A 73-year-old man presented to the emergency department with a 4-day history of nonproductive cough that worsened at night. He did not have fever, chills, headache, myalgias, rhinorrhea, nasal congestion, sore throat, hemoptysis, chest pain, or dyspnea.

Upper or lower respiratory tract infections (i.e., pneumonia, bronchitis, rhinosinusitis, and nonspecific upper respiratory infection) account for the majority of cases of acute cough (lasting <3 weeks), regardless of the patient's age. I would inquire about exposure to persons with similar symptoms. The absence of fever, dyspnea, hemoptysis, and pleuritic chest pain reduces the likelihood of pneumonia, although these features are frequently absent in elderly patients with pneumonia. Although they are more often identified as causes of chronic cough than as causes of acute cough, I would strongly consider other, noninfectious causes, such as hay fever, bronchial hyperreactivity, postnasal drip, or gastroesophageal reflux disease. The worsening of cough at night is consistent with postnasal drip, gastroesophageal reflux disease, and congestive heart failure. In this elderly man, aspiration caused by swallowing dysfunction (with central or peripheral causes), irritation of the lower airways by a foreign body, inflammation, or cancer are also possible.

The patient had type 2 diabetes mellitus, hypertension, a systolic heart murmur, and gastroesophageal reflux disease, and he had undergone coronary-artery bypass surgery. The murmur was believed to be caused by aortic stenosis, but this could not be confirmed, since he had declined echocardiographic evaluation. His medications were aspirin, metformin, lisinopril, simvastatin, and ranitidine.

The history of coronary artery disease, hypertension, and possible aortic stenosis increases my suspicion that the patient has congestive heart failure, and I would look for signs of this on physical examination. The patient also has gastroesophageal reflux disease, and the cough may reflect inadequate control by the H₂-receptor antagonist. Angiotensin-converting–enzyme (ACE) inhibitors are a frequent cause of cough; it would be helpful to know how long the patient has been taking this type of medication, as well as the aspirin, which may induce bronchospasm or exacerbate gastroesophageal reflux disease.

The patient reported that he did not have orthopnea or paroxysmal nocturnal dyspnea, and none of his medications had been started recently. On examination, he appeared to be comfortable, was afebrile, and had a regular pulse of 85 beats per minute, a respiratory rate of 16 breaths per minute, a blood pressure of 157/90 mm Hg, and an oxygen saturation of 98% in room air.
gen saturation of 99% while breathing ambient air. The oropharynx was normal on examination. There was no jugular venous distention. Cardiovascular examination showed a normal S,
S,
without an S,
S,
; there was a grade 3/6 midysystolic murmur that radiated to the carotid arteries. The lungs were clear on auscultation. He had no peripheral edema. A chest radiograph was normal (Fig. 1). The emergency department physician thought the patient’s cough was probably related to the use of lisinopril and advised that the drug be replaced with an angiotensin-receptor blocker, with follow-up by the primary care physician.

The normal vital signs, results of chest examination, and chest radiograph substantially reduce my concern about pneumonia or other pulmonary parenchymal diseases. Upper respiratory infection, bronchitis, postnasal drip, and gastroesophageal reflux disease are my leading diagnoses.

Since lisinopril had not recently been prescribed, I would not have discontinued it as my first step. Although the normal results of the lung examination and the absence of jugular venous distention and peripheral edema argue against congestive heart failure, I remain concerned about this possibility. Hepatojugular reflux (defined as a sustained increase in the jugular venous pressure of >3 cm after 15 seconds of 35 mm Hg of abdominal pressure) may be a more sensitive indicator of increased pulmonary-capillary wedge pressure. I would obtain an echocardiogram to assess the murmur and left ventricular function.

One week later, the patient returned to the clinic and reported that, despite the change in medication, the cough had worsened. It was present throughout the day but remained particularly bothersome at night and disrupted sleep. No new symptoms had developed.

Worsening at night and difficulty sleeping are common with cough associated with upper respiratory infection and could be caused by exacerbating factors such as dry air or postnasal drip. Since the patient’s illness remains most compatible with an acute respiratory tract illness, I would try symptomatic therapies, including dextromethorphan and inhaled albuterol, since these may have a modest benefit in reducing the severity and frequency of cough in adults with acute bronchitis. Because cough may be the only symptom of reflux, I would also initiate more aggressive acid suppression with a proton-pump inhibitor.

Another possibility that should be considered in adults with persistent cough is pertussis. In adults who have had previous infection with Bordetella pertussis or immunization against it, a persistent cough may be the only symptom. In contrast, persons without prior exposure to pertussis (through vaccination or natural infection) have the typical paroxysmal cough and inspiratory whoop, as well as post-tussive vomiting and syncope, more frequently. Immunity associated with childhood vaccination wanes after 5 to 10 years, so I would inquire about risk factors for exposure to pertussis — particularly recent contact with children, adolescents, or adults with a cough syndrome or known pertussis. In the absence of risk factors for pertussis, I would not test for the infection unless the cough persisted for more than 2 to 3 weeks, because the overwhelming majority of acute cases of cough are due to self-limited viral infections.

On further questioning, the patient stated that he felt well between coughing spells and was able to engage in his usual activities. His heartburn was well controlled. He did not have inspiratory whoop or post-tussive vomiting. He had not regularly or recently been in contact with children or adolescents, but he recalled that approximately 2 weeks before his cough began, he had visited a friend who had a cough, and he noted that a cough had recently developed in a few other friends.

Acute cough is usually caused by a virus (e.g., influenza virus, respiratory syncytial virus, or rhinovirus) with a short incubation period. The report
of contacts with a similar cough is common, especially during the winter months, but could represent exposure to *B. pertussis*, which has a longer incubation period (approximately 1 to 2 weeks).

When seen in the clinic, the patient was not in distress. The lungs were normal on auscultation and percussion. A repeat chest radiograph was normal. A nasopharyngeal-swab specimen was obtained for *B. pertussis* testing; 2 days later, the direct fluorescent antibody test was reported to be negative. On telephone follow-up, the patient reported that the cough was unchanged and remained quite bothersome.

I agree with the decision to obtain a repeat chest radiograph in this elderly patient with persistent cough. Although direct fluorescent antibody testing for pertussis has the advantage of a 1-to-2-day turnaround time, it, like culture, has poor sensitivity (usually <50%). I would not consider pertussis to be sufficiently ruled out on the basis of the results of direct fluorescent antibody testing. Polymerase-chain-reaction (PCR) testing is more sensitive and is preferred for the ruling out of pertussis. Laboratory confirmation of suspected pertussis is important for public health reasons, as well as for avoiding unnecessary testing (e.g., bronchoscopy or computed tomography).

Since the results of microbiologic testing may not be available for a week or more, and because pertussis is highly contagious, antimicrobial treatment should be initiated when testing is ordered, and positive cases should be reported to the local health department. When pertussis has lasted more than 7 to 10 days, antimicrobial therapy has little symptomatic benefit, but it reduces the risk of transmission. Postexposure prophylaxis should be offered to close contacts of patients with laboratory-confirmed cases, regardless of their age or vaccination status.

One week later, *B. pertussis* was reported to have been isolated from the nasopharyngeal specimen obtained at the previous clinic appointment. The patient was treated with oral erythromycin for 14 days, and the case was reported to the local health department. The patient’s friends with cough were treated for presumed pertussis. Household members and persons with prolonged close contact to the patient received chemoprophylaxis. The patient returned for a follow-up visit 1 month after completing antibiotic therapy and reported minimal improvement in the cough; he was concerned that he was still contagious.

Unfortunately, most adults with pertussis can expect to cough for at least 3 months. Antimicrobial treatment initiated after 1 to 2 weeks of symptoms has little effect on the duration of the cough. The persistence of cough for 2 months in this patient is typical of pertussis infection. He should not be contagious after appropriate antibiotic treatment, and the prolonged cough should not be considered an indicator of persistent infection.

The patient was reassured that he was no longer contagious and was informed that prolonged cough was typical of pertussis infection, despite treatment with antibiotics. The cough gradually resolved over the next 3 months.

**Commentary**

Cough is one of the most common symptoms for which patients see their primary care physicians. The differential diagnosis for cough is broad and encompasses disorders that range from those that are relatively benign to those that are potentially life-threatening. As noted by the discussant, the duration of cough at the time of presentation is a useful first step toward narrowing the differential diagnosis. The most common causes of acute cough (lasting <3 weeks) are self-limited, viral upper respiratory infections. Chronic cough (lasting >8 weeks) is most often attributable to gastroesophageal reflux disease, asthma, the upper-airway cough syndrome (formerly called postnasal drip), cigarette smoking, or use of ACE inhibitors. Persistent cough can result in rare but severe complications, such as broken ribs or even intracranial hemorrhage; it can also lead to social isolation.

An important, but often overlooked, cause of cough in adults is infection with *B. pertussis*. Pertussis is often thought of as a childhood infection; however, several recent studies have shown that it is the cause of 12 to 32% of cases of prolonged cough (lasting >2 to 3 weeks) in adolescents and adults. Another misconception is that childhood vaccination against *B. pertussis* confers lifelong immunity, but in fact, immunity wanes after 5 to 10 years and rarely lasts more than 12 years.

Pertussis was a devastating illness until a whole-cell vaccine was introduced in the United States in the late 1940s. The widespread vaccination of children led to a dramatic decline in the
incidence of pertussis, from a peak of more than 250,000 cases per year to a nadir of 1010 cases in 1976. However, the incidence has steadily risen since the early 1980s, with cyclic epidemic peaks approximately every 4 years, as in the prevaccine era. In 2005 there were 25,616 reported cases of pertussis in the United States; this increase has been attributed to increased transmission of B. pertussis, waning vaccine-induced immunity among adults and adolescents, heightened awareness and reporting, and the use of PCR testing for diagnosis.

Adolescents and adults with unrecognized pertussis are a reservoir of infection for infants and children. The disease is far more severe in children and may be fatal in infants, among whom the incidence appears to be increasing. To reduce the rate of transmission from adolescents and adults to infants and children, recent recommendations call for booster vaccinations of adolescents and adults with the new acellular pertussis vaccine (Tetanus Toxoid, Reduced Diphtheria Toxoid, and Acellular Pertussis Vaccine, Adsorbed).

The classic paroxysmal cough of pertussis consists of several rapid, harsh expirations followed by a dramatic inspiratory whoop. Once seen or heard, it is not soon forgotten. In adolescents and adults, a prolonged cough is usually the most notable symptom, but pertussis may also result in complications such as sinusitis, pneumonia, posttussive emesis or syncope, or rib fractures. Other potentially helpful clinical clues that occur during the catarrhal phase are excess lacrimation and conjunctival injection and hemorrhage.

Laboratory diagnostic tests for B. pertussis infection include bacterial culture, direct fluorescent
antibody staining, PCR testing, and serologic testing (i.e., with the enzyme-linked immunosorbent assay). Because of its high specificity, culture of the organism from nasopharyngeal secretions is the standard for diagnosis, but the sensitivity of culturing is only 30 to 60%. The advantage of the rapid results of direct fluorescent antibody testing is offset by its low sensitivity and specificity. PCR testing detects nonviable organisms and has increased sensitivity and specificity; it is replacing direct fluorescent antibody testing but is still costly and not universally available. The PCR assay appears to be better than culture for diagnosing pertussis in previously vaccinated adults, among whom recovery rates are particularly low, but false positive results may occur. Serum testing is also not widely available and is further hampered by lack of standardization.

Current recommendations call for culture or the PCR assay to be used as confirmatory tests to diagnose pertussis. Since B. pertussis preferentially resides in ciliated respiratory epithelium, clinicians must obtain specimens from the posterior nasopharynx, not the anterior nares or throat (Fig. 2). Cotton swabs inhibit the growth of B. pertussis on culture, and calcium alginate swabs may interfere with PCR assays; thus, Dacron swabs may be optimal for both. The sensitivity of culture is reduced by delayed transport to the laboratory and delayed plating of the specimen, as well as previous vaccination, recent antibiotic use, and prolonged illness.

Because of the public health implications of pertussis, the thresholds for testing and initiating treatment should be the same. Antibiotic treatment administered within the first week of illness can decrease the duration and severity of the cough; later administration is unlikely to affect the course of symptoms but helps reduce spread of the infection. Unfortunately, the diagnosis is often not considered during the catarrhal phase. Erythromycin therapy usually eliminates the organism within 5 days; without treatment, patients remain contagious for 1 month or more. Macrolide therapy is recommended for both treatment and postexposure prophylaxis: for adults, 500 mg of erythromycin four times daily for 14 days; 500 mg of azithromycin once on day 1, followed by 250 mg daily on days 2 through 5; or 500 mg of clarithromycin twice daily for 7 days. The predictive value of the classic symptoms of pertussis (paroxysmal cough, whoop, and post-tussive emesis) among previously vaccinated adolescents and adults is unclear, and these symptoms also occur in adults with cough caused by other agents. A recent report of outbreaks of respiratory illness that were by mistake initially attributed to pertussis, mainly on the basis of PCR testing, further highlights the diagnostic challenge posed by the frequently nonspecific symptoms of pertussis in adults and the limitations of currently available laboratory tests.

In subacute conditions, early follow-up allows the outpatient clinician to continue to gather data, assess the patient’s response to interventions, and reassess the differential diagnosis. Close follow-up (both in person and by telephone) in the present case, as well as recognition of the possibility of pertussis and knowledge of how best to test for it, facilitated earlier diagnosis than often occurs in adults with this infection.

Supported by an Advanced Career Development Award from the Health Services Research and Development Program of the Department of Veterans Affairs (to Dr. Saint).

Dr. Gonzales reports receiving consulting fees from CC Ford Healthcare and grant support from Abbott Laboratories. No other potential conflict of interest relevant to this article was reported.

REFERENCES

10. Preventing tetanus, diphtheria, and...


Copyright © 2007 Massachusetts Medical Society.