

FAST FACTS AND CONCEPTS #200 NON-OPIOID ANTI-TUSSIVES

Sean Marks MD and Drew A Rosielle MD

Background Cough is a common and at times distressing symptom. *Fast Fact* #199 discussed opioids for the symptomatic treatment of cough. This *Fast Fact* will address non-opioid anti-tussives.

Controversies Commonly used prescription and over-the-counter anti-tussive formulations which contain some combination of antihistamines (e.g. diphenhydramine), a mucolytic (e.g. guaifenesin), and/or dextromethorphan are often used for acute cough due to upper respiratory infections and acute bronchitis. Evidence for these agents in the acute setting is poor (either no better than placebo or sweet syrup) and cannot be recommended. Due to concerns about inadvertent overdose and lack of efficacy, these products are now being *actively* discouraged for use in the pediatric setting.

Centrally-acting non-opioid anti-tussives

- *Gabapentin*: the pathophysiology of refractory chronic cough is thought to resemble central sensitization as seen in neuropathic pain. A randomized, double-blind placebo controlled trial demonstrated that gabapentin can meaningfully improve cough-specific quality of life and reduce cough frequency and severity compared with placebo. Doses up to 1800 mg a day were studied.
- *Other neuromodulating agents*: paroxetine, amitriptyline, and benzodiazepines have been anecdotally reported to have efficacy in chronic, refractory cough but lack published controlled evidence.

Peripherally-acting anti-tussives

- *Sweet syrups* are commonly used as cough suppressants, whether as bases for prescription elixirs (such as codeine with guaifenesin) or home remedies (honey, simple syrup). The mechanism of action is unknown; some authors hypothesize it acts as a protective barrier to sensory receptors in the throat that heighten the cough reflex. A few controlled trials have shown sweet syrups reduce coughing in upper respiratory infections.
- *Benzonatate* inhibits cough by anesthetizing stretch receptors in the respiratory tract. Its duration of action is 3-8 hours; dosed at 100-200 mg three times a day. No published controlled studies confirm its effectiveness but multiple uncontrolled studies support its use. Side effects are uncommon but include sedation, headache, bronchospasm, and nausea. Empirically many experts recommend adding it to an opioid.
- *Antihistamines and anticholinergics* are often part of combination anti-tussive elixirs with or without an opioid. Anticholinergics such as hyoscyamine and scopolamine are most helpful in the setting of copious upper respiratory secretions leading to cough. See *Fast Fact* #109 for dosing information.
- *Expectorants* thin bronchial secretions and ease expectoration. Examples include guaifenesin (200-400 mg every 4 hours) and nebulized acetylcysteine or hypertonic saline. Empirically they have been recommended for severe, chronic, wet coughs. Because they may increase fluid in the respiratory tract, they are not recommended if the cough reflex is diminished.
- *Nebulized local anesthetics* are thought to work by anesthetizing afferent receptors in the respiratory tract. There have been no trials evaluating their effectiveness; anecdotally they have been reported to be effective for refractory cough. Published regimens include lidocaine 2% solution, 5 mL nebulized every 6 hours; and bupivacaine 0.25%, 5 mL nebulized every 8 hours. Bronchospasm is a potential side effect.
- *Other agents* such as bronchodilators and corticosteroids have not been shown to be effective apart from specific indications (e.g. for COPD or asthma exacerbations).

Recommendations Treatment for cough should be directed at the underlying cause if feasible and consistent with a patient's prognosis and goals of care. When symptomatic treatment for a distressing cough is necessary, it is reasonable to start with an opioid product, adding benzonatate if needed. A trial of anticholinergics and expectorants for the indications described above is reasonable, but they should be stopped after a couple days if they have no effect. Sweet syrups appear to be helpful in upper respiratory

infections; their role otherwise is uncertain. If these strategies fail to control distressing symptoms, gabapentin should be tried for chronic cough.

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Authors' Affiliations: Medical College of Wisconsin, Milwaukee, WI (SM); University of Minnesota Medical School and Fairview Health Services, Minneapolis, MN (DAR).

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