Cough: Pharmacologic and Nonpharmacologic Remedies

Michael D. Shepherd, MD, Assistant Professor; Department of Family Medicine, University of Tennessee College of Medicine, Chattanooga

Mechanism of cough: receptors in epithelium of larynx, trachea, and bronchus trigger cough and send message to brain; glottis closes with short inspiration, leading to forceful expiration (involves diaphragm, contraction of chest muscles, and increased chest pressure); forcefulness of cough can cause injury

Chronic cough: upper respiratory — allergy; vasomotor rhinitis; postnasal drip; sinusitis; postinfectious cough; lower respiratory — aspiration (especially in elderly patients); asthma; chronic obstructive pulmonary disease; allergic inflammation; abscess; bronchiectasis; tumor; cystic fibrosis (especially in children); drugs (eg, angiotensin-converting enzyme inhibitors)

Specific treatments: allergic rhinitis — inhaled nasal steroids; oral and inhaled antihistamines; intramuscular or oral steroids can be used, but not recommended; cough-variant asthma — small airway disease seen on spirometry; identify allergy component; start with leukotriene receptor antagonists; inhaled bronchodilators; inhaled and oral corticosteroids; gastroesophageal reflex disease — proton pump inhibitor; postviral syndrome — transient hypersensitivity of airways with twitchy cough; same treatment as cough-variant asthma; if patient has no airway hypersensitivity, use ipratropium or tiotropium; drug-related cough — stop medication

Other causes of cough: common cold; upper airway cough syndrome; allergic rhinitis; bronchitis; pneumonia; acid reflux; cigarette smoking; in children — foreign bodies; respiratory syncytial virus; asthma; allergic rhinitis; habitual psychologic cough; cystic fibrosis

Duration of cough: acute — most commonly caused by upper respiratory infection (URI); lasts ≤ 3 wk; subacute — lasts 3 to 8 wk; chronic — lasts ≥ 8 wk; study found mean duration of cough nearly 18 days, but patients felt cough associated with common cold should last 3 to 7 days (with bronchitis 7-9 days)

Treatment of cough: corticosteroids and epinephrine (especially in emergency department); dexamethasone and prednisolone; inhaled budesonide; mist and steam recommended, although not highly effective in clinical trials

Pertussis ("whooping cough"): caused by Bordetella pertussis; cough can last 3 to 4 wk; bronchodilators ineffective; corticosteroids not recommended (no good data); treat with macrolides and trimethoprim-sulfamethoxazole (TMP-SMZ); antitussives discouraged

Cough medicines: opiates — dextromethorphan (synthetic opiate); codeine (no scientific evidence for efficacy); hydrocodone (some evidence of efficacy); morphine; corticosteroids — modify inflammatory response of airway; ipratropium and tiotropium block efferent cough receptors, but do not work by bronchodilation (alter mucociliary factors); work in postviral syndrome; guaifenesin — usually used in combination with, eg, hydrocodone; inhibits sensitivity of cough reflex (more in patients with upper respiratory illness, compared to patients without illness); benzonatate (eg, Tessalon Perles, Zonatuss) — active on stretch receptors in lungs and upper airway; not approved for use in children; problem with fatigue, sedation, headaches, dizziness, disorientation, and confusion; benzonatate plus guaifenesin — more effective than either alone; dextromethorphan — available over-the-counter in lozenges, gels, liquids, and extended-release form; not recommended for children; hydrocodone — reduces cough; more effective when mixed with, eg, chlorpheniramine, guaifenesin; teratogenicity seen in animal studies; codeine — little evidence of efficacy, compared to placebo; metabolized into morphine; 1% to 7% of patients (including children) tend to rapidly metabolize codeine into morphine (associated with multiple deaths in children given codeine for pain relief following tonsillectomy and appendectomy); gabapentin — not recommended for acute cough, but may be helpful in refractory cough lasting 7 to 9 wk; start slow (300 mg 1-2 times daily); randomized trials saw high confidence factor and low number needed to treat; side effects include fatigue, sedation, and nausea; effective and well tolerated in patients with refractory cough

Honey: recommended by World Health Organization and American Academy of Pediatrics for children ≥ 1 yr of age for treatment of URI; meta-analysis found that children who took honey had greater mean improvement in severity and "bothersomeness" of cough

Alternative treatments: Glycyrrhiza glabra — studies showed 81% reduction in cough, compared to 62% with codeine; herbal tea with honey — steam and drinking hot water helpful in lubricating airway; others — ginger and honey; honey with warm milk or coconut milk at bedtime; eucalyptus rub; lemon-honey cough syrup — boil 1 lemon for 10 min; cut in half and extract juice; add glycerin and 2 Tbsp of honey; take 1 tsp every 4 hr; ginger-honey cough syrup — mix 1/4 tsp of ginger with cayenne pepper; add 1 Tbsp of honey, 1 Tbsp of apple cider vinegar, and 2 Tbsp of water; mix and take 1 tsp every 4 hr; theobromine — found in dark chocolate; found to inhibit cough; study used 1000 mg of theobromine twice daily; unsweetened dark chocolate has 450 mg per ounce; 150 mg in sweetened dark chocolate; blocks sensory nerves in trachea, larynx, and bronchi

Educational Objectives
The goal of this program is to improve management of persistent cough and pertussis in children. After hearing and assimilating this program, the clinician will be better able to:
1. Describe common causes of chronic cough.
2. Recommend appropriate antitussive agents for patients with cough.
3. Identify risk factors for severe pertussis.
4. Recognize patients and family members who may benefit from treatment of pertussis and/or prophylaxis.
5. Select an effective antibiotic for treatment of pertussis.

Faculty Disclosure
In adherence to ACCME Standards for Commercial Support, Audio-Digest requires all faculty and members of the planning committee to disclose relevant financial relationships within the past 12 months that might create any personal conflicts of interest. Any identified conflicts were resolved to ensure that this educational activity promotes quality in health care and not a proprietary business or commercial interest. For this program, the faculty and planning committee reported nothing to disclose.
Pertussis in Children: The 100-Day Cough

Ellen Laves, MD, Clinical Instructor of Health Sciences, Department of Pediatrics, University of California, San Francisco, School of Medicine

Epidemiology: with advent of diphtheria, tetanus, pertussis (DTP) or whole-cell pertussis vaccine, rate of pertussis fell to slightly >1000 cases in 1976; slightly >25,000 cases in 2005; in 2010, >9000 cases in California alone

Cocccobacilli: gram-negative; difficult to culture; bind to respiratory cilia and secrete toxin that paralyzes cilia, interfering with clearance of secretions; cough is reaction to damaged cilia, and can persist after clearance of bacteria; incubate for 1 to 2 wk, but incubation period can last up to 3 wk; infection spontaneously clear without treatment within 2 to 4 wk; some individuals can remain contagious for up to 6 wk

Phases: catarrhal — acute infection; most difficult phase to recognize; lasts 1 to 2 wk; characterized by mild fever, cough, and rhinorhea; children frequently diagnosed with URI or acute otitis media; paroxysmal — most classic and easily recognized phase; lasts 1 to 6 wk; characterized by paroxysms of cough, posttussive emesis, gagging, and poor feeding and dehydration if cough disruptive; presentation can be atypical (especially in infants [primary manifestation often autonomic instability, with reports of, eg, apnea, bradycardia]); convalescent — severity of coughing episodes gradually improves; can last for weeks to months

Complications: apnea; bradycardia; pneumonia (usually due to secondary bacterial infection); less common — seizures; encephalopathy; pneumothorax; pneumomediastinum; rib fracture; rectal prolapse; intracranial hemorrhage

Risk factors: age — 86% of hospitalizations occurred in infants 0 to 3 mo of age (fewer hospitalizations in infants 0 mo of age [may be due to, eg, passive immunity from mother, 3-wk incubation period]); data show 100% of infants who died and 100% of infants who required extracorporeal membrane oxygenation were 0 to 3 mo of age; 95% of infants who required mechanical ventilation 0 to 3 mo of age; >88% of infants with apnea, respiratory distress, and pneumonia 0 to 3 mo of age; according to Centers for Disease Control and Prevention (CDC) data, 80% to 90% of deaths occurred in infants 0 to 3 mo of age; younger children have more complicated courses with pertussis; risk for severe pertussis decreases with age; vaccination status — children should be vaccinated at 2, 4, and 6 mo of age; vaccination decreases rate of hospitalization; study found that infants 2 to 11 mo of age at risk and need vaccine for severe pertussis (ie, children requiring intensive care unit [ICU] hospitalization or mechanical ventilation, or children who died) had lower odds of developing severe pertussis with progressive number of doses of diphtheria and tetanus toxoids and acellular pertussis vaccine, adsorbed (DTP); cough duration — in patients with pertussis that required intensive care, apnea common in those with cough lasting ≤1 wk (suggests severe pertussis less likely with further progression); another study found that as time to diagnosis progressed beyond 2 wk, odds of developing severe pertussis significantly decreased; prematurity — CDC data show 51% of fatal infant cases occurred in infants born <37 wk gestational age (GA); 29% of fatal infant cases occurred in infants <35 wk GA; data limited; summary — infants <3 mo of age at significantly increased risk for severe pertussis; unimmunized or infants behind on immunization at risk; higher risk associated with short (<2 wk) cough duration; prematurity and other health issues (eg, need for O2 therapy, cardiac history, severe neurologic problems) associated with increased risk

Testing: culture — gold standard; 100% specific; relatively insensitive; requires live bacteria; most sensitive during catarrhal phase; sensitivity decreases with antibiotic use; polymerase chain reaction (PCR) testing — more sensitive than culture; does not require live bacteria; can be used within first 3 wk of cough; not affected by antibiotic treatment; since test characteristics not standardized, risk for false-positive results higher; CDC recommendations — obtain culture within first 2 wk of cough onset; perform PCR testing up to 4 wk after cough onset; culture and PCR recommended as diagnostic tools

Treatment and prophylaxis: purpose — decrease transmission in community; shorten contagiousness to 5 days; patients who present during paroxysmal phase showing results of toxinn-mediated disease (bacteria may be “long gone”; treat from public health standpoint rather than to attenuate disease severity); important to inform parents that treatment may not change disease course; if patient presents during catarrhal phase, then treatment can lessen severity; prophylaxis given to index patient within 21 days of cough onset can prevent symptomatic infection; who should be treated — all patients with positive pertussis test; patients at high risk for severe disease (eg, infants, women in third trimester of pregnancy, patients with preexisting health conditions, patients >65 yr of age) who have pertussis-like symptoms; who should be given prophylaxis — patients at high risk for severe disease; patients who come into regular contact with high-risk patients (eg, health care workers, day care workers, people with young infant at home)

Treatment algorithm: determine whether patient at high risk for severe pertussis (consider age, health status, pregnancy status); consider degree of concern for pertussis; determine who patient comes into contact with (eg, young child or pregnant mother at home); high clinical suspicion for pertussis in young (eg, 28 day of age) infant — test and treat infant; provide prophylaxis to individuals at high risk; “lukewarm” clinical suspicion for pertussis in high-risk patient — test and provide prophylaxis to high-risk contacts as needed; high clinical concern for pertussis in low-risk child — test and treat child; provide prophylaxis to high-risk contacts; low concern for pertussis in adolescent 15 yr of age who has infant sibling at home — test adolescent; treat and provide prophylaxis as needed; low likelihood of pertussis in adolescent 15 yr of age with no risk for exposure to others — offer supportive care; take-home points — “if you think it’s pertussis, treat for pertussis” (no need to wait for test results); clinical concern modified by community

Medications: azithromycin — 5-day course; dose varies depending on age: for infants <6 mo of age, 10 mg/kg per day for 5 days; for infants ≥6 mo of age, 10 mg/kg per day 1, followed by 5 mg/kg on days 2 through 5; others — erythromycin; clarithromycin; TMP-SMZ; not 5-day courses; erythromycin associated with risk for hypertrophic pyloric stenosis (counsel families about this; treatment for specific symptoms)

Fully immunized term infant 3.5 mo of age presenting with 3 wk of paroxysmal cough: acceptable to send infant home with good return precautions; CDC recommends testing with PCR and culture; infant at low risk for severe pertussis; acceptable to test and treat infant during visit; no high-risk contacts (no need to provide prophylaxis to family members)

Boy 11 yr of age presenting with 3 wk of paroxysmal cough and posttussive emesis: lives at home with healthy parents; child at low risk for severe pertussis; if physician convinced that child has pertussis, acceptable to test and treat child; no high-risk contacts (no need to provide prophylaxis to family members)

Boy 16 yr of age with paroxysmal cough and posttussive emesis: lives at home with healthy infant sister (2 mo of age) and parents; boy at low risk for severe pertussis, but pertussis clinically suspected; test and treat boy; provide prophylaxis to infant sister (high-risk contact) and parents (who come into contact with sister)

Fully immunized infant 2.5 mo of age presenting with 15 days of paroxysmal cough: no apneic episodes; lives with mother who runs day care center; infant at high risk for severe pertussis; clinical suspicion for pertussis high; test and treat infant; provide prophylaxis to mother; reasonable to consider hospitalization
High-risk contacts: young infants; pregnant women; elderly individuals; individuals with other health conditions; individuals who work in day care setting

Infant 28 days of age presenting with staccato, forceful paroxysmal cough for 8 days: no apneic events; lives with parents and 16-year-old brother who has posttussive emesis; infant at high risk for severe pertussis; since infant <3 mo of age, not fully immunized, and coughing for 8 days, consider hospitalization; test and treat infant and brother; data about prophylaxis limited

High-risk criteria for severe pertussis: age <3 mo; lack of immunization or underimmunization; short cough duration; prematurity; other health conditions

Take-home points: pertussis associated with serious complications; presentation can be atypical; consider risk factors for severe pertussis when considering disposition; use PCR and culture to diagnose pertussis; treat patients with clinical pertussis or positive PCR or culture; provide prophylaxis to individuals at risk for severe pertussis and individuals who come in contact with high-risk patients

Acknowledgments

Dr. Shepherd spoke in Chattanooga, TN, at the 28th Annual Family Medicine Update, presented June 12-15, 2013, by the Department of Family Medicine at the University of Tennessee College of Medicine. Please visit https://utcomchat.org/ for more information from this sponsor. Dr. Laves spoke in San Francisco, CA, at Annual Review in Family Medicine: Controversies and Challenges in Primary Care, presented December 9-10, 2013, by the University of California, San Francisco, School of Medicine. Visit www.cme.ucsf.edu/cme/ for information about upcoming courses from this sponsor. The Audio-Digest Foundation thanks the speakers and the sponsors for their cooperation in the production of this program.

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Estimated time to complete the educational process:

Review Educational Objectives on page 1 Take pretest 5 minutes 10 minutes

Listen to audio program 60 minutes Review written summary and suggested readings 35 minutes Take posttest 10 minutes
COMBATING THE PERSISTENT COUGH

To test online, go to www.audiodigest.org and sign in to online services.
To submit a test form by mail or fax, complete Pretest section before listening and Posttest section after listening.

1. Chronic cough is defined as cough lasting:
   (A) ≥2 wk (B) ≥4 wk (C) ≥6 wk (D) ≥8 wk

For questions 2-4, match the antitussive agent in Column I with its description in Column II.

<table>
<thead>
<tr>
<th>Column I</th>
<th>Column II</th>
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<tbody>
<tr>
<td>2. Guaifenesin</td>
<td>(A) Modifies inflammatory response of airway; metabolized into morphine</td>
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<td></td>
<td>(B) Usually used in combination with other agent; inhibits sensitivity of cough reflex</td>
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<tr>
<td>3. Benzonatate</td>
<td>(C) Active on stretch receptors in lungs and upper airway; not approved for use in children; associated with</td>
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<td>fatigue, sedation, and confusion</td>
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<tr>
<td>4. Gabapentin</td>
<td>(D) Not recommended for acute cough; effective and well tolerated in patients with refractory cough</td>
</tr>
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5. Which of the following is recommended by the World Health Organization and American Academy of Pediatrics for treatment of upper respiratory infection in children ≥1 yr of age?
   (A) Honey ** (B) Codeine (C) Benzonatate (D) Dextromethorphan

6. Severity of coughing episodes gradually improves during the _____ phase of pertussis.
   (A) Catarrhal (B) Paroxysmal (C) Convalescent ** (D) Posttussive

7. A study found that most hospitalized infants who required mechanical ventilation or had apnea, respiratory distress, and/or pneumonia were in which of the following age groups?
   (A) 0 to 3 mo of age ** (C) 3 to 6 mo of age
   (B) 2 to 4 mo of age (D) >6 mo of age

8. Choose the correct statement about use of polymerase chain reaction testing for pertussis.
   (A) Recognized as gold standard for diagnosis of pertussis
   (B) Requires live bacteria
   (C) Can be used within first 3 wk of cough **
   (D) Results affected by antibiotic treatment

9. Pertussis in infants is treated with a 5-day course of:
   (A) Erythromycin (C) Clarithromycin
   (B) Azithromycin ** (D) Trimethoprim-sulfamethoxazole

10. Short cough duration and prematurity are high-risk criteria for severe pertussis in infants.
    (A) True ** (B) False

Answers to Audio-Digest Family Practice Volume 62, Issue 14: 1-B, 2-B, 3-A, 4-C, 5-D, 6-D, 7-A, 8-B, 9-D, 10-A