CORRESPONDENCE

Inhalation fever: a proposed unifying term for febrile reactions to inhalation of noxious substances

Sir,—The comments by Rylander and Malmberg¹ and Greenburg² on our note describing inhalation fever (1992;49:40) deserve a reply.

One example of inhalation fever, organic dust toxic syndrome (ODTS), was carefully defined at an international meeting in Sweden in 1985.³ The definition requires fever, chills, and cough without chest x ray film changes or serious abnormalities of pulmonary function. (Readers will note the remarkable similarity of this definition to that generally accepted for metal fume fever.) In their letter, Rylander and Malmberg correctly state that there are reactions to organic dust and other noxious substances that may cause a variety of lung diseases. Our experience with many cases of inhalation fever suggests that the febrile reaction to inhaled fumes and particulates presents a predictable clinical picture that often causes little, if any, demonstrable damage to the lung. The febrile response, by definition, is uniformly present. Therefore, it is imperative to include the word fever in the name. The value of the word fever is further supported by the fact that several of these illnesses are already called fever by the workers who are affected—for example, mill fever.

We know of no proved human histopathological correlate of inhalation fever except for the ODTS case reported by Emanuel. That very ill patient's lung was characterised by a non-specific obliterative bronchiolitis with neutrophils in the terminal bronchiole, alveoli, and interstitium. The report did not describe a process limited to the alveolus. Therefore a specific term like alveolitis seems to be unjustified given the information at hand. Short of a lung biopsy it is impossible to make the diagnosis of alveolitis with certainty, evidence from bronchoalveolar lavage notwithstanding. The use of the term alveolitis may, in fact, confuse clinicians who associate that term with allergic alveolitis (hypersensitivity pneumonitis) such as farmer's lung.

For years inhalation fever has been mistaken for allergic alveolitis. Most knowledgeable people in the field agree that allergic alveolitis is a very rare disease. We believe the reason that allergic alveolitis had high reported prevalence rates in the past was due to the fact that inhalation fever was confused with allergic alveolitis.⁵

We also believe that the term toxic is not particularly helpful as it too is a non-specific term. It might give the false impression that the condition has something to do with toxic gases or that the condition is caused by toxins.

In conditions caused by inhalation of contaminated mist from humidifiers the separation in the nomenclature into two conditions is already a fact—the terms humidifier fever and humidifier lung are used.⁵ We suggest inhalation fever as an embracing term for all the febrile conditions caused by inhalation of noxious substances. To be more specific terms such as humidifier inhalation fever, metal fume inhalation fever, and so on could be used.

The concerns of Greenburg are noteworthy. He cautions us to wait for further evidence before "lumping" the many entities described in inhalation fever together. His counsel is sound. On the other hand, the clinical picture for these exposures is compellingly similar as is the outcome in virtually all the reported cases. When disorders are this similar it is usually safe to think of them in a similar fashion. Although we have no proof that the pathophysiology is the same it certainly is possible given the highly predictable way in which subjects react to substances as diverse as zinc, cadmium, silo dust, wheat, and complex polymers.

In the absence of histopathological evidence of alveolitis and the close similarity of all the various febrile illnesses appearing after inhalation of noxious substances we believe that the term inhalation fever helps rather than hinders the understanding of these illnesses. The use of hypothetical names that are unsupported by histopathology or plausible pathophysiology seems to be overreaching our current state of ignorance. We believe that inhalation fever best meets the important mandate of utility—keep it simple.

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- 1 Rylander R, Malmberg P (letter). *Br J Ind Med* 1992;49:296.
- 2 Greenburg M (letter). *Br J Ind Med* 1992 49:455.
- 3 doPico GA. Health effect of organic dusts in the farm environment. Report on diseases *Am J Ind Med* 1986;10:261-5.
- 4 Grant IW, Blyth W, Wardrop VE, Gordon RM, Pearson JC, Mair A. Prevalence of farmer's lung in Scotland: a pilot survey, *BMJ* 1972;1:530-634.
- 5 Baur X, Behr J, Dewair M, Ehret W, Fruhmman G, Vogelmaier C, Weiss W, Zinkernagel V. Humidifier lung and humidifier fever, *Lung* 1988;166:113-24.

A case-control study of malignant and non-malignant disease among employees of a fibreglass manufacturing facility

Sir,—Presenting analyses of smoking and respiratory diseases among fibreglass workers in advance of the availability of exposure histories makes the case-control study by Chiazzie *et al* (1992;49:326-31) impossible to interpret. Not only is the odds ratio for lung cancer potentially confounded by exposure to fibreglass (and other exposures present), there is the serious possibility of a multiplicative risk involving smoking and a mineral fibre, as has been clearly shown for asbestos and suggested for silica.¹ The unusually high odds ratio observed by Chiazzie *et al* for lung cancer and smoking (23.5) is an indication of an important non-smoking effect.

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- 1 Goldsmith DF, Guidotti TL. Combined silica exposure and cigarette smoking: a likely synergistic effect. In: Goldsmith DF, Winn DM, Shy CM, eds. *Silica, silicosis, and cancer*. New York: Praeger, 1986; 451-9.

Authors' reply

Sir,—We obviously disagree with the assertion by Mirer and Park that presenting the result of smoking analyses makes our case-control study¹ impossible to interpret.

It is the inadequacy or total omis-

sion of smoking data in the analysis of respiratory disease risk for an occupational cohort that makes a study difficult if not impossible to interpret. Smoking has been an unaccounted for confounder in many occupational epidemiology studies of risk for lung cancer. The epidemiological evidence is clear that analysis of respiratory disease risk in any cohort must start with a consideration of the impact that smoking has on that analysis.

The assertion that the risk associated with a known carcinogen-smoking may itself be confounded by a substance which has not been proved to be a human carcinogen represents faulty logic at best. Further, the notion of a multiplicative risk with regard to fibreglass is speculative and not supported by data from human epidemiological studies.

The results of our study with respect to smoking and mortality from lung cancer are consistent with the results reported by Enterline *et al* in 1987. They conducted a case-referent study and reported the results of a logistic regression analysis for respiratory cancer among fibrous glass workers drawn from the entire TIMA cohort. They entered into their model the variables year of birth, age at termination of the study (1982) or at death, smoking, time weighted cumulative exposure, and an interaction term between smoking

and exposure to fibre. Neither the interaction term between smoking and exposure nor the cumulative exposure were statistically significant and the authors state that "year of birth, age, and smoking were the only variables that were statistically significant in this analysis."² Furthermore, table 18 of that paper gives a maximum likelihood estimate of the log odds ratio for smoking among fibrous glass workers of over 14, consistent with the results in our paper.

Mirer and Park choose to ignore the data we present on prevalence of smoking among the subjects of the study. Only 3% of the lung cancer cases never smoked cigarettes. Not only was the prevalence of cigarette smoking among all employees extremely high among the study subjects, our data suggest that the prevalence for Newark seems to be sufficiently greater than the corresponding United States data to suggest that the previously reported excess of lung cancer for Newark (based on United States death rates) may be accounted for by differences in the prevalence of cigarette smoking between white male subjects in Newark and the United States.

Our page shows that after incorporation of the most extensive exposure determination ever undertaken in this industry, it is clear that smoking is the most important factor in risk for lung cancer for this population.

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- 1 Chiazze L, Watkins DK, Fryar C. A case-control study of malignant and non-malignant respiratory disease among employees of a fibreglass manufacturing facility. *B J Ind Med* 1992;49:326-33.
- 2 Enterline PE, Marsh G, Henderson V, Callahan C. Mortality update of a cohort of US man-made mineral fibre workers. *Ann Occup Hyg* 1987;31:625-56.

NOTICE

Bryan and Tempest Industrial Audiometry Courses, 17-19 March and 21-23 April 1993

These are two three day courses offering training and audiometry for industrial medical staff, safety officers, and others concerned with hearing in industry. The courses, which comply with the syllabus recommended by the British Society of Audiology, have the approval of the Society. The course will be held at the Wendover Hotel, Eccles, Manchester. Full details are available from: Dr W Tempest, Kismet, Croyde Road, St Annes, FY8 1EX. Telephone (0253) 712550.