PALLIATIVE PEARLS
BY ENCLARA PHARMACIA

Underlying Causes and Management of Cough
December 2016

Patient Case
RH is a 71-year-old male with a primary diagnosis of colon cancer with suspected metastases. Co-morbidities include asthma and open-angle glaucoma. He has no known drug allergies and lives at home with his wife.

RH reports a new productive cough and throat clearing. He is otherwise comfortable and ambulatory. He is able to expectorate thick sputum that is not purulent or blood-tinged. RH is afebrile and has no audible wheeze. He reports an itchy throat and the cough being worse at night and when he is lying down. His wife tells you he just got over a "head cold".

Current medications include:

- Morphine extended-release 30mg PO BID for pain
- Hydrocodone-acetaminophen 5-325mg 1 tablet PO Q.I.D. PRN pain
- Dexamethasone 4mg PO Daily for pain and appetite
- Metoclopramide 5mg PO Q.I.D. PRN for nausea
- Albuterol 0.083% nebulizer solution 1 ampule Q.I.D. PRN for shortness of breath
- Latanoprost 0.005% one drop OU QHS for glaucoma
- Brimonidine 0.15% one drop OU BID for glaucoma

What are some underlying causes of cough?

Acute cough is a tool to clear the airways of mucus and foreign bodies when regular transport via cilia is insufficient. When cough becomes chronic, it can be disruptive, distressing, and physically exhausting.1

Involuntary cough is initiated when rapidly adapting "irritant" receptors (RARs) are stimulated. RARs are present in the epithelium of the upper and lower airways and respond to a variety of chemical **(i.e., smoke), inflammatory (i.e., histamine) and mechanical (i.e., sputum) stimuli. At the end of life,** lack of energy, muscle weakness, failed attempts to expectorate sputum and the inability to coordinate an effective swallow result in ineffective, persistent coughing. RAR stimulation may also lead to bronchoconstriction and mucous hypersecretion.1

What conditions are associated with cough?

Chronic cough is associated with both malignant and non-malignant conditions.

The most common malignancies associated with cough involve cancers of the airways, lungs, pleura, and mediastinum either from the presence of primary tumor or metastasis1. Other cancer related causes of cough are listed below:

- Directly associated with tumor
  - Obstruction
  - Atelectasis
  - Fistula(s)
- Indirectly associated with tumor
  - Pleural effusion
  - Pericardial effusion
  - Treatment-induced pneumonitis (chemotherapy, radiation)

Non-Malignant1 causes of cough are outlined below:

- Acute
  - Acute bronchitis or laryngitis
  - Infection: Common cold, pneumonia, bacterial sinusitis, pertussis, aspiration
  - COPD exacerbations
  - Environmental irritant
- Chronic
  - Lung disease: asthma, chronic bronchitis, bronchiectasis, pleural disease, interstitial lung disease, COPD
  - Post-nasal drip syndrome
  - Post-infection cough
  - GERD
  - Heart failure
  - ACE inhibitor therapy
  - Smoking

How is cough managed?

Symptom-directed treatment for cough includes the following:

Cough suppression:

- Opioids, including morphine, hydrocodone and codeine

- Alternatives for cough refractory to opioids
    - Gabapentin and pregabalin
    - Benzonatate

Bronchoconstriction:

- Inhaled bronchodilators such as albuterol and/or ipratropium

Inflammation and mucus production

- Oral corticosteroids

Adjuvants, symptom specific:

- Antihistamines
- Decongestants

Thick sputum in patients able to hydrate and expectorate:

- Guaifenesin
- Nebulized saline
- Aceytlcysteine

Intractable cough, most serious cases: Local anesthetic such as nebulized lidocaine

- Lidocaine 2% solution nebulized with normal saline - average doses are 2 to 5ml in 1ml NSS every 4 hours PRN. Give first dose under observation as there is potential for initial reflex bronchoconstriction. Refrain from eating or drinking for at least 30 minutes, due to risk of choking.

Pharmacist Assessment

History of asthma: Asthma exacerbations are typically associated with cough, chest tightness, dyspnea and wheezing. As RH exhibits only cough and other symptoms are absent, we can rule this out as a contributor. Asthma is currently under control with the use of daily albuterol nebulizer treatments.

History of glaucoma: Anticholinergics, such as homatropine (contained in Hydromet®/Hycodan®), and antihistamine therapy (i.e., promethazine-containing cough syrups, diphenhydramine) can worsen angle closure glaucoma (narrow-angle). RH has well-controlled open-angle glaucoma and temporary use of anticholinergics and/or antihistamines should not contribute to a clinically significant increase in intraocular pressure. It is prudent however, to monitor for any visual changes.

Current pain management with opioids: Use of cough products containing an opioid will increase risk for sedation and respiratory depression, especially in patients taking high-dose opioids for pain management. Prior to concurrent use, assess level of tolerance to opioids and use reduced dosages if initiated.2

Other considerations: When other upper respiratory symptoms such as nasal congestion are present, use caution if initiating combination products containing decongestants (phenylephrine, pseudoephedrine). Patients with poorly controlled cardiovascular disease

should avoid decongestants, as they can increase blood pressure. Decongestants also have CNS adverse effects including anxiety, restlessness and reports of hallucinations and psychosis – elderly patients are more sensitive to these effects.

Recommendations to manage cough for RH

RH's acute cough is likely related to his recent "head cold". No obvious signs of bacterial infection are present so an antibiotic is not warranted. Considering he has some sinus drainage, an itchy throat, and worsened symptoms when lying down, post-nasal drip is a probable source for the cough.

RH needs an agent that will help dry up the post-nasal drip and assist in thinning his thick sputum. He was started on a regimen of hydrocodone-homatropine 5mg-1.5mg/5mL syrup (Hydromet®/Hycodan®), 5mL PO QHS for 10 days. RH was advised to increase his fluid intake and omit his night-time breakthrough pain medication dose when taking his cough medication – both contain the same amount of hydrocodone.

An alternative recommendation is Guaifenesin 100mg/5mL syrup; 5mL PO after meals and HS taken with Loratadine (Claritin) 10mg PO Daily.

For additional information on this topic, please review these references:

Enclara Pharmacia's On Demand Educational Webinar, "Management of Less Common but Troubling Symptoms in Hospice: Pruritus, Hiccups, Cough, Muscle & Bladder Spasm". Click here to log in.

1. Von Gunten C, Buckholz G. Palliative care: Overview of cough, stridor, and hemoptysis. In: UpToDate, Bruera E, Savarese DMF (Eds.), UpToDate, Waltham, MA. 2016 Apr 11. Accessed 2016 Dec 8.
2. Clinical Pharmacology: Elsevier/Gold Standard. 2016. [Accessed 2016 Dec]. Available from: www.clinicalpharmacology-ip.com
3. PL Detail-Document, Treatment of Cough in Adults. Pharmacist's Letter/Prescriber's Letter. February 2015
4. Irwin RS, Baumann MH, Bolser DC, et al. Diagnosis and management of cough executive summary: ACCP evidence-based clinical practice guidelines. *Chest*. 2006 January;129 (1Suppl):1S-23S.
5. Gibson PG, Vertigan AE. Gabapentin in chronic cough. *Pulmonary Pharmacology & Therapeutics*. 2015;35: 145-148.
6. Ryan NM, Birring SS, Gibson PG. Gabapentin for refractory chronic cough: A randomized double-blind, placebo-controlled trial. *Lancet.* 2012;380: 1583–89.
7. Mark B. Bromberg (editor) Motor Neuron Disease in Adults Oxford University Press, 2014. Page 266

8. Alexander Slade, Sinisa Stanic Managing excessive saliva with salivary gland irradiation in patients with amyotrophic lateral sclerosis Journal of the Neurological Sciences 352 (2015) 34–36
9. Clinical Pharmacology: Elsevier/Gold Standard. 2015. [Accessed 2016 Jul]. Available from: www.clinicalpharmacology-ip.com

