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Prevention of occupational asthma

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ABSTRACT: This paper focuses on the prevention of asthma caused by exposure to sensitizing agents in the workplace. Control of exposure (primary prevention) is the most direct method of reducing the number of incident cases. Screening programmes are also necessary as a "safety net", and have value as secondary prevention, because early detection may improve long-term prognosis.

It is recommended that regulatory or advisory bodies with responsibility for occupational asthma publish a guidance document on occupational asthma explaining their current concepts. Surveillance activities provide information on how common asthma is relative to other occupational lung diseases, and on the relative frequency of occurrence of asthma caused by different agents. Publication of a list of sensitizing agents would aid those with responsibility for control of exposure in the workplace. Epidemiological research on exposure-response relations is necessary as a background to prevention. This paper recommends such studies. Immunotoxicological research also has a role in testing hypotheses that cannot be tested in human subjects. Some standardization of screening programmes in industry is desirable. A short symptoms questionnaire is economical and acceptable to workers, but there are other approaches. Finally, evaluative research on prevention measures gives information on their effectiveness and efficiency.
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Scope

The incidence of asthma caused by workplace exposures will not fall unless those with responsibility for prevention have a clear idea of what they are trying to prevent. This report focuses on the prevention of asthma caused by exposure to sensitizing agents in the workplace. It would be wrong to assume that asthma induced or exacerbated by irritant exposures to chemicals in the workplace is of no importance. On the contrary, there is no information on the relative frequency of different types of asthma in the workplace; types related to irritant exposures may be the most frequently-occurring types in some industries.

This report does not include working definitions for specific purposes of public health practice, clinical work, or epidemiological research. Such definitions grow from an understanding of conceptual definitions, and take their final form depending upon several factors, including the context of the investigation (for example clinical practice as opposed to workplace screening), availability of resources, and potential for bias.

Approach to prevention

The importance of primary prevention underpins the writing of this paper. Control of the exposures causing asthma is the most direct way of reducing the number of incident cases. In order to achieve control, these exposures must be named; several hundred sensitizing agents are currently known to cause asthma; the relative frequency of occurrence of asthma caused by different agents can only be known by national surveillance; those responsible for prevention can only know where to take action if a list of sensitizing agents is published. Secondly, the relationship between exposure and response must be quantified by longitudinal epidemiological studies and by inference from animal experimentation. Thirdly, the effectiveness of control measures in reducing the incidence of asthma must be measured.

No control measure can be assumed to eliminate asthma short of elimination of the causal agent. Therefore, cases of asthma will develop and screening programmes are needed to detect them. Detection is useful as secondary prevention because there is evidence that patients with occupational asthma who promptly cease exposure to the causal agent have a better long-term prognosis than those who do not. Detection is also useful as a way of monitoring primary prevention measures to control exposure though it would be wrong for monitoring to rely on the detection of cases rather than on assessment of the workplace.

Methods of prevention

Because this paper envisages direct prevention as taking place in the workplace, another underlying assumption behind its writing is that the people with primary

responsibility for prevention are in the workplace: managers and supervisors, worker representatives, and health and safety professionals working within industry. It does not assume that regulatory bodies, physicians outside industry, academic institutions, and others concerned with occupational health and safety have no influence. It is clear that they have considerable influence. However, in general, such agencies and individuals have no direct authority to control the work process and, where their influence is felt, they act indirectly through those with such authority. Those with responsibility are usually less knowledgeable than advisors and regulators about asthma and its relation to work, but more knowledgeable about practical ways in which control measures can be implemented. Successful prevention depends on co-operation between employers, workers and their representatives, regulators, and medical and nonmedical specialist advisors.

Summary of recommendations

This paper recommends that regulatory or advisory bodies with responsibility for occupational asthma publish a guidance document on occupational asthma explaining their current concepts. Surveillance activities give information on how common asthma is relative to other occupational lung diseases, and on the relative frequency with which different agents cause asthma. Publication of a list of sensitizing agents would aid those with responsibility for control of exposure in the workplace. Epidemiological research on exposure-response relations is necessary as a background to prevention. The paper recommends such studies. Immunotoxicological research also has a role in testing hypotheses that cannot be tested in human subjects. Some standardization of screening programmes in industry is desirable. A short symptoms questionnaire is economical and acceptable to workers, but there are other approaches. Finally, evaluative research on preventive measures gives information on their effectiveness and efficiency.

Asthma

Asthma is common, found in up to 10% of adults [1]. Scadding's definition is widely quoted: "variable dyspnoea due to widespread narrowing of peripheral airways in the lungs, and varying in severity over short periods of time, either spontaneously or as a result of treatment" [2].

Asthma and bronchial hyperresponsiveness

Bronchial hyperresponsiveness is generally accepted as the defining physiological characteristic; although it is not the only characteristic of asthma, nor is it found exclusively in asthma. Its severity is variable, and it may not be detectable in every patient with asthma on each occasion of testing. Bronchial hyperresponsiveness is normally expressed in terms of response to inhaled histamine or acetylcholine, or its analogues [3, 4]. This response relates well to indices of the severity of asthma: the minimum treatment needed to control symptoms [5], response to bronchodilator, diurnal variation in lung function [6], and airway narrowing on exercise [7], after inhalation of cold air [8], or of dusts and aerosols [9].

Occupation and asthma

Any occupation where dusts, vapours or gases are inhaled is a potential cause of lung disease, or may exacerbate pre-existing lung disease. There are several ways in which occupational exposures cause or provoke asthma.

Exacerbation of asthma. Firstly, asthma may be exacerbated by work involving exercise or exposure to cold, dust or irritants to which hyperresponsive airways react. For example, people with asthma, but not normals, react with airway narrowing to sulphur dioxide at concentrations lower than recommended occupational standards [10]. There is a prior history of symptoms, no latent interval of symptom-free exposure, and symptoms are improved by drug treatment and by avoiding heavy exposure to the provoking agent. The term "irritants", as used here, does not imply a specific mechanism, such as stimulation of irritant receptors and reflex bronchoconstriction.

Pharmacologically active agents. Pharmacologically active substances may be used at work, and have been invoked as explanations for work-related asthma. For example, hexamethylene diisocyanate has *in vitro* anticholinesterase activity, though it has no measurable *in vivo* cholinesterase inhibition in guinea-pigs [11]. It is not clear how commonly this occurs. It is not clear whether provocation of airway narrowing by pharmacological means should be regarded as a form of "irritant response", as described above.

Heavy exposures and irritant-induced asthma. Heavy exposure to irritants in industrial accidents causes pulmonary oedema and also airway mucosal damage [12]. Survivors may have bronchial hyperresponsiveness, which persists for months, and perhaps longer [13]. This irritant-induced asthma has been termed "reactive airways dysfunction syndrome" [14]. It is not clear whether this represents the severe end of the spectrum of "irritant responses". Less extreme exposures of volunteers give a temporary increase in bronchial responsiveness [15]. The inflammatory response to viral respiratory tract infection [16], or influenza immunization [17], is accompanied by temporarily increased bronchial responsiveness.

Sensitization. Lastly, exposure at work causes sensitization, which, in a proportion of those affected, is associated with asthma. Although asthma caused by chemicals is sometimes discussed as a separate category from asthma

caused by biologically-derived agents, there is no evidence that the asthma is qualitatively different. Allergic asthma caused by work is, therefore, discussed here, regardless of the nature of the causal agent.

The term "allergy" was first used by VON PIRQUET [18] for any altered response to foreign material, either immunity or hypersensitivity, but its use for immunity has lapsed. There is no evidence that allergic asthma caused by an occupational exposure differs from that caused by common allergens, such as pollens or house dust. The term "allergy" is often used to imply an immunoglobulin E (IgE)-mediated mechanism. Asthma caused by some occupational exposures is IgE-mediated, for example to rat urine [19]; although it is not always possible to detect specific IgE antibodies in every case at the time of testing. With some other causes of occupational asthma, for example Western red cedar wood, it is possible that other immunological mechanisms mediate the asthma in a high proportion of patients. The symptoms and physiological findings are indistinguishable from those in IgE-mediated asthma. The term "sensitization" is used here, rather than "allergy", to avoid implying that IgE is the only immunological mechanism in occupational asthma.

Clinically, there is a latent interval of weeks to years, and patients may have no prior history of asthma, unless they are already hypersensitive to some other allergen. After sensitization, there may be responsiveness at extremely low levels of exposure. Potentially fatal attacks of asthma can occur after exposures which are orders of magnitude below those which irritate. Often the only way that symptoms can be minimized is by leaving the job. The clinical picture is, thus, different from irritant-induced asthma, where, although there is nonspecific airway hyperresponsiveness to a range of airway irritants, patients do not have extreme and specific sensitivity to low concentrations of the causal agent.

The pattern of response is not specific to a particular agent. For example, the acid anhydrides, a group of low molecular weight agents, can cause IgE-mediated asthma, stimulate specific immunoglobulin G (IgG) and other antibody production, exacerbate pre-existing asthma, and cause direct toxicity to the airways and lung parenchyma, if inhaled in sufficient concentration [20].

Sensitizer-induced asthma

Mechanism

In the airways, the inhaled antigen links to antibody, which starts a chain of mediator release leading to smooth muscle contraction, mucosal oedema and mucus hypersecretion. The physiological evidence of these processes is airway narrowing, which may be immediate, late or dual [21].

Late asthmatic response

It is thought that the late response is the response component which most closely resembles spontaneously-occurring asthma. The late response is maximal at 4–8 h after exposure. Increases in nonspecific bronchial responsiveness occur in parallel with the late response, and were first reported by COCKCROFT *et al*. [22]. It may be weeks before baseline values are regained, and during this time the patient experiences a heightened response to irritants and exercise, with increased diurnal variation in airway calibre. This phenomenon resembles the increase in bronchial responsiveness after infection or irritant exposure described above, and the common factor is likely to be airway mucosal inflammation, which HOGG [23] has suggested increases mucosal permeability, allowing chemical mediators to reach smooth muscle and irritant receptors.

Terminology

The term "occupational asthma" is often used loosely. In this paper, two types of occupationally-induced asthma are recognized: sensitizer-induced asthma (or allergic asthma) and irritant-induced asthma (reactive airways dysfunction syndrome). In both pathways to asthma, a work exposure has caused a fundamental change in the worker's airway response to his work and home environment. This is qualitatively different from work-exacerbated asthma, where work exposure is only one of many triggers which provoke asthma attacks. The complexity of the interactions between occupational and nonoccupational factors, and between asthma and other airway diseases, has been discussed in more detail by HENDRICK [24]. He makes the important points that defining one's terms "is not simply a matter of semantics, because the attendant problems of recognition, management, prevention, and compensation may differ profoundly" and that an unduly broad definition "assumes a license that few would consider helpful".

HARBER [25] has recently delineated 12 "occupation-asthma interactions". As well as categories of no relationship and uncertain relationship, he includes the two causal pathways noted in this paper: induction by a sensitizer or by a high-level toxic exposure. He identifies permanent and temporary exacerbation of asthma symptoms as separate categories. He comments that workplace factors may indirectly worsen asthma by, for example, precluding the use of medication. He states that there may be factors at work which improve the severity of asthma. He proposes that asymptomatic bronchial hyperresponsiveness may become symptomatic with a work exposure, and includes the development of symptoms earlier than otherwise would have occurred as a separate interaction. Finally, he comments that asthma may limit the worker's ability to carry out his work, or may increase his future risk at work.

Importance: frequency estimates

BLANC [26] has published from the US 1978 Social Security Administration Survey of Disability and Work, a survey of over 6,000 persons weighted towards benefit

applicants and those with activity limitation. A self-reported diagnosis of asthma was noted in 7.7% of respondents, and 15.4% of these reported that it was "caused by bad working conditions".

The best national data for occupational asthma appear to be from Finland [27]. There were 156 cases in a working population of about 2.2 million in 1981 [28], a crude annual incidence rate of 71 per million. In Finland, the condition is assumed to be mediated through a sensitization mechanism. Workplace or laboratory challenge testing is normally required to establish the diagnosis. The United Kingdom currently has a voluntary scheme for surveillance of work-related and occupational respiratory disease (SWORD) which noted 554 cases in a working population of about 25 million in 1989 [29], a crude annual incidence rate of 22 per million. The cases are of physician-diagnosed "occupational or work-related" asthma, and reports come from most of the country's specialist chest physicians and an unknown proportion of specialist occupational physicians. Asthma is the most common disease in the SWORD data. Some rates for comparison are 13 per million for malignant mesothelioma, 13 per million for all pneumoconioses, 5 for allergic alveolitis (hypersensitivity pneumonitis) and 1 for byssinosis.

Underestimation of frequency. The UK estimate for asthma in 1989 is assumed to be an underestimation, with the true rate closer to that reported from Finland, as regional rates varied from 8–63 per million, and a large part of the variation is thought to be explained by ascertainment. 1989 was the first year of the UK scheme, whereas the Finnish Occupational Disease Register dates from 1964, with improvements in 1975. There has been an increase in number of cases of occupational asthma in Finland from less than 10 per year in the 1960s to 80 in 1976 [27], presumably reflecting increased ascertainment.

Denominators for frequency estimates. In these analyses from Europe, the population denominator for each estimate is the working population. KESKINEN *et al*. [27] estimated that less than one-quarter of the Finnish working population is exposed to the more common causes of occupational asthma. SWORD data show considerable variation in incidence by occupational group, from less than 10 to 114 per million, with much higher rates in some subgroups; for example, 639 per million in coach and spray painters. Very much higher rates have been noted in individual workplaces or working groups, so that the unit of incidence (or, more commonly, prevalence) is usually percent rather than per million [30, 31]. For example, around a quarter of a cohort of platinum refinery workers developed both a positive skin-prick test to platinum salts and also respiratory symptoms in up to 4 yrs of follow-up, most within the first year [32]. Examples of cross-sectional studies are more numerous; an early example in the platinum-refining industry estimated that 46% of workers had occupational asthma [33].

Importance: morbidity

Occupational asthma is an important source of morbidity in the general community, because the onset of allergic asthma appears to represent a fundamental switch in the individual's way of responding to his environment. Once switched on, asthma does not, in general, go away. Several follow-up studies show that asthma, although improved, does persist after elimination or reduction of exposure to Western red cedar [34], solder fume [35], toluene diisocyanate [36], tetrachlorophthalic anhydride [37], snow crab [38] and various agents [39, 40]. These studies report persistent symptoms in up to 100% of patients; most also report persistent bronchial hyperresponsiveness; two were able to note persistent specific immunological responsiveness to the causal agent [37, 38]; one study suggested a plateau of improvement at about 2 yrs after cessation of the causal exposure [38]. Therefore, sensitization in the workplace is a source of new cases of adult-onset asthma in the community.

Importance: severity

Lastly, occupational asthma is important, because the asthma may be severe. Death is possible in an acute attack of asthma [41]. Severe attacks requiring hospitalization are not uncommon. In the US programme to eradicate screwworm fly by aerial distribution of irradiated screwworms, 70% of pilots and dispersers developed allergic symptoms in around two weeks to six months after joining the programme, and there were several emergency landings performed because of severe asthmatic symptoms [42].

The chronic asthma remaining after cessation of exposure is usually of mild to moderate severity. Early diagnosis and early removal from exposure are good prognostic factors [34, 39]. Patients who remain in exposure may remain stable with medication, respiratory protective equipment, and modifications to work, or may deteriorate despite such measures [36]. Bronchodilator treatment at the same time as allergen exposure is known to suppress the immediate asthmatic response, allow exposure to a greater dose of allergen, and increase the size of the late asthmatic response [43].

Prevention of sensitizer-induced asthma

Preventive measures are conventionally grouped as primary, secondary and tertiary prevention [44]. Primary preventive action prevents occupational exposure, and, if appropriate, any other determinants of occupational asthma. Secondary prevention aims to detect asthma early and take appropriate and timely action to minimize its duration and severity. Tertiary prevention is applicable only to patients with established asthma, as the aim is prevention of deterioration and complications by means of appropriate health care. Primary and secondary prevention take place in the workplace, and are addressed further here. Tertiary prevention in occupational asthma, although sometimes carried out by physicians with specialist expertise in occupational medicine, is essentially the same as effective management of any type of asthma [45, 46].

Attitudes to prevention

Adverse influence of concepts of allergy. It used to be assumed that there was little to be done to prevent sensitizer-induced asthma, because the cause was "constitutional", *i.e.* inherent to the individual. There has been a suggestion that laboratory animal allergy could be associated with HLA B15 and DR4 [47]. In occupational medicine, this way of thinking has often led to a focus on making the workers fit for the hazards of work, rather than making the work environment safe for all, or most, workers. Some workplace programmes consist almost entirely of systems to monitor the health of exposed individuals, with little attention to the workplace. Managers with responsibility for health and safety often believe that asthma cannot be controlled and is the province of doctors, rather than of occupational hygienists and safety engineers.

Confusion between induction and provocation of asthma. This view has been encouraged by confusion between the levels of allergen exposure which will elicit symptoms in sensitized individuals and the levels of exposure sufficient to induce the sensitized state in persons who are not sensitized. Sensitized patients may develop attacks of asthma after very low exposures. For example, in inhalation challenge tests with tetrachlorophthalic anhydride, patients with occupational asthma caused by this chemical showed late and dual asthmatic responses after 30 min exposures to airborne levels orders of magnitude lower than those recommended as occupational standards [48]. Patients with occupational asthma caused by colophony in solder responded to only a few breaths of solder fume, whereas unaffected individuals carry out hand-soldering operations over a normal workshift [49].

Exposure-response relations

There is, however, no evidence to suggest that the exposure-response relations for asthma induction are any different from those for the induction of other diseases. In a cross-sectional study of British bakers, for example, indices associated with occupational asthma were related to either duration of exposure or intensity of exposure measured as an 8 h time-weighted average of inhalable dust [50]. In a study in the US, the prevalence of laboratory animal allergy increased with number of hours per week of exposure, and with number of species handled [51]. Much of the epidemiological data on occupational asthma is derived from surveys of its prevalence in population cross-sections, rather than of its incidence in cohorts. Because asthma often leads to severe respiratory symptoms, it is common for affected workers to leave exposure by leaving the employer, or transferring to alternative work with no or low exposure. This healthy-worker survival bias is the probable explanation for a lack of exposure-response relations observed in some populations. For example, in a group of pharmaceutical research workers, symptoms consistent with occupational asthma caused by laboratory animals showed no relationship with job type, and showed an inverse relationship with increasing duration of exposure [52].

Effect of short-term high exposures. The assumption that intensity and duration of exposure are equivalent is questionable for many occupational diseases. In asthma, there is some evidence that short periods of high exposure could be more important than the equivalent dose accumulated at a lower exposure over a longer time. In one of the few longitudinal studies, WEILL *et al.* [53] followed workers exposed to toluene diisocyanate (TDI). Of 12 who developed asthma in 5 yrs, half had been exposed to spills of TDI. Animal models of asthma caused by subtilisin and by isocyanates have shown an increase in percentage of guinea-pigs sensitized by inhalation with increasing concentration of sensitizing agent [54]. The animal model of asthma caused by subtilisin suggests that long-term exposure to low levels of enzyme had less effect than an equivalent dose administered over a short time [55].

Exposure windows. It is possible that exposure during a time "window" shortly after first exposure is the major determinant of occupational asthma. The latent interval between the first exposure to a sensitizing agent and the development of asthma appears to be short for most agents, and most cases that will develop appear to do so in the first year or two of exposure [32, 56]. Exposure accumulated later may not increase the risk further.

Potency. Some occupational allergens appear to be exceptionally potent sensitizing agents; the effect occurs at low levels of exposure. For example, the hessian sacks used to transport castor beans are recycled for transport of green coffee bean. The sacks contain enough castor bean antigen to sensitize dock workers unloading coffee [57]. The sacks are also recycled to make upholstery felt, and this has been responsible for sensitization of furniture workers [58].

Methods of measurement. Another source of confusion is that there have, until recently, been few ways of measuring high molecular weight allergens, and these allergens represent a major class of agents that cause occupational asthma [31]. The field has developed in recent years and techniques of immunoassay are proliferating [59, 60].

Primary prevention

Elimination of the sensitizing agent is the most secure way of preventing exposure. If this is not practicable, it means reduction in exposure, combined or not with measures to limit the numbers of people exposed. It also means control of any other known determinants, where they are susceptible to control. In occupational asthma, atopy and smoking have been proposed as additional determinants. CORN [61] has provided a general description of the assessment and control of environmental exposure, with special reference to allergenic agents. He lists 20 control methods. Fifteen relate directly to primary prevention: elimination, substitution, isolation, enclosure,

ventilation, process change, product change, housekeeping, dust suppression, maintenance, sanitation, work practices, personal protective devices, waste disposal practices, administrative controls. CORN [61] includes "medical controls" as a sixteenth method. Four are indirectly related to primary prevention, in that they are needed in order to carry out the remaining sixteen: education, labelling and warning systems, environmental monitoring and management programmes.

Prevention by elimination. There are several examples of successful elimination of exposures causing asthma. VENABLES *et al.* [62] investigated an outbreak of asthma in a steel-coating plant, where at least 21 cases of occupational asthma developed in a workforce of around 200. Simple outbreak investigation techniques suggested that toluene diisocyanate was the cause. This was confirmed by inhalation challenge testing of the two index cases. The isocyanate had been introduced into the process by a supplier. When it was replaced by a different chemical, no new cases developed and a repeat survey showed that the existing cases had improved.

Prevention by reduction of exposure. Good examples of prevention by exposure reduction come from enzyme detergent production [63], and platinum refining [64]. After the epidemics of occupational asthma caused by *Bacillus subtilis* enzyme detergents in the 1960s and early 1970s, enzyme was handled as a liquid slurry rather than a dust; it was encapsulated; some plant was enclosed; exhaust ventilation was increased; protective clothing was modified; education and administrative systems were set up; and job applicants deemed at increased risk of allergy were excluded from employment. These measures led to a reduction in measured enzyme exposure and also in occupational asthma caused by enzyme. A similar package of multiple measures, with particular reliance on enclosure of processes, was used to reduce exposure to platinum salts. It has been noted previously that when multiple measures are used it is impossible to separate the effects of one component of a package from another [30]. Formal evaluation of the effectiveness or efficiency of control measures is still unusual in any area of preventive medicine.

Restriction of employment. In the examples of asthma caused by enzyme detergents and platinum salts, quoted above, the criterion for increased risk of allergy was atopy, defined as a history of allergic illness, or a positive skin-prick test to common environmental allergens. Depending on how a positive skin-prick test is defined, this approach may mean denying employment to around a third of job applicants, only a proportion of whom would develop occupational asthma [52]. It does not eliminate the problem because the association with atopy is not absolute. Other pre-employment screening criteria besides atopy are used [65]. NEWILL *et al.* [66] have made theoretical estimates of the efficacy of these various pre-employment screening criteria for preventing laboratory animal allergy [65]. The study suggests that screening procedures are introduced without consideration of their likely effects, or evaluation of their actual effects, and that the use of screening as a method of preventing laboratory animal allergy was premature. Some pre-employment tests are carried out quite appropriately for reasons other than the prevention of occupational asthma. Pre-exposure clinical data are useful as a baseline for results obtained during later health monitoring. It also seems wise to identify the rare individual with marked respiratory impairment as he should not be exposed to further risk of impairment.

Control of smoking and of respiratory irritants. Smoking has been shown to be a risk factor for the development of specific IgE antibody against occupational agents [32, 67–69], although not necessarily for asthma [56]. Smoking [70] potentiates experimental sensitization of animals. This adjuvant effect is shared with irritant gases, such as ozone and sulphur dioxide [71–73]. This raises the interesting possibilities that: firstly, programmes to reduce smoking may have the additional benefit of preventing IgE-mediated sensitization; and secondly, attention to control of respiratory irritants may have the same effect. Control of respiratory irritants would also control their direct toxic effects on the airways, which were noted above.

Respiratory protection. A helmet respirator (Racal) has been shown to be partially effective in reducing the consequences of exposure in patients with occupational asthma due to laboratory animals [74], and to aluminium potroom emissions [75]. This is a form of incomplete tertiary prevention but it raises the possibility that respiratory protective equipment may have some role in preventing the induction of sensitization and asthma. Some workers exposed to respiratory sensitizers use respiratory protection for that reason, by individual preference or in following an employer's policy.

Secondary prevention

Methods. Secondary prevention includes the periodic screening tests that are used in industry. The proportion of employers with an asthma risk who offer screening to their workforce is unknown. A wide variety of questionnaires are in use. Some employers use spirometric tests, but often without any attempt to time the tests so as to have a high probability of detecting asthma. A small number use skin-prick tests with specific antigens, for example enzyme extract [63], and complex platinum salts [64]. It is the impression of this author that most employers would welcome guidance on choice of appropriate screening tests and on quality control procedures for their conduct.

Symptoms questionnaires. The best known respiratory symptoms questionnaire is that published by the Medical Research Council in the United Kingdom [76]. It has given rise to others, such as that published by the American Thoracic Society. The roots of the Medical Research Council questionnaire and of its progeny lie in the

bronchitis research conducted in the 1950s and 1960s. Asthma was of interest only as a potential modifying variable. The questions are not suitable for detecting asthma. Some fresh approaches to questionnaire design for asthma have been made in recent years. MORTAGY and colleagues [77] published a questionnaire on "bronchial irritability" symptoms. A similar questionnaire was published under the sponsorship of the International Union against Tuberculosis and Lung Diseases [78]. Another was developed by VENABLES and co-workers [79]. All three questionnaires aim to note variable symptoms provoked by known triggers of asthma, such as cold air. All show that "bronchial irritability" symptoms are associated with bronchial hyperresponsiveness. Questions about improvement in symptoms at weekends and on holiday are widely-used, but have not been standardized or validated. A short questionnaire would have many advantages as a first-line screening tool for exposed workers.

Pulmonary function tests. BURGE [80] has observed that spirometry is an insensitive technique for detecting asthma, even when two measurements are made, before and after the workshift. Peak flow records over several weeks are both sensitive and specific for occupational asthma. They are feasible tests in surveys and interpretation of the resultant graphs by an experienced observer is reproducible [81]. However, this is a highly labour-intensive technique and unlikely to gain acceptance as a first-line screening tool. It would be better applied in a second phase of screening.

Immunological tests. It is not clear whether evidence of sensitization precedes the development of asthma. Sensitization can be detected, for example, by means of skin-prick tests or testing for serum specific IgE antibody. One study made use of routinely-collected occupational health screening data in order to assemble and follow a cohort of platinum refinery workers [32]. This showed that symptoms were as likely to be noted after as before detection of a positive skin-prick test to platinum salts. The symptoms variable studied was any lower respiratory tract symptoms, so it is possible that use of a tailored questionnaire would have shown different results. It is, however, also possible that it is difficult to achieve fine detail about the timing of onset of symptoms in other than a research setting. More information is needed before recommending immunological tests as suitable for the early detection of asthma.

Procedures. It is as important to have a practicable procedure for investigating workers who have positive screening tests. If a worker has occupational asthma, his prognosis is improved by early detection and prompt removal from exposure [34, 39]. From a public health viewpoint, one worker with occupational asthma is evidence that primary prevention has failed. His working conditions should be reviewed in case some failure of control has occurred. Workers with similar exposures should be tested in case others are affected. A proactive approach and systematization of the procedures following detection of a case of occupational asthma should ensure action is taken promptly.

Tertiary prevention

This report does not address the care of the affected worker. Once he has developed asthma his situation is entirely different. He will experience attacks of asthma after exceedingly low exposures. These attacks may be severe. He is at risk of death in an acute attack [41]. The appropriate treatment is prompt removal from exposure with preservation of income. In many countries, there is often a conflict between removal from exposure and preservation of income. This conflict can be resolved politically (by bargaining within a firm, or nationally through the party political process) and is not a strictly medical or scientific issue. It is, however, important that employers and employee representatives are fully aware of what constitutes good medical practice in the management of patients with sensitizer-induced asthma.

Recommendations

There is a great deal that could be done to prevent occupational asthma. The following strategy is implementable with existing knowledge, and would go some way towards prevention:

1. National regulatory or advisory bodies, or other agencies with responsibility for prevention, should publish a guidance document on the prevention of occupational asthma. This should establish general principles, such as terminology, rather than enumerate details.
2. Existing surveillance should be extended, or new surveillance established, to collect information on clinical diagnoses of occupational asthma. This could be combined with collection of data on other occupational lung diseases. It could also be combined with estimation of the relative frequency of sensitizer-induced asthma, irritant-induced asthma, and work-exacerbated asthma.
3. Existing lists of sensitizers that cause asthma should be collated, in order to publish a list that could form the basis for standards in product-labelling and exposure control strategies. Such a list would require regular updating.
4. Prospective epidemiological studies should be carried out of exposure-response relations. Such studies also allow scope for studying the effect of modifying variables, such as family history of asthma, or personal smoking. They can also act as a framework for additional studies, for example on the time course of sensitization.
5. Agreement should be reached on a short questionnaire, which could form the basis for screening tests in industry, or on other forms of screening.
6. Pilot prevention projects in industry should be encouraged, coupled with evaluative research to assess their effectiveness and efficiency.

Guidance document

Agreement on a guidance document would clarify an agency's view of the definition of occupational asthma, its causes, mechanisms, natural history and consequences. This document can form the basis of guidance statement, with a target audience consisting of those with a professional interest in occupational asthma. It is suggested, in addition, that a short summary document is composed, for distribution, as necessary, to a wider audience.

Surveillance

Few countries have national case-finding for occupational lung disease. The frequency with which asthma occurs in relation to the pneumoconioses and other occupational lung diseases is information which aids in setting priorities for preventive activities and for research. The relative frequency of asthma caused by different sensitizers is, similarly, useful information.

The SWORD project [29] in the UK collects simple data from specialist physicians. The Sentinel Event Notification System for Occupational Risks (SENSOR) in the US has been described by BAKER [82] and MATTE *et al*. [83]. Unlike SWORD, SENSOR does not aim to include all specialists who might make a diagnosis of occupational asthma; it includes diagnostic criteria for occupational asthma; it is not anonymous; and it is accompanied by intervention in the workplace.

List of sensitisers

Purpose of list. Several hundred agents are known to cause occupational asthma by inducing specific sensitization. These should be drawn together into a list. The list is intended for use in controlling exposure by indicating materials and processes in industry which are a hazard because they may cause asthma. It thus indicates areas and processes where exposure controls should be applied, and identifies occupational groups at risk of asthma who should be offered health screening programmes. Such a "controlled exposure" list could form the basis for regulations on, for example, safe handling, permissible exposure, and product-labelling.

Lists of occupational sensitizing agents can be used for other purposes. For example, physicians who see patients with possible occupational asthma need a list of agents as a focus for taking occupational histories. Such a list should include agents forming the "controlled exposure" list above, and additionally should include agents which are suspected to cause asthma.

Criteria for list. Chan-Yeung's list [31, 84] is, perhaps, the one consulted most frequently by English-speaking physicians with an interest in occupational asthma. The UK government has published a consultative document on respiratory sensitizers, which will form the basis of an Approved Code of Practice under the regulations on Control of Substances Hazardous to Health; this document will contain a list [85]. There may be other reputable lists.

This paper recommends to responsible agencies that existing lists be, firstly, collated. Clinical practice has changed in this century and in many centres today there is considerable reliance on tests, such as immunological tests or bronchial provocation tests, which were not available to physicians 20 or 30 yrs ago. Therefore, this report recommends, secondly, that explicit criteria for inclusion be determined retrospectively by inspection of the relevant publications about these agents. This process will have the benefits of codifying and formalizing the process of professional judgement where this was not made clear by an author; of identifying gaps in the medical literature where an agent is accepted in professional practice to cause asthma but where the published explicit evidence is slight; and of providing a rationale for updating the list as new sensitizers are introduced to industry and cause asthma.

Generating the list. There are several approaches to generating such a list. This paper recommends that one person, rather than a group, is responsible for the initial draft. It further recommends that inclusion criteria should be applicable by nonspecialists with experience in regulation and also practicable for at least 5 yrs from publication. To allow for debate and disagreement, a consultation period is recommended between initial and final publication for active solicitation of comments from practising physicians, academic institutions, regulatory bodies, and trade union representatives.

The final list should be widely disseminated and should then be updated regularly, say annually. This could be accomplished by means of an annual literature search, supplemented by active solicitation of new candidates for the list. Those meeting the inclusion criteria can then be published.

Describing exposure-response relations

Primary prevention measures to control exposure to agents which cause asthma must be informed by knowledge of exposure-response relations and of the factors which modify these relations. This paper suggests that these should be studied by means of prospective longitudinal studies with measurement of allergen exposure. Suitable populations are those at high risk of sensitization and asthma and with good markers of response to exposure.

Studies in animals can test hypotheses about sensitization that have been generated in epidemiological studies, and may also be the only way to obtain information on mechanisms.

Screening

This paper recommends use of a validated, reproducible questionnaire on work-related respiratory symptoms for use in screening programmes for detecting cases of occupational asthma and also in epidemiological research.

Such a questionnaire would normally be used in conjunction with other tests but may, in some settings, be used alone. The design of the questionnaire and details of its validation will vary according to the context of its use.

Evaluation of pilot prevention projects

The need is for studies that will give clear-cut answers which can be generalized to other populations with comparable exposures and, possibly, populations with different exposures. Topical general questions include: Does a measure to reduce exposure reduce the subsequent incidence rate of sensitization and of asthma? and, Does a screening programme to detect cases of asthma at an early stage reduce the subsequent functional impairment and consequent disability?

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