Work-related Asthma

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This medical discussion paper will be useful to those seeking general information about the medical issue involved. It is intended to provide a broad and general overview of a medical topic that is frequently considered in Tribunal appeals.

Each medical discussion paper is written by a recognized expert in the field, who has been recommended by the Tribunal’s medical counsellors. Each author is asked to present a balanced view of the current medical knowledge on the topic. Discussion papers are not peer reviewed. They are written to be understood by lay individuals.

Discussion papers do not necessarily represent the views of the Tribunal. A vice-chair or panel may consider and rely on the medical information provided in the discussion paper, but the Tribunal is not bound by an opinion expressed in a discussion paper in any particular case. Every Tribunal decision must be based on the facts of the particular appeal. Tribunal adjudicators recognize that it is always open to the parties to an appeal to rely on or to distinguish a medical discussion paper, and to challenge it with alternative evidence: see Kamara v. Ontario (Workplace Safety and Insurance Appeals Tribunal) [2009] O.J. No. 2080 (Ont Div Court).
Introduction

Asthma is a common condition that can start at any age. It usually has no known cause, although there is a genetic component (i.e. it often occurs in other family members) and it often is associated with allergy (it has been estimated that up to 80% of children who develop asthma have an allergic component, and up to 50% of adults with asthma). The association with allergy is often manifest by a personal and/or family history of allergic rhinitis (hayfever-like symptoms) or eczema. Allergic responses in asthma are associated with production by the affected individual of IgE antibodies that are directed at specific proteins or glyco-proteins that are foreign to the body, and usually are inhaled, e.g., cat proteins, dust mite proteins, fungal proteins. These proteins and glyco-proteins are termed allergens.

Work-related Asthma

Work-related asthma is the term used to describe asthma that is either caused or aggravated by exposures at work (Fig 1).

Figure 1 - Sub-types of work-related asthma
Among adults who develop asthma for the first time (termed adult-onset asthma), it has been estimated that 10-15% may have asthma that is CAUSED by work, and this is termed OCCUPATIONAL ASTHMA (OA). When this occurs it is usually due to an ALLERGIC response or sometimes a response that behaves in a similar way to an allergic response but for which the mechanism is unclear (these responses that behave like an allergic response are also termed SENSITIZATION). Less commonly high level irritant exposures can cause IRRITANT-INDUCED OA. The other subgroup of work-related asthma, besides OA, is WORK-EXACERBATED ASTHMA, as will be discussed later.

**Occupational Asthma (OA)**

The most clear mechanism for OA is an allergic response to an inhaled protein or glyco-protein in the workplace, such as animal proteins (e.g. in animal care workers or veterinarians or in farmers), or food or plant proteins (such as wheat or other proteins in bakers, bell pepper proteins in greenhouse workers, natural rubber latex proteins in healthcare workers using powdered latex gloves, or glyco-proteins from fungi). Other examples include inhaled proteins from insects or enzymes. There are numerous inhaled proteins or glyco-proteins that have caused OA by an allergic mechanism and it seems likely that almost any inhaled foreign protein might cause such a response in a susceptible worker. However, among those who are exposed, only a minority will develop this response (10% or less), and the reasons to explain this susceptibility in some individuals are not fully understood. There is some association with the extent of exposure i.e. lower exposures are associated with asthma in a smaller proportion of workers than higher exposures. However, even at very low exposure levels, some workers can become “sensitized” (i.e. develop specific IgE antibodies) and can then develop OA, likely associated with genetic susceptibility. Workers who develop specific IgE antibodies to a work agent can also develop allergic nasal symptoms (allergic rhinitis) that often precede or coincide with the development of OA.

Important aspects of the allergic response causing OA are: a) that there is a “latent period" of exposure before sensitization: i.e. the worker has exposure to the causative agent for weeks or even years before the first onset of symptoms – since this is an immunologic response, it cannot cause symptoms on the very first day of exposure; b) however once OA has developed with sensitization, then exposure, even to low levels of the causative agent will trigger asthma symptoms – unless symptoms are suppressed by asthma medications; c) the asthmatic response in a patient with OA can start within minutes of each exposure (an immediate response), or may be most noticeable 4-6 hours after the onset of exposure (a late response), or there can be a combined immediate and late response.

Some chemicals can also cause OA through a demonstrable allergic response, such as complex platinum salts and other metal salts, acid anhydrides (used to make plastics), persulphates (in hairdressers) and penicillin (e.g. in pharmaceutical workers).
Other chemicals can also cause occupational asthma and have similar features as with sensitization associated with IgE antibodies, but through mechanisms that are not fully understood, and usually without demonstrated specific IgE antibodies.

These chemicals causing sensitization by unclear mechanisms include diisocyanates and western red cedar dust: specific IgE antibodies can be identified in only a minority of those with well-documented OA caused by these agents, and they most commonly cause an isolated late response in those who have OA caused by them. Other chemicals that can cause OA by unclear mechanisms include acrylic compounds, quaternary ammonium compounds, and aldehydes such as glutaraldehyde and formaldehyde. Most chemicals that have caused occupational asthma have highly reactive molecular side-chains.

Lists have been compiled of the reported causes of OA with or without specific IgE antibodies. These are often divided into high-molecular-weight sensitizers (typically the proteins and glycoproteins) and low-molecular-weight sensitizers (typically the chemicals). Over 300 agents have been reported, some described in just a few case reports, and others in large groups of workers (and no list is completely comprehensive as new additional causes are described each year). Among the chemical sensitizers, diisocyanates and plicatic acid (in western red cedar) have been most thoroughly investigated.

Diisocyanates are very reactive chemicals used to make polyurethane products, such as in 2-part polyurethane spray paint systems, spray foam insulation for homes, urethane coatings, polyurethane foam for furnishings, used in cars (seating, headrests, bumpers etc.). They are also used in moulds in foundries, and as adhesives in particle board and oriented strand board. These chemicals have been the most common single cause of OA in many industrialized regions including Ontario, for several years. Due to this, there is a medical surveillance system in Ontario that was developed by the Ontario Ministry of Labour. This limits allowable exposure levels and requires regular questionnaires and breathing tests among those who have this exposure, in order to detect OA early.

**Diagnosis of OA caused by a sensitizer**

Since asthma can begin at any age and can occur without a cause from work, the new onset of asthma in a worker is not always due to the work exposure but may have started coincidental to the workplace for unknown reasons. Although OA should be suspected in any working adult who develops asthma, it has been recommended that objective tests be performed in such patients and the diagnosis of OA cannot be reliably made solely on the basis of identified exposure to a known sensitizing agent and the new-onset of asthma.
Several consensus documents or guidelines have been developed for the diagnosis of OA from several different countries, with a similar recommended approach. The medical history should document details of respiratory symptoms, and the timing of symptoms in relation to work exposures and days or holidays off work.

**Objective diagnosis of asthma**

There should be objective tests to confirm a diagnosis of asthma: this requires demonstration of a significant bronchodilator response on spirometry (12% and 180ml increase in FEV1 after a bronchodilator) or a positive methacholine challenge (PC20 8mg/ml or less). However, although these tests can confirm a diagnosis of asthma, they do not prove causation from work. In addition, if the tests are performed during a period that the patient is away from work, then normal findings do not exclude the possibility of OA, since patients with OA can sometimes have complete clearing of asthma when off work. Conversely, if these tests are completely normal during a period of time that the patient is working and has symptoms (especially within 24 hours of the implicated work exposure) then it is very unlikely that the patient’s symptoms are due to asthma, and another diagnosis should be considered (as detailed later).

**Support for an occupational cause of asthma**

In a worker with asthma, and a history suggesting OA, additional tests may support a work causation, such as demonstration of specific IgE antibodies to the work sensitizer (when these tests are available), although these tests can be positive even in some workers with no symptoms. These antibodies may be detected by allergy skin tests or blood tests for specific IgE antibodies using a solution containing the suspected causative protein from work (e.g. wheat in bakers or animal extracts in those working in laboratories with animals). Although several extracts are available for assessing specific IgE to work proteins, there also are numerous work sensitizers for which there are no reliable skin tests or blood tests. In addition, the presence of specific IgE antibodies without other objective tests that confirm asthma does not prove the diagnosis of OA, since the IgE tests can be positive in some exposed workers who have no symptoms.

Other tests that show changes in asthma during working periods compared with periods off work are useful (such as serial peak flow readings and serial methacholine challenges and/or induced sputum cytology).

Peak flow readings are obtained by asking the worker to use a small hand-held machine to measure a breathing test several times a day, while at work and while off work, over several weeks and to record the result in addition to keeping a record of symptoms, asthma medication use and location and/or work exposures. This can allow an estimate of changes in asthma during periods at work and off work (preferably including at least 10 days away from the work exposure), and help to determine the probability of work-related asthma. However, most often these charts are self-recorded and therefore are considered somewhat less objective than the other tests for work-
related asthma. The peak flow result is also affected by worker-effort, and potentially may be falsely low at the end of a working day when the patient may be tired. There may be other factors that can affect results such as absence of exposure to the work sensitizer during the recording period, or an intercurrent respiratory viral infection. Use of an electronic peak flow meter or portable spirometer can be helpful to provide a more objective record of results, but these are expensive and not commonly used in practice.

Methacholine challenge testing is often used as a diagnostic test for asthma, especially if the baseline FEV1 on spirometry is normal and there is no significant bronchodilator response. The test provides a measure of airway reactivity, and is typically increased in asthma (recorded as a PC20, with a lower PC20 representing greater airway hyperresponsiveness). The test can be performed towards the end of a typical work week with symptoms (when the airways hyperresponsiveness would be expected to be worst), and can also be performed after a period of 10 days or longer away from work (when there may be some improvement in airway hyperresponsiveness). An improvement in PC20 of three-fold or greater when away from the work exposure is very suggestive of OA. However, this test may not show significant improvement off work in all patients with OA, so absence of significant improvement in PC20 off work does not exclude the diagnosis of OA. In addition, there can be other factors besides the work exposure that can affect the result of a methacholine challenge test and such factors need to be considered in the interpretation of results, including a recent cold, exposure to relevant common environmental allergens (e.g., cat), and use of asthma medications before the test.

Another feature of asthma with an allergic response is the finding of inflammation in the airways typically with increased eosinophils (a type of white blood cell that is common in allergic responses). This can be assessed by performing an induced sputum test (currently performed in only a few centres in Ontario). If the test is repeated at the end of a work period and again when away from the implicated work exposure (similar to the paired measures of methacholine challenge), then the finding of a significant reduction in sputum eosinophils when off work vs. during work periods suggests an allergic airway response at work. This can occur as a feature of OA, and less commonly can occur as a more isolated finding of eosinophilic bronchitis (see further detail below). As with the other tests above, there can be false positive and negative results. The test can be affected by recent use of inhaled steroid medications for asthma, and by exposure to non-work-related allergic triggers. In addition, some patients with OA from a sensitizer do not have significant sputum eosinophils but instead have an increase in neutrophils (that also can be seen in chronic bronchitis or in infective bronchitis).

Specific laboratory challenge tests are considered a “gold standard” for diagnosis, but carry some risk, are very time-consuming and are not always a practical option. For these reasons they are seldom currently performed in Ontario.
Combinations of tests, and estimating probability of occupational asthma

A combination of tests has been recommended for diagnosis when feasible since each individual test can be falsely negative or positive. In addition some tests may not be feasible (such as antibody tests for most chemical sensitizers, and serial tests at work and off work in a patient who has already left work and cannot return).

The course of asthma in a worker who has left work and is not able to undergo objective testing may allow some estimate of probability of OA. If there was an objective assessment that confirmed asthma while working and if there is comparative evidence showing significant improvement since leaving work where there was a known sensitizer (and the improvement cannot be explained on the basis of asthma medications or other exposures), then this provides some support for OA. Lack of improvement does not rule out OA but makes it somewhat less likely. A history of previous childhood asthma or aspirin sensitivity and nasal polyps also does not rule out OA, but without other supporting information, the diagnosis becomes less likely.

Irritant-induced OA

This refers to OA induced by a high level irritant exposure, usually from an accident or fire at work. Unlike OA from a sensitizer there is usually no latency period – asthma symptoms generally start within 24 hours after the accidental exposure. The exposure may be high levels of irritating gases, fumes, smoke or dusts, and typically asthma symptoms are severe enough to lead to an unscheduled visit to the emergency department or health care provider within 24 hours. Typically symptoms persist for at least 3 months, with no preceding respiratory disease, and pulmonary function changes of asthma are documented (a significant bronchodilator response and/or positive methacholine challenge as detailed earlier).

When all the above features are present, a diagnosis of Irritant-induced OA can be made with confidence (initially termed Reactive Airways Dysfunction Syndrome, RADS). Difficulty in diagnosis arises when these typical findings are not all present: e.g. symptoms start several days after the exposure, or do not lead to a physician visit initially, or symptoms last for less than 3 months, or have cleared before pulmonary function tests were performed and were then normal, or if the worker had a significant smoking history and possible preceding COPD. No additional tests can be performed to clarify the diagnosis and decisions may have to be reached on the balance of probabilities with the information available.

Some information suggests that there is an increased risk of developing asthma from exposures to workplace irritants that are not massive, e.g. to spray cleaning products, but currently this cannot be clearly determined for an individual worker and cannot be distinguished from the coincidental onset of asthma.
Work-related Asthma

Work-exacerbated Asthma

In addition to OA, work exposures can aggravate or exacerbate (transiently worsen) asthma in workers who have asthma that is not caused by work. Individuals with asthma have more reactive airways and typically asthma symptoms can be worsened with exposure to cold dry air, by exercise, by exposure to dusts, smoke, fumes or sprays or by exposure to common environmental allergens to which the patient has an allergic response. Even without an allergic response, these exposures are likely to lead to asthma symptoms and transient airway narrowing, especially if asthma is severe or not well controlled. If such exposure occurs at work and worsens asthma symptoms, this is termed WORK-EXACERBATED ASTHMA.

It has been estimated that work-exacerbated asthma occurs in up to 25% of workers with asthma. It can commonly cause a short-term worsening of symptoms that may lead to no time off work or a few days off work. Less often, especially if the triggering exposure occurs on a daily basis at work, it may lead to more prolonged worsening of asthma and greater time off work. If the worker developed their asthma coincidentally while working and then has daily worsening of symptoms at work, then there may be suspicion of OA, especially if there is also a known exposure to a sensitizer. The worker should then be investigated as thoroughly as possible as indicated above, to try to identify whether the diagnosis is truly OA as described earlier or work-exacerbated asthma. Some of the tests used to diagnose OA may also be positive in patients with daily or frequent work-exacerbated asthma, e.g., peak flow readings, symptom scores and medication needs may worsen at work, and in a few patients there can be an improvement in methacholine PC20 when away from work. Specific IgE antibodies to a specific work agent would not be expected in work-exacerbated asthma, and an improvement in induced sputum eosinophils would not be expected in work-exacerbated asthma.

It has generally been considered likely that work-exacerbated asthma results in temporary worsening of asthma. It is not known whether work-exacerbated asthma can cause permanent worsening of asthma severity. This is difficult to determine since asthma is a variable condition and studies over time have suggested that unrelated to the workplace, about one third of those with asthma will worsen, one third improve and one third stay the same. Therefore, for an individual with asthma (that has not been caused by work), it is difficult to determine whether an aggravation at work has changed the long-term course of their asthma.

Other Difficulties in Diagnosis

A definite diagnosis of asthma requires pulmonary function tests showing the changes as described under OA. Asthma-like symptoms are more common than true asthma, and can have other causes, e.g., rhinitis (nasal symptoms), or gastro-oesophageal reflux can result in a cough that may mimic asthma, and bronchitis or other lung disease (such as bronchiectasis) may cause similar symptoms.
Some patients develop laryngeal symptoms that also may mimic asthma but have a different mechanism. This is termed “irritable larynx syndrome” and in some patients may include “vocal cord dysfunction syndrome”. It may occur as the sole cause of symptoms or may coexist with asthma and can then be a reason for poor response to asthma management. It typically causes symptoms of neck tightness, hoarseness, difficulty breathing in and wheezing when breathing in. It is important to recognize since it is different from asthma, and requires different treatment. This diagnosis is usually confirmed by assessment of the upper airway by an ear-nose-and- throat specialist with expertise in this disorder.

Another condition that is uncommon but can cause asthma-like symptoms and can be caused by sensitization to a work agent is eosinophilic bronchitis. This term refers to an inflammation of the airways, that can be caused by a sensitizer at work and can cause cough and chest tightness but the breathing tests for asthma are typically normal in this condition. This can be diagnosed by induced sputum cytology testing if available, ideally repeated both at the end of a working week and after a period off work to identify any work-related changes. If caused by work, the management is similar to that of OA.

**Management of work-related asthma**

This discussion paper is focused mainly on diagnosis. Management of work-related asthma differs dependent on the type of work-related asthma. The key management of OA due to a sensitizer is to completely avoid further exposure to that substance. This will usually require a change in work to a different area or different workplace where there is no airborne exposure to the agent (use of a respirator is not an adequate alternative). In addition medications are used as for other asthma, and exposure to other asthma triggers should be controlled. Asthma does not always clear after removal from exposure, but usually improves. However patients with OA who move to a different work area or different workplace could then develop work-exacerbated asthma if exposed to asthma triggers at work.

Patients with OA from an irritant exposure and those with work-exacerbated asthma may be able to continue the same work but may require modifications to reduce potential exposure to irritant agents that may exacerbate their asthma (short term use of respirators may be appropriate to prevent asthma symptoms associated with transient exposures). Asthma medications should be optimized and exposures to relevant asthma triggers outside the work environment should be minimized.

**Further resources**

**Work-related asthma web tool** (developed as an educational tool on work-related asthma)

http://lung.ca/workrelatedasthma/
Additional reading


