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## What are the indications for evaluating a patient with cough for pertussis?

### ■ EVIDENCE-BASED ANSWER

Pertussis should be considered in infants with apnea or severe coughing illnesses of any duration, and in older children or adults with prolonged cough (eg, longer than 2 weeks), especially if accompanied by inspiratory whoop or household exposure to a prolonged cough illness (strength of recommendation [SOR]: **B**, based on consecutive cohort studies with poor reference standards). Coughing paroxysms, posttussive vomiting, and absence of fever, while typical of pertussis, are of little help in distinguishing it from other causes of prolonged coughing illnesses (SOR: **B**, based on consecutive cohort studies with poor reference standards).

### ■ EVIDENCE SUMMARY

Pertussis is an important cause of cough in all age groups. Ten prevalence studies of adolescents and adults seeking medical attention for a prolonged cough (defined variously as >1–4 weeks) found acute pertussis in 12% to 32%.<sup>1</sup>

While cough longer than 2 weeks, inspiratory whoop, posttussive vomiting, coughing paroxysms, and absence of fever are commonly associated with pertussis, relatively few studies have assessed the sensitivities and specificities of these symptoms. The **Table** summarizes results from 5 cohort series of children and adults with laboratory-confirmed pertussis. Comparison groups were variously defined by negative pertussis cultures, negative pertussis serology, or serologic confirmation of other respiratory infections. Likelihood ratios (LR) were calculated from the data presented in each paper.

The magnitude and variability of these likelihood ratios suggest that individual symptoms may be of limited help in distinguishing pertussis from other causes of prolonged cough. Combinations of symptoms may be slightly more helpful. In a study comparing 10 patients with culture-confirmed pertussis with 10 patients with serologically confirmed mycoplasma pneumonia, the combination of cough >14 days and whoop had a sensitivity of 80%, a positive LR (LR+) of 8 and a negative LR (LR-) of 0.22.<sup>2</sup> A cohort series of children aged <5 years with suspected pertussis compared 33 with positive cultures to 55 with negative cultures. The constellation of spasmodic cough and lymphocytosis (>10,000) had a sensitivity of 83%, a LR+ of 2.5, and a LR- of 0.25. Cough >14 days with whoop and vomiting had a sensitivity of 67%, a LR+ of 3.2, and LR- of 0.42.<sup>3</sup>

Infants aged <6 months with pertussis are at particular risk for atypical presentations and serious complications. In a US series of 18,500 infants with pertussis, apnea was seen in 64% of infants under 1 month and in 44% between 6 and 11 months. Forty percent of the 6- to 11-month-olds had received at least 3 doses of pertussis vaccine.<sup>4</sup> A British study of 126 infants aged <5 months admitted to the pediatric intensive care unit with apnea, bradycardia, or respiratory failure found that 20% had pertussis. Apnea as a predictor of pertussis had a sensitivity of 68% and a specificity of 60%.<sup>5</sup>

Pertussis should be considered early in the evaluation of young infants with cough. In a case-control study comparing 15 fatal cases of pertussis with 32 who survived (infants aged <6 months), the mean number of days from symptom onset to hospital admission were 5.3 (fatal) and 8.6 (survivors). Rates of apnea on admission were 40% and 52%.<sup>6</sup> A case series of 9 infants aged <7 weeks requiring admission to an intensive care unit for pertussis found that 8 had been sick for less than 4 days at the time of admission. All 9 presented with poor feeding and cough, and 5 had experienced apnea.<sup>7</sup>

### ■ RECOMMENDATIONS FROM

TABLE

**Clinical features of pertussis**

History	Sensitivity	Specificity	LR+	LR-
Cough >2 weeks <sup>3,12</sup>	84%–100%	35%–36%	1.3–1.5	0–0.44
Cough >3 weeks <sup>3,12</sup>	75%–97%	51%–59%	1.8–2.0	0.06–0.42
Whoop <sup>3,10–12</sup>	37%–90%	49%–96%	1.6–9.2	0.18–0.66
Posttussive vomiting <sup>3,10,11,13</sup>	28%–84%	45%–84%	0.9–2.2	0.36–1.0
Paroxysms <sup>3,12,13</sup>	68%–94%	15%–45%	1.1–1.4	0.29–0.71
Household exposure <sup>11,13</sup>	20%–50%	73%–91%	1.9–2.2	0.68–0.88
Afebrile (temp <38°C) <sup>11–13</sup>	62%–96%	12%–54%	0.8–1.1	0–1.7
Lymphocytosis <sup>3</sup>	88%	57%	2.0	0.21

LR+ = positive likelihood ratio: sensitivity/(1–specificity); † LR– = negative likelihood ratio: (1–sensitivity)/specificity.

**OTHERS**

The Centers for Disease Control and Prevention and the World Health Organization describe the clinical case definition for pertussis as a cough illness lasting at least 2 weeks with at least 1 of the following: paroxysms of coughing, inspiratory whoop, or posttussive vomiting, without other apparent cause. Laboratory criteria for diagnosis include a positive *Bordetella pertussis* culture or a positive polymerase chain reaction (PCR) for *B pertussis*.<sup>8,9</sup>

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#### ■ CLINICAL COMMENTARY

##### **Infants may have complications; evaluate if there is apnea or significant cough**

Immunity to pertussis wanes following vaccination, leaving many adolescents and adults susceptible to infection. In older children and adults, there is often little in the clinical presentation that distinguishes chronic cough due to pertussis from that associated with other causes. Clinicians should consider evaluating for pertussis in older children and adults with chronic cough (>2 weeks) if there is reason to suspect they have been exposed, if the cough is associated with inspiratory whoop, or if the individual has household or frequent contact with infants.

Infants may suffer severe complications from pertussis, and should receive evaluation when presenting with apnea or significant cough of any duration. In current practice, evaluation usually includes obtaining a nasopharyngeal swab for culture and PCR, though these tests may be insensitive, especially in later phases of illness. The usefulness of single, quantitative immunoglobulin G titers with comparison to pop-

impact the epidemiology of pertussis in the US.

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## **Does quinine reduce leg cramps for young athletes?**

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#### ■ EVIDENCE-BASED ANSWER

Very little evidence exists regarding the use of quinine for cramps in young adult athletes. Quinine may be an effective treatment for heat cramps in athletes (strength of recommendation [SOR]: **C**, 1 case series involving 2 patients). Quinine is better established as an effective treatment for nocturnal leg cramps in the general adult population (SOR: **A**, 1 meta-analysis and 2 randomized controlled trials).

#### ■ EVIDENCE SUMMARY

Leg cramps (heat cramps) in athletes are defined as painful involuntary muscle contractions, usually in the large muscle groups of the legs, which occur during or in the hours following exercise. Oral quinine is sometimes used to treat nocturnal leg cramps in the general adult and elderly populations. However, its use is controversial secondary to concerns regarding efficacy and safety.

Efficacy of quinine in young athletes has not been well studied. A case series reported on 2 athletes: 1 college basketball player and 1 professional football player.<sup>1</sup> The basketball player experienced heat cramps during games that were resistant to hydration and dietary treatment. A regimen of 60 mg oral quinine sulfate taken 1 hour before game time and again at half-time eliminated cramps during the first game and the subsequent 15 games. The football player's heat cramps were only partially improved with oral electrolyte repletion and oral hydration. However, he suffered no further cramps after initiating a regimen of 120 mg oral quinine sulfate