GERIATRIC PHARMACIST

BOOT CAMP

Gastrointestinal Disorders in the Older Adult

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Supported in part by an educational grant from the ASCP Foundation.

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Meet the Speaker

- Education & Training:
  - PharmD, University of Rhode Island
  - MEd, Northeastern University
  - PGY-1 Pharmacy Practice Residency, Hospital of Saint Raphael, New Haven, CT
- Associate Clinical Professor, Assistant Dean for Academic Affairs and Assessment, PharmD Program Director, Northeastern University, Boston, MA
- Board Certified Geriatric Pharmacist (2011) and Board Certified Pharmacotherapy Specialist (2013)
- ASCP Fellow (2020)
- Research areas: Geriatrics, internal medicine, scholarship of teaching and learning

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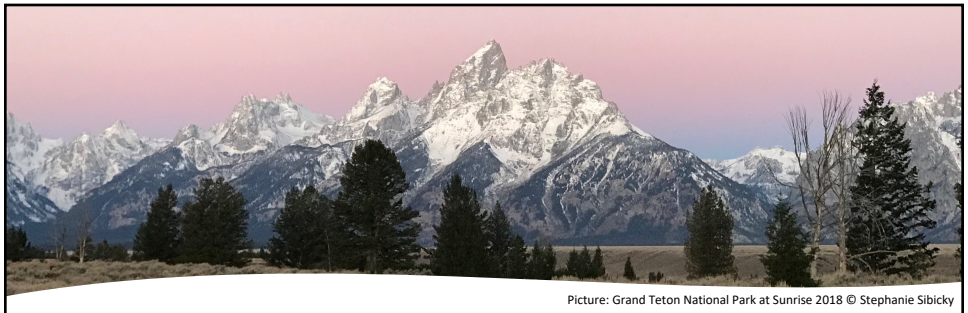

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Disclosures

Stephanie Sibicky does not have relevant financial relationships with ineligible companies.

None of the planners for this activity have relevant financial relationships to disclose with ineligible companies.

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Learning Objectives

1. Determine therapeutic options for diarrhea, constipation, gastroesophageal reflux disorder, nausea, vomiting, and anemia in the older adult.
2. Interpret gastrointestinal clinical findings and incorporate functional status into therapeutic decision-making.
3. Resolve and/or prevent gastrointestinal medication-related problems.
4. Apply gastrointestinal therapy recommendations and person-specific goals to senior patient cases.

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Outline

Please refer to Reference Sheet for additional information about medications mentioned!

Review:

- Age-related changes to the gastrointestinal (GI) tract
- Pharmacokinetic changes

Disease-state overview:

- Diarrhea
- Constipation
- GERD
- Nausea/Vomiting
- Anemia

GERD – gastroesophageal reflux disease

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Patient Case – Alex

Alex is a 72-year-old patient at your medicine clinic. They have several chronic conditions that are well managed overall. Their medication list is complex and has not been updated recently. Alex has worsening symptoms of GERD/heartburn over the past 5-7 years that have become so bothersome they are affecting Alex's quality of life.

Alex is overwhelmed with their chronic conditions and would like to get off any unnecessary medications, if possible, except their GERD treatment because of current symptoms.

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Alex's Medical History

- PMH:
  - Anemia (unspecified)
  - Chronic kidney disease (stage 2)
  - Hyperlipidemia
  - Hypertension (stage 2)
  - Osteoarthritis (knee)
  - Osteoporosis
  - Type 2 diabetes
  - Vitamin D deficiency
- Allergy to trimethoprim/ sulfamethoxazole (rash)
- Medications:
  - Amlodipine 10 mg PO daily
  - Aspirin 81 mg PO daily
  - Ferrous sulfate 325 mg PO twice daily
  - Ibandronate 150 mg PO every month
  - Ibuprofen 400 mg PO q4-6 hours as needed
  - Lisinopril 40 mg PO daily
  - Metformin 1000 mg PO twice daily
  - Meloxicam 15 mg PO daily
  - Bismuth subsalicylate PO as needed
  - Semaglutide (injectable) 1 mg every week (dose increased 1 week ago)
  - Rosuvastatin 20 mg PO daily

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Review

AGE-RELATED CHANGES TO GI TRACT	DISTRIBUTION

• Decreased saliva, swallowing capabilities, dentition
• Decreased gastric acid and increase in pH
• Smaller liver mass and blood flow = decreased first-pass effect, metabolism
• Small intestine remains mostly unaffected
	• Absorption = minimal changes
	• Distribution = decreased albumin
	• Metabolism =
	  • Altered depending on extraction ratio of medications
	  • May have reduction in Phase I (CYP450)
	• Elimination =
	  • Increased comorbidities leads to alterations
	  • Possible p-glycoprotein alterations

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Diarrhea

- Older adults at increased risk due to:
  - Exposure (e.g., living in residential facilities, hospitalizations)
  - Physical condition, such as frailty
  - Comorbidities
  - Increase in medication use
- Higher morbidity and mortality secondary to dehydration and electrolyte disturbances
- Definition: ≥ 3 unformed stools in 24 hours + enteric symptom (nausea, vomiting, abdominal cramps, tenesmus, urgency, and/or flatulence)
- Can be acute (1-7 days) or chronic (weeks to months)

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Riddle MS, et al. Am J Gastroenterol. 2016 May;111(5):602-22.
Dawod E, at al. Clin Geriatr Med. 2021 Feb;37(1):103-117.

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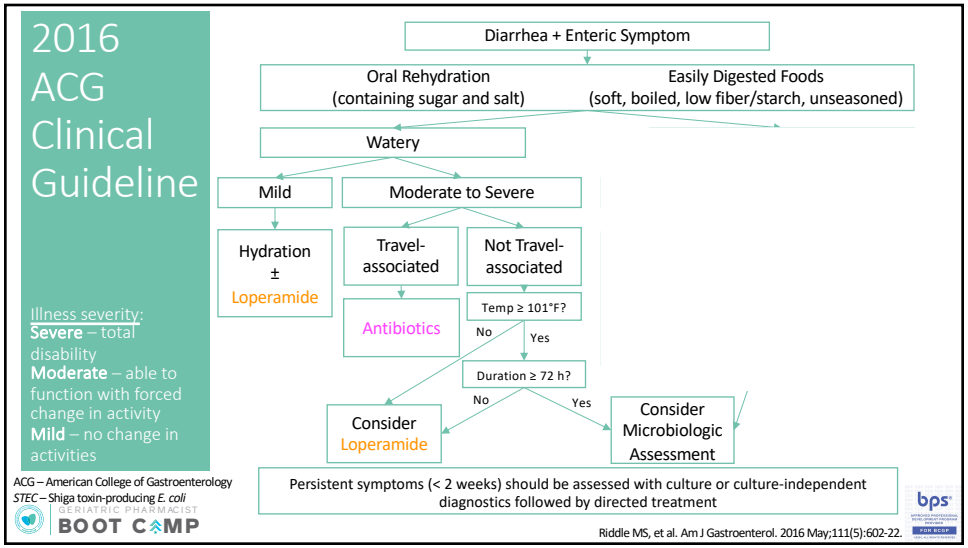
2016 ACG Clinical Guideline
Illness severity:
Severe – total disability
Moderate – able to function with forced change in activity
Mild – no change in activities
Diarrhea + Enteric Symptom
Oral Rehydration (containing sugar and salt)
Easily Digested Foods (soft, boiled, low fiber/starch, unseasoned)
Watery
Mild
Moderate to Severe
Hydration ± Loperamide
Travel-associated
Not Travel-associated
Antibiotics
Temp ≥ 101°F?
No
Yes
Duration ≥ 72 h?
No
Yes
Consider Loperamide
Consider Microbiologic Assessment
Persistent symptoms (< 2 weeks) should be assessed with culture or culture-independent diagnostics followed by directed treatment
ACG – American College of Gastroenterology
STEC – Shiga toxin-producing E. coli
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Riddle MS, et al. Am J Gastroenterol. 2016 May;111(5):602-22.

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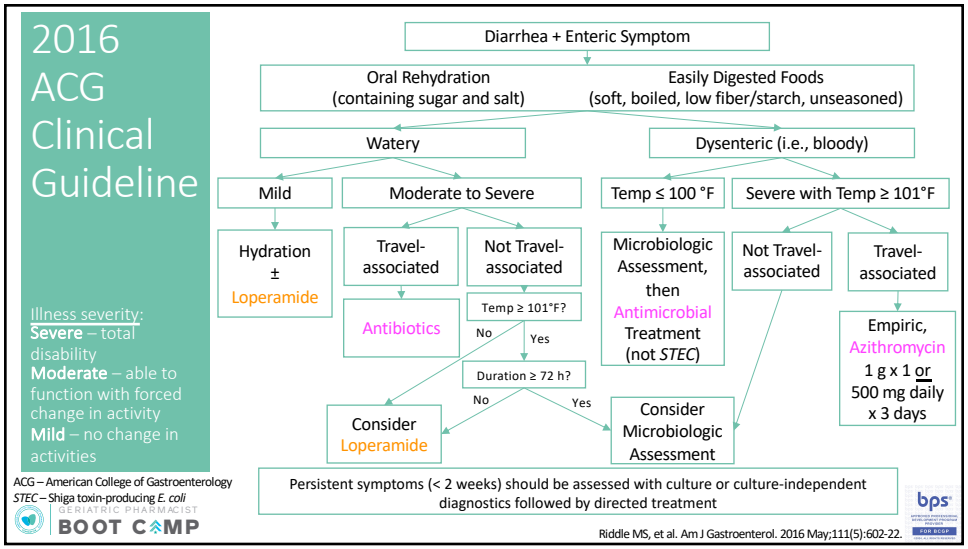
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Mild – no change in activities
Diarrhea + Enteric Symptom
Oral Rehydration (containing sugar and salt)
Easily Digested Foods (soft, boiled, low fiber/starch, unseasoned)
Watery
Dysenteric (i.e., bloody)
Mild
Moderate to Severe
Temp ≤ 100 °F
Severe with Temp ≥ 101°F
Hydration ± Loperamide
Travel-associated
Not Travel-associated
Microbiologic Assessment, then Antimicrobial Treatment (not STEC)
Not Travel-associated
Travel-associated
Antibiotics
Temp ≥ 101°F?
No
Yes
Empiric, Azithromycin 1 g x 1 or 500 mg daily x 3 days
Duration ≥ 72 h?
No
Yes
Consider Loperamide
Consider Microbiologic Assessment
Persistent symptoms (< 2 weeks) should be assessed with culture or culture-independent diagnostics followed by directed treatment
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Infectious Diarrhea

- Viral
  - Predominant type, norovirus is most common
  - 90% of norovirus-associated deaths are in older adults > 65 years old
  - Supportive care, no FDA-approved treatment
  - Potentially associated with COVID-19
- Bacterial
  - Often more severe with fever, most common *Salmonella* and *Campylobacter*
  - Stool studies (culture, PCR) guide therapy
  - Antibiotics for immunocompromised, severe inflammatory disease, travel-associated, *Clostridioides difficile*
- Parasitic (e.g., *Giardia*)

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Riddle MS, et al. Am J Gastroenterol. 2016 May;111(5):602-22.
Dawod E, at al. Clin Geriatr Med. 2021 Feb;37(1):103-117.
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Medication-Associated Diarrhea

KEY: Osmotic | Inflammatory | Promotility | Secretory

Antibiotics: clindamycin, beta-lactams, quinolones	Chemotherapy: 5-FU, methotrexate, irinotecan, cisplatin, rituximab	Anti-constipation: magnesium-containing, lactulose, PEG	Sugar alcohols: mannitol, sorbitol, xylitol	ACE-inhibitors
NSAIDs	SSRIs	AChE-inhibitors	Promotility: metoclopramide, erythromycin	Digoxin
Metformin	Misoprostol	Caffeine	Simvastatin	Herbals: St. John's wort, aloe vera, turmeric

5-FU – 5-fluorouracil; PEG – polyethylene glycol; ACE – angiotensin-converting enzyme;
NSAIDs – nonsteroidal anti-inflammatory drugs; SSRI – selective serotonin reuptake inhibitors; AChE – acetylcholinesterase

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Dawod E, at al. Clin Geriatr Med. 2021 Feb;37(1):103-117.

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Other Diarrheas in Older Adults

Overflow
- Often overlooked
- Caused by constipation
- No antidiarrheals

Lactase deficiency
- High prevalence in older adults (> 50%)
- Replacement or FODMAP diet

Malabsorption
- Impaired carb and fat digestion
- Pancreatic or biliary insufficiency

IBD and IBS-D

Celiac disease

Tube feedings

FODMAP – fermentable oligosaccharides, disaccharides, monosaccharides, and polyols; IBD – inflammatory bowel disease; IBS-D – irritable bowel syndrome, diarrhea predominant

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Dawod E, at al. Clin Geriatr Med. 2021 Feb;37(1):103-117.
Shiller LR. Gastroenterol Clin N Am. 2009 Sep;38(3):481-502.

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Diarrhea: Non-pharmacologic Treatment

- Oral rehydration solutions (ORS)
  - Prevents dehydration and electrolyte losses
  - Examples include World Health Organization (WHO)-ORS, Pedialyte
  - Watch sugar concentrations in sports drinks like Gatorade
  - Caution with comorbidities like heart failure, chronic kidney disease
- Food changes
  - BRAT (bananas, rice, apples, toast) limits other foods
  - Can include soft, bland, unseasoned, broths/soups, oatmeal, crackers
  - Avoid dairy, alcohol, green-leafy vegetables, and greasy, spicy, acidic, and sweet foods

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Shiller LR. Gastroenterol Clin N Am. 2009 Sep;38(3):481-502.

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Diarrhea: Non-prescription Treatment

PROBIOTICS	• Most benefit for prevention of antibiotic-associated diarrhea (AAD) with *Lactobacillus* or *Saccharomyces* strains • In older adults, no positive effect of probiotic use and reduced risk of AAD (RR 0.94, 95% CI 0.76-1.15) compared to younger adults (RR 0.47, 95% CI 0.4-0.56) • Benefit if started early, separate from antibiotics by at least 2 hours
BISMUTH SUBSALICYLATE	• Antimicrobial (bismuth), antisecretory and anti-inflammatory (subsalicylate) • Useful if fever or dysentery • 3.7X greater odds of diarrhea relief compared to placebo (95% CI 2.1-6.3, p < 0.001) • Available in multiple formulations (e.g., tablet, chewable, liquid) • Temporary darkening of tongue & stools important counseling point • Caution for patients on anticoagulants

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Brum JM et al. Dig Dis Sci. 2021 jul;66(7):2323-35.

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Diarrhea: Opioid-like Antimotility Agents

LOPERAMIDE	• Mu-opioid receptor agonist, anti-peristaltic • Only if NO fever or dysentery • Decreases symptoms about one day earlier than placebo, better reduction compared to bismuth • Concern at high doses for arrhythmias including QTc-prolongation (boxed warning) and opioid-effects (e.g., euphoria, "high")
DIPHENOXYLATE-ATROPINE	• Diphenoxylate chemically similar to meperidine; atropine added to prevent misuse • Concern for opioid and anticholinergic side effects • Loperamide more effective in cross-over trials • Listed on the American Geriatrics Society Beers Criteria to avoid use
TINCTURE OF OPIUM	• Chemotherapy-related or treatment-resistant chronic diarrhea • Safety concern with dosing and confusion with paregoric

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Dawod E, at al. Clin Geriatr Med. 2021 Feb;37(1):103-117.
Shiller LR. Gastroenterol Clin N Am. 2009 Sep;38(3):481-502.

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Other Treatments for Diarrhea

- Lactase enzymes or restriction/alternatives
- Bile acid sequestrants (cholestyramine, colestipol, colesevelam)
  - For bile acid-related malabsorption or IBS-D
  - Different formulations available (e.g., powder, tablet, granules)
- Eluxadoline (Viberzi®)
  - For IBS-D, mu- and kappa-opioid receptor agonist and delta-opioid antagonist
  - 100 mg twice daily (75 mg if intolerant or eGFR < 60 mL/min/1.73 m^3)
  - Concern for pancreatitis or biliary disorders (contraindicated if no gallbladder)
- Alosetron (Lotronex®)
  - For women with IBS-D who failed 6-months of conventional treatment, 5-HT_3 antagonist
  - Modified REMS program after severe constipation and ischemic colitis
  - 0.5 mg twice daily (reduce to once daily if constipation), titrate in 4 weeks to 1 mg twice daily

5-HT3 – 5-hydroxytryptamine (serotonin) 3; REMS – risk evaluation and management strategy

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Dawod E, at al. Clin Geriatr Med. 2021 Feb;37(1):103-117.
Shiller LR. Gastroenterol Clin N Am. 2009 Sep;38(3):481-502.

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Self-Assessment Question #1

Alex mentions that they have been experiencing watery diarrhea, no fever, and has taken bismuth subsalicylate for 2 days with no relief.

Which of the following medications is MOST appropriate?

A. Alosetron
B. Loperamide
C. Oral vancomycin
D. Diphenoxylate/atropine

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Constipation

- Age-related increase in prevalence
  - > 65 years old: 26% women, 16% men
  - > 85 years old: 34% women, 26% men
- Up to 80% of older adults in nursing facilities

PRIMARY			SECONDARY
Normal Transit	**Slow Transit**	**Anorectal Dysfunction**	Neurologic conditions (e.g., Parkinson's), hypothyroidism, hypercalcemia, malignancy, medications, diet, lifestyle
Most common (functional constipation); may also include IBS-C (pain and discomfort with defecation)	Primary deficits in gut innervation (neuropathic) or the muscle itself (myogenic)	Increased rectal compliance, impaired sensation, impaired coordination of pelvic muscles	

IBS-C – irritable bowel syndrome with constipation

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Dumic I et al. Can J Gastroenterol Hepatol. 2019 Jan 17;6757524
Lucak S et al. Clin Geriatr Med. 2021 Feb;37(1):85-102.

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Additional Causes of Constipation

Lifestyle

- Diet:
  - Low fiber
  - High fiber
  - High protein
  - Low overall intake or anorexia
  - Dehydration
- Sedentary lifestyle
- Ignoring defecation urge or holding

Medications

- Antacids
- Anticholinergics
- Antihistamines
- Antidepressants (e.g., TCAs, SNRIs)
- Calcium channel blockers
- Clonidine
- 5-HT_3 antagonists
- NSAIDs and opioids
- Calcium, iron, aluminum supplements
- Diuretics

TCAs – tricyclic antidepressants; SNRIs – serotonin and norepinephrine reuptake inhibitors

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History and Physical Assessment

- Consider challenges with history if cognitive or physical impairments
- What is "normal" or "constipated" to the patient?
- Other important considerations:
  - Depression or psychiatric conditions
  - Ability to perform ADL/IADL
  - Nutrition and environment
- Physical exam of abdomen and anal/perineal area
- Rule out other causes (e.g., metabolic, anemia, TFTs)
- Explore imaging if necessary

ADL – activities of daily living; IADL – instrumental activities of daily living;
TFTs – thyroid function tests

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Diagnosis – Rome IV Criteria

- Functional constipation (must have ≥ 2 of the following for past 3 months, symptom onset 6 months):
  1. Straining during > 25% of defecations
  2. Lumpy or hard stools (BSFS 1-2) > 25% of defecations
  3. Sensation of incomplete evaluation > 25% of defecations
  4. Sensation of anorectal obstruction/blockage > 25% of defecations
  5. Manual maneuvers to facilitate > 25% of defecations (e.g., digital evacuation)
  6. Fewer than 3 soft, bowel movements per week
  7. Loose stools rarely present without use of laxatives
  8. Insufficient criteria for IBS
- Opioid-induced constipation includes above, but in the context of initiating, changing, or increasing opioid therapy

BSFS – Bristol Stool Form Scale

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Mearin F et al. Gastroenterology. 2016 Feb 18:S0016-5085(16)00222-5.
Image @Jaipasdepseudo / Wikimedia Commons / CC-BY-SA-3.0 / No changes made to original

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General Treatment Approach

If possible, stop/change medication that contributes to constipation

LIFESTYLE MODIFICATIONS
Increase fiber, eat regularly, drink fluids, increase mobility

Osmotic Laxative

Stimulant Laxative

Suppositories/ Enema

If 2 laxatives tried at highest dose with no effect after 6-8 weeks, consider prucalopride or lubiprostone

Consider discontinuation after 2-4 weeks of normal stool passage. May need slow withdrawal. Use for duration of constipating medication.

UNABLE TO SWALLOW?
1. Osmotic laxative as syrup orally or via g-tube
2. Stimulant laxative per rectum

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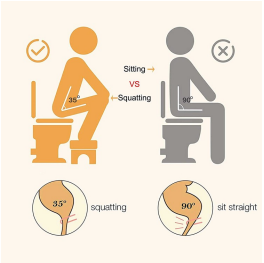
Lifestyle and Diet Modification

- Encourage daily movement as much as possible
- Scheduled defecation, limit toilet time to 3-8 minutes
- Stool diary
- Breathing techniques and manual maneuvers (e.g., splinting)
- Stool for under feet while toileting
- Fiber
  - Soluble less gas than insoluble
  - Recommended daily amount: women 20-28 g, men 30-38 g
  - Increase fiber by ≈ 5 g/week and increase as tolerated + increase fluid intake to 5-8, 8-ounce glasses/day



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Lucak S et al. Clin Geriatr Med. 2021 Feb;37(1):85-102.
Image: https://m.media-amazon.com/images/I/61p9PpiiWlL._AC_SL1500_.jpg

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Bulk-Forming Laxatives (Soluble Fiber)

- Increase water absorbency of stool and increase stool mass
- Accessible, low cost, easy to use, generally safe
- Avoid if immobile, on fluid restriction, GI obstruction, or cannot swallow effectively
- Inconsistent evidence regarding efficacy
  - Meta-analysis included four studies comparing to placebo, small population
  - Psyllium had non-statistically significant ↑ in BM vs. placebo
  - Polycarbophil had less gas than psyllium
- Side effects include bloating and flatulence

Psyllium | Methylcellulose | Polycarbophil | Wheat Dextrin

BM – bowel movements

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Kang SJ et al. J Neurogastroenterol Motil. 2021 Oct 30;27(4):495-512.
Lucak S et al. Clin Geriatr Med. 2021 Feb;37(1):85-102.

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Osmotic Laxatives

- Secretion of intestinal water increases stool frequency and peristalsis
- Side effects include bloating, cramping, flatulence
- May result in electrolyte disturbances (magnesium) and volume overload, caution in renal and cardiac conditions

POLYETHYLENE GLYCOL	LACTULOSE & SORBITOL	SALINE LAXATIVES (magnesium hydroxide, citrate)
• Systematic review found efficacy with improving stool frequency and consistency • Better than lactulose, psyllium • Use once daily, increase dose as tolerated	• Systematic review found efficacy with improving stool frequency and consistency • Synthetic disaccharide, osmotic effect due to undigested sugar • Lactulose > sorbitol	• Poorly absorbed, hyperosmolar solutions • Can result in hypermagnesemia if renal failure (diminished reflexes, somnolence, bradycardia, heart block)

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Kang SJ et al. J Neurogastroenterol Motil. 2021 Oct 30;27(4):495-512.
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Stimulant Laxatives

- Peristalsis through direct irritation of intestinal smooth muscle
- Alters water and electrolyte transport, fluid accumulation
- Daily use may lead to hypokalemia, salt wasting, protein deficiency

BISACODYL	• Oral tablet and suppository/enema • Onset of action for oral tablets may be longer for older adults (typically 6-10 hours, up to 12 in older adults)
SENNOSIDES	• Oral tablet and syrup • Onset of action for oral tablets may be longer for older adults (typically 6-12 hours, up to 12 in older adults) • Take at bedtime to achieve BM in the morning • Can cause melanosis coli with chronic use

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Kang SJ et al. J Neurogastroenterol Motil. 2021 Oct 30;27(4):495-512.
Lucak S et al. Clin Geriatr Med. 2021 Feb;37(1):85-102.

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Other Treatment for Constipation

- Stool softeners:
  - Mechanism includes lowering the surface tension of stool allowing water to enter
  - Evidence regarding efficacy is weak, many study limitations
  - Used for patients who cannot strain after surgeries, in combination with stimulant for opioid-induced constipation (OIC)
  - May contribute to polypharmacy with little to no added benefit
- Suppositories: Glycerin (osmotic), bisacodyl (stimulant)
- Enemas: Tap water, soap suds, mineral oil
- Probiotics: Maybe? limited quality evidence, most with *Bifidobacterium*

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Hawley PH et al. J Palliative Med. 2008;11(4):575-81.

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OIC: 2019 AGA Guideline

- Laxatives (PEG, bisacodyl) are first-line for OIC
- For laxative refractory (failure of 2 laxatives) recommends naldemedine, naloxegol, and methylnaltrexone over no treatment
- No recommendations for lubiprostone or pricalopride due to lack of evidence at publication

PERIPHERALLY ACTING μ-OPIOID RECEPTOR ANTAGONISTS
Specifically block receptors in the GI tract, inhibiting delay in GI transit time
Consider if score on Bowel Function Index ≥ 30
Do not use if obstruction present
Can cause GI perforation, need to monitor for opioid withdrawal

AGA – American Gastroenterological Association

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Crokett SD et al. Gastroenterology. 2019 Jan;156(1):218-26.

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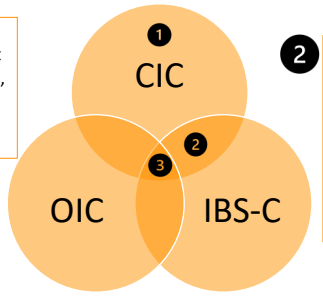
Chronic Idiopathic Constipation (CIC) and IBS-C

- CIC predominantly in women, fiber and laxative failure
- 10-20% of older adults with IBS, including IBS-C

1 **PRUCALOPRIDE (MOTEGRITY®)**
Selective 5-HT_4 receptor agonist
Stimulates peristalsis, secretions, motility
Limited data in older adults, seems favorable

3 **LUBIPROSTONE**
Chloride channel activator
Increases fluid secretion and transit time



2 **LINACLOTIDE (LINZESS®) & PLECANATIDE (TRULANCE®)**
Guanylate cyclase-C receptor agonists
Cause downstream chloride and bicarbonate secretion
Some subgroup analysis data in older adults; seem to be well tolerated

5-HT4 – 5-hydroxytryptamine (serotonin) 4

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Chang L et al. Am J Gastroenterol. 2023;118(6):936.

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Self-Assessment Question #2

Which of the following is first-line for constipation secondary to sedentary lifestyle and insufficient fiber intake?

A. Lubiprostone
B. Docusate sodium
C. Polyethylene glycol
D. Bisacodyl suppository

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GERD

- Reflux of gastric contents into the upper GI tract and/or lungs
- Incidence similar to younger adults (6-23%), sixth most common disorder in nursing home residents
- Symptoms:
  - Can be atypical in older adults (weight loss, anemia, dysphagia)
  - Often more severe due to decreased sensitivity to pain
- Older adults are at an increased risk of complications (Barrett's esophagus, severe esophagitis, ulcers, strictures)
- Increased risk of medication-related GERD due to polypharmacy
- Diagnosis with EGD may be preferred in older vs. younger adults

EGD – esophagogastroduodenoscopy

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Dumic I et al. Can J Gastroenterol Hepatol. 2019 Jan 17;6757524.
Otaki F et al. Clin Geriatr Med. 2021 Feb;37(1):17-29.

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Additional Causes of GERD

Lifestyle

- Diet
  - Alcohol
  - Chocolate
  - Caffeine
  - Fatty and/or spicy foods
- Tobacco smoking
- Sedentary (lying down or reclining)
- Excess weight

Medications

- NSAIDs
- Potassium
- Iron
- Bisphosphonates
- Calcium channel blockers
- Beta-blockers
- Anticholinergics
- TCAs
- Opioids
- Nitrates
- Diazepam

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Dumic I et al. Can J Gastroenterol Hepatol. 2019 Jan 17;6757524.
Chait MM. World J Gastrointest Endosc. 2010 Dec 16;2(12):388-98.
Katz PO et al. Am J Gastoenterol. 2022 Jan1;117(1):27-56.

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GERD: Treatment Overview

Non-pharmacologic

Avoid trigger foods, eating 2-3 hours before bedtime

Elevate head of bed (e.g., wedge inserts)

Weight loss, smoking cessation

Pharmacologic

H2RA ⇄ PPI (Step-Up / Step-Down)

Antacids As Needed

H2RA – histamine-2 receptor antagonist; PPI – proton pump inhibitor

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Otaki F et al. Clin Geriatr Med. 2021 Feb;37(1):17-29.
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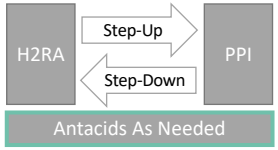
Pharmacologic: Antacids and Alginate

- Antacids (e.g., aluminum, calcium, magnesium)
  - Neutralize gastric pH
  - Rapid symptom relief (5-10 minutes), lasts 30-60 minutes
  - Limited long-term efficacy
  - Can alter absorption of other medications
  - Side effects: Constipation (aluminum- or calcium-containing), diarrhea (magnesium-containing), milk alkali syndrome
  - Avoid aluminum and magnesium if renal impairment
- Sodium alginate
  - Anti-reflux "barrier" formed by viscous gum floating in stomach
  - Better for post-prandial symptoms or mild disease



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Otaki F et al. Clin Geriatr Med. 2021 Feb;37(1):17-29.

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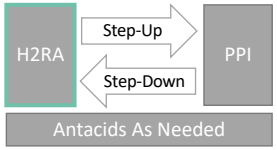
Pharmacologic: H2RAs



- Decrease secretion of acid by blocking histamine receptor on gastric parietal cell
- Can have tachyphylaxis within 2-6 weeks
- Step-up therapy:
  - Start H2RA + lifestyle for 1 week, then increase dose for total of 2 weeks
  - If symptoms continue, change to PPI
- Step-down therapy:
  - Can switch to H2RA as "taper" down from 8-weeks of PPI therapy
  - Can use for intermittent symptom relief, nocturnal symptoms
- Side effects:
  - Risk for altered mental status, especially if CrCl < 50 mL/min (dose reduce)
  - Vitamin B12 deficiency, thrombocytopenia

Famotidine
Cimetidine
Nizatidine

CrCl – creatinine clearance

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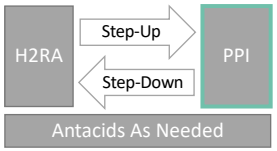
Pharmacologic: PPIs



- Irreversible inhibition at parietal cell H^+/K^+ ATPase pump thereby suppressing acid secretion
- Step-up therapy from H2RA or initial option for those with frequent (≥2 episodes per week) or severe symptoms, erosive esophagitis (EE)
- Efficacy:
  - Faster symptom relief, more effective than H2RA
  - Nearly 80% of patients at 8 weeks
  - No substantial clinical differences between products
- Take 30-60 minutes before first meal
- Daily administration provides better control than as needed

Esomeprazole
Dexlansoprazole
Lansoprazole
Omeprazole
Pantoprazole
Rabeprazole

CrCl – creatinine clearance

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Additional PPI Considerations

IN GENERAL:

- Use lowest effective dose to relieve symptoms
- Initial phase is 8 weeks, can extend up to 8 additional
- Can switch to another PPI if first ineffective (different potencies)
- Maintenance dosing (often daily) for Barrett's/EE, chronic NSAID use + bleeding risk
- Prolonged use may require taper to avoid rebound hypersecretion of acid
- Opportunity for deprescribing

SIDE EFFECTS:

- Mild including headache, nausea, abdominal pain, diarrhea/constipation, rash, dizziness
- Long-term/severe including osteoporosis, infection (*C. difficile*, pneumonia), hypomagnesemia, hypocalcemia, vitamin B12 deficiency, interstitial nephritis, atrophic gastritis, drug-induced SLE
- Conflicting data about association with dementia and altered mental status

SLE – systemic lupus erythematosus

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Otaki F et al. Clin Geriatr Med. 2021 Feb;37(1):17-29.
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Pilotto A et al. Drugs Aging. 2010 Jul 1;27(7):545-58.

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Other Options for GERD

Prokinetics (e.g., metoclopramide)	Prucalopride	Baclofen	Sucralfate	Vonoprazan
• Limited data available • Consider adverse events (e.g., CNS effects including dystonia and tardive dyskinesia)	• One off-label use study showed improvement in motility and reduction in acid exposure • Potential use in the future	• Reduces LES relaxation, belching • Use limited by side effects (e.g., dizziness, somnolence)	• Unabsorbed, minimal side effects • Limited data about efficacy in GERD outside of pregnancy	• Potassium competitive acid blocker (PCAB) • Indicated for erosive and non-erosive GERD and *H. pylori* treatment • Higher potency, longer duration of action, faster onset

CNS – central nervous system

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Pilotto A et al. Drugs Aging. 2010 Jul 1;27(7):545-58.
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Patient Case – Back to Alex

You ask Alex about their GERD symptoms to learn more. Alex tells you that they have had heartburn most of their adult life. They have symptoms 1-2 days/week and sometimes it feels like food "gets stuck" when swallowing.

These symptoms have been worse over the last 5-7 days and Alex did not want to start a PPI because of the "bad press" they receive.

Alex did see a gastroenterologist who performed an EGD. There were no signs of erosive esophagitis.

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Thinking about Alex…

- Any causes of heartburn you can identify?
- Any risks for untreated GERD symptoms?
- Should Alex start treatment?

- Medications:
  - Amlodipine 10 mg PO daily
  - Aspirin 81 mg PO daily
  - Ferrous sulfate 325 mg PO twice daily
  - Ibandronate 150 mg PO every month
  - Ibuprofen 400 mg PO q4-6 hours as needed
  - Lisinopril 40 mg PO daily
  - Metformin 1000 mg PO twice daily
  - Meloxicam 15 mg PO daily
  - Bismuth subsalicylate PO as needed
  - Semaglutide (injectable) 1 mg every week (dose increased 1 week ago)
  - Rosuvastatin 20 mg PO daily

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Self-Assessment Question #3

Which of the following interventions is MOST appropriate for Alex at this time?

A. Stop ibandronate
B. Start calcium carbonate as needed
C. Start famotidine twice daily
D. Start omeprazole 20 mg as needed

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Nausea/Vomiting (N/V)

CNS	Vestibular	Chemoreceptor Trigger Zone (CTZ)	Vomiting Center	GI Tract & Heart
Cortex Thalamus Hypothalamus Meninges	H_1 receptor M_1 receptor	Chemoreceptors D_2 receptor NK_1 receptor 5-HT_3 receptor	H_1 receptor M_1 receptor NK_1 receptor 5-HT_3 receptor	Mechanoreceptors Chemoreceptors 5-HT_3 receptor

- Antagonism of these receptors is the basis of antiemetic medication
- N/V often studied together, includes chemotherapy-induced (CINV), chronic unexplained (CUNV), and postoperative (PONV)
- Associated with many disease states (e.g., constipation, anxiety, pain)
- Side effect of most medications

H_1 – histamine type 1; M_1 – muscarinic type 1; D_2 – dopamine type 2; NK_1 - neurokinin type 1

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Heckroth M et al. J Clin Gastroenterol. 2021 Apr 1;55(4):279-99.

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N/V - Assessment

- Rule out obstruction, mesenteric ischemia, acute pancreatitis, myocardial infarction
- History – duration of symptoms (chronic > 1 month), recent food intake, frequency, severity, characteristics of vomitus
- Correct fluid and electrolyte disturbances related to vomiting
- Goals of therapy to relieve symptoms and remove underlying cause

MIGRAINE	VESTIBULAR	GASTROENTERITIS
Dopamine antagonists, prochlorperazine, serotonin antagonists	Antihistamines, anticholinergics	Dopamine antagonists, serotonin antagonists

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Heckroth M et al. J Clin Gastroenterol. 2021 Apr 1;55(4):279-99.

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Antiemetic Drug Targets and Affinities

Drug	D_2	H_1	M_1	5-HT_2 / $_3$ / $_4$	NK_1
Aprepitant					+++
Chlorpromazine	++++	++	+		
Domperidone	++++			-/-/+	
Haloperidol	++++	+			
Scopolamine	+	+	+++		
Metoclopramide	+++			-/+/++	
Olanzapine	++	+	+	++/-/-	
Ondansetron				-/++++/-	
Prochlorperazine	++++	++		+/-/-	
Promethazine	++	++++	++		

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Glare PA et al. Drugs. 2008;68(18):275-90.

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D_2 Antagonists

CredibleMeds.org is a great source for checking medications for QTc prolongation!

PHENOTHIAZINES

- Prochlorperazine, chlorpromazine, promethazine
- Limited efficacy studies, placebo effect noted
- Side effects limit use (e.g., dystonia, tardive dyskinesia, hypotension)
- Prochlorperazine has lowest risk of QTc prolongation
- AGS Beers Criteria for anticholinergic properties

BUTYROPHENONES

- Haloperidol, droperidol
- Potentiates effects of opioids
- Dose-dependent risk of QTc prolongation
- Contraindicated in Parkinson's disease

BENZAMIDES

- Metoclopramide, trimethylbenzamide, domperidone (IND only, GI specific)
- Side effects include anxiety, depression, hyperprolactinemia, QTc prolongation, tardive dyskinesia (box warning with long-term use)

AGS – American Geriatrics Society; IND – investigational drug

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AGS. J Am Geriatr Soc. 2023 Jul;71(7):2052-81.
Heckroth M et al. J Clin Gastroenterol. 2021 Apr 1;55(4):279-99.

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5-HT_3 Antagonists & Olanzapine

- 5-HT_3 Antagonists
  - Cornerstone of therapy for CINV, PONV
  - Evidence suggests all have similar efficacy and tolerability
  - Palonosetron has higher binding affinity and longer half-life
  - Side effects include headache, asthenia, constipation, dizziness
  - Caution for QTc prolongation and serotonin syndrome

Ondansetron | Granisetron | Dolasetron | Palonosetron

- Olanzapine
  - D_2 antagonist and 5-HT_2 antagonist
  - Used for both acute and delayed CINV
  - Has dose-dependent anticholinergic effects

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Heckroth M et al. J Clin Gastroenterol. 2021 Apr 1;55(4):279-99.

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Other Treatments for N/V

ANTICHOLINERGICS	• Example: Scopolamine • Use: Motion sickness, PONV • Recommended to avoid on AGS Beers Criteria
ANTIHISTAMINES	• Examples: Diphenhydramine, dimenhydrinate, meclizine • Use: Motion sickness • Recommended to avoid on AGS Beers Criteria
NEUROKININ RECEPTOR ANTAGONISTS	• Examples: Aprepitant, fosaprepitant, netupitant, rolapitant • Use: CINV, PONV • More efficacious when used with serotonin antagonists
CANNABINOIDS	• Example: Dronabinol • Use: CINV
BENZODIAZEPINES	• Examples: Lorazepam, alprazolam • Use: Adjunctive to reduce anxiety
STEROIDS	• Examples: Dexamethasone • Use: With serotonin antagonists for CINV

GERIATRIC PHARMACIST BOOT CAMP

AGS. J Am Geriatr Soc. 2023 Jul;71(7):2052-81.
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Anemia

- Definition
  - Men: Hgb < 13.5 g/dL
  - Women: Hgb < 11.5 g/dL
- Prevalence
  - 17% overall in those > 65 years old
  - 12% in community-dwelling, 40% in hospitalized, and 47% in nursing home residents
  - Increases with age, men > women
- Etiology
  - Nutritional deficiencies
  - Anemia of chronic disease (ACD) or inflammation (AI)
  - Kidney disease
  - Idiopathic
  - Clonal hematopoiesis
  - Blood loss
  - Hematological malignancy
  - Aplastic anemia

Hgb - hemoglobin

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Katsumi A et al. Geriatr Gerontol Inr. 2021 Jul;21(7):549-54.

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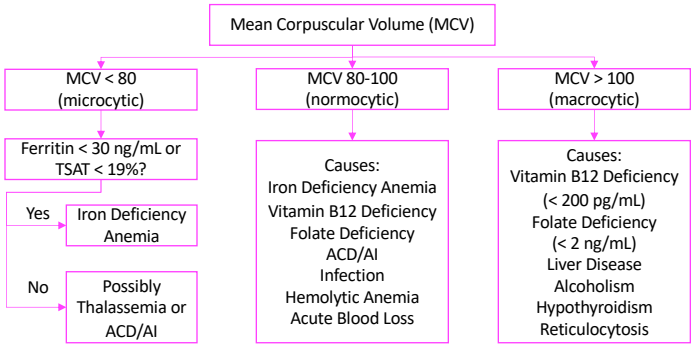
Assessing Anemia



	Iron Deficiency	ACD/AI
Serum Iron	↓	↓
TSAT	↓	↓
TIBC	↑	↓
Ferritin	↓	Normal

	B12	Folate
MMA	↑	Normal
Homocysteine	↑	↑/Normal

TSAT – transferrin saturation;
TIBC – total iron binding capacity;
MMA – methylmalonic acid

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Joosten E. Geriatr Gerontol Int 2018 Mar;18(3):373-79.

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Iron Deficiency Anemia in Older Adults

- Most common cause of anemia, usually GI bleeding and/or malabsorption, medications (e.g., NSAIDs, anticoagulants)
- Ferritin < 50 ng/mL may be more appropriate as a cut off, low hepcidin levels
- Often asymptomatic, but typical (e.g., fatigue, paleness, pica, glossitis)

GIB – gastrointestinal bleed, Fe – iron

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Joosten E. Geriatr Gerontol Int 2018 Mar;18(3):373-79.

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Treatment for Fe-Deficiency Anemia

- Ganzoni formula: Total Fe supplementation = target Hgb – actual Hgb x 2.4 x weight (kg) + 500
- Recommended daily dose varies
  - Typically, between 60-200 mg elementary Fe/day
  - Doses ≥ 60 mg increases hepcidin up to 24 hours, reducing absorption
  - Can use lower doses and/or every other day dosing
  - Can give with vitamin C for additional absorption
- Available as oral or IV (if inpatient, available, intolerant to oral, or oral not working)
- Duration 3-6 months to replete iron stores or ferritin > 100 ng/mL
- Side effects include nausea, constipation, diarrhea, abdominal pain, black stools

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Joosten E. Geriatr Gerontol Int 2018 Mar;18(3):373-79.

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Iron Formulations

ORAL		INTRAVENOUS	
Ferrous sulfate	20-30% elemental Fe/mg	**Ferric carboxymaltose**	50 mg/mL elemental Fe
Ferrous fumarate	≈ 30% elemental Fe/mg	**Ferumoxytol**	30 mg/mL elemental Fe
Ferrous gluconate	10-14% elemental Fe/mg	**Ferric gluconate**	12.5 mg/mL elemental Fe Test dose if multiple allergies
Polysaccharide-iron complex	Number of mg in name of product (e.g., Ferrex 150 – 150 mg elemental Fe)	**Iron sucrose**	20 mg/mL elemental Fe Test dose if multiple allergies
		Iron dextran	50 mg/mL elemental Fe Test dose required

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Joosten E. Geriatr Gerontol Int 2018 Mar;18(3):373-79.

55

Vitamin B12 Deficiency in Older Adults

- Increased probability in men and those who avoid dairy, meat, gastric bypass/bariatric surgery, taking metformin
- Hypochlorhydria caused by *H. pylori*, atrophic gastritis, antacids
- Most patients are asymptomatic, some with neurological findings
- If symptomatic or impaired absorption, give IV supplementation
- For most, supplement until deficiency resolved, encourage diet
- Dosing
  - Cyanocobalamin 1000 mcg IM/deep subq 1-3 times a week for 1 week, then 1000 mcg weekly for 4-8 weeks, then monthly
  - Oral tablets 1000-2000 mcg once daily

IM – intramuscular; subq - subcutaneous

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Katsumi A et al. Geriatr Gerontol Inr. 2021 Jul;21(7):549-54.

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Folate Deficiency in Older Adults

- Usually caused by dietary deficiency, impaired absorption
  - Foods are fortified with folic acid (cereal, grains)
  - Also found in green leafy vegetables
  - Alcohol, anticonvulsants, methotrexate
- Recommended daily allowance 200 mcg/day
  - Typically give 1-5 mg daily
  - Encourage diet
- Treatment with folic acid can mask hematologic abnormalities of vitamin B12 deficiency
- Complete response to therapy should take 2-4 weeks

GERIATRIC PHARMACIST BOOT CAMP

Katsumi A et al. Geriatr Gerontol Inr. 2021 Jul;21(7):549-54.

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Other Treatment for Anemia

- Blood loss
  - Warrants investigation of where bleed is coming from, if occult
  - Restrictive strategy: Transfusion indicated when Hgb is ≤ 7 g/dL (≤ 8 g/dL if going to surgery or have severe cardiovascular condition)
  - Will receive iron in transfusion as well (1 unit ≈ 200-250 mg iron)
- ACD/AI
  - Categorized as hyperinflammatory state (lifetime exposure to antigenic stimuli and free radicals)
  - Linked to CKD, heart failure, pulmonary arterial hypertension, atherosclerosis
  - Associated with retention of iron in reticuloendothelial system, reduced erythropoietin (EPO) production, elevated eryptosis

GERIATRIC PHARMACIST BOOT CAMP

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Katsumi A et al. Geriatr Gerontol Inr. 2021 Jul;21(7):549-54.

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Treatment for Anemia of Inflammation

- Control underlying chronic condition
- Evaluate for Fe deficiency, treat if TSAT < 20 %, ferritin < 100 ng/mL before determining need for erythropoietin-stimulating agents (ESA)
- ESA indication for anemia due to CKD or chemotherapy, off-label for anemia of inflammation
  - Epoetin alfa: Dose to nearest vial size, 50-100 units/kg once weekly
  - Darbepoetin alfa: 0.45 mcg/kg once every 4 weeks
- Monitoring
  - To start, Hgb < 10 g/dL or ≤ 1 g/dL increase every 2 weeks
  - Dose adjustments:
    - if Hgb does not increase by > 1 g/dL after 4 weeks, increase 25%
    - If Hgb increases > 1 g/dL in a 2-week period, reduce 25%

Use lowest dose sufficient to reduce the need for a blood transfusion

Side effects include hypertension, headache

Box warning regarding thrombosis risk, MI, stroke, VTE, death

MI – myocardial infarction; VTE – venous thromboembolism

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Katsumi A et al. Geriatr Gerontol Inr. 2021 Jul;21(7):549-54.

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Two Years Later…

- Alex comes to the clinic for their wellness exam. Alex's chief concern today is shortness of breath and fatigue.
- You receive the following labs (normal range):

RBC 4.2 (3.92-5.13)	WBC 4.1 (3.4-9.6)	Serum iron 90 (60-170)
Hgb 10.5 (11.6-15)	MCV 110 (80-95)	Serum ferritin 50 (12-150)
Hct 38 (35.5-44.9)	MCH 33 (37-31)	Vitamin B12 80 (200-900)
Platelets 225 (157-371)	TIBC 300 (250-450)	Folate 10 (2-20)
Reticulocyte 0.8 (0.5-1.5)		

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Self-Assessment Question #4

Which type of anemia does Alex have?

A. Anemia of blood loss
B. Microcytic anemia
C. Macrocytic anemia
D. Normocytic anemia

GERIATRIC PHARMACIST BOOT CAMP

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GERIATRIC PHARMACIST

BOOT CAMP

Gastrointestinal Disorders in the Older Adult

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Supported in part by an educational grant from the ASCP Foundation.

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