

Occupational asthma – time for prevention

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NORDMAN H. Occupational asthma — time for prevention. *Scand J Work Environ Health* 1994;20 special issue:108—15. Incidence figures show that occupational asthma is increasing. It often takes a deteriorating course. Follow-up studies of workers suffering from the disease have uniformly reported persistence of symptoms over long periods, even among formerly exposed workers. New initiators of occupational asthma are continuously being reported. Still “old” agents, such as diisocyanates and flours, remain major causes. There seems to be some disconnection in the dialogue between the medical and the technical parties involved. For prevention, it is essential to ensure that important information not only reaches those who are responsible for designing and maintaining processes, but that it is presented in an intelligible form. Occupational asthma has become an important occupational disease that merits high priority. Recent achievements should facilitate preventive actions. However, prevention is a multidisciplinary enterprise needing the commitment of industrial hygienists and engineers, chemists, and allergologists, in addition to that of occupational health personnel.

KEY TERMS — exposure assessment, exposure control, primary prevention, registers, review, risk identification, secondary prevention, surveillance systems.

Occupational asthma is likely to be the most common occupational respiratory disorder today (1, 2). It is also one of the few increasing occupational diseases (figure 1). The assumption that occupational asthma recovers after cessation of exposure has been refuted; there are several studies showing the persistence of asthma in workers who have been removed from exposure (3, 4). The scientific interest in the disease has increased tremendously. Reports, extensive reviews, and textbooks are flooding the market, new causative agents are being recognized, prevalence figures from a variety of work environments are becoming known, mechanisms are becoming understood, and diagnostics are improving. However, with a few exceptions (5—7), prevention is mostly dealt with briefly or not at all in reports and reviews on occupational asthma. The increasing numbers of causative agents and rising incidence figures are shoving the prevention of occupational asthma high up the ladder of priorities. This article reviews various possibilities and difficulties associated with the prevention of occupational asthma.

Definition of occupational asthma

Occupational asthma as a medicolegal diagnosis

Occupational asthma is largely a medicolegal diagnosis. Definitions may have to be adjusted in accordance with national legislation. Several definitions

have been suggested. One widely adopted definition was suggested by Newman Taylor (8): “reversible airway narrowing causally related to exposure in the working environment to airborne dusts, gases, vapours, or fumes [p 241].” This definition seems to correspond to the medical and legal demands of several countries, including Great Britain, Canada (9), and Finland.

Occupational asthma through a pathophysiological mechanism

To most physicians occupational asthma signifies asthma initiated by sensitizers involving a period of sensitization. The preceding definition of occupational asthma includes bronchoconstriction induced by irritants and leading to inflammatory airway narrowing [ie, the “reactive airway dysfunction syndrome” (RADS)] (10), as well as to pharmacological bronchoconstriction, as seen in the form of byssinosis and grain fever (11). RADS is, by and large, always due to accidental exposure to irritants. The prevention of RADS is, therefore, rather straightforward. The mechanisms inducing the variable airflow obstruction seen in the cotton dust industry and in workers exposed to grain dust are not fully understood. For both there is a marked relationship between airflow obstruction and degree of exposure. This article focuses on asthma as a consequence of sensitization, and it adopts, in that respect, a more recent definition of occupational asthma, as suggested by Smith (12).

Prevention at different stages

Primary prevention generally means controlling the exposure that eventually leads to asthma. *Secondary*

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prevention implies early detection aiming at the prevention of impairment and disability from asthma. Secondary prevention can also involve the detection of symptoms (eg, rhinitis, cough) and other indications [eg, specific immunoglobulin (Ig) E antibodies] of sensitization that can precede the outbreak of asthma (7, 9); as the objective is to avert the triggering of occupational asthma, this form of prevention could be considered to be primary as well. Management of occupational asthma, sometimes discussed under the topic of *tertiary prevention*, implying prevention of asthma from deterioration, is not included in the objectives of this review.

Primary prevention

The control of environmental exposure involves several steps, such as the identification of risks at the workplace, epidemiologic surveys, exposure assessments, and setting hygienic limits to monitor health at the workplace. It also demands cooperation between medical, chemical, technical, engineering, and labor protection experts.

At the workplace, exposure can be controlled in many ways. The safest measure is to prevent potential initiators of asthma from being used or to prevent the agent from entering the breathing air at the workplace. Less efficient measures include ventilation and dust suppression systems aiming at the reduction of emissions and air concentrations. Finally, the worker may, in situations such as maintenance or operational disturbances, have to be protected from inhaling the potentially noxious substance.

Many measures to prevent exposure are purely engineering control methods, while others imply worker participation. The most essential measures of

preventing exposure were outlined by Schilling (13) as follows: (i) elimination or diminution by substitution, redesign of a process or improved work methods, (ii) total enclosure of the process, (iii) segregation of a process, (iv) control by dilution and local exhaust ventilation, (v) dust suppression, (vi) good housekeeping, including disposal of waste, (vii) personal protection, (viii) training for health and safety, and (ix) maintaining control by environmental and health monitoring. These measures still form the core of exposure control.

To the list should be added maintenance of processes and control systems (14). One would also like to add, as a separate issue, the control of microbial growth, which seems to be becoming more and more important in the prevention of hypersensitivities. In bakeries and farming, storage mites may be as important sensitizers as grain dust (15). Molds in conjunction with humidifying the work environment, as well as molds as a consequence of water damage in buildings, are also current issues (16).

Risk identification. In any potentially hazardous work environment a risk assessment ought to be carried out. Ideally, the risk should be predicted, and detrimental health effects averted. A prerequisite is that information about potential sensitizers be available. There have been attempts to compile lists of sensitizing agents in some countries, and such a list has been published in England, as referred to by Venables (7). In the future, member states of the European Union (EU) will adopt the EU directives for listing and labeling chemicals. The listed substances have thus far not undergone any uniform classification procedure. Some may be potent sensitizers,

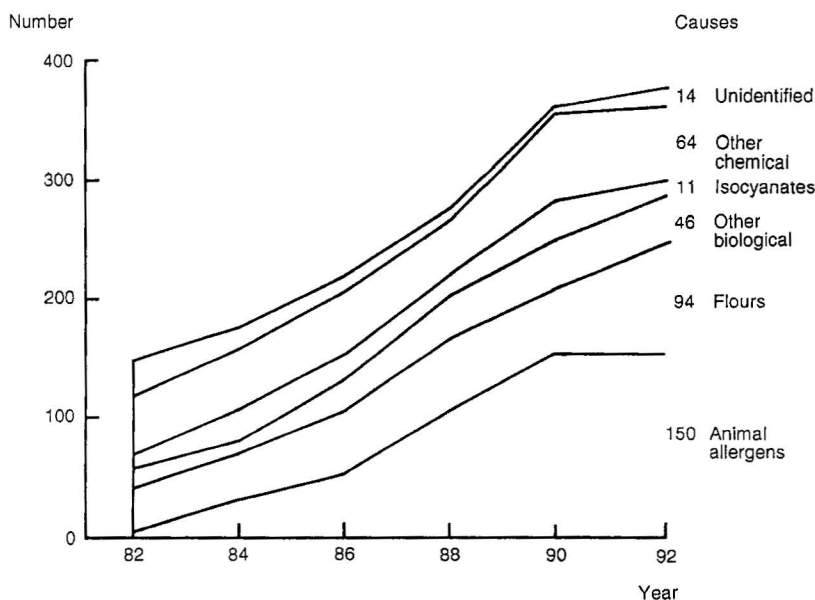


Figure 1. Incidence of occupational asthma in Finland 1982-1992, according to major causes (from the Finnish Register on Occupational Diseases). The numbers listed with the causes are the numbers of cases in 1992.

while others may have caused sensitization on a single occasion. Data on exposure intensities needed for sensitization are scarce and far from exact (17, 18). Regardless of their imperfections the available lists have been useful in that they have facilitated product labeling and risk assessments at the workplace.

A classification system for chemicals was recently suggested (19). A Nordic expert group pointed out the need for uniform terminology and common criteria for classifying sensitizing chemicals. The proposed system uses the same approach as that for carcinogenic substances adopted by the International Agency for Research on Cancer (20). Data are categorized as human evidence, evidence from animal studies, and supporting evidence. Data can be classified as "sufficient evidence," "limited evidence," and "information does not permit conclusions." Group I includes substances for which there is sufficient human evidence that they initiate specific hypersensitivity of the airways, group IIA is for probable initiators for which limited human or supporting evidence is available, and group IIB for possible initiators. In group III, data do not permit classification, and group IV is for chemicals that probably do not sensitize the airways. It is too early to evaluate the usefulness of the classification system, which, apart from classifying chemicals, helps to define areas in which information is lacking and research needed.

Exposure assessment. In avoiding harmful exposure, it is necessary to know at what levels a substance can initiate asthma and what levels can provoke asthma in workers who have already developed asthma. Allergens such as pollen and mold spores are measurable. As regards fungi, the most common methods measure viable spores, which may comprise as little as 1% of the total allergenic material. More recently developed immunoassays allow the measurement of protein allergens. These very sensitive methods are based on the determination of mono- or polyclonal antibodies. There are methods for directly measuring immunoglobulin (Ig) binding and others using inhibition techniques (21, 22). The assessment of aeroallergens makes it possible to monitor allergens in the work environment, as well as to study exposure-response relationships, which hopefully in the near future will generate data for occupational health limits based on the sensitizing properties of various airborne allergens.

Dissemination of information. The steady increase of occupational asthma in most industrial countries over the last 20 years points to the fact that prevention has been unsuccessful. Despite the body of information that has accumulated, and which undoubtedly facilitates preventive action, the situation has changed little. Isocyanates still cause the most com-

mon form of chemically induced asthma, the importance of organic acid anhydrides is increasing, and asthma caused by flour, laboratory animals and red cedar is not declining (2, 23, 24) (figure 1). How can the modest preventive results possibly be explained or defended? Do they reflect indifferent and nonchalant attitudes or ignorance, are both workers and employers inadequately informed, are compensation systems inadequate, are repercussions too mild to discourage violations?

One reason for the negative trend seems to be that information does not reach the right forum, or information is disseminated in a form unintelligible to the receiver. For example, information on diisocyanates exists in abundance. It is well known that diisocyanate-induced asthma persists for a long time and may become permanent. Nevertheless, substitutes have not been introduced, and cars are painted as before at a high price in terms of health.

Biotechnological achievements have made it possible to produce enzymes at lower costs. New commercial applications of enzymes are swiftly being invented. Throughout the 1980s the baking industry increased the use of enzymes. Reports on asthma among bakers initiated primarily by alpha-amylase have been published at an increasing rate during the last few years (25–27). Similarly, preliminary results show a prevalence of about 10% in two recently studied research laboratories (28, 29). Considering the enzyme-induced problems in the detergent industry during the late 1960s, the present situation appears to be unnecessary. There were distinct solutions to the enzyme problem which should have guided the use of powdered enzymes in other industries (30, 31). The lessons were poorly learned.

The preceding examples illustrate one reason for preventive failure: industry is not receiving or not seeking help from experts in occupational medicine during the planning of new processes or the redesign of old ones. This field is open for activities on both sides.

Susceptible persons. Preplacement and periodic examinations are carried out to ensure that the worker is physically and mentally fit for a particular job, but also to identify persons who may be particularly susceptible to a certain type of exposure. Symptoms from the airways, such as asthma and chronic bronchitis, undoubtedly render job applicants less suitable for tasks involving exposure to nonspecific irritants because their disease may deteriorate, not because of an increased risk of sensitization. The decision does not depend on whether the symptoms have an atopic etiology or not.

Atopy, defined as the capacity to produce IgE-type antibodies readily when exposed to common environmental allergens, is a predisposing factor in several work environments associated with exposure to high-molecular weight substances. It is also a char-

acteristic of some 30% of any working population, and therefore preemployment screening based on atopy would affect a substantial number of job applicants.

Sensitization has been demonstrated to be more common among atopic laboratory animal handlers (28, 29), detergent industry workers (31, 32), and workers exposed to grain dust (33, 34) or locusts (35) than among nonatopic persons. Among atopic laboratory animal handlers, asthma is a significantly more common outcome of sensitization than among nonatopics (28, 29). As a consequence preplacement screening for applicants to work involving laboratory animal handling has been suggested (36). The criteria have obviously been used to some extent (37), although colleagues have unanimously declared that the criteria, among them atopy, do not identify a significant proportion of applicants who would develop disease (ie, the sensitivity, specificity, and predictive value of the suggested criteria are far too low) (9, 28, 37–39).

There are obvious explanations for the low predictive value of atopy. First, IgE-mediated occupational asthma is frequently developed by persons without any evidence of atopy, and, second, occupational asthma is caused by mechanisms unrelated to atopy (ie, not IgE-mediated).

Atopy is of little relevance to the development of asthma as a result of exposure to most low-molecular weight chemicals, such as formaldehyde (40), diisocyanates (41), and some organic acid anhydrides (42).

Interestingly, Venables and her co-workers (43) showed that tobacco smoking in a tetrachlorophthalic anhydride plant was a stronger risk than atopy with respect to the development of specific IgE antibodies. This finding corroborated earlier results from a coffee roastery (44). Smoking was also strongly associated with skin sensitization to platinum salts (45), and a similar association has been shown in some other environments as well. Although the association between smoking and the development of specific IgE antibodies is not a uniform observation even in studies on organic anhydrides (42), it seems reasonable to advise workers to refrain from smoking in industries in which such a risk has been demonstrated.

Secondary prevention

Every new case of occupational asthma is a result of the failure of primary prevention, the intention of which is to prevent the exposure that causes asthma. In daily practice, the risk of sensitization is identified through observations of detrimental effects. What is alerting the health personnel is complaints of symptoms in relation to work by one or several workers. Thus effective secondary prevention is important. There is evidence showing that early diagnosis followed by removal from exposure affects the

prognosis of the person in question favorably as compared with one whose exposure continues (3, 4, 46).

Some strategies for the early detection of occupational asthma in the workplace have been suggested, but there is no consensus as to the approach of choice. Structured questionnaires have been tested and found sensitive enough although they are not very specific (47). Still, questionnaires or personal interviews afford the best way to define those who should be subjected to intensified surveillance or specific investigations. Sensitization by high-molecular weight proteins that cause IgE-mediated allergy can be detected by routine skin testing at suitable intervals. Repeated skin prick tests do not involve any additional risk of sensitizing the worker (31). As sensitization per se is no disease, and the predictive value of specific IgE antibodies is low with respect to the development of occupational asthma, there is little rationale for any other action than intensified surveillance of such symptomless workers.

If the exposure is to a low-molecular weight chemical, routine skin tests have a low sensitivity. In isocyanate-induced asthma IgE antibodies have been found in about 20% of subjects reacting to a specific inhalation test and exclusively among those who showed an immediate reaction. Moreover, only about half of the immediate reactors displayed IgE antibodies (48). This and similar experiences by other authors (49) render routine skin testing with conjugates rather meaningless. The presence of specific IgE antibodies may aid the diagnosis, although the absence of antibodies does not preclude the diagnosis. Allergic rhinitis may precede occupational asthma, but the predictive value of the condition has not been assessed. Action is often taken on the empirical experience that continuing exposure will trigger asthma in workers suffering from specific allergic rhinitis. This assurance is probably correct, but ought to be demonstrated.

The role and usefulness of bronchial hyperresponsiveness in occupational asthma is not as yet clear. Increased bronchial hyperresponsiveness is a feature in most workers with occupational asthma (50). However, a normal responsiveness of the bronchi in workers with occupational asthma is not rare (51). An increased bronchial hyperresponsiveness is associated with a late asthmatic reaction, which it precedes, whereas immediate reactions appear to be unrelated to changes in bronchial reactivity (52). Sometimes bronchial hyperresponsiveness is induced by occupational agents that do not cause simultaneous airway obstruction (53). It seems as if bronchial hyperresponsiveness is a consequence of occupational exposures rather than a risk factor for the development of occupational asthma. Repeated measurements of the nonspecific reactivity of the bronchi is useful, both in the diagnostics and management of occupational asthma.

Accurate diagnostics

There are three distinct reasons why one should always try to reach a specific etiologic diagnosis of occupational asthma: (i) when replacing or re-educating the diseased worker, one needs to know what specific exposures to avoid in the future, (ii) the specific provocation test affords the most important means of identifying new initiators of occupational asthma in the work environment, and (iii) registers on the incidence and causes of asthma are no better than the information fed into them.

During the last few years recommendations have been made for the diagnostics of occupational asthma (54, 55). The specific inhalation provocation test has been regarded as the "gold standard" with which the sensitivity and specificity of other diagnostic tests can be compared. Although inhalation challenge tests undoubtedly represent the most reliable way of diagnosing occupational asthma, the method may not be incontestable. Specific inhalation challenges are not always practicable, the asthma may be too unstable, the offending agent is unknown, or the provocation situation can, on the whole, not be arranged. A short provocation situation does not necessarily correspond to a continuous 8-h daily exposure. The sensitivity to the substance may have vanished since the last exposure or during sick leave. For ethical reasons, occupational exposure limits should not be exceeded in an exposure chamber, although it may often be the situation at work. Finally, safety aspects do exist. Reactions may be severe (56) and the increase in bronchial hyperresponsiveness may continue for weeks and even months after a challenge test. Recurrent nocturnal asthma may also result. It is both likely and desirable that inhalation challenge tests become more and more common in the routine diagnostics of occupational asthma. It is, therefore, pertinent to emphasize that challenges should definitely be performed only in centers with sufficient experience with provocation testing.

In situations in which challenge tests are impractical, the diagnosis has to be done relying on other combined information. If the exposure to an agent known to initiate asthma can be ascertained and the medical history is suggestive of occupational asthma, the diagnosis can often be made with a fairly high probability by the demonstration of bronchial asthma, confirmation of work-related airway obstruction, and the demonstration of specific antibodies. Serial peak flow measurements and measurements of nonspecific bronchial responsiveness have proved useful in the demonstration of work-related bronchoconstriction (54).

Surveillance programs

In times of economic recession resources are allocated with increasing stringency to areas of priority. When priorities are set, it is necessary to know

both the occurrence and incidence trends of a particular disease relative to those of other diseases. This situation applies strongly to occupational asthma, which is recognized as both underdiagnosed and underreported (1, 57, 58). National incidence figures, if available at all, have been suffering from varying degrees of inaccuracy (59).

In 1987 a system for the surveillance of work-related and occupational respiratory disease (SWORD) was started in Great Britain. It involves pulmonary and occupational physicians, members of the British Thoracic Society and the Society of Occupational Medicine, who voluntarily participate by reporting new cases of occupational respiratory diseases on a monthly basis. The year 1989 was the first for reporting. An overall incidence of 22 cases of occupational asthma per million of the working population was reported with a regional range of 8–63. The most frequently reported occupational disorder turned out to be occupational asthma (26%), followed by mesothelioma (16%) and pneumoconiosis (15%) (1). Thus, from the point of view of the need for preventing occupational asthma, SWORD generated important and novel information from the very beginning. Compliance was surprisingly good among pulmonary physicians during the first year. It remains to be seen whether the enthusiasm can be sustained in the future.

In Finland, the Register of Occupational Diseases was established in 1964. The Act on the Supervision of Labor Protection, which became effective in 1974, requires physicians to report every case of occupational disease. The coverage is considered fairly good, although not complete. According to the Finnish Register, the overall incidence of occupational asthma in Finland in 1990 was 152 per million of the work force. This figure is based on 375 new reported cases and a work force of 2.47 million. According to rather loose figures for total exposed categories (information obtained for 1989 and 1990 at the Central Statistical Office of Finland), the highest incidence was found among bakers, 4000 per million bakers per year. Spray painters had an incidence of 3100 and electronic assemblers 720 per million (60). These figures are higher than those reported by Meredith (2): bakers 334 per million, spray painters 658 per million, and electronic equipment assemblers 175 per million. The rather large differences between the Finnish register and SWORD can be accounted for by a variety of reasons, for example, the number and type of agents included in the prescribed national lists (61), differences in national legislation, compliance with a voluntary system as compared with a mandatory one, diagnostic differences, and some others. A more careful analysis of the data would probably yield valuable information.

In the United States, the National Institute for Occupational Safety and Health (NIOSH) has launched the Sentinel Health Notification System for Occupational Risks (SENSOR) for the surveillance of new

cases of occupational diseases. It is, so far, too early to evaluate the efficiency of this system (57).

The need for reliable surveillance systems appears to be recognized and, hopefully, more and more countries will see the advantages and the necessity of having registers for occupational disorders.

Epidemiologic surveys

Epidemiologic studies have been deemed useful in the prevention of occupational asthma (6, 62). Epidemiologic studies can clarify rates of occurrence in a given work environment and relate the occurrence of occupational asthma to the degree of exposure. Studies can be designed to identify causes. An epidemiologic approach is likewise useful in assessing the effect of intervention measures. Much has also been learned about individual risk factors for the development of occupational asthma.

The vast majority of epidemiologic surveys on occupational asthma have been cross-sectional and have resulted in rough estimates of the occurrence of occupational asthma in a certain work environment at a given time. Prevalence studies on hypersensitivity, especially occupational asthma, are particularly vulnerable to selection bias, notably survivor bias. This problem is frequently overlooked. Clinical asthma initiated specifically by an agent present at the workplace is likely to force a change of work tasks or the work environment. Such changes can take place already at a stage of rhinitis, conjunctivitis, or coughing. Consequently, the work force would be likely to be depleted of workers with work-related asthma. In environments in which the agent causes a typical IgE-mediated sensitization, such as in the handling of laboratory animals or in the baking industry, selection can also apply to atopy. The opposite may be true for an unexposed reference population. A personal or family history of allergy may lead the worker to a clean environment free of sensitizers or irritants. Selection may take place due to allergies in the family or through vocational guidance and preemployment examinations. Part of the selection bias in prevalence studies can be controlled if the reasons for leaving work are studied among those who have left during the last 10 years.

The need for cohort studies has been recognized (6, 7). However, cohort studies are connected with difficulties of their own, and the paucity of such data from most environments is probably due to a lack of feasibility. Selection bias applies to this design as well, unless quitters can be accounted for. The ideal set-up of newcomers is rare; such a design also takes into account those newcomers whose symptoms cause resignation within days or weeks and leaves such workers out of work records. From the point of view of prevention longitudinal studies are still needed.

Case-referent studies nested in cohorts would seem to be the design of choice in the study of host factors and exposure aspects (62, 63).

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