

Work-related asthma

Work-related asthma can be responsible for up to 25% of all adult asthma.

MOHAMED F JEEBHAY, MB ChB, DOH, MPhil (Epi), MPH (Occ Med), PhD

Professor, Centre for Occupational and Environmental Health Research, School of Public Health and Family Medicine, University of Cape Town

Mohamed Jeebhay is a Professor of Occupational Medicine at the University of Cape Town. He convenes the occupational medicine specialist training programme at UCT and co-manages the Fogarty International Centre programme aimed at promoting research and training in occupational and environmental health in southern Africa. His main research interest focuses on risk factors, surveillance and interventions for occupational allergy and asthma. He has served on many statutory technical committees related to OSH in South Africa. He is on the editorial board of Current Allergy & Clinical Immunology and the International Journal of Maritime Health.

E-mail: Mohamed.jeebhay@uct.ac.za

Occupational lung diseases such as asthma, COPD and pneumoconioses caused by exposure to airborne particulates are a major contributor to mortality and disability globally. However, work-related asthma remains under-recognised, poorly managed and inadequately compensated.^{1,2}

Work-related factors, depending on the industry, can be responsible for up to 25% of all adult asthma cases. International reviews suggest that the median proportion of adult cases of asthma attributable to occupational exposure is 16% and for work-exacerbated asthma around 10%.^{3,4}

Definition

Work-related asthma (WRA) can be broadly defined as (i) occupational asthma (OA) or asthma caused by specific agents in the workplace, and (ii) work-exacerbated asthma (WEA) or pre-existing asthma worsened by moderate-to-low level workplace exposures (e.g. dusts, smoke, fumes, sprays, cleaning agents) and

physical factors (e.g. cold air, humidity, strenuous work) (Fig. 1).⁴

There are two major forms of occupational asthma: (i) allergic (sensitiser-induced) asthma characterised by a latency period required for developing allergic sensitisation prior to the development of symptoms; and (ii) irritant-induced (non-immunological) asthma, characterised by rapid onset of asthma following single or multiple exposures to high levels of irritant compounds (e.g. chlorine and glutaraldehyde spills, smoke from fires, bleach and ammonia mixtures, sulphur dioxide and chlorine gas). Among these two major patterns, much higher proportions (70 - 90%) of allergic compared with irritant-induced OA are reported.¹

Epidemiology

The reported mean annual incidence of OA in developing countries is less than 2 per 100 000 compared with very high rates of up to 18 per 100 000 in Scandinavian countries.¹ This low figure is attributed to uneven industrial development, under-recognition and the

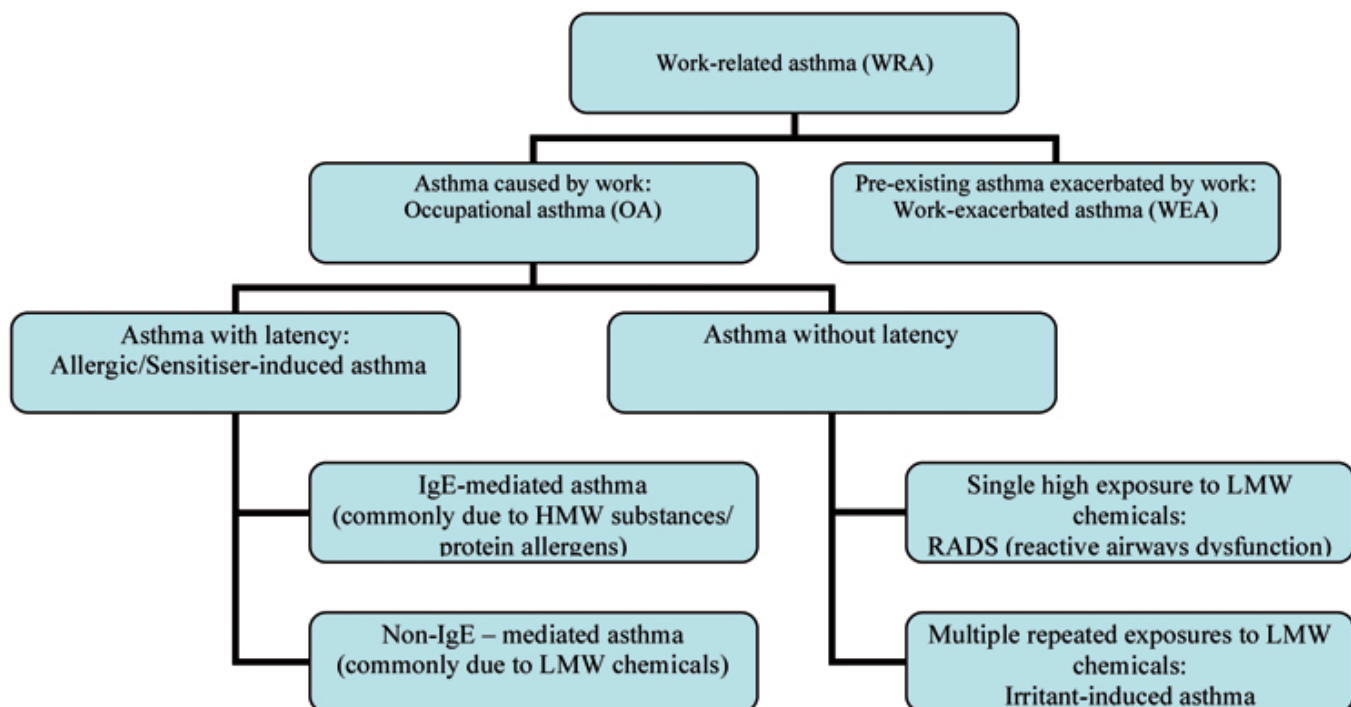


Fig. 1. Classification of work-related asthma.

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Reference: 1. Sciechitano R, Aalbers R, Ukena D, et al. Efficacy and safety of budesonide/formoterol single-inhaler therapy versus a higher dose of budesonide in moderate to severe asthma. *Curr Med Res Opin* 2004; 20(9): 1403-1418. 2. Global initiative for Asthma. Global strategy for asthma management and prevention. Revised 2006. Available at www.ginasthma.org.

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Asthma

relatively under-developed or non-existent surveillance systems in most countries, resulting in a large proportion of cases being unreported. Despite the relatively lower incidence (1.8/100 000) in South Africa, provincial differences exist, with a much higher incidence reported in the Western Cape (2.5/100 000), comparable with the USA and other European countries.⁵

High-risk industries and occupations

The patterns of WRA are quite diverse in various countries, demonstrating an array of economic activities associated with the disease. There are however some common industries and occupations that appear to be consistently associated with a higher incidence of OA.⁶ These include bakers and pastry makers, spray painters, especially in the car manufacturing industry, health

care workers and platinum refinery workers (Table I).⁵ In South Africa, a large proportion of epidemiological studies have been conducted in various food processing workplaces, reporting a much higher prevalence of work-related allergic asthma in grain (wheat) milling plants (17%) and bakeries (13%) than in animal processing plants (fish: 2%, poultry: 12%) (Table II). A

much high prevalence of WRA (15 - 30%) has also been reported among workers handling isocyanates in automotive repair shops and in chemical processing activities. Chemical processing plants such as platinum refineries appear to cause a much higher disease burden than vanadium plants. The prevalence of WRA in wood-working operations such as sawmills and furniture

Table I. Common industries /and or jobs associated with work-related asthma in developing countries

- Manufacturing: car/coach spray painters, bakers and pastry makers, grain milling, chemical/foam/plastic product workers, metal/electric/electronic workers, lumber/wood product workers, rubber product workers, pharmaceutical workers
- Health care and social work: health service workers
- Agriculture, forestry and fishing: farmers
- Service work: janitors/cleaners/ housekeepers
- Mining: platinum and vanadium refinery workers

Adapted from reference 1.

Table II. Epidemiological studies of work-related asthma in South Africa

Type of workforce (author, yr published)	N	Outcome measure	Agent/s implicated	Prevalence/ incidence (%)
Biological agents				
Grain mill (Jeebhay 2000, 2005)	111	Work-related grain dust allergic asthma*	Wheat, storage pests (mealworm, cockroach, storage mites)	17 %
(Yach 1985)	582	Asthma symptoms		23 - 25%
Grain mill (Bartie 2004)	84	Work-related asthma symptoms	Maize, storage pests (weevils)	7%
Soybean processing (Mansoor 2004)	115	Work-related soybean allergic asthma*	Soybean	IR: 2 per 1 000 person months
Supermarket bakeries (Baatjies 2009)	517	Occupational asthma	Cereal flour (wheat, rye) and fungal alpha-amylase	13%
Poultry processing (Rees 1998)	134	Asthma symptoms	Feed, poultry matter (feathers, droppings, serum)	12%
Seafood processing (Jeebhay 2008)	594	Occupational asthma	Fish products, fish parasite (Anisakis)	2%
Vineyards (Jeebhay 2007)	207	Work-related spider mite allergic asthma*	Spider mite	6%
Experimental laboratory (Lopata 2004)	10	Work-related locust allergic asthma*	Locust matter (wings, faeces, body)	30%
Hospitals (high risk) (Potter 2001)	717	Work-related latex allergic asthma*	Natural rubber latex protein	9%
Furniture plant (Pitt 1985)	27	Work-related asthma symptoms	Wood dust (yellow wood, stinkwood, blackwood, imbuia)	7%
Sawmill plant (Fox 2004)	392	Asthma	Wood dust (pine wood)	3%
Chemical agents				
Chemical processing/ packaging (Soderlund 1993)	20	Work-related asthma	Toluene di-isocyanate	30%
Automotive spraypainting (Randolph 1997)	40	Asthma symptoms	Hexamethylene di-isocyanate	10 - 15%
Platinum refinery (Calverley 1995)	78	Platinum salt sensitivity	Platinum salts	24 month CI: 41%
Vanadium plant (Irsigler 1999)	1440	Asthma symptoms	Vanadium pentoxide	24 month CI: 11%

CI: cumulative incidence, IR: incidence rate.

* Work-related asthma symptoms + allergic sensitisation with or without spirometry changes.

Adapted from reference 1.

plants appears to be much lower (3 - 7%). Notably absent are epidemiological studies on irritant-induced asthma, despite the presence of large industries where high-risk exposures may be more prevalent. As for studies on WEA, a recently published study of supermarket bakery workers reported a prevalence of 3% in this group.⁷

Causative agents

There are more than 350 agents known to cause OA, which are broadly classified into high molecular weight substances (proteins) and low molecular weight substances (chemicals).⁴ In most industrialised countries the main causes of asthma include isocyanates, cereal flour/grain dust, welding fumes and wood dust (Table III).¹ Exposure to animal epithelia, hairs and secretions is commonly reported among laboratory animal workers and agricultural workers. Latex allergy-related asthma appears to be less common due to the introduction of latex-free gloves in most health care settings. However, the introduction of new agents (hair dyes, hair fixing, hair waving solutions) containing persulfates in the hairdressing industry and domestic household cleaning sprays are emergent causes.

In developing countries the spectrum of agents causing OA is more diverse and less consistent.¹ Between 1997 and 1999 SORDSA, the surveillance programme in South Africa, reported isocyanates (a component of automotive spray paints and polyurethane foam products), latex proteins, flour and grain, and platinum salts as the most common agents.⁵ In a study of patients presenting with acute asthma in emergency casualty units at two large public hospitals the most commonly cited exposures were cleaning agents, dyes and paints.⁸

Diagnosis

While approaches to the diagnosis of WRA may vary between various countries, a stepwise approach is often used in most countries, the extent of the investigation being largely dependent on the definition subscribed to, the purpose of the investigation and the level of diagnostic capabilities available. The recently published ACCP Consensus Statement outlines the approach recommended for

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the diagnosis and management of WRA.⁴ The panel recommended that WRA (OA and WEA) should be considered in all adult patients with new-onset or worsening asthma through taking an appropriate history. Thereafter, the diagnosis of asthma should be confirmed and the patient investigated to determine the presence of WRA, performing these tests, whenever possible, *prior* to advising the patient to change jobs. The following approach can be used:

Assess the probability of WRA based on history

In all individuals, document the onset and timing of symptoms, medication use and their temporal relationship to periods at and away from work. The following questions can be asked of any patient with asthma that starts or becomes worse during work:

- Were there any symptoms prior to working in this current job?

- Were there any changes in work processes in the period prior to the onset of symptoms?
- Was there an unusual work exposure within 24 hours before onset of initial asthma symptoms?
- Do asthma symptoms differ during times away from work such as weekends, holidays or other extended times away from work?
- Are there symptoms of allergic rhinitis and/or conjunctivitis that worsen with work?

An occupational history is crucial in assessing the probability of being exposed to a respiratory sensitiser or irritant. The important points to cover are:

- Take a history of the job duties and duration.
- Obtain a list of the hazardous exposures (obtain material safety data sheets (MSDs) for products used by the individual), and cross-check against a list of known agents causing OA from reliable sources, e.g. <http://www.asmanet.com/asmapro/agents.htm>.
- Assess the level of airborne exposures of the job (degree of dustiness).
- Determine the use of protective devices/equipment (respiratory, goggles, gloves).
- Determine the presence of respiratory disease in coworkers.

Work-related asthma should be considered in all adult patients with new-onset or worsening asthma.

Confirm the diagnosis of asthma

Confirmation of asthma requires the demonstration of reversible airways obstruction. Using spirometry, significant reversibility is defined as a post-bronchodilator increase of $\geq 12\%$ accompanied with a 200 ml increase in FEV₁. Serial PEFr monitoring over a 2-week period demonstrating a diurnal variation of $\geq 20\%$ is also considered to be diagnostic for asthma.

Establish the work-relatedness of asthma

Serial PEFr testing using a portable peak flow meter is currently the most practical test that can be used to assess

Table III. Commonly reported causes of occupational asthma in developing countries

- * Cleaning agents
- * Thermal degradation products (plastics, rubber)
- * Latex proteins
- * Isocyanates
- * Cereal flours/grain dust
- * Agricultural chemicals and products (pesticides, organic dusts)
- * Metallic products (platinum, chrome, nickel)
- * Solvent petroleum derivatives
- * Wood dust
- * Welding fumes

Adapted from reference 1.

Asthma

work-relatedness in patients who are still working. Its main drawbacks are requirements for daily recording of PEFR and dependence on the individual's compliance. For PEFR to yield meaningful results, recordings need to be done 4 times daily over a 4-week period, with 2 weeks doing usual work and 2 weeks away from work. On each occasion, 3 efforts are conducted, with the highest of the 3 efforts recorded. A specially designed chart is most appropriate. Record daily as (yes/no) adverse responses to workplace exposure, tight chest, flu symptoms, and any use of inhaled bronchodilator (indicate frequency of use). It is critical that exposure days are clearly recorded.

Determine whether WEA and/or OA is present

Diagnostic criteria for the various entities of work-related asthma used by the workers' compensation dispensation in South Africa are outlined in Table IV.

The presence of WEA should be considered highly probable in individuals who have asthma not caused by work but

whose pre-existing asthma subsequently worsens while working. This assessment is usually based on changes in symptoms, medication use, and/or lung function temporally related to work.

In individuals with suspected sensitiser-induced OA, immunological tests should be performed (skin prick testing or *in vitro* specific IgE assays) to identify sensitisation to specific work allergens when these tests are technically reliable and available, e.g. Phadia ImmunoCAP. Serial PEFR monitoring may be useful where immunological tests against low-molecular-weight chemicals (that commonly cause non-IgE-mediated reactions) are not available. Should the PEFR results be equivocal, the patient should be referred to a specialised centre for a nonspecific challenge test (methacholine or histamine) to document nonspecific airway responsiveness while the individual is still working in the job in question. The test should also be repeated during a period (optimally at least 2 weeks) away from the work exposure to identify work-related changes.

In very rare circumstances, when the diagnosis or causative agent is equivocal, a specific inhalation challenge test (the reference standard for occupational asthma) with the agent concerned is performed in South African facilities.

In all individuals, document the onset and timing of symptoms, medication use and their temporal relationship to periods at and away from work.

Management

Early diagnosis and early avoidance of further exposure are the cornerstones of patient management for WRA.

Table IV. Diagnostic criteria for work-related asthma compensable under the Workers' Compensation system in South Africa

Occupational asthma (immunological) as per Circular Instruction 176*

Requires all 4 criteria (A - D):

- (A) A medical practitioner's diagnosis of asthma and physiological evidence of reversible airways obstruction or airways hyperresponsiveness
- (B) An occupational exposure preceding the onset of asthmatic symptoms
- (C) An association between symptoms of asthma and work exposure
- (D) An exposure and/or physiological evidence of the relationship between asthma and the workplace environment (Requires D1 and preferably one or more of D2 - D5):
 - (1) Workplace exposure to agent reported to give rise to occupational asthma
 - (2) Work-related changes in FEV₁ or PEFR
 - (3) Work-related changes in serial testing of nonspecific bronchial hyperresponsiveness (e.g. methacholine challenge test)
 - (4) Positive specific bronchial challenge test
 - (5) Positive skin prick test or raised specific IgE antibody level to the suspected agent

Occupational asthma (irritant-induced) as per Circular Instruction 177*

Requires all 5 criteria:

- (1) Medical history indicating the absence of pre-existing asthma-like complaints
- (2) Onset of symptoms after a single or multiple exposure(s), incident(s) or accident (s)
- (3) An occupational exposure to a gas, smoke, fume, vapour or dust with irritant properties
- (4) Onset of symptoms within 24 hours of exposure with persistence of symptoms for at least 3 months. (An association between symptoms of asthma and exposure)
- (5) Presence of airflow obstruction on pulmonary function tests and/or presence of nonspecific bronchial hyperresponsiveness on tests done at least 3 months after exposure

Work-aggravated asthma as per Circular Instruction 184*

Requires all 5 criteria:

- (1) Medical history indicating pre-existing asthma or history of asthmatic symptoms, prior to the start of employment or exposure to the known aggravating agent
- (2) Presence of work-related exposures preceding and/or associated with the onset of an asthmatic attack or the worsening of symptoms
- (3) Presence of work-related factors known to aggravate asthma symptoms (e.g. cold air, dusty work, chemical or biological irritants, indoor air pollutants, physically strenuous work, second-hand smoke)
- (4) Increase in symptoms or medication requirements, or documentation of work-related changes in PEFR or FEV₁ after start of employment or occupational exposure
- (5) Presence of reversible airflow obstruction and/or nonspecific bronchial hyperresponsiveness on pulmonary function testing

* As published in the Government Gazette, Republic of South Africa, Pretoria (<http://www.labour.gov.za/programmes/>)

Exposure avoidance

Patients with sensitiser-induced OA, whenever feasible, should be relocated to a job category without exposure or, if this is not possible, they should be moved to an area of low exposure. Evidence-based guidelines for the management of OA indicate that the likelihood of improvement or resolution of symptoms or of preventing deterioration is greater in workers who have no further exposure to the causative agent, in workers who have relatively normal lung function at the time of diagnosis, and in workers who have shorter duration of symptoms prior to diagnosis or prior to avoidance of exposure.⁶ The use of respirators is usually ineffective.

Early diagnosis and avoidance of further exposure are key to the management of patients with work-related asthma.

In individuals with irritant-induced OA or WEA, the ACCP guidelines advise optimising asthma treatment and reducing the exposure to the relevant workplace triggers. If this is not successful, changing jobs to a workplace with fewer triggers in order to control asthma is recommended. However, patients with reactive airways dysfunction syndrome (RADS) can continue to work in the same job provided measures are taken to prevent further exposures to high concentrations of irritant agents.

Optimising asthma treatment

Pharmacological treatment of WRA does not differ from therapy of other types of asthma, and should comply with the GINA asthma guidelines.⁹ Efforts should be made to increase the use of inhaled corticosteroids early after the diagnosis, as this has been shown to improve the prognosis.⁴ General measures such as cessation of smoking and avoidance of exposure to common aeroallergens to which the patients may also be sensitised, or to environmental irritants, should always be recommended.

Ongoing follow-up and assessment of impairment/disability

Impairment and disability evaluation should be carried out as soon as the

asthma is stabilised and 2 years later, and patients should be counselled regarding compensation.¹⁰

Assist with workers' compensation claim

WRA has serious socio-economic consequences. About one-third of workers with OA are unemployed at 6 years after diagnosis and are known to suffer financially.⁶ Recent initiatives in South Africa have attempted to address these issues such that the workers' compensation dispensation covers all types of WRA (Table IV).¹ Physicians should support the affected workers in the application of a worker's compensation claim, and should report occupational disease to the corresponding worker's compensation system and the Department of Labour. The detailed workers' compensation submission procedures are outlined elsewhere.^{11,12} Assistance can be sought from referral clinics for occupational diseases located at the National Institute for Occupational Health (Gauteng), Groote Schuur Hospital (Western Cape) and King Edward Hospital (KwaZulu-Natal).

References

- Jeebhay MF, Quirce S. Occupational asthma in the developing and industrialised world: a review. *Int J Tuberc Lung Dis* 2007; 11(2): 122-133.
- Jeebhay MF, Omar F, Kisting S, Edwards D, Adams S. Outcome of worker's compensation claims submitted by the Workers' Clinic in Cape Town. *Occupational Health Southern Africa* 2002; 8: 4-7.
- Toren K, Blanc PD. Asthma caused by occupational exposures is common – a systematic analysis of estimates of the population-attributable fraction. *BMC Pulmonary Medicine* 2009; 9: 7. doi:10.1186/1471-2466-9-7.
- Tarlo S, Balmes J, Balkissoon R, et al. Diagnosis and Management of Work-Related Asthma. American College of Chest Physicians Consensus Statement. *Chest* 2008; 134(3): 1S-41S.
- Esterhuizen TM, Hnizdo E, Rees D. Occurrence and causes of occupational asthma in South Africa – results from SORDSA's Occupational Asthma Registry, 1997-1999. *S Afr Med J* 2001; 91: 509-513.
- Nicholson PJ, Cullinan P, Newman Taylor AJ, Burge PS, Boyle C. Evidence-based guidelines for the prevention, identification and management of occupational asthma. *Occ Env Med* 2005; 62: 290-299.
- Baatjies R, Lopata AL, Sander I, et al. Determinants of asthma phenotypes among supermarket bakery workers. *Eur Respir J* 2009; 34(4): 825-833.
- Buck RG, Miles AJ, Ehrlich RI. Possible occupational asthma among adults presenting with acute asthma. *S Afr Med J* 2000; 90: 884-888.
- Bateman ED, Hurd SS, Barnes PJ, et al. Global strategy for asthma management and

prevention: GINA executive summary. *Eur Respir J* 2008; 31: 143-178.

- American Thoracic Society ad hoc Committee on impairment/disability in subjects with asthma. Guidelines for the evaluation of impairment/disability in patients with asthma. *Am Rev Respir Dis* 1993; 147: 1056-1061.
- Jeebhay MF. Setting up an occupational health service – legal provisions and practical considerations. *South African Journal of Continuing Medical Education* 1996; 14: 1321-1327.
- Adams S, Jeebhay M. How to claim compensation for work-related injuries or diseases. In Mash B, Blitz-Lindeque J, eds. *South African Family Practice Manual*, 2nd ed. Pretoria: Van Schaik Publishers, 2006: 226-230.

In a nutshell

- Work-related factors, depending on the industry, can be responsible for up to 25% of all adult asthma cases.
- WRA is under-recognised, poorly diagnosed and managed, and inadequately compensated in South Africa.
- WRA should be considered in all adult patients with new-onset or worsening asthma through taking an appropriate history.
- WRA can be broadly classified into occupational asthma (OA) and work-exacerbated asthma (WEA).
- OA is commonly caused by isocyanates, cereal flour/grain dust, natural rubber latex gloves and cleaning agents.
- Reactive airways dysfunction syndrome (RADS) is caused by exposure to high levels of irritant compounds (e.g. chlorine, ammonia, sulphur dioxide, fire smoke, glutaraldehyde).
- WEA is due to exacerbation of pre-existing asthma to workplace exposures (e.g. dusts, smoke, fumes, cleaning agents) and physical factors (e.g. cold air, strenuous work).
- Early diagnosis by a physician and avoidance of further exposure are the cornerstones of patient management for WRA.
- Physician assistance with a worker's compensation claim will ensure preservation of income and improved quality of life of individuals with WRA.