

## CORRESPONDENCE

### Glutaraldehyde induced asthma in endoscopy nursing staff

We read with interest the paper on glutaraldehyde and symptoms in endoscopy nursing staff.<sup>1</sup> It is reported that there was an absence of objective evidence of the physiological changes associated with asthma. Peak expiratory flow (PEF) records from 17 cases were analysed by the OASYS-2 computer program, and three of these had OASYS-2 scores less than 2.5. These cases were thought not to show asthma because PEF diurnal variability was less than 15%. We have recently shown that increased diurnal variability is not found in most workers with occupational asthma.<sup>2</sup> Part of the explanation may be that the acrophase (time of maximum PEF in a 24 hour period) in normal and asthmatic people occurs at around 1600 with a trough about 12 hours later. Any deterioration in lung function due to exposure in the workplace is superimposed on the normal circadian rhythm. Thus, if a worker starting work in the morning has a fall in PEF that continued throughout the day while at work, the maximum PEF occurring at the time of the acrophase might be reduced. This would tend to reduce the diurnal variability. Even in non-occupational asthma there is considerable overlap of PEF variability with that occurring in normal people.<sup>3</sup> Use of non-linear PEF meters significantly underestimates variability in PEF<sup>4</sup> but even when PEF readings are linearised, an absence of an increase in diurnal variability does not exclude asthma. An OASYS-2 score greater than 2.5 has a specificity of 94% for diagnosing occupational asthma.<sup>5</sup> We suspect that, provided peak flow records were of adequate quality, the three cases with OASYS-2 scores greater than 2.5 did indeed have occupational asthma.

Since 1995, 29 cases of occupational asthma due to glutaraldehyde have been reported to SHIELD, the West Midlands reporting scheme for occupational asthma. A study of 24 workers referred to the Occupational Lung Disease Clinic in Birmingham with respiratory symptoms temporally related to glutaraldehyde exposure found that 16 had a definite occupational effect evident on their PEF records.<sup>6</sup> Five of eight workers with equivocal PEF records underwent specific bronchial provocation tests to 2% glutaraldehyde, all of which were positive as were three challenge tests in workers with suggestive PEF records. The challenge subjects included two in whom PEF diurnal variability was less than 10%. Of the subjects, seven out of 24 also had positive specific IgE to glutaraldehyde.

The sensitivity of serial PEF records in showing occupational asthma drops dramatically if less than three to four weeks of recordings are performed or if they are of inadequate quality—for example, less than four readings a day. We have found that objective evidence of asthma induced by glutaraldehyde can be obtained in a large proportion of workers with respiratory tract

symptoms temporally related to exposure to glutaraldehyde when adequately sought after.

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- 1 Vyas A, Pickering CAC, Oldham LA, *et al.* Survey of symptoms, respiratory function, and immunology and their relation to glutaraldehyde and other occupational exposures among endoscopy nursing staff. *Occup Environ Med* 2000;57:752-9.
- 2 Anees W, Burge PS. Diurnal variability of peak expiratory flow and non-specific bronchial reactivity in workers with occupational asthma. *Eur Respir J* 2000;16:520s.
- 3 Higgins BG, Britton JR, Chinn S, *et al.* The distribution of peak expiratory flow variability in a population sample. *Am Rev Respir Dis* 1989;140:1368-72.
- 4 Miles JF, Miller MR. Influence of peak flow meter non-linearity on recorded PEF variability. *Thorax* 1992;47:891.
- 5 Burge PS, Pantin CF, Newton DT, *et al.* Development of an expert system for the interpretation of serial peak expiratory flow measurements in the diagnosis of occupational asthma. *Occup Environ Med* 1999;56:758-64.
- 6 Di Stefano F, Siriruttanapruk S, McCoach JS, *et al.* Glutaraldehyde: an occupational hazard in the hospital setting. *Allergy* 1999;54:1105-9.

#### Vyas *et al* reply

Anees *et al* raise a very important issue in terms of the physiological criteria on which a diagnosis of occupational asthma should be based and in particular the clinical significance of small work related declines in peak expiratory flow. We fully accept that a lack of an increase in diurnal variation does not exclude a diagnosis of occupational asthma. The pattern of peak flow measurements in occupational asthma quite often shows a marked difference in the mean peak flow on working days compared with days away from work without any increase in diurnal variation. Burge *et al* refer to the phenomenon of small work related changes in their publication<sup>1</sup> and raise the question as to whether this represents asthma or other lung pathology. Their opinion at that time was that it was unclear what was the importance of these small changes. The example that they give in their article showed, taking the lowest peak flow recording during the working week and the highest on days away from work, a variation in peak flow in excess of 20% which we would accept as compatible with asthma and from the pattern illustrated probable occupational asthma. The small group of workers that we studied had diurnal variations in peak flow ranging between 5.7% and 9.8% and taking the worst working day peak flow and the best day off work peak flows, a variation between 11% and 13.5% (our peak flow recordings were linearised). This degree of variation does not satisfy the British Thoracic Society criteria for a diagnosis of bronchial asthma, neither do they satisfy a positive challenge response in bronchial challenge study. We have seen similar patterns of peak flow recordings in textile workers exposed to dust, both with and without notable contamination with endotoxin. We took the view that the small peak flow changes were due to an irritant effect and postulate the same mechanism in this group exposed to glutaraldehyde. The clinical histories provided by these workers does not suggest increasing respiratory symptoms with continued exposure. Although it is possible that the changes that we

have reported may represent a very mild form of occupational asthma, the clinical picture and the small physiological variation in peak flow, in our opinion is more consistent with an irritant airway response than the development of occupational asthma. Our paper is not intended to suggest that glutaraldehyde is not capable of inducing occupational asthma, for which there is convincing published evidence, in addition to our own personal experience. Our paper reports the findings of an epidemiological survey of a large population of currently exposed endoscopy nurses and has shown that while respiratory symptoms occur in this group, the lung physiology and the immunology have not supported a suggestion of a high prevalence of occupational asthma at current exposure levels.

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- 1 Burge PS, Pantin CF, Newton DT, *et al.* Development of an expert system for the interpretation of serial peak expiratory flow measurements in the diagnosis of occupational asthma. *Occup Environ Med* 1999;56:758-64.

### Glutaraldehyde induced asthma in endoscopy nursing staff

The recent article by Vyas *et al*<sup>1</sup> raises some concerns to which I would be grateful if they could respond.

(1) In the abstract one of the objectives is stated as finding the nature and incidence of symptoms experienced by a large sample of hospital endoscopy nurses. The study design is cross sectional and used an adapted version of the MRC questionnaire for respiratory symptoms. This study design normally records disease prevalence rather than incidence.<sup>2</sup> It would be helpful to know if the questionnaire sought information on new symptoms in a given period in the past, or the presence of symptoms.

(2) For the purposes of the study, work related symptoms of contact dermatitis were defined as contact skin rash, which occurred when working on the endoscopy unit and could not be attributed to known non-occupational agents. It is not clear what validation process was performed before this section of the questionnaire in the study was used. The authors have indicated that eight of the 13 subjects with a positive test to IgE specific to latex had work related symptoms of dermatitis, and indicate that this is non-significant. The authors' definition of contact dermatitis would have resulted in staff with contact urticaria answering positively to this section. As such, the presence of IgE specific to latex could well be of importance as staff would have used latex gloves.

(3) Cross sectional studies are enhanced by the inclusion of ex-employees. In this study only 18 of 68 ex-employees participated in this study. All 18 were among 26 staff who had left within the past 5 years for health reasons. As such a selection bias exists and the interpretation of the frequency of work related symptoms in ex-employees should be cautious. Also, it is noted that eight of the 18 ex-employees continue to work as nurses and may experience work related symptoms from circumstances related to current workplaces rather than endoscopy suites. The absence of a control group of nurses working in areas

without exposure to glutaraldehyde would have been of help in interpreting the results obtained.

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- 1 A Vyas, C A C Pickering, L A Oldham, *et al.* Survey of symptoms, respiratory function, and immunology and their relation to glutaraldehyde and other occupational exposures among endoscopy nursing staff. *Occup Environ Med* 2000;57:752-9.
- 2 Last JM. *A dictionary of epidemiology*. Oxford: Oxford University Press, 1995.

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## NOTICE

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### North American Congress of Clinical Toxicology Conference. 4-9 October 2001. Montreal, Canada.

The 2001 North American Congress of Clinical Toxicology will be held in Montreal, Canada, 4-9 October, 2001. This annual congress allows an opportunity for physicians, pharmacists, nurses, and scientists from around the world to participate in the sharing of a wide variety of toxicological issues. As well as platform and poster sessions, the program will offer a number of symposia, and other traditional and novel special sessions. Obtain the program details at [www.clintox.org](http://www.clintox.org) or contact Contemporary Forums Conference Management, 11900 Silvergate Drive, Dublin, CA 94568, USA. Phone 001 925 8287100 Extention 0.

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## BOOK REVIEWS

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### Toxicology of the lung: 3rd edition.

Edited by: D E GARDNER, J D CRAPO, R O MCCLELLAN. (Pp 416; £110.00) 1999. USA: Taylor and Francis Books. ISBN: 1 56032 801 0.

This is the 3rd edition of what has become a standard work in the fields of inhalation toxicology and air pollution science. The editors have, again, put together a series of chapters by recognised authorities: some pick up and develop topics considered in the 2nd, and even 1st editions; others deal with new problems. Some potential buyers will be wondering why they should pay £110.00 for this

edition when the 2nd (1993) still contains much of relevance and importance. The answer is that we are living in a period when air pollution science is advancing rapidly: much of what was thought about the effects, or lack of effects, of air pollutants on health in the early 1990s is no longer believed today. This book provides an invaluable update.

It is not possible to review all chapters in detail but a few that seemed particularly important are: Harkema on the nasal airways (replacing K T Morgan in the second edition); cytokines and regulation of pulmonary inflammation by Driscoll; epidemiological approaches to investigating outdoor and indoor air pollution by Samet and Jaakkola; environmental asthma by Frew and colleagues (possibly the first United Kingdom—although not the first European—contribution to this series), and chemical studies of air pollutants by Frampton and Utell. So a lot of well known names and the usual competent reviews. There is rather less anatomical material and lung cell biology in this edition than in previous ones. To the air pollution specialist the chapter by Graham and colleagues from the United States Environmental Protection Agency (EPA) is a jewel. They have provided us with an update on the criteria air pollutants (known in Europe as the classic air pollutants) in about 35 pages. Brilliant! Almost like a condensed EPA staff paper and indispensable for workers in countries, such as the United Kingdom, where resources are, in comparison with the United States EPA, limited. The tabulation of data from epidemiological studies on the effects of particles makes this chapter especially valuable. The problem of particles is dealt with in more detail by Roger McClellan in a long and very detailed chapter (11). This is in effect an “all you need to know” chapter and takes us from sources of particles and deposition in the lung, through evidence of effects, to standard setting and needs for research. McClellan expands on standard setting in a later chapter and this, too, is good. Despite this I was left with a feeling that someone of McClellan’s distinction could have gone further and given us more of his own views. The United States regulatory system in both the ambient and the occupational context is extraordinarily rigid and legalistic. Need it be like this? Do ambient air quality standards help? Given recent epidemiological work do we need animal to man extrapolation in setting air quality standards? As the honours papers used to say: discuss! A book of this type should do more than present the facts, it should give us the arguments: in this alone the book is limited.

Well then, worth £110.00? Yes, I think so. The updating chapters, alone, are worth it. I hope the editors will soon be thinking about a 4th edition: let us have more arguments—especially about the usefulness and validity of current regulatory practices.

R L MAYNARD

### Principles of toxicology: environmental and industrial applications, 2nd edition.

Edited by: P L WILLIAMS, R C JAMES, S M ROBERTS. (Pp xvii + 1-603; £). 2000. New York: John Wiley. ISBN: 0 471 29321 0.

The declared intention of the book is to present “. . . compactly and efficiently the scientific basis to [sic] toxicology as it applies to the workplace and the environment”, and it succeeds at a practical level.

The editors and authors all come from the eastern half of the United States, which gives a particular cast to the topics covered, and particularly to the sources cited and the approach to the evaluation of data. They have still served the reader well by the breadth of the coverage and the clarity of the presentation.

The three main sections cover: the principles of toxicology; areas of concern including reproduction, carcinogenicity, the effects of metals, pesticides, solvents and natural toxins; and applications including risk assessment, occupational and environmental health, epidemiology, and the control of hazards in the work place. Each topic is followed by a concise summary and a short, reasonably up to date list of references and suggested reading (not distinguished). There are some graphs, diagrams, and occasional illustrative sketches and grainy photographs.

The strong points of the book are its breadth in its chosen areas (although workplace related matters get more attention than environmental issues—for example, lead gets almost four times the space of dioxins) and clarity. Its weaknesses are the parochialism and the simplicity imposed by the coverage of many topics. Information and its evaluation are presented more as “givens” than as opportunities for arguments to illustrate principles and their modification in practice. Although the book seems to be directed towards practical users of toxicological decisions it does not cover the sources of information, nor does it offer a guide even to the multifarious United States agencies involved; federal activities seem less important than state or local actions. Other countries and even international bodies with which the United States may cooperate are omitted.

None the less, this would be a useful book to have as a quick source of information and as a guide to some of the principles underlying the successful application of toxicology some of the time and in some circumstances. In a contrary way, it would be an ideal base for high level students to identify deficiencies in its very pragmatic approach to toxicology and to learn by remedying them with knowledge from elsewhere.

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