Occupational Asthma

Syazili Mustofa[1], Dimas Trend Pinaka Baladika[2]

[1]Departement of Biochemistry, Physiology and Molecular Biology, Medical Faculty, Universitas Lampung, Indonesia

[2]Student, Department of Pulmonology and Medical Respiratory, Medical Faculty, Universitas Lampung, Indonesia

Abstract

Asthma is a respiratory disease commonly found in general medical practice and in various fields of study. Twenty five percent of adult-onset asthma is occupational asthma. Occupational asthma has become the most prevalent occupational lung disease in developed countries. Allergens that cause occupational asthma are commonly found in work place such as animal proteins, plant proteins, metal transition, chemical substances, etc. Pathogenesis of disease are based on immunologically mediated with participation of specific IgE, immunologically mediated without evidence of participation of IgE and non-immunologic. The diagnosis of occupational asthma does not differ from the diagnosis of general asthma. The difference is that the diagnosis of occupational asthma must be reassured that the exposure to allergens involves a contact to irritating substance within workplace. The best treatment would be to avoid allergens in the workplace.[1,2]

Key words: Occupational asthma (OA), allergens, workplace

Corresponding author: Dr.Si. dr. Syazili Mustofa, S.Ked, M.Biomed., Address: Jl. Soemantri Brodjonegoro No. 1, Bandar Lampung, Lampung, Indonesia. Phone: 081929345909, e-mail syazilimustofa.dr@gmail.com

Introduction

Asthma is a disease with many variations (phenotype), usually characterized by chronic airway inflammation. Asthma has two key defining features: a history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, and variable expiratory airflow limitation.[3] By definition of occupational asthma (OA) and asthma are the same, the difference is due to causes and conditions which are attributable to a particular occupational environment. The definition issued by the American College of Chest Physicians further stipulates that OA refers to de novo asthmas or the recurrence of previously quiescent asthma (ie, asthma as a child or in the distant past that has been in remission) induced by either sensitization to a specific substance, which is termed sensitizer-induced OA, or by exposure to an inhaled irritant at work, which is termed irritant-induced OA.[2]

Respiratory sensitization to an occupational agent is one of very few well established causes of adult asthma. It is thus potentially preventable and furthermore offers a rare opportunity to cure an asthmatic patient of their disease. Moreover, it seems to be a costly disease. In the UK, the total lifetime costs of cases of occupational asthma reported are estimated to be up £100 million each year.[4,5] In Indonesia, the author did not find the particular data enough. For these reasons, the disease has a high profile in industrial legislation in most of the developed world. Therefore, especially faculty of medicine, University of Lampung provides a special place for the field of agromedicine to provide understanding about occupational asthma to governments, companies, and communities working in the industry.

Types of Occupational Asthma

The guideline on medical practice of the American College of Chest Physicians (ACCP) 2008 divides OA into two categories: sensitizer-induced occupational asthma and irritant-induced asthma.[1,2,6]

1. *Sensitizer induced occupational asthma* is caused by physical contact with allergens in the workplace. The contact may occur in two ways:

1.1 High molecular weight sensitizers, such

as protein from animals which occurs in cattle farming, honey bee farming or seafood preparation process. High molecular weight allergens from plants such as dyes, latex, starch, or high molecular weight allergen from fungi such as mushroom spore contacted by mushroom farmers or a scientist in a laboratory.[1,2,6]

1.2 Low molecular weight sensitizers: mostly chemical or initial substance used in industrial manufacturing of other chemical substance such as organic solvents or organic compounds of metals.[1,2,6]

2. *Irritant induced occupational asthma* is caused by physical contact with substance irritant to the respiratory system at high level within a short period of time which can directly damage the tissue within the respiratory tract of the patient.[1,2,6]

Etiology

Although there are hundreds of agents used in the workplace that can cause OA, 50% to 90% of reported cases have been associated with exposure to flour, diisocyanates, latex, persulfate salts, aldehydes, animals, wood dusts, metals, and enzymes.[2,7]

Figure 1. Principal agents causing sensitizer induced OA[2]

Source/chemical class	Agent	Workers/occupations at risk
HMW agents		
Animals	Laboratory animals (mice, rats)	Research laboratory workers
	Cows	Farmers
	Seafood (fish, crustaceans, and molluscs)	Seafood processors, fishermen, aquaculturists
	Insects (eg, flies, locusts, worms, spiders, predatory mites/bugs, parasitoidal wasps, and nematodes)	Laboratory workers, fish food producers, fruit growers, biological pest control in greenhouses
	Animal-derived products:	Food processors, bakers
	• Milk/egg proteins, bovine serum albumin	Natural dye producers
	• Carmine from *Dactolylopius coccus*	
Plants	Flour (wheat, rye, barley, buckwheat)	Bakers, pastry/pizza makers, millers
	Latex (natural rubber latex from Hevea tree, *Ficus benjamina*)	Health care workers, laboratory technicians, floral workers
	Spices (eg, aniseed, cinnamon, coriander, fennel, and nutmeg)	Food industry
	Beans, seeds (eg, coffee, soybean, linseed, and lupine)	Food processors
	Roots, leaves (tea, chamomile, and henna)	Tea and herbal tea processors, hairdressers
	Ornamental plants	Horticulture
	Pollen (tomato, bell pepper, broccoli, and saffron)	Greenhouse workers
	Gums (acacia, guar, tragacanth, and psyllium)	Food industry, carpet manufacturing, pharmaceutical and health care workers
	Plant-derived products: colophony	Electronic soldering
Enzymes from various origins	α-Amylase, maxatase, alcalase, cellulase, papain, bromelain, pancreatin	Baking product production, bakers, detergent production, pharmaceutical industry, food industry
Molds	Various species	Biotechnology plants, waste management, wood workers, greenhouse workers, food industry
LMW agents		
Isocyanates	Toluene diisocyanate, methylene diphenyl-diisocyanate, hexamethylene diisocyanate	Polyurethane production, plastic industry, insulation, molding, spray painting
Acid anhydrides	Phthalic, trimellitic, maleic, tetrachlorophthalic anhydrides	Epoxy resin workers
Acrylates	Cyanoacrylates, methacrylates, plain acrylates	Adhesives, printing inks, paints and coatings, dental care, beauty care
Amines	Polyamine epoxy resin hardeners	Construction coatings, adhesives, plastic composites manufacturing, pipe relining
Biocides	Formaldehyde, glutaraldehyde, quaternary ammonium compounds, chlorhexidine, triclosan	Health care workers, cleaners
Drugs	Penicillin derivatives, cephalosporins, clarithromycin, minoxidil, ferrimanitol ovalbumin, glucosamine	Pharmaceutical workers, health care workers
Persulfate salts	Hair bleach	Hairdressers
Reactive and other dyes	Reactive black 5, pyrazolone derivatives, vinyl sulphones	Textile workers, food industry workers
Metals	Platinum salts, chromium, nickel, cobalt	Metal refinery, metal alloy production, electroplating, welding
Metal working fluids	Uncertain causal agent(s): biocides (eg, isothiazolinone derivatives, and bismorpholine), microorganisms, metals	Metal cutting
Woods	Red cedar, iroko, obeche, oak, and others	Sawmill workers, carpenters, cabinet and furniture makers

raise this possibility due to fear of job-loss or reduction in income if changes need to be made at work. Potentially greater education of workers about OA by web educational tools, brochures, and other means and standardized inclusion of questions in primary care regarding worsening of asthma symptoms with work and improvement off work (on weekend or holidays) may lead to greater recognition of OA. Other aspects of history include details of exposure at the onset or worsening of asthma symptoms. Changes in the work process that coincide with the onset of symptoms may help identify a culprit agent. Obtaining material safety data sheets can be helpful in identifying exposure in the work place and should be made available to the worker on request.[1,8]

The history should also include questions about high exposure to an irritant agent at work coinciding with the initial onset of asthma symptoms that would suggest irritant-induced asthma. Work exacerbated asthma causes symptoms worse at work, which may occur on a single occasion with an unusual exposure at work or may occur more regularly with exposure to irritants or common allergens at work differentiating asthma that has coincidentally started while working from occupational asthma can be challenging.[1,8]

Table 1. Occupational Respiratory History for Suspected Occupational Asthma[8]

1. While at your current job, have you had wheezing, cough, chest tightness, or shortness of breath?
2. If you answered yes, do these symptoms occur immediately after coming to work?
3. If you answered yes, do these symptoms begin hours after coming to work? If so, how many hours?
4. If you answered yes, do these symptoms continue after coming home from work? If so, within how many hours and how long do these last?
5. If you answered yes, do the symptoms decrease on weekends or vacations?
6. How long were you working at your current job before you first noticed respiratory symptoms?
7. Are you a current smoker, former smoker? If yes, record pack-years.
8. Have you ever been diagnosed with asthma, allergic rhinitis, chronic bronchitis, or chronic obstructive pulmonary disease? If yes, provide details.
9. Have you experienced nasal or eye symptoms (sneezing, itching of the nose or eyes) that begin or worsen at work? If yes, provide details.
10. If the patient does have asthma, list the required controller and rescue medication, frequency of exacerbations, and relation of these to work exposure.

Stepwise Evaluation of OA Due to a Workplace Sensitizer

Step1: Establishing Asthma Diagnosis

The first step in the diagnostic workup is to obtain a clinical and occupational history as described earlier. If a worker reports work related lower respiratory symptoms consistent with possible work-related asthma, the next step is to objectively confirm asthma by showing reversibility in forced expiratory volume in 1 second (FEV_1) after inhaled bronchodilator. Simple spirometry testing should be performed before and after 2 to 4 inhalations of albuterol delivered by a metered-dose inhaler. An increase in FEV_1 of at least 12% after bronchodilator treatment confirms asthma but alone is not sufficient to establish a diagnosis of OA.[1,2,8]

If reversibility in FEV_1 cannot be demonstrated, methacholine challenge testing is recommended. The methacholine test is performed by having the patient inhale nebulized saline, which is followed by inhalation of incremental doses of methacholine (0.125-25 mg/ml) every 5 to 10 minutes until a 20% decrease from the post saline FEV_1 is observed or until all challenge doses have been delivered without any decrease in FEV_1. The provocative concentration eliciting an FEV_1 decrease of 20% is referred to as the methacholine PC_{20} with a positive test reaction defined as PC_{20} no higher than 16 mg/ml.[1,2,8]

Step 2: Determining Workplace Connection

Once asthma is confirmed, a decrease in lung function during the work shift concomitant with exposure to a suspect

causative agent is required for confirming OA. The preferred approach is to perform a specific inhalation challenge (SIC) in a specialized laboratory. The SIC is considered the diagnostic gold standard for OA. Serial measurement of peak expiratory flow rate (PEFR) during work and away from work exposure is the alternative approach for confirming OA from an occupational sensitizer. OA is confirmed by consistent decreases in PEFR on days at work while exposed to a suspect causative agent that increases on days away from work. Workplace monitoring of PEFR has a sensitivity of 81% and a specificity of 74% for correctly identifying OA.[1,2,8]

Utility of Allergy Testing for OA

Whenever appropriated, specific IgE testing with high molecular weight (HMW) occupational allergens should be conducted with skin prick testing and or serum specific IgE. It should be emphasized that specific IgE determines sensitization status, but alone does not establish or exclude an OA diagnosis. A positive skin test or serum specific IgE assay reaction can assist in establishing causation of OA especially if allergen exposure to that substances is associated with work related decreases in PEFR.[1,2,8]

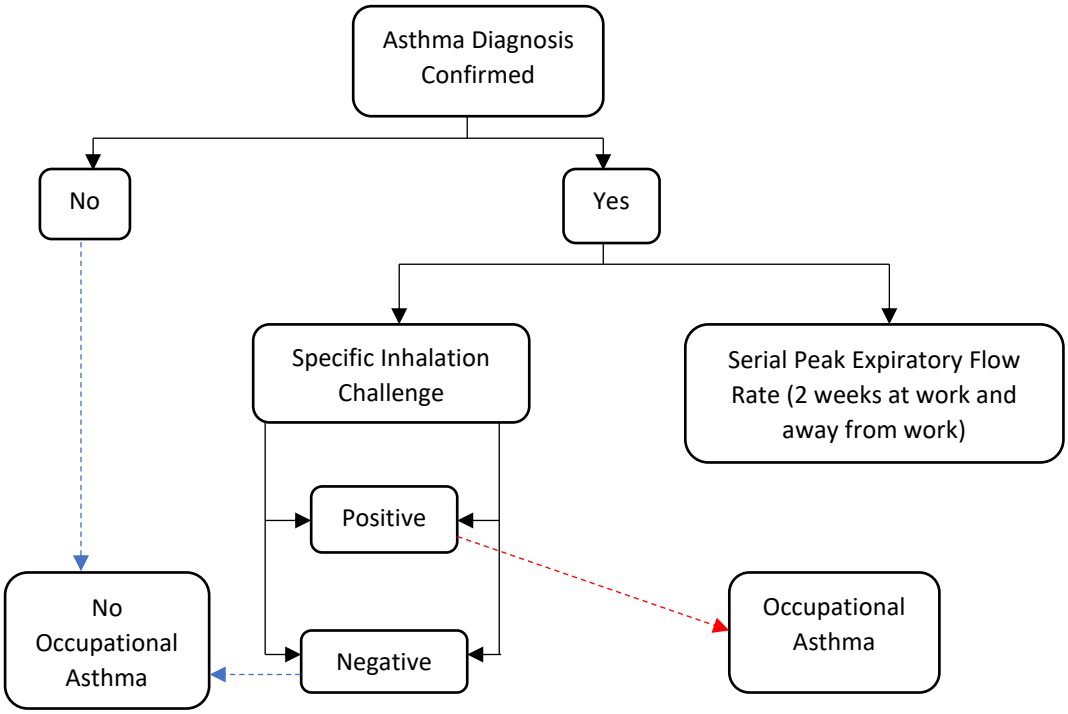

Figure 2. Stepwise approach to evaluating the worker with work related lower respiratory symptoms. Asthma is confirmed by reversibility in forced expiratory volume in 1 second (FEV_1) or with methacholine testing. If asthma is present, then occupational asthma (OA) is confirmed by a positive specific inhalation challenge (if available) or serial monitoring of peak expiratory flow rate for 2 weeks at work and 2 weeks away from work.[8]

Pathogenesis

Pathogenesis of disease are based on 3 causes as follows :[1,9,10]

1. Immunologically mediated with participation of specific IgE, like that for general asthma, is a stimulation of the immune system through classic IgE antibody mediated mechanism.
2. Immunologically mediated without evidence of participation of IgE is a stimulation of antibody which is not done through IgE. The pathogenesis mechanism remains unclear but some studies explain that the disease may be caused by certain change in the chemical structure of the underlying

allergen.

3. Non immunologic, irritant mediated is caused by a quick contact to intense substance that irritates respiratory system.

Prevention and Treatment

Occupational asthma is partly preventable. If feasible, primary prevention is the best approach. According to the Canadian Center for Occupational Health and Safety (CCOHS), better educational programs for workers, management, medical professionals, *etc.*, is the most important way for the prevention of occupational asthma. This will enable these at-risk groups to identify specific hazards and to apply preventive measures accordingly. Ongoing education of health care professionals may also lead to earlier diagnosis and better prognosis. The reduction or avoidance of a specific hazardous exposure is most effective for those persons who suffer from irritant-induced occupational asthma. By reducing the duration of exposure and the concentration of the causative agent, the probability of falling sick may be significantly reduced. Exposure may also be reduced through the use of face masks or improved ventilation.

Recovery is directly dependent on the duration and the level of exposure to the causative agent. Depending on the severity of the symptoms, the condition of the patient can improve dramatically during the first year after removal of exposure. Additionally, transfer of the patient form the hazardous environment and causative agents, medical and pharmacological interventions are necessary.[4,6]

Conclusion

Adult-onset asthma may be the result of an exposure to allergens in workplace. Several hundred agents in the workplace have been identified as capable of inducing occupational asthma, most are airborne proteins or highly reactive chemicals. In most cases, a sufficiently accurate diagnosis can be achieved through a combination of careful history, appropriate immunology and the comparison of serial measurements of lung function made at work and at home. Occupational asthma is potentially preventable. Preventive action should be focused on exposure control.

References:

1. Maneechaeye, W., Mitthamsiri, W., Sangasapaviliya, A. & Pradubpongsa, P. Asthma in Workers : An Overview. (2018) **6**, 121–124.
2. Cullinan, P., Vandenplas, O. & Bernstein, D. Assessment and Management of Occupational Asthma. *J. Allergy Clin. Immunol. Pract.* (2020):**8**; 3264–3275.
3. Reddel, H. *et al.* Pocket guide for asthma management and prevention (for adults and children older than 5 years). *Glob. Initiat. Asthma* 46 (2020).
4. Mahlknecht, S. V. Occuparional asthma review. *Occup. asthma* (2011): 2(2) **;**76–81
5. Chan-Yeung, M. & Malo, J. L. Aetiological agents in occupational asthma. *Eur. Respir. J.* (1994):**7**;346–371.
6. Dao, A. & Bernstein, D. I. Occupational exposure and asthma. *Ann. Allergy, Asthma Immunol.* (2018):**120**; 468–475
7. Reilly, M. J., Wang, L. & Rosenman, K. D. The Burden of Work-related Asthma in Michigan, 1988–2018. *Ann. Am. Thorac. Soc.* (2020):**17**; 284–292
8. Cullinan, P. & Newman Taylor, A. J. Occupational Asthma. *Allergy Allerg. Dis. Second Ed.* (2009):**2**;1687–1711.
9. Tarlo, S. M. & Lau, A. Update on the management of occupational asthma and work-exacerbated asthma. *Allergy, Asthma Immunol. Res.* (2019):**11**;188–200