

Diarrhea, Constipation, and Irritable Bowel Syndrome

728-655

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Learning Objectives

- Identify common medication causes of diarrhea and constipation
- Design a regimen to prevent and treat diarrhea or constipation
- Institute treatment for IBS depending on presenting symptoms

Reading Assignment

Pharmacotherapy. A Pathophysiologic Approach, 11th edition. Chapter 53. Diarrhea, Constipation and Irritable Bowel Syndrome. Pages 543-559

Reading guide for Chapter 53

The chapter's key concepts can be an initial roadmap for the chapter.

Use the learning objectives to guide your reading. The learning objectives have been chosen because of their relevance to immunology pharmacotherapy and are the source of the exam questions.

The majority of the self-assessment questions align with the content of the lecture.

Study questions:

1. Compare loperamide and diphenoxylate/atropine.
2. What is the role of fiber in the management of constipation?
3. What is irritable bowel syndrome?

Research Clerkship








- Opportunity to do research with a faculty member during clerkship year
- Permission to register by October 5.

Research Area	Faculty
Opioid use	Lim
Immunology and transplant	Hayney
Infectious diseases	Rose
Neurology and cannabinoids	Schmitz
Substance Use Disorders	Wenthur

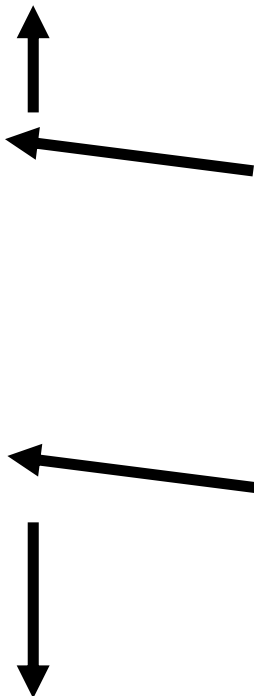


Continuum of bowel function

Bristol Stool Chart

Type 1		Separate hard lumps, like nuts (hard to pass)
Type 2		Sausage-shaped but lumpy
Type 3		Like a sausage but with cracks on the surface
Type 4		Like a sausage or snake, smooth and soft
Type 5		Soft blobs with clear-cut edges
Type 6		Fluffy pieces with ragged edges, a mushy stool
Type 7		Watery, no solid pieces. Entirely Liquid

Source: Henderson MC, Tierney LM, Smetana GW: *The Patient History: An Evidence-Based Approach to Differential Diagnosis*: www.accessmedicine.com
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- Death
- Bowel necrosis
- Bowel obstruction
- Constipation
- Abdominal distention
- Bloating
- Normal bowel function**
- Diarrhea
- Cramps
- Dehydration
- Electrolyte abnormalities
- Death

Diarrhea

Acute

Less than
14 day

Infectious

Persistent

14-29 days

Medical
condition

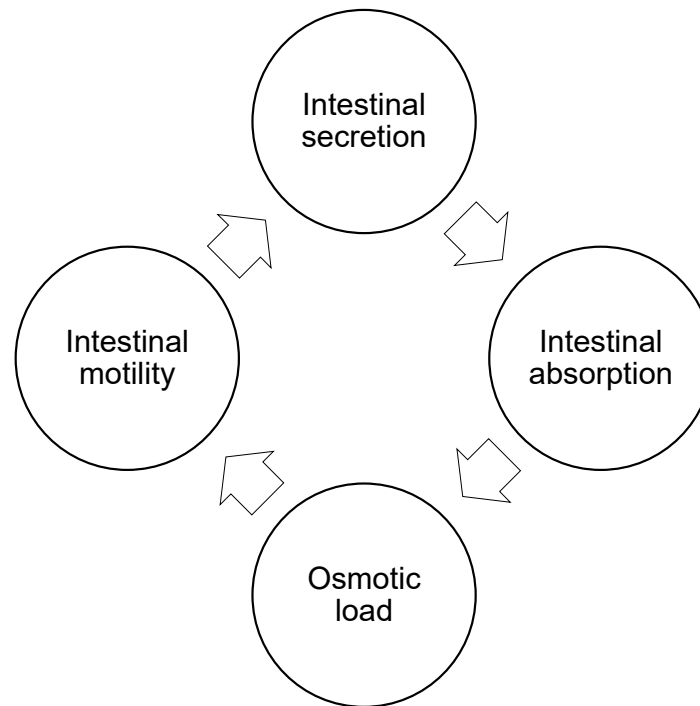
Chronic

30 or more
days

Medical
condition



Pathophysiology



Medication induced causes-diarrhea

- Challenge: find a package insert that does not list diarrhea as an adverse effect!
- See table 53-2.
- Consider sorbitol—often in liquid medications



Acute diarrhea

- Gastroenteritis
 - Common causes food, water
 - Viruses, bacteria
- Prevention
 - Food safety
 - Hand washing and hygiene
 - Immunizations (rotavirus, cholera)
 - Travel precautions

 Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

Food Safety

[Spanish](#)

4 STEPS TO FOOD SAFETY



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Travel Clinic


School of Pharmacy
UNIVERSITY OF WISCONSIN-MADISON

Self care exclusions

Patient age	Under age 6 months or weight under 8 kg, pregnancy
Onset/History	Lack of response to oral rehydration
Symptoms/Characteristics/Location	Persistent fever 102.2F, signs of severe dehydration/ large volumes out, severe abdominal pain Alarm symptoms



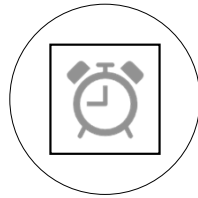
Self care alarm symptoms



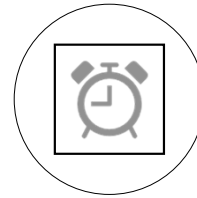
SEVERE
DEHYDRATION



FEVER



PERSISTENT
BLOOD IN
STOOL



UNEXPLAINED
CHANGE IN
BOWEL HABITS



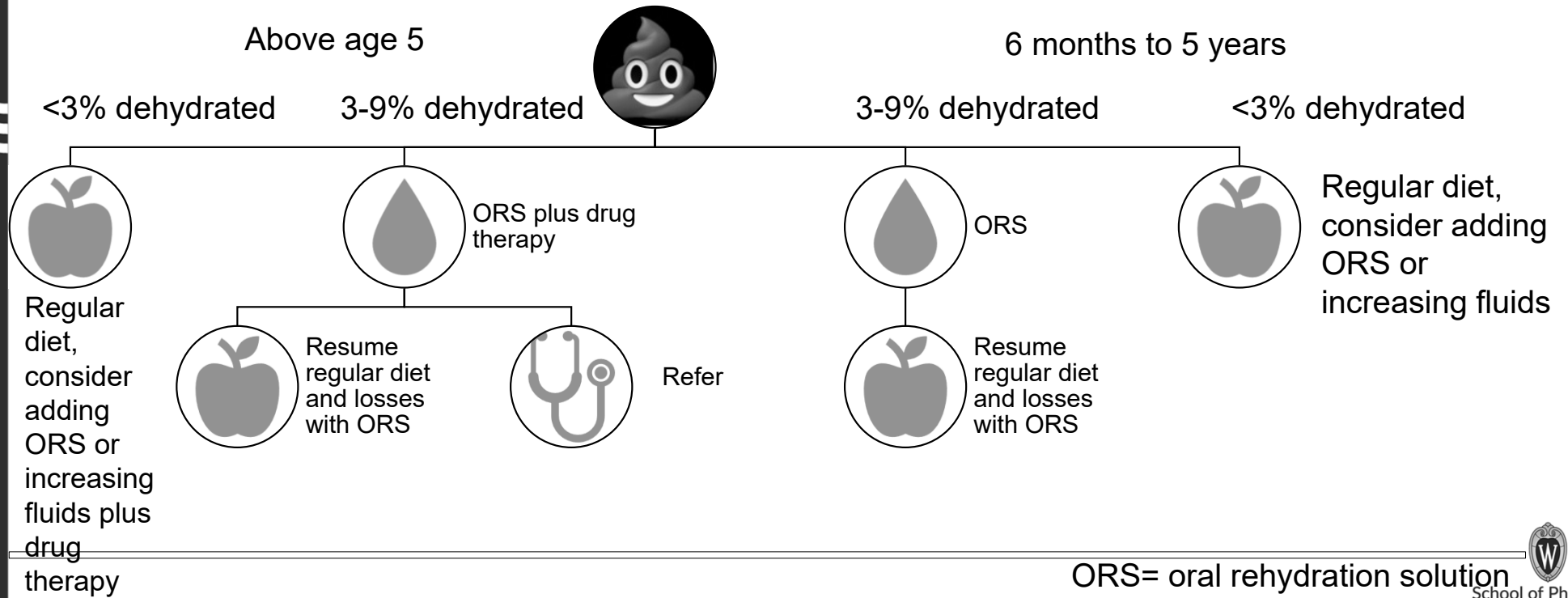
UNEXPLAINED
WEIGHT LOSS



	Self-treatable		Not Self-treatable
	Minimal/no dehydration	Mild/moderate dehydration	Severe dehydration
% body wt loss	Less than 3	3-9	More than 9
Mental status	Good, alert	Normal, fatigued/restless, irritable	Apathetic, lethargic, unconscious
Thirst	Normal, might refuse	Thirsty and eager	Poor/unable to drink
Heart rate	Normal	Normal to increased	Fast or if severe low
Pulse quality	Normal	Normal to decreased	Weak, thread, cannot find
Breathing	Normal	Normal to fast	Deep
Eyes	Normal	Slightly sunken	Deeply sunken
Tears	Present	Decreased	Absent
Mouth and tongue	Moist	Dry	Parched
Skin fold	Instant recoil	Recoil less than 2 sec	Recoil more than 2 sec
Capillary refill	Normal	Prolonged	Prolonged/minimal
Extremities	Warm	Cool	Cold, mottled, cyanotic
Urine output	Normal to decreased	Decreased	Minimal
Unformed stools	Less than 3	3-5	6-9
Other	Afebrile, normal BP/P	Afebrile or fever, normal BP or mild orthostatic changes	Fever above 102.2F, low BP, dizzy

Adapted from Krinsky DL et al. Handbook of Nonprescription Drugs. 19th ed.

Treatment algorithm- diarrhea



ORS= oral rehydration solution



Treatment categories-diarrhea

Antimotility

- Diphenoxylate
- Loperamide
- Opium tincture

Adsorbents

- Kaolin-pectin
- Polycarbophil

Antisecretory

- Bismuth subsalicylate
- Lactase



Individual therapy-oral rehydration solutions (ORS)

Action	Provide fluid, electrolytes and calories (glucose) to maintain/replace		
Product	Precautions/side effects	Dosing	Notes
Powder, solution, popsicles		Age 6 months-5 years 50-100 mL/kg over 3-4 hours for 4-6 hours. Extra 10 mL/kg for each loose stool Age 6 and up 2-4L over 3 hours. Extra for ongoing losses	Different flavors available More palatable when chilled
Soda/juice	Carbonation may or may not be palatable		
Sports drink			Different flavors available Vary in electrolyte/glucose content

75 mEq/L sodium for rehydration

Individual drug therapy- antimotility

Action			
Mu receptor activity to reduce peristalsis, anticholinergic			
Medication	Precautions/side effects	Dosing	Notes
Diphenoxylate/ atropine	Confusion, drowsiness	Age 2 and up Solution, tab	C-V substance
Loperamide	BOX: Euphoria, Torsades/sudden death with higher than max dose	Age 2 and up Solution, tab	Max 16 mg/day Take with plenty of fluids
Opium tincture or paregoric	1 mL=morphine 10 mg		C-II substance Drops or mLs



Individual drug therapy-adsorbents

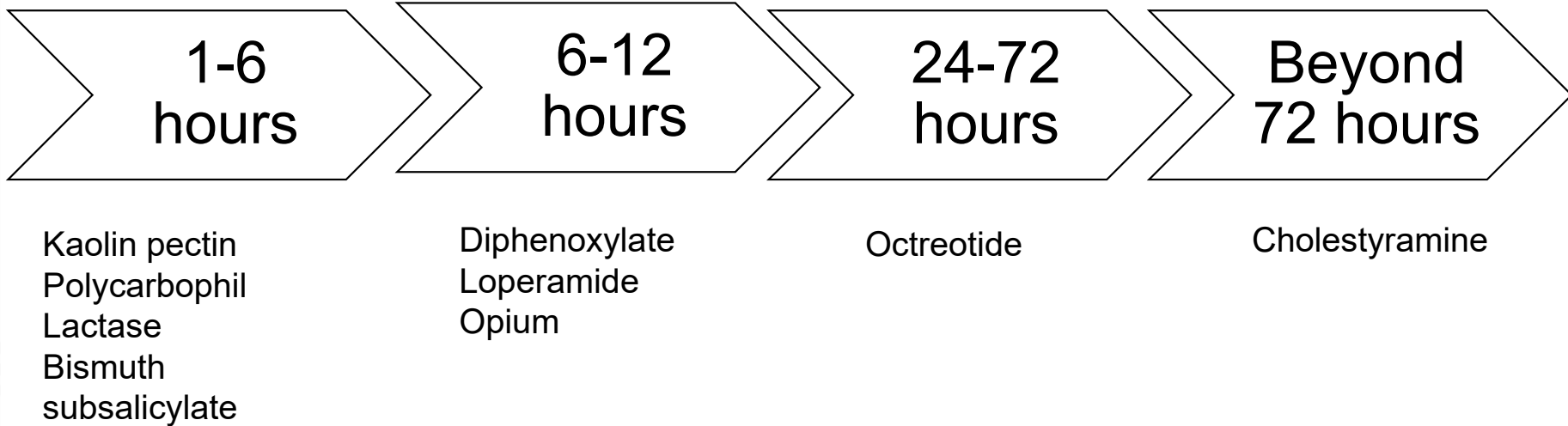
Action		Absorbing excess intestinal fluids (non-specific)	
Medication	Precautions/side effects	Dosing	Notes
Kaolin-pectin		30-120ml after each loose stool	Read label
Polycarbophil		2 tabs chewed 4x/day or after loose stool (NMT 12 tabs/day)	Can absorb 60x its weight in water Take with 8 oz water
Action	Binding bile acids limits their cathartic effects		
Cholestyramine	Binding other medications	Daily up to 4 times daily Powder	Drink shortly after mixing (2-6 oz non-carbonated fluid) with meals



Individual drug therapy-antisecretory

Action	Salicylate has antisecretory effects		
Medication	Precautions/side effects	Dosing	Notes
Bismuth subsalicylate	Salicylate containing	Suspension, tab 2 month and older	If chew tab allow to dissolve before swallowing Tongue may darken
Lactase		Age 4 and up	If related to lactose intolerance
Action	Blocks serotonin release, inhibits intestinal secretion and increased absorption		
Octreotide	Injection site pain, can cause gall/biliary stones	Subcutaneous	Can convert to depot

Timeline for activity



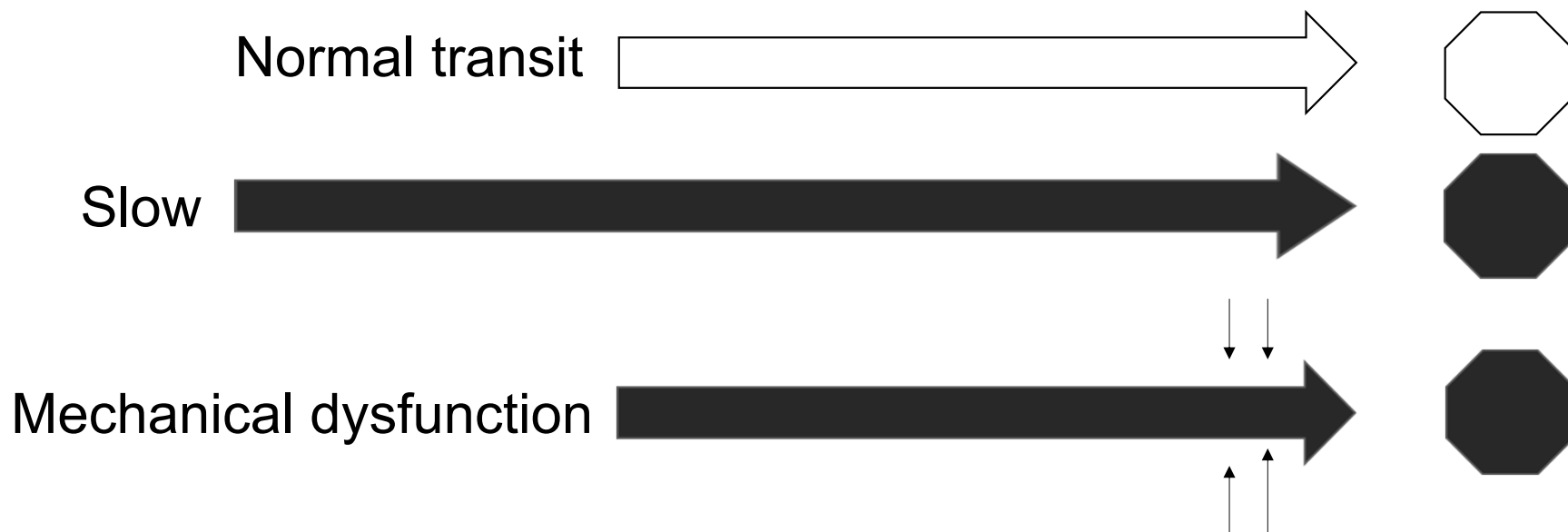
Cost comparison

\$	Lactase, bismuth subsalicylate
\$\$	Diphenoxylate/atropine, loperamide, opium, cholestyramine
\$\$\$	Octreotide

\$=less than \$10/month, \$\$=\$10-50/month, \$\$\$ greater than \$50/month. If inpatient only medication cost shown per day.



Pathophysiology-primary constipation



Medication induced causes-constipation

- Challenge: find a package insert that does not list constipation as an adverse effect!
- See table 53-6.



Self care exclusions

Patient age	Age less than 2
Onset/History	Symptoms lasting more than 14 days or recurring over 3 months Daily self-initiated laxative use
Symptoms/Characteristics/Location	Fever, intense abdominal pain, significant distention/cramping/flatulence, nausea/vomiting, anorexia Alarm symptoms

If caused by medications intervene/refer
If caused by condition refer



Self-care alarm symptoms



RECURRENT
NAUSEA/VOMITING



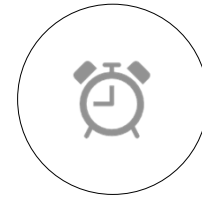
UNEXPLAINED
ANEMIA



HEMATEMESIS



WT LOSS
(UNINTENTIONAL
MORE THAN 10%)



FAMILY HISTORY
OF MALIGNANCY



Fiber recommendations

- Daily goal 25-35 g/day (based on 14 g/1000 kcal)



3.4 g	3.5 g	4 g	7 g	8 g	9 g	15 g
1 whole	1 ounce	2 slices	¼ cup	1 cup	1 bar	1 cup

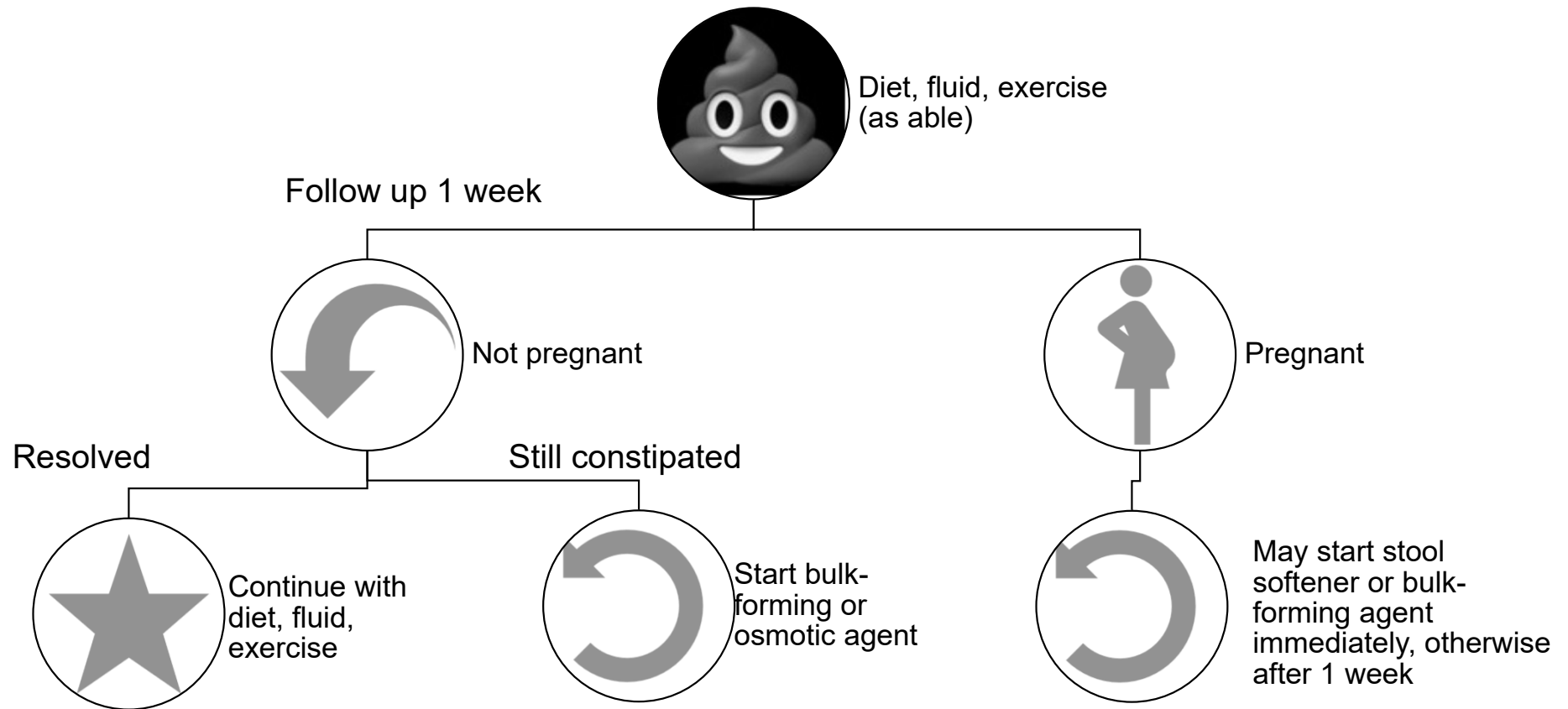


Dietary impact on bowel function

- Choice of foods (fat, fiber) impact on GI transit
- Food security may impact access
- Be aware of referral options (food pantries, programs based on income)



Treatment algorithm- constipation



For opioid induced constipation use laxatives as first-line treatment.

Strong recommendation, moderate quality evidence. AGA 2019 Guideline on medical management of OIC.

Order/prescription verification

- Discontinue PRN orders if a scheduled order replaces it
- Order sets with multiple options
- Consider optimal time of day
- Bowel preparation



Treatment categories-constipation

Bulk-forming laxative

- Methylcellulose
- Polycarbophil
- Psyllium

Guar gum

Emollient laxative

- Docusate
- Mineral oil

Stimulant laxative

- Bisacodyl
- Senna

Osmotic laxative

- Polyethylene glycol 3350
- Lactulose
- Sorbitol

Magnesium salts
Glycerin
Sodium phosphate

Intestinal Secretagogue

- Lubiprostone
- Linaclotide
- Plecanatide

Prucalopride

Opioid Antagonist

- Methylnaltrexone
- Naloxegol
- Naldemidine

Alvimopan



Individual drug therapy- bulk forming

Action				Providing bulk in intestines and increased water content			
Medication	Precautions/side effects	Dosing	Notes				
Methylcellulose		Age 6 and up Cap or powder	Mix with 8 oz liquid				
Polycarbophil		Age 6 and up	Can absorb 60x it's weight in water Take with 8 oz water				
Psyllium	Anaphylaxis possible with inhaled powder	Age 1 and up Cap or powder	Mix with 8 oz liquid				
Guar gum		Powder					

Watch sugar/calorie content. Sugar-free versions available though avoid with phenylketonuria



Individual drug therapy-emollient/stool softener

Action	Water and liquid enter stool to hydrate and soften		
Medication	Precautions/side effects	Dosing	Notes
Docusate sodium	Can cause throat irritation	Age 2 and up Capsule, liquid, enema	Combination tablet with senna
Docusate calcium			
Docusate potassium			
Mineral oil	Aspiration causing pneumonia	Age 6 and up Liquid Oral, NG, rectal	Absorption of fat-soluble vitamins impaired



Individual drug therapy-stimulant laxative

Action	Irritated nerves stimulate colonic motility, decreased water absorption		
Medication	Precautions/side effects	Dosing	Notes
Bisacodyl		Age 2 and up Oral, suppository	
Senna	Abd cramps	Age 2 and up Oral, liquid	Combination tablet with docusate



Individual drug therapy-osmotic laxative

Action	Draws water into intestine to hydrate and soften		
Medication	Precautions/ side effects	Dosing	Notes
Polyethylene glycol 3350		Age 2 and up Daily dose should be sufficient	mL/tsp, g, capful, packet Mix 4-8 oz liquid
Magnesium	Many interactions related to med timing	Age 2 and up PO, solution, IV	Numerous salts mL vs. bottle
Lactulose/ sorbitol/glycerin		Generally daily dosing or less Okay for peds Liquid, suppository	Mix lactulose with juice, water, milk
Sodium phosphate	Use caution in CKD Bloating, abd pain	Age 2 and up Solution, enema	If PO take with 8 oz cool water plus 8 oz additional water



Individual drug therapy- intestinal secretagogue

Action		Stimulate fluid secretion via Cl channel or guanylate cyclase receptor in enterocytes		
Medication	Precautions/side effects	Dosing		Notes
Lubiprostone	Dyspnea, nausea, hypotension			Take with food to lessen nausea
Linaclootide	18 and up only			Take before first meal to avoid diarrhea due to fat
Plecanatide	18 and up only			
Prucalopride	Headache, dizziness, fatigue, suicidal ideation			



Individual drug therapy- opioid antagonist/PAMORA peripherally acting mu opioid receptor antagonist

Action	Block receptors in gut restoring GI motility, no impact on pain relief action		
Medication	Precautions/side effects	Dosing	Notes
Methylnaltrexone	May cause opioid withdrawal GI: abd pain, gas, nausea	Oral/Subcutaneous	
Naldemidine	GI: abd pain, diarrhea		CYP3A4 substrate interactions
Naloxegol	Severe abd pain, GI perforation		CYP3A4 substrate interactions, avoid grapefruit juice
Alvimopan	Avoid opioids 7 days prior to use. Risk of MI, hypokalemia Japanese pts increase GI side effects	Begin day prior to surgery, resume day after surgery	Inpatient use less than 7 days, REMS

Timeline for activity

1-6
hours

Magnesium
Bisacodyl PR
Glycerin PR
Sodium phosphate

6-12
hours

Bisacodyl PO
Senna
Mineral oil

24-72
hours

Docusate
Lactulose
Polyethylene
glycol 3350
Sorbitol
Methylcellulose
Polycarbophil
Psyllium
Guar Gum
Alvimopan
Methylnaltrexone
Naldemidine
Naloxegol
Lubiprostone
Linaclotide
Plecanatide
Prucalopride

Beyond
72 hours

Dietary fiber
Exercise



Cost comparison

\$	Docusate, bisacodyl, senna, polyethylene glycol 3350, lactulose, sorbitol, glycerin, sodium phosphate, magnesium, methylcellulose, polycarbophil, psyllium, guar gum, mineral oil
\$\$	
\$\$\$	Alvimopan, methylnaltrexone, naldemidine, naloxogol, lubiprostone, linaclotide, plecanatide, prucalopride

\$=less than \$10/month, \$\$=\$10-50/month, \$\$\$ greater than \$50/month..



Probiotics

- Effectiveness species, dose, disease-specific
 - Cochrane review 5 billion CFU or more per days significantly more effective
- Duration of therapy depends on indication
 - Begin at onset of symptoms and continue as symptoms persist
- Safe for infants, children, adults, older adults
- Use caution if immune compromised/vulnerable



Myths related to constipation

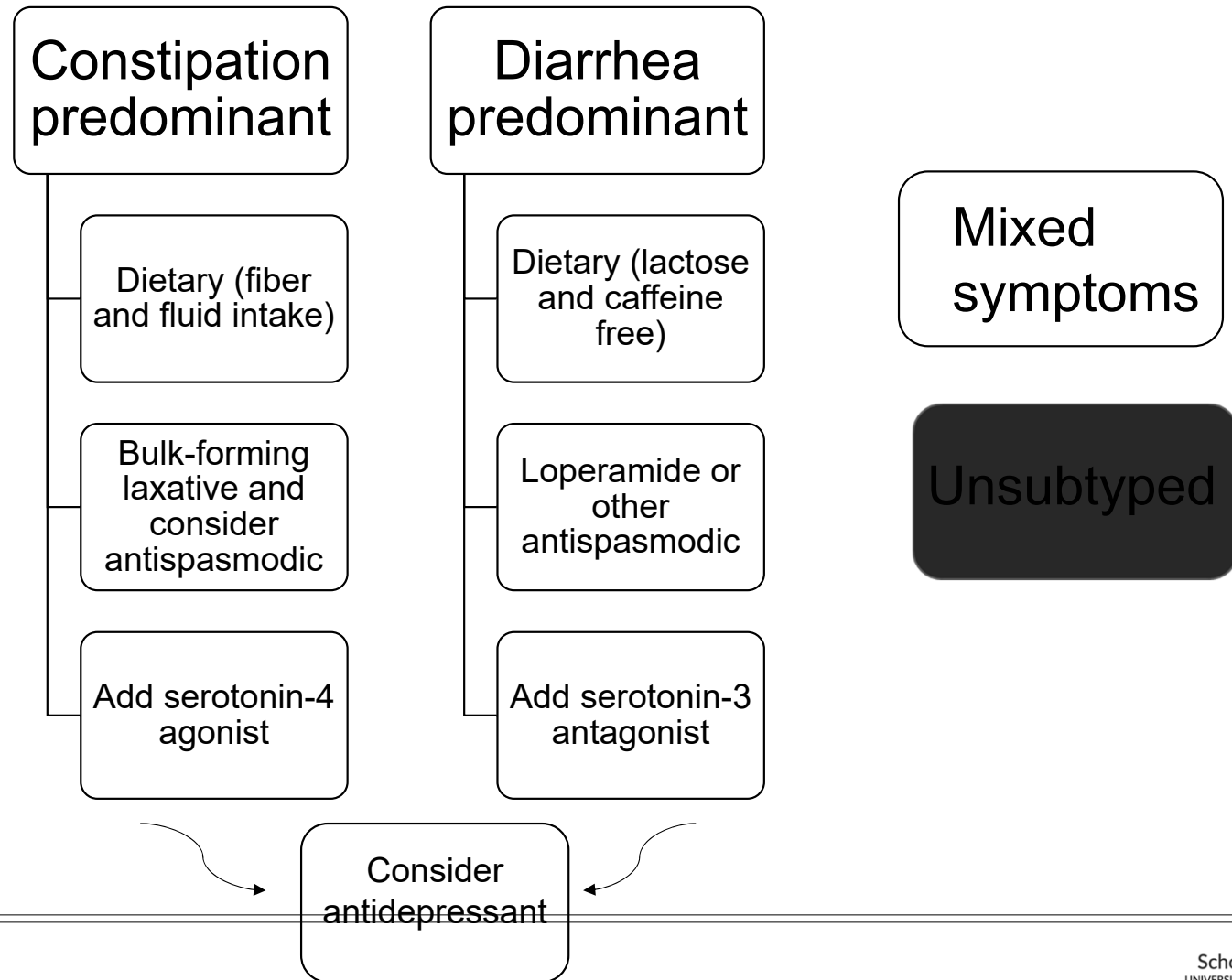
- Diets lacking fiber cause constipation
- Increasing fluid intake treats constipation
- Limited physical activity causes constipation
- Chronic laxatives cause damage
- Tolerance develops to laxatives
- People becoming physically dependent to laxatives



Irritable Bowel Syndrome (IBS)

- Brain-gut disorder. Those affected due to predisposition or environmental exposure, an abnormal stress response, combined with psychological distress and infection/inflammation results in IBS symptoms.
- Definition- chronic abd pain and altered bowels) in absence of organic cause. Depending on diagnostic criteria symptoms for 3-6 months..
- Prevalence 5-15% in North America/Europe and females 2:1 in North America

IBS



Individual drug therapy-constipation predominant

Action	5HT4 stimulates peristaltic reflex and intestinal secretion		
Medication	Precautions/side effects	Dosing	Notes
Tegaserod	MI/CVA/TIA/angina Suicidality Headache/abd pain	30 min prior to a meal	Females less than 65
Action	Sodium/hydrogen exchanger 3 inhibitor to increase water, faster transit		
Tenapanor		Immediately prior to a meal	Not yet available



Individual drug therapy-diarrhea predominant

Action	Mixed opioid receptor activity to reduce abd pain and diarrhea		
Medication	Precautions/side effects	Dosing	Notes
Eluxadoline	Alcohol increases pancreatitis risk	With food	C-IV substance
Action	Serotonin antagonist reducing visceral pain, colonic transit and secretions		
Alosteron	BOX: ischemic colitis, constipation	Twice daily	
Action	Antimicrobial may modify gut biome and gas		
Rifaximin	Peripheral edema, dizziness, fatigue		Used 14 days or less

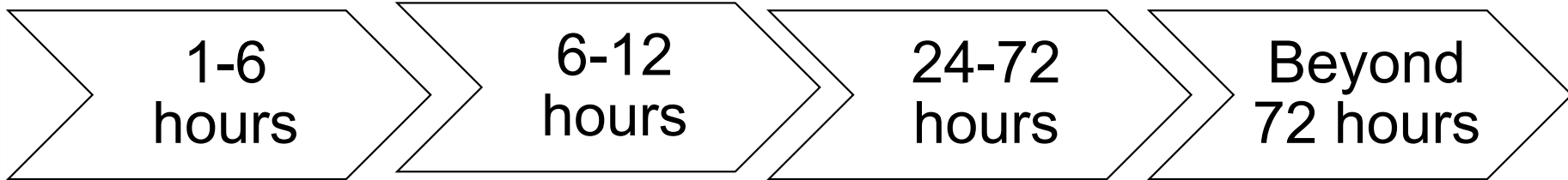


Antidepressants for IBS diarrhea-predominant

- Tricyclic antidepressants—benefit demonstrated
- SSRI—conflicting results
 - Duloxetine gradual improvement in symptom severity and quality of life over 12 weeks
- Either TCA or SSRI useful for treating IBS abdominal pain
 - Avoid TCA if constipation predominant



Timeline for activity



Alosteron
Rifaximin
Eluxadoline

Tegaserod



Cost comparison

\$	
\$\$	
\$\$\$	Tegaserod, eluxadoline, rifaximin, alosteron

\$=less than \$10/month, \$\$=\$10-50/month, \$\$\$ greater than \$50/month. If inpatient only medication cost shown per day.



Patient counselling

- Rectal administration of medications handout
- Body positioning recommendations
- Most common side effects relate to underlying condition (cramping, gas, bloating, diarrhea/constipation)
- Can interact/bind with other medications
- Encourage fluids, diet and exercise as applicable



Summary

- OTC treatment often means paying shelf price
- Product selection: timing, cost, prior experience, concurrent conditions,
- If you anticipate diarrhea/constipation happening educate and offer management/treatment options