Abstract—Background: Epidemiologic issues of testing, treatment, prevention, immunization, mandated reporting, and post-exposure prophylaxis do not often intrude on the Emergency Department management of the well-appearing adolescent or adult with a couple of weeks of cough. Objectives: Considering that waning immunity to pertussis, the only vaccine-preventable disease with increasing cases and deaths in the United States, is responsible for 12–35% of such illness, such issues need to be considered. Discussion: Mostly self-limited in adults, transmission of pertussis to infants places them at risk for hospitalization and death. Pertussis is highly contagious (80% transmission), and atypical presentations are the rule in adults (cough alone) and infants (apnea, bradycardia, poor feeding). Treatment in the first few weeks can impact the clinical course, and later treatment can still prevent transmission. Clinical features like paroxysmal cough, inspiratory “whoop,” and post-tussive emesis have mildly increased predictive values and may be absent in adults. Testing is unreliable after 3 weeks of cough. Treatment reduces communicability within 5 days and is suggested without regard to test results within 3 weeks of cough onset for those aged > 1 year (within 6 weeks of cough for < 1 year). Reporting requirements are based on the clinical case definition: ([Cough $\geq$ 2 weeks] + [paroxysms OR whoop OR post-tussive emesis]). Lower reporting thresholds are appropriate during an outbreak or when vulnerable populations are at risk. Post-exposure prophylaxis is recommended for at-risk contacts. Tdap is encouraged for all adults. Conclusion: Practical recommendations consistent with the most current guidelines are offered. Published by Elsevier Inc.

Keywords—pertussis; prevention; epidemiology; diagnosis; treatment

INTRODUCTION

Adults or adolescents with persistent cough frequently present to Emergency Departments (EDs). Once life threats and significant illness have been ruled out, there are additional and potentially serious epidemiologic issues that are often not addressed.

TYPICAL CASE SCENARIO

Clinical Information

An adolescent or adult, without significant comorbidities, presents to your ED with 2–3 weeks of cough. She saw
another provider about 10 days ago, was diagnosed with “bronchitis” and treated with an albuterol inhaler and a cough medicine containing hydrocodone. The cough continues, is non-productive, occasionally better with the inhaler and cough medicine, and has caused the patient to vomit once or twice. There is no history of fever. She is afebrile and well appearing with an occasional cough. There is no respiratory distress; vital signs are normal and oxygen saturation is 99%. Lungs are clear, with no edema. The remaining physical examination is unremarkable. A chest X-ray study is negative. There is mild subjective improvement after nebulized albuterol + ipratropium, and no change in the examination.

**Diagnosis and Disposition**

Your patient continues to look well. You diagnose “persistent bronchitis” and consider antibiotics (recognizing the limited evidence to support the use of antibiotics in “acute bronchitis” – usually defined as ≤3 weeks of cough) (1). Possibly adding some steroids to go with the inhaler, you discharge the patient for follow-up with their primary care physician.

**DISCUSSION: CLINICAL AND EPIDEMIOLOGICAL ISSUES: WHAT ABOUT ADULT PERTUSSIS IN THIS PATIENT?**

Caused by *Bordetella pertussis*, this highly contagious respiratory illness (80% secondary attack rate) has four classic phases in children (Table 1). Atypical pertussis occurs in adolescents, adults, and in infants under 1 year of age (2).

Although easier to diagnose, “classic” cases are currently less frequent than the atypical ones. Like our clinical scenario, adolescents and adults with pertussis often present with cough for only 2–3 weeks. Among general practitioners in France, pertussis was considered as infrequently as 6% of the time in adult patients presenting with cough of over 14 days duration, even though such patients have a pretest probability of pertussis of 12–35% (3–5). The only clinical features that “modestly” increase the pretest probability of pertussis in adults are post-tussive emesis (Likelihood Ratio [LR] = 1.8) and inspiratory whoop (LR = 1.9). Paroxysmal cough is common, less often reported, less severe, and non-specific (LR = 1.1) (5). Thirty-nine percent of pertussis polymerase chain reaction (PCR)-positive patients in one outbreak had only 1–2 weeks of cough (median 12 days) and none of the other case-definition symptoms of pertussis (paroxysmal coughing, “whoop,” or post-tussive emesis) (6).

Infants may have no paroxysms or cough at all, presenting with poor feeding, apnea, or bradycardia. Infants are the group at highest risk for serious illness or death (7).

### Table 1. Classic Stages of Clinical Pertussis in Children

<table>
<thead>
<tr>
<th>Stage</th>
<th>Clinical Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incubation Stage (7–10 days)</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>Catarhral Stage (1–2 weeks)</td>
<td>Resembles URI, the most infectious</td>
</tr>
<tr>
<td>Paroxysmal Stage (1–6 weeks)</td>
<td>Multiple coughs during single exhalation, then an inspiratory “whoop”*</td>
</tr>
<tr>
<td>“Whooping Cough”</td>
<td>Post-tussive emesis or cyanosis</td>
</tr>
<tr>
<td>Convalescent Stage (2–12 weeks)</td>
<td>Gradual recovery</td>
</tr>
<tr>
<td></td>
<td>Exacerbations recur</td>
</tr>
<tr>
<td></td>
<td>“The 100-day cough”- China</td>
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</tbody>
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* URI = upper respiratory infection.


Atypical infections occur in immunized adolescents and adults due to waning immunity and issues of vaccine efficacy. The original whole-cell pertussis vaccine was dramatically effective when it was introduced in the 1940s. However, cases have been increasing again since the 1980s as a result of waning immunity, which rarely lasts more than 12 years (8). Childhood cases are still the least frequent. Forty-four percent of pertussis cases now occur in adolescents or adults, and infants under 1 year of age have the highest reported rates of pertussis (9). The vaccine is poorly effective in the first year of life, and most infants receive little passive immunity from their mother. The waning immunity of adults in the home limits any benefit of herd immunity. Household members are the primary source of 76–83% of infant pertussis (10). Pertussis “boosters” were not recommended until 2006, when the newly licensed Tdap (tetanus, diphtheria, and pertussis) vaccine replacedTd, with the specific goals of protecting adults and “reducing the reservoir of pertussis in the population at large” (11).

**Increasing Incidence**

Pertussis is the only vaccine-preventable disease with increasing numbers of cases and deaths in the United States (US) (12). For example, in 2010, 9143 cases of pertussis (including 10 infant deaths) were reported from California, the most since 1947 (13).

**Diagnosis**

The diagnosis of pertussis is a clinical one. Positive testing is not required for presumptive diagnosis or treatment. The clinical case definition for pertussis from both the Centers for Disease Control and Prevention (CDC) and the American College of Chest Physicians is the same: “cough illness lasting for ≥2 weeks and one of the following: paroxysms of coughing, inspiratory “whoop,” or post-tussive vomiting, without another apparent cause (12,14).
Differential Diagnosis

The differential diagnoses of pertussis include infections caused by other etiologic agents, including adenoviruses, respiratory syncytial virus, Mycoplasma pneumoniae, Chlamydia pneumoniae, and other Bordetella species such as B. parapertussis, and rarely, B. bronchiseptica or B. holmesii (12).

Complications

Infants. Unvaccinated or incompletely vaccinated infants under a year of age are the primary concern. Their immunity is weak, their presentations atypical, and they are at the highest risk for hospitalization and death (usually due to secondary bacterial pneumonia). More than half of infants <1 year of age who get pertussis are hospitalized (11). Eighty-nine percent of Canadians admitted for pertussis were under 6 months of age, and most deaths were in those under 3 months (15). Dehydration, poor feeding with malnutrition and weight loss, sleep disturbance, and encephalopathy also occur.

Although prompt treatment is most beneficial, early clinical diagnosis is difficult. Apnea may be the only symptom, with minimal cough. The best protection for infants is prevention by vaccination of household contacts, plus the early treatment of suspected cases in the home, coupled with post-exposure therapy for the infant.

Adults. Complications in adults are largely cough-induced and include urinary incontinence, herniated disc, sudden hearing loss, carotid dissection, inguinal hernia, fractured ribs, intracranial hemorrhage, and cough syncope. Hospitalization rates can range from 3% to 12%. Angina, encephalopathy, pneumonia, and death can occur, especially in the very elderly (11).

Epidemiologic Issues: Testing, Treatment, Reporting, and Post-exposure Prophylaxis

Pertussis is rarely considered in the differential diagnosis of cough in adults and adolescents, so it is rarely reported (3). Rossi-Foulkes et al. note that although board preparation materials for pediatricians cover pertussis extensively, similar tools for the Internal Medicine and Family Practice board examinations provide no information on the public health issues addressed here (16). Search of a commonly used bank of 1839 emergency medicine review questions from the Council of Emergency Medicine Residency Directors found no reference to “pertussis” or “whooping cough.”

Testing. Chest radiographs are negative. Commonly available tests (nasopharyngeal culture and PCR) are most sensitive early in the clinical course. PCR has optimal sensitivity during the first 3 weeks of cough, with increasing false negatives after the fourth week (17). Culture (the “gold standard” with 100% specificity) has very low sensitivity after 2 weeks of cough (15–45% within 21 days of onset of cough; ≤1–3% if ≥3 weeks) and results may take as long as 2 weeks to return (11). The CDC recommends that PCR and culture be done together whenever testing is done. Technique is important for PCR testing, using either Dacron swabs or nasopharyngeal washings. Other tests (serology, direct fluorescent antibody, gel electrophoresis) are not well standardized and not “confirmatory.” Only 44% of patients aged ≥15 years with clinical pertussis have laboratory evidence of infection (18).

Testing may be more likely positive in childhood pertussis cases. Children are often seen earlier in the course of a cough illness than adults, when tests are more accurate.

Treatment. Most previously immunized adults or adolescents we see in the ED with prolonged cough will eventually recover without antibiotics. Their partial immunity generally results in milder illness than that seen in infants and young children. Treatment is most effective in lessening symptoms if offered early in the disease, during the first 1–2 weeks before coughing paroxysms occur (the time when pertussis is most difficult to diagnose). Extra vigilance during outbreaks or in families may aid in early diagnosis and effective early treatment. “Clinicians should strongly consider treating before test results if clinical history is strongly suggestive, or the patient is at risk for severe or complicated disease, e.g., infants” (19). A major value of later treatment is the ability of that intervention to eliminate B. pertussis from the nasopharynx and prevent transmission to more vulnerable populations. For that reason, the CDC recommends treatment at any time within 3 weeks of cough onset for those over a year of age, and within 6 weeks of cough onset for those younger. The period of communicability is reduced to 5 days after treatment with antibiotics. Coughing (symptomatic) household members of a pertussis patient should be treated as if they have pertussis (12). Earlier treatment and prevention of transmission may reduce the considerable burden of adult pertussis: loss of work, prolonged symptoms, and multiple provider visits (11). There are no proven treatments for pertussis-induced cough; steroids and beta-agonists are not effective.

Macrolide antibiotics eradicate B. pertussis within 5 days. Recommendations include azithromycin (for 5 days) and clarithromycin (7 days). These have fewer gastrointestinal side effects, easier dosing, and better compliance than erythromycin (which is recommended for 14 days). In infants <1 month of age, azithromycin is preferred due to concerns for infantile hypertrophic
pyloric stenosis, which is associated with erythromycin. Trimethoprim/sulfamethoxazole for 14 days is an alternative for patients who cannot tolerate macrolides and who are not pregnant, nursing, or <2 months of age. Doses are standard, except for infants <6 months, for whom azithromycin is recommended at 10 mg/kg/day for 5 days. No work or school is recommended for patients with suspected pertussis until completion of at least 5 days of antimicrobial therapy (12).

**Reporting.** US physicians are legally required to report pertussis cases when **clinically suspected.** Recognizing the difficulties with testing, reporting requirements are based on the clinical case definition: “A cough illness lasting at least 2 weeks with one of the following: paroxysms of coughing, inspiratory ‘whoop’, or post-tussive vomiting, without other apparent cause (as reported by a health professional).” In an outbreak, “a case may be defined as a cough illness lasting at least 2 weeks” (9).

Historically, physicians report a minority of suspected pertussis cases to health departments (16). Of urgent care providers in Utah, only 19% knew that clinically diagnosed pertussis was reportable (20). There is some increase in reporting during outbreaks, most from positive laboratory tests. Adults are rarely reported.

**Post-exposure prophylaxis (PEP).** Individuals with pertussis are most infectious during the initial catarrhal period and for the first 2 weeks of spasmodic cough, but can remain infectious for up to 6 weeks, especially in the case of non-immune infants. Post-exposure chemoprophylaxis (with the same antibiotic regimens used for treatment) is recommended within 3 weeks of exposure for close contacts of patients with clinically suspected pertussis who are at risk of severe disease and death. These include infants, pregnant women in their third trimester (because they will soon have contact with a newborn), and those that are immunocompromised (personal communication with S.W. Martin, Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention; January 12, 2012). The same pretest probability of pertussis (12–35%) that may lower one’s threshold for macrolide therapy in the persistently coughing adolescent or adult may not seem high enough to warrant reporting those same patients as “clinically suspected” pertussis, because up to 90% will not have the disease. Balancing the knowledge that up to 39% of adult pertussis patients may have cough only against the difficulty of health department follow-up for all persistently coughing adults, the best solution may be to report suspected adult pertussis in those who clearly meet the reporting standard ([(Cough ≥2 weeks] + [paroxysms OR whoop OR post-tussive emesis]), with a lower reporting threshold for those who may put others at risk (workers in child care, schools, and health care; caretakers of infants under a year of age). Reporting threshold should fall during an outbreak, because the false-positive rate will also fall with an increase in prevalence. I consider reporting adults: 1) in an outbreak; 2) with household transmission from a diagnosed case; or 3) with a “Super-classic” (my words) clinical case. Additionally, I will likely report those patients I choose to test, insuring health department follow-up on test results.

**CONCLUSION**

**Adult Pertussis: Summary and Practical Approach to Epidemiologic Concerns**

**Testing.** Given the generally low sensitivity, testing is not recommended after 3 weeks of cough, and is most useful for public health surveillance and case finding during an outbreak. The CDC recommends treating anyone you test. **Treatment.** Early treatment may benefit the patient; later treatment reduces transmission. Treat within 3 weeks of cough if >1 year of age, within 6 weeks of cough onset if <1 year.

**Reporting and post-exposure prophylaxis.** Reporting and PEP are the areas in which the greatest uncertainties exist with regard to appropriate clinician behavior in the context of current CDC recommendations and health department requirements.

**Reporting.** Reporting is mandated for this difficult clinical diagnosis, yet few doctors do so, “almost never” for adults. CDC epidemiologists note that: Nonspecific symptoms, atypical presentation and difficulties associated with laboratory diagnosis make pertussis diagnosis challenging, especially in adults who often present late in the clinical course. Reporting decisions should be based on clinical presentation and available epidemiologic information (personal communication with S.W. Martin, Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention; January 12, 2012). The same pretest probability of pertussis (12–35%) that may lower one’s threshold for macrolide therapy in the persistently coughing adolescent or adult may not seem high enough to warrant reporting those same patients as “clinically suspected” pertussis, because up to 90% will not have the disease. Balancing the knowledge that up to 39% of adult pertussis patients may have cough only against the difficulty of health department follow-up for all persistently coughing adults, the best solution may be to report suspected adult pertussis in those who clearly meet the reporting standard ([(Cough ≥2 weeks] + [paroxysms OR whoop OR post-tussive emesis]), with a lower reporting threshold for those who may put others at risk (workers in child care, schools, and health care; caretakers of infants under a year of age). Reporting threshold should fall during an outbreak, because the false-positive rate will also fall with an increase in prevalence. I consider reporting adults: 1) in an outbreak; 2) with household transmission from a diagnosed case; or 3) with a “Super-classic” (my words) clinical case. Additionally, I will likely report those patients I choose to test, insuring health department follow-up on test results.

**Prophylaxis.** See above. Recommendations for pertussis prophylaxis are analogous to those for influenza during the 2009–2010 pandemic: to “consider” prophylaxis for persons with increased risk for complications who were close contacts of “confirmed, probable, or suspected” cases, during that person’s infectious period (for pertussis, 21 days of cough onset). In the absence of a doctor–patient relationship, most ED prophylaxis will
likely consist of discharge instructions with that recommendation.

**Prevention.** Give or recommend Tdap to all adults, regardless of age, who have not had it (regardless of the interval from their last Td), with particular emphasis on parents-to-be, health care workers, and caretakers of infants. This includes pregnant women in the third trimester (>20 weeks) or immediately postpartum for those not who have not had it previously (21).

**Recommendations**

Consider adding these epidemiologic concerns related to pertussis and its serious consequences in infants to your approach to the persistently coughing adolescent or adult. What is their Tdap status? The best evidence is that Tdap likely protects for at least 10 years (22–24). Ask about associated symptoms of paroxysmal cough, whooping, and post-tussive emesis. Are they in close contact with vulnerable populations, or secondarily with others with such contact? Consider discussing/recommending post-exposure prophylaxis for their vulnerable contacts. If you are going to treat “persistent bronchitis,” use a macrolide.

Consider pertussis in infants under a year of age with a cough illness, apnea, poor feeding, or bradycardia. Inquire about persistently coughing family members and their Tdap vaccination status. Consider adding pertussis PCR and culture to Respiratory Syncytial Virus or other testing you might do in such infants. Consider macrolide therapy in seriously ill infants at risk for pertussis.

Offer or advise Tdap to adults or adolescents who have not received it, with particular emphasis on pregnant women and their families.

Utilize your local health department. Give them a call. Health department concerns often center on preventing additional cases in the workplace or in schools and other groups of school-age children (clubs, teams). They are often contacted regarding issues of school exclusion, appropriate treatment, contact assessment, or prophylaxis recommendations. Opinions, practices, and resources will vary, and your local agency sets the standard. Look for changes and more specific guidance in an outbreak. Take advantage of their services: counseling, second opinion, case finding, free pertussis testing, and free immunizations (Tdap). They can give your patient or their teacher a call and take many problems off your hands.

Consider reporting. Advise isolation for 5 days if treating.

**REFERENCES**

ARTICLE SUMMARY

1. Why is this topic important?
Highly contagious, pertussis is the only vaccine-preventable disease with increasing cases and deaths in the United States. The common Emergency Department approach to persistently coughing adults places infants at risk for serious illness.

2. What does this review attempt to show?
Epidemiologic issues of testing, treatment, prevention, immunization, mandated reporting, and post-exposure prophylaxis should play a role in our management of some well-appearing patients with persistent cough. This is an area in which more antibiotic prescribing for “bronchitis” and prophylaxis may save lives.

3. What are the key findings?
Treatment of pertussis within the first few weeks can impact the clinical course, and later treatment can still prevent transmission. Clinical features like paroxysmal cough, inspiratory “whoop,” and post-tussive emesis have only mildly increased predictive values and may be absent in adults. Testing is unreliable after 3 weeks of cough.

4. How is patient care impacted?
We should be increasing our consideration of pertussis in daily practice. Incomplete or remote immunization status and primary or secondary exposure to vulnerable contacts (infants and pregnant women) should provoke considerations of treatment, post-exposure prophylaxis, immunization, and reporting.