Work-Related Asthma

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Objective: Summarize developed evidence-based diagnostic and treatment guidelines for work-related asthma (WRA). **Methods:** Comprehensive literature reviews conducted with article critiquing and grading. Guidelines developed by a multidisciplinary expert panel and peer-reviewed. **Results:** Evidence supports spirometric testing as an essential early test. Serial peak expiratory flow rates measurement is moderately recommended for employees diagnosed with asthma to establish work-relatedness. Bronchial provocation testing is moderately recommended. IgE and skin prick testing for specific high-molecular weight (HMW) antigens are highly recommended. IgG testing for HMW antigens, IgE testing for low-molecular weight antigens, and nitric oxide testing for diagnosis are not recommended. Removal from exposure is associated with the highest probability of improvement, but may not lead to complete recovery. **Conclusion:** Quality evidence supports these clinical practice recommendations. The guidelines may be useful to providers who diagnose and/or treat WRA.

INTRODUCTION

Asthma is a common, chronic disorder of the airways that involves a complex interaction of airflow obstruction, bronchial hyperresponsiveness, and underlying inflammation with increased airway responsiveness to a variety of stimuli being typical.[1–5] Work-related asthma (WRA) includes both asthma of an occupational origin (occupational asthma [OA]) and work-exacerbated asthma (WEA). OA includes sensitizer-induced asthma, resulting from sensitization to an antigen in the workplace, and irritant-induced asthma, induced by workplace exposures to irritants (Table 1). Each condition has the potential for considerable acute morbidity, long-term disability, and adverse impact on income and quality of life.[6–12]

The most common form of occupational lung disease in many industrialized countries, with approximately 10% to 15% of all prevalent adult cases attributed to occupational factors,[6–8,10,12–14] OA is further classified into OA with latency or OA without latency. OA without latency is less common, and is believed to represent 5% to 15% of all OA cases.[1,15] The percentage of new-onset adult asthma attributable to occupational causes is considered to be much higher, up to a third of all cases.[16,17] The frequency of WEA, defined as preexisting reactive airways disease that is made temporarily or permanently worse due to occupational exposures, is substantially more common than OA.[18]

The predisposing factors for developing OA with latency are not well known. Atopy is the primary established risk factor, operating largely with respect to high molecular weight (HMW) antigens such as animal proteins. It has been proposed that human leukocyte antigen class-2 alleles may be a risk factor for the development of OA resulting from low molecular weight agents.[11,19,20] Medical management and compensation decisions require a thorough assessment of suspected OA, which may be mistaken for non-OA unless a detailed history, including occupational history, and appropriate medical tests are performed to support an association with work.[21]

GUIDELINE FOCUS/TARGET POPULATION

The American College of Occupational and Environmental Medicine (ACOEM) created its evidence-based Work-related Asthma Guideline to primarily address diagnostic options to help determine whether an employee has asthma, and whether the asthma is related to workplace exposures (Fig. 1). It was designed to present health care providers—who are the primary target users—with evidence-based guidance on the evaluation and treatment of WRA. This report summarizes findings from that Guideline (138 pages, 497 references) and addresses the following questions developed by the Evidence-based Work-related Asthma Panel:

1. Is there evidence on how to identify workers who are at higher risk of developing occupational asthma?
2. What evidence is there for the diagnosis of occupational asthma?
3. Is there evidence that different diagnostic modalities are needed for workers with new onset of symptoms or worsening of previous asthma symptoms?
4. Are there diagnostic tests that can assist in differentiating occupationally related asthma from nonoccupational asthma?
5. Is there evidence on treatment options that differ for occupationally related asthma from nonoccupational asthma?
6. What management options are available for occupational asthma?
7. Is removal from work necessary in all cases of occupationally related asthma?

The primary target population is working-age adults, although the literature searches included articles addressing all adults. Thus, it is recognized that the principles may apply more broadly.

GUIDELINE DEVELOPMENT PROCESS

A detailed methodology document specified evidence selection, scoring, incorporation of cost considerations, and formulation of recommendations.[22,23] The aim was to identify the highest quality evidence on any given topic. Guidance was drafted using tables that abstracted the evidence and which were forwarded to the multidisciplinary Panel that reviewed the evidence and finalized the text and recommendations.

EVIDENCE REVIEW AND GRADING

All evidence related to WRA in searching four databases (*PubMed*, *EBSCO*, *Cochrane Library*, and *Scopus*) was included in this guideline. The comprehensive searches for evidence were performed through September 2012 for diagnostic studies and February 2014 for management studies to help ensure complete study capture. The search strategies retrieved a total of 10,598 articles that were screened, with all potentially appropriate study abstracts reviewed and evaluated against specified inclusion and

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TABLE 1. Types of Work-Related Asthma

Nomenclature	Term	Defining Features
Sensitizer-induced OA	OA with latency of allergic or presumed immunological mechanism: not necessarily IgE	Immunological/hypersensitivity component and diagnostic tests include measures of specific sensitization (eg, skin-prick test, serum specific IgE, circulating IgC against the antigen or skin sensitization)
Irritant-induced OA	OA without latency	No allergic component and worker is not sensitized to an agent; rather, the agent causes inflammatory responses through irritant mechanisms
WEA or aggravated asthma	WEA or aggravated asthma (no latency period)	Worker has prior or concurrent history of asthma not induced by that workplace. The worker is not sensitized to an agent at work, but is irritated by a ''non-massive'' exposure (eg, cold, exercise, non-sensitizing dust, fumes, or sprays) that provokes an asthmatic reaction

IgE, immunoglobulin E; OA, occupational asthma; WEA, work-exacerbated asthma. Adapted from the American College of Chest Physicians.

exclusion criteria. Searches were supplemented with articles from personal files and reference reviews. A total of 497 articles were retrieved of which 157 met the inclusion criteria. Of those, 114 were included as high- or moderate-quality studies in evidence-based guideline development. The remaining 43 studies were deemed low-quality and excluded.

All included studies were scored for quality. Recommendations were graded from (A) to (C) in favor and against the specific diagnostic test or treatment, with (A) level recommendations having the highest quality body of literature. Quality evidence was developed into evidence-based recommendations. Expert consensus was employed for insufficient evidence (I) to develop consensus guidance. Recommendations and evidence tables were reviewed and amended by the multidisciplinary Panel. This guideline achieved 100% Panel agreement for all developed guidance.

COMMENTS AND MODIFICATION

Guidance was developed with sufficient detail to facilitate assessment of compliance (Institute of Medicine [IOM]) and auditing/monitoring (Appraisal of Guidelines for Research and Evaluation).[24,25] Alternative options to manage conditions are provided in other ACOEM guidelines when comparative trials are available. The only Appraisal of Guidelines for Research and Evaluation[25] and IOM criterion[24] not followed was incorporation of the views of the target population. In accordance with the IOM's *Trustworthy Guidelines*, this guideline underwent external peer review by four external reviewers, and subsequent revisions to the guidance, and detailed records of the peer-review processes have been kept, including responses to external peer reviewers.[24]

This guideline is updated at least every 3 years or more frequently should evidence require it. All treatment recommendations are guidance based on synthesis of the evidence plus expert consensus. These recommendations are for practitioners, and decisions to adopt a particular course of action must be made by trained practitioners on the basis of available resources and the particular circumstances presented by the individual patient.

CLINICAL RECOMMENDATIONS

Sixteen diagnostic recommendations were formulated for diagnostic testing, of which 11 were ultimately recommended and five were not recommended (Table 2). There were nine recommendations formulated for the management of WRA, of which five were recommended and four were not (Table 3).

SPIROMETRY TESTING

Spirometry, performed alone or in conjunction with pre- and postbronchodilator testing, is an important component of the evaluation and management of persons with possible WRA.[26–32] Spirometry with bronchodilator administration has three distinct potential roles when WRA is a concern:

1. Determining whether asthma is present;
2. If asthma is present, helping inform the conclusion about whether the asthma is work related; and
3. Monitoring response to therapy and possible return to work.

Spirometry with bronchodilator is not invasive, has few adverse effects, and is low-to-moderate cost and high in yield for complications and other respiratory problems. As its value lies in correlation with clinical information and observation, spirometry with bronchodilator is a recommended integral part of the evaluation of WRA.

PEAK EXPIRATORY FLOW RATES

Serial peak expiratory flow rate monitoring is moderately recommended (evidence level B) to diagnose WRA in patients already diagnosed with asthma by other methods. Six moderate-quality studies support the use of peak expiratory flow rate for the diagnosis of OA and WRA; however, peak expiratory flow rate is heavily dependent upon the worker's efforts and assumes worker honesty in performing and recording the test results.[33–40]

NONSPECIFIC BRONCHIAL PROVOCATION TESTING

Nonspecific bronchial provocation testing has been evaluated in quality studies that utilized methacholine, histamine, and mannitol as provocative testing agents. Four high-quality and 12 moderate-quality studies were used in formulating recommendations of nonspecific bronchial provocation testing as an investigational tool for the diagnoses of OA and WRA.[41–57] Nonspecific bronchial provocation testing is strongly recommended (evidence level A) to diagnose general asthma, and moderately recommended (evidence level B) to diagnose WRA. The Panel supports the American Thoracic Society's guideline for interpreting the methacholine dose that would result in a positive test.[58]

SPECIFIC IMMUNOLOGICAL TESTING

Specific immunological testing was evaluated separately for HMW and low molecular weight antigens. There were six high- and 12 moderate-quality studies used in the formulation of recommendations for specific immunological testing.[50,51,57,59–73] The Panel evaluated the difference between immunoglobulin E (IgE) and IgG tests. IgE testing for HMW antigens is strongly recommended (evidence level A) when specific testing reagents have been validated and are commercially available. Testing of IgG for HMW antigens is not recommended (evidence level C) for use as a diagnostic tool; however, this test may be efficacious as a marker for exposure to the antigen. IgE testing to low molecular weight antigens is not recommended (evidence level I).

