CORRESPONDENCE

Measurement of vitamin D, metabolites in smelter workers exposed to lead and cadmium

We note with interest the paper of Chalkley et al on the measurement of vitamin D metabolites in smelter workers, where they suggest that exposure to both cadmium (Cd) and lead (Pb) increased the concentration of 1,25 dihydroxyvitamin D. We also reported a significant association between blood Pb concentrations and serum 1,25 dihydroxyvitamin D in Pb workers. However, our subjects were not occupationally exposed to Cd and in vivo measurements of tibial Pb, as an index of cumulative exposure, were also made. Our data suggested that the increase in 1,25 dihydroxyvitamin D was associated with blood Pb, not reflecting recent or current exposure rather than tibial Pb, and that the relation was not significant in those subjects with blood Pb <60 µg/dL. Our study found no effect on serum calcium, phosphate, or parathyroid hormone concentrations.

We think that it is important to highlight the difference between this Pb-induced renal effect in adults and the reported opposite finding in children of a decrease of serum 1,25 dihydroxyvitamin D associated with increasing blood Pb. Whatever the cellular or biochemical events that cause such contrary findings between children and adults, we should renew our caution in any sort of extrapolation from dose effect relations or “no observable effect levels” derived from adult, occupational studies to other potentially susceptible groups such as children. It is also feasible that biomarkers of nephrotoxic effect may have different usefulness or applicability in studies of adults and children. The maturing kidney during childhood and lifestyle habits, such as hand-mouth contact, means that children with potential exposure to any nephrotoxin should remain a group of special concern for professionals in environmental medicine or public health.

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Pb and 1α,25(OH)2 D concentrations, we thought that a direct comparison of our work with theirs was not possible due to the difference in the concentrations of Pb exposure, the fact that they had measured tibial Pb, and also that our subjects were primarily exposed to Pb. Mason and Chettle raise two separate issues, the first about the correlation between blood Pb and plasma 1α,25(OH)2 D, and the second draws attention to the need for caution when assuming that values derived from adult studies may be applied to children.

About the correlation between blood Pb and plasma 1α,25(OH)2 D, our interest lay in the fact that concurrent exposure to Cd seemed to enhance the positive correlation between blood Pb and plasma 1α,25(OH)2 D, at concentrations below the appearance of lead toxicity, with no threshold effect.

The second point raised was not an intentional part of our study, as we only mentioned the results of other studies on children in our discussion to suggest possible mechanisms for these opposite findings. However, we want to respond with this suggestion of caution when extrapolating results obtained from adults to children and also that children may be more susceptible to environmental hazards than adults. We found that serum MCH concentrations were significantly increased in children who did not wash their hands before eating compared with those who did (Chalkley SR, Hardman T, Strehlow CD, et al). Report on project to study the impact of lead in gasoline regulations in the UK; 1999, manuscript in preparation).

In London schoolchildren with concentrations of mean cell volume (MCV), mean cell haemoglobin (MCH), and serum ferritin below the reference ranges, the blood Pb and erythrocyte protoporphyrin (EPP) concentrations were significantly higher than those found in children whose MCV, MCH, and serum ferritin were below the reference ranges. Monitoring the concentrations of Pb in air in the school playgrounds indicated that these children were all exposed to similar concentrations of Pb in air (Chalkley SR, Hardman T, Strehlow CD, et al). Report on project to study the impact of lead in gasoline regulations in the UK; 1999, manuscript in preparation).

Exposure-response relations of α-amylase sensitisation in British bakeries and flour mills

Error—The publication of this paper by Nieuwenhuijsen et al was accompanied by an unusually high level of media interest in the United Kingdom with typical banner headlines that read “exposure to α-amylase is a significant health risk for those employed in bakeries and flour mills.” The authors’ press release included a comment that “urgent action is needed to reduce these high levels of fungal amylase and the high sensitisation rates of up to 30%.” Although the assay for amylase and the data on exposure response are new, the risk of sensitisation to fungal amylase in bread bakeries has been recognised for some time. On the basis of research carried out within one of the large food companies in the United Kingdom, the trade organisations representing the milling and baking industries have taken a proactive stance in both proposing exposure standards and producing training material to reduce the risk of sensitisation to fungal amylase.

Unfortunately the authors of the paper have not made mention of these facts.

On a slightly more disturbing note, there are two conclusions in the paper which are difficult to justify on the basis of the data presented. The first is the statement that “exposure to α-amylase is a significant health risk.” Although there is no dispute about the high prevalence of markers of sensitisation to amylase, in this case a positive serology or the large numbers with respiratory symptoms, these are essentially independent observations. To show a causal relation between the observations would require detailed historical taking (rather than a respiratory questionnaire) to establish the relation between the occurrence of symptoms and working patterns which give rise to high levels of amylase exposure. It is worth noting that there are reasons quite apart from sensitisation which could explain the high level of symptoms. The groups of milling and baking employees with the highest exposures to fungal amylase are also those who may have high total inhalable dust exposures (>10 mg/m3).

It is entirely possible that their symptoms (the health effect) may simply be the result of a non-specific irritant response.

The second conclusion which is difficult to defend is that amylase produces a health risk in flour mills. Unlike the data from the dispensing and mixing category in bread bakeries, which show a consistently high exposure in a group who handle fungal amylase relatively concentrated form (bread improvers), the conclusion on risk in flour mills is based on limited and inconsistent data. Essentially it relates to a small sample with a high arithmetic mean (of a respiratory questionnaire) to establish the relation between the occurrence of symptoms and working patterns which give rise to high levels of amylase exposure. It is worth noting that there are reasons quite apart from sensitisation which could explain the high level of symptoms. The groups of milling and baking employees with the highest exposures to fungal amylase are also those who may have high total inhalable dust exposures (>10 mg/m3).

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In summary, it seems a pity that a paper which presents new and important data on sensitisation in bakery workers should be spoiled by pressing the interpretation of findings too far.

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Authors’ reply—Although the statement that “urgent action is needed to reduce these high levels of fungal amylase and the high sensitisation rates of to 30%” was not ours, but that of OEM’s press release, we support this conclusion and greatly welcome the initiatives that apparently have already been taken by the bakery industry. We suggest, however, that the organisations take care if they want to use the results of the studies in one of the large food companies to set an exposure standard given the limited information on exposure including the representativeness, level, duration, and definition of exposure (workers with “regular” exposure), the labour turnover, including many how many left and why, bearing in mind the aims of the studies and the basic statistical analyses. The main aim of the other papers seemed to be to categorise any sensitisation into diagnostic categories—for example, respiratory irritations or occupational asthma, and to describe their overall (relatively low) prevalence rather than exploring any exposure-response relation as we aimed for in our work. “We found that the overall prevalence of sensitisation was relatively low (about 5%) and that only by categorising workers by exposure levels and taking into account movement of workers it was possible to detect a proportion of the workers become sensitised (about 30%).” This is important information for the prevention of sensitisation.

We do not agree with the suggestion by Smith et al that sensitisation is not a relevant endpoint. In the previous study in The Netherlands sensitisation to α-amylase was strongly associated with reported work related respiratory symptoms, of both upper and lower airways. In this study we found no association, but this could, for example, be due to the movement of workers away from exposure or the relatively short duration of exposure. We further know from other studies among workers exposed to typical high molecular weight sensitised workers have more symptoms that non-sensitised workers, and that the likelihood of the presence of symptoms in sensitised workers is associated with the amount of exposure. Few longitudinal studies are available, but the limited evidence published suggests that sensitised workers develop bronchial hyperresponsiveness and symptoms soon after sensitisation. It is likely that those who become sensitised to α-amylase are more likely to develop occupational asthma (when exposed) than those not sensitised, and reducing the risk of sensitisation will reduce the risk of occupational asthma. We acknowledge that respiratory symptoms occur in the absence of sensitisation. The concentrations at which these symptoms occur are not well described, but it is unlikely that these symptoms occur below the inhalable dust or allergen concentrations at which sensitisation occurs. For risk assessment purposes it seems therefore reasonable to take sensitisation as a critical end point for the risk evaluation.

For exposure-response modelling as performed in our studies, there is no need to include a cross section of the whole industry as long as the study is not hampered by different forms of bias, well known to most epidemiologists. Whether the risk assessment is appropriate for other exposed populations than the study population is a matter of generalisability and comparability. Other exposure setting, where workers are exposed to the same allergens, but possibly at different concentrations, are usually within the limits of generalisability. A well designed exposure assessment study throughout the United Kingdom baking and milling industry would be welcomed, and would provide information on exposure levels and for risk assessment. We found detectable, and sometimes high, concentrations of α-amylase at half the flour milling sites, site 1 and site 10, among, for example, flour millers, packers, and cleaners (hygiene). As we stated in our paper, the great majority of those sensitised was exposed to non-detectable or very low concentrations of α-amylase, and only a small proportion to high concentrations. We think that these high concentrations of α-amylase should be reduced. This would most likely lead to a reduction in sensitisation in α-amylase.

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**Guidance on the development of educational and training curricula.**

**Edited by:** MARTIN FITZPATRICK, SAVIER BONNEFOY. (PP 198; SW.FR45) WHO. ISBN: 92 890 1350 8.

The authors of this book have given them- selves a very broad objective which in itself is unachievable: to define content and methods for teaching environmental health in Europe (east and west). The book wants to show the administrators as well as those who want to build up curricula and those who teach in it, how to do this. Also it considers all different level of teaching. In this context the scheme about different levels of training is quite useful.

The book provides background information for the development of training programmes in environmental health, it describes the application of existing methods for teaching environmental health topics, however, the tables of who teaches what, and who needs what, are sometimes contradictory. The obvious aim of not forgetting anybody in any list about who should be taught what and what should be taught by whom and which fields should be covered, are not completely consistent. For instance, basic areas of attitudinal competence start with “caring attitudes towards people” and “active concerns for public health”. In the disciplines covering the field of environmental health, however, medicine and public health are not mentioned (page 33).

The annexes give detailed contents of curricula for different environmental health professionals which might be used as a check list for existing courses or stimulate teachers to expand on certain topics but on the whole remain superficial and do not help to design a teaching programme. The book might also be useful in harmonising some of the environmental health teaching programmes in Europe. It does not help anybody who wants to learn something about environmental health, but this is probably not only in this context it is unable to bridge the gap between what should be taught on which level and the content to be taught, its usefulness therefore will remain restricted to those who want to build up a traditional curriculum for environmental health personnel and are looking for teachers in different fields. There might be a need for such a book in parts of Europe.

**URSULA ACKERMANN-LIEBRICH**

### Analysis of hazardous substances in biological materials, volume 6.


This publication is volume 6 of a series on this topic produced by the Deutsche Forschungs- gemeinschaft Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area. The sections of these books are distilled from meetings of a standing working subgroup of the Commission to which numerous guests and ad hoc experts are invited to contribute. As a result, the material presented has been scrutinised and reviewed by many leaders in the field and, therefore, represents an extremely reliable and authoritative consensus of opinion. As with the previous issues, the format consists of a monograph which covers the use and occurrence of each substance or substance group, the associated health hazards, metabolic and excretion data, exposure limits, and biological tolerance values. This is followed by an account of the recommended method for analysis of the compounds in biological fluids. This is presented in great detail such that a laboratory analyst with the requisite equipment to hand should be able to reproduce the method with minimum effort. Each method is also designed to detect trace concentrations of interest for environmental medicine and that for occupational medicine.

This volume deals with aluminium, amniotines, hydrazines, pentachlorophenol, phenols and pyrethroid metabolites, thorium, and uranium in the manner already described. Also there is an introductory chapter on inductively coupled mass spectrometry (ICP-MS) which is probably the most powerful technique yet devised for trace element analyses. One important feature of ICP-MS is the facility to screen biological samples for increased concentrations of a whole series of contaminants for increased concentrations of a whole series of contaminants of interest to environmental medicine and that for occupational medicine.

What are the implications of demographic change for British Medicine? The BMJ, in conjunction with the Debate of the Age, are holding this one day conference to examine the possible effects of an ageing society on the practice of medicine, medical education, and medicine’s institutions.

With plenary sessions and a choice of six different workshops, this conference will be highly interactive and educational. Contributors include: Sir Donald Irvine, London;
This publication, like the previous five volumes in the series, is a valuable work of reference which is aimed primarily at analytical chemists, although much of the review material will interest occupational physicians and provides useful background information on what analyses are possible, limits on sample collection, and guidance on interpreting the analytical data.

Brian Widdop


The American Conference of Governmental Industrial Hygienists’ book of threshold limit values (TLVs) is regarded as an essential reference book for industrial hygienists and occupational physicians worldwide. This new edition is, as before, pocket sized but now ring bound and contains even more information. The book is often used only for looking up TLVs: this is a great pity. The introductory textual material is particularly valuable and provides a concise introduction to the principles of standard setting in regulatory toxicology. For example, an admirably short and clear explanation of the log normal distribution of short term exposure measurements likely to occur in conjunction with well controlled processes is provided. This leads to a transparent explanation of the derivation of excursion limits. The appendices provide further valuable information. Carcinogens, substances of variable composition, PTFE/decomposition products, welding fumes, and mixtures are all considered. Appendix D focuses on particles and defines the descriptors used to describe particle mass functions. The change of the median cut off point for a respirable particulate matter sample (now 4.0 μm compared with 3.5 μm in previous editions) is noted.

The second half of the book deals with biological exposure indices. Biological specimens—for example, urine—are easy to collect and even easier to collect inappropriately—for example at the wrong time of day or over the wrong period. The background information explains the theoretical background to biological sampling.

The third part of the book deals with physical agents: noise, vibration, ergonomic factors, ionising radiation, lasers, non-ionising radiation, and thermal stress. Here too the explanatory notes are clear and concise.

In summary: this is an indispensible book. It is a great deal more than a list of standards and deserves to be read thoroughly. Highly recommended.

R.L. Maynard


Reviewing a book of nearly 2000 pages is a challenge. Should one dip and skip, read a series of chapters in vain or simply use it?

I’ve had Rom beside me for 6 months and have used it to look up knotty problems of environmental and occupational medicine: it has proved unfailingly excellent. Looking things up has led to reading many whole chapters and this has had no hardship: chapters are divided, balanced, and, blessedly, not too long.

This book is organised into three large sections and 136 chapters. A chapter thus averages just over 13 large, double column pages. Reading the thoughtful introductory chapter led me to:

“Importantly, the journal of the faculty of occupational medicine in the United Kingdom has changed its name from the British Journal of Industrial Medicine to Occupational and Environmental Medicine.”

Excellent! The first section continues with chapters on our specialty—history, its methods, its successes and its failures. In chapter 9 the pace changes: a series of chapters on the immune system, molecular biology, carcinogenesis, a whole chapter on P53 tumour suppressor gene, and other rather biochemical topics follow. These are hard going in places—but the short chapter format lets the reader reach the end of each without collapse. How many occupational and environmental physicians will read these chapters? My guess is: too few.

The next batch of chapters deals with the lung (chapters 19-44, a monograph in themselves) and then other organ systems (chapters 45-67). The chapters on the lung begin with Lippmann on particle deposition, later on ozone, and cover all the standard areas of occupational pulmonology. Air pollutants are well represented, including Utell on SO2 and H2SO4 aerosols and Guidotti on respiratory irritants. Rom contributes chapters on asbestos related diseases and on silicates and benign pneumoconioses.

The coverage is impressive: even volcanic ash is discussed. Picking out individual chapters is always invidious but Becklake’s chapter on occupational exposures as a cause of chronic airways disease struck me as a particularly judicious account of what has been a vexed question: the section on the implications of the recent shift of opinion in other areas must be read by all occupational physicians.

Chapters on specific problems: metals, organic chemicals, and radiation follow. Here I’ve dipped and skipped as I needed to find out things. Aluminium, lead, and cadmium have all been problems to me and the chapters have helped. Benzene and 1,3-butadiene seem interminable problems in the air pollution field and here, too, the chapters have been helpful. The chapter by Silbergeld and Thomas on dioxins and related compounds was an invaluable find: the links with endocrine toxicology are better explained here than I could reasonably have hoped.

The chapters (113-123) on environmental issues are helpful; well known names abound: Samet, Dockery, Spengler, Devlin. Gulf War syndrome has been mentioned, as have the effects of global warming. The book ends with chapters on broader issues including regulatory systems, law, and ethics. Roger McClellan on risk assessment is particularly excellent. Who is this book intended for? At £149.00 it is expensive but extraordinary value for money and should be considered by anybody training in occupational and environmental medicine. Indeed, 6 months’ selective reading would form an excellent course of study! For the consultant dealing with problems a bit outside his or her personal area of expertise it is an outstanding guide; for the toxicologist interested in the health effects of individual compounds it is invaluable. In conclusion: the best reference book currently available on occupational and environmental medicine.

R.L. Maynard


This reasonably priced small book published by the World Health Organisation targets the need for early rapid assessment in natural disasters. It is designed to be used by local health staff who are described as being unlikely to have a team of experts on hand to give advice. It is a useful document for this purpose but is also helpful for those with an interest in disaster medicine, public health, infectious diseases, epidemiology, environmental health, emergency planning, and toxicology. It is a book for the doers, not the examination candidates.

The opening chapter on rapid health assessment provides detailed guidance of the purpose and process for preparedness for health assessment. The checklist approach is well laid out and helps by listing tasks for preparedness for any health assessment. Details of organisations needing to be included in plans are given but not aids—such as information for contact to international agencies and organisations.

Most of the book concentrates on infectious diseases. Chapters are targeted at epidemics of infectious origin, outbreak survey and control, and outbreaks of acute diarrhoea. Sudden impact natural disasters has an elegant four staged approach of reviewing likely processes and activities in the first 5 days with the likelihood of emergency plans being fully implemented by day 5. This will be reassuring to many local responders who may well be among the casualties and have difficulty in providing a comprehensive response immediately. Chapters on sudden population displacements, nutritional emergencies, and complex emergencies are also included.

The chapter on chemical emergencies provides an excellent start for any acute or chronic incident impact assessment. It covers the process of conducting the assessment by considering the following five issues:

- The need to confirm the existence of a chemical emergency—by a quick visit to the site by a person with knowledge of handling dangerous goods or chemicals, who can provide preliminary precautions (but not mentioning fire brigade or other trained emergency professionals)—with health personnel undertaking a differential diagnosis and examining sentinel cases (the need for safety is not mentioned here)
- Identifying the type of chemical and their reaction by-products—here mention is made of the signs that can be provided by chemical information centres. Internationally

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the process through the International Programme of Chemical Safety has been to establish Poisons Information Centres, with few countries having specialist chemical information centres, therefore this advice may be confusing:

- Determining the population at risk and health impact—including a valuable comment on the need for a case definition but does not recommend early biological and environmental sampling.

- Assessing the local response capacity—comments on the vulnerability of health care facilities to chemical contamination. This section does draw attention to the need for protective equipment and decontamination facilities. A useful checklist of all the many issues that affect health impact assessment in a chemical incident is included. Although detailed, covering 13 different critical issues, it is not complete as it really considers acute not chronic incidents. This is not surprising considering the complexity of the investigation and management of chemical emergencies.

My main concern is that sources of information and advice are not given for any of these emergencies. The three organisations who collaborated in the preparation of this book are mentioned—interestingly enough none of these were a chemical information centre.

 VIRGINIA MURRAY

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