REVIEW ARTICLE

How to diagnose and treat work-related asthma

Key messages for clinical practice from the American College of Chest Physicians Consensus Statement

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KEY WORDS

asthma, irritant-induced asthma, occupational asthma, work-exacerbated asthma, work-related asthma

ABSTRACT

Work-related asthma is common among adult asthmatics, either asthma initially caused by work (occupational asthma) or pre-existing asthma worsened by work factors (work-exacerbated asthma). Appropriate management depends on both correct diagnosis and on recognition of etiology. Following a systematic literature review, the American College of Chest Physicians enpaneled a group of experts that reviewed this material, extended the literature review, and developed a "Consensus Statement on the Diagnosis, and Management of Work-Related Asthma", published in 2008. This article addresses the main practical aspects of that Consensus Statement, including clinical clues to diagnosis of work-related asthma from the medical history, exposure assessment, targeted diagnostic tests, and directed patient management. The range and importance of preventive measures are also addressed.

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Introduction This review addresses the key practical aspects of the American College of Chest Physicians "Consensus Statement on the Diagnosis, and Management of Work-related Asthma", published in 2008 as a Supplement in the Chest[1], and it is freely available online at http://chestjournal.org/cgi/content/abstract/134/3_suppl/1S, where a full membership of the Expert Panel is listed. This review also summarizes key differences between this statement and the British document, "Standards of Care for Occupational Asthma", published in the same year.[2]

An initial systematic literature review commissioned for this project[3,4] led to a consensus of the panel members that work-related asthma is unlikely to be investigated through randomized controlled clinical studies and related methodologies. Thus, this topic does not lend itself to a systematic assessment of evidence using the GRADE system[5] or similar approaches. In response to this limitation, the Statement took an approach in which the strength of "the best available evidence" was assessed by the Panel members. For this reason, the resulting review took the form of a Consensus document comprised of statements of suggested practice rather than the graded recommendations more typical of a practice guideline.

The first key message for clinicians from the Statement is that the occupational contribution to the prevalence of this disease is substantial, accounting for up to 15% of all adult asthma. Work-related factors, therefore, should be considered in the assessment of all persons whose asthma started while working or who are currently working with this disease. A second key message, directly related to the first, is the recognition that not all work-related asthma is occupational asthma. Occupational asthma is defined as the new onset of asthma due to exposure(s) at work. In contrast, and much more common (in some studies affecting up to 25% of working asthmatics)[6], is the occurrence of work-exacerbated asthma, i.e., asthma that was present before the work exposure, but then is aggravated or exacerbated by conditions on the job (this can be chemical exposures, but could also include physical conditions such as changes in temperature or exertional demands). Together, occupational asthma and work-exacerbated asthma

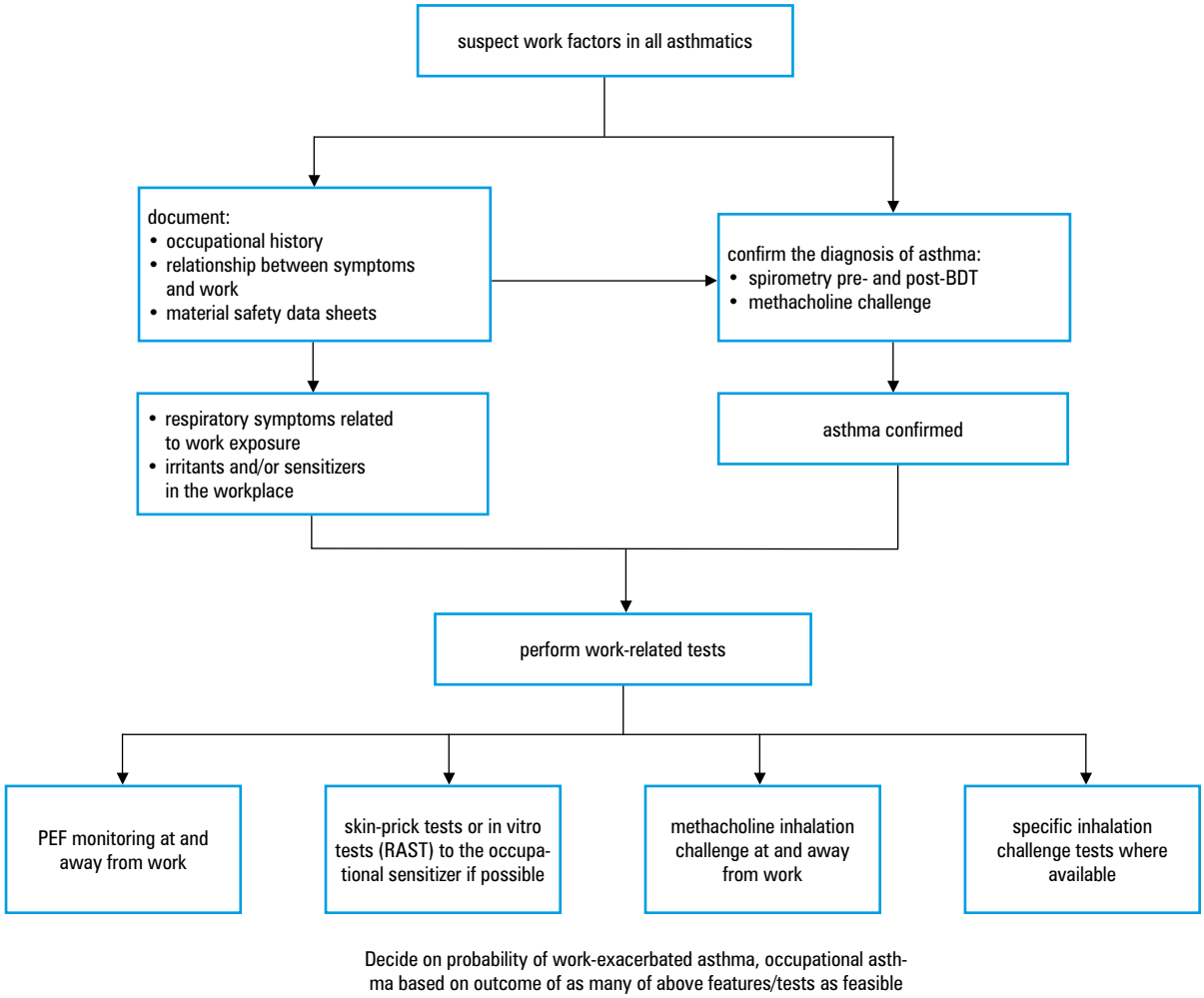

FIGURE This flowsheet illustrates the approach to diagnosis of work-related asthma (reproduced with permission from Diagnosis and Management of Work-related Asthma, American College of Chest Physicians Consensus Statement. Chest 2008;134:1S-41S http://www.chestjournal.org/content/134/3_suppl/1S/suppl/DC2 web supplemental material. Abbreviations: BDT – bronchodilator test, PEF – peak expiratory flow, RAST – radioallergosorbent test

comprise the spectrum of work-related asthma. Although both subsets of work-related asthma are addressed in the document of the American College of Chest Physicians (ACCP), it is important to recognize that the British document focuses only on occupational asthma.

Occupational asthma can be subdivided into:
1 asthma that is caused by a workplace sensitizer (a high or low molecular weight substance that causes a specific asthmatic response by an identified immunoglobulin E-associated response or through other presumed anamnestic immunologic responses)
2 asthma that is caused by a high-level irritant exposure at work (irritant-induced asthma, which is also referred to as reactive airways dysfunction syndrome [RADS]).[7] Occupational asthma from a specific sensitizing agent is the more common scenario in most case surveillance series. In terms of large molecular weight sensitizing agents, such asthma can be due to organic inhaled material such as flour (bakers), animal proteins (veterinarians, farmers), plant proteins (greenhouse workers, farmers), or fungal spores (contaminated office buildings). Low molecular weight occupational sensitizers include diisocyanates (used in polyurethanes that are the key component of a wide variety of commercial products such as spray paints, foam insulation, and sealants), acid anhydrides (in epoxy compounds), amines, and acrylic compounds (in glues and other polymers). The foregoing was a short list: there are over 300 recognized occupational sensitizers with new agents reported each year.[8] The practical message is that although suspicion of occupational asthma is increased in a patient with asthma who works as a baker, a farmer, or in another job well-recognized to cause occupational asthma, the absence of a high-risk occupation cannot be used to exclude occupational asthma. Thus, additional questions as to possible workplace relationships need to be asked, whatever the job or presumed exposure. Similarly, although work-exacerbated asthma may be expected when a patient with pre-existing asthma starts work in a smoke-filled foundry or is expected to undertake significant exertion in a hot environment, exacerbation can also occur in an established asthmatic domestic cleaner exposed to cleaning products in the home that he/she is cleaning or in an office worker when construction is being done in their building. Therefore, the range of both potential sensitizers and potential exacerbating factors to be considered is very wide and multiple factors often can co-exist in the same workplace environment.

The diagnosis of either occupational asthma or work-exacerbated asthma likely will be missed without asking every working asthmatic about the relationship of their asthma to their work. FIGURE

illustrates the approach. Worsening from work exposures may occur with every work shift or may be intermittent. Symptoms may be worse almost immediately at work or only after several hours, even after leaving work at the end of a shift or during the night. The most useful questions to initially determine a possible work component to asthma as noted in the ACCP document are:

1 Were there changes in work processes in the period preceding symptoms?

2 Was there an unusual work exposure within 24 h before the onset of initial asthma symptoms? (a positive response would suggest irritant-induced asthma)

3 Do asthma symptoms differ during times away from work such as weekends or holidays or other extended times away from work?

4 Are there symptoms of allergic rhinitis and/or conjunctivitis that are worse with work? (a positive response would suggest specific sensitization at work)

5 Are co-workers affected?

Negative responses to all of these questions suggest a lower probability of work-related asthma. One or more positive response is not sufficient for a diagnosis but should prompt further investigation. Both the ACCP and the British documents advise investigations to confirm or rule out work-related asthma. Objective confirmation of asthma as a generic diagnosis should be sought in all patients, since other conditions can mimic asthma and will require different management. A key practical aspect is to perform the tests for diagnosis of asthma (bronchodilator response manifest by spirometric assessment or a test of airway hyperresponsiveness by methacholine or histamine challenge) preferably during a work week or at least when the asthmatic has had recent symptoms. The rationale for this temporal consideration is that these tests may be normal and yet not exclude work-related asthma, if performed after removal of the relevant exposure and at a time when the patient has not had recent symptoms. This caveat is especially relevant with recent-onset asthma.

After establishing the diagnosis of asthma, and when work-related asthma is suspected from the clinical history, the next diagnostic step is to establish its relationship to work. In this diagnostic algorithm there are different pathways to establish a diagnosis of:

1 occupational asthma from an irritant exposure

2 occupational asthma from a sensitizer

3 work-exacerbated asthma.

Occupational asthma from an irritant exposure can be diagnosed based on the criteria described by Brooks[7] used for the diagnosis of RADS, and later modified for irritant-induced asthma.[9] These include establishing that one or more high-level irritant exposures occurred, with the new onset of asthma symptoms within 24 h of the exposure, usually leading to an emergency department visit or unscheduled outpatient physician visit. Asthma symptoms must continue for at least 3 months after the exposure and pulmonary function testing must confirm reversible airway obstruction or airway hyper-responsiveness. Moreover, other lung disease should be reasonably excluded. If all criteria are met, then the term *RADS* or *irritant induced asthma* can be used; the latter term is also applied using somewhat more broadly defined criteria for acuity of exposure and response.[10]

Occupational asthma from a sensitizer is further investigated by objective tests providing evidence of specific sensitization whenever possible. The ACCP panel consensus found that skin tests, when available, usually showed greater sensitivity than in vitro tests, and therefore were preferable. In contrast, the British document favored in vitro tests, perhaps reflecting less availability of specialists performing allergy skin tests or the potential advantage of having centralized immunologic testing. However, on a practical level, both skin test extracts and in vitro specific IgE antibody assays are often not available for occupational allergens, and if available, usually do not consist of standardized allergen extracts. Also, the prevalence of exposed workers who are sensitized is greater than the prevalence with clinical occupational asthma. Therefore, although these tests can add to the likelihood of a positive or negative diagnosis, it is preferable to also have additional diagnostic tests showing functional asthma changes associated with workplace exposures.

One functional test that is advised in the ACCP document, as in the British guidelines, is that of serial peak expiratory flow rate (PEFR) readings performed over multiple working days as well as periods off work. These PEFR readings are best performed in triplicate at least four times a day (e.g., pre-shift, mid-shift, post-shift, and bedtime, with similar times on days off work). It is important to recognize that they are effort dependent and require careful patient instruction. Additional helpful information is obtained by concurrent recording by the patient of symptom scores and asthma "reliever" medication use (e.g., short-acting β-agonist inhalers). An example of the sheet that can be used is provided in the web-supplement to the ACCP document, "A physician pathway to diagnosis" (http://www.chestjournal.org/content/134/3_suppl/1S/suppl/DC2).

An important difference between the ACCP and the British document is in their approaches to the interpretation of PEFR meter results. The British advise using a computerized system (OASYS)[11,12] rather than visual expert interpretation of plotted PEFR graphs. The ACCP document does not favor one method over another, noting that results from either have been shown to be comparable.[12] With either method, significant worsening of PEFR during periods at work compared with periods off work (preferably 2 or more weeks at work and 10 days or more off work), supports concurrent worsening of asthma from

work. Nonetheless, such findings cannot always distinguish occupational asthma from work-exacerbated asthma.[13]

The other functional asthma test advised by the ACCP consensus panel is the use of measures of airway responsiveness (such as methacholine challenge) performed serially at more than one point in time, for example towards the end of a working period and near the end of a period away from the suspected work factor(s), preferably after at least 10 days away, such as the end of a holiday period without exposure. A significant improvement away from the work exposure, usually taken as an increase of at least a 4-fold concentration (two doubling doses) needed to cause a 20% fall in forced expiratory volume in one second (provocative concentration – PC_{20}) compared with the PC_{20} during a working period, is supportive of sensitizer-induced occupational asthma in the presence of other compatible findings from history. It is well recognized that tests of airway responsiveness may change due to other exposures, such as a nonoccupational allergen exposure or an upper respiratory infection, or failure to stop bronchodilators for an appropriate time before the test. In the absence of such confounding factors, however, the ACCP panel advised this as a useful contributing diagnostic test. In contrast, the British document did not include this assessment in its diagnostic algorithm. Nonetheless, support for this approach in the diagnostic work-up for occupational asthma has been voiced elsewhere by UK experts.[14]

In (the relatively few) centres where induced sputum for cytology to assess eosinophils can also be performed during a working period and at the end of a period away from exposure, preliminary reports support the diagnosis of sensitizer-induced occupational asthma in those who have a greater proportion of sputum eosinophils during a working period.[15,16] Based on these preliminary data, the addition of these tests was supported, when available, by the ACCP document.

Specific inhalation challenge (SIC) tests with a suspected work sensitizer are available in relatively few centres. Moreover, SIC may carry significant risk, if not performed in specialized facilities under close supervision. When available, a SIC provides a useful option as a diagnostic test. It can be especially helpful if the patient has left the implicated work exposure and cannot return for the above tests of functional work-related asthma changes. As with any of the previous tests, the SIC is not perfect and can be falsely positive or negative.[17]

The ACCP document emphasizes (and the British document concurs) that a combination of diagnostic tests should be performed when the diagnosis of sensitizer-induced occupational asthma is suspected. Thus, the probability of the etiological diagnosis can best be determined from the combined results of the history and several different clinical investigations. Investigations are most reliably performed while the patient is still working and removal from work before arriving at a diagnosis is not advised unless there are clear supervening safety concerns.

Work-exacerbated asthma can range from a single short-term worsening of asthma at work (e.g., worsening symptoms for a few hours or days) up to daily worsening at work on a consistent basis. A single short-term exacerbation may be documented by history alone (increased symptoms and increased bronchodilator use associated with an exposure at work). In that situation, further investigations are not likely to be feasible or necessary, unless similar episodes recur frequently enough to be documented by means of a symptom and peak flow diary. At the other end of the spectrum, however, work-exacerbated asthma with symptom worsening on a daily or near-daily basis can be investigated in a similar manner as for sensitizer-induced occupational asthma. This can include allergy tests when appropriate (such as for dust mites or pets in domestic cleaners, or pollens and fungal spores in outdoor workers), PEFR monitoring and/or methacholine challenge testing during work periods and periods off work to assess the presence of a work relationship. Of note, some exacerbating factors, such as cold air or exercise, are less likely to be associated with a shift in methacholine responsiveness compared with triggers such as common allergens. Typically, if specific challenge tests to occupational sensitizers are performed in patients with work-exacerbated asthma, they will be negative.[15]

Management **Occupational asthma from a sensitizer** The ACCP consensus advises that workers with occupational asthma should no longer work with exposure to the causative sensitizer.[1,3] It is recognized that this may not be easy to achieve, for example, in a work process where the causative agent cannot be removed or a worksite where the worker cannot be moved to a separate building or separately ventilated area. Furthermore, significant socio-economic consequences can occur if the worker has to change job or job duties, even if a workers' compensation system provides some support in lieu of lost wages. Nonetheless, the medical outcome of asthma is best with early removal of the offending exposure, when disease is milder and more likely to remit or resolve altogether. The only agent documented to date for which greatly reduced exposure (as compared to complete removal) appears to offer a comparable improvement in prognosis is natural rubber latex from glove use in healthcare workers. In that instance, low protein, powder-free latex gloves for co-workers, along with the use of latex-free gloves for the sensitized worker, appears to be safe and to allow continued work in the same job.[18]

Other aspects of management of occupational asthma are the same as for nonoccupational asthma: limiting exposure to relevant nonoccupational and occupational environmental triggers, pharmacologic measures, and education as to asthma control.

Support of the worker through the appropriate compensation system when available should be provided to assist replacement of income loss, cover the costs of asthma medications, and provide job retraining as appropriate.

Occupational asthma from an irritant Occupational asthma caused by an irritant exposure at work can generally be managed as for nonoccupational asthma, with the exception that there should be a review of occupational hygiene measures to minimize the likelihood that the workplace conditions that caused the initial irritant exposure recur (e.g., preventing the mixing of cleaning agents that release irritant fumes). In addition, it should be recognized that those who have developed asthma from an irritant exposure at work and have on-going asthma on return to their usual job may subsequently have work-exacerbated asthma from work conditions that previously may have not caused any symptoms. These cases should be managed as others with work-exacerbated asthma.

Work-exacerbated asthma Management of work-exacerbated asthma includes optimizing asthma control by reducing exposure to relevant asthma triggers, both at work and off work, as well as pharmacologic asthma treatment. Reduced exposure may be achieved by better ventilation or other occupational hygiene measures at work, use of an appropriate respirator for short-term irritant exposures, and, in some cases, there may be a need to move the worker to a different work assignment.

Prevention The ACCP Consensus Statement prominently supports steps designed to prevent work-related asthma. Such preventive measures can be divided into primary, secondary, and tertiary preventive measures. Primary actions comprise measures that prevent workers from developing work-related asthma in the first place. Such strategies include avoidance of the use of sensitizers or strong irritant agents (e.g., avoiding unnecessary use of natural rubber latex gloves and instead, substituting non-latex gloves), optimizing measures to reduce exposures to sensitizers or strong irritants by occupational hygiene measures to enclose processes, use robotics instead of workers in high-exposure areas, improve ventilation, and, as the least preferred option, short-term use of respiratory protective devices. Air sampling to ensure that approved exposure concentrations are not exceeded, and joint worker-management approaches to enhance compliance with safety measures are also components of primary prevention.

Secondary prevention comprises early detection of work-related sensitization, rhinitis, or asthma (specifically relevant to sensitizer-induced occupational asthma) by medical surveillance measures that may include periodic respiratory questionnaires, spirometry, and relevant immunologic screening for specific antibodies to work sensitizers, when available. Limited available evidence suggests some benefit from such programs for workers exposed to disocyanates or enzymes, and among bakers (who have multiple potential exposures).[19-21]

Tertiary prevention comprises optimum treatment of those with work-related asthma to reduce morbidity, using all of the management measures described above. Workers' compensation can also be considered as a component of tertiary prevention, limiting socioeconomic impacts.

As with diagnosis and management of work-related asthma, it is unlikely that randomized, controlled trials will be conducted to identify the relative benefits of different preventive strategies. However, time series strongly indicate a benefit from a combination of preventive measures to reduce occupational asthma from natural rubber latex[22] and also have suggested earlier diagnosis and improved outcome with preventive measures for diisocyanate-induced asthma,[23] serving as models of high- and low-molecular weight occupational sensitizers.

Finally, as with all guidelines, practice parameters, and similar documents, the ACCP Consensus Statement will need dissemination and implementation in order to be maximally effective. As co-authors of the Statement, we greatly appreciate the invitation to contribute this review to the journal; we hope that it will provide the reader with an overview of some practical aspects, and stimulate interest to review and implement the full Statement.

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ARTYKUŁ POGLĄDOWY

Jak rozpoznawać i leczyć astmę związaną z pracą zawodową

Uzgodnione stanowisko American College of Chest Physicians – główne przesłania dla praktyki klinicznej

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SŁOWA KLUCZOWE

astma, astma wywołana czynnikiem drażniącym, astma zaostrzana wywoływaną pracą, astma zawodowa, astma związana z wykonywaną pracą

STRESZCZENIE

Astma związana z pracą zawodową jest często spotykana wśród dorosłych astmatyków – jest to albo astma wywołana przez czynniki zawodowe (astma zawodowa), albo wcześniej istniejąca astma ulegająca zaostrzeniu pod wpływem czynników zawodowych. Prawidłowe leczenie zależy zarówno od właściwego rozpoznania choroby, jak i od ustalenia etiologii. Po dokonaniu systematycznego przeglądu piśmiennictwa American College of Chest Physicians powołało grupę ekspertów, którzy dokonali szczegółowej oceny tego materiału, poszerzyli go i opracowali „Uzgodnione stanowisko dotyczące rozpoznawania i leczenia astmy związanej z pracą zawodową", opublikowane w 2008 roku. Niniejszy artykuł przedstawia główne aspekty praktyczne tego Stanowiska, w tym wskazówki kliniczne do rozpoznawania astmy związanej z pracą zawodową na podstawie danych z wywiadu, ocenę narażenia na czynniki zawodowe, ukierunkowane badania diagnostyczne oraz sposoby leczenia, jak również zakres i znaczenie środków zapobiegawczych.

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