

Occupational asthma: an approach to diagnosis and management

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Case

A 40-year-old woman comes to the family practice clinic for a routine annual visit. She reports a 6-month history of progressively severe episodic shortness of breath, cough, wheeze and chest tightness. You question her about associated symptoms, the timing and frequency of the symptoms, and triggering or exacerbating factors. You ask about environmental exposures in the home and workplace and any temporal associations of the symptoms with such exposures, including any change in severity of symptoms on weekends or holidays, as is your routine for patients with new-onset or worsening asthma. She reports that symptoms typically worsen in the evenings and that they cleared while she was at home over the Christmas holidays. You note from your records that at the time of her previous visit she was working at an electronics factory, and you question her more closely about possible exposures to chemicals at work, but she is unsure what compounds are used. The results of a physical examination are normal.

Asthma is a common condition, often starting or recurring in adult life. For example, in a recent survey about 4% to 6% of men and 5% to 10% of women 20 to 44 years of age in 6 Canadian cities reported current use of asthma medication.¹ Occupational asthma from various causes is being diagnosed with increasing frequency. This article reviews the classification, diagnosis, investigation and management of occupational asthma.

Classification of work-related asthma

Aggravation of pre-existing or coincidental asthma

Workplace exposures to potential irritants, such as cold, dry air, dusts, smoke, fumes and sprays, or exertion at work may aggravate asthma, especially in patients with moderate or severe forms of the disease and in those not receiving optimal treatment. Such aggravation of pre-existing disease is different from occupational asthma (i.e., asthma caused by some aspect of the workplace). Optimization of asthma management and, if needed, reduction of workplace exposures to respiratory irritants often allow patients with this type of work-related asthma to continue in the same job.

Occupational asthma

Occupational asthma is asthma caused by some aspect of the workplace environment.² It is important to distinguish

occupational asthma from aggravation of pre-existing asthma, because the management and compensation can differ. The more common type of occupational asthma, accounting for over 90% of cases, is sensitizer-induced occupational asthma, caused by an IgE-mediated or other immune response to specific workplace agents: high-molecular-weight sensitizers (such as animal proteins, flour or natural rubber latex) and low-molecular-weight chemicals (such as diisocyanates, colophony [a pine resin product] or epoxy compounds). Once a person has been sensitized to one of these materials, even exposure to extremely low quantities will exacerbate the asthma. The less common form of occupational asthma, accounting for about 7% of cases, is irritant-induced occupational asthma, which occurs after accidental exposure to very high inhaled concentrations of a workplace irritant. Given that both forms account for only a small proportion of all cases of adult asthma (about 10%)³ and can be caused by numerous workplace agents,⁴ the diagnosis of occupational asthma can easily be overlooked in primary care practice unless it is routinely considered in the assessment of new-onset asthma in a working adult.

Irritant-induced occupational asthma should be suspected if the symptoms first began within 24 hours after accidental exposure to a high inhaled concentration of a workplace irritant, whereas sensitizer-induced occupational asthma should be suspected if the symptoms begin during a period when the patient is working, are worse at work or in the evenings after work, and diminish during weekends or holidays. If any of these situations apply, further investigations are needed.

Diagnosis of occupational asthma

Irritant-induced occupational asthma

The most definitive form of irritant-induced asthma⁵ is reactive airways dysfunction syndrome.⁶ The diagnostic criteria for reactive airways dysfunction syndrome are shown in Table 1. Patients with this or the less strictly defined forms of irritant-induced asthma^{5,6} may be entitled to provincial workers' compensation for asthma caused by the workplace. Furthermore, modification of the work environment may be required to reduce exposure to aggravating irritants and to reduce the risk of future accidental exposures affecting the same worker or others.

Sensitizer-induced occupational asthma

Some examples of the more than 250 agents that can cause sensitizer-induced occupational asthma are listed in Table 2. If this form of occupational asthma is suspected from the patient's history, objective investigation is required to confirm or refute the diagnosis,^{7,8} since the implications for the patient's work situation differ for this and other

forms of work-related asthma. Patients with confirmed sensitizer-induced occupational asthma should have no further exposure to the causative agent, since the best outcome is achieved with early diagnosis and complete avoidance of exposure.⁹ These measures will probably result in economic loss, even if a compensation claim is accepted, so an objectively confirmed diagnosis is very important.

Approximately 96% of people with sensitizer-induced

Table 1: Features of various forms of work-related asthma

Feature	Aggravation of pre-existing or coincidental asthma	Irritant-induced occupational asthma (RADS)	Sensitizer-induced occupational asthma
History			
Symptoms of asthma	Yes	Yes	Yes
Onset	Before or during working life	Within 24 h of exposure to large quantities of a respiratory irritant (usually severe enough to require medical attention at that time)	Onset or recurrence of condition during working life
Relation to work schedule	Worse on one or more days while at work		Symptoms worsen during or after a work shift and diminish when away from work (evenings, weekends, holidays)
Other	Exposure at work to asthma-aggravating factors such as dusts, smoke, fumes	Persistence of symptoms for at least 12 weeks, but no previously documented evidence of asthma or other chronic lung disease	Exposure to a known sensitizer†
Typical investigations*			
General	Objective evidence of asthma‡	Objective evidence of asthma‡	Objective evidence of asthma‡
Serial peak expiratory flow rates	Worse during work periods than when off work§	Not relevant unless the irritant was also a sensitizer	Worse during work periods than when off work§
Changes in response to methacholine challenge	No difference between work periods and when off work	Not relevant unless the irritant was also a sensitizer	Worse at end of a work week than at end of a holiday period
Other challenges	Negative response to challenges with specific agents from workplace	Not relevant unless the irritant was also a sensitizer	Positive response to challenges with suspected agent or agents from workplace
Immunologic tests	Negative response to workplace sensitizer	Not relevant unless the irritant was also a sensitizer	Positive response to workplace sensitizer
Other			Review patient's history and MSDSs to assess possible exposure to a respiratory sensitizer in the workplace
Management			
Symptoms	Improve treatment of asthma¶	Treat asthma¶	Treat asthma¶
Exposure	Reduce exposure to workplace irritants if necessary (by use of mask or change in work area)**	Reduce exposure to workplace irritants if necessary (by use of mask or change in work area)	Prevent further exposure to workplace sensitizer
Compensation	Initiate compensation claim if time has been missed because of workplace exposure	Initiate compensation claim	Initiate compensation claim
Other measures			Notify authorities such as ministry of labour to implement industrial hygiene measures and possible medical surveillance

Note: RADS = reactive airways dysfunction syndrome, MSDS = material safety data sheet.

*For sensitizer-induced occupational asthma, some investigations may not be needed or may not be feasible, but combinations of tests increase the diagnostic certainty.

†New sensitizers are described each year.

‡Airway hyperresponsiveness on challenge with histamine or methacholine; airflow limitation with significant responsiveness to bronchodilator (at least 12% increase in forced expiratory volume in the first second).

§Analyzed in conjunction with symptom and medication diaries.

¶As in the Canadian asthma consensus guidelines.¹⁰

**Person can usually remain in the same job.

occupational asthma have a history consistent with this diagnosis. However, the specificity of history is poor, and only 25% of those with an appropriate history actually have sensitizer-induced occupational asthma.¹⁰ Thus, a negative history is more reliable in excluding a diagnosis than a positive history is in confirming it. The wide differential diagnosis for patients with a history suspicious for sensitizer-induced occupational asthma includes asthma coincidental to the workplace, unrelated asthma that is aggravated by exposure to nonspecific irritants at work and nonasthmatic causes of asthma-like symptoms (such as rhinitis with post-nasal drip, acute or chronic bronchitis, gastroesophageal reflux or cardiac asthma).

The steps in diagnosing sensitizer-induced occupational asthma are presented in Table 1. Patients with suspected sensitizer-induced occupational asthma should be referred as soon as possible to a specialist (a respirologist, an allergist or an occupational physician) with expertise in this area. However, the investigations (as outlined in Table 1) are most helpful if they can be performed while the patient is still working in the suspected causative work area; the primary care physician may be able to initiate some of these.

Assessments and investigations

Confirm asthma

The initial diagnostic step is to objectively confirm or refute the diagnosis of asthma by means of pulmonary function tests before and after administration of a bronchodilator, with or without a histamine or methacholine challenge test, according to a standard protocol.¹¹ These investigations should be arranged while the patient is still employed and should take place within 24 hours of the patient's usual work exposure. Normal results at that time, especially a normal response to methacholine challenge, virtually exclude a diagnosis of occupational asthma (although a few patients with diisocyanate-induced asthma but normal results on methacholine challenge have been described).¹²

Assess exposure

Affected patients may not be aware of the chemicals to which they are exposed at work. Additional information can be obtained from the workplace in the form of material safety data sheets (MSDSs). Employers are required to have an MSDS available on site for any hazardous material that accounts for 1% or more of any workplace substance. The specialist should review the MSDSs for all agents to which the patient may have airborne exposure, including those used by coworkers. Further details on chemicals not listed on the sheets can be requested by phoning the contact number given on the MSDS (usually the manufacturer of the hazardous material).

Assess relation between asthma and the workplace

Several studies,^{7,8} including guidelines from the Canadian Thoracic Society,⁸ have assessed the value of investigations for occupational asthma. Each investigative measure (Table 1) can have false-positive and false-negative outcomes. It is therefore important for the physician interpreting the test results to be aware of confounding factors⁸ and to undertake as many investigations as are feasible for an individual patient. Such comprehensive testing and interpretation usually requires referral to a specialist.

Serial monitoring of peak expiratory flow and paired methacholine challenges

Peak expiratory flow meters are inexpensive and can be given to the patient in a primary care setting. The patient records peak expiratory flow rate (PEFR) 4 times a day and completes symptom and medication diaries during periods of regular work and periods off work (e.g., weekends and holidays).¹³ The flow meters are useful as a component of an occupational asthma investigation, but patients must be instructed as to correct use. If possible, medications (other than as-needed bronchodilators) are kept at stable, regular dosages during this period, sufficient to control but not com-

Table 2: Examples of workplace sensitizers to which workers in various professions may be exposed*

Occupation	Potential sensitizers
Health care workers	Natural rubber latex in gloves Glutaraldehyde used in sterilization of endoscopy equipment and development of x-ray film Penicillin and other aerosolized or powdered medications
Woodworkers	Dusts from red cedar and other woods Phenol formaldehyde resins in particle board Diisocyanates in glues
Automotive workers	Diisocyanates or epoxy compounds in spray paints Diisocyanates in manufacture of rigid or flexible polyurethane foam and glues
Electronic workers	Colophony or amines in soldering flux Acrylic glues
Welders and other metal workers	Metal dusts or fumes (e.g., nickel, cobalt, chromium) Coolants containing pine products or other sensitizers
Food processors and animal workers	Food or animal protein allergens (e.g., egg processors exposed to egg proteins, bakers exposed to wheat and fungal amylase)
Farmers or gardeners	Animal, plant, insect and fungal allergens
Cleaners and laboratory workers	Enzymes or cleaning agents

More than 250 sensitizers have been reported to cause occupational asthma.

pletely suppress symptoms. Compliance in completing the symptom, medication and PEFr diaries is often poor. However, in cases where the patient has kept records with enough information to assess the relation between symptoms and work schedule over several weeks of work and over a holiday period, the sensitivity and specificity of serial PEFrs has been higher (at 73% and 100% respectively) than for other, more objective tests.¹⁴ Nonetheless, differences in symptoms and PEFr readings between periods at work and periods off work may not be sufficient to distinguish aggravation of asthma from occupational asthma. Performing methacholine challenges at the end of a work week and again at the end of a holiday period can provide additional helpful information. A threefold or greater decline in methacholine reactivity (i.e., an increase in PC₂₀, the provocation concentration of methacholine causing a 20% drop in forced expiratory volume in the first second) after a period away from work is strongly supportive of occupational asthma, rather than aggravation of asthma; however, lack of a change of this magnitude does not exclude occupational asthma, since hyperresponsiveness may persist for several months or years.

Immunological tests

A positive skin prick response to an agent from the workplace supports a diagnosis of occupational asthma if it is associated with appropriate pulmonary function changes, but is not diagnostic as a sole investigation. Immunological tests (skin tests or *in vitro* assays for specific IgE antibodies¹⁵) are often limited by the lack of commercially available or standardized reagents.

If the patient has left the implicated workplace and cannot or will not return on a trial basis for the workplace-related peak flow and methacholine testing, an objective physiological diagnosis may require challenges with specific agents in a specialized facility (usually an academic centre specializing in occupational lung disease).

Management

Aggravation of pre-existing asthma

For patients with aggravation of pre-existing asthma, the best approach is to optimize medical management of the asthma, by limiting exposure to relevant environmental allergens and nonoccupational irritants such as tobacco smoke and by prescribing appropriate medications and providing suitable education to ensure that the patient understands how to use the drugs and the importance of compliance.¹⁶ The patient can usually stay in the same job, but it may be necessary to reduce exposure to nonspecific workplace triggers,⁸ for example by moving to a different work area, making changes in the ventilation system or in work processes, or using an appropriate respirator for short-term exposures to irritants, as advised by an occupational hygienist familiar with the exposures.¹⁷ If the asthma is severe, then a change in

occupation to a relatively sedentary job in a clean environment may be needed to enable the patient to continue work.

Irritant-induced occupational asthma

Workers with occupational asthma induced by exposure to an irritant at work should be managed in the same way as those with aggravation of pre-existing asthma, with the addition of appropriate precautions⁸ (e.g., health and safety education, better workplace containment of respiratory irritants, improved ventilation and use of respiratory protection as necessary¹⁷) to ensure that there is no risk of further exposure to high inhaled concentrations of the irritant (Table 1).

Sensitizer-induced occupational asthma

For a patient with occupational asthma induced by a respiratory sensitizer, a workers' compensation claim should be pursued, if applicable. Once the decision on the claim has been made, steps should be taken to prevent further exposure to the agent,⁸ and the worker should receive the same types of medical treatment as people with nonoccupational asthma (Table 1). In addition, the provincial ministry of labour or a workplace physician (or both) should be notified as to the possible risk of occupational asthma in other workers because of continuing exposure to the causative agent.

Case revisited

This patient's work consisted of soldering electronic parts for a small company. Her symptoms worsened in the evenings on workdays and diminished on weekends and holidays. MSDSs from the workplace indicated that the soldering flux used at the site contained colophony, a pine resin product that is known to be a respiratory sensitizer.¹⁸ She was not aware of any coworkers with similar symptoms. Pulmonary function tests performed near the end of a work week confirmed asthma. Regular use of an inhaled steroid was prescribed, along with an inhaled bronchodilator when needed. She was referred to a respirologist for assessment of possible occupational asthma. Before the assessment, she was instructed to record symptoms, serial PEFrs and medication use. She brought this documentation, along with copies of the MSDSs from her workplace, to the appointment with the specialist for interpretation. Assessment by the respirologist confirmed occupational asthma, likely secondary to exposure to colophony: the variability in her PEFr was worse on working days, and methacholine hyperresponsiveness was 3 times as great (i.e., methacholine PC₂₀ was 3 times lower) at the end of a work week than at the end of a holiday period. A workers' compensation claim was submitted and accepted, and she was retrained for office work. The symptoms cleared 3 months after she left her previous position, and she needed no further medication. The provincial ministry of labour reviewed conditions in the workplace and advised modifications to the ventilation system to reduce workers' exposure to fumes from the soldering flux.

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Key points

- If new-onset asthma develops during a person's working life, occupational asthma should be considered.
- Exposure to irritants in the workplace commonly aggravates underlying asthma, but this condition is managed differently from occupational asthma, and compensation also differs.
- Occupational asthma should be suspected if symptoms began within 24 hours of exposure to high levels of an irritant at work (irritant-induced occupational asthma) or if symptoms worsen while the person is at work or shortly after he or she leaves work and diminish on weekends and holidays (sensitizer-induced occupational asthma).
- Objective investigations are needed, because a diagnosis of occupational asthma often has significant implications for the person's working situation. Furthermore, a history consistent with occupational asthma has poor specificity for the diagnosis.
- Unless the patient's asthma is severe and cannot be controlled, the primary care physician should advise the patient not to stop working until the diagnosis has been confirmed.
- Early referral to a specialist is usually needed for full investigation.
- The primary care physician can initiate investigations to confirm that the symptoms are due to asthma and to begin serial monitoring of peak flow.
- In cases of sensitizer-induced occupational asthma, early, accurate diagnosis and avoidance of further exposure are associated with the best prognosis.
- A patient with irritant-induced occupational asthma may be able to continue with his or her job, with changes in the workplace, if necessary, to prevent further high-level exposure to irritants.
- Patients with workplace aggravation of existing asthma should be assessed to ensure that measures to manage the asthma are optimal. Although measures to reduce exposure to workplace irritants may be required, such patients are often able to continue working in the same job.

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