CHEST

Clinically Diagnosing Pertussis-associated Cough in Adults and Children

CHEST Guideline and Expert Panel Report

*Abigail Moore, BM, BCh; Anthony Harnden, MD; Cameron C. Grant, MD; Sheena Patel, MPH; Richard S. Irwin, MD, Master FCCP; on behalf of the CHEST Expert Cough Panel**

BACKGROUND: The decision to treat a suspected case of pertussis with antibiotics is usually based on a clinical diagnosis rather than waiting for laboratory confirmation. The current guideline focuses on making the clinical diagnosis of pertussis-associated cough in adults and children.

METHODS: The American College of Chest Physicians (CHEST) methodologic guidelines and the Grading of Recommendations, Assessment, Development, and Evaluation framework were used. The Expert Cough Panel based their recommendations on findings from a systematic review that was recently published on the topic; final grading was reached by consensus according to Delphi methodology. The systematic review was carried out to answer the Key Clinical Question: *In patients presenting with cough, how can we most accurately diagnose from clinical features alone those who have pertussis-associated cough as opposed to other causes of cough?*

RESULTS: In adults, after pre-specified meta-analysis exclusions, pooled estimates of sensitivity and specificity were generated for only 4 clinical features: paroxysmal cough, posttussive vomiting, inspiratory whooping, and absence of fever. Both paroxysmal cough and absence of fever had high sensitivity (93.2% [95% CI, 83.2-97.4] and 81.8% [95% CI, 72.2-88.7], respectively) and low specificity (20.6% [95% CI, 14.7-28.1] and 18.8% [95% CI, 8.1-37.9]). Inspiratory whooping and posttussive vomiting had a low sensitivity (32.5% [95% CI, 24.5-41.6] and 29.8% [95% CI, 18.0-45.2]) but high specificity (77.7% [95% CI, 73.1-81.7] and 79.5% [95% CI, 69.4-86.9]). In children, after pre-specified meta-analysis exclusions, pooled estimates of sensitivity and specificity were generated for only 1 clinical feature in children (0-18 years): posttussive vomiting. Posttussive vomiting in children was only moderately sensitive (60.0% [95% CI, 40.3-77.0]) and specific (66.0% [95% CI, 52.5-77.3]).

CONCLUSIONS: In adults with acute (< 3 weeks) or subacute (3-8 weeks) cough, the presence of whooping or posttussive vomiting should rule in a possible diagnosis of pertussis, whereas the lack of a paroxysmal cough or the presence of fever should rule it out. In children with acute (< 4 weeks) cough, posttussive vomiting is suggestive of pertussis but is much less helpful as a clinical diagnostic test. Guideline suggestions are made based upon these findings and conclusions.

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KEY WORDS: cough; evidence-based medicine; guidelines; infectious disease

ABBREVIATIONS: CDC = Centers for Disease Control and Prevention

AFFILIATIONS: From the Department of Primary Heath Care Sciences (Drs Moore and Harnden), University of Oxford, Oxford, England; Department of Paediatrics, Child and Youth Health (Prof Grant), University of Auckland, Auckland, New Zealand; CHEST Organization (Ms Patel); and the Division of Pulmonary, Allergy, and Critical Care Medicine (Dr Irwin), Department of Medicine, UMass Memorial Medical Center, Worcester, MA.

*Collaborators from the CHEST Expert Cough Panel are listed in the Acknowledgments.

DISCLAIMER: American College of Chest Physician guidelines are intended for general information only, are not medical advice, and

Summary of Recommendations:

1. For adult patients complaining of acute cough (< 3 weeks in duration) or subacute cough (3-8 weeks), we suggest that clinicians should specifically assess for the 4 key characteristics of paroxysmal cough, post-tussive vomiting, inspiratory whooping, and absence of fever in ruling in or out a clinical diagnosis of pertussis. (Grade 2C)

Remark: Paroxysmal cough is defined as recurrent prolonged coughing episodes (ie, an expiratory phase with multiple burst of outflow) with an inability to breathe during spells. Posttussive vomiting is defined as vomiting induced by coughing. Inspiratory whooping is defined as a continuous inspiratory airway sound with a whooping quality to it. Fever is defined as any body temperature above the normal of 98.6°F (37°C).

2. For adult patients complaining of acute or subacute cough, we suggest that clinicians consider that the cough is unlikely to be due to pertussis if the patient has a fever or the cough is not paroxysmal in nature. (Grade 2C)

3. For adult patients complaining of acute or subacute cough, we suggest that clinicians consider that the cough is likely to be caused by pertussis if there is posttussive vomiting or is associated with an inspiratory whooping sound. (Grade 2C)

4. For children complaining of acute cough (< 4 weeks in duration), we suggest that clinicians should specifically assess for the 3 classical characteristics of paroxysmal cough, posttussive vomiting, and inspiratory whooping. (Ungraded consensus-based statement)

5. For children complaining of acute cough, we suggest that clinicians consider that the cough could be caused by pertussis if there is posttussive vomiting. (Grade 2C)

6. For children complaining of acute cough, we suggest that clinicians consider that the cough could be caused by pertussis if there is paroxysmal cough or inspiratory whooping. (Ungraded consensus-based statement)

Introduction

Pertussis (whooping cough), caused by *Bordetella pertussis,* is a highly contagious respiratory tract infection that can be associated with significant morbidity and mortality, particularly in young infants.

Pertussis causes an acute cough that can often become persistent and is classically associated with paroxysms of coughing, inspiratory whooping, and posttussive vomiting. However, clinical judgment also plays an important role in diagnosis. This is reflected in the clinical definitions used by the World Health Organization,[1] Centers for Disease Control and Prevention (CDC),[2] and Public Health England[3] (Table 1).

There are several recognized laboratory methods to confirm a diagnosis of pertussis; culture (100% specific), polymerase chain reaction (88%-100% specific), serology (72%-100% specific),[4,5] and oral fluid testing (91%-99% specific).[6] These are used variously by the different health organizations (Table 2).[1-3]

The treatment of pertussis has been the subject of a Cochrane systematic review.[7] There are several effective antibiotics; these eliminate *B pertussis* but do not alter the clinical course of the illness. However, treatment should be initiated as soon as possible after onset of illness to prevent spread of the disease.[3] The decision to treat with antibiotics is therefore frequently based on a clinical diagnosis rather than waiting for laboratory confirmation.

Because reviews of laboratory diagnosis and treatment have recently been published[7] and diagnosis is usually made clinically, the current guideline focuses on making the clinical diagnosis of pertussis-associated cough in adults and children.

Materials and Methods

The methodology of the CHEST Guideline Oversight Committee[8,9] was used to select the Expert Cough Panel Chair and the international panel of experts to synthesize the evidence and to develop the recommendations and suggestions that are contained within this article. In addition to the quality of the evidence, the recommendation/suggestion grading also includes a strength of recommendation dimension, used for all CHEST Guidelines.[8,9] In

CORRESPONDENCE TO: Abigail Moore, BM, BCh, Radcliffe Primary Care Building, Radcliffe Observatory Quarter, Woodstock Rd, Oxford, OX2 6GG, England; e-mail: abigail.moore@phc.ox.ac.uk

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TABLE 1] Clinical Case Criteria

Health Organization	Clinical Judgment	Cough > 2 Wk	Inspiratory Whooping	Posttussive Vomiting	Paroxysms of Coughing	Apnea	Epidemiological Contact
WHO[1]	A case diagnosed as pertussis by a physician OR	A person with a cough lasting at least 2 wk with at least one of the following symptoms:	Inspiratory whooping OR	Posttussive vomiting (ie, vomiting immediately after coughing) without other apparent cause	Paroxysms (ie, fits) of coughing	…	…
CDC[2]	In the absence of a more likely diagnosis	A cough illness lasting ≥ 2 wk with one of the following symptoms:	Inspiratory whooping OR	Posttussive vomiting OR	Paroxysms of coughing	Apnea (with or without cyanosis) for infants < 1 y only	…
PHE[3]	Without an apparent cause	Acute cough lasting for ≥ 14 d plus one or more of the following:	Inspiratory whooping OR	Posttussive vomiting OR	Paroxysms of coughing	Undiagnosed apneic attacks in young infants OR	Someone with signs and symptoms consistent with pertussis who has been in contact with a confirmed case in the previous 21 d OR someone who is known to be part of any ongoing outbreak investigation in a specific group of people

CDC = Centers for Disease Control and Prevention; PHE = Public Health England; WHO = World Health Organization.

the context of practice recommendations, a grade 1 recommendation is a strong recommendation and applies to almost all patients, whereas a grade 2 recommendation is weak and conditional and only applies to some patients. The strength of recommendation here is based on consideration of three factors: balance of benefits to harms, patient values and preferences, and resource considerations. Harms incorporate risks and burdens to the patients that can include convenience or lack of convenience, difficulty of administration, and invasiveness. These, in turn, impact patient preferences. The resource considerations go beyond economics and should also factor in time and other indirect costs. The authors of these recommendations or suggestions have considered these parameters in determining the strength of the recommendations or suggestions and associated grades.

The findings of a systematic review and meta-analysis that was carried out to be the basis of this guideline and has recently been published[10] were used to support the evidence graded recommendations or suggestions. The first, second, and third authors of this current guideline article were among the authors of the systematic review and meta-analysis. The process of review of previous studies identified in the systematic review included assessment using the QUADAS-2 (a quality assessment tool for diagnostic accuracy studies) in the domains of patient selection, index tests, reference standard, and flow and timing.[11] When the quality of studies included in the systematic review[10] were checked using DART (Documentation and Appraisal Review Tool),[12] similar quality results were found. A highly structured consensus-based Delphi approach was employed to provide expert advice on all guidance statements. The total number of eligible voters for each guidance statement did not vary because none was recused from voting on any particular statements because of any potential conflicts of interest. A lay person representing the interests of patients participated in the process and voting. Transparency of process was documented. Further details of the methods related to conflicts of interests and transparency for all CHEST guidelines have been published in e-Table 1 and elsewhere.[8,9]

Based on the systematic review and meta-analysis[10] and the Delphi methodology described, the writing group developed guideline recommendations or suggestions. These then underwent review and consensus agreement through an online anonymous voting survey by the full cough panel. For a recommendation or suggestion to be accepted, it had to be voted upon by 75% of the eligible Cough Panelists and achieve ratings of strongly agree or agree by 80% of the voting panelists. Agreement was achieved by 87.24% to 95.75% of those voting on the current recommendations or suggestions. No panelist was excluded from voting.

Because a paroxysmal cough figures heavily in making a clinical diagnosis of a pertussis-associated cough, we have defined it as recurrent prolonged coughing episodes (ie, an expiratory phase with multiple burst of outflow) with an inability to breathe during spells.

Results

The recommendations that follow are based upon the recently published high-quality systematic review[10] that included a comprehensive search of multiple databases restricted to the English language. The systematic review followed all the standards of the National Academy of Medicine (previously referred to as the Institute of Medicine).[13] After generating the key clinical question for the systematic review, population, index test, reference test, and target

TABLE 2] Recognized Laboratory Methods to Confirm a Case

Health Organization	Culture	Polymerase Chain Reaction	Serology	Oral Fluid Testing for Anti-pertussis Toxin IgG
WHO[1]	X	X	X	…
CDC[2]	X	X	…	…
PHE[3]	X	X	X	X

See Table 1 legend for expansion of abbreviations.

condition elements were derived to inform the literature review (Table 3).[10] The authors of the review systematically searched the following databases: CINAHL (EBSCHost from 1982 to 2016), Embase (OvidSP from 1974 to 2016), Medline & Medline In-Process (OvidSP from 1946 to 2016), and SCI-EXPANDED/CPCI-S (Web of Science Core Collection from 1945 to 2016). The search strategy combined MeSH headings with free text search terms for whooping cough and clinical symptoms. The search was supplemented by review of reference lists of included articles and relevant review articles as well as by contacting authors of studies to request additional relevant data where it was apparent that it was likely to have been collected but not published. The full search strategy can be found in e-Appendix 1 of the systematic review.[10]

After the initial screening of articles, full text review, data extraction, and quality assessment, 53 articles were identified for descriptive analysis and meta-analysis.[10] These articles included 23,796 subjects, of whom 4,149 (17.4%) had a laboratory diagnosis of pertussis. Thirty-six of the 53 articles had a prospective design, 12 were retrospective, and 5 were case-control. From these 53 studies, 41 clinical characteristics (ie, index tests) were assessed for diagnostic accuracy, including 9 cough characteristics as well as other clinical and demographic features (Table 4).[10] After excluding from the meta-analysis studies at high risk of bias (28 studies), pooled estimates of sensitivity and specificity were generated by meta-analysis (Table 5).[10,14-29]

Evidence and Recommendations

Key Clinical Question: In patients presenting with cough, how can we most accurately diagnose from clinical features alone those who have pertussis-associated cough as opposed to other causes of cough?

Summary of the Evidence in Adults and Interpretation: After pre-specified meta-analysis exclusions, pooled estimates of sensitivity and specificity were generated for only 4 clinical features in adult patients: paroxysmal cough, posttussive vomiting, inspiratory whooping, and absence of fever. Both paroxysmal cough and absence of fever had high sensitivity and low specificity (Table 5, e-Table 2).[10] This means that a patient without these features is unlikely to have a diagnosis of pertussis (few false-negatives). Inspiratory whoop and posttussive vomiting had a low sensitivity but high specificity. This means that a diagnosis of pertussis should be considered in a patient with these features (few false-positives).

1. For adult patients complaining of acute cough (< 3 weeks in duration) or subacute cough (3-8 weeks), we suggest that clinicians should specifically assess for the 4 key characteristics of paroxysmal cough, posttussive vomiting, inspiratory whooping, and absence of fever in ruling in or out a clinical diagnosis of pertussis. (Grade 2C)

Remark: Paroxysmal cough is defined as recurrent prolonged coughing episodes (ie, an expiratory phase with multiple burst of outflow) with an inability to breathe during spells. Posttussive vomiting is defined as vomiting induced by coughing. Inspiratory whooping is defined as a continuous inspiratory airway sound with a whooping quality to it. Fever is defined as any body temperature above the normal of 98.6°F (37°C).

2. For adult patients complaining of acute or subacute cough, we suggest that clinicians consider that the cough is unlikely to be due to pertussis if the patient has a fever or the cough is not paroxysmal in nature. (Grade 2C)

TABLE 3] Population, Index Test, Reference Test, and Target Condition Elements Derived to Inform the Literature Review[10]

Population	Index Test	Reference Test	Target Condition
People of any age, sex, ethnicity, and nationality attending either primary or secondary care settings with cough	Any presenting clinical characteristic of pertussis-associated cough	Laboratory diagnostic tests for pertussis, including culture, PCR, and serology	*Bordetella pertussis*

PCR = polymerase chain reaction.

TABLE 4] Index Tests

Index Test	No. of Studies
Cough characteristic	
Paroxysmal cough	36
Posttussive vomiting	36
Whooping cough	28
Worse at night	16
Productive cough	12
Wheeze	12
Any cough	7
Cough duration	6
Stridor	3
Other respiratory symptoms/findings	
Apnea	21
Cyanosis	16
Rhinorrhea	10
Shortness of breath	9
URTI symptoms	6
Respiratory distress/hypoxia	5
Chest crackles	5
Sore throat	5
Sneezing	4
Sinus pain	3
Hoarseness	2
Posttussive gagging	2
Other clinical features	
Fever	28
Headache	5
Chest pain	5
Feeding difficulties	4
Lymphocytosis	4
Facial discoloration	3
Myalgia	3
Conjunctival changes	3
WBC count	3
Fatigue	2
Sweating	2
Seizure	2
Posttussive syncope	2
Clinical judgment	
Meets CDC/WHO clinical definition	8
Clinical suspicion	2
Patient demographics	
Vaccinated	19
Exposure to contact	16
Comorbidity	6
Smoking	5
Previous whooping cough	4

(Continued)

TABLE 4] *(Continued)*

This table includes clinical characteristics, examination findings and patient demographic characteristics, and number of studies in which these were recorded. Reprinted from Moore et al.[10] URTI = upper respiratory tract infection. See Table 1 legend for expansion of other abbreviations.

3. For adult patients complaining of acute or subacute cough, we suggest that clinicians consider that the cough is likely to be caused by pertussis if there is posttussive vomiting or is associated with an inspiratory whooping sound. (Grade 2C)

Summary of the Evidence in Children and Interpretation: After pre-specified meta-analysis exclusions, pooled estimates of sensitivity and specificity were generated for only one clinical feature in children: posttussive vomiting. Posttussive vomiting in children (ages 0-18) was only moderately sensitive and specific (Table 5, e-Table 2).[10]

4. For children complaining of acute cough (< 4 weeks in duration), we suggest that clinicians should specifically assess for the 3 classical characteristics of paroxysmal cough, posttussive vomiting, and inspiratory whooping. (Ungraded consensus-based statement)

5. For children complaining of acute cough, we suggest that clinicians consider that the cough could be caused by pertussis if there is posttussive vomiting. (Grade 2C)

6. For children complaining of acute cough, we suggest that clinicians consider that the cough could be caused by pertussis if there is paroxysmal cough or inspiratory whooping. (Ungraded consensus-based statement)

Discussion

The systematic review used to form the basis of this guideline is the largest on this topic to date.[10] The broad inclusion criteria were designed to capture the full spectrum of pertussis presentation but meant that there was significant variation in included study characteristics—including different study designs (case-control and retrospective/prospective cohort), those in

TABLE 5] Meta-analysis: Pooled Estimates of Sensitivity and Specificity

Clinical Feature on Which Meta-analysis Performed	Age Category	No. of Studies	Sensitivity % (95% CI)	Specificity % (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)
Paroxysmal cough[14-20]	Adults	7	93.2 (83.2-97.4)	20.6 (14.7-28.1)	1.17 (1.10-1.25)	0.33 (0.15-0.71)
Posttussive vomiting[14-21]	Adults	8	32.5 (24.5-41.6)	77.7 (73.1-81.7)	1.45 (1.19-1.79)	0.87 (0.79-0.96)
Inspiratory whooping[14-19,22]	Adults	7	29.8 (18.0-45.2)	79.5 (69.4-86.9)	1.46 (1.07-1.97)	0.88 (0.77-1.00)
Absence of fever[14-16,20,23]	Adults	5	81.8 (72.2-88.7)	18.8 (8.1-37.9)	1.01 (0.86-1.18)	0.97 (0.49-1.90)
Posttussive vomiting[24-29]	Children	6	60.0 (40.3-77.0)	66.0 (52.5-77.3)	1.76 (1.26-2.48)	0.61 (0.40-0.91)

Reprinted from Moore et al.[10]

specialist populations (eg, outbreaks), and used different reference standards. While the systematic review was done according to rigorous methods, it did have limitations. For example, while assessment of quality meant that those at resultant high risk of bias were excluded from meta-analysis, heterogeneity in the remaining studies meant that only 4 characteristics could be analyzed in this way. Because the review excluded non-English studies, potentially relevant studies may have been missed. In addition, the systematic review was published in 2017, and it was based upon a literature search that was last updated in June of 2016, and studies published since this time have not been taken into account. Although data were analyzed separately for adults and children, it is important to note that the "children" category includes studies with both older children (up to 18) and young infants who may also have very different presentations of pertussis.

A second systematic review has been written on this topic within the last year. Compared with the systematic review used to compile this guideline, Ebell et al[30] used a more restrictive search strategy in Medline only and included only prospective cohort studies. Eight unique references were included compared with the systematic review used for this guideline. However, these references were excluded from our systematic review for the following reasons: 4 had no comparison group, 2 compared pertussis with parapertussis, 1 had no clinical information, and 1 was not in English. In Ebell et al,[30] meta-analysis was done for all index tests with no comment on heterogeneity, and index tests were only analyzed separately in adults and children for paroxysmal cough, whooping cough, and posttussive vomiting. For these reasons, it was felt that the findings of Ebell et al should not be taken into account in compiling this guideline.

The existing clinical criteria in use by multiple health agencies (Table 1)[1-3] contain the index tests shown in the meta-analysis to be useful in the diagnosis of pertussis and recommended/suggested by this guideline. The presence of whooping or posttussive vomiting is common to the CDC, Public Health England, and World Health Organization clinical criteria, whereas paroxysms of coughing is included by just the CDC and World Health Organization. Apnea and cyanosis are mentioned in relation to infants aged < 1 year in the CDC criteria and were shown in forest plots in the systematic review (e-Appendix 2)[10] to be moderately sensitive and specific in children.

Areas for Future Research

To advance the field, a number of research endeavors to address the gaps in knowledge should be undertaken. These include conducting further large prospective studies in primary care of patients presenting with acute or subacute cough, particularly in infants and children. To improve on the problems in study design identified by the systematic review, the following would be needed: detailed epidemiological/baseline characteristics of included patients, time since symptom onset recorded rather than acting as inclusion criteria, clear definitions of clinical characteristics recorded, characteristics recorded at presentation and ideally subsequently in a symptom diary. It would also be helpful to assess clinical judgment as part of this. Individual patient analysis would help assess the diagnostic utility of different symptoms in combination.

Conclusions

Cough due to pertussis in adults and children has been the sole focus in this update, compared with one of many causes of postinfectious cough in the 2006 CHEST Cough Guidelines.[31] This guideline focuses on how to make the clinical diagnosis of pertussis because this is how the decision to treat with antibiotics is usually made. This guideline is based upon a high-quality systematic review, and it identifies gaps in our knowledge and areas for future research; we therefore believe it advances the field.

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***CHEST Expert Cough Panel Collaborators:** Kenneth W. Altman, MD, PhD (Baylor College of Medicine, Houston, TX), Elie Azoulay, MD, PhD (University of Paris, Paris, France), Alan F. Barker, MD (Oregon Health & Science University, Portland, OR), Donald C. Bolser, PhD (College of Veterinary Medicine, University of Florida, Gainesville, FL), Surinder S. Birring, MBChB, MD (Division of Asthma, Allergy and Lung Biology, King's College London, Denmark Hill, London, United Kingdom), Fiona Blackwell, MD, PhD (Department of Medical Oncology, Manchester, England), Louis-Philippe Boulet, MD, FCCP (Universitaire de cardiologie et de pneumonlogue de Quebec [IUCPQ], QC, Canada), Sidney S. Braman, MD, FCCP (Mount Sinai Hospital, New York, NY), Christopher Brightling, PhD, FCCP (University of Leicester, Glenfield Hospital, Leicester, United Kingdom), Priscilla Callahan-Lyon, MD (Adamstown, MD), Anne B. Chang, PhD, MPH (Royal Children's Hospital, Queensland, Australia), Terrie Cowley (The TMJ Association, Milwaukee, WI), Paul Davenport, PhD (Department of Physiological Sciences, University of Florida, Gainesville, FL), Ali A. El Solh, MD, MPH (University at Buffalo, State University of New York, Buffalo, NY), Patricio Escalante, MD, FCCP (Mayo Clinic, Rochester, MN), Stephen K. Field, MD (University of Calgary, Calgary, AB, Canada), Dina Fisher, MD (University of Calgary, Respiratory Medicine, Calgary, AB, Canada), Cynthia T. French, PhD, FCCP (UMass Memorial Medical Center, Worcester, MA), Cameron Grant, MB ChB, PhD (University of Auckland, Auckland, New Zealand), Peter Gibson, MBBS (Hunter Medical Research Institute, New South Wales, Australia), Philip Gold, MD, MACP, FCCP (Loma Linda University, Loma Linda, CA), Susan M. Harding, MD, FCCP (Division of Pulmonary, Allergy and Critical Care Medicine, University of Alabama at Birmingham, Birmingham, AL), Anthony Harnden, MB ChB, MSc (University of Oxford, Oxford, England), Adam T. Hill, MB ChB, MD (Royal Infirmary and University of Edinburgh, Edinburgh, Scotland), Richard S. Irwin, MD, Master FCCP (UMass Memorial Medical Center, Worcester, MA), Peter J. Kahrilas, MD (Feinberg School of Medicine, Northwestern University, Chicago, IL), Joanne Kavanagh, MBChB (Division of Asthma, Allergy and Lung Biology, King's College London, Denmark Hill, London, England), Karina A. Keogh, MD (Mayo Clinic, Rochester, MN), Kefang Lai, MD, PhD (First Affiliated Hospital of Guangzhou Medical College, Guangzhou, China), Andrew P. Lane, MD (Johns Hopkins University School of Medicine, Baltimore, MD), Kaiser Lim, MD (Mayo Clinic, Rochester, MN), Mark Lown, PhD, MRCGP (University of Southampton, Southampton, England), J. Mark Madison, MD, FCCP (UMass Memorial Medical Center, Worcester, MA), Mark A. Malesker, PharmD, FCCP (Creighton University School of Pharmacy and Health Professions, Omaha, NE), Stuart Mazzone, PhD, FCCP (University of Melbourne, Victoria, Australia), Lorcan McGarvey, MD (The Queen's University Belfast, Belfast, Ireland), Alex Molasoitis, PhD, RN (Hong Kong Polytechnic University, Hong Kong, China), Abigail Moore, BM BCh (University of Oxford, Oxford, England), M. Hassan Murad, MD, MPH (Mayo Clinic, Rochester, MN), Mangala Narasimhan, DO, FCCP (Hofstra-Northwell Health, Manhasset, NY), Peter Newcombe, PhD (School of Psychology University of Queensland, Queensland, Australia), Huong Q. Nguyen, PhD, RN (Kaiser Permanente, Pasadena, CA), John Oppenheimer, MD (UMDNJ-Rutgers University, Morristown, NJ), Mark Rosen, MD, Master FCCP (Icahn School of Medicine at Mount Sinai, New York, NY), Bruce Rubin, MEngr, MD (Virginia Commonwealth University, Richmond, VA), Richard J. Russell, MBBS (University of Leicester, Glenfield Hospital, Leicester, England), Jay H. Ryu, MD, FCCP (Mayo Clinic, Rochester, MN), Sonal Singh, MD, MPH (UMass Memorial Medical Center, Worcester, MA), Jaclyn Smith, MB ChB, PhD (University of Manchester, Manchester, England), Maeve P. Smith, MB ChB, MD (University of Alberta, Edmonton, AB, Canada), Susan M. Tarlo, MBBS, FCCP (Toronto Western Hospital, Toronto, ON, Canada), Anne E. Vertigan, PhD, BAppSc (SpPath) (John Hunter Hospital, New South Wales, Australia), and Miles Weinberger, MD, FCCP (University of Iowa Hospitals and Clinics, Iowa City, IA).

Endorsements: This guideline has been endorsed by the American Association for Respiratory Care (AARC), the American College of Allergy, Asthma, and Immunology (ACAAI), and the American Thoracic Society (ATS).

Additional information: The e-Tables can be found in the Supplemental Materials section of the online article.

References

1. World Health Organization. WHO-recommended surveillance standard of pertussis. http://www.who.int/immunization/monitoring_surveillance/burden/vpd/surveillance_type/passive/pertussis_standards/en/. Accessed January 15, 2017.
2. Centers for Disease Control and Prevention. Pertussis/whooping cough (Bordetella pertussis) 2014 case definition. https://wwwn.cdc.gov/nndss/conditions/pertussis/case-definition/2014/. Accessed February 9, 2018.
3. England PH. Pertussis factsheet for healthcare professionals. 2016; https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/562472/HHC_Factsheet_Pertussis.pdf. Accessed February 21, 2018.
4. Wendelboe AM, Van Rie A. Diagnosis of pertussis: a historical review and recent developments. *Expert Review of Molecular Diagnostics*. 2006;6(6):857-864.
5. Prevention CfDCa. Diagnosis Confirmation. 2017; https://www.cdc.gov/pertussis/clinical/diagnostic-testing/diagnosis-confirmation.html. Accessed January 22, 2018.
6. Litt DJ, Samuel D, Duncan J, Harnden A, George RC, Harrison TG. Detection of anti-pertussis toxin IgG in oral fluids for use in diagnosis and surveillance of Bordetella pertussis infection in children and young adults. *Journal of Medical Microbiology*. 2006;55(pt 9):1223-1228.
7. Altunaiji S, Kukuruzovic R, Curtis N, Massie J. Antibiotics for whooping cough (pertussis). *Cochrane Database of Systematic Reviews*. 2007;3:CD004404.
8. Lewis SZ, Diekemper R, Ornelas J, Casey KR. Methodologies for the development of CHEST guidelines and expert panel reports. *Chest*. 2014;146(1):182-192.
9. Lewis SZ, Diekemper RL, French CT, Gold PM, Irwin RS; CHEST Expert Cough Panel. Methodologies for the development of the management of cough: CHEST guideline and expert panel report. *Chest*. 2014;146(5):1395-1402.

10. Moore A, Ashdown HF, Shinkins B, et al. Clinical characteristics of pertussis-associated cough in adults and children: a diagnostic systematic review and meta-analysis. *Chest*. 2017;152(2):353-367.

11. Whiting PF, Rutjes AW, Westwood ME, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Annals of Internal Medicine*. 2011;155(8):529-536.

12. Diekemper RL, Ireland BK, Merz LR. Development of the documentation and Appraisal Review Tool for systematic reviews. *World J Meta-Anal*. 2015;3(3):142-150.

13. Eden J, Levit L, Berg A, et al, eds; Institute of Medicine (US) Committee on Standards for Systematic Reviews of Comparative Effectiveness Research. 5, Standards for reporting systematic reviews. In: *Finding What Works in Health Care: Standards for Systematic Reviews*. Washington, DC: National Academies Press (US); 2011. https://www.ncbi.nlm.nih.gov/books/NBK209507/. Accessed November 12, 2018.

14. Craig AS, Wright SW, Edwards KM, et al. Outbreak of pertussis on a college campus. *The American Journal of Medicine*. 2007;120(4):364-368.

15. Miyashita N, Akaike H, Teranishi H, et al. Diagnostic value of symptoms and laboratory data for pertussis in adolescent and adult patients. *BMC Infectious Diseases Dis*. 2013;13:129.

16. Park S, Lee SH, Seo KH, et al. Epidemiological aspects of pertussis among adults and adolescents in a Korean outpatient setting: a multicenter, PCR-based study. *Journal of Korean Medical Science*. 2014;29(9):1232-1239.

17. Park WB, Park SW, Kim HB, Kim EC, Oh M, Choe KW. Pertussis in adults with persistent cough in South Korea. *European Journal Of Clinical Microbiology & Infectious Diseases: official publication of the European Society of Clinical Microbiology*. 2005;24(2):156-158.

18. Rosenthal S, Strebel P, Cassiday P, Sanden G, Brusuelas K, Wharton M. Pertussis infection among adults during the 1993 outbreak in Chicago. *The Journal Of Infectious Diseases*. 1995;171(6):1650-1652.

19. Strebel P, Nordin J, Edwards K, et al. Population-based incidence of pertussis among adolescents and adults, Minnesota, 1995-1996. *The Journal Of Infectious Diseases*. 2001;183(9):1353-1359.

20. Wright SW, Edwards KM, Decker MD, Zeldin MH. Pertussis infection in adults with persistent cough. *JAMA*. 1995;273(13):1044-1046.

21. Bock JM, Burtis CC, Poetker DM, Blumin JH, Frank MO. Serum immunoglobulin G analysis to establish a delayed diagnosis of chronic cough due to Bordetella pertussis. *Otolaryngology—Head And Neck Surgery: official journal of American Academy of Otolaryngology-Head and Neck Surgery*. 2012;146(1):63-67.

22. Siriyakorn N, Leethong P, Tantawichien T, et al. Adult pertussis is unrecognized public health problem in Thailand. *BMC Infectious Diseases*. 2016;16:25.

23. Teepe J, Broekhuizen BD, Ieven M, et al. Prevalence, diagnosis, and disease course of pertussis in adults with acute cough: a prospective, observational study in primary care. *The British Journal Of General Practice: The Journal of the Royal College of General Practitioners*. 2015;65(639):e662-e667.

24. Cengiz AB, Yildirim I, Ceyhan M, Secmeer G, Gur D, Kara A. Comparison of nasopharyngeal culture, polymerase chain reaction (PCR) and serological test for diagnosis of pertussis. *The Turkish Journal Of Pediatrics*. 2009;51(4):309-316.

25. Ghanaie RM, Karimi A, Sadeghi H, et al. Sensitivity and specificity of the World Health Organization pertussis clinical case definition. *International Journal Of Infectious Diseases: IJID: Official Publication Of The International Society for Infectious Diseases*. 2010;14(12):e1072-e1075.

26. Harnden A, Grant C, Harrison T, et al. Whooping cough in school age children with persistent cough: prospective cohort study in primary care. *BMJ (Clinical research ed.)*. 2006;333(7560):174-177.

27. Kayina V, Kyobe S, Katabazi FA, et al. Pertussis prevalence and its determinants among children with persistent cough in urban Uganda. *PloS One*. 2015;10(4):e0123240.

28. Strebel PM, Cochi SL, Farizo KM, Payne BJ, Hanauer SD, Baughman AL. Pertussis in Missouri: evaluation of nasopharyngeal culture, direct fluorescent antibody testing, and clinical case definitions in the diagnosis of pertussis. *Clinical Infectious Diseases: An Official Publication Of The Infectious Diseases Society Of America*. 1993;16(2):276-285.

29. Wymann MN, Richard JL, Vidondo B, Heininger U. Prospective pertussis surveillance in Switzerland, 1991-2006. *Vaccine*. 2011;29(11):2058-2065.

30. Ebell MH, Marchello C, Callahan M. Clinical diagnosis of Bordetella Pertussis infection: a systematic review. *J Am Board Fam Med*. 2017;30(3):308-319.

31. Braman SS. Postinfectious cough: ACCP evidence-based clinical practice guidelines. *Chest*. 2006;129(1 Suppl):138S-146S.