

# Managing Less Common But Troublesome Symptoms in Hospice and Palliative Care

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## Objectives

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1. List several common causes of pruritis in hospice patients and the types of medications that can provide symptom relief
2. Discuss a step-wise approach for managing cough in hospice patients.
3. Review medications that can be useful for treating hiccups at end of life.

# General Principles

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Symptom  
management in  
hospice and home  
care patients

Common underlying  
conditions

Frequency, duration  
and severity of  
symptom

Any new  
medications?

Patient history:

- What has been done thus far?
- What works?
- What doesn't work?

Avoiding  
polypharmacy

# Pruritus

# Pruritus: Overview

- Unpleasant or irritating skin sensation that results in a desire to scratch
- Complex physiology, poorly understood mechanisms
  - not just histamine; also potentially serotonin, opioid, neuropathic
- In hospice/palliative care, common causes of severe pruritis include
  - cholestatic pruritis in disorders of liver or biliary duct
  - uremic pruritis in chronic renal disorders
  - paraneoplastic pruritis in the context of malignancy
  - HIV associated pruritis
  - medication-induced pruritis
    - *Angiotensin-converting enzyme (ACE) inhibitors (and other antihypertensives)*
    - *Opioids*
    - *Chemotherapy*
    - *Antimicrobials (Bactrim, macrolides, PCN)*
    - *Anticonvulsants*
  - *medication-related allergies (sulfa based meds, etc.)*

# Pruritus: Assessment

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- Onset, location and duration of itchiness
- Presence/absence of rash
  - Pruritus in the absence of a rash may be indicative of cholestatic jaundice or other metabolic or hematologic disorder
  - For pruritus with a rash, the appearance of any lesions can be useful for differential diagnosis

# Pruritus: Non-Pharmacological Management

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- Keep nails short
- Wear loose fitting cotton clothing
- Avoid hot or frequent showers
- Avoid abrasive washcloths/sponges
- Avoid deodorant soaps
  - *Use emollient gels/ointment or aqueous creams instead*
- Apply emollients (petroleum jelly, hypoallergenic lotions, vitamin A&D ointment) immediately after bathing to seal moisture in the skin



# Pruritus: Localized

Pharmacotherapy (TOPICAL) - General	
Class	Select Medications
Antihistamines	Diphenhydramine (Benadryl®) Cream: Apply to affected area(s) TID Doxepin cream?
Corticosteroids	Apply to affected area(s) BID-QID: <ul style="list-style-type: none"> <li>• Hydrocortisone 0.5-2.5%</li> <li>• Triamcinolone acetonide 0.025%</li> <li>• Fluocinolone acetonide (Synalar®)</li> <li>• Betamethasone dipropionate 0.025-0.1% (Diprolene®)</li> <li>• Fluocinonide (Lidex®)</li> <li>• Triamcinolone acetonide 0.5%</li> </ul>
Emollients/ Protectants	As needed application: Bag Balm, Calamine lotion, Zinc oxide
Anesthetics	<ul style="list-style-type: none"> <li>• Lidocaine cream, ointment: Apply BID-TID PRN</li> <li>• Lidocaine patch</li> <li>• Methol/camphor (Sarna®): Apply PRN</li> </ul>

# Pruritis: Diffuse

## Pharmacotherapy (ORAL) - General

Class	Select Medications	Considerations
Oral Antihistamines	<b>H<sub>1</sub> (Histamine) blockers:</b> <ul style="list-style-type: none"> <li>Diphenhydramine (Benadryl®) 25mg PO Q6H</li> <li>Hydroxyzine HCl (Atarax®) 10mg PO Q6H</li> <li>Loratadine (Claritin®) 10mg PO daily, (also cetirizine, etc)</li> </ul> <b>H<sub>2</sub> blockers:</b> famotidine (Pepcid®)	<ul style="list-style-type: none"> <li>For urticaria</li> <li>“older” antihistamines provide sedating effect;</li> <li><b>Pruritis from paraneoplastic syndromes, uremia, cholestasis does not respond to antihistamines</b></li> <li>No benefit in atopic dermatitis</li> <li>H2 blocker can be added for allergic reactions that don’t respond to H1 blocker alone</li> </ul>
Oral Corticosteroids	<ul style="list-style-type: none"> <li>Prednisone 10-30 mg PO daily</li> <li>Methylprednisolone (Medrol® Dosepak™) per pak instructions</li> <li>Dexamethasone (Decadron®) 4 – 8 mg PO daily</li> </ul>	<ul style="list-style-type: none"> <li>Typical course of 7 days, no need to taper</li> </ul>
Other	<ul style="list-style-type: none"> <li>Gabapentin (Neurontin®)</li> <li>Pregabalin (Lyrica®)</li> <li>Paroxetine (Paxil®)</li> </ul>	<ul style="list-style-type: none"> <li>Neuropathic pruritus can occur with damage to nervous system</li> <li><b>Neurogenic itch is centrally regulated and is thought to be mediated through opioid and serotonin receptors hence unresponsive to antihistamines</b></li> <li>These medications may hinder the transmission of nociceptive sensations to the brain, thereby also suppressing pruritus</li> </ul>

Anand, Sheeba. "Gabapentin for pruritus in palliative care." *American Journal of Hospice and Palliative Medicine*® 30.2 (2013): 192-196.

Gleeson, Aoife. "Management of less common symptoms in palliative care." *Medicine* 48.1 (2020): 43-47.

# Pruritus: Specific Source

Pharmacotherapy	
Source	Select Medications
Uremic pruritis	Gabapentin, pregabalin; sertraline; maybe cannabinoids, capsaicin
Cholestasis	<b>Gabapentin makes it worse!</b> Cholestyramine, colestipol <i>What happened to colsevelam (Welchol®)?</i>
	<b>1<sup>st</sup> Line</b> Rifampin Naltrexone ( <b>don't use if on opioids</b> ) Sertraline (75-100 mg/d) (paroxetine, mirtazapine 15-30 mg/day)
	<b>2<sup>nd</sup> line</b>
Psychogenic pruritis	Paroxetine, sertraline, doxepin, mirtazapine, olanzapine, gabapentin
HIV associated	Indomethacin ( <i>hydroxyzine?</i> )

Siemens, Waldemar, et al. "Pharmacological interventions for pruritus in adult palliative care patients." *Cochrane database of systematic reviews* 11 (2016).  
 Düll, Miriam M., and Andreas E. Kremer. "Newer approaches to the management of pruritus in cholestatic liver disease." *Current Hepatology Reports* 19.2 (2020): 86-95.  
 Buteau, Anna, and Jason Reichenberg. "Psychogenic pruritus and its management." *Dermatologic Clinics* 36.3 (2018): 309-314.

# Pruritis: When in Doubt, Try Paroxetine

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- For patients in palliative care settings who mainly suffered from pruritus related to solid tumors, hematological malignancies, and various non-malignant or idiopathic conditions, the selective serotonin reuptake inhibitor (SSRI) paroxetine has been shown to be effective.
- Because serotonin might have a role in pruritus secondary to malignant disease, as well as cholestasis, uremia, and opioids, it is reasonable to try the drug. In order to reduce adverse effects, patients should start with small doses, such as 5 to 10 mg nightly. Effects can usually be observed within 24 to 48 hours.

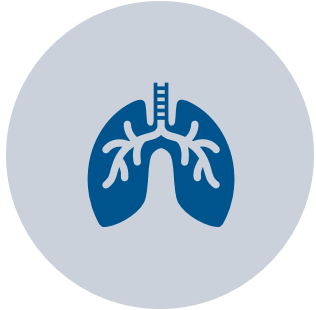
Medication	Indication(s)	Dosing	Adverse Effects, Concerns
Cholestyramine	<b>Cholestasis</b> , solid tumors and paraneoplastic disorders, uremia	Initial: 4 g PO taken 30 minutes before breakfast and 30 minutes after breakfast. As needed, add 2 doses at lunchtime (before and after the meal) or at dinnertime (before and after the meal) Maximum: 16 to 32 g/day	Nausea, constipation, abdominal discomfort, flatulence, unpleasant taste. Often poorly tolerated. <b>Breakfast dosing time effective as pruritogens are stored in the gallbladder overnight.</b> MANY drug interactions, commonly requires dose spacing. <b>Take one hour before or 4-6 hours after other medication to avoid absorption impairment.</b>
Doxepin	Cholestasis, <b>psychogenic</b>	Initial: 10 to 25 mg PO HS; Increase by 25 mg/day. Maximum: 75 to 300 mg per day in divided doses.	Drowsiness, xerostomia <b>Powerful H<sub>1</sub> effect</b> (more than hydroxyzine or diphenhydramine). QTc prolongation if dose over 100 mg per day.
Gabapentin	Lymphoma, opioid-induced, <b>uremia</b>	Initial: 100 mg PO TID. Hemodialysis patients: 100 to 300 mg PO once after HD Maximum: up to 1200 mg/day.	Drowsiness, dizziness, fatigue, ataxia, peripheral edema, visual disturbances, unsteadiness. <b>Adjust dose for reduced renal function. In extended therapy, (optimally) reduce dose over a minimum of one week.</b> Few drug interactions.
Methylnaltrexone	Cholestasis	Initial: 12 mg SC daily Repeat dosing every 1 to 2 days PRN.	Abdominal pain, flatulence, nausea. Contraindicated in known or suspected GI obstruction or if an increased risk of recurrent obstruction. Costly. Acts peripherally
Mirtazapine	<b>Psychogenic</b> ; Cholestasis, lymphoma, solid tumors and paraneoplastic disorders, uremia if failure of other treatments,	Initial: 7.5 to 15 mg PO HS. If partial relief after one week, increase by 15 mg. Maximum: 30 mg/day.	Drowsiness, but may be beneficial for itch suffering at HS. Weight gain. No anxiety or nausea at start of use (unlike SSRI's). Few drug interactions. Use caution if history of seizures. Discontinuation symptoms have been reported upon abrupt withdrawal; reduce dose gradually if possible. <b>Therapeutic effect may disappear after 4 to 6 weeks.</b> Clearance is reduced in moderate and severe renal function. Administer with caution in hepatic impairment
Naloxone	Cholestasis, opioid-induced, psychogenic	Initial: 0.2 mcg per kg per minute IV infusion. Double the infusion rate every 3 to 4 hours PRN Maximum: 0.8 mcg/kg/min.	Withdrawal syndrome: if on opioids (reversing analgesia), or if high endogenous opioids (e.g., in cholestasis, liver damage or uremia). May change to PO naltrexone after 24 to 48 hours of use.

Medication	Indication(s)	Dosing	Adverse Effects/Concerns
Ondansetron	Cholestasis, opioid-induced, psychogenic, uremia	Initial: 4 mg PO,SC, IV once or twice daily. Maximum: 8 mg TID.	Headache, constipation, diarrhea, xerostomia, increased liver enzymes, fever. Single 4 mg IV may be effective for 4 hours; 8 mg IV effective for 16 hours.
Paroxetine	Cholestasis, <b>psychogenic</b> , solid tumors and paraneoplastic disorders, opioid induced, if failure of other treatments	Initial: 5 to 10 mg PO daily. Increase by 10 mg per day, every 4 to 5 days. Maximum: 20 mg/day.	<b>Nausea and vomiting, especially first 3 days.</b> Drowsiness. Lower or less frequent dosing may be needed in severe renal impairment (CrCl less than 30 mL/min). Lower and less frequent dosing may be necessary in patients with severe hepatic impairment. Use caution in seizure disorder patients. <b>Pruritus may return within 3 days if discontinued.</b> Avoid abrupt discontinuation as may increase risk of serious discontinuation symptoms; <b>gradual dose reduction</b> and monitoring recommended. <b>Antipruritic effect may disappear after 2-3 months for some patients</b>
Rifampin	<b>Cholestasis</b>	Initial: 75 mg PO daily. Double dose every week PRN. Maximum: 300 mg BID.	MANY drug interactions; assess risk prior to initiation. Do not drink alcohol while taking. Take 1 hour before or 2 hours after a meal with a full glass of water. To avoid long term adverse effects, (hepatitis, hemolytic anemia, renal failure, thrombocytopenia) stop if pruritus completely resolves.
Sertraline	<b>Cholestasis</b>	Initial: 25 mg PO daily. Adjust by 25 mg per day every 4 to 5 days. Maximum: 100 mg/day.	Insomnia, nausea. <b>Duration of antipruritic effect sustained throughout full treatment use, unlike paroxetine.</b> Use caution in seizure disorder patients. No adjustment needed in renal impairment.

# Cough

# Cough: Overview

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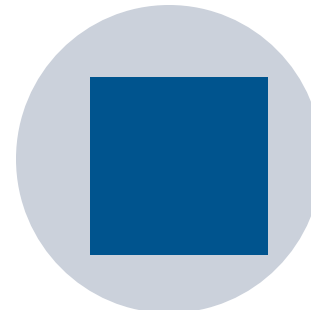
Cough is a normal complex physiological mechanism intended to protect the lungs through the clearance of mucus and foreign matter from the airways.



It is under both voluntary and involuntary control



Presents as either wet, productive of sputum, or dry, unproductive of sputum



Symptoms range from mildly irritating to deeply distressing leading to muscle strain, fatigue, interrupted sleep, pain and rib fractures



# Cough: Causes

	Cancer related	Cancer unrelated
Respiratory system	Airways involvement Chemotherapy Pleural effusion Pleural involvement Pulmonary involvement Radiation therapy Tracheoesophageal fistula	Asthma Bronchiectasis COPD Infections Interstitial lung disease Postnasal drip Pulmonary embolism Sarcoidosis
Other systems	Lymphangitis carcinomatosis Mediastinal involvement Pericardial effusion Superior vena cava syndrome	Congestive heart failure Gastroesophageal reflux Hepatic abscess Tympanic irritation

Homsj, Jade, Declan Walsh, and Kristine A. Nelson. "Important drugs for cough in advanced cancer." *Supportive care in cancer* 9.8 (2001): 565-574.

# Medications That Cause Cough

Medication	
ACE Inhibitors	
Sitagliptin	Also rhinorrhea, dyspnea, wheezing
Calcium Channel Blockers	With/without reflux symptoms
Fentanyl (intravenous)	Bronchoconstriction
Latanoprost ophthalmic	
Topiramate	
Phenytoin	Nocturnal cough
Methotrexate	
Omeprazole	Worse at night

Shim JS, Song WJ, Morice AH. Drug-induced cough. *Physiol Res*. 2020 Mar 27;69 (Suppl 1): S81-S92.

Ding H, et al. Drug-induced chronic cough and the possible mechanism of action. *Ann Palliat Med* 9.5 (2020): 3562-3570.

## Cough: Assessment

Evaluate	Presence of any comorbidities, fever, wheezing, and smoking history
Assess	For associated symptoms - pleuritic chest pain, shortness of breath
Obtain	A thorough drug history
Evaluate	Presence/absence of sputum. If present: <ul style="list-style-type: none"><li>• Color and consistency</li><li>• Purulence</li></ul>

• Blood - hemoptysis is suggestive of an invasive lung tumor

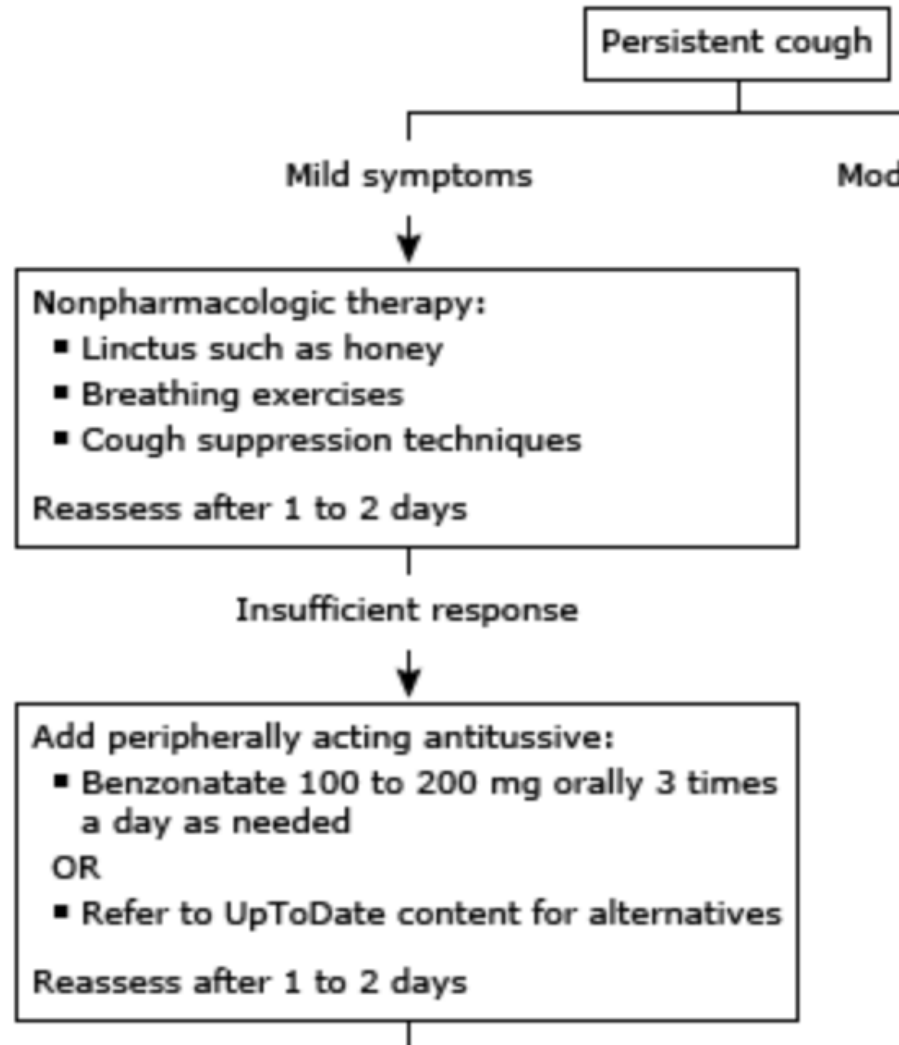
# Cough Management

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Treat underlying causes of cough when indicated:

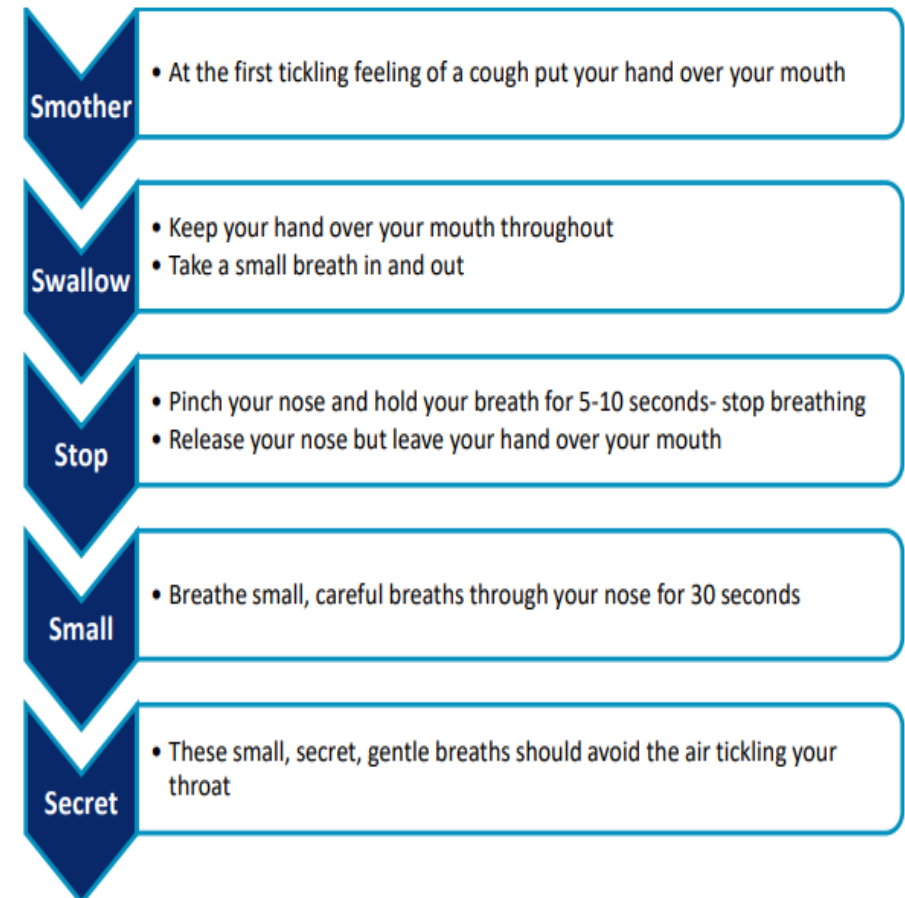
- Allergies, post-nasal drip: Ipratropium, antihistamines, decongestants, nasal steroids
- GERD: H2 blockers, PPIs
- Heart failure: Diuretics
- Purulent (respiratory infection): Antibiotics
- Excess secretions: Expectorants, patient positioning, anticholinergics

# Cough Management



## The Stop Cough Technique: (The 5 S's)

Practice this technique at least 5 times a day for a week when you first start this exercise



Adapted from: Estfan B, LeGrand S. Management of cough in advanced cancer. *J Support Oncol* 2004; 2:523.  
Graphic 131668 Version 3.0  
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# Cough Management




# Cough Management: Opioids

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Opioids are a mainstay of pharmacologic therapy for palliative care patients with moderate to severe chronic cough, particularly those with intrathoracic cancer.



In a 2013 meta-analysis of trials evaluating various treatments for chronic cough (which included only a few trials with cancer patients), opioids reduced cough severity (standardized mean difference 0.55, 95% CI 0.38-0.72) and cough frequency (rate ratio 0.57, 95% CI 0.36-0.91) compared with placebo. They also improved quality of life. No opioid was superior to another.



A 2015 systematic review of trials examining interventions for cough in patients with primary or metastatic cancer also noted some positive effect with opioids ([morphine](#), [codeine](#), and dihydrocodeine)

# Cough Management: Opioids

## Opioid Products

- Long-acting agents:
  - *Hydrocodone/chlorpheniramine (Tussionex®) 10mg hydrocodone/8 mg chlorpheniramine per 5 mL dosed q 12 hours*
    - Taper dose by 25-50% every 2-4 days to d/c if prolonged use
- Short-acting agents:
  - *Guaifenesin/codeine (Cheratussin®) 100 mg guaifenesin/10 mg codeine per 5 mL*
    - Do not exceed 120 mg/day codeine, 2400 mg guaifenesin from all sources; taper to d/c if long-term use
  - *Hydrocodone/homatropine (Hycodan®) 5 mg hydrocodone/1.5 mg homatropine per 5 mL or per tab*
    - Max 6 tabs or 30 ML per day



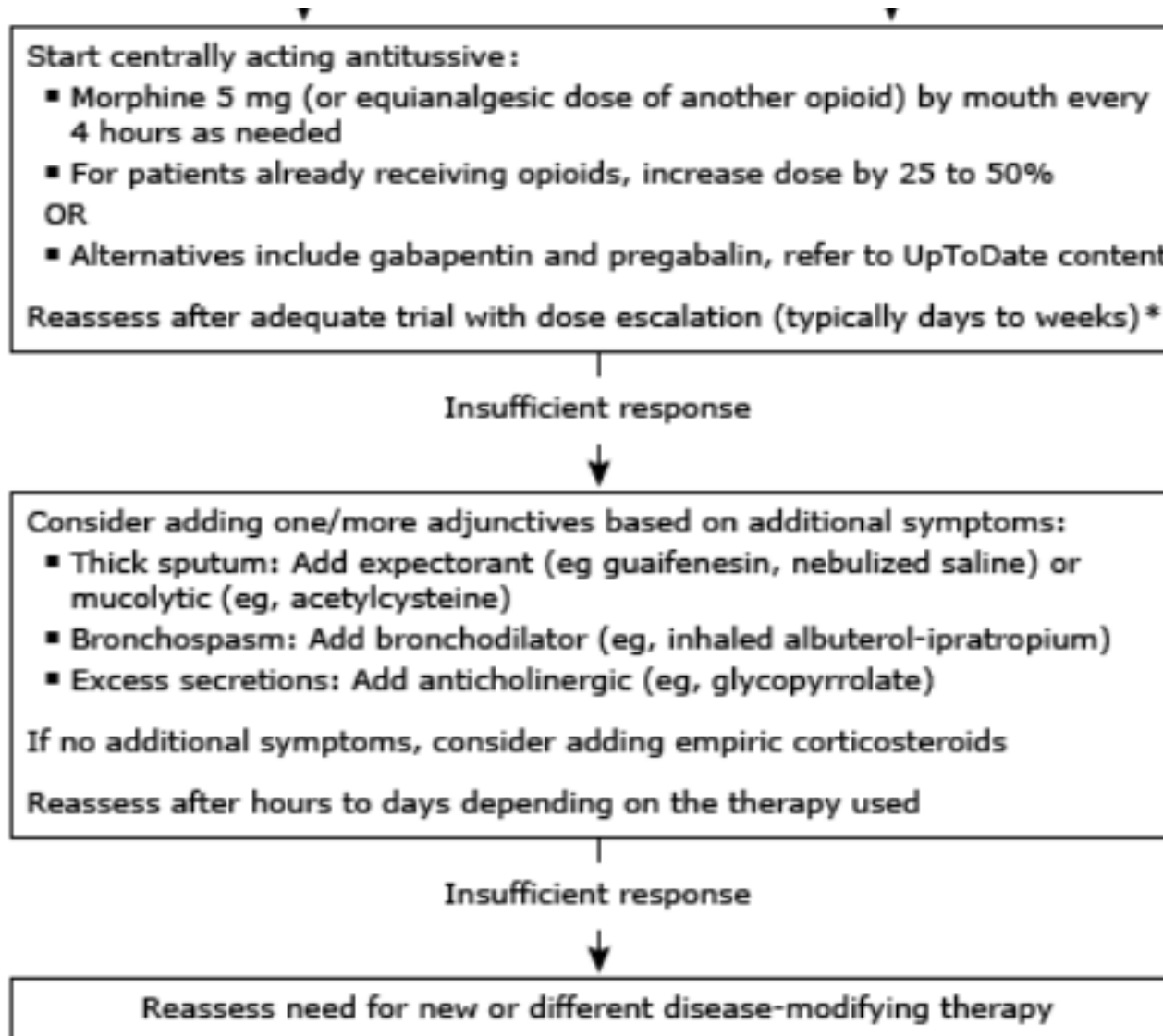
### *Gabapentin*

- 300 mg per day with gradual increases up to max of 900 twice daily
- Sedation usually decreases 1-3 days after each dose escalation

### *Pregabalin*

- *75 mg daily and gradually increased over a week to 300mg/day max*

# Cough Management



# Cough Management: Adjuncts

## Thick Sputum

- Guaifenesin
  - *available as single product (Robitussin® Mucinex®) and in combination with many other products in liquid and tablet form*
    - Codeine
    - Acetaminophen
    - Phenylephrine
    - Dextromethorphan
- nebulized saline or acetylcysteine
- ? benefit to acetylcysteine over saline
  - *Sodium Chloride 0.9% Neb: 1 amp via neb every 2 hours PRN*

## Bronchospasm (chest tightness, occurs with activity, wheezing, etc.)

- Bronchodilators
  - Albuterol MDI/Neb: 2 puffs/1 vial inhaled every 4 hours PRN
  - Ipratropium MDI/Neb: 2 puffs/1 vial inhaled every 4 hours PRN
- Corticosteroids
  - Prednisone 20mg PO daily
  - Dexamethasone 4mg PO daily
  - Beclomethasone inhaled 200 mcg twice daily

# Nebulized Lidocaine



The efficacy of nebulized lidocaine (10-400 mg) for suppression of intractable cough has been reported in 6 descriptive studies and 1 small controlled clinical trial. Intractable cough was defined as patient-reported cough despite use of common cough suppressants; prior failed treatments were specified in some studies. 15-21



In 1 case series, nebulized lidocaine 1-4% (10–20 mg) every 4 to 6 hours as needed, preceded by albuterol 5 mg, produced nearly instantaneous relief of intractable cough in 21 patients who had obstructive, restrictive, or infective airway disease 15 In another case series, 3 patients with intractable cough secondary to upper respiratory tract infection were treated with a single nebulization session of lidocaine 10 mg and bupivacaine 5 mg. The cough stopped and did not recur.



The use of higher doses of nebulized lidocaine (400 mg, preceded by albuterol 2-5 mg) to suppress intractable cough was noted in 3 patients with cough secondary to lung cancer, with immediate effects that persisted for 1 week or more



Preservative-free lidocaine solution for injection administered via nebulization has been reported to cause initial bronchoconstriction in individuals with baseline bronchial hyperreactivity (eg, asthma, COPD, hay fever)

# Clinical Considerations

Treat cough only if necessary to ease breathing or to provide comfort

Throat lozenges may provide relief for constant throat irritation

Administer expectorants (e.g., guaifenesin) with full glass of water

Avoid cough suppressants with a productive cough, as decreased mucus clearing may lead to mucus plugging and airway obstruction; however, cautious use of suppressants at night may aid sleep

ACE-I cough not sensitive to opioids

Hallucinations, serotonin syndrome with dextromethorphan and SSRIs

Hydrocodone 5 mg = codeine 30 mg

Histamine release, hypotension more likely to occur with hydrocodone than other opioids; also hiccups and myoclonus

Be aware of potential benzonatate toxicity in children

Home remedies can work!

# Hiccups

# Hiccups: Overview

Hiccups (singultus) are involuntary, intermittent, spasmodic contractions of the diaphragm and intercostal muscles

They are caused by a disruption in the reflex arc between the phrenic and vagus nerve and the central reflex center (brainstem)

- disturbances of phrenic or vagus nerve
- disturbance of CNS
- produced by toxic/metabolic disturbance or drugs
- psychogenic

**Males more often (5x) affected (especially TALL men!)**

Hiccup bout: Lasting from a few seconds to 48 hours

Persistent hiccups: Lasting > 48 hours but < 1 month

Intractable hiccups: Lasting > 1-2 month

### Comorbidities with an increased prevalence of hiccups:

- Gastrointestinal disorders (GERD, PUD, erosive esophagitis, others)
- CNS disorders
- Infectious disease
- Metabolic changes and toxins
- Psychogenic causes

### Medications:

- Chemotherapy
- Sulfonamides and other antibiotics
- Barbiturates
- Benzodiazepines
- Corticosteroids



## Hiccups: Assessment

1

Review existing medical diagnoses and patient-specific habits to find a cause for hiccups in the hospice patient (although often unidentified)

2

Review prescribed medications for possible cause of hiccups

3

Assess for GI disease (GERD or dyspepsia) or local irritation of the diaphragm due to gastric distension, hepatomegaly, or disease progression

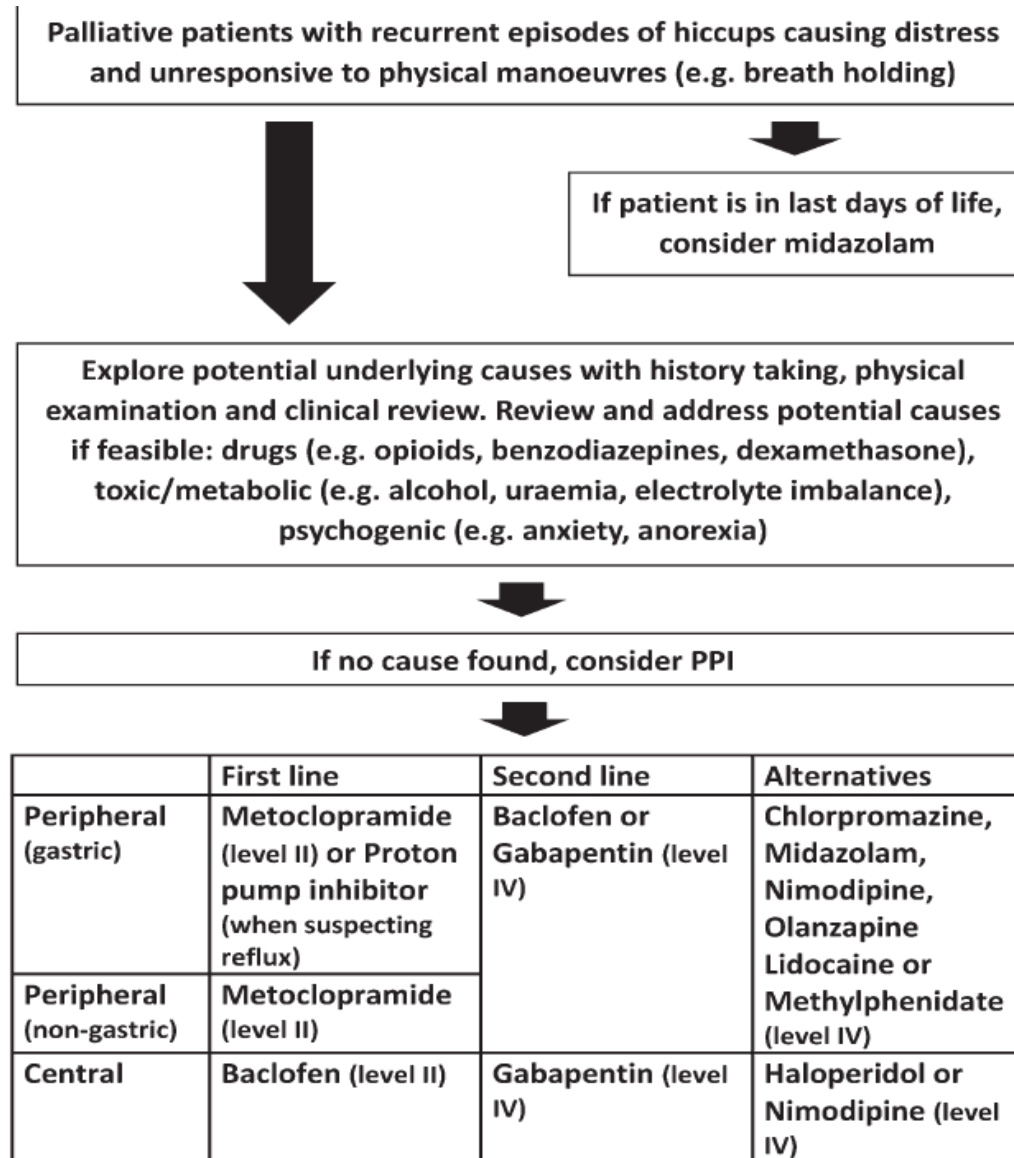
# Hiccups: Management

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## Non-pharmacologic Therapy

- Holding breath, hyperventilating, breathing into a paper bag
- Gargling; sipping iced water or drinking water rapidly, drinking water while “holding breath”
- Dietary interventions:
  - *Eating something very tart (e.g., lemon juice, pineapple juice or vinegar) or sucking on a lemon; eating ginger; eating something very sweet*
- Trial keeping patient NPO for 24 hours
- **Decrease/stop benzodiazepines, steroids**

# Hiccups Treatment Algorithm



**Table 3** Summary of medication dosages

Medication(s)	Dosage
Baclofen	5–15 mg three times a day
Metoclopramide	10 mg three times a day
Gabapentin	100–400 mg three times a day
Midazolam	10–60 mg/24 hours SC
Haloperidol	1–4 mg/24 hours SC/oral/intramuscular
Omeprazole	20 mg twice a day
Chlorpromazine	10–50 mg three times a day intravenous/oral

SC, subcutaneous.

Jeon, Yong Suk, Alison Mary Kearney, and Peter Graham Baker.  
"Management of hiccups in palliative care patients." *BMJ Supportive & Palliative Care* 8.1 (2018): 1-6.

# Dry Mouth

# Dry Mouth: Overview

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## Causes

- more than 500 commonly used medications
  - TCAs, bladder meds, decongestants, bronchodilators, antihypertensives, diuretics, antihistamines, sedative/hypnotics, muscle relaxants
- radiation therapy for cancers of the head and neck.
- autoimmune conditions

## Treatments

- relieve clinical symptoms and improve QOL of patients
- therapies include sialagogues and saliva substitutes, as well as general measures such as sipping water or chewing gum that contains xylitol
- Honey? Acupuncture? Coconut Oil

# Dry Mouth: Sialagogues

- Cevimeline (Exovac®)
  - 30 mg cap; indicated for Sjogren's syndrome
  - 30 mg q 8 h
- Pilocarpine (Salagen®)
  - 5 mg, 7.5 mg tab
  - Radiation induced: 5 mg po q 8h; may titrate up to 10 mg po q 8h, not to exceed 30 mg/d
  - Sjogren's syndrome: 5 mg q 6 h
  - Dose reduction in moderate hepatic impairment; not recommended in severe
- Comparable effectiveness but more AE with pilocarpine (**sweating**, nausea, abdominal pain, flushing, increased urinary frequency, diarrhea, bronchospasm, hypotension, bradycardia)
- Many drug interactions, contraindications (asthma, glaucoma, cardiac) with both

# Dry Mouth: Artificial Saliva



Also referred to as saliva substitutes



Artificial saliva is usually a mix of buffering agents, cellulose derivatives, and flavoring agents.

*Cellulose derivatives increase viscosity and help lubricate the oral cavity*  
*Glycerin coats tongue, teeth, gums to reduce moisture loss*  
*Xylitol may help increase saliva production*



Rinses, sprays, gels, oils, swabs, dissolving tabs, others



All provide short term relief



Patient preference re: taste, mode of use, etc.



**QUESTIONS?**



**THANK YOU!**