Occupational asthma

Dr H Pahad, MBBCH (Wits), FCP (SA), FCCP
Private Specialist Physician and Pulmonologist, Milpark Hospiital
Council Member of the National Asthma Education Programme

Correspondence: Rooms (011) 482 1436, Fax (011) 482 5984

Introduction

More than 250 substances found in the workplace cause occupational asthma (OA).

Occupational asthma is characterised by variable airflow limitation and airway hyperresponsiveness due to precipitants in the workplace.[1] Work-related asthma can be an exacerbation of asthma that was previously subclinical or in remission (work-aggravated asthma), a new onset of asthma caused by a sensitising exposure (asthma with latency) or asthma that results from a single heavy exposure to a potent respiratory irritant (asthma without latency, irritant asthma or the reactive airways dysfunction syndrome). ***(SA Fam Pract 2003;45(10): 35-40)***

Epidemiology

Occupational asthma is the most common form of occupational lung disease in the developed world, and appears to be increasing in frequency.[2-6] Five to fifteen percent of new cases of asthma in working adults are caused by occupational exposure. Occupational asthma accounted for nearly 30% of work-related pulmonary disorders in the United Kingdom in 1994.[7]

Environmental determinants

The types and intensity of antigen exposure are the most important determinants of OA. A dose-response relationship between the level of exposure and prevalence of disease has been documented for several types of OA, including illness related to Western red cedar, colophony (soft-core solder) and acid anhydride.[8]

Isocyanates, which are low molecular weight compounds involved in the production of plastics and rubber, are the most common aetiologic agents, accounting for approximately 20% of OA cases. Exposure to very high concentrations of isocyanates can also lead to the development of the reactive airways dysfunction syndrome.[9] **(See table 1)**

Pathogenesis

OA can result from immunologic or nonimmunologic mechanisms.[10] Agents which induce OA by immunologic mechanisms are characterised by a latency between exposure and the development of symptoms.

Immunologic, IgE Mediated:

High molecular weight agents (e.g., animal proteins and flour) act as complete antigens and induce the production of specific IgE antibodies. Certain low molecular weight occupational agents (platinum salts, trimellitic anhydride) also induce specific IgE antibodies, probably by acting as haptens and binding with proteins to form functional antigens. These agents affect mostly atopic subjects.[11]

Regardless of the characteristics of the initiating antigen, reactions between specific IgE antibodies and antigens lead to a cascade of events, which result in an influx of inflammatory cells into the airway and the release of inflammatory mediators.

The presence of sensitisation to occupational agents can be detected by skin tests, radioallergosorbent tests (RAST) or enzyme-linked immunosorbent assay (ELISA)

Immunologic, non-IgE Mediated Reactions

Many low molecular weight agents, including isocyanates and plicatic acid, cause OA but do not consistently induce specific IgE antibodies.[12,13] The ability of low molecular weight agents to induce asthma may depend upon its chemical structure.

Nonimmunological Reactions

These agents are characterised by absence of a latency period.

Three mechanisms may explain symptoms in these patients

- Acute airway injury from accidental exposure to high dose of irritant may lead to RADS (Reactive Airways Dysfunction Syndrome)[14] (e.g. chlorine, ammonia, smoke).
- Some low molecular weight agents have pharmacologic properties that may cause bronchoconstriction.[15,16] (e.g. isocyanate may block beta-2 adrenergic receptors).
- Agents may stimulate sensory nerves to release substance P and other neuropeptides.[17] Neuropeptides affect a variety of cells in the

Table 1: Major causes of occupational asthma

Low molecular weight chemicals	Occupation at risk
Isocyanates (e.g. toluene diisocyanate, diphenylmethane, diisocyanate, hexamethylene diisocyanate, naphthalene diisocyanate)	Polyurethane workers, roofers, insulators, painters
Anhydrides (e.g. trimellitic anhydride, phthalic anhydride)	Manufacturers of paint, plastics, epoxy resins
Metals (e.g. chromic acid, potassium dichromate, nickel sulfate, vanadium, platinum salts)	Platers, welders, metal and chemical workers
Drugs (e.g. beta lactam agents, piperazine derivatives, psyllium, sulphathiazole, organophosphate)	Pharmaceutical workers, farm workers
Miscellaneous (e.g. formaldehyde, dimethylethanolamine, ethylene oxide, pyrethrin, polyvinyl chloride vapour)	Laboratory workers, textile workers, paint sprayers
High molecular weight organic chemicals	
Animal proteins (e.g. domestic animals, birds, mice, fish glue)	Farmers, veterinarians, poultry processors, laboratory workers, bookbinders, postal workers
Plan proteins (e.g. wheat, grain dust, coffee beans, tobacco dust, cotton, tea)	Farmers, bakers, textile workers, food processors
Wood dust (e.g. Western cedar, mahogany, oak, redwood)	Carpenters, woodworkers
Dyes (e.g. anthraquinone, carmine, paraphenyl diamine, henna extract)	Fabric and fur dyers, beauticians
Fluxes (e.g. colophony, soft core solder)	Solderers, electrical workers
Enzymes (e.g. pancreatic extracts, trypsin, Bacillus subtilis, bromelain pectinase)	Pharmaceutical workers, food processors, plastic workers, detergent manufacturers

airways, resulting in cough, smooth muscle contraction and mucous production[18] (e.g. isocyanate).

Pathology

Irrespective of mechanisms of induction of asthma, the pathology in the airways of subjects with OA is similar to that seen in patients with nonoccupational asthma.[19]

Clinical features

The clinical history in patients with possible OA should encompass occupational exposure to potential provocative agents and the pattern of development of symptoms in addition to conventional historical elements.[20]

All asthmatic subjects should be questioned not only about their occupation, but also about their current and past exposures at work. As example, a "clerk" can be exposed indirectly to a sensitising agent depending upon the company and environment in which he/she works.

Symptoms of OA classically are first present only at work, and disappear or improve while away from work. With high-molecular weight (HMW) proteinous agents, rhinoconjunctivitis symptoms often precede symptoms of OA.[21]

The latency period between the onset of exposure and the onset of symptoms is highly variable. In general the latency period is shorter with exposure to low-molecular weight agents (LMW), such as isocyanates and plicatic acid (Western cedar), than with HMW agents.[22]

The other clinical features are similar to those found in patients with non-occupational asthma.

Diagnosis

Diagnostic Criteria

Diagnosis of OA should include both the diagnosis of asthma and the establishment of a relation between the asthma and work. The diagnosis of asthma is based on a compatible history and the presence of airflow limitation or, in the absence of airflow limitation, the presence of pharmacologically induced bronchial hyperresponsiveness.[10]

An occupational cause should be sought for all asthma of new onset in adults. The disease should be suspected in a person exposed at work to agents known to cause OA.

A detailed assessment of workplace exposure may help determine the specific type of OA. The assessment should include a detailed history of specific job duties and work processes for both patient and co-workers.

A history of improvement of symptoms during weekends and holidays and a worsening on return to work suggests, but does not confirm OA. Runny and itchy eyes and nose and sneezing often accompany respiratory symptoms.

An algorithm for the clinical investigation of OA is shown in Figure 1.

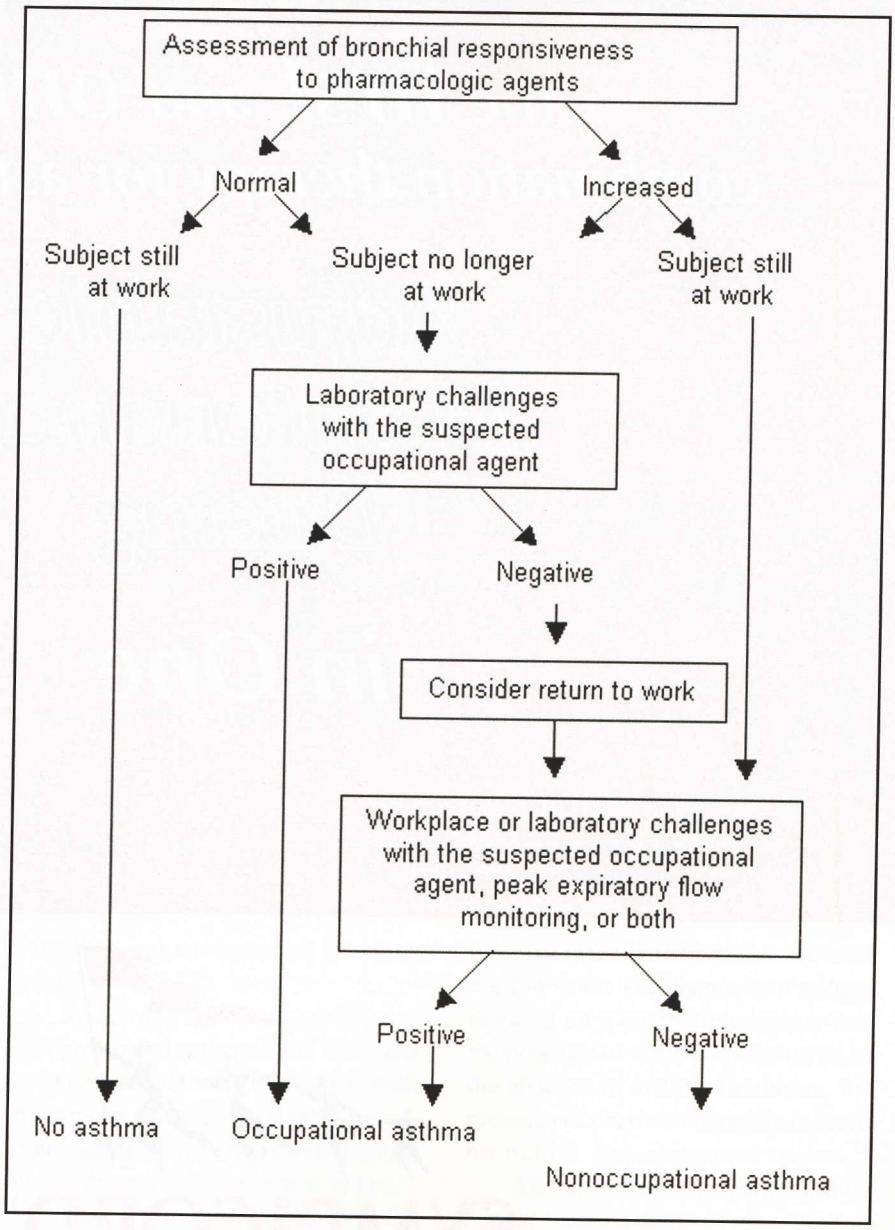
- Peak expiratory flow rate (PEFR) monitoring - Is a useful method in the investigation and assessment of OA.[23-25] Monitoring is carried out by asking the subject to record his/her PEFR at least four times per day for a period of at least two weeks at work and during a similar period away from work. However, there are a number of potential problems to this approach, including the reproducibility of readings, compliance and honesty of subjects, interpretation of results, and sensitivity and specificity compared with specific inhalation challenges. Newer portable peak flow meters store values electronically, enabling falsified patient logs to be identified.

- Nonspecific bronchoprovocation testing – To obtain more objective evidence of an occupational relationship of symptoms, nonspecific bronchial hyperresponsiveness can be measured at the end of the work period and at the end of the period away from work. The absence of bronchial hyperresponsiveness when the subject is at work, and has symptoms, virtually excludes OA.

- Spirometry – Monitoring of FEV1 in the workplace by a skilled technician should be encouraged. Comparison with data from a non-exposure day can confirm work-related exacerbations of asthma.

- Skin testing – Skin test reagents are not available for documenting hypersensitivity to most occupational agents, but the technique is feasible for some HMW agents, such as animal or plant proteins. The presence of immediate skin test reactivity reflects IgE – specific sensitisation. A negative test virtually excludes the possibility that OA is caused by that specific antigen.

Figure 1: Algorithm for the Clinical Investigation of Occupational Asthma



Treatment

A favourable prognosis is dependent on rapid diagnosis and early removal of the patient from further exposure. Improvement tends to plateau two years after cessation of exposure.[26] Most patients show incomplete resolution of asthma even after many years.[27]

Patients with OA generally deteriorate if they remain in the same job and fatal cases have occurred among workers with ongoing workplace exposure to provocative antigens.[28-29]

Treatment of OA does not differ from that of nonoccupational asthma, but it cannot substitute for effective elimination of exposure to precipitating antigens. Respiratory protection devices, such as powered filtering respirators, provide incomplete protection and also cannot substitute for removal from the offending antigen(s).

Prevention

Monitoring and control of the level of potential allergens may decrease the number of individuals who become sensitised in the workplace.

Atopic individuals who wish to enter high-risk workplaces require follow-up examinations for early detection of sensitisation and nonspecific bronchial hyperresponsiveness. Smoking cessation

should be advised. Management of persons with pre-existing asthma is more problematic. Frequent objective measures of lung function should be obtained, and if asthma control is deteriorating a therapeutic trial of removal from the work environment is indicated.

Impairment and disability evaluation

Once the diagnosis of OA is made, patients should be referred to compensation boards or similar agencies when appropriate. Patients should be evaluated for temporary impairment and disability when their asthma is under good control.[30] Evaluation of permanent impairment and disability should take place after two years, when improvement has plateaued.[31] In addition to the assessment of lung function, it is recommended that the assessment include the degree of pharmacologically induced bronchial hyperresponsiveness and airway reversibility, the minimal amount and types of medication required for maintaining control and the effect on quality of life.[10]

Conclusion

Knowledge of OA has expanded in recent years. There is greater recognition of aetiologic agents, as well as improved diagnostic methods and better understanding of pathogenesis and natural history. Despite considerable advances, there is still much to be learned. Although occupational diseases such as asbestosis and silicosis may be eradicated with time because of better preventative measures, it is unlikely that OA will ever disappear because of the constant introduction of new chemicals into workplaces.

References

1. Bernstein L, Chan-Yeung M, Malo J-L, Bernstein D (Eds). Definition of Occupational Asthma. Asthma in the Workplace, Mercel Dekker, 1993, p. 1.
2. Reilly MJ, Rosenman KD, Watt FC, et al. Surveillance for occupational asthma – Michigan and New Jersey, 1988 – 1992. MMWR CDC Surveill Summ 1994;43:9-17.
3. Lagier F, Cartier A, Malo JL. Statistiques médico-légales sur l'asthme professionnel au Québec de 1986 à 1988. Rev Mal Respir 1990;7:337-41.
4. Keskinen H, Alanko K, Saarinen L. Occupational asthma in Finland. Clin Allergy 1978;8:569-79.
5. Meredith SK, Taylor VM, McDonald JC. Occupational respiratory disease in the United Kingdom 1989; a report to the British Thoracic Society and the Society of Occupational Medicine by the SWORD project group. Br J Ind Med 1991;48:292-8.
6. Conteras GR, Rosseau R, Chan-Yeung M. Occupational respiratory diseases in British Columbia, Canada in 1991. Occup Environ Med 1994;51:710-2.
7. Meredith S, Nordman H. Occupational asthma: Measures of frequency from four countries. Thorax 1996; 51:435.
8. Chan-Yeung M, Malo JL. Epidemiology of occupational asthma. In: Asthma and Rhinitis, Busse W, Holgate S (Eds), Blackwell Scientific Publications, 1995,p.44.
9. Lemière C, Malo JL, Boutet M. Reactive airways dysfunction syndrome induced by exposure to a mixture containing isocyanate: Functional and histopathologic behaviour. Allergy 1996; 51:262.
10. Cahn-Yeung M, Malo JL. Occupational asthma. N Engl J Med 1995; 333:107.
11. Grammer LC, Zeiss CR, Yarnold PR, Shaughnessy MA. Human leucocyte antigens (HLA) and trimellitic anhydride (TMA) immunological lung disease. Respir Med 2000; 94:964.
12. Tse KS, Chan H, Chan-Yeung M. Specific IgE antibodies in workers with occupational asthma due to western red cedar. Clin Allergy 1982; 12:249.
13. Karol MH, Alarie Y. Antigens which detect IgE antibodies in workers sensitive to toluene diisocyanate. Clin Allergy 1980; 10:101.
14. Brooks S, Bernstein I. Reactive airways dysfunction syndrome. In: Asthma in the Workplace, Marcel Dekker, New York, 1993; p.533.
15. Butcher BT, Karr RM, O'Neil CE, et al. Inhalation challenge and pharmacologic studies of toluene diisocyanate (TDI) – sensitive workers. J Allergy Clin Immunol 1979; 64:146.
16. Chan-Yeung M, Giclas PM, Henson PM. Activation of complement by plicatic acid, the chemical compound responsible for asthma due to western red cedar (Thuja plicata). J Allergy Clin Immunol 1980; 65:333.
17. Chitano P, Di Blasi P, Lucchini RE, et al. The effects of toluene diisocyanate and of capsaicin on human bronchial smooth muscle in vitro. Eur J Pharmacol 1994; 270:167.
18. Mapp CE, Chitano P, Fabbri LM, et al. Evidence that toluene diisocyanate contracts guinea pig bronchial smooth muscle by activating capsaicin-sensitive sensory nerves. J Pharmacol Exp Ther 1991; 256:1082.
19. Fabbri LM, Danieli D, Crescioli S, et al. Fatal asthma in a subject sensitized to toluene diisocyanate. Am Rev Respir Dis 1988; 137:1494.
20. Malo JL, Ghezzo H, L'Archeveque J, et al. Is the clinical history a satisfactory means of diagnosing occupational asthma? Am Rev Respir Dis 1991; 143:528.
21. Malo JL, Lemière C, Desjardins A, Cartier A. Prevalence and intensity of rhinoconjunctivitis in subjects with occupational asthma. Eur Respir J 1997: 10:1513.
22. Malo JL, Ghezzo H, D'Aquino C, et al. Natural history of occupational asthma: Relevance of type of agent and other factors in the rate of development of symptoms in affected subjects. J Allergy Clin Immunol 1992; 90:937.
23. Burge PS, O'Brien IM, Harries MG. Peak flow rate records in the diagnosis of occupational asthma due to colophony. Thorax 1979; 34:308.
24. Burge PS, O'Brien IM, Harries MG. Peak flow rate records in the diagnosis of occupational asthma due to isocyanates. Thorax 1979; 34:317.
25. Moscato G, Godnic-Cvar J, Maestrelli P, et al. Statement on self-monitoring of peak expiratory flows in the investigation of occupational asthma. J Allergy Clin Immunol 1995; 96:295.
26. Malo JL, Cartier A, Ghezzo H, et al. Patterns of improvement in spirometry, bronchial hyperresponsiveness, and specific IgE antibody levels after cessation of exposure in occupational asthma caused by snow-crab processing. Am Rev Respir Dis 1988;138:807.
27. Chan-Yeung M, Malo JL. Natural history of occupational asthma. In: Asthma in the worjkplace, Bernstein IL, Chan-Yeung M, Malo JL, Bernstein DI (Eds), Mercel Dekker, 1993, p.299.
28. Comté J, Kennedy SM, Chan-Yeung M. Outcome of patients with cedar asthma with continuous exposure. Am Rev Respir Dis 1990; 141:373.
29. Fabbri LM, Danieli D, Crescioli S, et al. Fatal asthma in a subject sensitized to toluene diisocyanate. Am Rev Respir Dis 1988; 137:1494.
30. National Asthma Education Program. Guidelines for the diagnosis and management of asthma. Bethesda, Md.: Public Health Service, 1991. (DHHS publication no. (NIH) 91-3042.)
31. Chan-Yeung M. Occupational asthma. Chest 1990;98: Suppl: 148s-161s.