: Tablets: 20 mg once daily
  - Administration:
    - Best if taken 30 minutes before a meal when treating GERD
    - Tablets should be swallowed whole, do not chew, crush, or split
  - Adverse Reactions:
    - Headache, abdominal pain, diarrhea, nausea, vomiting
  - Dosage Forms:
    - Tablet Delayed Release: 20 mg

# Histamine H<sub>2</sub> Antagonists

- To be used if PPIs are not available or are contraindicated
- Less effective than PPIs in symptom relief and healing rates of erosive esophagitis
- Tachyphylaxis can develop within 6 weeks of initiation, limiting long-term use
- Mechanism of Action:
  - Competitive inhibition of histamine at the H2 receptors of the gastric parietal cells. This inhibits gastric acid secretion. Gastric volume and hydrogen ion concentration are reduced
- Gastric pH begins to increase within 30 minutes of the dose
- Pediatric Considerations:
  - Have been associated with an increased risk for developing acute gastroenteritis and community acquired pneumonia
  - Increase incidence of Necrotizing Enterocolitis (NEC) in VLBW neonates

# Histamine H<sub>2</sub> Antagonists

- Ranitidine

- Dosing:
  - Infants, children, and adolescents < 16 yrs: 5-10 mg/kg/day divided twice daily (max 300 mg/day)
  - Adolescents > 16 yrs: 150 mg twice daily
- Administration:
  - Administer with meals and/or at bedtime
- Adverse Reactions:
  - Abdominal pain, constipation, diarrhea, headache
- Products:
  - Capsule: 150 mg and 300 mg
  - Tablet: 75 mg and 150 mg
  - Syrup: 15 mg/mL

# Histamine H<sub>2</sub> Antagonists

- Nizatidine
  - Dosing:
    - Infants and children ≤ 11 yrs: 5 mg/kg/dose twice daily (max 300 mg/day)
    - Children ≥ 12 yrs and adolescents: 150 mg twice daily
  - Administration:
    - May administer with or without food
    - Do not administer or mix capsule contents with apple juice
  - Adverse Reactions:
    - Diarrhea, vomiting, headache, irritability, cough, nasal congestion, rhinitis
  - Products:
    - Capsule: 150 mg and 300 mg
    - Solution: 15 mg/mL

# Histamine H<sub>2</sub> Antagonists

- Famotidine

- Dosing:

- Suspension:

- Infants < 3 months: 0.5 mg/kg/dose once daily for up to 8 weeks; if not effective after 2 weeks, may increase to 1 mg/kg/dose once daily
    - Infants ≥ 3 months, children, and adolescents ≤ 16 years: 0.5 mg/kg/dose twice daily ( max 40 mg/dose); doses up to 1 mg/kg/dose twice daily have been used

- Tablets:

- Children and adolescents ≥ 40 kg: 20 mg twice daily for up to 6 weeks; may use 40 mg twice daily for up to 12 weeks

- Administration:

- Can be taken without regard to meals
    - May administer with antacids

- Adverse Reactions:

- Constipation, diarrhea, dizziness, headache

- Products:

- Tablets: 20 mg and 40 mg
    - Solution: 40 mg/5 mL

# Histamine H<sub>2</sub> Antagonists

- Cimetidine
  - Dosing:
    - Adolescents ≥ 16 years: 30 to 40 mg/kg/day in 4 divided doses (max 400 mg/dose)
  - Administration:
    - Administer with food; do not give with antacids
  - Adverse Reaction:
    - Increased risk of liver disease and gynecomastia
  - Dosage Forms:
    - Solution: 300 mg/5 mL
    - Tablet: 200 mg, 300 mg, and 400 mg

# Antacids

- Mechanism of Action:
  - Directly buffer gastric acid in the stomach or esophagus to reduce heartburn and allow for mucosal healing of the esophagus
- Limited evidence that antacids can lead to symptom relief in infants and children
- Use is not without risk:
  - Aluminum containing products can lead to aluminum toxicity
  - Calcium containing products can lead to a triad of hypercalcemia, alkalosis, and renal failure
- Chronic therapy is generally not recommended in pediatric patients for the treatment of GERD

# Prokinetic Agents

- Mechanism of Action:
  - Improve contractility of the body of the esophagus, increasing lower esophageal sphincter pressure, and increasing the rate of gastric emptying
- Metoclopramide:
  - The most common prokinetic agent
  - Although it has shown to decrease GERD symptoms, there is a risk of significant adverse effects
  - Black Box Warning for tardive dyskinesia
    - A serious movement disorder that is often irreversible
    - Risk increases with duration of treatment and total cumulative dose
  - Adverse Reactions:
    - CNS depression, restlessness, extrapyramidal symptoms, and neuroleptic malignant syndrome

# Prokinetic Agents

- Other prokinetic agents:
  - Bethanechol
  - Erythromycin
- There is insufficient evidence to support the routine use of prokinetic agents for the treatment of GERD in infants or older children
- Should only be considered for use following specialist recommendations and as a last-line agent

# Gastroesophageal Reflux

- There needs to be regular assessment of the ongoing need of long-term acid suppression therapy in infants and children with GERD
  - Generally a 4 to 8 week course of treatment is recommended for typical symptoms
- H<sub>2</sub> antagonists and PPIs are not recommended for the treatment of crying/distress in otherwise healthy infants

# Constipation

- Defined as:
  - A condition that persists for 2 or more weeks with some of the following symptoms:
    - Hard stool
    - Painful bowel movements
    - Decreased frequency of bowel movements
    - Inability to completely empty the lower colon
- Accounts for approximately 5% of all pediatric outpatient visits and 25% of GI referrals

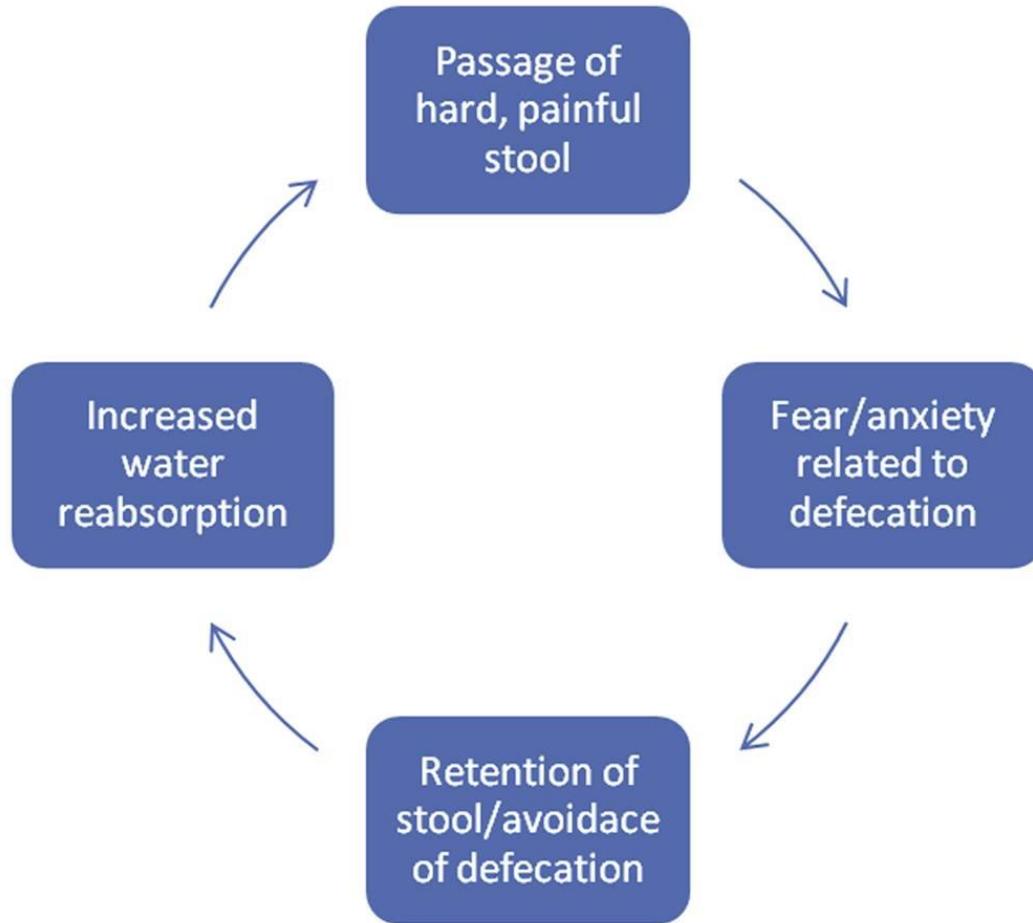
# Causes of Constipation

- Neurologic
  - Hirschsprung's Disease
    - Genetic disorder, can be associated with other syndromes, such as Trisomy 21
    - Delayed passage of meconium
  - Obstructive
    - Imperforated anus
    - Pelvic mass
  - Endocrine/Metabolic
    - Hypothyroidism
    - DM
    - CF
    - Celiac Disease
  - Opiates

# Causes of Constipation

- Functional
  - Most common form of constipation
  - Constipation without evidence of pathological condition
  - Commonly caused by painful bowel movements which results in the child purposely withholding stool
    - Difficulty with toilet training
    - Anxiety related to when and where bowel movements take place
    - Change in the child's normal routine

# Functional Constipation



# Clinical Practice Guidelines

- Evidence-Based Recommendations from ESPGHAN and NASPGHAN in 2014: Evaluation and Treatment of Functional Constipation in Infants and Children
- Recommendations are based on a combination of comprehensive and systematic review of literature along with expert opinion

# Treatment of Functional Constipation

- Determine whether impaction is present
- Treat the impaction
- Initiate treatment with oral medications
- Provide education and follow-up
- Adjust medication as necessary

# Treatment of Functional Constipation

- Impaction
  - Necessary to treat before beginning maintenance therapy
  - 1<sup>st</sup> line – Polyethylene Glycol (PEG) with or without electrolytes  
1-1.5 gram/kg/day for 3-6 days
  - If PEG is not available, an enema once per day for 3-6 days if recommended

# Treatment of Functional Constipation

- Maintenance Treatment
  - Should continue for at least 2 months
  - All symptoms should be resolved for at least 1 month prior to discontinuation of treatment
  - Treatment should be decreased gradually
  - Early treatment has a positive effect on recovery
  - Follow those with a history of constipation closely and restart treatment promptly if necessary

# Treatment of Functional Constipation

- 1<sup>st</sup> line – Polyethylene Glycol (PEG) with a starting dose of 0.4 g/kg/day
- The addition of enemas is not recommended
- Lactulose can be used as 1<sup>st</sup> line treatment if PEG is not available
- MOM, mineral oil, and stimulant laxatives may be considered as an additional or 2<sup>nd</sup> line treatment

# Oral Laxatives

- PEG (Polyethylene Glycol) 3350 (Miralax)
  - Osmotic laxative
  - Causes water retention in the stool, increasing stool frequency
  - Dosing:
    - Infants, children, and adolescents: 0.4 g/kg/day, with a range of 0.2-0.8 g/kg/day; higher doses of 1 g/kg have been used
  - Administration:
    - Dissolve powder in 4-8 ounces of water, juice, soda, coffee, or tea
  - Adverse reactions:
    - Cramping and flatulence
  - Onset of action:
    - 1-3 days
  - Superior to other osmotic agents in palatability and acceptance by children

# Oral Laxatives

- Lactulose
  - Osmotic laxative
  - Distention promotes peristalsis and elimination of ammonium from the body
  - Dosing:
    - Infants, children, and adolescents: 1 to 2 g/kg/day (1.5 to 3 mL/kg/day) divided once or twice daily
  - Administration:
    - Oral solution: may mix with fruit juice, water, or milk
    - Crystals for oral solution: dissolve contents of packet in 120 mL water
  - Adverse reactions:
    - Abdominal cramping and flatulence
  - Onset of Action:
    - 24 to 48 hours to produce a bowel movement
  - Products:
    - Solution: 10 gram/15 mL
    - Packets: 10 gram

# Oral Laxatives

- Milk of Magnesia (Magnesium Hydroxide)
  - Osmotic laxative
  - Retention of fluid distends the colon and produces increased peristaltic activity
  - Dosing:
    - 2-5 years: 400 to 1200 mg/day in single or divided doses
    - 6-11 years: 1200 to 2400 mg/day in single or divided doses
    - 12-18 years: 2400 to 4800 mg/day in single or divided doses
  - Administration:
    - Liquid doses may be diluted with a small amount of water prior to administration. All doses should be followed by 8 ounces of water if patient  $\geq$  2 years of age
  - Use with caution in those with renal impairment, could lead to accumulation of magnesium
  - Onset of Action:
    - 30 minutes to 6 hours
  - Products:
    - Suspension: 400 mg/5 mL

# Oral Laxatives

- Mineral Oil
  - Lubricant laxative
  - Decreases water absorption, softens stool, lubricates the intestine
  - Dosing:
    - Children and adolescents: 1 to 3 mL/kg/day in 1 or 2 divided doses (max 90 mL/day)
  - Administration:
    - Tastes better chilled
    - Give on an empty stomach and at least 2 hours before or after other medications
  - Adverse reactions:
    - Abdominal cramps, diarrhea, nausea
  - Onset of Action:
    - 6 to 8 hours
  - Risk of lipid pneumonitis if aspirated
    - Avoid in infants
    - Avoid in patients in prolonged supine position or those with difficulty swallowing

# Oral Laxatives

- Bisacodyl
  - Stimulant laxative
  - Directly irritates smooth muscle of the intestine, alters water and electrolyte secretion producing fluid accumulation and laxation
  - Dosing:
    - Children  $\geq$  3 years to 10 years: 5 mg once daily
    - Children  $>$  10 years and adolescents: 5 to 10 mg once daily
  - Administration:
    - Give on an empty stomach with water
    - Swallow tablets whole
    - Do not break or chew enteric-coated tablet
  - Adverse reactions:
    - Abdominal cramps, electrolyte disturbance, nausea
  - Onset of Action:
    - 6 to 12 hours
  - Products:
    - Delayed release tablet: 5 mg

# Oral Laxatives

- Senna
  - Stimulant laxative
  - Acts as a local irritant on the colon, which stimulates peristaltic activity
  - Dosing:
    - Syrup (8.8 mg sennosides/5 mL)
      - Children 2 to 5 years: 2.5 to 3.75 mL at bedtime; not to exceed 3.75 mL twice daily
      - Children 6 to 11 years: 5 to 7.5 mL at bedtime; not to exceed 7.5 mL twice daily
      - Children  $\geq$  12 years and adolescents: 10 to 15 mL at bedtime; not to exceed 15 mL twice daily
    - Tablet (8.6 mg sennosides/tablet)
      - Children 2 to 5 years:  $\frac{1}{2}$  tablet at bedtime; not to exceed 1 tablet twice daily
      - Children 6 to 11 years: 1 tablet at bedtime; not to exceed 2 tablets twice daily
      - Children  $\geq$  12 years and adolescents: 2 tablets at bedtime; not to exceed 4 tablets twice daily

# Oral Laxatives

- Senna (continued)
  - Dosing
    - Chewable tablet (15 mg sennosides/tablet)
      - Children 6-11 years: 1 tablet once or twice daily
      - Children  $\geq$  12 years and adolescents: 2 tablets once or twice daily
  - Administration:
    - Give at bedtime with water
    - Syrup can be taken with juice or milk or mixed with ice cream to mask taste
  - Adverse reactions:
    - Abdominal cramps, diarrhea, nausea, vomiting
  - Onset of Action:
    - 6 to 24 hours

# Rectal Laxatives/Enemas

- Bisacodyl
  - Stimulant laxative
  - Dosing (rectal):
    - Suppository:
      - Children ≥ 2 to 10 years: 5 mg (1/2 suppository) once daily
      - Children > 10 years and adolescents: 5 to 10 mg once daily
    - Enema:
      - Children ≥ 12 years and adolescents: 10 mg once daily
  - Administration:
    - Suppository:
      - Remove foil and insert pointed end first
      - Retain for 15 to 20 minutes
  - Products:
    - Suppository: 10 mg
    - Enema: 10 mg/30 mL

# Rectal Laxatives/Enemas

- Sodium Phosphate (Fleet)
  - Osmotic laxative
  - Draws water into the lumen of the gut, causing distention and peristalsis
  - Dosing (rectal):
    - Children 2 to 4 years: administer **one half** contents of one 2.25 ounce pediatric enema
    - Children 5 to 11 years: administer the contents of one 2.25 ounce pediatric enema
    - Children  $\geq$  12 years and adolescents: administer the contents of one 4.5 ounce enema
  - Administration
    - Preparation for **one half bottle** administration: unscrew cap and remove 30 mL of liquid, replace cap and administer as usual
  - Adverse reactions:
    - Hyperphosphatemia, hypocalcemia, abdominal distension, vomiting
  - Products:
    - Enema: 133 mL (118 mL deliverable)
    - Pediatric Enema: 66 mL (59 mL deliverable)

# Rectal Laxatives/Enemas

- Mineral Oil
  - Lubricant Laxative
  - Dosing (rectal):
    - Children 2 to 11 years: administer **one half** the contents of a 4.5 ounce as a single dose
    - Children  $\geq$  years and adolescents: administer the contents of one 4.5 ounce bottle as a single dose
  - Products:
    - Enema: 135 mL

# Fiber

- Increasing intake of fiber, through dietary changes or fiber supplements is often recommended for the treatment of constipation
  - The evidence base for this practice is weak
  - Can have either beneficial or adverse effects in children
  - The use of fiber supplements to treat functional constipation is not recommended in the guidelines
- A balanced diet is recommended and can include:
  - Whole grains
  - Fruit
  - Vegetables
- A reasonable target for dietary fiber can be calculated as the child's age + 5 to 10 grams/day
  - Example: 11 to 16 grams per day for a 6 year old child

# Fiber

- It may be reasonable to avoid any dietary changes during the initial treatment phase of constipation
- For those with a history of impaction, extra fiber intake should only be initiated after several months of successful treatment with laxatives, once rectal tone has been restored
- Adequate intake is important once laxative therapy has been discontinued

# Acute Gastroenteritis

- Defined as diarrheal disease of rapid onset, with or without nausea, vomiting, fever, or abdominal pain
  - Involves increased stool frequency or altered consistency that is unrelated to chronic conditions
- Worldwide:
  - 68% of diarrheal disease occurs in young children
  - 5<sup>th</sup> leading cause of death in children, accounting for 2.5 million deaths
- United States:
  - Causes significant morbidity in children under the age of 5 years
  - 1.5 million office visits, 200,000 hospitalizations, and 300 deaths in children each year

# Acute Gastroenteritis

- Viruses account for 75% to 90% of acute infectious gastroenteritis
  - Is normally self-limited
  - Treated with supportive measures
- Approximately 20% of cases are due to bacteria
- Less than 5% caused by parasitic infections, in which diarrhea typically persists for at least 14 days
- Causative microorganisms vary with season and climate

# Acute Gastroenteritis

- Obtain history from the family:
  - Onset and duration of symptoms
  - Fluid intake and output
  - “Red Flag” symptoms that would require aggressive treatment
    - Examples: altered mental status, petechial rash, rapid breathing, toxic appearance, and those infants < 6 months of age
- Vomiting and diarrhea are not specific to gastroenteritis and other diagnoses will need to be ruled out
- Stool studies not routinely needed for mild illness

TABLE 2

## Differential Diagnosis of Diarrhea or Vomiting in Children

Symptom or sign	Possible diagnosis
Altered mental status	Central nervous system infection, sepsis
Bilious vomiting	Bowel obstruction
Blood or mucus in the stool (particularly if lasting more than two weeks)	Inflammatory bowel disease
Dyspnea	Pneumonia
Fever	Infections such as otitis media and urinary tract infection can cause nausea and vomiting in children
Localized abdominal pain, abdominal distention, or rebound tenderness	Surgical abdomen (e.g., appendicitis)
Neck stiffness or bulging fontanelle	Meningitis
Nonblanching rash	Toxic shock syndrome
Recent antibiotic use (e.g., ampicillin)	Antibiotic adverse effect

Information from reference 1 and 13.

# Acute Gastroenteritis

- Goals of treatment:
  - Prevent dehydration
  - Treat dehydration
    - Initial fluid repletion
    - Replace ongoing fluid losses
      - For infants: continue breastfeeding
      - For children: may start an age appropriate diet after the initial rehydration
      - Milk products do not need to be avoided
  - Reducing the duration and severity of symptoms

# Acute Gastroenteritis

- Hydration status:
  - Physical exam is the best way to evaluate hydration status
- Clinical Dehydration Scale
  - Evaluates 4 clinical features to estimate the degree of dehydration
  - Most useful in identifying moderate to severe dehydration

TABLE 3

#### Clinical Dehydration Scale

Characteristic	0 points	1 point	2 points
Appearance	Normal	Thirsty, restless, or lethargic but irritable when touched	Drowsy, limp, cold, sweaty, comatose
Eyes	Normal	Slightly sunken	Very sunken
Mucous membranes	Molst	Sticky	Dry
Tears	Tears	Decreased tears	Absent tears

**Scoring:** 0 points = less than 3% dehydration; 1 to 4 points = mild (3% to 6%) dehydration; 5 to 8 points = moderate to severe (more than 6%) dehydration.

*Information from reference 16.*

# Acute Gastroenteritis

- Mild Dehydration
  - 6% or less
  - Managed at home
  - Oral rehydration therapy (ORT)
    - World Health Organization (WHO) recommendations:
      - After each loose stool:
      - Children < 2 years of age: 50 to 100 mL
      - Children 2-10 years of age: 100 to 200 mL
      - Children > 10 years of age: as much volume as they want

# Acute Gastroenteritis

- Moderate to Severe Dehydration
  - More than 6% dehydration
  - Includes oral rehydration plus medication if needed
    - To decrease nausea and vomiting
    - To improve tolerance of the oral rehydration solutions
  - Provide education on how to properly administer the rehydration solution: to newborns with a syringe and with a spoon in older infants.

TABLE 4

## WHO Guidelines for Administering ORS in Children

Weight*	Age*	Approximate amount of ORS (mL) to give in the first four hours
Less than 5 kg (11 lb)	Younger than four months	200 to 400
5 to 7.9 kg (11 lb to 17 lb, 7 oz)	Four to 11 months	200 to 400
8 to 10.9 kg (17 lb, 10 oz to 24 lb)	12 to 23 months	600 to 800
11 to 15.9 kg (24 lb, 4 oz to 35 lb)	Two to four years	800 to 1,200
16 to 29.9 kg (35 lb, 4 oz to 65 lb, 15 oz)	Five to 14 years	1,200 to 2,200
30 kg (66 lb, 2 oz) or more	15 years or older	2,200 to 4,000

**Note:** If the patient wants more ORS than shown, give more. Encourage breastfeeding mothers to continue breastfeeding the child. For infants younger than six months who are not breastfed: if using the old WHO ORS solution (90 mEq per L of sodium), add an extra 100 to 200 mL of clean water; this is not necessary if using the new reduced osmolality ORS (75 mEq per L of sodium).

ORS = oral rehydration solution; WHO = World Health Organization.

\*—Use the patient's age only if the weight is not known. The approximate amount of ORS required (in mL) can also be calculated by multiplying the patient's weight in kg by 75.

Adapted with permission from World Health Organization. *The treatment of diarrhoea: a manual for physicians and other senior health workers*. 2005. <http://apps.who.int/iris/bitstream/10665/43209/1/9241593180.pdf>. Accessed January 3, 2018.

# Acute Gastroenteritis

## Oral Rehydration Therapy (ORT)

- Is as effective as IV hydration in treating mild to moderate dehydration
- When compared to IV fluids, ORT is:
  - Less costly
  - Less invasive
  - Easier to administer
- Best to use a standard, commercially prepped solution or one from the WHO (World Health Organization)
  - Osmolarity between 200 to 310 mOsm/L
  - Do not use homemade solutions
  - Half strength apple juice is an option in mild dehydration

# Acute Gastroenteritis

## Composition of oral rehydration solutions (ORS) and commonly used beverages

	Carbohydrate (g/L)	mEq/L			Osmolarity (mOSM/kg H <sub>2</sub> O)
		Sodium	Potassium	Base (HCO <sub>3</sub> <sup>-</sup> )	
<b>Oral rehydration solutions</b>					
CeraLyte	40	70	20	10	235
Enfalyte	30	50	25	30	200
Pedialyte	25	45	20	30	250
Rehydralyte	25	75	20	30	310
WHO (1975)	20	90	30	30	310
WHO (2002)	13.5	75	20	30	245
<b>Commonly Used Beverages (not appropriate for repletion therapy)</b>					
Apple juice	100 to 150	3	20	0	700
Chicken broth	0	250	5	0	450
Colas	100 to 150	2	0.1	13	550
Gatorade	45	20	3	3	330
Ginger Ale	90	3.5	0.1	3.6	565
Tea	0	0	0	0	5

# Acute Gastroenteritis

- Ondansetron
  - Antiemetic – selective 5-HT<sub>3</sub> receptor antagonist which blocks serotonin
  - Dosing:
    - Oral: Infants and children 6 months to 10 years,  $\geq 8$  kg:
      - 8 to 15 kg: 2 mg/dose
      - > 15 to 30 kg: 4 mg/dose
      - > 30 kg: 8 mg/dose
  - Administration:
    - May administer without regard to meals
    - ODT: Remove from blister pack when needed. Using dry hands, place tablet on tongue and allow to dissolve; swallow with saliva
  - Adverse Reactions:
    - Fatigue, headaches, malaise, constipation, diarrhea
    - Rare: prolonged QT interval
  - Onset of Action:
    - 30 minutes
  - Products:
    - Solution: 4 mg/2 mL
    - Tablet: 4 mg and 8 mg
    - ODT Tablet: 4 mg and 8 mg

# Acute Gastroenteritis

## Antidiarrheal Agents

- NOT ROUTINELY USED

- Loperamide

- Acts on circular and longitudinal intestinal muscles, through the opioid receptor, to inhibit peristalsis and prolong transit time

- Dosing:

- 2 to 5 years weighing 13 to <21 kg: 1 mg with first loose stool followed by 1 mg/dose after each additional loose stool (Max 3 mg/day)

- 6 to 8 years weighing 21 to 27 kg: 2 mg with first loose stool followed by 1 mg/dose after each additional loose stool (Max 4 mg/day)

- 9 to 11 years weighing 27.1 to 43 kg: 2 mg with first loose stool followed by 1 mg/dose after each additional loose stool (Max 6 mg/day)

- Children ≥ 12 years and adolescents: 4 mg with first loose stool followed by 2 mg/dose after each additional loose stool (Max 8 mg/day)

- Administration:

- Drink plenty of fluids

- Adverse Reactions:

- Dizziness, abdominal cramps, constipation, nausea

- Products:

- Tablet: 2 mg

- Liquid: 1 mg/7.5 mL and 1 mg/5 mL

# Prevention of Acute Gastroenteritis

- Handwashing
  - Primary means of preventing gastroenteritis
  - No evidence that antibacterial soaps work better than non-antibacterial soaps
  - The addition of alcohol-based hand sanitizers in addition can reduce gastroenteritis in offices and daycares/schools by 30%
- Breastfeeding
  - Exclusive breastfeeding for 4 months and partial breastfeeding thereafter are associated with lower rates of acute gastroenteritis in the first year of life and with decreased rates of hospitalization
- Probiotics
  - Some evidence demonstrates that daily administration of probiotics can reduce the incidence of acute infectious diarrhea without adverse effects
  - More studies are needed to determine which specific strains and dosages of probiotics are most helpful

# Prevention of Acute Gastroenteritis

- Vaccines
  - Rotavirus Vaccine
    - Oral, live, attenuate vaccine
    - Reduces the risk of severe gastroenteritis, hospitalization, and death
    - Dosing: Series should be completed with the same product
      - Rotarix:
        - Infants 6 to 24 weeks of age: Oral: 1 mL per dose for 2 doses, the first dose given at 6 weeks of age, followed by the second dose given  $\geq$  4 weeks later. The 2 dose series should be completed by 24 weeks of age
        - RotaTeq:
          - Infants 6 to 32 weeks of age: Oral: 2 mL per dose for 3 doses, the first dose given at 6 to 12 weeks of age, followed by subsequent doses at 4 to 10 weeks intervals. The 3 dose series should be completed by 32 weeks of age
      - Adverse Reactions:
        - Irritability, diarrhea, flatulence, vomiting
        - Rare: intussusception and Kawasaki Disease
      - Before availability of rotavirus vaccine, nearly all children experienced an infection by 3 to 5 years of age

# **Clostridium *difficile*** **(C. *difficile*)**

- Important cause of antibiotic-associated diarrhea
- One of the most common health care-associated pathogens
- Less common in children than adults
- Manifestations range from asymptomatic colonization to fulminant colitis
- Asymptomatic colonization is common in neonates and infants. C. *difficile* can be detected in 25 to 50% of neonates and in 40 to 70% of infants
  - With both toxigenic or nontoxigenic strains
- No clear association between the detection of C. *difficile* toxins and diarrheal illness in children younger than 2 year of age

# *C. difficile* Risk Factors

- Recent antibiotic exposure
- Hospitalization
- Underlying complex chronic conditions:
  - Malignancy
  - Solid organ transplant
  - IBD
- Gastrostomy or jejunostomy tubes
- Acid suppressing medications
  - H<sub>2</sub> antagonists > PPIs

# C. *Difficile* Symptoms

- Diarrhea
  - Begins either during or several weeks after antibiotic therapy
  - Acute onset, mild to moderate diarrhea is the most common symptom
  - May be watery and profuse, some children have > 10 stools per day
  - Visible blood is uncommon, occurring in < 15% of cases
  - Fever and lower abdominal cramping are common
- Pseudomembranous Colitis
  - Inflammation of the colon associated with an overgrowth of *C. difficile*
  - Uncommon in children
  - Normally occurs during or within 21 days after administration of  $\geq 1$  antibiotic
  - Fever, prolonged diarrhea, abdominal pain and distention, leukocytosis and increased band counts, blood or mucus in the stool, fecal leukocytes
  - Severe infections can lead to:
    - Hypoalbuminemia, sepsis, ascites, intestinal perforation

# C. *Difficile* Symptoms

- Fulminant Disease
  - Characterized by ileus, toxic megacolon, hypotension, or shock
  - Can present with:
    - Fever, diarrhea, severe lower abdominal pain, abdominal distension, hypovolemia, leukocytosis, hypoalbuminemia, lactic acidosis
    - Bowel perforation is a potential complication
    - Will need aggressive treatment and surgical consultation to assess the need for surgical intervention

## Extracolonic Findings:

- Rare in children
- Can include:
  - Skin and soft tissue infections
  - Bacteremia
  - Osteomyelitis

# *C. difficile* Diagnosis

- Due to the high prevalence of asymptomatic carriage of toxigenic *C. difficile* in infants, testing should not be routinely recommended for neonates and infants  $\leq$  12 months of age with diarrhea
- Testing should not be routinely performed in children with diarrhea who are 1 to 2 years of age unless other infectious or noninfectious causes have been excluded
- Testing is recommended in those  $\geq$  2 years of age with prolonged or worsening diarrhea and risk factors (underlying IBD or immunocompromised) or exposures (antibiotics or the health care system)
- Those with unexplained and new-onset  $\geq$  3 unformed stools in 24 hours are the preferred target population for testing

# C. difficile Treatment

**Table 2. Recommendations for the Treatment of *Clostridium difficile* Infection in Children**

Clinical Definition	Recommended Treatment	Pediatric Dose	Maximum Dose	Strength of Recommendation/ Quality of Evidence
Initial episode, non-severe	<ul style="list-style-type: none"> <li>Metronidazole × 10 days (PO), OR</li> <li>Vancomycin × 10 days (PO)</li> </ul>	<ul style="list-style-type: none"> <li>7.5 mg/kg/dose tid or qid</li> <li>10 mg/kg/dose qid</li> </ul>	<ul style="list-style-type: none"> <li>500 mg tid or qid</li> <li>125 mg qid</li> </ul>	Weak/Low Weak/Low
Initial episode, severe/ fulminant	<ul style="list-style-type: none"> <li>Vancomycin × 10 days (PO or PR) with or without metronidazole × 10 days (IV)<sup>a</sup></li> </ul>	<ul style="list-style-type: none"> <li>10 mg/kg/dose qid</li> <li>10 mg/kg/dose tid</li> </ul>	<ul style="list-style-type: none"> <li>500 mg qid</li> <li>500 mg tid</li> </ul>	Strong/Moderate Weak/Low
First recurrence, non-severe	<ul style="list-style-type: none"> <li>Metronidazole × 10 days (PO), OR</li> <li>Vancomycin × 10 days (PO)</li> </ul>	<ul style="list-style-type: none"> <li>7.5 mg/kg/dose tid or qid</li> <li>10 mg/kg/dose qid</li> </ul>	<ul style="list-style-type: none"> <li>500 mg tid or qid</li> <li>125 mg qid</li> </ul>	Weak/Low
Second or subsequent recurrence	<ul style="list-style-type: none"> <li>Vancomycin in a tapered and pulsed regimen<sup>b</sup>, OR</li> <li>Vancomycin for 10 days followed by rifaximin<sup>c</sup> for 20 days, OR</li> <li>Fecal microbiota transplantation</li> </ul>	<ul style="list-style-type: none"> <li>10 mg/kg/dose qid</li> <li>Vancomycin: 10 mg/kg/dose qid; rifaximin: no pediatric dosing</li> <li>...</li> </ul>	<ul style="list-style-type: none"> <li>125 mg qid</li> <li>Vancomycin: 500 mg qid; rifaximin: 400 mg tid</li> <li>...</li> </ul>	Weak/Low Weak/Low Weak/Very low

Abbreviations: IV, intravenous; PO, oral; PR, rectal; qid, 4 times daily; tid, 3 times daily.

<sup>a</sup>In cases of severe or fulminant *Clostridium difficile* infection associated with critical illness, consider addition of intravenous metronidazole to oral vancomycin.

<sup>b</sup>Tapered and pulsed regimen: vancomycin 10 mg/kg with max of 125 mg 4 times per day for 10–14 days, then 10 mg/kg with max of 125 mg 2 times per day for a week, then 10 mg/kg with max of 125 mg once per day for a week, and then 10 mg/kg with max of 125 mg every 2 or 3 days for 2–8 weeks.

<sup>c</sup>No pediatric dosing for rifaximin; not approved by the US Food and Drug Administration for use in children <12 years of age.

# *C. difficile* Treatment

- Initial, non-severe:
  - Oral Metronidazole or Vancomycin
- Initial, severe:
  - Oral Vancomycin with or without IV Metronidazole
- First recurrence, non-severe:
  - Oral Metronidazole or Vancomycin
- Second or subsequent recurrence:
  - Oral Vancomycin in a tapered and pulsed regimen
  - Vancomycin followed by Rifaximin (for  $\geq 12$  years of age)
  - Fecal transplant

# *C. difficile* Treatment

- Metronidazole

- Used for the treatment of anaerobic and protozoal infections
- Dosing:
  - Children and adolescents:
    - Non-severe infection, initial or first recurrence: 7.5 mg/kg/dose 3 to 4 times daily for 10 days (max 500 mg/dose)
    - Severe/fulminant infection, initial: 10 mg/kg/dose IV every 8 hours for 10 days (max 500 mg/dose); use concomitantly with oral or rectal vancomycin
- Administration:
  - Oral: may give with food to minimize GI upset
- Adverse Reactions:
  - Abdominal discomfort, abnormal taste in mouth, diarrhea, nausea, dizziness, headache
- Products:
  - Capsule: 375 mg
  - Tablet: 250 mg and 500 mg
  - Suspension: commercially available as a compounding kit (50 mg/mL and 100 mg/mL) or an oral suspension could be compounded using tablets or powder (50 mg/mL)

# *C. difficile* Treatment

- Vancomycin
  - Miscellaneous antibiotic, can be used orally to treat *C. difficile*
  - Dosing:
    - Non-severe infection, initial or first occurrence: Children and Adolescents: 10 mg/kg/dose 4 times daily for 10 days (max 125 mg/dose)
    - Severe/fulminant infection, initial: 10 mg/kg/dose 4 times daily for 10 days (max 500 mg/dose)
    - Second or subsequent recurrence: Pulsed-tapered regimen: 10 mg/kg/dose 4 times daily for 10 to 14 days; then 10 mg/kg/dose twice daily for 7 days, then 10 mg/kg/dose once daily for 7 days, then 10 mg/kg/dose every 2 or 3 days for 2 to 8 weeks (max 125 mg/dose)
  - Administration:
    - Oral:
      - Oral solution (Firvanq): shake well before use
      - Solution can be made by using the powder for injection: reconstitute to 50 mg/mL, add the appropriate volume for the dose to 30 mL of water and administer orally or via NG tube

# *C. difficile* Treatment

- Vancomycin, continued:
  - Adverse Reactions:
    - Fatigue, headache, abdominal pain, diarrhea, nausea, vomiting, peripheral edema, UTI
  - Dosage Forms:
    - Capsule: 125 mg and 250 mg
    - Solution reconstituted (Firvanq): 25 mg/mL and 50 mg/mL (grape flavored)

# *C. difficile*

- Repeat testing should not be performed (within 7 days) during the same episode of diarrhea in the absence of changes to the clinical presentation
- Do not test asymptomatic patients
- If following successful treatment and cessation of diarrhea, the symptoms return, testing should be repeated since recurrence is common
  - Recurrence occurs in 12 to 30% of children
  - Generally occurs 1 to 3 weeks after initial episode
- There is no clinical value in repeat *C. difficile* testing to establish a cure
  - > 60 % of patient may remain positive for *C. difficile* even after treatment

# Inflammatory Bowel Disease

- Caused by a dysregulated mucosal immune response to the intestinal microflora
  - Occurs in those with a genetic predisposition
  - Includes:
    - Crohn Disease
    - Ulcerative Colitis
- Normally diagnosed in adolescence and in young adults
  - Peak incidence occurs between 15-30 years of age
  - But can occur at any age
- Common enough for pediatricians and other clinicians to encounter in practice
  - Incidence is on the rise

# Inflammatory Bowel Disease

- Types
  - Ulcerative Colitis (UC)
    - Is a diffuse, continuous inflammation of the colon extending from the rectum
    - 40-70% of patients can have mild inflammation of the upper GI tract
  - Crohn Disease (CD)
    - Can involve any area of the GI tract from the mouth to the anus
    - 20% of children can have perianal involvement
      - Skin tags
      - Fissures
      - Fistulas
      - Abscesses
  - IBD Unspecified
    - Those patients who cannot be classified as definitively having UD or CD

# Inflammatory Bowel Disease

## Clinical Presentation of IBD in Children and Adolescents

Presenting Symptom	Classification of IBD, % of Patients <sup>a</sup>	
	Crohn Disease	Ulcerative Colitis
General		
Weight loss	55-80	31-38
Fever	38	NA
Anorexia	2-25	6
Growth retardation	3-4	0
Lethargy	13-27	2-12
Gastrointestinal tract		
Abdominal pain	67-86	43-62
Diarrhea	30-78	74-98
Rectal bleeding	22-49	83-84
Nausea/vomiting	6	<1
Constipation	1	0
Perianal disease	6-15	0
Mouth ulcers	5-28	13

# Inflammatory Bowel Disease

## Box 2

### Suggested Initial Laboratory Evaluation for Suspected Inflammatory Bowel Disease in Children and Adolescents

#### Blood Laboratory Tests

Complete blood cell count (CBC) with differential

Inflammatory markers (C-reactive protein level, erythrocyte sedimentation rate)

Liver profile (levels of alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, bilirubin, and  $\gamma$ -glutamyl transferase)

Albumin level

#### Stool Examination

*Salmonella*, *Shigella*, *Campylobacter*, and *Yersinia* species, *Escherichia coli* O157, and *Clostridium difficile*

Ova and parasites

Occult blood

Fecal calprotectin or fecal lactoferrin

# Inflammatory Bowel Disease

- Treatment Goals:
  - Eliminate symptoms and restore quality of life
  - Restore normal growth
  - Eliminate complications
- Therapies for IBD:
  - Induce remission of active disease
  - Maintain remission
  - Some medications are only effective for either remission induction or maintenance, other medications are appropriate for both

# Inflammatory Bowel Disease Treatment

- Corticosteroids
  - Are effective for the induction of clinical remission
  - Numerous adverse effects with long-term use
- Enteral Nutrition Therapy
  - Treatment with exclusive enteral nutrition (100% of caloric needs from liquid formula) is as effective as corticosteroid therapy for inducing remission
  - Duration normally 8-12 weeks
- Aminosalicylates
  - Exert a topical anti-inflammatory effect on the intestinal mucosa
  - Can be given orally in formulations that release 5-aminosalicylic acid in the ileum or colon or topically via enema or suppository
  - Effective for induction and maintenance of remission
  - Sulfasalazine-not tolerated well due to sulfa-related adverse effects
  - Newer agents: Mesalamine, Balsalazide, Osalazine

# Inflammatory Bowel Disease Treatment

- Immunomodulators
  - Thiopurine drugs (azathioprine and mercaptopurine (6-MP))
  - Given their delayed onset, are mainly effective as maintenance therapy
  - Methotrexate is also being used for maintenance therapy
  - Can cause myelosuppression, elevated transaminase levels, and pancreatitis
- Anti-TNF Therapy
  - Monoclonal antibodies directed at TNF, a major pro-inflammatory cytokine in CD and UC
  - Typically used to treat IBD refractory to steroids or in those dependent to corticosteroids despite the addition of an immunomodulator
  - Superior to thiopurines for inducing complete mucosal healing of the intestine
    - Infusion: Infliximab
    - Subcutaneous injection: Adalimumab, Certolizumab, and Golimumab

# Inflammatory Bowel Disease

- Long-Term Issues

- Micronutrient deficiencies

- Can include: Vitamin D, vitamin B12, iron, folate
    - Due to chronic blood loss, intestinal malabsorption, chronic inflammation
    - Evidence that those with low vitamin D levels are more likely to have disease recurrence and levels should be maintained above 30 ng/mL to increase the likelihood of maintaining clinical remission

- Growth and bone health

- Decreased intake, malabsorption, corticosteroid use
    - Growth failure occurs in 40% of children with CD and 10% in those with UC
      - Close monitoring of linear growth and treatment should be directed at restoring normal growth
    - Bone metabolism is abnormal
      - Chronic inflammation may have the most profound effect
      - A dietary intake of 1000 to 1600 mg of elemental calcium and 800 to 1000 IU of vitamin D is recommended daily

# Inflammatory Bowel Disease

- Long-Term Issues, continued
  - Colon Cancer
    - Increased risk due to chronic inflammation
    - Those younger at diagnosis and with pancolitis are at higher-risk
    - 7 to 10 years after diagnosis, children should undergo colonoscopy with surveillance biopsy every 1 to 2 years
- Psychosocial Function
  - Have higher rates of depression and anxiety disorders
  - Can correlate with disease activity and sleep disturbances and corticosteroids may contribute
  - Refer patients for treatment when indicated

# Probiotics

- Contain microorganisms
  - Bacteria that are similar to those naturally occurring in the human gut
  - Can provide a health benefit when administered in adequate amounts
- Play an important role in the maintenance of immunologic equilibrium in the GI tract
  - The microbiome can be altered by diet, lifestyle, exposure to toxins, and antibiotic use
  - There is a relationship between disease, health, the immune system, and changes in the microbiome
- Available in two main forms:
  - Food
    - Yogurt with active cultures
  - Dietary supplements
    - Available over-the-counter or with a prescription
    - Generally available as a capsule or powder packet
    - Not regulated by the US Food and Drug Administration

# Probiotics

- Probiotic effectiveness can be species, dose, and disease specific
- Duration of use depends on the indication being treated
- One study found that a dosage of 5 billion colony-forming units or greater per day was significantly more effective than a lower dosage
- Gastrointestinal Conditions in which probiotics may be beneficial:
  - Acute Infectious Diarrhea
    - Should be started at the onset of symptoms and continue for 1 to 2 weeks
    - For traveler's diarrhea prevention, start 2 days prior to travel and continue throughout the trip
    - Not effective for diarrhea caused by a virus
  - Antibiotic-associated and *C. difficile* associated diarrhea
    - For prevention: start probiotics on the first day of antibiotic treatment and continue for 1 to 2 weeks following the completion of antibiotics
  - Ulcerative colitis
    - Can be effective for remission induction, but not for maintenance of remission
  - Constipation
    - Start at the onset of symptoms and continue while symptoms persist

# Probiotic Products

**Table 3. Select Probiotic Products\***

Product	Contents	Dose	Package size/count	Average retail price†
Activia yogurt	<b><i>Bifidobacterium animalis</i></b> subsp <i>lactis</i> DN-173 010	100 million CFUs per g	4 oz, 12 count	\$6
Align	<b><i>Bifidobacterium longum</i></b> subsp <i>infantis</i> 35624	1 billion CFUs per capsule	56	\$50
Bacid	<b><i>Lactobacillus acidophilus</i></b>	1 billion CFUs per capsule	50	\$20
Bio-K Plus	<b><i>Lactobacillus acidophilus</i></b> CL1285, <i>casei</i> LBC80R	12.5 billion CFUs per capsule 50 billion CFUs per 3.5-oz bottled beverage	15 12	\$17 \$27
Culturelle	<b><i>Lactobacillus rhamnosus</i></b> GG	10 billion CFUs + 200 mg inulin per capsule	50	\$40
DanActive	<b><i>Lactobacillus casei</i></b> subsp <i>immunitas</i> , <i>delbrueckii</i> subsp <i>bulgaricus</i> <b><i>Streptococcus thermophilus</i></b>	1 billion CFUs per 3.1-oz bottle	8	\$5
Florastor	<b><i>Saccharomyces boulardii</i></b>	1 billion CFUs per capsule	50	\$50

# Probiotic Products, Continued

Garden of Life Raw Probiotics Ultimate Care	<i>Bifidobacterium lactis, longum</i> <i>Brettanomyces anomalus</i> <i>Debaryomyces hansenii</i> <i>Kluyveromyces marxianus</i> <i>Lactobacillus acidophilus, brevis, bulgaricus, casei, fermentum, helveticus, kefir, kefiranofaciens, kefirgranum, parakefir, plantarum, rhamnosus</i> <i>Lactococcus cremoris, lactis, lactis biovar diacetylactis</i> <i>Leuconostoc cremoris, dextranicum, lactis, mesenteroides</i> <i>Saccharomyces cerevisiae, exiguum, turicensis, unisporus</i> <i>Streptococcus thermophilus</i> <i>Torulaspora delbrueckii</i>	100 billion CFUs per capsule	30	\$35
iFlora Multi-Probiotic	<i>Bifidobacterium bifidum, breve, lactis (infantis), lactis HN019, longum</i> <i>Lactobacillus acidophilus, brevis, bulgaricus, casei, gasseri, lactis, paracasei, plantarum, rhamnosus, salivarius</i> <i>Streptococcus thermophilus</i> NutraFlora scFOS (fructooligosaccharide)	32 billion CFUs per 2-capsule serving	60	\$25
Jamieson Probiotic Sticks	<i>Bifidobacterium longum</i> <i>Lactobacillus helveticus</i>	3 billion CFUs per powder stick	30	\$25
Kefir	<i>Bifidobacterium brevis, lactis, longum</i> <i>Lactobacillus acidophilus, casei, plantarum, reuteri, rhamnosus</i> <i>Leuconostoc cremoris, lactis subsp diacetylactis</i> <i>Saccharomyces florentinus</i>	7 to 10 billion CFUs per 8 oz	12	\$40

# Probiotic Products, Continued

Kefir	<i>Bifidobacterium brevis, lactis, longum</i> <i>Lactobacillus acidophilus, casei, plantarum, reuteri, rhamnosus</i> <i>Leuconostoc cremoris, lactis subsp diacetylactis</i> <i>Saccharomyces florentinus</i>	7 to 10 billion CFUs per 8 oz	12	\$40
Lactinex	<i>Lactobacillus acidophilus (gasseri), helveticus (bulgaricus)</i>	1 million CFUs per tablet 100 million CFUs per packet	50 12	\$20 \$20
Probiotic-10	<i>Bifidobacterium bifidum, breve, longum</i> <i>Lactobacillus acidophilus, casei, paracasei, plantarum, rhamnosus, salivarius</i> <i>Streptococcus thermophilus</i>	25 billion CFUs per capsule	50	\$15

*continues*

CFU = colony-forming unit.

\*—Limited to species and dosage studied.

†—Pricing from various online retailers, excluding shipping.

# Probiotic Products, Continued

**Table 3. Select Probiotic Products\*** (continued)

Product	Contents	Dose	Package size/count	Average retail price†
Ultimate Flora	<b><i>Bifidobacterium breve, lactis, longum</i></b> <b><i>Lactobacillus acidophilus, bulgaricus, casei, paracasei, plantarum, rhamnosus, salivarius</i></b>	30 billion CFUs per capsule	30	\$25
USANA Probiotic	<b><i>Bifidobacterium BB-12</i></b> <b><i>Lactobacillus rhamnosus LGG</i></b>	12 billion CFUs per 1-g packet	14	\$30
VSL#3	<b><i>Bifidobacterium breve, infantis, longum</i></b> <b><i>Lactobacillus acidophilus, delbruekii subsp bulgaricus, paracasei, plantarum</i></b> <b><i>Streptococcus thermophilus</i></b>	450 billion CFUs per packet 225 billion CFUs per 2-capsule serving	30 60	\$90 \$50

CFU = colony-forming unit.

\*—Limited to species and dosage studied.

†—Pricing from various online retailers, excluding shipping.

# Probiotics

- Safety:
  - There is a lack of clear guidelines on when to use probiotics and as to what would be the most effective strain to use for treating GI conditions
  - Probiotics are generally considered safe, but caution should be used in those who are immunocompromised
    - Risk of probiotic related bacteremia, fungemia, positive blood cultures
  - Long-term effects are unknown and further studies need to be conducted to evaluate the safety and effectiveness of probiotics

# Questions



# References

- Lightdale J, Gremse D, Section on Gastroenterology, Hepatology, and Nutrition. Gastroesophageal reflux: management guidance for the pediatrician. *Pediatrics*. 2013;131(5):e1684-e1695.
- Rosen R, Vandenplas Y, Singendonk M, et al. Pediatric Gastroesophageal Reflux Clinical Practice Guidelines: Joint Recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition. *J Pediatr Gastroenterol Nutr*. 2018;66(3):516-554.
- Tabbers MM, DiLorenzo C, Berger MY, et al. Evaluation and treatment of functional constipation in infants and children: evidence-based recommendations from ESPGHAN and NASPGHAN. *J Pediatr Gastroenterol Nutr*. 2014;58(2):258-274.
- Blackmer AB, Farrington EA. Constipation in the pediatric patient: an overview and pharmacologic considerations. *J Pediatr Health Care*. 2010;24(6):385-399.
- Sood MR. Chronic functional constipation and fecal incontinence in infants and children: treatment. Hoppin AG, ed. UpToDate. Waltham, MA: UpToDate Inc. <https://uptodate.com> (Accessed on July 22, 2019.)
- Lexicomp Online, Pediatric and Neonatal Lexi-Drugs Online, Hudson, Ohio: Wolters Kluwer Clinical Drug Information, Inc.; 2019; July 12, 2019.
- Hartman S, Brown E, Loomis E, Russell HA. Gastroenteritis in children. *American Family Physician*. 2019;99(3):159-165.
- Matson DO. Acute viral gastroenteritis in children in resource-rich countries: management and prevention. Torchia MM, ed. UpToDate. Waltham, MA: UpToDate Inc. <https://uptodate.com> (Accessed on July 1, 2019.)
- Freedman S. Oral rehydration therapy. Kim MS, ed. UpToDate. Waltham, MA: UpToDate Inc. <https://uptodate.com> (Accessed on July 1, 2019.)
- McDonald LC, Gerding DN, Johnson S, et al. Clinical Practice Guidelines for Clostridium difficile Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). *Clinical Infectious Diseases*. 2018;66(7):e1-e48.
- Crews J. Clostridioides (formerly clostridium) difficile infection in children: clinical features and diagnosis. Torchia MM, ed. UpToDate. Waltham, MA: UpToDate Inc. <https://uptodate.com> (Accessed on July 9, 2019.)
- Rosen M, Dhawan A, Saeed S. Inflammatory bowel disease in children and adolescents. *JAMA Pediatr*. 2015;169(11):1053-1060.
- Wilkins T, Sequoia J. Probiotics for gastrointestinal conditions: a summary of the evidence. *American Family Physician*. 2017;96(3):170-178.