# Managing Common Non-Pain Symptoms

Emily Peterson, MD
UCLA Family Medicine PGY3

# Symptom Management

Why do we care?

- Common in both inpatient and outpatient settings
- Quality of life
- Often treatable
- Can be manifestations of other problems
- Healthcare cost, length of stay

# Overview

Nausea/vomiting

Constipation

Pruritus

Dyspnea

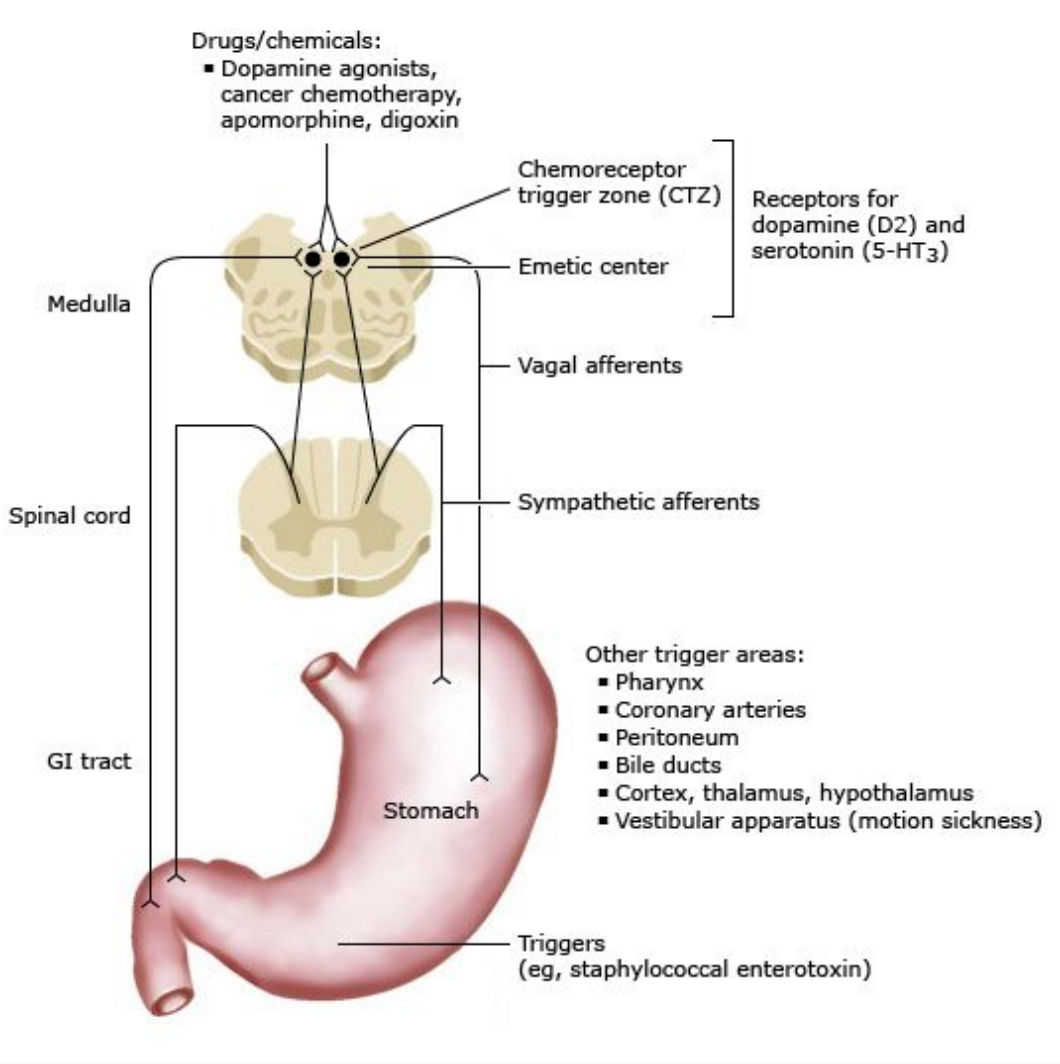
# Nausea & Vomiting

# Nausea/Vomiting

Physiology: reflex to get rid of ingested toxins/substances.

5 neurotransmitters mediate vomiting:

1. Muscarinic (M1)
2. Dopamine (D2)
3. Histamine (H1)
4. Serotonin (5HT3)
5. Substance P (NK1)



# Nausea/Vomiting: Assessment

1. Evaluate for life-threatening disorders - obstruction, mesenteric ischemia, pancreatitis, MI, etc.
2. Assess for complications - fluid depletion, hypokalemia, metabolic alkalosis
3. Treat cause if possible, otherwise manage symptoms

# Nausea/Vomiting: Etiology

Wide range of causes:

- Obstruction
- Infections
- Medications → abx, opioids, chemotherapy, antidepressants
- Intracranial pathology
- Vestibular
- Postoperative
- Dehydration
- Migraine
- Pregnancy
- Cannabis hyperemesis

# Nausea/Vomiting: Management

1. **Antidopaminergics (D2 antagonists)** → medication-induced, toxin-induced (including postop and chemotherapy-associated)
    a. Haldol (IV less likely to prolong QTc), olanzapine (chemo-induced), chlorpromazine (risk of sedation)
    b. Prochlorperazine (risk of QTc prolongation, risk of hypotension and extrapyramidal side effects, shorter-acting), trimethobenzamide
    c. Promotility: metoclopramide (QTc prolongation, tardive dyskinesia - slower dosing (over 15 min) has less risk of akathisia with same efficacy (Tura *et al., 2012*)
    d. Dromperidone: dopamine antagonist with poor BBB penetration so less dystonia, anxiety but not available in US
2. **5HT3 antagonists**
    a. Ondansetron, granisetron (QTc prolonging), palonosetron

# Nausea/Vomiting: Management

3. **Antihistamines, anticholinergics**
    a. Antihistamines: promethazine (QTc prolonging), meclizine, diphenhydramine (QTc prolonging)
    b. Anticholinergics: scopolamine
4. **Miscellaneous**
    c. NK1 antagonists - aprepitant
    d. Dexamethasone
    e. Cannabinoids: dronabinol, nabilone
    f. TCAs: amitriptyline
    g. Anxiolytics: anticipatory N/V

# Opioid-Induced Nausea/Vomiting

- Can stimulate CTZ at base of 4th ventricle, can also directly stimulate vestibular apparatus to cause vertigo
- Constipation
- Tolerance in 3-7 days
- Management
  - Dose adjustment
  - Switch opioids
  - Antiemetics

# Summary:

Opioid-induced → dose adjust, switch opioid, wait for tolerance, meds: antidopaminergics, anticholinergics, antihistamines

Antidopaminergics → best for postop, chemo-induced, opioid-induced, other toxins, migraine

5HT3 antagonists → best for chemo-induced, postop, gastroenteritis, migraine

Antihistamines, anticholinergics → best for vertigo-related

If predominantly nausea, try antidopaminergic

If predominantly vomiting, try 5HT3 antagonist. (Glare *et al.* 2011, Becker *et al.* 2010)

# Constipation

# Constipation: Etiology

1. Solid waste
2. Water content
3. Motility
4. Lubrication
5. Bonus: medication-induced - opioids, anticholinergics (TCAs, antidepressants, scopolamine, oxybutinin, promethazine, benadryl), lithium, verapamil, iron, etc.

# Constipation: Management

1. Solid waste - fiber
2. Water content - hydration, PEG, magnesium, sorbitol/lactulose
3. Motility - senna
4. Lubrication - docusate, glycerin suppositories, mineral oil suppositories

# Opioid-Induced Constipation

- Prevalent: 45-90% of patients on opioids
- Can cause significant mortality, common reason to d/c opioids, increased hospital length of stay
- Physiology: ineffective GI motility, inhibition of mucosal fluid transport, interferes with defecation reflex
- Duration of therapy
- Do not develop tolerance
- **All patients on opioids should have a consistent bowel regimen regardless of opioid dose or duration of therapy**

# Opioid-Induced Constipation: Management

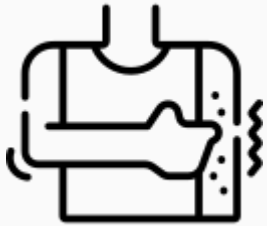
- Nonpharmacologic
- Pharmacologic:
  - Stimulant laxatives: senna, bisacodyl
  - Osmotic laxatives: lactulose, sorbitol, PEG, Mg citrate
  - Rectal laxatives
- Newer therapies:
  - Naloxone - mu opioid receptor antagonist
  - Methylnaltrexone - peripheral mu opioid receptor antagonist
  - Naloxegol - pegylated naloxone
  - Alvimopam - peripheral mu opioid receptor antagonist
  - Lubipristone - selective chloride channel-2 activator
  - Prucalopride - serotonin receptor type 4 agonist

# Pruritus

# Pruritus

Physiology: poorly understood, stimulation of skin itch via unmyelinated peripheral C-fibers, histamine and non-histamine pathways

Scratching: inhibits local circuits and stimulates pain receptors to inhibit itch sensation, release of endogenous opioids



# Pruritus - Etiology and Assessment

Acute vs chronic

If diagnosis unknown:
1. Group 1: inflamed skin
2. Group 2: noninflamed skin
3. Group 3: chronic secondary lesions

If diagnosis known:
1. Dermatologic
2. Systemic
3. Neurologic
4. Psychogenic

Assess for presence/absence of skin lesions
Labs: LFTs, CBC, TSH, renal function, other based on history

# Pruritus - Management

Skin care - emollients, avoid irritants, lifestyle modifications

Topical cooling agents - calamine, menthol, cold compresses

Treat underlying cause if possible:

- Dry skin, moisture, irritation, derm conditions
- Hepatic failure
- Renal failure
- Hypothyroidism
- Hematologic
- Drugs
- Infections
- Allergy
- Psychogenic
- Itch-scratch cycle

# Pruritus - Management

- Antihistamines
- Topical steroids
- Topical tacrolimus
- Antidepressants - paroxetine, mirtazapine, doxepine in CKD, sertraline for cholestasis
- Zofran - opioid-induced pruritus, cholestasis, uremia
- Cholestyramine - cholestatic pruritus
- Rifampin - cholestatic pruritus
- Gabapentin/pregabalin
- Opioid antagonists
- Emerging therapies: JAK inhibitors, IL-31 inhibitors, NK1 receptor antagonist

# Dyspnea

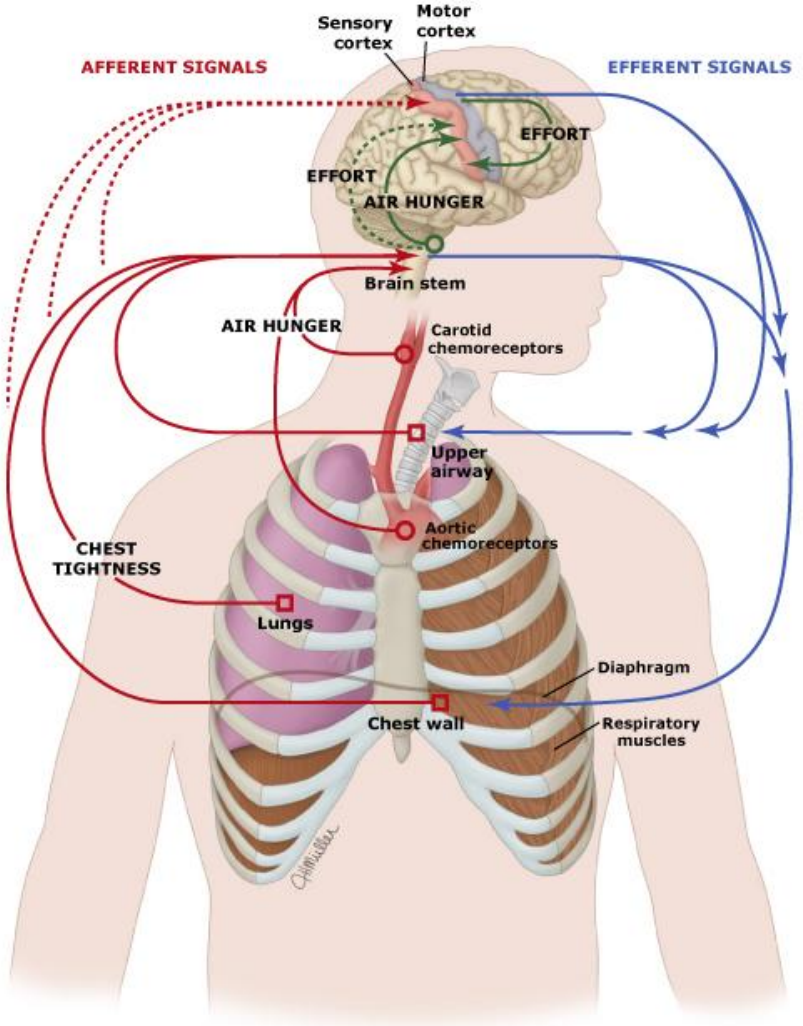
# Dyspnea

Definition: subjective experience of breathing discomfort comprised of distinct sensations that vary intensity (American Thoracic Society)

Consistently ranked as most distressing symptom (Tishelman *et al*., 2007)

Etiology:

- Pulmonary and cardiac



# Dyspnea: Assessment

Ensure equipment is working properly

Assess for triggers, time of symptom onset

- Cardiac: MI, CHF, tamponade
- Pulm: bronchospasm, PE, PTX, infection, anaphylaxis
- Workup: pulse ox, ABG/VBG, CXR, PFTs, etc. if appropriate

# Dyspnea: Management

- Reposition, airflow, modify activity level, mobility aids, etc. if chronic
- Consider discontinuing fluids
- Medications:
  - Opioids - end of life dyspnea
  - Antitussives
  - Anticholinergics (scopolamine) if secretions
  - Anxiolytics
  - Diuretics
  - Bronchodilators
  - Corticosteroids
- Oxygen - titrate to comfort vs pulse ox
- Thoracentesis, indwelling pleural catheter, pleurodesis if effusion

# Questions?

# Resources

Herndon CM, et al. Management of opioid-induced gastrointestinal effects in patients receiving palliative care. Pharmacotherapy. 2002; 22:240-250.

Tura P, Erdur B, Aydin B, Turkcuer I, Parlak I. Slow infusion metoclopramide does not affect the improvement rate of nausea while reducing akathisia and sedation incidence. Emerg Med J. 2012 Feb;29(2):108-12. doi: 10.1136/emj.2010.094367. Epub 2011 Feb 3. PMID: 21292793.

Davidson S, Zhang X, Khasabov SG, Simone DA, Giesler GJ Jr. Relief of itch by scratching: state-dependent inhibition of primate spinothalamic tract neurons. Nat Neurosci. 2009 May;12(5):544-6. doi: 10.1038/nn.2292. Epub 2009 Apr 6. PMID: 19349977; PMCID: PMC3006451.

Yosipovitch G. Epidemiology of itching in skin and systemic disease. In: Itch: Basic Mechanisms and Therapy, Yosipovitch G, Greaves MW, Fleischer Jr AB, McGlone F (Eds), Marcel Dekker, New York 2004. P.183.

Aquagenic pruritus in polycythemia vera: characteristics and influence on quality of life in 441 patients. Siegel FP, Tauscher J, Petrides PE. Am J Hematol. 2013;88(8):665. Epub 2013 Jul 8.

Podesta A, Lopez P, Terg R, Villamil F, Flores D, Mastai R, Udaondo CB, Companc JP. Treatment of pruritus of primary biliary cirrhosis with rifampin. Dig Dis Sci. 1991 Feb;36(2):216-20. doi: 10.1007/BF01300759. PMID: 1988266.

Tishelman C, Petersson LM, Degner LF, et al: Symptom prevalence, intensity, and distress in patients with inoperable lung cancer in relation to time of death. J Clin Oncol 25:5381-5389, 2007