PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #199
OPIOIDS FOR COUGH

Sean Marks MD and Drew A Rosielle MD

Background Cough is a common, and at times distressing, symptom. Up to 40% of advanced cancer patients report cough, and while a smaller percentage find their cough distressing, severe cough can lead to dyspnea, nausea/vomiting, sleep impairment, chest and throat pain, and impaired communication. This *Fast Fact* will focus on the use of opioids for the symptomatic treatment of cough. *Fast Fact* #200 will address other agents for cough.

Etiologies & Evaluation Common etiologies of cough include infections of the upper and lower airway, asthma and COPD, lung cancer or lung metastases, interstitial pulmonary processes (such as lymphangitic tumor spread or pulmonary edema), gastroesophageal reflux, aspiration, and drugs. Common drug causes include ACE inhibitors, NSAIDs, and inhalant medications. Evaluating for reversible causes is appropriate if consistent with the goals of care and prognosis. If feasible, treatment should be directed at the underlying cause. Many patients however will benefit from symptomatic therapy for a distressing cough while waiting for acute therapy to work or have a chronic cough not amenable to treatment (e.g. cough due to advanced lung cancer).

Opioids are the only clearly effective centrally-acting anti-tussive drugs and are thought to work by suppressing the brainstem cough center through mu and kappa opioid receptor agonism. They are the first-line symptomatic treatment for severe, distressing cough. All opioids used to treat cough have typical opioid side effects such as sedation, constipation, and nausea.

- *Codeine:* Duration of action is 4 hours; usual adult dose is 10-20 mg every 4-6 hours. It has shown to be effective for acute and chronic cough in several placebo-controlled trials. It is available alone or as an elixir with guaifenesin.

- *Dextromethorphan:* Duration of action 3-6 hours; usual adult dose is 10-20 mg every 4-6 hours. It is the most commonly used anti-tussive. Confirmed to be as effective as codeine for cough in multiple studies. It is available alone or as an elixir with guaifenesin. Note: dextromethorphan inhibits the cytochrome P450 system and thereby affects the metabolism of many drugs. Dextromethorphan can also cause a serotonin syndrome if used with serotonergic drugs such as antidepressants.

- *Hydrocodone:* Duration of action 4-6 hours; usual dose 5-10 mg every 4 hours. Hydrocodone is only available as a combination product in the US: as a short-acting elixir with the anticholinergic drug homatropine or as an extended release elixir with the antihistamine chlorpheniramine (dosed at 10 mg every 12 hours). These other agents magnify hydrocodone's sedative effects, and limit the maximum dose a patient can take. Hydrocodone has been shown to be as effective as codeine in head to head studies but with fewer gastrointestinal side-effects. For this reason it is considered by many experts as the anti-tussive of choice (Homsi 2001).

- *All opioid* analgesics have anti-tussive activity and their use has been mostly based on convention; there is no strong evidence that any one opioid has superior efficacy for cough. For patients already taking opioids for pain, it is unclear whether adding a second opioid such as codeine for cough is effective. One uncontrolled, open-label study showed hydrocodone to be helpful in this setting; it has not been repeated (Homsi 2001).

Fast Fact #200 will discuss non-opioid agents for cough, as well as address some general treatment strategies.

References

1. Homsi J, Walsh D, Nelson KA. Important drugs for cough in advanced cancer. *Support Care Cancer.* 2001; 9:565-74.
2. Estfan B, LeGrand S. Management of cough in advanced cancer. *J Support Oncol.* 2004; 2:523-7.
3. Von Gunten CF. Interventions to manage symptoms at the end of life. *J of Pall Med.* 2005; 8(1): 88-94.
4. Adam J. *Pan-Glasgow palliative care algorithm 2005 – Palliation of cough*. Palliative Care Formulary 2nd Edition. Radcliffe Medical Press Ltd. 2002.
5. Davis CL. ABC of palliative care: breathlessness, cough and other respiratory problems. *BMJ.* 1997; 315: 931-4.
6. Homsi J, Walsh D, Nelson KA, Sarhill N, Rybicki L, LeGrand SB, Davis M. A phase II study of hydrocodone for cough in advanced cancer. *Am J Hospice Palliat Care.* 2002; 19:49-56.
7. Turturro MA, Paris PM, Yealy DM, Menegazzi JJ. Hydrocodone versus codeine in acute musculoskeletal pain. *Ann Emerg Med.* 1991; 20:1100-03.
8. Irwin RS. Complications of cough. *Chest*. 2006; 129:54S-58S.
9. Homsi J, et al. Symptom evaluation in palliative medicine: patient report vs systematic assessment. *Support Care Cancer.* 2006; 14:444-453.
10. Chung KF. Currently available cough suppressants for chronic cough. *Lung* 2008 [E-pub ahead of print, available Oct 2, 2007]. DOI: 10.1007/s00408-007-9030-1.

Conflict of Interest Statement: the authors have disclosed no relevant conflicts of interest.
Authors' Affiliations: Medical College of Wisconsin, Milwaukee, WI (SM); University of Minnesota Medical School and Fairview Health Services, Minneapolis, MN (DAR).

Version History: Originally published March 2008. Copy-edited in June 2009. 2nd edition published in July 2013; minimally revised to reflect that gabapentin is a newly appreciated centrally acting anti-tussive; copy edited again July 2015.