CORRESPONDENCE

Glutaraldehyde induced asthma in endoscopy nursing staff

We read with interest the paper on glutaraldehyde and symptoms in endoscopy nursing staff.¹ 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.² 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.³ Use of non-linear PEF meters significantly underestimates variability in PEF⁴ 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.⁵ 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.⁶ 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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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 publication¹ 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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Glutaraldehyde induced asthma in endoscopy nursing staff

The recent article by Vyas *et al*¹ 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.² 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.
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NOTICE

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 or contact Contemporary Forums Conference Management, 11900 Silvergate Drive, Dublin, CA 94568, USA. Phone 001 925 8287100 Extention 0.

BOOK REVIEWS

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.

A D DAYAN

CORRESPONDENCE

Personal exposure of children to nitrogen dioxide

We read with interest a recently published study on personal exposure of asthmatic children to nitrogen dioxide (NO₂), relative to concentrations in outdoor air.¹ In their results, the authors did not find:

"...significant correlation... between each child's weekly mean personal exposures and mean outdoor concentrations for the corresponding periods";

"...marked evidence of seasonality" on personal exposure.

They concluded: "...at low concentrations, changes in NO₂ in outdoor air... contribute little to variations in personal exposure to the pollutant." We think that these conclusions cannot be drawn from the method used to evaluate outdoor concentrations. Besides, we report different findings on a seasonal trend at higher concentrations of personal exposure.

We performed a study to evaluate the annual distribution of personal exposure to NO₂ in school children of Novara, a small city in north west Italy (about 110 000 inhabitants) and to study determinants of this exposure. Exposure to NO₂ was measured with passive samplers (Palmer's tubes) in 310 school children aged 5-14 years. The children wore the tubes for 5 days a week, in each season of the year.

The possible differences in personal measurements were assessed by analysis of variance (ANOVA) and Tukey's tests. Information about the sources of potential exposure was collected by a questionnaire. The relative risk for these variables was estimated with a multiple regression model (logit). The annual average of 6200 measurements was 42.7 µg/m³ with a significant difference between seasons, and higher values in winter. The only factor associated with increased personal exposure was to live along busy streets, and then only for children from playschool (3-6 years). Even if the designs of two studies are different, at this point it is possible to make some comparisons.

Firstly, at higher concentrations of NO₂ exposure, as in those reported by Linaker *et al.*,¹ the seasonal changes in concentration in outdoor air contribute significantly to variations in exposure within individual people. On the other hand, the role of risk factors present at home, and the differences between children are not clear. We think that our results depend on the habits of most children to spend many hours every day in many different occupations away from home, reducing the individual differences caused by domestic sources of NO₂.

Secondly, we think that only one measurement station, as used by Linaker *et al.*,¹ is inappropriate to evaluate the real impact of outdoor concentrations on personal exposure, because outdoor concentrations of pollutants are, in our and in other studies,^{2,3} related to traffic density in each street.

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The bones and hormones of deep water divers and pilots of high performance aircraft

I have hypothesised that paternal hormone concentrations around the time of conception partially control the sex ratio (proportion male) of resulting offspring. Low concentrations of the testosterone/gonadotropin ratio are associated with subsequent daughters.¹ Such low offspring sex ratios have been reported by operators of high performance aircraft²⁻⁴ and deep water divers.⁵⁻⁶ In accordance with my hypothesis, low testosterone/gonadotropin ratios in men have been reported in association with changes in gravitation (as are experienced by operators of high performance aircraft)⁷⁻⁸ and strongly suspected in association with changes in atmospheric pressure (as are associated with deep water diving).⁹⁻¹⁰ It is now clear that high performance aircraft pilots are at increased risk of degenerative lesions of the cervical spine¹¹ and that deep water divers are also subject to skeletal degeneration.¹²⁻¹³ Low testosterone concentrations are an established risk factor for osteoporosis and bone fractures in men.¹⁴⁻¹⁵ So I suggest that the suboptimal bones of men in these two forms of occupation (deep water diving and operating high performance aircraft) are, at least partially, hormonally mediated consequences of these forms of occupational exposure. The point should be investigated.

Moreover the hormone profile of a low testosterone/gonadotropin ratio is established as associated with many illnesses in men¹⁶ as is exposure to deleterious chemicals—for example, the nematocide DBCP¹⁷ and dioxin¹⁸—and to non-ionising radiation.¹⁹ So the question arises: what is the medical importance of this hormone profile in men who are in the workforce or who are serving members of the armed forces and who seem to be clinically well? Does it indicate immunological compromise?

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NOTICE

International course "Principles and methods of epidemiologic research" by K J Rothman. 27-31 October 2002. Lunteren, The Netherlands.

Topics:

- Causation and inference
- Epidemiological measures
- Cohort and case-control studies
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Enrollment is open to researchers having basic knowledge of epidemiology and biostatistics and at least some working experience. Closing date for enrollment is June 14, 2002. Course fee: Euro 1 150 (including accommodation and meals).

For further information please contact: Ms Astrid van Alst, course secretary, Department of Epidemiology and Biostatistics (252), UMC Nijmegen, PO Box 9101, NL 6500 HB Nijmegen, The Netherlands. Tel + 31 24 3619132; Fax + 31 24 3613505; email: A.VanAlst-mie.kun.nl

CORRECTION

Gluteraldehyde induced asthma in endoscopy nursing staff. E WACLAWSKI. 2001;58:544.

The last sentence should read: The *presence* of a control group of nurses working in areas without exposure to gluteraldehyde would have been of help in interpreting the results obtained.

BOOK REVIEWS

The urban atmosphere and its effects. Edited by: BRIMBLECOMBE P, MAYNARD R. (Pp 374; .) 2001. London: Imperial College Press. ISBN 186094 064 1

For graduate students trying to move beyond a basic understanding of the effects of air

pollution on our health and urban environment, a book such as this is greatly needed. The volume of literature on that subject and its level of complexity is huge, and the gulf between it and basic texts is growing rapidly. This book seeks to bridge that gulf by tackling the key issues in the field of air pollution research.

A collection of work by people with expertise in each of the chosen fields, this book succeeds to varying degrees with its aim, with some chapters succeeding to a greater extent than others. Statistical issues in analysis of air pollution time series are complex indeed, and Hurley succeeds in demonstrating these complexities without making them seem intimidating. Maynard also provides a very clear introduction to the effects of non-biological particles on health, which gives readers a clear understanding of causality in epidemiological studies, and introduces the issues surrounding the key question as to who dies during episodes of particulate pollution. Cancer and air pollution is another difficult area dealt with skilfully by Rushton. People without an epidemiological background are introduced to the concepts of epidemiological studies, and confounding in particular. Other highlights are the lucid discussions of mechanisms of toxicity of gaseous pollutants, and an introduction to the concept of risk measurement and management at the population level.

Other contributions did not seem to work so well. The introductory chapter would not

give a reader new to the field a clear picture as to how composition, sources, and levels of air pollution have changed, and the discussion of alternative fuels was dominated by discussion of regulations in the United States and took a long time to get down to business. The final chapter about information resources gives a basic introduction on where to find information, but essentially is a list of where to find information on *any* subject—an advanced reader would possibly be better served by introducing key elements against which studies in this field can be critically appraised.

Inevitably, there are some terms that are not explained by the authors, which would make some sections difficult to understand for people from a different scientific background to that of the authors. Addition of a glossary would have helped. The ordering of the chapters seemed at times to be illogical but good editing means that all sections are relatively easy to read and follow. The print quality of some of the figures is poor, which is a shame, because there are relatively few of them.

Overall, this book succeeds at a very difficult task. A graduate student will leave this little volume neither overwhelmed by the complexity of the subject, nor seeing as simple the task of unravelling the vast and growing body of knowledge in the field of air pollution research. In that, the book succeeds, and I would recommend it to my research students as a way into this fascinating subject.

S WALTERS

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Patty's industrial hygiene, Volumes 1–4, 5th edition. Edited by: HARRIS RL. (Pp 3453; £577 for all four volumes, £166 each if purchased separately.) 2000. Chichester, West Sussex, UK: John Wiley and Son. ISBN 0 471 29784 4

This is a comprehensive occupational hygiene textbook written from a North American perspective. There are 67 chapters in four separate volumes, a total of 3453 pages covering everything from hazard recognition to control of emissions from industrial processes. Each volume is available separately although there is a discount for those who decide to purchase the four volumes together.

The first edition of *Patty's industrial hygiene* was produced over 50 years ago, with each subsequent edition being produced at about 10 year intervals. The scope of the work has continued to expand as occupational hygienists have become involved with a wider range of problems. This edition brings together updated material that was previously published in *Patty's industrial hygiene and toxicology* and *The theory and rationale of industrial hygiene*. These books are mainly intended as a reference source for the professional occupational hygienist, but they provide such a diverse range of material that it is likely that anyone involved with occupational health would find much of interest within them.

Volume 1 comprises 18 chapters that deal with recognition and evaluation of hazardous substances. There are seven new chapters with the remainder updated to a greater or lesser extent. The new sections include contributions on occupational dermatitis, aerosol science, endocrine disrupters, and multiple chemical sensitivity. The remaining parts cover basic toxicology and measurement of hazardous substances.

Volume 2 comprises sections on physical agents (seven chapters), engineering control plus personal protective equipment (six chapters) and biohazards (two chapters). The chapters on biohazards are both new to this edition of *Patty's industrial hygiene*. Much of the material in the section on physical agents is specific to the United States, for example the use of 5 dB adjustment for noise exposure rather than 3 dB, which is used in Europe. There is also extensive reference to specific sections within United States legislation and guidance. The revised chapter on non-ionising radiation has not been included in the paper version book and we are left with a one page addendum to the chapter written for the fourth edition to describe the research on the potential adverse effects of low frequency magnetic fields and cellular telephones. An editorial note suggests that a revised chapter may be included in the CD-ROM version of the book.

Volume 3 contains 18 chapters on legal, regulatory, and managerial aspects of occupational hygiene practice. Most of this volume is specific to United States legislation, although three chapters are of more general interest: pharmacokinetics and unusual work schedules, the biological basis of occupational exposure limits, and a chapter on biological monitoring. The chapter on pharmacokinetics and unusual work schedules by Dr Dennis Paustenbach is a particularly useful review of this topic that is accessible to the general reader and provides practical advice about how to evaluate the risks for people who have to work very long periods or non-standard shift patterns.

Volume 4 has a further 16 chapters that cover specialised areas and associated professional topics. This book has chapters on occupational health nursing, epidemiology,

ergonomics, occupational safety, fire and explosions, indoor air quality, air pollution, and hazardous wastes.

There is an uneven feel to these books, with the consequence that the reader is uncertain of what to expect before beginning a chapter. The level of the material varies from straightforward introductory standard to complex discussions of specific technical issues—for example, there is a long chapter on the statistical interpretation of monitoring data. Some chapters—such as the one dealing with man made mineral fibres—seem ill conceived because the material is unlikely to be relevant a few years from now. Several of the chapters use imperial units, others have either SI units or a mixture of systems, which in my opinion serves to confuse the reader. Each chapter has an extensive bibliography, but there is no standardisation of the format of the citations. A minor but annoying point when the content of a reference is not apparent from the material quoted.

One major omission is a discussion of the recent developments in assessment and control of dermal exposure. This is an area of occupational hygiene practice that has seen considerable research efforts, both to develop new techniques to measure hazardous substances contaminating the skin and to evaluate the effectiveness of gloves and clothing in protecting people at work. Otherwise these books are a comprehensive source of information about occupational hygiene in the United States. For European occupational health practitioners there are many individual chapters that are both interesting and informative. However, overall these books are not good value for money for people working outside North America.

J CHERRIE

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