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# Occupational asthma in Australia

## Highlights

About 9–15% of adult-onset asthma cases can be attributed to exposures at work. Precise data are not available, but based on research from Australia and overseas, there may be as many as 1,000–3,000 new cases of occupational asthma each year in Australia. People with occupational asthma often have to change jobs or careers to relieve their symptoms; hence, work disruption and economic hardship are common consequences of the disease.

Occupational asthma is a type of asthma where the cause is often acknowledged. Individuals at high risk of developing this disease include those with a family history of asthma, previous sensitisation to one or more allergens, exposure to tobacco smoke, and, most importantly, employment in a high-risk workplace.

Numerous workplace agents (300–400 to date) can cause occupational asthma in susceptible individuals. Among the most common causes of occupational asthma in Australia are wood dust from trees such as the Western red cedar, isocyanates (the raw materials used in polyurethane products), paint fumes, solvents, latex, and flour. Manufacturing and health/community services tend to be the industries with the workplaces of highest risk.

Although not curable, occupational asthma is largely preventable through actions that avoid or reduce exposure to workplace sensitisers and irritants. The ability to predict which people are likely to develop occupational asthma is mixed and requires further investigation and review. There is also a need to gather more systematic data on the causes, prevalence, incidence and impact of occupational asthma in Australia.

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## Introduction

Asthma is a chronic inflammatory disease of the airways that affects more than 2 million Australians. A great deal has been learned about this complex disease in recent years, including the factors that provoke attacks or worsen symptoms. However, the exact causes are largely unknown and the relationships between the key characteristics of asthma (see Box 1) are not fully understood (O'Byrne & Inman 2003; Pearce et al. 1999; Prescott & Tang 2004). Asthma can develop at any time in life but it has been estimated that about 50–60% of all cases develop in adulthood (Flattery et al. 2006). Among adult-onset cases, clear causal relationships can sometimes be established between the disease onset and exposure to agents in the workplace.

Asthma caused by exposure to agents in the workplace is commonly referred to as occupational asthma. Together with pre-existing asthma provoked or worsened by environmental conditions or substances at work (work-aggravated asthma), it is one of the most commonly reported occupational respiratory disease in Australia and other developed countries (ASCC 2006; Banks & Jalloul 2007; Elder et al. 2004; McDonald et al. 2000; Newman Taylor et al. 2004).

Occupational exposure accounts for up to 15% of new asthma cases in adults. However, as a type of asthma with known causes, occupational asthma is largely preventable through the effective control of exposure to causal agents. This bulletin addresses several key questions regarding this form of asthma:

1. What is occupational asthma? (How is it defined, what are the different types, and in what ways does is differ from 'normal' and work-aggravated asthma?)
2. What causes it? (What are the factors that increase the risk of occupational asthma and which occupations present the greatest risks?)
3. How common is the disease? (What is the prevalence and incidence of occupational asthma in Australia?)
4. What are its consequences? (How does occupational asthma affect the individual and the health-care system?).

Accurate measures of the prevalence and incidence of occupational asthma can be used to target where interventions are needed and to monitor and evaluate their effects. This bulletin includes a discussion of the monitoring and surveillance of the disease and its risk factors.

**Box 1: Definition and characteristics of asthma**

*Asthma is defined by the expert panel of the National Asthma Education and Prevention Program, US National Heart, Lung, and Blood Institute, as:*

*'… a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role, in particular, mast cells, eosinophils, T lymphocytes, neutrophils, and epithelial cells. In susceptible individuals, this inflammation causes recurrent episodes of wheezing, breathlessness, chest tightness, and cough, particularly at night and in the early morning. These episodes are usually associated with widespread but variable airflow obstruction that is often reversible either spontaneously or with treatment. The inflammation also causes an associated increase in the existing bronchial hyperresponsiveness to a variety of stimuli' (National Asthma Education and Prevention Program 1997:3).*

## About occupational asthma

Occupational asthma is new-onset asthma in which the underlying cause is exposure to an agent at work. It is distinguished from work-aggravated asthma in that the individual has not had asthma previously. That is, in occupational asthma, workplace exposures cause new cases of asthma, while in work-aggravated asthma, workplace exposures provoke (or 'trigger') symptoms of existing asthma. Up to 15% of cases of asthma in working-age adults can be attributed to exposures in the workplace (Balmes et al. 2003; Blanc & Toren 1999).

Occupational asthma can be either allergic or non-allergic (see Box 2). Allergic occupational asthma is often referred to as sensitiser-induced occupational asthma, while non-allergic occupational asthma is commonly referred to as irritant-induced occupational asthma. Sensitisers are agents that make the airways sensitive so that they react to subsequent exposure to the same agent and often to other sensitisers, irritants and triggers such as cold air. Therefore, people with sensitiser-induced occupational asthma are sensitised to at least one allergen in their workplace, which on subsequent exposure causes an allergic immune response in the airways. Irritants are agents, such as chemicals, that cause adverse reactions in the airways, particularly localised inflammation.

Approximately 90% of occupational asthma is sensitiser-induced, with the remaining 10% being irritant-induced (Henneberger et al. 2003; Newman Taylor et al. 2004; Tarlo & Liss 2003). Some people with work-aggravated asthma may also be sensitised to agents in the workplace and develop occupational asthma (Banks & Jalloul 2007).

Whereas sensitiser-induced occupational asthma involves an allergic immune response, irritant-induced occupational asthma occurs shortly after a high level of exposure at work to a respiratory irritant such as a gas, smoke, fume or vapour (Alberts 1996; Chatkin et al. 1999). It may result from a single or multiple high-level irritant exposures. While the precise mechanism involved in irritant-induced occupational asthma is not known (Lombardo & Balmes 2000; Mapp et al. 2005), inflammation following injury to the bronchial epithelium is a likely initial stage.

In sensitiser-induced occupational asthma, there is a time delay between first exposure and the onset of symptoms (Youakim 2001). The time delay can vary depending on biological variability, the causal agent and the management of exposure. The delay can be many years; however, occupational asthma is most likely to develop in the first years of exposure for workers exposed to agents such as isocyanates, laboratory animal allergens, platinum salts and enzymes (Newman Taylor et al. 2004). For irritant-induced occupational asthma, the sudden onset of asthma occurs within hours of exposure to very high concentrations of inhaled irritants in the workplace (Vandenplas & Malo 2003).

### Box 2: Allergic and non-allergic asthma

*Approximately 65–80% of asthma cases are the result of an allergic immune response occurring in the airways (Court et al. 2002; Faniran et al. 1999; Miraglia Del Giudice et al. 2002; Plaschke et al. 1999). People with this form of asthma are sensitised to at least one allergen in their environment and are therefore said to have allergic (or immunologic) asthma. Their allergic immune response is mediated by certain antibodies, especially immunoglobulin E (IgE), and is often referred to as IgE-mediated hypersensitivity (or Type 1 hypersensitivity). Pre-existing allergic sensitisation, or atopy, is an important risk factor for the development of allergic asthma (Faniran et al. 1999; Illi et al. 2001; Lombardo & Balmes 2000). Other risk factors include a family history, tobacco smoking and exposure to allergens (e.g. house dust mites, cats, cockroaches, pollen and moulds).*

*In contrast with allergic asthma, non-allergic (or non-immunologic) asthma does not involve sensitisation and may be caused by a chemical irritant or virus, among other yet-to-be-discovered causes (Novak & Bieber 2003). Risk factors for non-allergic asthma include tobacco smoking and exposure to irritants in the workplace. Non-allergic asthma is less frequently associated with a family history of asthma (Nieves et al. 2005).*

*Allergic and non-allergic asthma share more similarities than differences. For example, even though the risk factors for the two types are different, the inflammatory response in the airways is very similar and the symptoms are essentially the same (Novak & Bieber 2003). An important difference involves the specificity of airway hyperresponsiveness (AHR) that people with allergic or non-allergic asthma tend to have. People with allergic asthma typically have specific airway AHR, which means their airways respond and narrow when re-exposed to small amounts of the original sensitising agent. They usually also have non-specific AHR, in which their airways narrow when exposed to non-specific triggers such as exercise, cold air, air pollutants, viruses, and some medications and food preservatives. Those with non-allergic asthma usually have non-specific AHR, but they tend not to have specific AHR (Youakim 2001).*

## Reactive airways dysfunction syndrome

Irritant-induced occupational asthma results from one or more exposures to a respiratory irritant. A subtype of irritant-induced occupational asthma is 'reactive airways dysfunction syndrome' (RADS), which results from a single exposure to high concentrations of an irritant (Brooks et al. 1985). RADS occurs within 24 hours of a single exposure large enough to cause injury to the airways. Unlike other types of occupational asthma, RADS is typically not preceded by sensitisation.

People with RADS have respiratory symptoms that persist for at least 3 months. The acute symptoms are probably associated with airway inflammation following epithelial injury—but the reasons for the persistence of symptoms are unclear (Alberts 1996). Whereas allergic occupational asthma is induced only by sensitisers, RADS can be caused by substances that are purely irritants as well as those that may act as sensitisers for other people, provided the exposure is at irritant level (Banks 2001). A substance such as toluene diisocyanate may be a sensitiser for some people and, at higher concentrations, an irritant for others (Banks 2001; Chatkin et al. 1999).

RADS is characterised by reversible bronchial constriction as well as airway inflammation and hyperresponsiveness (as with sensitiser-induced occupational asthma). However, RADS is not associated with a latency period between exposure and onset of symptoms (unlike sensitiser-induced occupational asthma), and people with RADS do not have subsequent attacks when exposed to small amounts of the causal irritant (Alberts 1996). To distinguish it from irritant-induced occupational asthma of a delayed or progressive nature, RADS may be best considered as 'acute irritant-induced asthma' or as 'sudden-onset irritant-induced asthma' (Francis et al. 2007; Mapp et al. 2005; Vandenplas & Malo 1997).

In terms of persistence of symptoms, use of health-care services, days off work, and applications for workers' compensation, the impact of RADS is at least as great as that of other occupational and work-aggravated asthma (Henneberger et al. 2003). However, accounting for probably less than 1% of adult asthma, RADS is relatively rare in Australia (Johnson et al. 2006b).

## Occupational risk factors

Risk factors for asthma are anything that increases the chance of developing the disease. These include factors that predispose an individual to developing asthma, agents that cause the onset of asthma, and factors that trigger or worsen symptoms in those with existing disease. Asthma may actually be a cluster of related diseases rather than a single disease (Burke 2003; van Woerden 2004; Wardlaw et al. 2005). Consequently, the causes and risk factors for asthma are varied.

In occupational asthma, exposure to certain agents at work causes new cases of the disease; whereas in work-aggravated asthma, symptoms are made worse or more frequent by exposure to triggers at work. This section describes some of the known risk factors for occupational asthma. These include tobacco smoking, previous allergic sensitisation and genetic predisposition (Newman Taylor et al. 2004; Venables & Chan-Yeung 1997). However, findings from several studies, including cohort studies, show that the level of exposure to workplace sensitisers and irritants is most important for developing occupational asthma (Gautrin et al. 2003; Newman Taylor 2002; Sastre et al. 2003; Tarlo et al. 1997). In other words, if exposure does not occur, the disease will not occur (Curran & Fishwick 2003).

## Causal agents (sensitisers and irritants)

There are numerous agents (at least 300–400 to date) that have been cited as causing occupational asthma. In Finland, an estimated 30% of the total workforce is exposed to respiratory pollutants in the workplace, and about 13.5% are exposed to occupational sensitisers (Rantanen & Lehtinen 1992, cited in Reijula et al. 1996). Data from the Finnish Registry of Occupational Diseases show that about 69% of occupational asthma cases are caused by flours, grain dusts, fodders and the skin, hairs and secretions of animals (Karjalainen et al. 2000).

Occupational asthma is caused by workplace agents that have either a high or low molecular weight (Table 1). Common high molecular weight substances include latex, flour, grains, enzymes and laboratory animal antigens; common low molecular weight causal agents include isocyanates and Western red cedar dust.

**Table 1: Selection of high and low molecular weight agents causing occupational asthma**

| High molecular weight agents | Low molecular weight agents |
|---|---|
| **Animal** | **Chemicals** |
| Animal allergens (e.g. dander, urine) | Isocyanates (e.g. toluene diisocyanate) |
| Crustaceans (prawns, crabs) | Acid anhydrides |
| Egg protein | Complex amines |
| Bird products | Reactive dyes |
| Arthropods | Methyl methacrylate |
| **Plants** | Glutaraldehyde |
| Grain dust | Formaldehyde |
| Coffee bean dust | **Metal salts, dusts or fumes** |
| Wheat flour | Platinum |
| Rye flour | Cobalt |
| Soy flour | Chromium |
| Latex | Nickel |
| Plant allergens (e.g. pollens) | **Wood dusts** |
| **Fungi** | Western red cedar |
| Moulds | Redwood |
| Yeasts | Oak |
| **Enzymes** | **Pharmaceuticals** |
| Pancreatin | Penicillins |
| Pepsin | Tetracycline |
| Trypsin | **Other** |
| Fungal amylase | Colophony in solder flux |
| Alcalase | Aluminium potroom emissions |

*Sources:* Chan-Yeung & Malo (1994); Lombardo & Balmes (2000); Mapp et al. (2005); Venables & Chan-Yeung (1997).

The distinction between high molecular weight (HMW) and low molecular weight (LMW) agents is important as it appears that the size of the causal agent affects the disease mechanism—the mechanism for HMW agents being better understood (Youakim 2001). High molecular weight agents, such as animal and vegetable proteins, seem to act through immunoglobulin E (IgE)-mediated hypersensitivity. That is, they cause sensitiser-induced occupational asthma by stimulating the production of IgE antibodies in an early-phase allergic immune response (Mapp et al. 2005).

On the other hand, LMW agents, which include organic and inorganic compounds, cause a less well-defined immune response that generally does not involve an IgE-mediated allergic immune response (Mapp et al. 2005). This includes the majority of LMW chemicals, such as isocyanates, Western red cedar and acrylates. However, some LMW agents usually do act through IgE-mediated hypersensitivity; these include acid anhydrides, platinum salts and reactive dyes (Sastre et al. 2003; Vandenplas et al. 2003; Venables & Chan-Yeung 1997).

Most of the studies demonstrating a direct relationship between allergen exposure at work and occupational asthma also showed a positive exposure–response relationship for sensitisation. This means that higher exposure to many of the causal workplace agents increases the risk of sensitisation and occupational asthma, particularly for agents acting through IgE-mediated hypersensitivity, such as flour allergens, laboratory animal allergens, acid anhydrides, platinum salts and enzymes (Sastre et al. 2003).

### *At-risk occupations*

At-risk occupations are those in which workers may be exposed to sufficient levels of causal agents to develop occupational asthma. Surveillance systems and population-based studies have found the occupations with the greatest risk for occupational asthma to be farming, painting, cleaning, baking, animal handling (e.g. veterinary care and laboratory technicians) and chemical work (Karjalainen et al. 2000; Kogevinas et al. 1999; Newman Taylor et al. 2004; Reijula et al. 1996). Other at-risk occupations include nursing, welding, food processing, dentistry, laboratory work, storage work, and work in the timber, forestry, electrical, electronic production, metal, plastics, rubber, and textile industries (Newman Taylor et al. 2004).

When causal agents are examined individually, the incidence of asthma can vary greatly and covers a wide variety of occupations (Table 2).

**Table 2: Selected causal agents, incidence and occupations in which exposure may occur**

| Agent | Incidence in exposed subjects | Associated occupations |
|---|---|---|
| Isocyanates | Approximately 5% | Adhesive industry, automotive industry, carpenter, chemical industry, coachworks, foundry worker, joiner, mechanic, metallurgist, painter, plastics industry, tinsmith |
| Wood dust | 3.4–13.5% | Builder, carpenter, joiner, model builder, paper industry, polisher, sander, saw mill employee, woodcutter |
| Flour and grain dust | Proportional to the frequency and duration of the exposure to the risk and directly related to the workplace conditions for some agents<br>5–24% for others | Animal breeder, animal foodstuffs industry, baker, butcher, cannery factory employee, coffee packer, combine harvester driver, confectioner, cook, delicatessen employee, docker, food industry, grocer, miller, pastry cook, pizza maker, seed packer |
| Animals | 10–32% | Animal breeder, biologist, food processing industry, pet shop employee, pharmaceutical industry, veterinary surgeon |
| Latex | 2.9–5.5% and attains 8% in subjects who are regularly exposed to this product | Toy manufacture, hospital staff, surgical glove manufacture, medical personnel, nurse, surgeon, textile industry |
| Formaldehyde | 30% | Carpenter, chemical industry, cosmetics industry, embalmer, foundry worker, hairdresser, laboratory staff, medical personnel, nurse, paper industry, plastics industry, rubber industry, tanner |
| Platinum salts | 10% with precautions in place (>50% initially) | Chemist, dentist, electronic components industry, electronics industry, jeweller, metallurgist, nurse, photographer, refinery worker |

*Source:* Asmapro (2006).

### *In Australia*

An occupational respiratory surveillance scheme in Victoria and Tasmania (Surveillance of Australian Workplace Based Respiratory Events—SABRE) reports on the causal agents of occupational asthma cases in these states. Wood dust from trees such as the Western red cedar (accounting for 13.5% of reported diagnoses) and isocyanates (5.8%) were the most common causal agents reported in the first 3.5 years of the scheme (Elder et al. 2004). Other causal agents commonly reported in Victoria and Tasmania were paint fumes, aluminium potroom gas/fumes, solvents, latex, flour and products of thermal combustion such as tobacco smoke. It should be noted, however, that the distribution of high-risk industry sectors, such as underground mining, differs in these two states compared to the rest of Australia (Elder et al. 2004). Findings from SABRE, therefore, may not be representative of Australia as a whole.

## Tobacco smoking

There is evidence that tobacco smoking worsens work-aggravated asthma (Mapp et al. 2005). There is also some evidence that tobacco smoking contributes to the risk of occupational asthma by increasing the likelihood of sensitisation by some causal agents (Lombardo & Balmes 2000; Youakim 2001). However, for some agents, studies provide conflicting evidence and the role of tobacco smoking is less clear. For example, when combined with smoking, exposure to isocyanates, platinum salts, salmon and snow crab

increases the risk of occupational asthma compared to exposure alone (Newman Taylor et al. 2004), but the relationship between smoking and the risk of developing occupational asthma is unclear when the causal agent is laboratory animals, enzymes or acid anhydrides (Newman Taylor et al. 2004).

## Previous allergic sensitisation

Atopy is the tendency to produce IgE antibodies in response to exposure to low, usually harmless doses of common allergens (Johansson et al. 2001). The result of such exposure is an IgE-mediated allergic immune response, as seen in most cases of occupational asthma. Many studies have found that people with previous allergic sensitisation, particularly those with other IgE-mediated allergies, are more likely to be sensitised to agents encountered in the workplace, especially HMW substances (Huovinen et al. 1999; Jaakkola et al. 2006; Lombardo & Balmes 2000; Plaschke et al. 2000; Porsbjerg et al. 2006; Wolfe et al. 2000; Xuan et al. 2002).

In particular, it has been shown that in workers exposed to isocyanates, detergent enzymes, laboratory animals, other animals, some reactive dyes, or flour, atopy increases the risk of occupational asthma (Newman Taylor et al. 2004). However, the evidence for an association between atopy and occupational asthma is conflicting for some agents. For example, some studies have failed to demonstrate an association involving isocyanates or detergent enzymes, as well as associations for agents such as cork, crab, salmon, platinum salts, and glutaraldehyde (Newman Taylor et al. 2004).

Occupational rhinitis (hay fever) is an IgE-mediated condition that frequently co-exists in people with sensitiser-induced occupational asthma (Huovinen et al. 1999; Malo et al. 2004; Nicholson et al. 2005). There is some evidence that the risk of developing occupational asthma is highest within a year of the onset of occupational rhinitis (Karjalainen et al. 2003; Nicholson et al. 2005). It has also been reported that people develop rhinoconjunctivitis—a combination of rhinitis and conjunctivitis (infection or inflammation of the membrane lining the eyelids)—before the onset of sensitiser-induced occupational asthma (Grammer et al. 2002; Malo et al. 1997; Mapp et al. 2005; Nicholson et al. 2005).

## Genetic predisposition

Asthma most likely occurs when environmental factors affect genetically susceptible individuals (Yang et al. 2007). The role of genetic susceptibility, or predisposition, in asthma has been demonstrated in studies of families, which have shown that approximately 50% of asthma risk is genetically determined (Cookson 2002; Host & Halken 2000). In particular, studies of twins demonstrate that genetically identical individuals (identical twins) have a higher probability of both individuals developing asthma than genetically similar but not identical individuals (fraternal twins) (Duffy et al. 1990). Also, gene variants have been found that are more common in people with asthma than in those without asthma.

Genetics may partly explain why an individual is allergic to a specific allergen (such as house dust mite or cat dander) but not another. Similarly, genetic predisposition may explain why not all individuals exposed to the same agent develop occupational asthma. For example, although diisocyanates are the LMW agents responsible for most cases of occupational asthma, only 5–10% of exposed workers develop the disease (Piirila et al. 2001).

The inheritance of asthma appears to be caused by multiple genes rather than a variation in a single gene, which means that the overall contribution of an individual gene or an individual gene variant may be quite low. Current knowledge suggests that asthma, and occupational asthma in particular, is a disease in which a large number of genetic variants are linked to subtle but harmful responses of the immune system and airways to environmental stimuli (Clarke et al. 2000; Patino & Martinez 2001).

Studies have shown that variants of certain genes may predispose a person to occupational asthma caused by a number of agents. For example, during the inflammation process, reactive oxygen damages tissues and causes some of the symptoms seen in asthma. Glutathione S-transferase (GST) is a family of enzymes that protects cells from reactive oxygen (oxidative stress) by acting as an antioxidant (McCunney 2005; Romieu et al. 2004). Variants of the GST gene may be particularly important in protecting against immune responses to diisocyanate exposure (Piirila et al. 2001). The gene for another enzyme, N-acetyltransferase, may also be involved in diisocyanate-induced occupational asthma, especially when toluene diisocyanate is involved (Wikman et al. 2002).

Class II human leucocyte antigens (HLAs) have been shown to be important in occupational asthma caused by exposure to LMW chemicals, including acid anhydrides, isocyanates and platinum salts. In a study of Canadian workers that developed occupational asthma due to plicatic acid from the Western red cedar tree, 43% had one of two variants of the HLA DQB1 gene, while only 13% of the reference population had either of the gene variants (Horne et al. 2000). The HLA class II proteins are associated with the immune system's recognition of foreign substances, such as viruses, bacteria and allergens. They have a crucial role in the immune response as they bind to parts of the proteins from these foreign entities and present them to white blood cells (T cells). The T cells then mount an immune response against those foreign (non-self) entities. Certain variants of the HLA genes have also been associated with IgE production following exposure to house dust mites and soybeans (Hizawa et al. 1998; Soriano et al. 1997). Other variants have been associated with sensitivity to apple, pollen, cockroach allergens, platinum salts and isocyanates (Balboni et al. 1996; Bignon et al. 1994; Donfack et al. 2000; Kim et al. 2001; Mapp et al. 1997; Senechal et al. 1999; Stephan et al. 1999).

As yet, there are no strong candidates for a genetic role in irritant-induced occupational asthma (Mapp 2003). However, among cases of irritant-induced occupational asthma that does not occur within 24 hours of exposure—that is, those that do not qualify as RADS—there may be an irritant–susceptibility interaction (Brooks et al. 1998).

While several associations between occupational asthma and gene variants have been made, the evidence is often conflicting and the relative contribution of the genes in determining susceptibility is not known. In any event, the dose of the causal agent absorbed by an individual is the main factor influencing who develops occupational asthma (Gautrin et al. 2003; Newman Taylor 2002).

## Prevalence and incidence

As with asthma in general, obtaining accurate estimates of the number of existing and new cases of occupational and work-aggravated asthma is challenging. Occupational asthma is a difficult disease to diagnose as there is no single validated clinical questionnaire. Nor is there a single criterion for interpreting changes in lung function, such as peak expiratory flow rates or bronchial hyperresponsiveness to specific agents (Moscato et al. 2003). There are also varying definitions of the disease and exposure (Lombardo & Balmes 2000). Notwithstanding these difficulties, administrative and survey data sources provide some indication of the prevalence and incidence of occupational and work-aggravated asthma. Before these data are examined, it is important to consider the proportion of adult-onset asthma that can be attributed to occupational exposures.

### Attributing asthma to occupational exposures

Systematic reviews of studies from various countries have concluded that 9–15% of asthma cases in working-age adults can be attributed to occupational exposures (Balmes et al. 2003; Blanc & Toren 1999; Newman Taylor et al. 2004). This includes occupational (new-onset) asthma and reactivated pre-existing asthma (asthma that has been asymptomatic for a long time). Put another way, up to 15% of adult-onset asthma could be prevented if exposure to known occupational agents were avoided. In Australia, from a survey of about 5,300 adults aged 18–49 years in New South Wales in 2000–01, an estimated 9.5% of adult-onset asthma cases were due to occupational exposures (Johnson et al. 2006b). This estimate falls within the now widely cited and accepted 9–15% range.

### Prevalence

The prevalence of occupational and work-aggravated asthma is usually estimated by population-based cross-sectional studies that rely on self-reports or, less commonly, clinical diagnosis. Case-control and clinical cohort studies are less common but normally involve clinical diagnosis.

Population-based surveys—which typically rely on self-reports and do not contain strict criteria for work-related onset—are usually best suited for estimating the prevalence of work-aggravated asthma rather than occupational asthma. Results from such surveys suggest that work-aggravated asthma may be quite common. Surveys in Australia, the United States of America and Finland have found that 20–25% of workers with asthma report worse symptoms at work (Abramson et al. 1995; Henneberger et al. 2002;

Saarinen et al. 2003). The Australian study by Abramson and colleagues (1995) included adults in Victoria with a history of asthma or with symptoms of asthma. In Finland, Saarinen and colleagues (2003) found work-aggravated asthma among 10% of workers with child-onset asthma.

Overall, the prevalence of occupational and work-aggravated asthma in Australia is difficult to determine from available data. Based on estimates from the National Health Survey, 2.2% of asthma among adults in 2004–05 was reportedly work-related. This estimate is not limited to adult-onset cases.

## Incidence

The incidence (new cases during a given period) of occupational asthma is most often estimated from case-based surveillance systems and medico-legal statistics, usually relying on physician reports.

### *Surveillance systems*

Occupational asthma is considered a sentinel health event in some industrialised countries. That is, the disease has such implications for workplace health and safety that each new case serves as a warning for greater exposure prevention or control.

The Surveillance of Work-related and Occupational Respiratory Disease (SWORD) system was introduced in the United Kingdom in 1989. It is a sentinel network operating under the Health and Occupation Reporting Network whereby specialists in thoracic and occupational medicine voluntarily report new cases of work-related respiratory disease.

A small number of states in the United States of America have surveillance and intelligence programs for occupational asthma as part of the Sentinel Event Notification Systems for Occupational Risks (SENSOR). SENSOR is a state-based program funded by cooperative agreements awarded by the National Institute for Occupational Safety and Health. Physician reporting of occupational diseases is mandatory under SENSOR, but the requirement for supplementary hospitalisation data varies between states.

Other systems that have operated or are still in use include the Notifiable Occupational Disease System in New Zealand, the Physician-based Surveillance System of Occupational Respiratory Disease in Quebec, Canada, the Surveillance of Work-related and Occupational Respiratory Diseases in South Africa system, and the Swedish Register of Reported Occupational Disease.

It is generally accepted that the recognition and reporting of work-related cases is less than systematic and therefore schemes such as SENSOR and SWORD probably underestimate the incidence of occupational asthma (Draper et al. 2003; McDonald et al. 2000; Romero Jajosky et al. 1999). SWORD is also limited by not including consultations with general practitioners (McDonald et al. 2000).

Finland has one of the most comprehensive occupational asthma notification systems. Physicians in Finland are required to report all known or suspected cases of occupational disease to provincial labour protection authorities, which pass the information on to the Finnish Registry of Occupational Diseases (FROD). Insurance companies also report every new case of occupational disease to FROD. Duplication of cases is removed from the system, which covers about 95% of the workforce (Karjalainen et al. 2000). Due to strict criteria for the diagnosis of occupational asthma, mild cases requiring occasional medication tend not to be included in the register (Reijula et al. 1996).

### *In Australia*

Two surveillance systems in Australia generate data on the incidence of occupational asthma. One is based on notification of diagnosed cases, the other on workers' compensation claims.

#### Surveillance of Australian Workplace Based Respiratory Events

The Surveillance of Australian Workplace Based Respiratory Events (SABRE) is an occupational respiratory disease surveillance (notification) system that has operated in Victoria and Tasmania since 1997 and in New South Wales since 2001. The system involves voluntary and anonymous reporting by respiratory and occupational physicians of occupational respiratory events encountered in their practices. The coverage is incomplete in that it does not include all physicians who see cases of occupational respiratory diseases.

Data from Victoria and Tasmania show that asthma is the most commonly reported occupational respiratory disease in these states. From November 1997 to October 2004, there were about 820 reported diagnoses of occupational respiratory disease (Sim et al. 2005). Of these diagnoses, about 265 (32.5%) were of occupational asthma and about 200 (24.5%) were of non-malignant pleural plaques.

In contrast, the SABRE system in New South Wales contains about 3,190 diagnoses of occupational respiratory disease reported between January 2001 and November 2007 (SABRE 2008). Of these diagnoses, 930 (29%) were of non-malignant pleural plaques, but only 80 (3%) were of occupational asthma.

The differences between the states in the reporting of occupational asthma may be due to actual differences in disease incidence (and causal factor prevalence), but it might also be due to under-reporting or under-diagnosis (Johnson et al. 2006a).

The lack of complete coverage across and within states means that SABRE data cannot be considered representative of Australia as a whole. A senate inquiry into workplace exposure to toxic dust held in May 2006 recommended that the SABRE scheme operate nationally and be compulsory (Senate Community Affairs References Committee 2006).

### The National Data Set for Compensation-based Statistics

The National Data Set for Compensation-based Statistics (NDS) consists of accepted workers' compensation claims. That is, it contains data from Commonwealth, state and territory workers' compensation agencies on cases that result in death, permanent disability or temporary disability involving 5 or more days off work. NDS data are used for occupational health and safety indicators. The data are available online via the Office of the Australian Safety and Compensation Council interactive database of national workers' compensation statistics (ASCC 2008).

In the 5-year period from 2000–01 to 2004–05, there were about 2,660 accepted claims for respiratory diseases, about 395 of which (about 15%) were for asthma. During this period there were also about 945 accepted claims for asbestosis (about 36% of all accepted claims for respiratory diseases). Whereas the number of accepted claims for asbestosis has increased from about 155 in 2000–01 to about 245 in 2004–05 (from 32% to 40% of accepted respiratory disease claims), accepted claims for asthma have fallen from about 95 to about 70 (20% to 11%).

In 2004–05, about 51% of the accepted asthma claims were for female workers, and about 33% were for workers aged 45–54 years. Manufacturing (25%) and health/community services (23%) were the industries with the highest proportion of accepted claims. About 11% of those with an accepted claim for asthma in 2004–05 were absent from work for 6 months or more.

NDS data do not cover all occurrences of occupational asthma as they do not include military personnel, self-employed workers, cases not claimed and cases not compensated under general Commonwealth, state and territory workers' compensation legislation. Furthermore, the percentages reported may not be exact as the data are adjusted for confidentiality purposes (hence the rounding to the nearest '5').

Another shortcoming of the NDS, and similar compensation-based systems, is that timely diagnosis and the establishment of work-relatedness cannot be guaranteed. Consequently, many cases of asthma are not recognised as work-related and therefore not included in the database. This is often the situation with diseases that follow a long period of exposure or if there is a long latency between exposure and symptoms.

#### *Incidence rates*

A recent international study by Kogevinas et al. (2007) estimated the incidence rate of occupational asthma to be 250–300 cases per million people per year. This study included data from 13 countries, including Australia. Malo and Gautrin (2007), however, suggest that the Kogevinas et al. (2007) incidence rate probably underestimates the incidence of all types of asthma in the workplace, but overestimates the incidence of occupational asthma.

### *In Australia*

An incidence rate of 250–300 cases per million workers per year as found by Kogevinas et al. (2007) would equate to about 2,400–2,900 cases of occupational asthma in Australia in 2003, given a labour force of about 9.5 million in that year.

Estimates from the Australian Burden of Disease and Injury Study suggest that there were 78,493 new (incident) cases of asthma in 2003 (AIHW: Begg et al. 2007). About 20,570 of these were in working-age adults (i.e. 15–64 years). Applying a population-attributable risk of 9–15% to this estimate, there may have been between 1,850 and 3,090 new cases of asthma in 2003 due to workplace exposures, giving an annual incidence rate of 195–325 cases per million workers per year (Table 3). This incidence rate range is similar to that proposed by Kogevinas et al. (2007), and includes a lower estimate similar to the average rate of 174 per million workers per year found in Finland by Karjalainen et al. (2000) and an upper estimate similar to the peak rate of 386 per million working-aged adults per year found by Reijula et al. (1996).

Some studies have attributed around 20% of adult-onset asthma to workplace exposures. For example, Johnson et al. (2000) estimated that 18% of adult-onset asthma in high-risk occupations and industries in Canada could be prevented by avoiding exposure to known occupational agents. However, a population-attributable risk of 15% appears to be a reasonable upper limit based on the findings of comprehensive reviews and meta-analyses (such as Balmes et al. 2003; Blanc & Toren 1999). On the other hand, in view of Malo and Gautrin's (2007) observation, an attributable risk of 5% as found by Reijula et al. (1996) in Finland may be a more conservative lower limit for estimating the incidence of occupational asthma in Australia than the 9% concluded by Blanc and Toren (1999), or the 9.5% found by Johnson et al. (2006b). When 5% is used as the lower boundary for the estimate, it gives a lower number of 1,030 new cases in 2003. Overall, this gives an estimated annual incidence rate of 110–325 cases per million workers per year (Table 3).

Allowing for a considerable degree of imprecision in these estimates (such as that which may be caused by the lag between exposure and disease onset in some cases, labour force participation patterns, and the ratio of males to females in new cases of asthma compared with new cases of occupational asthma), they point to a problem that is much larger than suggested by the available surveillance and compensation statistics.

**Table 3: Incidence of occupational asthma in Australia**

| Population-attributable risk (per cent) | Estimated number of cases (2003) | Incidence rate (cases per million workers per year) |
|---|---|---|
| 5 | 1,030 | 110 |
| 9 | 1,850 | 195 |
| 15 | 3,090 | 325 |

*Note:* Estimates based on estimated number of new asthma cases in 15–64 year olds in 2003 (20,570) and labour force as of June 2003 (9,507,500).
*Source:* AIHW: Begg et al. 2007.

## Consequences

Deaths from occupational asthma are rare and only a handful of hospital separations in Australia can be identified as work-related. However, international studies have shown that occupational asthma is associated with considerable morbidity and economic burden (Larbanois et al. 2002; Vandenplas et al. 2003).

There is often loss of income and associated financial hardship among people with occupational asthma. Some people with the disease may have to change jobs or job duties to avoid exposure to the agent that caused their disease, reduce their participation in the workforce or take strict precautions against exposure whilst at work. Blanc et al. (1999) have found that almost a quarter of those aged 20–44 years in Sweden with occupational asthma reported having to change or leave jobs due to the effects on their breathing. Occupational asthma can cause reduced job performance and lost work days. It can also leave a person severely disabled and consequently lead to early retirement.

Unemployment rates are high among workers with occupational asthma, with around one-third of workers unemployed up to 6 years after diagnosis (Newman Taylor et al. 2004). Between 25% and 38% of people with sensitiser-induced occupational asthma have prolonged periods of work disruption and as many as 78% experience a substantial loss of income (Vandenplas et al. 2003).

Symptoms of occupational asthma are more likely to improve or even cease with an early intervention, such as early diagnosis and removal from exposure to the causal agent (Banks & Jalloul 2007; Newman Taylor et al. 2004; Venables & Chan-Yeung 1997). Many patients, however, fail to recover completely. Several years after removal from the causal agent, about 70% of people with sensitiser-induced occupational asthma still experience symptoms and non-specific bronchial hyperresponsiveness (Vandenplas et al. 2003). People with irritant-induced occupational asthma may recover within months of ceasing exposure, but in some cases the symptoms persist for years or may be permanent (Alberts 1996). Both the duration of symptoms before removal from the causal agent and the severity of asthma at diagnosis have been associated with persistence of asthma.

While removal from exposure to the causal agent increases the chance of improvement in health, it may also increase the financial impact, which may explain why almost one-third of workers with sensitiser-induced occupational asthma remain exposed to the causal agent (Vandenplas et al. 2003). There is evidence that a reduction in exposure is less effective than avoidance in reducing the worsening or persistence of symptoms and non-specific bronchial hyperresponsiveness (Vandenplas et al. 2003). However, those who do not at least reduce their exposure to the causal agent and remain in the same job generally experience worsening asthma symptoms (Venables & Chan-Yeung 1997).

The few available studies into the socioeconomic impact of work-aggravated asthma show that it is also associated with a sizeable socioeconomic impact. In two studies, the rate of unemployment and the proportion of people reporting a reduction in income did not differ significantly in comparison to those with occupational asthma (Cannon et al. 1995; Larbanois et al. 2002). For example, a reduction in income has been found in up to 60–65% of people with either occupational or work-aggravated (Cannon et al. 1995; Larbanois et al. 2002).

### *In Australia*

Focus groups have been conducted in Victoria to examine the experiences and health, social and economic burdens associated with occupational asthma (Sim et al. 2005). In agreement with international findings, people with occupational asthma experienced significant economic impact in both the short and long term. Sim and colleagues also identified large social impacts among people with occupational asthma, including negatively affected social status at and outside the workplace, loss of key friendships and support networks, negative impacts on personal sense of worth, and loss of faith in themselves and others.

Data from the Office of the Australian Safety and Compensation Council online database of national workers' compensation statistics show that a considerable proportion of accepted claims for asthma involve more than 12 weeks of time lost from work (Table 4), although the proportion has fallen in recent years.

**Table 4: Time lost from work associated with accepted claims for asthma, 2000–01 to 2004–05 (per cent of accepted claims)**

| Time lost | 2000–01 | 2001–02 | 2002–03 | 2003–04 | 2004–05 |
|---|---|---|---|---|---|
| 1 week to less than 2 weeks | 30.5 | 25.3 | 16.7 | 25.1 | 23.1 |
| 2 weeks to less than 12 weeks | 30.0 | 30.1 | 34.7 | 35.6 | 45.6 |
| 12 weeks to less than 26 weeks | n.a. | 15.7 | 13.9 | n.a. | 10.0 |
| 26 weeks or more | 24.6 | 21.0 | 27.8 | 27.3 | 11.4 |
| Permanent incapacity | 10.7 | 7.9 | 6.9 | 7.1 | 10.0 |

n.a. = data not available due to privacy restrictions.
*Source:* Online statistics interactive National Workers' Compensation Statistics databases (see ASCC 2008).

## Disease and exposure monitoring

Measuring the extent, impact and causes of occupational asthma has many practical implications. Effective disease and exposure monitoring improves the capacity to make decisions for cost-effective allocation of resources, target priority populations groups and monitor the impact of intervention strategies.

As a type of asthma with known causal agents, occupational asthma is largely preventable and amenable to the surveillance and monitoring of its risk factors, prevalence and incidence. In recent decades, knowledge of the mechanisms involved in sensitiser-induced occupational asthma has improved considerably. However, large gaps remain in our understanding of the mechanisms involved in irritant-induced occupational asthma and those involved in sensitiser-induced occupational asthma caused by exposure to LMW substances (Lombardo & Balmes 2000).

## Monitoring prevalence, incidence and impact

Population-based surveys, compensation statistics and surveillance systems give an indication of the extent and distribution of occupational asthma as well as the main causal agents and occupations involved (Curran & Fishwick 2003; Gautrin et al. 2003). Administrative databases (e.g. the AIHW's National Hospital Morbidity Database) and population-based surveys (e.g. the Australian Bureau of Statistics' National Health Survey) provide additional information on outcomes associated with occupational asthma. However, all of these sources have severe limitations; especially the lack of clear and reliable identifiers for occupational asthma.

Findings from population-based surveys can provide an indication of the prevalence of an occupational disease or condition. However, if the survey is not actually population-based, it may be subject to biases reflecting the 'healthy worker effect 'or 'survivor effect'. The healthy worker effect is a bias associated with a general tendency for workers to be healthier than the wider population (Garcia & Checkoway 2003). The survivor effect is a bias associated with the loss of susceptible or affected individuals from the working population (Garcia & Checkoway 2003). Population-based surveys also tend to have high sensitivity (ability to identify probable cases) but low specificity (ability to distinguish between cases and non-cases); hence leading to overestimation of estimates (Gautrin et al. 2003).

The National Workers' Compensation Statistics Database contains data from Commonwealth, state and territory workers' compensation agencies on cases of work-related disease and injury. In theory, these data can be used to indicate the incidence of occupational asthma, however the derived incidence would almost always be an underestimate as not all cases can or do claim compensation. That is, occupational asthma is not a condition that is compensated routinely (Australian Centre for Asthma Monitoring 2004). In general, compensation statistics do not give an accurate indication of occupational asthma incidence.

At present, the major available data source for monitoring the incidence of occupational asthma is the Surveillance of Australian Workplace Based Respiratory Events (SABRE) scheme in Victoria, Tasmania and, more recently, New South Wales. The SABRE database is collected specifically for monitoring work-related respiratory diseases such as occupational asthma. A number of limitations of SABRE data have been identified, such as a low participation rate associated with the voluntary nature of the scheme and the accuracy of the physician's identification of the causal agents (Australian Centre for Asthma Monitoring 2004; Sim et al. 2005). Surveillance/notification systems generally underestimate the incidence of occupational asthma. Besides a lack of universal coverage, this is because information from surveillance systems can be compromised by differences in defining cases of occupational asthma, recognition of the disease, attribution to work exposures, and motivation of the physician to report cases, especially when the system is voluntary (Gautrin et al. 2003; Karjalainen et al. 2000). They may also lack data from primary care settings (Curran & Fishwick 2003).

Occupational asthma can place a heavy economic and social burden on the affected individual. However, there is little information about the outcomes for individuals in Australia, such as changes in employment status, income, quality of life and functioning.

## Monitoring exposures

Although atopy and variants of the HLA class II genes are important risk factors for occupational asthma, the level of exposure is the most important determining factor (Gautrin et al. 2003; Newman Taylor 2002). This places a greater emphasis on monitoring and eliminating, or at least controlling, workplace exposures.

In general, the surveillance and monitoring of asthma risk factors, particularly environmental factors, is complicated by the conflicting evidence for causal roles of some of these factors and for the effectiveness of exposure-avoidance strategies, especially with respect to the onset of asthma (Australian Centre for Asthma Monitoring 2005).

Public (i.e. government) surveillance and monitoring of occupational asthma typically concerns the prevalence and incidence of cases (e.g. case notification, compensation claims, self-reports on population-based surveys). Exposure monitoring is usually conducted at the industry or workplace level in compliance with state and territory occupational health and safety legislation. For example, Victoria's Occupational Health and Safety Regulations 2007 outline the employer's duty to identify and record any hazardous substances in the workplace and to control the associated risk. The employer is also required under the regulations to undertake atmospheric monitoring, provided exposure standards are applicable and there is no requirement for health surveillance involving biological monitoring.

National exposure standards and codes of practice for airborne substances in the workplace, including those recognised as sensitisers, exist under the *National Occupational Health and Safety Commission Act 1985*. However, these standards and codes of practices are not enforceable unless adopted by relevant Commonwealth, state or territory legislation.

## Monitoring genetic predisposition

Genetic predisposition, or susceptibility, plays a significant role in the development of asthma. Researchers are currently examining how underlying genetic predisposition affects the response to an environmental exposure that may lead to the development of asthma. However, in most cases, the cause of asthma remains unknown and it is not currently possible to identify individuals that are likely to develop the disease.

Atopy and atopic diseases such as allergic rhinitis are strong risk factors for asthma; but not all atopic people develop asthma. So, although testing for atopy may be feasible for some specific sensitisers—a positive skin-prick test for acid anhydrides or platinum salts, for example, is a good predictor of occupational asthma (Cullinan et al. 2003)—in general, the presence of atopy is not a good predictor of occupational asthma development (Mapp et al. 2005; Youakim 2001). As yet, the interactions between personal susceptibility factors and environmental factors are not well enough understood to justify preemployment screening (Lombardo & Balmes 2000; Youakim 2001).

At present, information about the genetics of occupational asthma has greater implications for the development of prevention or treatment strategies through the understanding of the cause and nature of the disease.

## Glossary

**Allergen:** an antigen that causes IgE-mediated hypersensitivity (allergy).

**Allergic (or immunologic) asthma:** asthma that involves an allergic immune response in the airways. People with this form of asthma are sensitised to at least one allergen in their environment.

**Antibody:** an immune cell produced in response to a specific antigen.

**Antigen:** a substance that when recognised by the immune system as non-self causes the production of antibodies and an immune response.

**Atopy:** a tendency (usually inherited) to produce IgE antibodies in response to low doses of common allergens, leading to symptoms seen in asthma, allergic rhinitis and eczema.

**Causal agents:** factors that cause individuals to develop asthma. They include sensitisers and irritants.

**Gene:** the basic unit of heredity, comprised of deoxyribonucleic acid (DNA) and occupying a specific location on a chromosome.

**Gene variant:** a naturally occurring variation in the DNA of a gene. Gene variations are usually harmless and are part of the genetic diversity in humans. They are also called 'polymorphisms'.

**Genetic predisposition:** an inherited increased risk of developing a disease. It is also called genetic susceptibility.

**IgE (immunoglobulin E):** an antibody that binds to mast cells and, when in contact with an antigen, causes the mast cell to release inflammatory mediators such as histamine.

**IgE-mediated hypersensitivity:** also called 'Type 1 hypersensitivity', the immediate allergic immune response stimulated by re-exposure to specific antigens. As seen in atopic diseases such as allergic asthma and hay fever.

**Immune response:** the body's defensive reaction to foreign antigens.

**Incidence:** number of new cases during a given period.

**Inflammation:** local immune response to injury, infection or allergy. It involves increased blood flow, immigration of white blood cells and release of toxins resulting in redness, heat, swelling and pain.

**Irritant-induced occupational asthma:** non-allergic occupational asthma.

**Isocyanates:** highly reactive low molecular weight chemicals used in the production of polyurethane foams, coatings, adhesives and insulation materials.

**Mast cell:** an immune cell that releases histamine and other inflammatory mediators in an IgE-mediated immune response. Mast cells are found in connective tissue and do not circulate in the blood.

**Non-allergic (non-immunologic) asthma:** asthma that does not involve an allergic immune response. Instead of sensitisation, the asthma may be caused by a chemical irritant or virus.

**Occupational asthma:** new-onset asthma where the cause of the asthma is exposure to an agent at work.

**Prevalence:** the number or proportion of cases among a population at a given time.

**Risk factors:** any environmental, chemical, physiological, psychological or genetic factors that increase the risk of developing a health disorder or other unwanted condition or event. In asthma, risk factors include those that predispose people to develop the disease, cause the disease, or trigger symptoms.

**Sensitisation:** the process of becoming hypersensitive to an allergen.

**Sensitiser-induced occupational asthma:** allergic occupational asthma.

**T cell:** a white blood cell that activates or regulates an immune response (includes helper T cells, suppressor T cells and killer T cells).

**Triggers:** factors that evoke or worsen symptoms in people who already have asthma. Some may also be causal factors.

**Work-aggravated asthma:** pre-existing or coincident asthma made worse by workplace exposures.

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## Abbreviations

| | |
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| HLA | human leucocyte antigen |
| HMW | high molecular weight |
| IgE | immunoglobulin E |
| LMW | low molecular weight |
| NDS | National Data Set for Compensation-based Statistics |
| RADS | reactive airways dysfunction syndrome |
| SABRE | Surveillance of Australian workplace Based Respiratory Events |

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