

THE JOURNAL OF
ALLERGY
AND
CLINICAL IMMUNOLOGY

VOLUME 91

NUMBER 5

EDITORIAL

**The case for confirming occupational asthma:
Why, how much, how far?**

Occupational asthma is defined as "a disease characterized by variable airflow limitation and/or airway hyperresponsiveness due to causes and conditions attributable to a particular occupational environment and not to stimuli encountered outside the workplace."¹ It is now the most common occupational respiratory ailment.

**WHY SHOULD OCCUPATIONAL ASTHMA
BE CONFIRMED?**

The significant medical, social, and medicolegal implications of making a diagnosis of occupational asthma together with the development and improvement in diagnostic methods in recent years point to the need for confirming the diagnosis whenever feasible. It is known that the duration of symptoms after the onset of exposure influences the persistence of asthma once subjects are no longer exposed to the offending agent. Unlike patients with pneumoconiosis, most subjects who have occupational asthma are young. Advising a subject to leave his or her job and to

Abbreviations used:

PEFR: Peak expiratory flow rate

FEV₁: Forced expiratory volume in 1 second

retrain for a new job has an impact on quality of life.² Finally, it has been estimated that the cost of compensating one case of occupational asthma by the Worker's Compensation Board of Quebec is equivalent to \$40,000.³ Although it is reasonable to base a diagnosis of pneumoconiosis on a history of exposure to mineral dust and a chest radiograph that suggests fibrosis, this is not the case for occupational asthma. Both a history of exposure to mineral dust and lung fibrosis are rare occurrences in a general population. The presence of both variables in the same subject therefore makes the diagnosis highly likely without requiring the objective evidence of a lung biopsy. In the case of occupational asthma, the presence of asthma and exposure to agents now identified as causing occupational asthma (there are nearly 250 listed) are both common occurrences. The likelihood of having occupational asthma in the presence of asthma on the one hand and exposure to a potential causal agent on the other is not sufficiently high to make a diagnosis. Occupational asthma is unique in that we can confirm the diagnosis in a truly experimental and scientifically based manner.

From the Department of Chest Medicine, Hôpital du Sacré-Coeur, Montreal, Quebec, Canada. Reprint requests: Jean-Luc Malo, MD, Department of Chest Medicine, Hôpital du Sacré-Coeur, 5400 West Gouin, Montreal, Quebec, Canada H4J1C5.

J ALLERGY CLIN IMMUNOL 1993;91:967-70
Copyright © 1993 by Mosby-Year Book, Inc.
0091-6749/93 \$1.00 + .10 1/1/45638

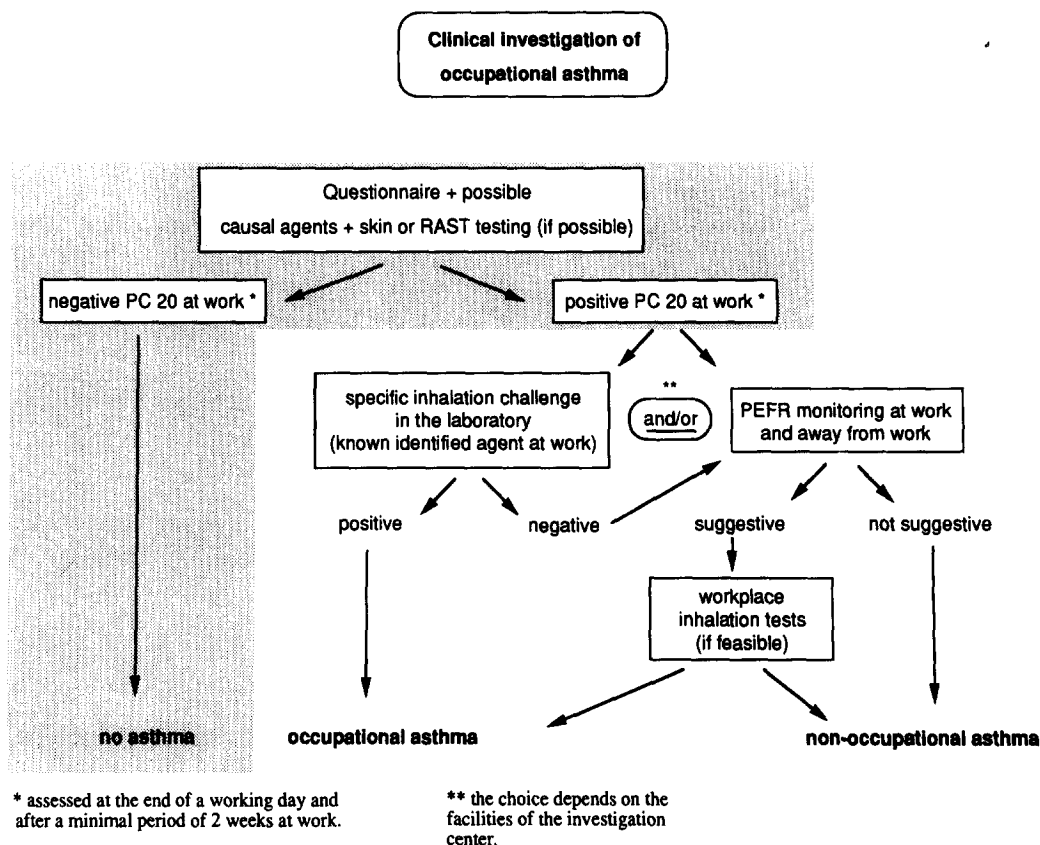


FIG. 1. Stepwise scheme for investigating occupational asthma. The *white zone* corresponds to the investigation that should be carried out in specialized centers, and the *gray zone* represents the steps that should be followed by allergologists, pneumologists, and internists in the initial step of the investigation. Reprinted from Bernstein IL, et al. Asthma in the workplace. New York: Marcel Dekker, Inc., 1993 (p. 113) by courtesy of Marcel Dekker, Inc.

HOW SHOULD OCCUPATIONAL ASTHMA BE CONFIRMED?

The article by Chan-Yeung et al. in this issue of the *JOURNAL* (pages 974-978) discusses the various means that can be used to investigate this condition. The decision tree is shown in Fig. 1. The questionnaire can suggest the presence of asthma symptoms at work only or shortly after a work shift, with improvement on weekends and vacations. Although the questionnaire is a sensitive tool, it is not specific enough to make a diagnosis. This is true of the closed questionnaire administered in epidemiologic surveys and the open medical history. The subject described by Chan-Yeung et al. had a history of common asthma, which is unusual because most subjects who have occupational asthma do not have preexisting asthma. This, however, does not exclude the possibility of occupational asthma, as the authors rightly suspected. The most important aspect of taking the history is to question every subject with asthma

about his or her workplace. A thorough list of all agents at the workplace should be obtained. If an agent known to cause asthma is present, an effort should be made to exclude or confirm the condition. In the case report by Chan-Yeung et al. glutaraldehyde, which has been described as causing occupational asthma, was present. Products known to cause occupational asthma are generally classified as high or low molecular weight agents, the threshold between the two being 1000 d. High molecular weight agents (e.g., antigens derived from flours or animals) are proteins, and immunologic testing (skin, specific IgE) can be performed. As for common inhalant allergens, the presence of immediate reactivity may simply reflect sensitization instead of a cause of asthma. However, the presence of skin reactivity and demonstration of bronchial hyperresponsiveness to a pharmacologic agent (methacholine/histamine) makes the diagnosis of asthma caused by the particular agent highly likely (80% likelihood).

Because the mechanisms of occupational asthma caused by low molecular weight agents are generally unknown, we must rely on bronchial hyperresponsiveness to pharmacologic agents, which is the hallmark of asthma, although it is not exclusive to the condition. The subject described by Chan-Yeung et al. was exposed to a low molecular weight agent, glutaraldehyde, and immunologic testing was not applicable. Bronchial hyperresponsiveness to pharmacologic agents can still be present months or even years after exposure ends. However, if bronchial hyperresponsiveness is absent, it should be reassessed when the subject is at work, preferably after 2 weeks on the job, in order to exclude occupational asthma. It is our experience that the absence of bronchial hyperresponsiveness to pharmacologic agents in such circumstances virtually excludes the diagnosis of occupational asthma. It is important to realize that all of the above steps in the investigation (questionnaire, study of the workplace environment, assessment of immediate immunologic reactivity in the case of high molecular weight agents, assessment of bronchial responsiveness) can be done in nonspecialized centers by practitioners of allergology, chest medicine, or internal medicine.

The other steps are usually reserved for specialized centers with specific expertise in the field of occupational asthma. Monitoring of peak expiratory flow rate (PEFR) must be carried out early in the investigation, when subjects are still at work. Monitoring cannot be carried out on subjects who are no longer exposed to the offending agent, as observed in the New Jersey SENSOR project.⁴ Of 70 subjects involved, only 14 underwent successful PEFR monitoring. However, if monitoring is done early on, when subjects are still at work, this method of assessing airway caliber for periods at work and away from work can be rewarding and generally offers good specificity and sensitivity in ascertaining the diagnosis⁵ in comparison with the gold standard, specific inhalation challenges.^{6, 7} However, there are several pitfalls to this approach: (1) it requires energy on the part of the investigator's team; (2) this approach is not devoid of risk because asthmatic reactions that are due to exposure at the workplace can occur, and there is no direct supervision to allow for early intervention in the case of such events; (3) interpretation is still based on visual examination, and no mathematical indices appear to be satisfactory⁷; (4) graphs can be difficult to interpret in the case of intermittent exposure to

the offending agent; (5) this approach requires good collaboration and honesty on the part of the subject; (6) changes in PEFR are not as sensitive as changes in forced expiratory volume in 1 second (FEV₁). It is likely, however, that the availability of instruments that can record FEV₁ and PEFR and store the information (time of assessment, physiologic results) on a computer chip in the near future will overcome these problems. Changes in bronchial responsiveness to pharmacologic agents are useful in confirming fluctuations in PEFR for periods at work and away from work,⁸ but they are far from constant. These changes are described in the article by Chan-Yeung et al., but they occurred at a time when baseline FEV₁ was lower, which made interpretation difficult.

Specific inhalation challenges still represent the gold standard in making the diagnosis. These tests can be performed in a hospital laboratory where environmental conditions can be controlled.⁹ These tests should be performed, at the initial step, with low doses and/or short duration of exposure in order to make this procedure safe. Some subjects can be highly reactive to the causal agent. In the case of isocyanates, efforts have been made to build smaller rooms to allow for more stable concentrations. There is usually no need to expose healthy subjects as a control group unless an immediate nonspecific, irritant reaction in the subject who undergoes challenges is documented. This pattern of reaction can, at times, be difficult to interpret. If this is the case, subjects with asthma and the same degree of bronchial responsiveness to pharmacologic agents can be used as a control group. Recent developments in closed-circuit methodology and smaller exposure chambers make obtaining dose-response curves with particles and isocyanates possible.^{10, 11} Chan-Yeung et al. have shown that these tests can also be carried out in the workplace under the close supervision of a technician. However, in this instance, the environment cannot be controlled, and every effort should be made to reproduce the usual working conditions. Authorization from the employer to carry out the tests should also be obtained.

CONCLUSION

Before advising a subject with asthma to leave his or her job because it is believed that the cause is the specific workplace, provisions for confirming the diagnosis should be made. Confirmation of the diagnosis is a stepwise procedure; a major

part of it takes place in nonspecialized centers. Once these steps have been followed, the subject should then be referred to a more specialized center.

Jean-Luc Malo, MD
Department of Chest Medicine
Hôpital du Sacré-Coeur
5400 West Gouin
Montreal, Quebec, Canada H4J1C5

I thank Katherine Tallman for kindly reviewing the manuscript.

REFERENCES

- Bernstein IL, Chan-Yeung M, Malo JL, Bernstein DI. Asthma in the workplace. New York: Marcel Dekker, 1993.
- Malo JL, Boulet LP, Dewitte JD, et al. A quality of life questionnaire for asthma: clinical validation of discriminative properties. *J ALLERGY CLIN IMMUNOL* (in press).
- Malo JL, Dewitte JD, Cartier A, et al. The Quebec system of compensation for occupational asthma: description, effectiveness and cost. (submitted for publication).
- Henneberger PK, Stanbury MJ, Trimbath LS, Kipen HM. The use of portable peak flowmeters in the surveillance of occupational asthma. *Chest* 1991;100:1515-21.
- Burge PS, O'Brien IM, Harries MG. Peak flow rate records in the diagnosis of occupational asthma due to isocyanates. *Thorax* 1979;34:317-23.
- Côté J, Kennedy S, Chan-Yeung M. Sensitivity and specificity of PC₂₀ and peak expiratory flow rate in cedar asthma. *J ALLERGY CLIN IMMUNOL* 1990;85:592-8.
- Perrin B, Lagier F, L'Archevêque J, et al. Occupational asthma: validity of monitoring of peak expiratory flow rates and non-allergic bronchial responsiveness as compared to specific inhalation challenge. *Eur Respir J* 1992; 5:40-8.
- Cartier A, Pineau L, Malo J-L. Monitoring of maximum expiratory peak flow rates and histamine inhalation tests in the investigation of occupational asthma. *Clin Allergy* 1984;14:193-6.
- Pepys J, Hutchcroft BJ. Bronchial provocation tests in etiologic diagnosis and analysis of asthma. *Am Rev Respir Dis* 1975;112:829-59.
- Cloutier Y, Lagier F, Lemieux R, et al. New methodology for specific inhalation challenges with occupational agents in powder form. *Eur Respir J* 1989;2:769-77.
- Vandenplas O, Malo JL, Cartier A, Perreault G, Cloutier Y. Closed-circuit methodology for inhalation challenge tests with isocyanates. *Am Rev Respir Dis* 1991;145:582-7.

AVAILABLE NOW! The FIVE-YEAR (1986-1990) CUMULATIVE INDEX TO THE JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY can be purchased from the Publisher for \$48.00. This comprehensive, 188-page reference guide is a current presentation of all topics included in the JOURNAL from January 1986 to December 1990 (volumes 77-86)—the past 10 volumes. It incorporates complete references to over 1500 original articles, abstracts, case reports, letters, editorials, and CME articles. It features 1662 subject headings, under which there are 5863 entries. Each subject entry lists the complete article title, author(s), volume, page, and year of publication. It also includes 5801 author entries, listing contributors, along with their respective titles, author-to-author referral, volume, page, and publication date.

To purchase, call or write: Mosby, 11830 Westline Industrial Dr., St. Louis, MO 63146-3318, or telephone FREE, Subscription Services, 1 (800) 453-4351 or 314-453-4351. PRE-PAYMENT REQUIRED. Make checks payable to Mosby. (All payments must be in US funds drawn on a US bank.) Price: \$48.00 in the US, \$54.35 in Canada, and \$51.00 international (price includes mailing charges).