ABSTRACT

Occupational asthma is one of the category of work-related asthma. The diagnosis of occupational asthma is established on the basis of a suggestive history of a temporal association between exposure and the onset of symptoms and objective test that these symptoms are caused by specific agent at work. Besides pharmacological treatment management of OA include removal from exposure or reduction of exposure through workplace control measures. Prevention of new cases is the best approach to reducing the burden of asthma attributable to occupational exposures.

INTRODUCTION

Occupational asthma (OA) is the most common occupational lung disease in the developed countries and Singapore. The incidence rate varies between different countries depending on working diagnosis, notification, surveillance and compensation systems. OA is under diagnosed because most physicians do not enquire about the work-relatedness of symptoms. Affected workers may leave their jobs before they can be diagnosed contributing to the “healthy worker effect”. OA is often under-diagnosed and under-reported.

It is important to recognise OA early as cessation of exposure to the agent improves prognosis of the disease. Proper management of a case also benefits the worker and employer in terms of improvement in productivity and saving of medical expenses. The primary healthcare physician should consider the possibility of occupational causes in every adult with new onset asthma or an asthmatic patient with aggravation of symptoms.

DEFINITION AND CLASSIFICATION

There is no universally accepted definition of OA. The workplace can trigger or induce asthma leading to what is labeled as “work-related asthma” (WRA). Work-related asthma can then be divided into two general groupings: Work-aggravated asthma (WAA) and Occupational asthma (OA). (Table 1)

Work-aggravated asthma (WAA) is asthma exacerbated by workplace exposure in an individual with a prior history of asthma. The asthma is triggered by nonspecific mechanism such as cold temperatures, excessive exertion, or exposure to irritant aerosols including dusts, fumes, vapors, and gases.

CAUSATIVE AGENTS

More than 300 agents that can cause OA have been reported. The primary healthcare physician should be familiar with the common ones. There are many publications and websites listing out asthma causative agents (asthmagens). One useful webpage of agents asthmagens is at: http://www.asmanet.com/asmapro/agents.htm. It is also useful to know the occupations associated with the causative agents and these are also found in the webpage: http://www.asmanet.com/asmapro/jobs.htm. OA however may be caused by unreported new agents and such cases should be referred for evaluation by the occupational respiratory physician.

The agents are classified either as high molecular weight (HMW) agents or low molecular weight (LMW) agents. Some examples of HMW agents include organic compounds like...
natural rubber latex, flour, seafood proteins, enzymes, animal proteins, synthetic adhesives etc. Examples of LMW agents include isocyanates, amines, acid anhydrides and antibiotics.

The agents that can cause RADS include inhaled smoke, fumes of acid such as acetic, sulphuric and hydrochloric acids; irritant gases such as chlorine, hydrogen sulphide, ammonia and phosgene; and vapours of toluene diisocyanate.

**DIAGNOSIS OF OCCUPATIONAL ASTHMA**

It is important to make accurate diagnosis of work-related asthma and distinguish between WAA and OA as the management and compensation differ. Inadequate evaluation may lead to a premature recommendation of employee removal from the workplace. Failure to remove a patient from harmful exposure may result in persistent asthma and has been associated with fatal asthma.

The diagnosis is made by:

1. Establishment of the presence of asthma;
2. Demonstration of the relationship between asthma symptoms and work, and;
3. Establishment of exposure to a specific causative agent.

**1. Establishment of the presence of asthma**

There should be objective evidence of asthma which include presence of asthma symptoms and signs, reversible airflow obstruction in spirometry, and non-specific airway hypersensitivity in methacholine or histamine challenge test. If evaluation fails to confirm the diagnosis of asthma, other causes of the respiratory symptoms should be sought, and the diagnosis of work-related asthma can be ruled out.

**2. Demonstration of the relationship between asthma symptoms and work**

A comprehensive occupational history is the first significant step in the diagnosis of OA. The assessment should focus on several key areas:

- **a) Job history details**
  The employment history, including past and present jobs should be taken. It is important to have the worker describe specific tasks and exposures. Sensitisation and asthma may have resulted from previous exposure in similar job tasks. Asthma may develop after a change in a manufacturing process, failures of the workplace ventilation systems, uncontrolled releases or spills and introduction of new chemicals in the workplace. Hence, it is useful to ask about such events.

  Evaluation of the list of suspected chemicals and the relevant Safety Data Sheet (SDS) is often very helpful. Employers are required under the Workplace and Safety Health Act to have SDS available for hazardous substances in the workplace. The SDS provides information of the chemical composition of products including health effects such as sensitisation and pulmonary effects.

- **b) Onset of symptoms**
  It is important to recognise the different asthmatic responses of OA so that diagnosis may not be missed. Three general temporal patterns for OA are described - immediate, late and dual asthmatic reactions. HMW agents typically produce immediate reactions. Symptoms begin 10 to 20 minutes following exposure and may gradually resolve with or without treatment over the next 1 to 2 hours. LMW agents commonly produce late reactions. Symptoms begin 3 to 4 hours after exposure and peak after 8 hours. If the late reaction occurs after the worker has left the workplace, the relation to work exposure may be missed. Dual reactions (an early reaction followed by a late one) and atypical reactions have also been described. Reaction patterns however cannot be used to identify suspected causative agents because they are not specific to the molecular-weight size grouping. Early, late, dual, and atypical reactions can occur with LMW and HMW substances.

  In the case of RADS, onset of asthma symptoms occurs within 24 hours after a high dose exposure and persists for more than three months.

  The improvement of asthmatic symptoms on weekends or vacations is typical of OA. However, it needs to be borne in mind that over time, a worker with OA may develop persistent symptoms, losing the temporal association of symptoms to work. Some cases of OA also respond to treatment initially without any symptoms until it becomes more severe.

- **c) Presence of other symptoms**
  Both LMW and HMW agents are associated with sensitisation of nasal and eye mucosa and are co-morbid conditions to work-related asthma. The patient may present with rhinitis and conjunctivitis even before the onset of asthma.

- **d) Presence of symptoms in co-workers**
  While OA may occur only in a susceptible worker, clusters of work-related asthma may occur for workers exposed to strong sensitiser or irritant. In such situation, a more comprehensive workplace investigation is needed.

**3. Establishment of exposure to a specific causative agent**

- **a) Immunological tests:**
  Immunological tests (skin tests or in vitro assay for specific IgE antibodies) are seldom done due to lack of commercially available or standardised reagents. A positive skin prick test to a workplace agent supports a diagnosis of OA if it is associated with pulmonary function changes, but not diagnostic as sole investigation. Presence of serum IgE antibody for known HMW antigens is an indication of prior exposure and sensitisation. The absence of an IgE antibody to a known workplace exposure is useful in ruling out Type I hypersensitivity to the agent, but does not exclude asthma mediated by other immunologic responses.
b) Serial peak expiratory flow rate

Serial peak expiratory flow (PEF) monitoring during periods at work and away from work is commonly used to demonstrate a workplace association to asthma. It is simple, inexpensive and usually acceptable to the worker and employer. Though it is limited by dependence on patient’s effort and measurement bias, it has been found to be both sensitive (96%) and specific (89%) for the diagnosis of OA. Various schedules of monitoring ranging from every 2 hours to 4 times a day have been recommended. PEFR measurements 4 times per day for 4 weeks have been found to be of high sensitivity and specificity.13

The worker is asked to record his/her readings for about 4 weeks with a continuous period of about one week away from work (e.g. weekends or vacation). Medication use, work tasks, the types of chemical exposures and asthma symptoms are also recorded. (Figure 1) Such monitoring ideally should be conducted with the patient not using any asthma control medications (e.g. inhaled corticosteroids or long-acting bronchodilators) as this may mask work-related pattern. However, if the patient requires medication, the monitoring can still be performed by keeping the dose to a minimum and uniform for periods at work and away from work.

A graph of the maximum, minimum and mean PEFR for each day gives a good visual picture of the pattern of work-relatedness, if any (Figure 2). A 20% or greater diurnal variability during period of exposure is used to diagnose OA.

c) Workplace assessment

A visit to the workplace may be required to verify history of exposure. Environmental monitoring is useful in documenting exposure to the specific agent. It is also useful in the assessment of risk and effectiveness of control measures based on the level of exposure. When interpreting the air levels, it has to be remembered that very minute quantity of asthagen may still cause sensitisation to the causative agent or trigger OA.

Specific inhalational challenge

Specific inhalation challenge (SIC) also known as specific bronchial provocation test is considered by some to be the ‘gold standard’ for objective diagnosis of OA. The greatest advantage of SIC is that a positive test confirms a diagnosis of OA to a specific agent. A sustained fall in FEV1 (Forced expiratory volume in one second) or PEFR of 20% or more from pre-challenge value in the absence of significant (more than 10%) changes after exposure to a control is considered positive.

Interpretation and performance of test however can be difficult at times. It may not be possible to reproduce the exact exposures in the workplace in terms of exposure time, concentration and nature of the agents. The possibility of interaction between different agents in causing the asthma is also difficult to exclude.

Not every case of OA needs to be diagnosed by SIC if there is strong evidence from other evaluation tools. There are risks involved besides the time and expense that is required.
from the patient as well as the investigating doctor. Some indications for SIC include:

1. Documentation of new (i.e. previously unreported) causative agents,
2. Identification of causative agent amongst multiple known agents,
3. Provision of objective evidence in a difficult case or where it is not possible to do a serial PEFR monitoring as in a patient who has already left employment.

Patients should be carefully selected for such a procedure. The test should be carried out in specialist departments with trained personnel to provide patient with significant periods of close observation and potential resuscitation if respiratory arrest occurs.

**MANAGEMENT**

**Pharmacological treatment**
Pharmacological treatment of OA is similar as for any case of asthma. However, it is not effective in preventing lung function deterioration in sensitiser-induced OA when the worker remains exposed to the causative agent.

**Removal from exposure**
Complete removal from exposure remains the most effective treatment of sensitiser-induced OA especially those with severe asthma. Earlier removal has been shown to be associated with greater improvement in symptoms, lung function and recovery. It may also prevent fatality.

While transfer of the worker from the job may be ideal it may mean significant loss of income to the worker and also the loss of a skilled worker for the employer. The objective, therefore, is to manage the asthma without exposing the patient to unacceptable risk and causing unacceptable financial hardship. Several factors can be used to guide the decision for transfer. These include the type of causative agent, exposure circumstances, condition of the worker, control measures in workplace and use of respirators. An acceptable compromise is to continue work for the same employer in a new area with less exposure, and using respirators and medication.

Patients with RADS/irritant-induced OA are more likely to be able to return to work and managed pharmacologically. Several case reports also show that the use of respirators allowed workers with OA exposed to laboratory animal allergens, aluminum pot room fumes, flour, cow dander and grains to continue with their jobs successfully.

The managing doctor should help the patient, employer and all parties involved to understand the condition and cooperate to find the best possible solution so that it will ultimately benefit both the worker and the employer.

**COMPENSATION**
Persons with OA may suffer from considerable financial expenses from long medical leave, loss of job opportunities and possible long-term medical expenses which they may continue to incur even after leaving the employment where they developed their asthma. They may have difficulty securing a job with a comparable salary.

In Singapore, all cases of OA are eligible for compensation. A case of OA is assessed using the FEV₁ but if this is normal, then an award of between 5% and 20% disability can be given depending on the minimum medication requirements. Such assessments should be made only after the patient is stabilised and there is adequate period since transfer from exposure to the causative agent.
PREVENTION

Primary prevention
Risk identification is one of the most important aspects of primary prevention. Relevant SDS should be made available to workers. Ideally there should be elimination of workplace exposures to known asthmagens. Workplaces can be encouraged to substitute such agents to totally enclose the process. However, this is not always practicable or cost effective, given the apparently low incidence of OA. Reduction of exposures to these agents through ventilation system and dust suppression may help to reduce the risk. The effective use of respiratory protection may also help reduce worker exposure.

Secondary prevention
The goal of secondary prevention is to identify preclinical changes in the disease. Health education of employers and workers to increase the awareness of the condition may result in earlier self-reporting. Periodic screening of workers at risk using spirometry, skin prick or specific antibody testing has been proposed, but the cost effectiveness of such a procedure has to be considered.

The use of a simple questionnaire at pre-employment and at periodic intervals may be a useful and relatively inexpensive screening test. The questionnaire should include symptoms of rhinitis and conjunctivitis (these often precede onset of OA induced by HMV agents) and respiratory symptoms for OA without latency.

CONCLUSION
OA will continue to affect many workers worldwide because of continuous influx of chemicals and change of manufacturing process. It is important to consider the possibility of work-related asthma in any adult patient with asthma. In patients where the history is suggestive, investigations should be properly conducted to confirm or exclude the diagnosis of OA, as the subsequent management of the case may have implications on the patient’s livelihood. There are also medico-legal considerations.

LEARNING POINTS
- It is important to differentiate the various categories of work-related asthma as management can be different.
- Identify occupational asthma early will improve the prognosis of the patient and reduce financial and social cost.
- Every new adult onset asthma and asthma with deterioration should be evaluated for possible occupational etiology.
- A comprehensive occupational history is essential in the initial assessment of a patient thought to have work-related asthma. Taking a good occupational history is an important first step to the diagnosis of occupational asthma.
- The latency period of OA can be immediate, delayed or dual. Hence the importance of watching out for symptoms even when the worker is not at work.
- All cases of suspected work-related asthma should be referred to the occupational health physicians to confirm the cause so that preventive measures can be implemented.

REFERENCES