PainWeek

ADVANCED EDUCATION

CERTIFICATION SERIES

Cardiopulmonary Symptoms

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Titles and Affiliations

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Disclosures

Learning Objectives

At the conclusion of this presentation the participant will be able to:

Identify pharmacologic and nonpharmacologic strategies for the treatment of dyspnea

Given an assessment and identified pathogenesis of a complaint of cough and recommend a treatment plan including nonpharmacologic and pharmacologic strategies

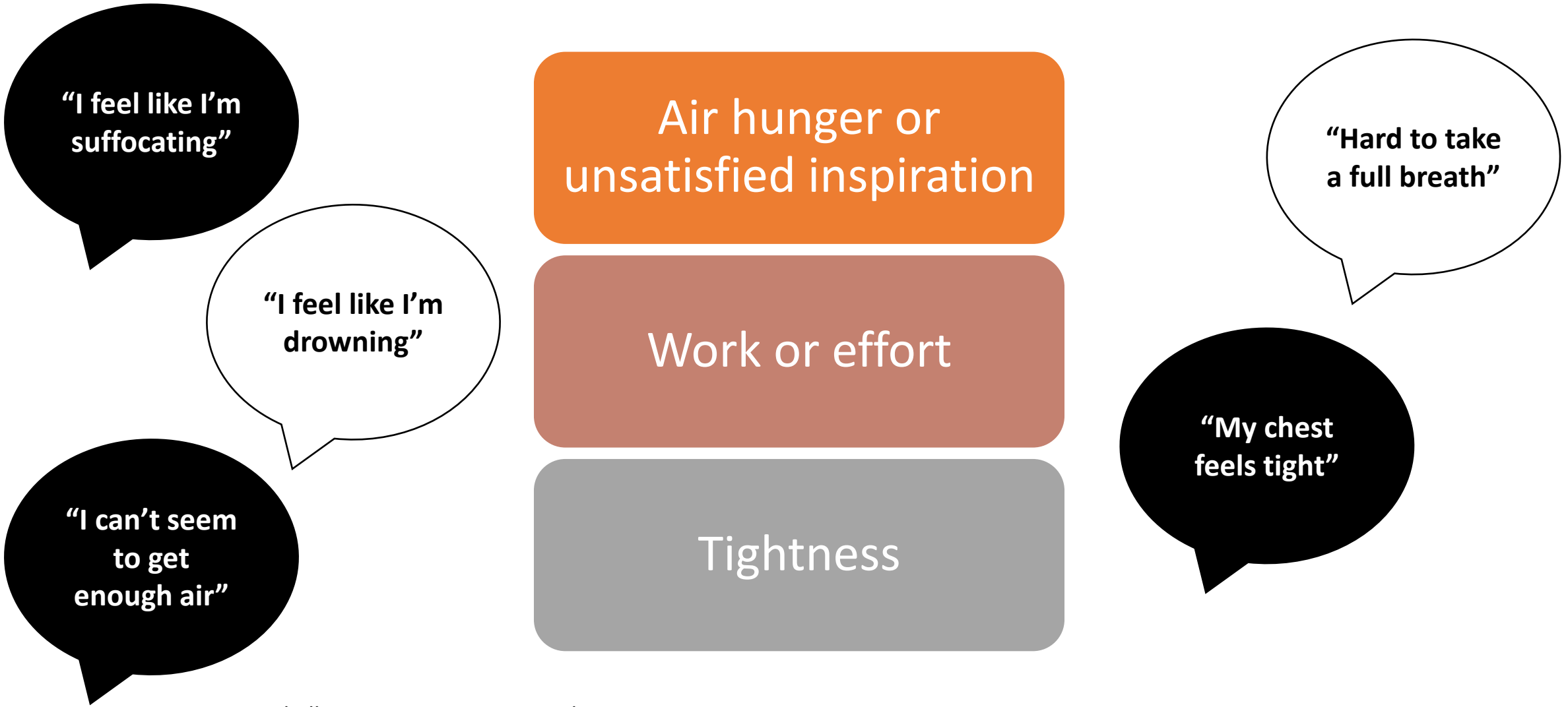
Given a simulated case of a patient with a complaint of hiccups, recommend nonpharmacologic and pharmacologic management strategies

Dyspnea

"A **subjective** experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity."

[American Thoracic Society]

Qualities of Dyspnea

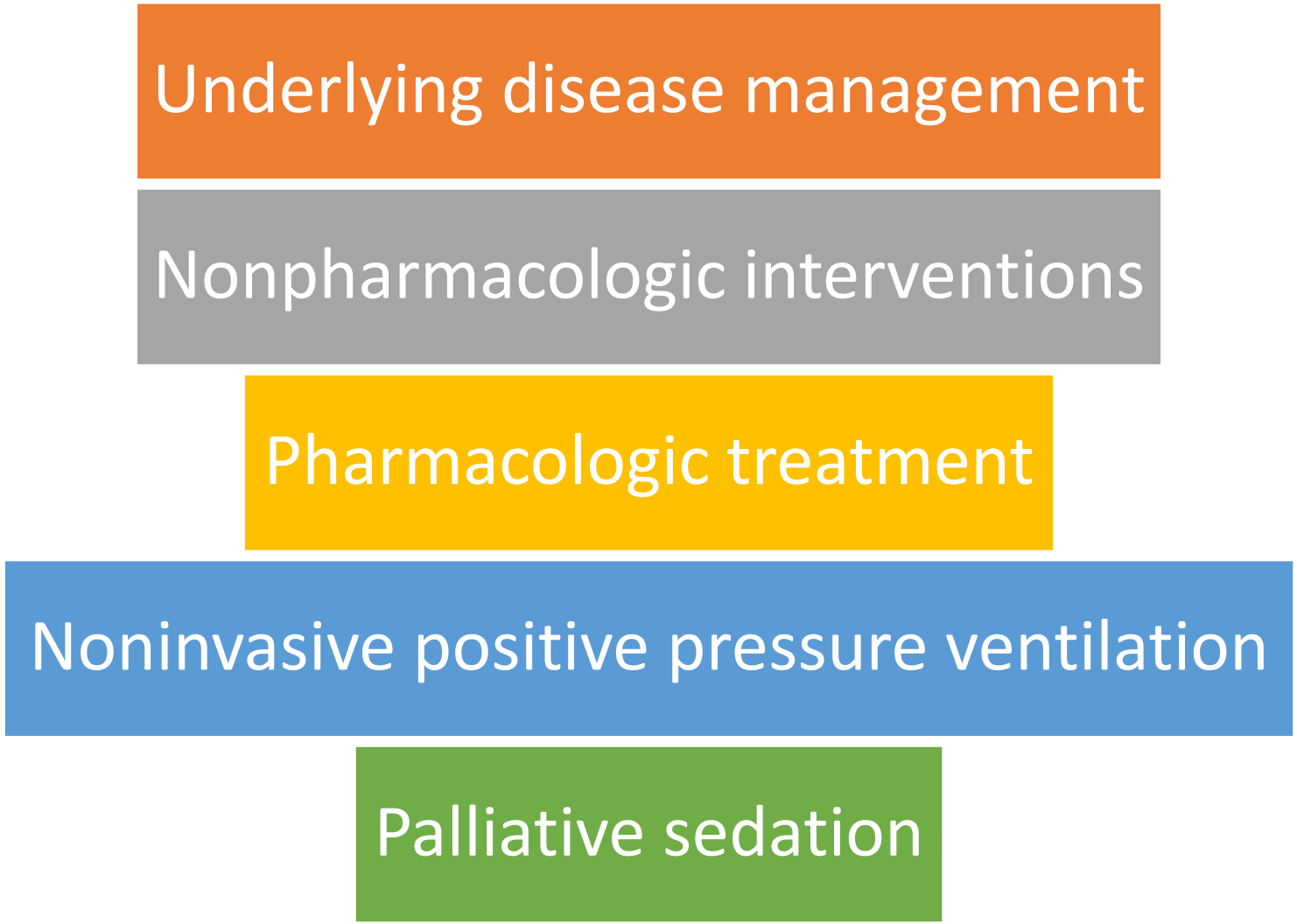


Parshall. *Am J Resp Crit Care Med*. 2012;185:435-452.

Causes of Dyspnea

Lung cancer/ other malignancy	Pleural or pericardial effusion	Pulmonary embolism	SVC obstruction	Infection
Pulmonary hypertension	Radiation- or drug-induced pneumonitis	Ascites	Asthma/ COPD	Bronchiectasis
Interstitial pulmonary fibrosis	Heart failure	Arrhythmia	Anemia	Anxiety/ Panic attack

Management of Dyspnea



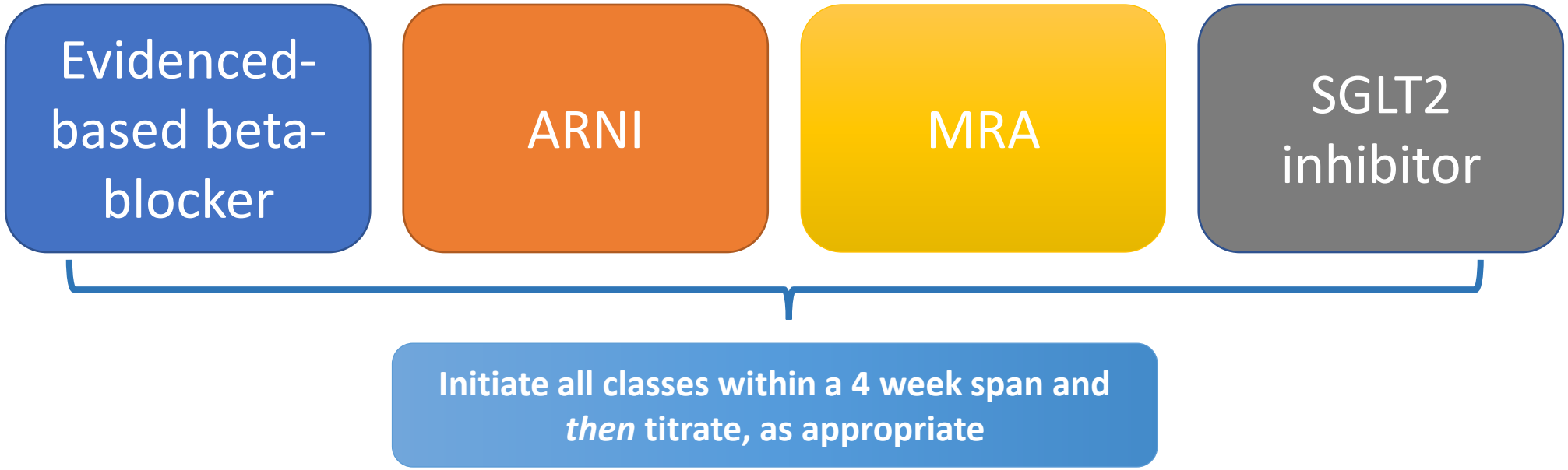
Oxford Textbook of Palliative Medicine. 5 ed. 2015:421-434.

Underlying Disease Management

- Cancer-directed therapy (eg, chemotherapy, immunotherapy, radiation)
- Guideline-directed medical therapy
  - Heart failure
  - COPD
  - Asthma
- Treatment of infection (antibiotics)
- Interventional management (eg, paracentesis, thoracentesis)

Maddox et al. *J Am Coll Cardiol*. 2021 Feb;77(6):772-810.
Global Initiative for Chronic Obstructive Lung Disease. *Am J Respir Crit Care Med*. 2021;203(1):24-36.
Expert Panel. *J Allergy Clin Immunol*. 2020 Dec;146(6):1217-1270.

Heart Failure – Rapid Sequence Initiation



ARNI, angiotensin-receptor neprilysin inhibitor; MRA, mineralocorticoid receptor antagonist; SGLT, sodium-glucose cotransporter

Greene. *JAMA Cardiol*. 2021;6:743-744.
Packer. *Eur J Heart Fail*. 2021;23:882-894.

Nonpharmacologic Interventions

- Cognitive behavioral therapy
- Breathing retraining
- Positioning
- Activity pacing/ energy conservation
- Walking aids
- Neuromuscular electrical stimulation
- Supportive counseling
- Acupuncture/acupressure
- Chest wall vibration
- Exercise
- Handheld fan
- Other
  - Relaxation
  - Guided imagery
  - Music therapy
  - Pet therapy

Nonpharmacologic Interventions

- Breathing retraining
  - **Pursed lip breathing**
    - Inhale normal breath slowly through nose with mouth closed
    - Exhale slowly through pursed lips (whistling or kissing position); twice as long as inhalation
    - Never try to force out the air
  - **Coordinated breathing**
    - Pursed lip breathing with inhalation before activity
    - Count out loud if holding breath
    - Use when anxious, active, wound-up

Pharmacologic Treatment

Opioids

- First line pharmacologic intervention

Benzodiazepines

- Have a role if anxiety is significant

Oxygen

- Lack of clear evidence of benefit overall
- Improved survival, quality of life, and neurophysiologic functioning in COPD
- Therapeutic trial can be considered
- Low risk intervention

“Among the remedies which it has pleased Almighty God to give to man to relieve his sufferings, none is so universal and so efficacious as opium.”

Thomas Sydenham, 1680

Opioids in Dyspnea

- Poorly understood – may act centrally, peripherally, or by reducing anxiety
- Reduce ventilatory response to carbon dioxide, hypoxia, inspiratory flow-resistive loading, and exercise
- Alter central perception of dyspnea
- Morphine found to decrease oxygen consumption both at rest and with exercise in healthy individuals

Uronis et al. *Int J COPD*. 2006;1(3):289-304.

Which Opioid? What Dose?

- Oral or parenteral opioids show favorable results
- Nebulized morphine is no better than plain saline alone
- Choose opioid, dose, and titration schedule based on individual patient characteristics:
  - Renal, hepatic function
  - Current and past opioid use
  - Opioid intolerance/allergy history

Starting Doses for Dyspnea

Opioid	Available Routes	Starting Dose (Adults)
Hydromorphone (Dilaudid®)	PO, SL, PR, SC, IV	1-2 mg PO q4h PRN
Morphine (Roxanol®)	PO, SL, PR, SC, IV	2.5-5 mg PO q4h PRN
Oxycodone (Roxicodone®)	PO, SL, PR	2.5-5 mg PO q4h PRN
Benzodiazepine	**Available Routes**	**Starting Dose (Adults)**
Alprazolam (Xanax®)	PO, SL, PR	0.25 mg PO q8h PRN
Clonazepam (Klonopin®)	PO, SL, PR	0.25 mg PO q12h PRN
Diazepam (Valium®)	PO, SL, PR, IM, IV	2 mg PO q8h PRN
Lorazepam (Ativan®)	PO, SL, PR, SC, IV	0.5 mg PO q6h PRN

Palliative Care Consultant. 4 ed. 2015;81-83.

Noninvasive Positive Pressure Ventilation

- Can assist fatigued muscles
- Enable patients to take a deeper breath
- Can limit communication and ability to eat
- May heighten anxiety in some patients

Oxford Textbook of Palliative Medicine. 5 ed. 2015:421-434.

Palliative Sedation

- Defined as “the intentional lowering of awareness towards, and including, unconsciousness for patients with severe and refractory symptoms.”
- Should only be considered after all available options have been exhausted
- Level of sedation should be proportional to the patient’s level of distress
- Raises ethical concerns
- Does not typically hasten death

AAHPM Statement on Palliative Sedation. Approved 12/5/14. aahpm.org/positions/palliative-sedation.

Patient Case

- EH is a 75yo female who was recently admitted to your hospice. She is weak, dyspneic at rest, and has been showing less and less interest in family members or anyone visiting. The patient's daughter tells you she knows her Mom is depressed and in pain but is afraid to ask for medication for fear she'll be labeled an "addict."
- PMH: CAD, COPD, diabetes, heart failure, hyperlipidemia, hypertension
- SH: Prior tobacco use (smoked 0.5-1 PPD from age 15-55), denies alcohol or illicit drug use

Patient Case (continued)

- Current medications:
  - Aspirin 81 mg po daily
  - Lisinopril 10 mg po daily
  - Metformin 500 mg po BID
  - Atorvastatin 40 mg po qhs
  - Cholecalciferol 1000 IU po daily
  - Furosemide 40 mg po daily PRN edema
  - Formoterol 12 mcg inh BID
  - Tiotropium 18 mcg inh daily
  - Albuterol 90 mcg/inh 1-2 puffs q4h PRN shortness of breath
  - Carboxymethylcellulose 1 drop 4 times daily
  - Dorzolamide 2% solution 1 drop BID
  - Travoprost 0.004% solution 1 drop qhs
  - Acetaminophen 650 mg po q4h PRN pain

Self-Assessment!

You just got off the phone with the hospice attending physician who estimates Mrs. EH's prognosis to be "several months." At this point in time, which of the following recommendations would you make?

A. Start a benzodiazepine to help treat the patient's dyspnea
B. Start a low dose opioid to help manage dyspnea and pain. Educate the patient and her family regarding why this class of medications is beneficial
C. Start an NSAID to help manage the patient's pain
D. Start nebulized morphine q4h PRN to help manage dyspnea and pain

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Edema

- Maintenance of euvolemia (normal fluid balance) is important
- Not all heart failure patients have fluid overload
- Ambulatory patients – pedal edema
- Bed-bound patients – sacral edema
- Pulmonary edema
  - Difficulty breathing, tachypnea (↑ RR), tachycardia (↑↑ HR), cyanosis, wheezing, crackles, orthopnea, paroxysmal nocturnal dyspnea (PND)

Lindenfield et al. *J Card Fail*. 2010;16:e1e194.

Edema Management in Heart Failure

- Loop diuretics ± thiazide diuretic
- Avoid medications that can worsen sodium/fluid retention
  - NSAIDs
  - Calcium-channel blockers (amlodipine, nifedipine)
  - Corticosteroids
  - Hormonal therapy (estrogen, progesterone, testosterone)
  - Pioglitazone (Actos®)
- Elevating extremities
- Compression stockings
- Salt restriction

Cough

- Estimated prevalence up to 80%
- Many potential etiologies
- If possible, treatment should target the underlying cause
- Productive cough
  - Consider antibiotics if life expectancy >2 weeks and treatment desired
  - Guaifenesin (if patient is able to expectorate)
- Nonproductive cough
  - Dextromethorphan
  - Benzonatate
  - Opioids

Physical Complications of Cough

- Chest wall pain
- Rib fracture
- Urinary incontinence
- Sweating
- Exhaustion
- Anorexia
- Insomnia

Etiologies of Cough

Allergens	Upper airway cough syndrome (postnasal drip)	Heart failure	Infection
Malignancy	Aspiration	Asthma/ COPD	GERD
Pleural effusion	Interstitial lung disease	Radiation-induced pneumonitis	Medications

Etiologies of Cough – Medications

- Angiotensin converting enzyme (ACE) inhibitors
- Angiotensin receptor antagonists (ARBs)
- Antibiotics
  - Amphotericin
  - Erythromycin
  - Aminoglycosides
  - Sulfonamides
- Inhaled steroids

Pharmacologic Treatment of Cough

	Adult Dosing	Additional Information
Guaifenesin	**IR:** 400 mg PO q4h PRN **ER:** 600 mg PO BID	Available in combination products with dextromethorphan or codeine
Nebulized saline	Inhale 3 mL via nebulizer q4h PRN	
Dextromethorphan	**IR:** 15 mg PO q4h PRN **ER suspension:** 60 mg PO BID	
Guaifenesin/dextromethorphan	10 mL PO q4h PRN 1 tab PO BID	
Guaifenesin/codeine	10 mL PO q4h PRN	C-V controlled substance
Hydrocodone/homatropine	5 mg PO q4h PRN	C-II controlled substance; homatropine dose is subtherapeutic to discourage deliberate abuse/overdose
Benzonatate	100 mg po TID PRN	Capsules must be swallowed whole
Lidocaine	Inhale 5 mL (1%) via nebulizer PRN	Avoid eating or drinking for 30-60 min after treatment to reduce risk of aspiration

Palliative Care Consultant. 4 ed. 2015;57-58.

Respiratory Secretions

- Increased secretions may occur during active stage of dying
  - “Terminal respiratory secretions”
- Patients are not usually bothered, but staff and family may be
- Suctioning may irritate and cause *increased* secretions
- Treatment:
  - Nonpharmacologic interventions
  - Anticholinergics
  - Expectorants
  - Mucolytics

Treatment of Respiratory Secretions

Medication	Adult Dosing	Additional Information
Atropine 1% ophthalmic solution	2 drops SL q4h PRN	1 drop of 1% atropine solution delivers approximately 0.5 mg atropine
Glycopyrrolate	0.2 mg SC q6h PRN 1 mg PO q6h PRN	Fewer CNS effects, more xerostomia than other anticholinergics; oral bioavailability is low
Hyoscyamine	0.125 mg SL q4h PRN	
Scopolamine	1 patch q72h 0.4 mg SC q6h PRN	Apply patch to hairless area behind ear; do not cut patch; patches not ideal for terminal secretions due to slow onset and more difficult titration

Others:

- Mucolytics: acetylcysteine nebulized saline
- Expectorants: guaifenesin

Palliative Care Consultant. 4 ed. 2015;191-192.

Hiccups (*Singultus*)

- Involuntary, intermittent, spasmodic contractions of the diaphragm and intercostal muscles, which result in sudden inspirations and end with abrupt closures of the glottis
- Frequency can range from 4-60 hiccups/min
- Can be classified by duration
  - **Acute: <**48 hours
  - **Persistent**: >48 hours
  - **Intractable**: >1 month
- Can result in exhaustion, fatigue, malnutrition, weight loss, and/or death

Associated Symptoms

- Nausea/vomiting
- Pain
- Fatigue
- Insomnia
- Psychological distress
  - Depression
  - Anxiety

Causes of Hiccups

Abdominal distension or gastroparesis	Hot chili pepper	Metabolic disorders (hyponatremia, hypokalemia, hypocalcemia)	Smoking/ alcohol
Excitement, anxiety, stress, fear	Cerebrovascular disease or accident	Brain, mediastinal, or esophageal masses	Intracranial injury
GERD	Large hiatal hernias	Cardiovascular disease (myocardial infarction, pericarditis, aortic aneurysm)	Medication-related (benzodiazepines, opioids, steroids, chemotherapy)

Clinical Evaluation of Hiccups

- Duration
- Relationship with meals
- Gastric symptoms
- Abdominal masses
- Signs of CNS injury/ malignancy
- Associated diseases
- Medications
- Labs*
- Imaging*
  - CT abdomen, brain
- Procedures*
  - Upper endoscopy

*Would likely not pursue such an extensive workup in hospice patients

Coradazzi. *Hosp Palliat Med Int J*. 2018;2(2):90-92.

Management of Hiccups

- Treatment should target underlying etiology (if possible)
  - Etiology may be multifactorial
- Many nonpharmacologic strategies
- Pharmacologic
  - Consider use of proton pump inhibitors first
  - Lack of robust evidence for most other medications used
  - Most available data is from case series
- Invasive procedures
  - Surgical phrenic nerve ablation
  - Phrenic nerve blockade with local anesthetic
  - Electrical stimulation of phrenic nerve (with a respiratory pacemaker)

Nonpharmacologic Approaches

- Vagal stimulation (eg, carotid massage, pulling knees to chest)
- Ocular compression
- Breath holding
- Breathing inside a bag
- Hyperventilation
- Drinking from far side of a glass
- Biting a lemon
- Nasal instillation of vinegar
- Producing a fright response
- Hypnosis
- Acupuncture

No strong evidence to support the use of any of these nonpharmacologic approaches.

Pharmacologic Treatment

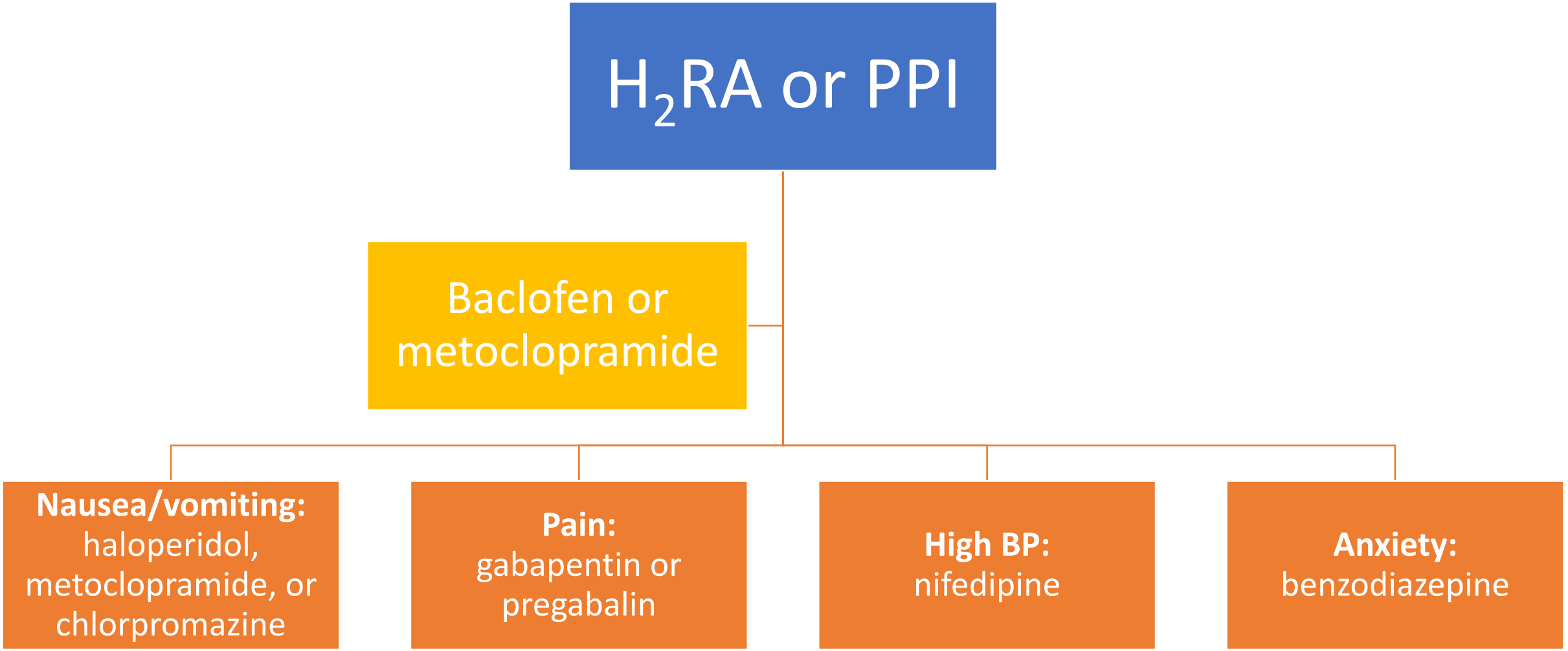
- Dopamine antagonists
- Antiepileptics
- Baclofen
- Others (limited data/success)
  - Carbamazepine 100-300 mg po q6-8h
  - Valproic acid, target dose 15-20 mg/kg/day
  - Phenytoin 100 mg po q8h
  - Nifedipine 10 mg po BID; gradually increase to 20 mg po TID
  - Amitriptyline 25-100 mg po qhs
  - Methylphenidate 5-10 mg po daily
  - Midazolam continuous infusion
  - Inhaled lidocaine

Pharmacologic Treatment of Hiccups

Medication	Adult Dosing	Adverse Effects	Evidence for Use
Chlorpromazine	10-50 mg po q8h; 10-50 mg in 500-1000 ml of NS over several hours	Drowsiness, dizziness, hypotension (especially with IV), urinary retention	2 large case series from the 1950s
Haloperidol	2-5 mg subq/po loading dose, followed by 1-4 mg po TID	Extrapyramidal symptoms (unlikely at low doses)	Case series
Metoclopramide	10 mg po q8h	Extrapyramidal symptoms	Case reports, case series, RCT; provided relief in hiccups due to GI causes
Gabapentin	100-400 mg po TID	Drowsiness, dizziness, ataxia, peripheral edema	Case reports, case series, systematic review, retrospective chart review
Pregabalin	75-150 mg po BID	Drowsiness, dizziness	Case report
Baclofen	5-20 mg po q8h	Drowsiness, dizziness, ataxia	Double-blind RCT; did not eliminate hiccups but provided symptomatic relief in some

Palliative Care Consultant. 4 ed. 2015;96-97.
Principles and Practice of Palliative Care and Supportive Oncology. 5 ed. 2022;258-262.

Treatment Algorithm



Patient JR

- JR is a 53yo male with past medical history significant for stage IV colon cancer (liver mets; recently received chemo), hypertension, anxiety, and insomnia who presents to the hospital with worsening abdominal pain, nausea/vomiting, reflux, and hiccups.
- Medications:
  - Amlodipine 5 mg po daily
  - Oxycodone ER 20 mg po q12h
  - Oxycodone 5 mg po q4h PRN pain 5-10
  - Sertraline 75 mg po daily
  - Lorazepam 0.5 mg po q6h PRN anxiety
  - Ondansetron 8 mg IV q8h PRN nausea/vomiting

Self-Assessment!

What would be a reasonable first-line approach for managing JR's hiccups?

A. Midazolam continuous infusion
B. Nifedipine 20 mg po q8h
C. Pantoprazole 40 mg po daily
D. Haloperidol 10 mg po q8h
E. C and D

Self-Assessment!

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