Common GI Disease in Outpatient Medicine

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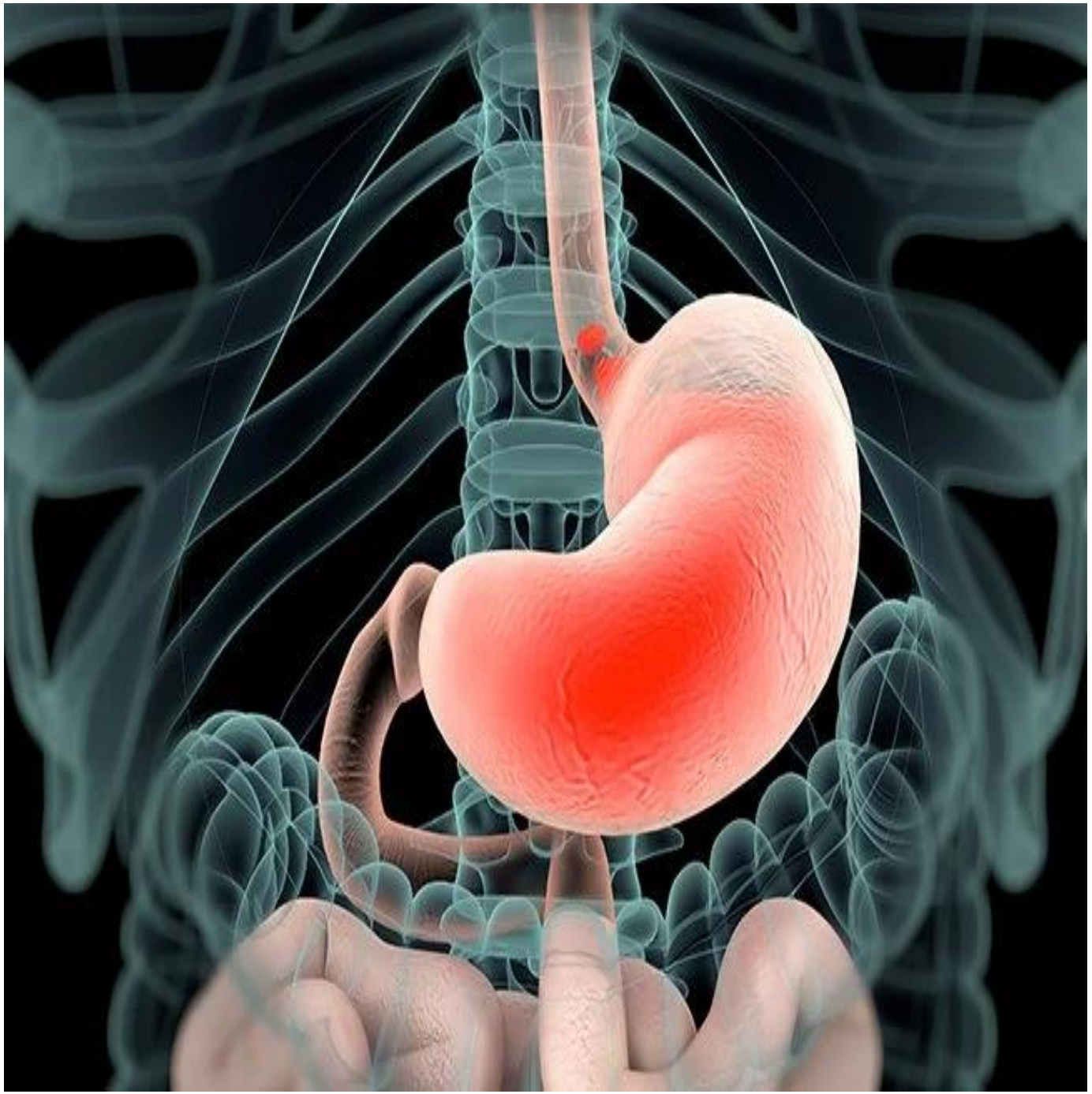

LEARNING OBJECTIVES ARE TO MASTER DIAGNOSIS AND TREATMENT OF THE FOLLOWING DISORDERS:

1. GERD
2. NAUSEA AND VOMITING
3. PEPTIC ULCER DISEASE
4. ABDOMINAL PAIN
5. BLOATING
6. GALLSTONE DISEASE
7. IBS-C and IBS-D

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GASTROESOPHAGEAL REFLUX DISEASE (GERD)

- Reflux of stomach contents into esophagus
- Most common symptoms are heartburn and regurgitation
- Prevalence up to 20% of the US population
- Defined as:
  - Frequent symptoms (2 or more times a week) **or**
  - Esophageal inflammation, ulcers/erosions, strictures or Barrett's
- Barriers are LES, diaphragm and gravity
  - Foods, lifestyle habits, and anatomic issues weaken barriers

Fass R. Proton-pump inhibitor therapy in patients with gastro-oesophageal reflux disease: putative mechanisms of failure. Drugs 2007

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TREATMENT OF GERD

- Lifestyle Modifications:
  - Wait 2-3 hours after eating
  - Raise the head of the bed 6-10 inches
  - Stop smoking and avoid alcohol:
    - Both relax the LES and are independent risk factors for esophageal cancer
  - Avoid chocolate, coffee, peppermint, greasy or spicy foods, tomato products, and alcoholic beverages
  - Weight loss if BMI > 25

TREATMENT OF GERD

- H2 Receptor Antagonists
  - On market 50 years and affordable
  - Initial treatment or maintenance of mild symptoms
- Proton Pump Inhibitors (PPI)
  - Irreversibly binding/inhibiting the H-K-ATPase pump of the parietal cell
  - Quantity of H-K-ATPase greatest after a prolonged fast

Wolfe et al. Acid suppression: optimizing therapy for gastroduodenal ulcer healing, gastroesophageal reflux disease, and stress-related erosive syndrome. Gastroenterology 2000

PPI

- Once daily preferred, but twice daily can be considered
- Choice of a PPI determined by patient preference and/or payer coverage
- Systematic review of 12 randomized trials examining different PPI dosing regimens found no consistent difference in symptom resolution and esophagitis healing rates
- If pills not tolerated an oral suspension of lansoprazole or powder formulation of omeprazole-sodium bicarbonate available
- Complete relief of heartburn with PPIs occurs at a rate of approximately 11.5% per week
- Endoscopic healing and symptom relief are achieved typically within 8 weeks

Ip S, et al. Comparative Effectiveness of Management Strategies for Gastroesophageal Reflux Disease. Evidence Report/Technology Assessment, Tufts-New England Medical Center
Chiba N, et al. Speed of healing and symptom relief in grade II to IV gastroesophageal reflux disease: a meta-analysis. Gastroenterology 1997

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ADVERSE EFFECTS OF PPI THERAPY

- **Gastrointestinal:**
  - Increased risk of Clostridioides difficile infection, enteric infections, and microscopic colitis
- **Malabsorption of minerals and vitamins:**
  - Hypomagnesemia due to reduced intestinal absorption
  - Long-term therapy use associated with vitamin B12 malabsorption
  - Causality between PPI therapy and bone fractures has not been established
- **Kidney disease:**
  - Associated with acute interstitial nephritis and chronic kidney disease (CKD) progression
- **Associations of unclear significance:**
  - Conflicting data on the association between PPI use and risk of dementia, pneumonia and/or death

Cheungpasitporn W, et al. Proton pump inhibitors linked to hypomagnesemia: a systematic review and meta-analysis of observational studies. Ren Fail
Khalili H, et al. Use of proton pump inhibitors and risk of hip fracture in relation to dietary and lifestyle factors: a prospective cohort study. BMJ 2012
Recker RR. Calcium absorption and achlorhydria. N Engl J Med 1985

TREATMENT GOALS

- **Discontinuing PPIs:**
  - Prescribe lowest dose and shortest duration possible
  - Gradually taper if treated longer than 6 months
  - No method for discontinuing PPI therapy proven effective
  - Studies demonstrate rebound acid hypersecretion following discontinuation of PPIs in long-term use

Björnsson E, et al. Discontinuation of proton pump inhibitors in patients on long-term therapy: a double-blind, placebo-controlled trial. Aliment Pharmacol Ther

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TREATMENT OF GERD

- Approximately 10 - 40% with GERD fail to respond to PPIs
- Most nonresponse is due to nonerosive reflux (NERD) or functional heartburn
  - With NERD the pooled symptomatic response rate to PPI once daily at four weeks is 37%
- With erosive esophagitis, pooled symptomatic response rate is 56%

Fass R. Therapeutic options for refractory gastroesophageal reflux disease. J Gastroenterol Hepatol 2012
Dean BB, et al. Effectiveness of proton pump inhibitors in nonerosive reflux disease. Clin Gastroenterol Hepatol 2004

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GERD CONSIDERATIONS: FUNCTIONAL HEARTBURN

- Estimated in 58% of patients with persistent heartburn despite PPI
- Rome IV criteria requires all the following criteria be fulfilled for the last 3 months with symptom onset at least 6 months prior to the diagnosis:
  - Burning retrosternal discomfort or pain
  - Absence of symptom relief despite optimal antisecretory therapy
  - Absence of evidence that GERD or eosinophilic esophagitis are the cause of symptoms
  - Absence of major esophageal motor disorders (achalasia, diffuse esophageal spasm, jackhammer esophagus)
- In population-based studies, anxiety and depression have been also been demonstrated to increase GERD-related symptoms

Savarino E, et al. Impedance-pH reflux patterns can differentiate non-erosive reflux disease from functional heartburn patients. J Gastroenterol 2012
Aziz Q, et al. Functional Esophageal Disorders. Gastroenterology 2016

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GERD CONSIDERATIONS: REFLUX HYPERSENSITIVITY AND EEM

Reflux hypersensitivity:

- Retrosternal symptoms of heartburn +/- chest pain and **normal esophagus**
- Rome IV criteria requires **all** the following criteria be fulfilled for the last 3 months with symptom onset at least 6 months prior to the diagnosis:
  - Retrosternal symptoms including heartburn or chest pain
  - Normal endoscopy and no evidence of eosinophilic esophagitis
  - No esophageal motor disorders
  - Normal pH–impedance monitoring

Extra-esophageal manifestations (EEM) of GERD:

- GERD is associated with asthma, chronic cough and ear, nose and throat problems

Mainie I, et al. Acid and non-acid reflux in patients with persistent symptoms despite acid suppressive therapy: a multicentre study using combined ambulatory impedance-pH monitoring. Gut 2006

Mizyed I, et al. Review article: gastro-oesophageal reflux disease and psychological comorbidity. Aliment Pharmacol Ther 2009

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ALARM FEATURES OF GERD

- Alarm features that may be suggestive of a gastrointestinal malignancy:
  - New onset dyspepsia age ≥60 years
  - Gastrointestinal bleeding
  - Iron deficiency anemia
  - Anorexia/unexplained weight loss
  - Dysphagia/odynophagia
  - Persistent vomiting
  - Gastrointestinal cancer in a first-degree relative

- Do not delay endoscopy with PPI trial in patients with any alarm symptoms
- Perform a repeat upper endoscopy if new alarm features developed since last endoscopy
- Biopsies of the esophagus should be obtained to rule out eosinophilic esophagitis

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AMERICAN COLLEGE OF GASTROENTEROLOGY GUIDELINES - GERD

- Classic GERD symptoms without alarm symptoms → 8-week trial of empiric PPIs once daily before a meal
- Discontinue PPIs if symptoms respond to an 8-week empiric trial of PPIs
- EGD if no response to 8-week empiric trial of PPIs or if symptoms return when PPIs are discontinued
- Diagnostic endoscopy +/- reflux monitoring in chest pain with negative cardiac workup
- Barium swallow study not recommended solely as a diagnostic test for GERD
- Endoscopy is primary test of choice in dysphagia, other alarm symptoms (weight loss and GI bleeding) and in patients with multiple risk factors for Barrett's esophagus

Katz et al. The American Journal of Gastroenterology: January 2022
Hirano I et al. ACG practice guidelines: Am J Gastroenterol 2007

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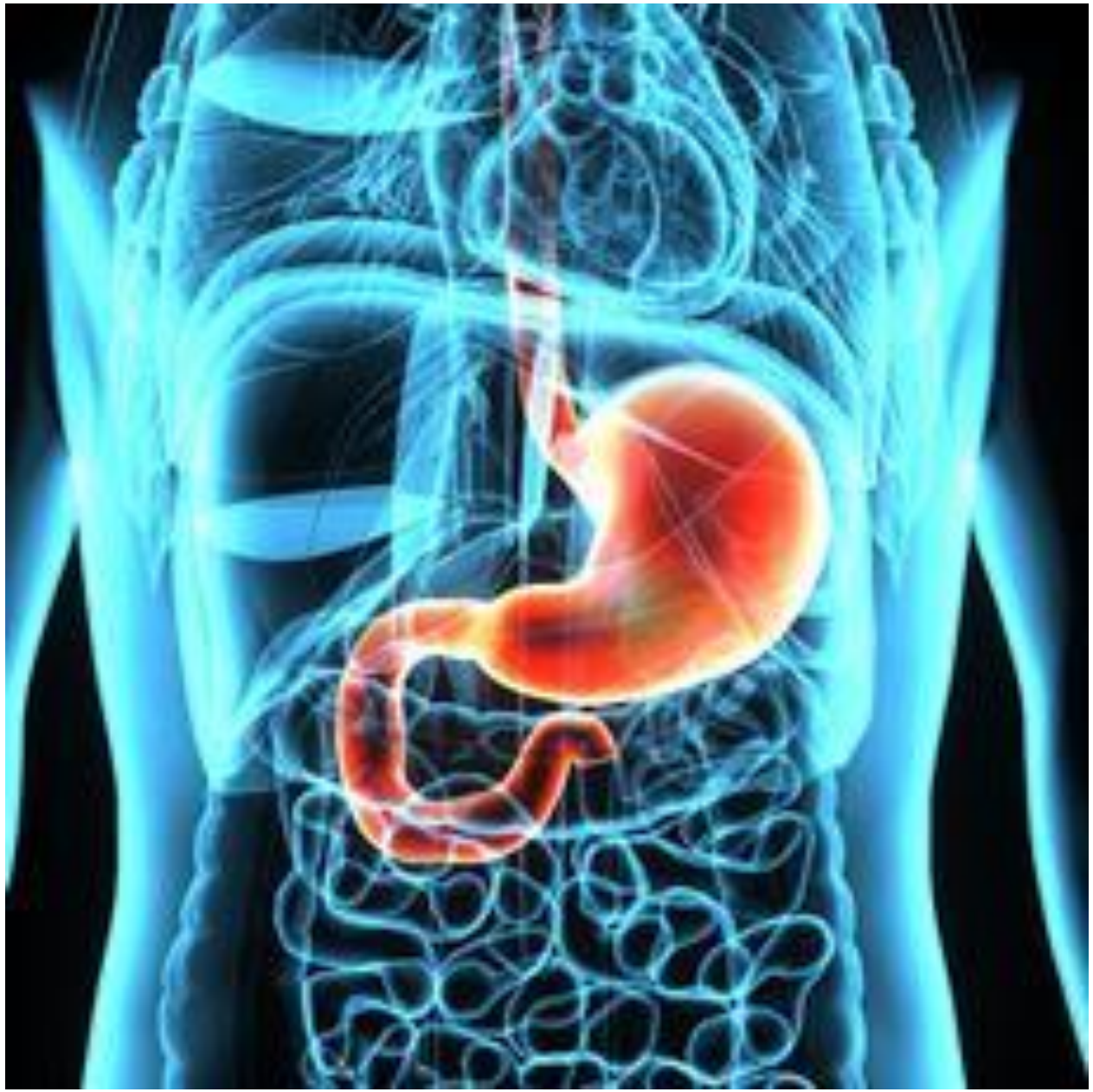

NAUSEA AND VOMITING

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NAUSEA AND VOMITING - DEFINITIONS

Nausea is the unpleasant sensation of needing to vomit

- Increased saliva in the mouth
- Can occur before or without vomiting

Vomiting is the forceful movement of gastric contents out through the mouth

- Lower esophageal sphincter relaxation
- Retrograde contraction proximal small bowel and antrum
- Muscles in the abdominal wall squeeze tightly
- Cricopharyngeal relaxation

Regurgitation is the effortless movement of stomach contents into mouth

- May be a manifestation of reflux disease or motility disorder

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NAUSEA AND VOMITING

- Estimated in United States exceeds $1 billion dollars per year in medical expenses (not including cost of missed work/lost productivity)
- Etiology should be sought with consideration of duration (chronic > 1 month)
- Metabolic complications of nausea and vomiting are fluid depletion, hypokalemia, and metabolic alkalosis
- Targeted therapy should be provided once identified (intra-abdominal infection, SBO or malignancy)

Metz A, et al. Nausea and vomiting in adults--a diagnostic approach. Aust Fam Physician 2007

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CAUSES – “MADIC”

Metabolic Derangements

- Kidney failure/uremia
- Hyperglycemia
- Hormonal disorders including diabetes, overactive thyroid (hyperthyroid) and underactive adrenal glands (Addison’s disease)

Abdominal Process

- Inflammation of the abdominal organs such as pancreatitis, Crohn’s disease or ulcerative colitis.
- Intestinal blockage from stomach or intestinal ulcers, cancers, tumors or inflammatory diseases like Crohn’s disease
- Slow intestinal movement such as slow emptying of stomach (gastroparesis), ileus or pseudo obstruction
- Pregnancy
- Postoperative nausea and vomiting occurs in one-third of surgical patients after receiving general anesthesia

Cao X, et al. An update on the management of postoperative nausea and vomiting. J Anesth 2017

CAUSES – “MADIC”

Drugs

- Nausea and vomiting can result from almost any medication
- Medicines such as chemotherapy for cancer and anesthetic agents often cause profound nausea and vomiting

Infection

- Infections of the gastrointestinal tract – virus, bacteria, parasitic gall bladder infections (cholecystitis), appendicitis, viral hepatitis and diverticulitis
- Infections outside the intestines such as pneumonia, bladder and kidney infections, meningitis and ear infections
- Acute gastroenteritis is second only to the common cold as a cause of lost productivity: Bacterial, viral, and parasitic pathogens cause this illness which is characterized by diarrhea and/or vomiting
- Vomiting is especially common with infections caused by rotaviruses, enteric adenovirus, norovirus, and Staphylococcus aureus

CAUSES – “MADIC”

CNS

- Motion sickness
- Alcohol intoxication
- Migraine headaches
- Other brain and nervous system disorders including tumors of the brain, seizures, head trauma and multiple sclerosis
- Vestibular neuritis is an acute labyrinthine disorder characterized by rapid onset of severe vertigo with nausea, vomiting and gait instability

Other

- Radiation therapy
- Psychiatric disorders such as anxiety, depression, anorexia nervosa and bulimia.
- Cyclic vomiting syndrome
- Physical or emotional pain
- Myocardial Infarction

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CONSIDERATIONS – NAUSEA AND VOMITING

- Common side effect of medications → opioids and cannabis
- Abdominal pain + vomiting → organic etiology (cholelithiasis)
- Abdominal distension + tenderness + vomiting → suggest bowel obstruction
- Vomiting of food eaten several hours earlier → gastric obstruction or gastroparesis
- Vomiting of blood or coffee grounds → UGIB
- GERD can present as chronic nausea without typical reflux symptoms
- Early morning vomiting → pregnancy
- Feculent vomiting → intestinal obstruction
- Bulimia → dental enamel erosion, parotid gland enlargement
- Headache + vomiting → migraine
- Consider infectious when multiple people affected

Bollom A, et al. Emergency Department Burden of Nausea and Vomiting Associated With Cannabis Use Disorder: US Trends From 2006 to 2013. J Clin Gastroenterol 2018
Brzana RJ, et al. Gastroesophageal reflux disease presenting with intractable nausea. Ann Intern Med 1997
Herrell HE. Nausea and vomiting of pregnancy. Am Fam Physician 2014
Hermont AP, et al. Tooth erosion and eating disorders: a systematic review and meta-analysis. PLoS One 2014

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DISORDERS ASSOCIATED WITH N/V

Nausea and vomiting of pregnancy

- Up to 74%of pregnant women suffer nausea and/or vomiting
- 50% have vomiting alone
- Some risk factors include female fetus, increased gravidity, multiple gestation, trisomy 21, previous hyperemesis of pregnancy, history of motion sickness or migraine headaches
- Nearly always begins within the first nine weeks of pregnancy

Gastroparesis

- Delayed gastric emptying diagnosed by scintigraphy gastric emptying testing Idiopathic and diabetic gastroparesis are the two most common groups

Herrell HE. Nausea and vomiting of pregnancy. Am Fam Physician 2014

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DISORDERS OF N/V

Functional nausea and vomiting:

The Rome IV criteria requires fulfillment of the **criteria for at least 3 months** with **symptom onset at least 6 months before diagnosis:**

- At least 1 day per week and/or 1 or more vomiting episodes per week
- Self-induced vomiting, eating disorders excluded
- Organic diseases excluded (EGD)

Cannabinoid hyperemesis syndrome:

May be associated with pathologic bathing behavior (prolonged hot baths or showers)

A systematic literature review by Venkatesan et al 2019 proposed these criteria should require:

- At least 3 episodes per year
- Cannabis use for greater than one year before symptom onset
- Average use greater than 4 times per week
- Resolution after cessation of cannabis use for at least 6 months

Stanghellini V, et al. Gastroduodenal Disorders. Gastroenterology 2016

Venkatesan T, et al. Role of chronic cannabis use: Cyclic vomiting syndrome vs cannabinoid hyperemesis syndrome. Neurogastroenterol Motil 2019

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DISORDERS OF N/V

Cyclic vomiting syndrome (Rome IV criteria must include all criteria):

- Vomiting is acute and lasts < 1 week
- At least 3 discrete episodes in the prior year and 2 episodes in the past 6 months, occurring at least 1 week apart
- Absence of vomiting between episodes
- Personal or family history of migraine headaches supports the diagnosis

Venkatesan T, et al. Guidelines on management of cyclic vomiting syndrome in adults by the American Neurogastroenterology and Motility Society and the Cyclic Vomiting Syndrome Association. Neurogastroenterol Motil 2019

TREATMENT: ANTIEMETICS AND PROKINETICS

Prochlorperazine (Compazine) - antiemetic that alleviates acute nausea and vomiting

- Associated with risks of hypotension and extrapyramidal side effects

Metoclopramide (Reglan) **-** dopamine receptor antagonist has combined antiemetic and prokinetic properties

- Associated with extrapyramidal side effects

Domperidone - penetrates the blood-brain barrier poorly therefore anxiety and dystonia are much less common than with metoclopramide

- Not approved for use in the United States
- The FDA domperidone investigational new drug section can be contacted at DomperidoneIND@fda.hhs.gov

Erythromycin - motilin receptor agonist that improves gastric emptying without improving nausea

- A systematic review of published clinical trials of oral erythromycin therapy for various types of gastroparesis revealed that all studies were methodically weak and demonstrated <50% clinical improvement

Furyk JS, et al. Drug treatment of adults with nausea and vomiting in primary care. BMJ 2014
Maganti K, et al. Oral erythromycin and symptomatic relief of gastroparesis: a systematic review. Am J Gastroenterol 2003

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TREATMENT – SEROTONIN ANTAGONISTS, TCA AND PACEMAKER

Ondansetron (Zofran) - serotonin antagonists (5-HT3)

- Cornerstone of therapy for acute emesis with chemotherapy agents
- Oral formulation has comparable efficacy to intravenous dosing
- Side effects are headache 15 to 20%, constipation 5 to 10%, and dizziness up to 10% of patients receiving IV and in 5% receiving oral formulation
- Electrocardiogram (ECG) interval changes appear to be most prominent one to two hours after a dose and are mostly small, clinically insignificant, and return to baseline within 24 hours

Amitriptyline - tricyclic antidepressant has a role both as abortive treatment and as prophylaxis for cyclic vomiting syndrome

Gastric electrical stimulation - via implanted electrodes can be considered in selected patients with gastroparesis that is refractory to conventional therapy

Perez EA, et al. Comparison of single-dose oral granisetron versus intravenous ondansetron in the prevention of nausea and vomiting induced by moderately emetogenic chemotherapy: a multicenter, double-blind, randomized parallel study. J Clin Oncol 1998

Navari RM, et al. Electrocardiographic and cardiovascular effects of the 5-hydroxytryptamine3 receptor antagonists. Ann Pharmacother 2003

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PEPTIC ULCER DISEASE (PUD)

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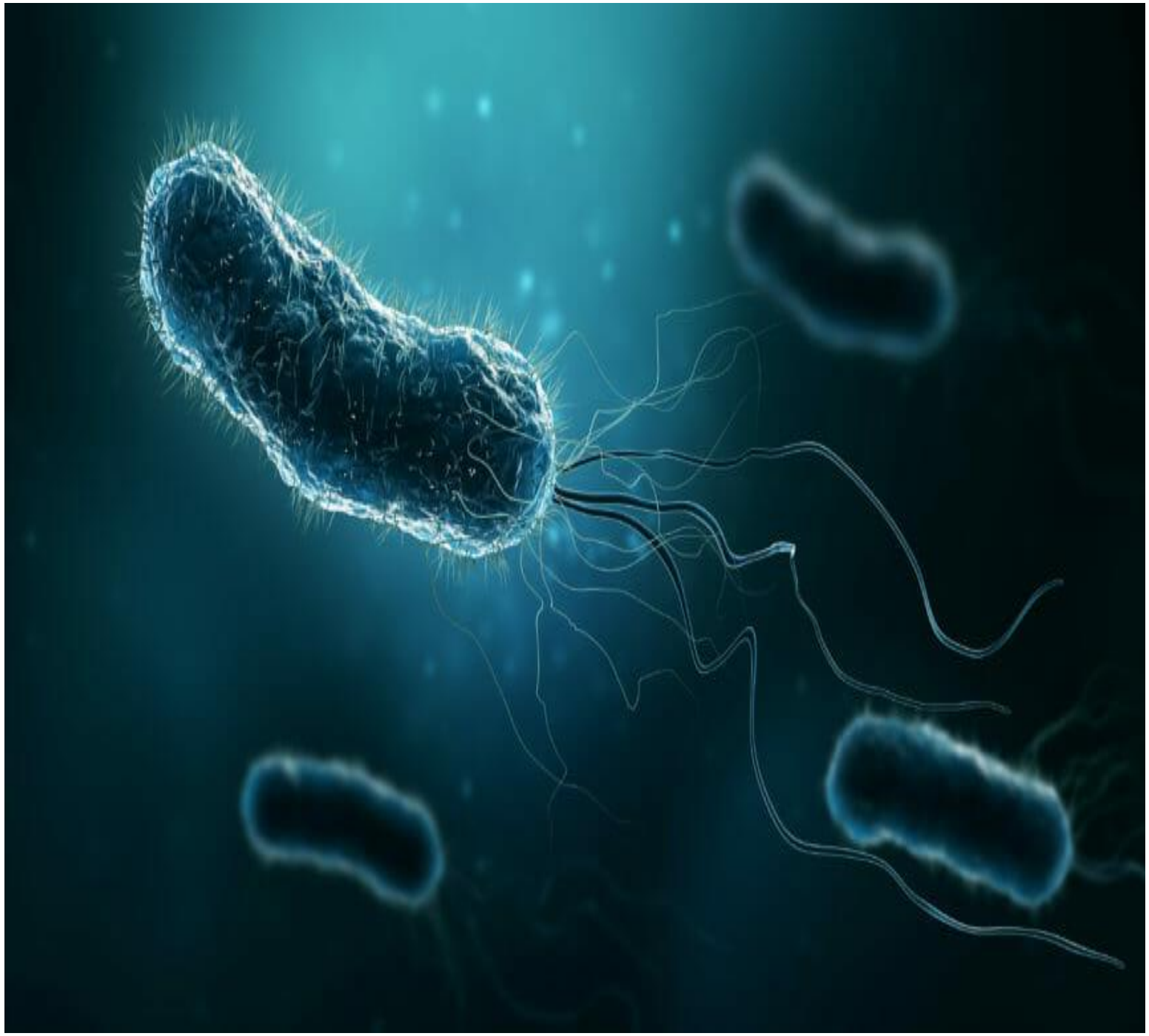

HELICOBACTER PYLORI

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PEPTIC ULCER DISEASE (PUD)

- Defect in the gastric or duodenal wall that extends through the muscularis mucosa into the deeper layers of the wall
- *Helicobacter pylori* (*H. pylori*) and nonsteroidal anti-inflammatory drugs (NSAIDs) are primary causes
- *Helicobacter pylori* (also called *H. pylori* or “HP”) is a gram – bacilli
  - Dr. Barry Marshall and Dr. J. Robin Warren were awarded the 2005 Nobel Prize in Medicine for this discovering *H. pylori’s* association with ulcers
- Treat with a goal of eradication
- Confirm eradication 4 or more weeks after the completion of therapy

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HELICOBACTER PYLORI TESTING INVASIVE

Biopsy urease testing

- Gastric biopsies placed in a pH reagent → urease cleaves urea and liberates ammonia (alkaline pH) resulting in color change
- Sensitivity and specificity of biopsy urease testing is 90 and 95% respectively

Histology

- Gastric biopsies can diagnose of *H. pylori* infection and associated lesions (atrophic gastritis, intestinal metaplasia, dysplasia, and mucosa-associated lymphoid tissue [MALT] lymphoma)
- Biopsies should be taken from both the antrum and body of the stomach
- Accuracy of histologic diagnosis increases with Giemsa stain
- Sensitivity and specificity of histology 95 and 98% respectively
- Sensitivity of histology decreased on PPI therapy due to proximal migration of *H. pylori* to corpus from antrum of stomach
- Density of *H. pylori* can vary at different sites and interpretation of histologic slides associated with interobserver variability

Chey WD, et al. Practice Parameters Committee of the American College of Gastroenterology. American College of Gastroenterology guideline on the management of Helicobacter pylori infection. Am J Gastroenterol 2007

Wright CL et al.The use of routine special stains for upper gastrointestinal biopsies. Am J Surg Pathol 2006

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HELICOBACTER PYLORI TESTING NONINVASIVE

Urea breath testing - hydrolysis of urea by H. pylori produces CO2 and ammonia

- The sensitivity and specificity of UBT are approximately 88 to 95% and 95 to 100%, respectively

Stool antigen assay

- Stool antigen testing can therefore be used to establish the initial diagnosis of *H. pylori* and to confirm eradication
- Of the available tests, stool antigen testing is the most cost effective in areas of low to intermediate prevalence of *H. pylori*
- The sensitivity and specificity of the laboratory-based monoclonal enzyme immunoassay 94 and 97%, respectively (decreased with recent use of bismuth compounds, antibiotics, and PPIs)

Serology

- Laboratory-based ELISA test to detect immunoglobulin G (IgG) antibodies is inaccurate and not recommended
- Sensitivity and specificity of 85 and 79%, respectively

Howden CW, et al. Guidelines for the management of Helicobacter pylori infection. Ad Hoc Committee on Practice Parameters of the American College of Gastroenterology. Am J Gastroenterol 1998
Kelly SM, et al. Isolation of Helicobacter pylori from feces of patients with dyspepsia in the United Kingdom. Gastroenterology 1994
Loy CT, et al. Do commercial serological kits for Helicobacter pylori infection differ in accuracy? A meta-analysis. Am J Gastroenterol 1996

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HP/PEPTIC ULCER DISEASE TREATMENT

- PPIs have higher healing rates compared to H2 blockers due to stronger acid suppression
- Encourage patients to stop smoking, limit alcohol intake, and avoid nonsteroidal anti-inflammatory drug (NSAID)
- Approximately 60% of peptic ulcers heal spontaneously and eradication of *H. pylori* leads to >90% healing rate
- **Always confirm *H. pylori* eradication**

Uncomplicated ulcer

- PPI given BID for 30 days, along with the antibiotic regimen to treat *H. pylori* (Pepto Bismol 525 mg + Flagyl 500 mg + Tetracycline 500 mg QID x 14 days)
- Eradication of *H. pylori* heals >90% of ulcers

Complicated ulcer

- PPI IV initially, then BID x 4 weeks minimum
- Dosing should be reduced to once daily for additional 8 weeks
- In patients with gastric ulcers discontinue antisecretory therapy only after ulcer healing has been confirmed by upper endoscopy

Yeomans ND, et al. A comparison of omeprazole with ranitidine for ulcers associated with nonsteroidal antiinflammatory drugs. Acid Suppression Trial: Ranitidine versus Omeprazole for NSAID-associated Ulcer Treatment (ASTRONAUT) Study Group. N Engl J Med 1998

Lam SK, et al. Does treatment of Helicobacter pylori with antibiotics alone heal duodenal ulcer? A randomised double blind placebo controlled study. Gut 1997

Li LF, et al. Cigarette smoking and gastrointestinal diseases: the causal relationship and underlying molecular mechanisms (review). Int J Mol Med 2014

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PEPTIC ULCER DISEASE MANAGEMENT

Duodenal ulcers - low risk of malignancy and no repeat EGD unless symptoms persist or recur

Gastric ulcers – follow up endoscopy recommended (with biopsies of the ulcer if still present) be performed after 8 to 12 weeks in patients with gastric ulcers and any one of the following:

- Symptoms persist despite medical therapy and/or etiology unclear
- Giant ulcer size >2 cm
- Biopsies not performed or inadequate sampling (up to 5% false negative sampling)
- Ulcer appears suspicious for malignancy
- Continued bleeding
- Age >50 years, Helicobacter pylori, immigrants from a region with high prevalence of gastric cancer [Japan, Korea, Taiwan, Costa Rica], family history of gastric cancer, the presence of adenoma, dysplasia or intestinal metaplasia)

ASGE Standards of Practice Committee, Banerjee S, Cash BD, et al. The role of endoscopy in the management of patients with peptic ulcer disease. Gastrointest Endosc 2010
Gisbert

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PEPTIC ULCER DISEASE MANAGEMENT

Maintenance antisecretory therapy is recommended in the following patients with peptic ulcer disease:

- Giant (>2 cm) peptic ulcer and age >50 years or multiple co-morbidities
- *H. pylori*-negative, NSAID-negative ulcer disease
- Failure to eradicate *H. pylori* (up to 30% recurrence in first year even with PPI therapy)
- Frequently recurrent peptic ulcers (>2 documented recurrences a year)
- Continued NSAID use

Safety and Pregnancy

- A meta-analysis of safety studies showed no significant adverse outcomes with PPI use in pregnant women
- Limited data with omeprazole and pantoprazole suggest that excretion in breast milk does occur but the levels are low

Gill SK, et al. The safety of proton pump inhibitors (PPIs) in pregnancy: a meta-analysis. Am J Gastroenterol 2009; 104:1541.JP, et al. Meta-analysis: Helicobacter pylori eradication therapy vs. antisecretory non-eradication therapy for the prevention of recurrent bleeding from peptic ulcer. Aliment Pharmacol Ther 2004

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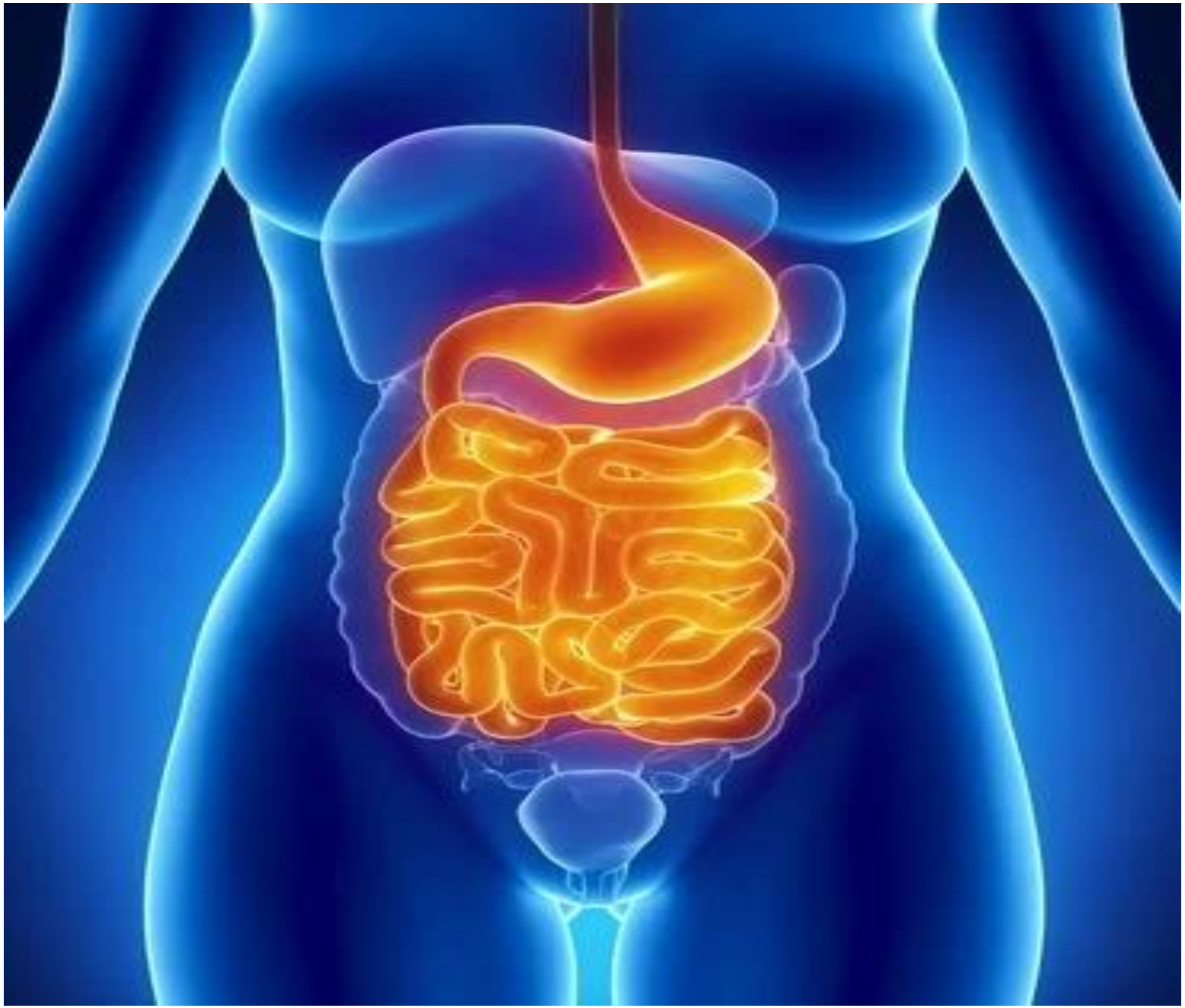

ABDOMINAL PAIN

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ABDOMINAL PAIN – HISTORY IS IMPORTANT

Location

Temporal elements - onset, frequency, and duration of the pain are helpful features

- Gradual- pancreatitis or sudden - peritonitis

Quality

- Burning - GERD or gnawing - PUD
- Colicky - gastroenteritis or cramping - SBO

Severity

- Intense pain – biliary, nephrolithiasis or acute mesenteric ischemia
- Dull pain - gastroenteritis is less marked

Precipitants or palliation

- Chronic mesenteric ischemia usually starts within one hour of eating
- PUD relieved by eating then recur several hours after a meal
- Pancreatitis relieved by sitting up and leaning forward
- Peritonitis improved by lying on back

Associated symptoms:

- Nausea, vomiting, diarrhea, constipation, hematochezia, melena, and changes in stool
- Jaundice, pruritis and changes in the color of urine and stool
- Dysuria, frequency, and hematuria
- Rashes
- Weight loss

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ABDOMINAL PAIN

Right Upper Quadrant Pain

CBC, CMP, lipase, US abdomen

Biliary colic, cholecystitis, cholangitis, SOD, hepatitis, PV thrombus, liver abscess

Epigastric Pain:

CBC, CMP, lipase, US abdomen
HP stool Antigen or EGD if suspicious of PUD

MI, pancreatitis, PUD, GERD, gastritis, functional dyspepsia, gastroparesis

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ABDOMINAL PAIN

Left Upper Quadrant Pain

CBC w Diff, lipase, CT Abdomen or US Abdomen

Splenomegaly, splenic infarct/abscess/rupture, constipation

Lower Abdominal Pain:

CBC w Diff, ESR/CRP, UA, CT abdomen and pelvis

Appendicitis, diverticulosis, nephrolithiasis, pyelonephritis, cystitis, colitis

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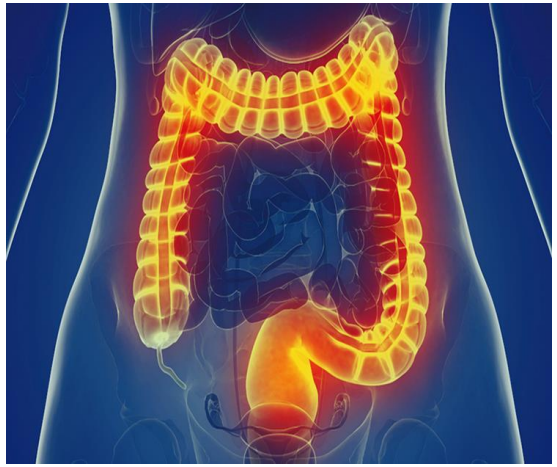
ABDOMINAL PAIN: DIFFUSE ABDOMINAL PAIN

CBC, CMP, lipase, B HCG, CT abdomen and pelvis

SBO, perforation, mesenteric ischemia, IBD, gastroenteritis, celiac, IBS, constipation, lactose intolerance, malignancy



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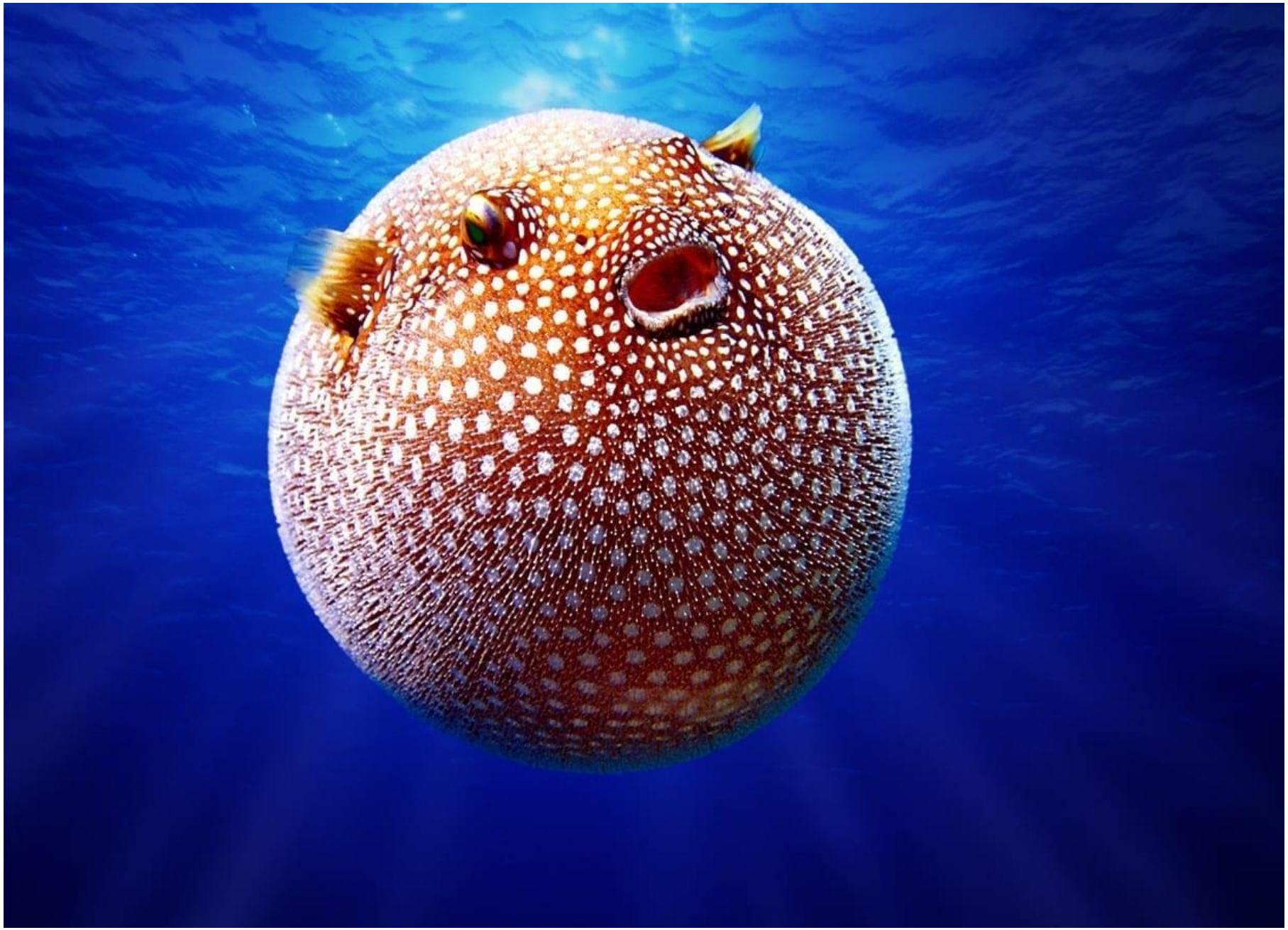

BLOATING AND FLATULENCE

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BLOATING AND FLATULENCE - BACKGROUND

- Volume of intestinal gas ~ 200 mL
- 500 - 1500 mL gas passed daily
- Humans pass gas 10 - 20 times daily

Levitt MD. Intestinal gas production. J Am Diet Assoc 1972

Levitt MD. Production and excretion of hydrogen gas in man. N Engl J Med 1969

Newcomer AD, et al. Prospective comparison of indirect methods for detecting lactase deficiency. N Engl J Med 1975

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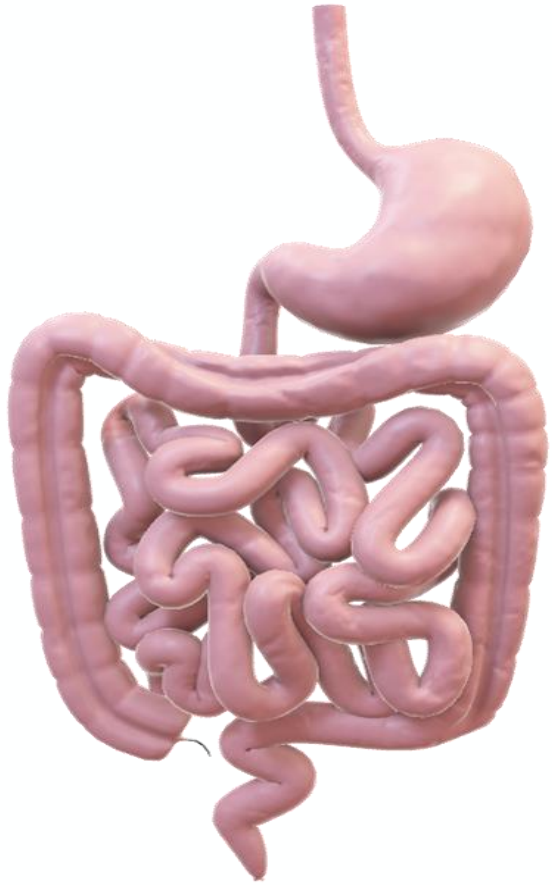
BLOATING AND FLATULENCE - CAUSES

- Excessive air swallowing
- Increased production
- Decreased absorption



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BLOATING AND FLATULANCE

- Alarm features:
  - Nocturnal defecation
  - Hematochezia
  - Diarrhea or steatorrhea
  - Vomiting or weight loss

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BLOATING AND FLATULANCE - TREATMENT

- Lactose intolerance –enzymes and avoidance
- Chronic Pancreatic Insufficiency – enzymes
- SIBO – antibiotics
- Celiac disease – gluten avoidance

de Roest RH, et al. The low FODMAP diet improves gastrointestinal symptoms in patients with irritable bowel syndrome: a prospective study. Int J Clin Pract 2013

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BLOATING AND FLATULANCE - TREATMENT

Dietary modification:

- Avoid gas-producing foods
- Low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) diet
- https://www.monashfodmap.com/about-fodmap-and-ibs/

Medications:

- Anticholinergic agents, opioids, and calcium blockers should be avoided because of their effects on gut motility
- Simethicone is relatively safe, SE includes diarrhea

de Roest RH, et al. The low FODMAP diet improves gastrointestinal symptoms in patients with irritable bowel syndrome: a prospective study. Int J Clin Pract 2013

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GALLSTONE DISEASE

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GALLSTONE DISESASE

Gallstones occur in up to 20% of American women by the age of 60 and 3 x more likely to develop stones than men

Cholesterol stones – 90% of stones and produced by imbalance in the production of cholesterol or the secretion of bile

Pigmented stones - primarily composed of bilirubin

Risk Factors for Development of Gallstones:

- Multiple pregnancies
- Family history of gallstones
- Hispanic or American Indian heritage
- Obesity
- Rapid loss of weight

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GALLSTONE DISESASE - SYMPTOMS

Asymptomatic (incidental) gallstones:

- Most individuals with gallstones are asymptomatic and stones found incidentally

Symptomatic gallstones:

- **Biliary colic** = intense, dull discomfort located in RUQ often associated with diaphoresis, nausea and vomiting

Atypical symptoms:

- Belching/regurgitation
- Early satiety
- Abdominal distension/bloating
- Epigastric or retrosternal burning
- Nausea or vomiting alone
- Nonspecific abdominal pain

Everhart JE, et al. Prevalence and ethnic differences in gallbladder disease in the United States. Gastroenterology 1999

GALLSTONE DISESASE

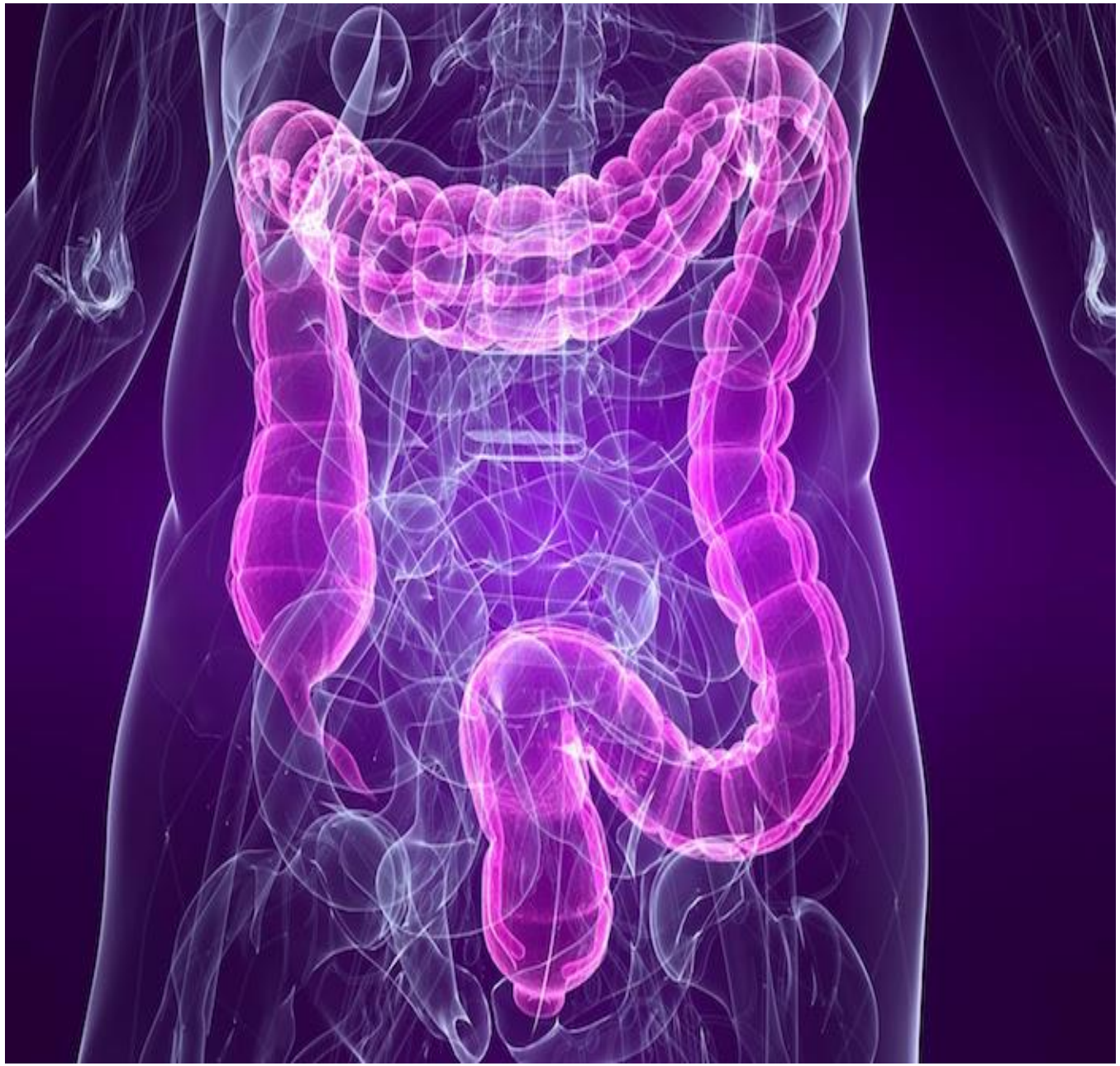
- Gallstone complications → acute cholecystitis, cholangitis, gallstone pancreatitis
- Sludge and microlithiasis are managed the same as gallstones

- Patients with biliary colic and gallstones should have cholecystectomy

- Asymptomatic patients with incidental gallstones should delay cholecystectomy to prevent unnecessary surgery

- Patients with increased risk of gallbladder cancer should undergo cholecystectomy
  - Biliary cyst
  - Gallbladder adenomas (polyp > 1 cm or rapid growth)
  - Porcelain gallbladder
  - Large gallstones (> 3 cm)

Diehl AK. Gallstone size and the risk of gallbladder cancer. JAMA 1983



IRRITABLE BOWEL SYNDROME

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IRRITABLE BOWEL SYNDROME (IBS)

Approximately 10 to 15% of adults and adolescents have symptoms consistent with IBS

Defined as recurrent abdominal pain at least one day per week in the last 3 months with >2 of the following:

- related to defecation
- associated with a change in frequency of stool
- associated with a change in form (appearance) of stool

Subtypes:

- IBS with predominant constipation (IBS-C)
- IBS with predominant diarrhea (IBS-D)
- IBS with mixed bowel habits (IBS-M)
- IBS unclassified

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IRRITABLE BOWEL SYNDROME - TREATMENT

Patients may benefit from exclusion of gas-producing foods; a diet low in fermentable oligo-, di-, and monosaccharides and polyols **(FODMAPs)**

- **Fermentable** - intestinal bacteria ferment undigested carbohydrate to produce gases
- **Oligosaccharides** (fructans) - found in wheat, rye, onions, garlic and legumes
- **Disaccharides** (lactose) - found in milk, soft cheeses and yogurts
- **Monosaccharides** (fructose) - found in honey, apples, high fructose corn syrups
- **Polyols** (sorbitol and mannitol) – found in some fruits, vegetables and sweeteners

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Foods suitable on a low-fodmap diet

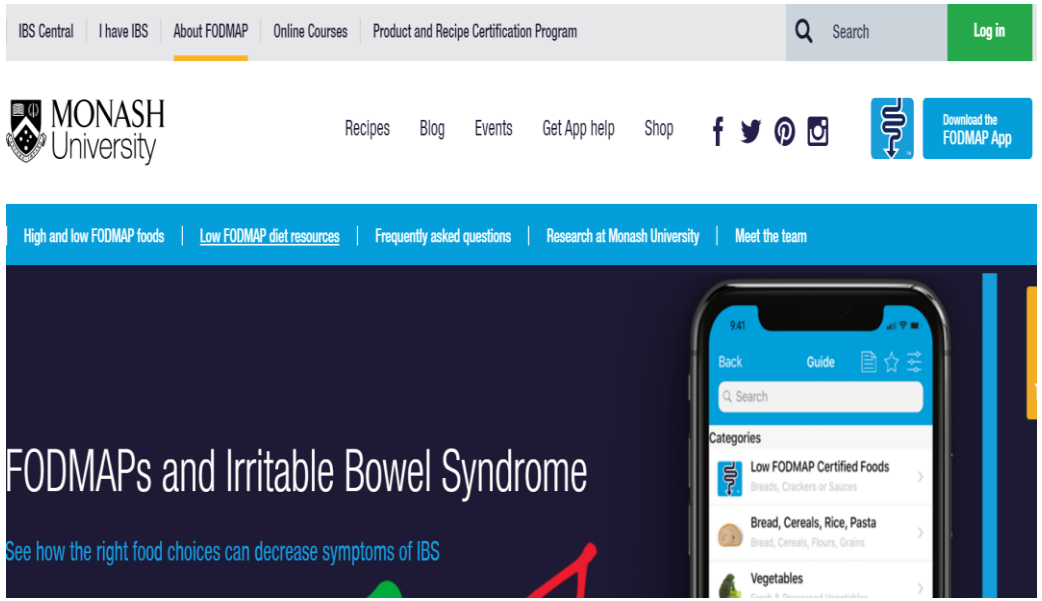
fruit	vegetables	grain foods	milk products	other
fruit banana, blueberry, boysenberry, canteloupe, cranberry, durian, grape, grapefruit, honeydew melon, kiwifruit, lemon, lime, mandarin, orange, passionfruit, pawpaw, raspberry, rhubarb, rockmelon, star anise, strawberry, tangelo Note: if fruit is dried, eat in small quantities	**vegetables** alfalfa, bamboo shoots, bean shoots, bok choy, carrot, celery, choko, choy sum, eggplant, endive, ginger, green beans, lettuce, olives, parsnip, potato, pumpkin, red capsicum (bell pepper), silver beet, spinach, squash, swede, sweet potato, taro, tomato, turnip, yam, zucchini **herbs** basil, chili, coriander, ginger, lemongrass, marjoram, mint, oregano, parsley, rosemary, thyme	**cereals** gluten-free bread or cereal products **bread** 100% spelt bread **rice** **oats** **polenta** **other** arrowroot, millet, psyllium, quinoa, sorgum, tapioca	**milk** lactose-free milk*, oat milk*, rice milk*, soy milk* *check for additives **cheeses** hard cheeses, and brie and camembert **yoghurt** lactose-free varieties **ice-cream substitutes** gelati, sorbet **butter substitutes** olive oil	**tofu** **sweeteners** sugar* (sucrose), glucose, artificial sweeteners not ending in '-ol' **honey substitutes** golden syrup*, maple syrup*, molasses, treacle *small quantities

Eliminate foods containing fodmaps

excess fructose	lactose	fructans	galactans	polyols
fruit apple, mango, nashi, pear, tinned fruit in natural juice, watermelon **sweeteners** fructose, high fructose corn syrup **large total fructose dose** concentrated fruit sources, large serves of fruit, dried fruit, fruit juice **honey** corn syrup, fruisana	**milk** milk from cows, goats or sheep, custard, ice cream, yoghurt **cheeses** soft unripened cheeses eg. cottage, cream, mascarpone, ricotta	**vegetables** artichoke, asparagus, beetroot, broccoli, brussels sprouts, cabbage, fennel, garlic, leek, okra, onion (all), shallots, spring onion **cereals** wheat and rye, in large amounts eg. bread, crackers, cookies, couscous, pasta **fruit** custard apple, persimmon, watermelon **miscellaneous** chicory, dandelion, inulin, pistachio	**legumes** baked beans, chickpeas, kidney beans, lentils, soy beans	**fruit** apple, apricot, avocado, blackberry, cherry, longon, lychee, nashi, nectarine, peach, pear, plum, prune, watermelon **vegetables** cauliflower, green capsicum (bell pepper), mushroom, sweet corn **sweeteners** sorbitol (420) mannitol (421) isomalt (953) maltitol (965) xylitol (967)

IBS Self Help and Support Group - www.ibsgroup.org

https://www.monashfodmap.com/about-fodmap-and-ibs/



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IRRITABLE BOWEL SYNDROME - TREATMENT

Exclude foods that increase flatulence:

- Beans, onions, celery, carrots, raisins, bananas, apricots, prunes, Brussels sprouts, wheat germ, pretzels, and bagels
- Alcohol
- Caffeine

Visceral hypersensitivity can exaggerate pain in IBS associated with gas-producing foods

Hasler WL, et al. Irritable bowel syndrome. In: Textbook of Gastroenterology, 4th ed, Yamada T (Ed), JB Lippincott, Philadelphia 2003
Zhu Y,et al. Bloating and distention in irritable bowel syndrome: the role of gas production and visceral sensation after lactose ingestion in a population with lactase deficiency. Am J Gastroenterol 2013

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IRRITABLE BOWEL SYNDROME - TREATMENT

- Empiric trial of a lactose-free diet should be considered in patients with persistent abdominal bloating despite exclusion of gas-producing foods
- Diagnosis of lactose intolerance can be confirmed with breath testing in patients who do not want to be on a lactose-restricted diet
- Incidence of lactose malabsorption is not higher in patients with IBS
- IBS + lactose intolerance have an exaggerated symptoms with lactose ingestion

Zhu Y, et al. Bloating and distention in irritable bowel syndrome: the role of gas production and visceral sensation after lactose ingestion in a population with lactase deficiency. Am J Gastroenterol 2013

IRRITABLE BOWEL SYNDROME - TREATMENT

- **Gluten** has been demonstrated to alter bowel barrier functions in patients with IBS-D
- **Nonceliac gluten sensitivity (NCGS)** is hypothesized as an underlying mechanism for IBS symptoms
- Symptomatic improvement seen with a gluten-free diet may be rather due to reduction of fructans
- Given the absence of serious side effects and potential benefit of psyllium, fiber should be considered in patients with IBS whose predominant symptom is constipation

Skodje GI, et al. Fructan, Rather Than Gluten, Induces Symptoms in Patients With Self-Reported Non-Celiac Gluten Sensitivity. Gastroenterology 2018

IRRITABLE BOWEL SYNDROME - CONSTIPATION

- **PEG** is inexpensive and has fewer side effects as compared with other osmotic laxatives (ex. lactulose, milk of magnesia)

- **Lubiprostone (Amitiza)** is a locally acting chloride channel activator that enhances chloride-rich intestinal fluid secretion
  - Used for treatment of IBS-C in women 18 years and older
  - 8 micrograms twice daily
  - Efficacy well demonstrated in two multicenter, placebo-controlled trials of 1154 IBS-C adults (92% women) randomly assigned to lubiprostone (8 mcg BID) vs placebo for 12 weeks (18% vs 10% response)
  - A follow-up open-label study that included 522 patients demonstrated that benefits of lubiprostone persisted or increased at 52 weeks

Rao S, Lembo AJ et al. A 12-week, randomized, controlled trial with a 4-week randomized withdrawal period to evaluate the efficacy and safety of linaclotide in irritable bowel syndrome with constipation. Am J Gastroenterol 2012

IRRITABLE BOWEL SYNDROME - CONSTIPATION

Guanylate cyclase agonists stimulates intestinal fluid secretion and transit

- **Linaclotide (Linzess**) dosed at 290 mcg QD
- The efficacy of linaclotide in the treatment of IBS-C has been demonstrated in two randomized controlled trials
- 26 weeks treatment → 38% vs 14% reported significant improvement

- **Plecanatide (Trulance)** dosed at 3 mg QD and is comparable to linaclotide in efficacy

Sodium/hydrogen exchanger 3 (NHE3) inhibitor reduces the absorption of sodium and phosphate and enhances intestinal fluid volume and transit

- **Tenapanor (Ibsrela)** efficacy demonstrated in two randomized, multicenter trials in adult patients
- 50 mg BID - Improvement in both average weekly complete spontaneous bowel movements and abdominal pain as compared with placebo

Rao S, Lembo AJ, Shiff SJ, et al. A 12-week, randomized, controlled trial with a 4-week randomized withdrawal period to evaluate the efficacy and safety of linaclotide in irritable bowel syndrome with constipation. Am J Gastroenterol 2012; 107:1714.

Chey WD, et al. Linaclotide for irritable bowel syndrome with constipation: a 26-week, randomized, double-blind, placebo-controlled trial to evaluate efficacy and safety. Am J Gastroenterol 2012

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IRRITABLE BOWEL SYNDROME - DIARRHEA

Loperamide 2 mg 45 minutes before a meal on regularly scheduled doses (max dose 16 mg/day)

- inhibit peristalsis, prolong transit time, and reduce fecal volume

Eluxadoline (Viberzi) combines a mu-opioid receptor agonist and a delta-opioid receptor antagonist

- Contraindicated in patients without gallbladder due to acute pancreatitis
- Efficacy demonstrated in two large studies with over 2427 IBS-D demonstrating a decrease in abdominal pain and improvement in stool consistency

In patients with persistent diarrhea bile acid sequestrants are beneficial **(cholestyramine)**

Alosetron (Lotronex) is a 5-hydroxytryptamine-3 receptor (5HT-3) antagonist

- Approved for severe IBS-D in females with symptoms > 6 months who failed conventional treatment
- Modulates visceral afferent activity by decreasing colonic motility and secretion while potentially improving abdominal pain

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IRRITABLE BOWEL SYNDROME - DIARRHEA

Antispasmodics and **peppermint oil** selectively inhibit GI smooth muscle by reducing colonic motor activity

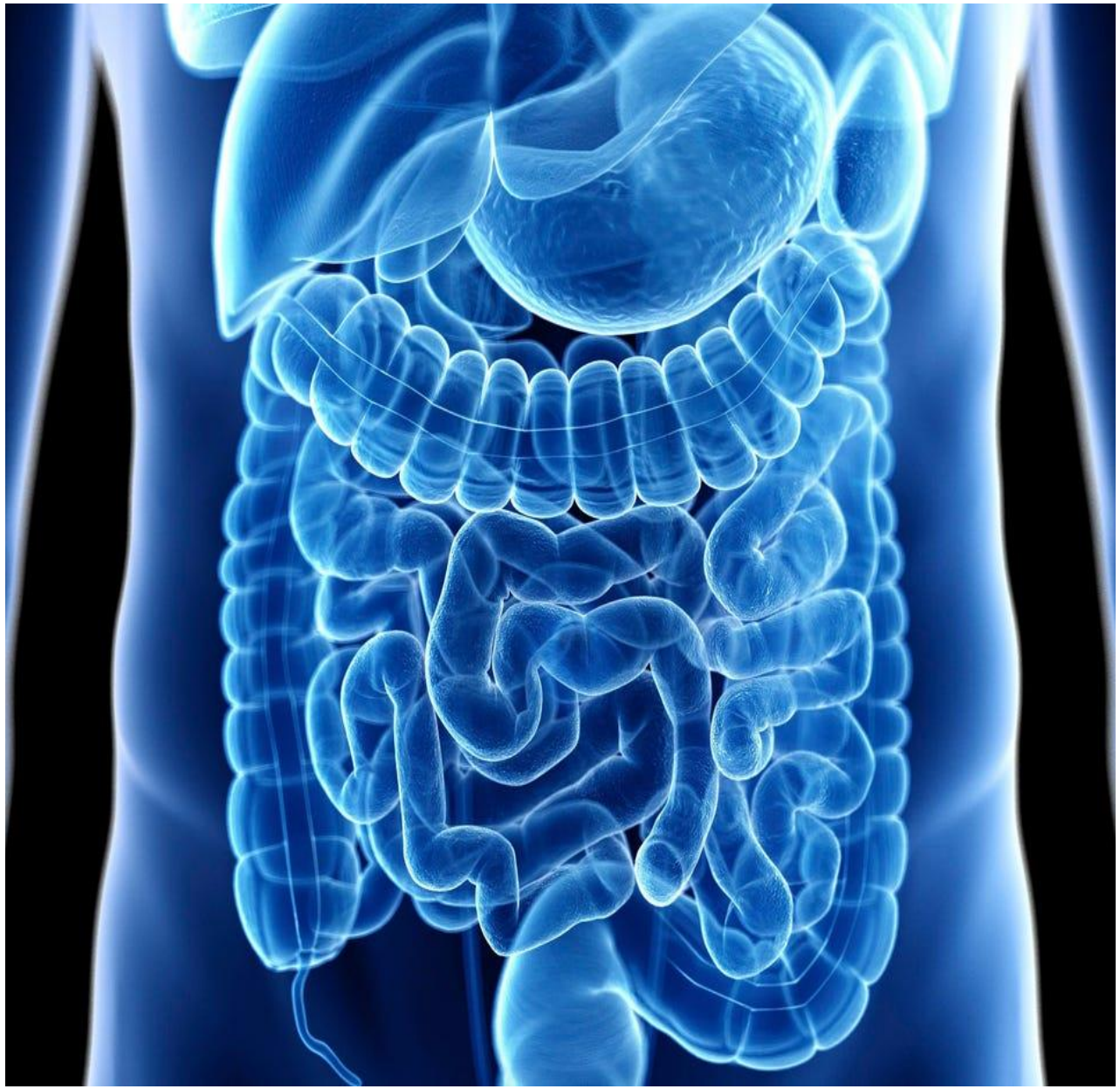
Reduction in postprandial pain, bloating, and urgency:

- Dicyclomine 20 mg orally four times daily as needed
- Hyoscyamine 0.125 to 0.25 mg orally or sublingually three to four times daily as needed

Tricyclic antidepressants (TCAs) slow intestinal transit time through anticholinergic properties and benefit IBS-D

- Amitriptyline 25 mg QHS

Ruepert L, et al. Bulking agents, antispasmodics and antidepressants for the treatment of irritable bowel syndrome. Cochrane Database Syst Rev 2011
Gorard DA, Libbet al. Effect of a tricyclic antidepressant on small intestinal motility in health and diarrhea-predominant irritable bowel syndrome. Dig Dis Sci 1995



TOPICS COVERED:

1. GERD
2. NAUSEA AND VOMITING
3. PEPTIC ULCER DISEASE
4. ABDOMINAL PAIN
5. BLOATING
6. GALLSTONE DISEASE
7. IBS-C and IBS-D

THANK YOU!

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