

SERIES 'OCCUPATIONAL ASTHMA'

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Management of occupational asthma

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ABSTRACT: The importance of occupational asthma and its management is usefully set in perspective by considering recent trends of increasing asthma incidence, morbidity and mortality in the population at large. The contribution to incidence made by asthma of occupational origin is of the order 20–100 cases per million workers per year; the individual worker's lifetime risk approaching 5% in some industrial environments.

Management of the affected industry inevitably follows different pathways from that of the affected individual, though both need to start from a definitive diagnosis. For the affected industry, managers must identify the causative agent and assess the extent of the problem. Affected workers can then be removed from hazardous settings, and meaningful strategies of prevention can be introduced. The most promising preventive measures involve improvements in industrial hygiene or the substitution of alternative agents in the manufacturing process. The role of worker selection (*i.e.* the exclusion of applicant workers who may be unduly susceptible because they smoke, or have existing airway hyperresponsiveness or atopy) is small and controversial. More valuable is a strict surveillance programme of workers perceived to be at risk, so that emerging disease is recognized promptly, before it poses any major threat of permanent ill-health.

Management choices beyond conventional medication and the avoidance of irritant environmental triggers are greatly limited for the affected individual worker. A change of job environment with complete cessation of exposure to the relevant asthma-inducing agent is to be favoured and offers the best chance of full recovery, but may not be practical if the worker is to avoid permanent unemployment. The alternative of continued work for the same employer in a new capacity with diminished exposure, possibly with medication and the use of respirators, may offer an acceptable compromise.

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Perspective

In most developed countries, there has been a disturbing steady increase in the morbidity and mortality of asthma over the last 10–20 yrs [1–4]. This is likely to be a consequence of increasing incidence and prevalence, though changes in diagnostic habit (labelling shift) may have confounded the issue, especially in the elderly. Increasing prevalence has been demonstrated even more dramatically in a number of developing countries. For example, inhabitants from rural areas of Africa have experienced a severalfold increase in the risk for developing asthma when they moved to urban environments [5]. Similarly, children from the pacific atoll of Tokelau were found to have developed asthma with similar prevalence to native New Zealand children, when they were evacuated to New Zealand following a typhoon which devastated the local economy [6]. A subsequent study of children remaining in Tokelau showed a substantially lesser prevalence. The explanation for such rapid changes worldwide must lie primarily with environmental (including occupational) rather than genetic factors.

Some perspective for the possible contribution of the occupational environment can be gained from the results of the Surveillance of Work-related and Occupational Respiratory Disease (SWORD) project [7]. This is a collaborative reporting system for lung disease considered to be occupational in origin by the reporting physician. It is a national system throughout Britain, which involves the great majority of practising consultants in respiratory medicine and occupational medicine. At the end of its first full year of operation (1989), asthma emerged as being by far the most commonly reported lung disease of occupational origin, and it accounted for 26% of all reports (554 of 2,101). The mean incidence for the whole working population was 22 per million per year, providing an overall lifetime risk for the development of occupational asthma of the order 0.1% for each worker. There were regional differences and the highest incidence was 63 per million per year. This is of similar magnitude to the figure of 71 per million per year reported as the net average incidence for the working population of Finland in 1981 (156 cases) [8]. Of particular interest was the suggestion that 25% of this population was then regularly

occupationally-exposed to known asthma-inducing agents. The overall lifetime risk for an individual worker consequently approaches 0.5% in Finland and in at least one region of Britain. Because these estimates depend on voluntary reporting of cases presenting to physicians, they are likely to underestimate significantly the true risk.

In addition to geographical variations in risk, there are far more profound differences between different industries. Thus, results from the SWORD project suggest that amongst library, professional and clerical workers the incidence of occupational asthma is small or negligible (of the order 0–2 per million per year). At the other end of the spectrum, for bakers, workers in the plastics and chemical industries, and spray painters, the incidence is of the order 400–650 per million per year, the 95% confidence intervals indicating that the overall lifetime risk of developing occupational asthma for individual workers may be as high as 4%. This certainly challenges, and probably exceeds, their risk of developing asthma for non-occupational reasons. Occupational factors are, therefore, likely to play a major role in asthma in the population at large, and its successful management should contribute significantly to the overall control of asthma in the general population.

Management of the affected industry

The general principles of managing an industry affected by occupational asthma are obvious and straightforward. They are illustrated in figure 1 [9] and need not be discussed in great detail. Because asthma is a common disease in the population at large, irrespective of the occupational environment, it is critical that a definitive diagnosis of occupational asthma is established. Many workers, during their working lifetimes, will develop asthma which has no relevance to the occupational environment, and some will develop asthma which, though unrelated causally, is nevertheless worsened in the occupational environment. The worker may, for example, be required to carry out heavy exertion where ambient air is either cold or polluted with irritants. Such exposures are likely to cause worsening symptoms and this may

simulate true occupational asthma. Full investigation is consequently essential when a particular workplace environment is first suspected to be a cause of occupational asthma.

Once a definitive diagnosis is established in at least one member of the workforce, there is a need to establish the extent of the problem throughout the entire workforce. Some clue to this may be gained from experience in similar industrial plants, but it is often necessary to carry out some form of survey within the particular plant now found to be affected. This may involve conventional questionnaires, spirometry (particularly measured across working shifts, though many true cases will escape detection if investigation is confined to a single day), and the measurement of non-specific airway responsiveness. This will help establish whether the individual presenting as the index case is the sole affected worker (in which case personal susceptibility may be the major factor rather than undue exposures to a potent asthma-inducing agent), or whether the problem is more widespread - indeed, suggesting an agent of appreciable sensitizing potency or one which is present at appreciable levels of exposure.

The affected industry should also identify the specific agent responsible; thereby, allowing improvements in industrial hygiene, so that exposure levels are minimized, or the development of an alternative manufacturing process, which eliminates the use of the particular asthma-inducing agent.

Prevention

Once occupational asthma is recognized as a hazard in a particular industry, three general preventative methods can be considered in the future control of the disease. These are essential components of management and so will be considered separately.

Exposure control

Most importantly, exposure levels need to be minimized through improvements in industrial hygiene and/or changes

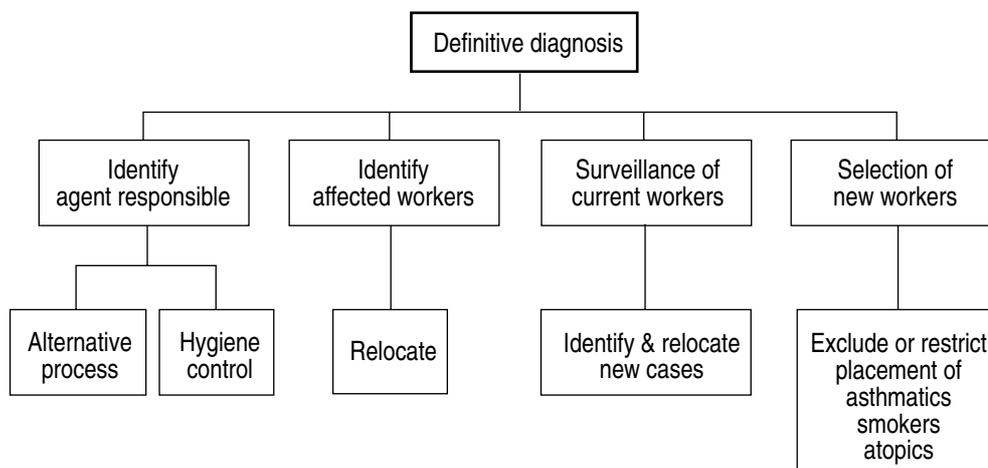


Fig. 1. — Management of the affected industry.

in the manufacturing process. These are the measures used directly in the management of the affected industry and have been discussed already.

Worker selection

In some studies of occupational asthma, a number of personal factors have been shown to be significant risk factors. The most prominent are pre-existing (or prior) asthma, atopy and smoking. The question consequently arises, whether the incidence of occupational asthma could be lessened by a pre-employment selection examination and the exclusion of particular individuals from the hazardous environment.

With regard to pre-existing (or prior) asthma, only a small minority of any group of job applicants would be selected by this criterion, and the great majority of subjects likely to develop occupational asthma would be left in the remaining, much greater group of subjects without previous evidence of asthma. Selection using this criterion would not, consequently, make much impact on the incidence of occupational asthma. Furthermore, the actual increase in risk in those with evidence of pre-existing or prior asthma has not generally been found to be of great degree, compared with those who were previously without asthmatic symptoms. Thus, in most industries, the majority of those excluded by such a process may not have developed occupational asthma anyway. The practical advantage of screening new workers in such a way is consequently of very limited value, quite apart from the ethical and practical considerations of job discrimination against those already disadvantaged by illness through no fault of their own. The individual with currently active asthma is, nevertheless, best advised to avoid occupations where the risk of developing asthma is considered high or moderate - particularly if his/her asthma is currently of such severity as to need regular medication or was itself occupational in origin. A further, perhaps stronger, argument is that the development of true occupational asthma is more difficult to recognize in those who are already asthmatic, and that a restrictive employment policy would valuably simplify any later problems of diagnosis.

Similar arguments apply to the measurement of non-specific airway responsiveness (AR) as a pre-employment screening procedure. There is currently no clear evidence that those who have no previous history of asthmatic symptoms but, nevertheless, have measurable levels of AR are at any greater risk of developing occupational asthma. What is clear, is that when AR is demonstrated in association with occupational asthma, it is most commonly an effect, not the cause, of the individual's occupational disease. Furthermore, AR is distributed unimodally, not bimodally, in the population at large, and can be readily demonstrated using methacholine or histamine tests and forced expiratory volume in one second (FEV₁) measurements in some 30-40%. If measurements of airway resistance are used, AR can be quantified in almost everyone. This implies that a screening procedure would require the selection of an arbitrary end-point to

define an "unacceptable" level of AR. Doubtless, some workers would fail one but pass the other, if duplicated tests were undertaken.

In some industries, atopy has been considered a more important risk factor for occupational asthma - particularly those in which the causative agent has high molecular weight agent and induces demonstrable specific immunoglobulin E (IgE) responses. It appears, however, that this particular variable is also unimodally distributed in the population at large, and that, again, there is no obvious point at which to separate those who are deemed to be atopic from those who are deemed to be nonatopic. With some definitions, as much as 30% of the general population could be defined atopic, an impractical proportion if one is to exclude atopic subjects from job opportunities - unless a particular industry is one in which the "atopy risk factor" is known to be very high indeed. This was once considered to be true in platinum refining, but the recent recognition of important smoking-atopy interactions has led to an invaluable reappraisal. In a longitudinal study of 91 workers, the relative risk for developing asthma among atopic compared with nonatopic individuals was approximately 2, and not statistically significant. Smoking, by contrast, was a significant predictor, the relative risk among smokers being approximately fivefold that of nonsmokers [10].

Furthermore, in many of the industries affected by occupational asthma, generally those in which low molecular weight agents are involved, there is little or no evidence that atopy increases risk. As with pre-existing asthma, employment selection against atopy is consequently likely to exclude many more subjects who would not have developed occupational asthma than those who would have become affected. At the same time, a greater number of cases is likely to arise from the larger group who are defined as non-atopic.

The effect of smoking is of particular interest at present, since there is increasing evidence that smoking enhances IgE responses and, therefore, augments any effect attributable to atopic sensitivity [11]. This suggests that smoking may be of little or no relevance in industries affected by occupational asthma for which atopy does not appear to be relevant. This appears to be so, and it is far from obvious that smoking is relevant in all industries affected by this disease. Indeed, there are a number of epidemiological surveys which suggest that smoking may exert a protective effect against the development of occupational asthma, and that it is the nonsmokers who run the greater risk [12]. Such a finding might be influenced by artefact, smokers with lung disease being less likely to recognize that they have occupational (rather than smoke-induced) lung disease. The possible protective effect of smoking should not be dismissed lightly, however, since there is persuasive evidence that smokers have a lesser risk for developing both extrinsic allergic alveolitis and sarcoidosis than nonsmokers, to say nothing of non-respiratory (but immunological) diseases, such as ulcerative colitis [13, 14].

In practical terms, therefore, all three factors are of considerable academic interest to the development of occupational asthma, but the case for using them as

pre-employment screening factors to exclude potential employees is not sustainable, except in exceptional circumstances. Thus, where adequate exposure control of particularly potent asthma-inducers cannot be satisfactorily achieved (e.g. platinum-refining), there may be justification for excluding atopic individuals who smoke, particularly if there is a past history suggesting active asthma.

Worker surveillance

The most practical approach in an industry known to be at risk for the development of occupational asthma is to provide a close surveillance system for all exposed employees. Ideally, this begins before employment, so that any changes are quickly detected. Such a programme should include an assessment of symptoms (possibly through a questionnaire or physician interview), spirometry, the measurement of airway responsiveness, and regular examination of the serum for the development of specific IgE antibodies in those industries (relatively few) where such antibody responses are detectable.

The chief principle is that occupational asthma, if recognized quickly, almost invariably resolves completely if exposure ceases immediately. Workers should, therefore, be aware that they should report any evolving symptoms immediately, so that a thorough medical evaluation can take place. Not all workers will readily admit to symptoms, however, particularly if these threaten continuing employment. It is essential, therefore, for all exposed workers to participate in a regular surveillance programme, follow-up investigations being carried out at regular intervals.

The precise time intervals will vary from industry to industry, according to the perceived level of risk, but a reasonable programme in an industry facing moderate risk might involve investigations after one, three and six months, followed by regular further evaluations at 6–12 monthly intervals. Serial measurements of airway responsiveness might prove to be particularly useful in this respect, since these may detect evolving changes attributable to occupational asthma before this becomes symptomatic.

Management of the affected individual

Again, the general principles are relatively obvious and straightforward. They are illustrated in figure 2 [9]. Once more a definitive diagnosis is critical so that asthma of true occupational origin is distinguished from asthma which has arisen coincidentally. If investigation indicates asthma of the latter type, there is no contraindication to continuing employment, but it should be recognized that such a worker may now be at increased risk of developing occupational asthma. There is also some risk of an error in diagnosis, and so such a worker should not be lost to continuing surveillance. Any evidence of deteriorating asthma could then lead to a re-evaluation.

Once it is clear that the asthma of an individual worker is indeed occupational in origin, there are essentially only two possible courses of management, apart from the use

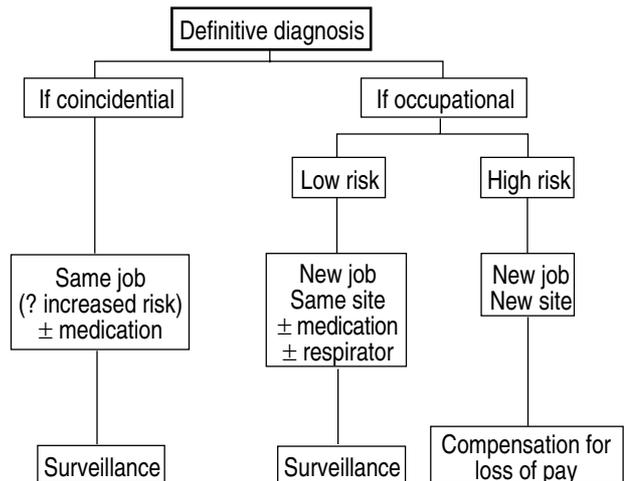


Fig. 2. – Management of the affected individual.

of conventional medication appropriate to any other asthmatic patient.

Firstly, the affected worker avoids any subsequent exposure to the relevant inducing agent. To be certain that such cessation truly occurs, the worker must be transferred to work in a completely different building, usually on a completely separate site. Even in a separate building the ambient air may be contaminated by neighbourhood emissions or by contaminated products (or fellow workers) passing from building to building. Such a job change is not always possible, and the affected worker may need to seek a new employer or become unemployed. The latter is, unfortunately, a far from uncommon outcome, though may be mitigated to some extent by the receipt of compensation.

Compensation is not, however, uniformly available, and complete cessation of exposure may not be readily achieved. Even when it is, the outcome is not necessarily one of quick and full recovery. When occupational asthma is detected soon after its onset and soon after exposure has first begun, symptoms usually resolve quickly (within days or weeks) and spirometry, together with levels of airway responsiveness, may quickly return to normal. In other circumstances, however, active asthma may persist, irrespective of there being no obvious continuing exposure to the initial inducing agent.

This unsatisfactory outcome is of some relevance to the alternative major course of action - namely that the worker continues working for his current employer, but in circumstances where levels of exposure can be appreciably reduced. This can be achieved by both industrial hygiene improvements and modifications to the manufacturing process, by changes of specific job within the same plant or site, and by the use of respiratory protection equipment, together with conventional medication. Such an approach may be the only practical alternative to lifelong unemployment, and may be the one favoured by the affected subject.

Such management is not without risk. In addition to the possible outcomes described already of active asthma resolving or continuing unchanged, this approach carries

some risk of worsening symptoms and of asthma continuing when exposure does eventually cease. There are occasional reports of fatalities in occupational asthma [15], and the particular risk of a heavy accidental exposure in the workplace could have catastrophic consequences.

Evaluating these various risks and deducing a recommended course of management for an individual affected worker is not easy and needs to be carried out separately from individual to individual. Not all physicians would necessarily reach the same conclusion, and a conclusion to approve continued work with reduced exposure may not be acceptable to the employer. It may also carry litigious risks, in certain countries, for the physician. In essence, the decision must depend on a full cost-benefit analysis for the individual concerned and his employer; and on close collaboration between the employee, his physician advisers (and possibly his trade union advisers), and the employer. All should understand the potential risks involved and the need for close regular surveillance. Written records should be kept of relevant discussions and the agreed programme for surveillance. The two following examples are intended to illustrate the two essential options available in the management of the individual case.

Complete cessation of exposure

The patient was a 38 year old research technician working with a new low-temperature bleach activating agent, sodium iso-nonanoyl oxybenzene sulphonate (SINOS). He developed symptoms classical of occupational asthma, having never previously had any suspicion of asthma. Investigation included a series of inhalation provocation tests using nebulized solutions of SINOS, delivered from a dosimeter in aliquots of 10 µl per inhalation [16]. Figure 3 illustrates a classical late asthmatic reaction, which was observed following challenge with SINOS, 32 µg. The mean of the baseline measurements

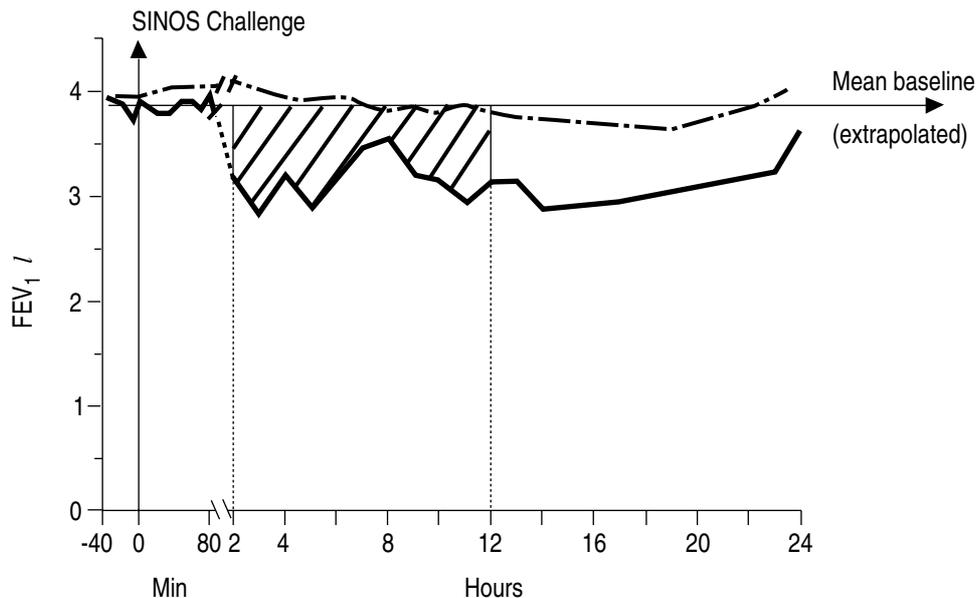


Fig. 3. - Inhalation challenge tests in SINOS worker, and definition of 2-12 h FEV₁ area decrement (shaded area). SINOS: sodium iso-nonanoyl oxybenzene sulphonate; FEV₁: forced expiratory volume in one second; — : SINOS, 32 µg; - - - : control (saline).

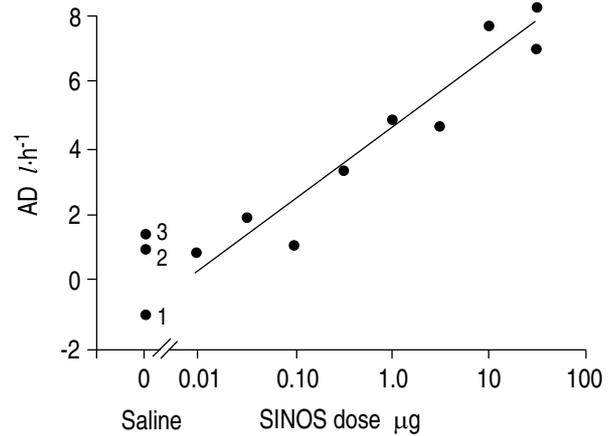


Fig. 4. - Relation of SINOS dose to area decrement (AD). SINOS: sodium iso-nonanoyl oxybenzene sulphonate. 1-3: control challenges.

of FEV₁ is extrapolated in the figure so that the late reaction could be quantified in terms of the area decrement (AD) from this mean, 2-12 h after the challenge exposure (the shaded area).

Figure 4 illustrates the results of the full series of these tests. Each challenge was administered on a separate day, there being a total of three control challenges with saline alone and nine challenges with increasing doses of SINOS. All tests were administered in a double-blind fashion.

SINOS challenges at doses of 0.01-0.1 µg produced no suspicion of any asthmatic response. The intermediate doses (0.32-3.2 µg) produced some suspicion of asthmatic reactions, whilst the higher doses (10-32 µg) produced classical and unequivocal late asthmatic reactions. The relationship of dose to response can be expressed by the regression equation:

$$AD = 4.53 + [2.14 \times \log \text{SINOS dose}]$$

(SE 0.29 0.24; p < 0.001 < 0.001)

This useful equation confirms that deteriorating lung function is significantly related to increasing exposures to SINOS (the slope), and it provides a constant term which is a measure of the spontaneous circadian change in ventilatory function, irrespective of SINOS exposure.

The point of interest in this case is that these particular investigations were carried out 2 yrs after the diagnosis was first established, and 2 yrs after the affected individual was moved to work in a completely separate institution owned by his employer, where there was no possibility of any continuing exposure to SINOS. He had recovered fully within a few weeks of leaving the initial plant, and had not only been without symptoms but had shown normal spirometry and undetectable levels of airway responsiveness (*i.e.* he failed to produce a 20% decrement in FEV₁ after 6,400 µg of methacholine by aerosol). At the end of the 2 yr period he had volunteered to join a larger study of other members of the workforce at the initial plant, hoping that the investigation would prove that he was no longer susceptible to SINOS. He wished to return to his initial, more satisfying job, where exposure levels to SINOS had been greatly diminished through industrial hygiene improvements. The study indicated that although he had shown a full clinical recovery from his occupational asthma, there was nevertheless continuing hypersensitivity to SINOS. As a result he was not permitted to return to the original factory. The repeated study did, however, show that some improvement had occurred during the 2 yrs, the slope of the regression equation diminishing from 3.27 (in 1986) to 2.14 (in 1988).

Continuing work at lesser exposure levels

The patient was a female process worker, aged 44 yrs, who had a similar classical history of occupational asthma, never having previously suffered asthmatic symptoms [17]. She used a polyethylene repair tape, which incorpo-

rated the cross-linking agent dicumyl peroxide, to repair broken electrical cables. Once the central conducting cable had been repaired elsewhere in the factory, her job was to restore continuity of the polyethylene insulating covering. She did this by winding the repair tape round the exposed conductor until the gap separating the two ends of the insulating sheath was closed. The repair was then heated in a small oven, which partially melted the polyethylene and allowed the cross-linking agent to join polyethylene molecules of the initial sheath with those of the repair. The process released some fume, which was largely extracted locally. Some, however, escaped into the working environment and was shown by provocation studies in the laboratory (fig. 5) to be the cause of her asthma. The results of a control day without challenge are also illustrated, together with a similar challenge when an insulating sheath not containing dicumyl peroxide was similarly heated. Only the fumes from the dicumyl peroxide containing tape produced an asthmatic reaction - also a classical late reaction.

Unlike the situation in the previous case, this lady's employer had no alternative plant in which she could be employed without the possibility of continuing exposure. She was also a divorcee, with responsibility for raising two small children in an area of high unemployment. Her prospects for new employment were recognized to be bleak and she was most anxious to continue working in the plant, if this could be done with reasonable safety. Furthermore, occupational asthma presumed to be caused by pyrolysis fumes emanating from heated dicumyl peroxide was not recognized for state compensation in Britain at the time. The fact that no previous case of this nature had been described (and that no fellow workers in the plant appeared to be affected) also meant that there would be considerable difficulties in her succeeding with a civil law suit, since this would involve proof of negligence on behalf of the employer. There were consequently very strong reasons for her to accept the management's offer of an alternative job in the same building - albeit,

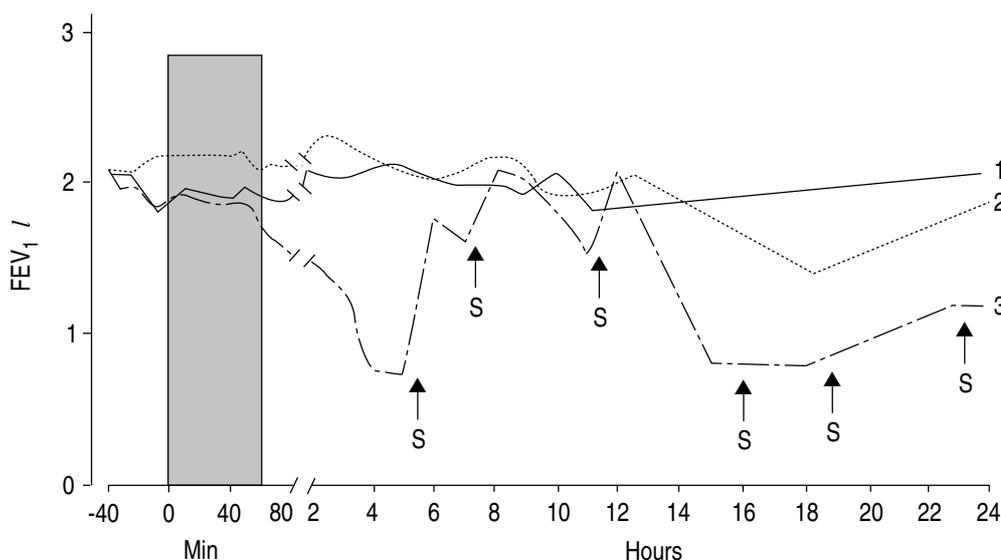


Fig. 5. - Inhalation challenge tests in dicumyl peroxide worker. 1: control day (—); 2: heated sheath without dicumyl peroxide (---); 3: heated sheath with dicumyl peroxide (.....); S: salbutamol; FEV₁: forced expiratory volume in one second. The shaded area indicates the period of challenge. No nocturnal measurements were taken on the control day.

based as distant as possible from this particular repair process. In addition, stronger extractor fans were fitted so that the risk of ongoing exposure, even at trivial levels, appeared small.

It was consequently agreed that she would return to work in these circumstances but would be followed by a regular surveillance programme. This involved frequent measurements of airway responsiveness (AR) as well as clinical evaluations by her local consultant chest physician. Table 1 illustrates the results of serial measurements of AR expressed as provocative dose of methacholine producing a 20% fall in FEV₁ (PD₂₀). Methacholine tests were carried out at least 12 h after her last use of an inhaled bronchodilator. She was otherwise treated conventionally, with a regular inhaled corticosteroid and an inhaled beta-agonist.

PD₂₀ measurements in our laboratory are normally repeatable within the range 0.5–2.0 × the initial measurement [18]. Thus, the initial measurement of 9.0 µg methacholine would not be considered to have changed significantly unless it fell below 4.5 µg (in which case there would be a significant increase in an AR) or above 18.0 (in which case AR would have significantly declined).

A diagnostic return to work study on November 14, 1985 led to a typical late asthmatic reaction and a significant increase in AR, which persisted for a few days but resolved within three weeks. There followed a period of a full year without exposure, during which she was entitled to state sickness benefit while her employer considered advice regarding further management of the apparent problem. Eventually, at the expiration of the

period for which sickness benefit was allowable, all parties agreed to the formal laboratory studies of December 16–18, 1986 illustrated in figure 5. These also led to a late asthmatic reaction and to a temporary increase in AR, which recovered to baseline levels within three weeks.

The agreed return to a new job in the same plant then took place from the beginning of 1987. For 2 yrs, progress was entirely satisfactory with regard to symptoms, spirometry, and measurements of AR. Since that time, however, there has been a significant increase in AR, though this was not initially accompanied by any apparent worsening in day-to-day symptoms. There was, however, some decline in the baseline FEV₁. More recently, she developed worsening symptoms and was treated briefly with an additional course of oral corticosteroids. This was reported to have restored her to her former level of well-being, following which a post-bronchodilator measurement of FEV₁ was recorded as 2.0 l, her best for some years. She and the physician immediately supervising her care consequently remained satisfied with her progress, though there is now objective evidence of worsening levels of AR. Whether this is truly an effect of her continued work in the plant is a matter of speculation, since it is possible that she has not been meaningfully exposed to the relevant agent throughout this time. Nevertheless, the possibility of minimal levels of continuing exposure does exist, and it is conceivable that this is of relevance to her developing increasing levels of AR. Her course, therefore, neatly illustrates the dilemma that may be faced in managing occupational asthma in this way.

On the one hand, she has worked successfully and supported her family for 4 yrs, and is personally fully satisfied with her progress. Furthermore, the earlier sickness leave of 12 months without any possibility of continuing exposure produced no sign of any improvement in her condition. It is likely, therefore, that had she continued to avoid exposure (and almost certainly become unemployed) she would still not have gained any obvious clinical benefit. On the other hand, she has certainly not improved since returning to work and her asthma may now be deteriorating.

Table 1. – Serial measurements of PD₂₀ methacholine

Date of measurement	PD ₂₀ µg
Off work 3 months, regular inhaled steroids and bronchodilators	
11.11.85	9.0
12.11.85	5.1
Return-to-work study (14.11.85)	
18.11.85	2.8
19.11.85	3.0
06.12.85	18.0
15.12.86	9.0
Laboratory tests (16–18.12.86)	
22.12.86	3.8
05.01.87	4.5
19.01.87	10.8
Return to new job in same factory building (Jan 1987)	
05.08.87	6.9
21.08.87	8.4
02.10.87	7.5
07.04.88	7.2
07.10.88	9.6
22.05.89	4.8
26.07.89	4.5
16.10.90	2.6

PD₂₀: provocative dose of methacholine producing a 20% fall in forced expiratory volume in one second.

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