CORRESPONDENCE

PBN as a possible bladder carcinogen

In their paper updating a previous investigation of the mortality of workers employed at a factory producing chemicals for the rubber industry, Sorohan, Hamilton, and Jackson plead for priority to be given for studies on the cancer experience of other working populations exposed to N-phenyl-β-naphthylamine (PBN).

It is, therefore, disappointing that the authors made no reference at all to studies conducted by the British Rubber Manufacturers’ Association (BRMA), and others, on rubber workers employed after 1950. These workers would have been exposed to PBN, and to other antioxidants still in use after the discontinuance (in 1949) of Nonox “S” and similar compounds, as well as to 2-naphthylamine (BNA). This contaminant, a potent human bladder carcinogen, was at a concentration (2500 ppm) sufficient to double the incidence of bladder cancer in those exposed.

A particular study† which singled out a large cohort of male rubber workers (2577) at a tyre factory, who experienced mixed exposure, but also exposure to PBN as the predominant antioxidant was followed, up to 1990. No excess of bladder tumours was found (25 observed, 24.1 expected; standardised incidence ratio (SIR) 104, 95% confidence interval (95% CI) 67 to 153). This result was confirmed in such a mixed exposure situation, where exposure can be confirmed in occupational hygiene terms, strongly suggests that whatever agents are being used they are not (under those conditions of manufacture) exerting a carcinogenic influence. Also a subcohort of 1322 men at the same factory, but employed before the end of 1949, who could be excluded from concomitant exposure to Nonox “S”, but who were exposed to PBN flowline, showed similar results (12 observed, 14.5 expected; SIR 83, 95% CI 43 to 145).

The rubber industry deserves to be reassured from such purposefully conducted studies as soon as possible.

There is no evidence that PBN is itself carcinogenic. As the authors indicate, it is not a proved animal carcinogen and it is not mutagenic to bacteria. If some dephenylation occurs in vivo, it probably does so to a very minor degree, and at a stage in the metabolic cycle that renders any metabolites relatively innocuous, or unavailable to the urothelium.†

It is one thing to cast suspicion of carcinogenicity at manufacturing industry, quite another to transpose this into the situation of open usage; I cite the auranine and magenta example in the dye industry. From the data shown in their figure, Sorohan et al essentially rely on only six cases of bladder tumour in a subcohort of 94 men, all allegedly exposed to PBN, but 52 of whom had mixed exposure to α-toluidine and to 2-mercaptobenzothiazole (MBT) as well. Three tumours related to this manufacturing industry, three to the 42 men allegedly exposed only to PBN.

The authors have undoubtedly shown that an excess of bladder tumours has occurred in the factory workforce studied, but on all the evidence presented, in my opinion, it is unjustifiable to ascribe a suspicion of carcinogenicity to PBN, when overall the epidemiological and other evidence available is more reassuring than not.

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Sorohan and Jackson reply—We agree with Veys that his study of workers exposed to phenyl-β-naphthylamine (PBN) while engaged in the manufacture of rubber tyres indicates that such workers do not experience increased risks of bladder cancer, and that the findings of his study need to be considered along with our own new findings in arriving at any overall evaluation. Our simple interpretation of the new findings was that “PBN (or a chemical reagent of chemical intermediate) did not contribute to the production of PBN at this factory in the 1930s or 1940s was a bladder carcinogen”, that other interpretations were possible and that all needed to be “treated with caution”. Our emphasis on the possible role of chemical intermediates matches the concerns of Veys—namely that epidemiological findings relating to workers engaged in the manufacture of a given chemical may be quite different to those pertaining to workers using the chemical. Clearly, large scale studies relating to both sets of circumstances should assist confident interpretation.

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Childhood cancer and possible exposure to benzene from traffic and petrol stations

In a study of childhood cancer and possible exposure to benzene from traffic and petrol stations Harrison et al found a non-significant increase in childhood leukaemia. In their conclusion they state that “... the data are overall rather reassuring in showing that any such effect, if real, is likely to be small in magnitude”. We think that this conclusions cannot be drawn from such limited material.

Firstly, they merge all types of leukaemia, whereas studies in adults have indicated that non-lymphocytic leukaemia is most strongly associated with benzene. An ecological Swedish study found an association between car density and NLL but not with other types of leukaemia or lymphoma.†

Secondly, the misclassification of exposure may be substantial in the study by Harrison et al. In Sweden wood burning makes a major contribution to the exposure to benzene in some areas. Probably the burning of other fuels for heating will also contribute. Children are transported in cars, stay in kindergartens, schools, sports areas, shopping areas, etc. for much of their days. Even if stationary sampling shows a different concentration of pollutants close to roads, that may not mean that the exposure of the children differs in the same way. A Danish study found that although front door concentrations of benzene were significantly higher in a city than in rural areas (8.9 v 1.9 µg/m³), there was almost no difference in the mean personal exposure of these children (5.4 v 4.5 µg/m³). Such misclassification of exposure leads to an understimation of the relative risk.

The important findings of Harrison et al and other studies† (see London Research Centre for further references) is that living in high populated areas, with a high traffic density and NLL but not with other types of leukaemia or lymphoma.†


Authors’ reply—Jarvholm and Forsberg quite rightly point out that studies in adults have indicated that exposure to benzene is associated with an excess of non-lymphocytic leukaemia (NLL) and implicitly criticise us for having merged all types of leukaemia. The reason for merging the leukaemias was because lymphocytic leukaemias accounted for 176 of 225 leukaemias in the West Midlands in the age group 0–14 years in the period 1993–7, and therefore non-lymphocytic types accounted for only a very few cases, with only 42 registrations of acute myeloid leukaemia over this period. It seemed very unlikely that we would be able to obtain a significant result from so few cases.

Jarvholm and Forsberg comment also on the potential for misclassification of exposure in our study. We do not think this very likely in the United Kingdom. Wood burning is almost unknown in the West Midlands.
corroboration, and indeed would not be consistent with United Kingdom smoke control laws. The inventory of air pollutant emissions for the corroboration indicates that 99% of benzene emissions to atmosphere arise from road traffic. Our paper gives some indication of the likely gradients between houses at the roadside and those in urban background locations. Although children are also exposed to benzene when travelling in cars, the duration of exposure is relatively short and our earlier paper on personal exposures to aromatic hydrocarbons suggests that this will be a minor contributor to overall exposure. It is exposure in the home and workplace (or in the case of children, in the school) which is dominant. It is likely that other sources of exposure are relatively similar on average for the more exposed and less exposed groups and therefore the main difference relates to the point of residence and the influence of outdoor air on indoor concentrations.

Järhovm and Forsberg cite a Danish study which showed significantly higher front door concentrations of benzene in a city than in rural areas. In the United Kingdom West Midlands the risk of childhood cancer is higher in rural than in urban areas which suggests that benzene exposure is unlikely to be a major factor and that other causal agents such as population mixing may be far more influential.1 None the less our results do suggest a slight excess of cancers for children living close to major roads and petrol stations and we wholly agree with Järhovm and Forsberg that this merits further investigation.

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Prevalence and risk factors for latex allergy: a cross sectional study in a United Kingdom hospital

EDITOR—We read with interest the cross sectional study of latex allergy of workers in a United Kingdom hospital.1 We have also tried to study healthcare workers in a district general hospital and have had problems with the response rate for skin prick testing and also blood taking. We have, however, used standardised and evaluated skin prick test materials from Stallergen (1:200) and the Pharmacia CAP for latex and have found a high percentage of symptomatic workers with positive skin tests and specific IgE. We also found that workers in general wards were exposed to as much airborne latex as those in operating theatres, accidents and emergency, and intensive care, areas which we previously thought of as high exposure. Median concentrations of latex in air were 0.44 µg/m³ in our high exposure areas and 0.48 µg/m³ in our lower exposure areas, perhaps because lower quality gloves were used in the general medicalwards.

We obtained questionnaires from 73% of our sample workers but only 60% response from symptomatic workers who were invited for skin prick testing and blood taking. There were a few significant differences between groups but there was a greater relation between the number of gloves worn a day than the hours of glove wearing. Work related symptoms relative to glove use are shown in the table.

Seven of 48 symptomatic workers had at least a 3 mm weal to the latex allergen and nine had positive RAST (≥0.7 kU/l). All skin prick positive workers had itching skin, four out of seven had eye irritation, two out of seven wheeze, and three out of seven rhinitis. Any study of this sort is likely to miss the most severely affected workers who cannot tolerate latex at present in the air in ordinary hospital environments.

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NOTICES


This annual conference 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 programme will offer symposia, and other traditional and novel special sessions.

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BOOK REVIEWS


The first edition of this famous book was published in 1969 and rapidly established itself alongside works by Comroe and Cotes as required reading for respiratory physiologists and especially for anaesthetists. This new edition—the original author having handed the torch to Lumb, maintains the high standards of its predecessors. As the editions have appeared changes in the arrangement of sections of the book have been made. These are most marked in this edition: basic principles, applied physiology, and the physiology of pulmonary disease now being the sections that contain the §33 chapters. The last section is a new venture and contains much new material. To keep the book to about 700 pages Lumb has excised some material that was in the earlier edition. This is recognised by the original author in his foreword. Casual readers will notice few changes—"tho' much is taken, much abides" and the quality is undiminished.

The book begins with a chapter, by the original author, on the atmosphere. This is outstanding and should be read by all physiologists. Did you know that half the expected life of this planet has passed? I didn’t and it is a sobering thought. The author makes the point that our atmosphere has dictated our physiology. Current concerns about antioxidants in the diet and their role in protecting the airways against free radical attack are reassessed by the chapter. Further details of oxygen radical formation see page 496: the chemistry is complex but elegantly explained. Section 1 continues with accounts of lung structure, elastic forces, resistance to gas flow, the control of ventilation (rate and particularly clear) and thence to the matching of ventilation and perfusion. This has always been a difficult chapter and some changes can be recognised. It is still difficult but recent advances in modelling of and the use of the MIGET technique have done much to simplify the theory. Discussion of the Riley, Fenn, Cournard model has been reduced—this may disappoint some. We have to paraphrase Saunders, this area has provided many with much quiet intellectual amusement and instruction) at the cost of a few pencils and some reams of paper only! Those proposing to follow a career in respiratory physiology should read the account given in earlier editions of this book. The "applied" sections of earlier editions appeared, I suspect, more to anaesthetists than to physicians. This should no longer be the case: Pregnancy, sleep, air pollution, and smoking for example are all now given chapters of their own: indeed, only one chapter is headed “anaesthesia”. This is a significant step; it provides an account of most of that which a respiratory physician or anaesthetist should know about pathophysiology. The chapter on acute lung injury is particularly good with an excellent account of the role of cytokines.

The book concludes with five appendices dealing with the maths and physics. The appendix on nomograms and correction charts will appeal to many: the great Siggard-Anderson—Fio2 nomogram remains as does the invaluable Pao2—Fio2, shunt nomogram (much photocopied!). Reading this book has been a pleasure. It is the best single volume account of pure and applied respiratory physiology now available. At £59.50 it is a bargain—buy it!

R. L. MAYNARD


The structure and functioning of the United States healthcare system is perceived by many as being analogous to an inscrutable labyrinth. Moreover, the medicolegal terrain in which physicians practice in the United States is extraordinarily litigious. Liang’s remarkably well researched, and excellently written, book Health law and policy provides healthcare practitioners with a lucid, detailed road map to avert legal pitfalls in the mine ridden, United States medicolegal landscape.

Although Liang’s book is a superb compendium specifically of United States medicolegal issues and principles, it is noteworthy that the legal systems of the United States and United Kingdom are rooted, similarly, in the soil of judge made, “common” law. As such, Liang’s expert examination of the amply developed body of United States medicolegal case precedents, spawned by the highly active legal system in America, may be of considerable instructive value to healthcare practitioners in the United Kingdom desiring to avoid entanglement in legal traps. Liang has a trio of document referees (in medicine, public policy, and law); and earns a living as a professor at an American law school. By virtue of his unusually wide ranging formal educational background, Liang is able to view the subject closely, and very carefully, penetrating and dissect multitudinous, timely issues residing at the interface of law and medicine. The book is configured into four parts, encompassing 16 chapters. An often and effectively used mantra of Liang is to identify a medicolegal concept; and then provide an illustrative case, based on a real life case, followed by a pithy legal discussion of the case illustration. Generally, the numerous cases and accompanying legal discussions brightly illuminate the adjoining textual material.

In part I of the book, Liang focuses readers’ attention on traditional areas of concern in the realm of law and medicine, including such topics as informed consent and confidentiality. In part II, Liang works assiduously to sketch the contours of the healthcare insurance structure in the United States. Modern delivery considerations—for example, physician reimbursement, fraud issues, health reform—comprise the subject of a third part. In a concluding part, on end of life considerations, Liang studiously elucidates advance directives and definitions of death, and attendant legal and policy issues.

In the preface, Liang states that the book is aimed at people interested in learning about the United States health enterprise. In this task, he is, indeed, quite successful. A distinguishing feature of the book, which finely tailors it to fit readers educated in fields outside the law, is that the author uses language understandable to non-lawyers. At the same time, Liang supplies copious quantities of medicolegal references. The book, as tailored, thus fits legal scholars as well.

It is important for readers to understand that the book is not a substitute for competent legal counsel. The book can capably assist the non-lawyer in recognising potential legal problems; but it is not a source enabling the non-lawyer to fully flesh out legal issues in existing manner, without the assistance of qualified counsel. Finally, although the book is presently up to date, a relevant and salient reality is that the medicolegal world explained so succinctly and carefully by Liang is changing rapidly, thus mitigating the book’s future, practical value to readers.

LEO UZYCH
Evaluation in occupational health practice, 1st edition

Evaluation of healthcare systems, with its significant use of qualitative data, has to date received far less attention in relation to conventional research methods. However, study designs such as randomised control trials are of limited use when occupational health services seek to describe their own practice or are asked to justify programmes to employers, who expect such activities to impact on the functioning of their organisations. The evaluation approach, developed partly in the social sciences, helps provide models for such researching questions. However, as the authors note, a great number of such studies have been heard in the BMJ and Occup Environ Med. Menckel and Westerholm's book coherently draws together the conventional study methods and these newer approaches. In doing so the potential researcher is encouraged to seek clarity of thought in the question to be addressed before the study design is selected, to consider the role and expectations of stakeholders, and to consider the wide range of potential outcomes from any occupational health programme.

The evaluation approach requires a knowledge of systems theory and this book provides a useful introduction that may help occupational health specialists see the workings of their own departments in a new light. The book has a consistent emphasis on occupational health experience and rarely strays into unnessary theory. The principal weakness is a lack of worked examples on common themes in occupational health practice—for example, management of sickness absence. However, as the authors observe, comparatively few evaluation studies have been published in the occupational health literature and this book will no doubt help correct this situation.

This thought provoking book encourages reflection on the daily practice of occupational health and offers a wide range of approaches that may be adopted to evaluate common practice. Such approaches may not, read not only to formal research but also to well informed management decisions on the development and impact of occupational health services. In conclusion this book is worthy of inclusion alongside standard texts of statistical and research methods, but is likely to be of greater use in the day to day management of occupational health services.

PHILIP WYNN

Occupational health: recognising and preventing work related disease and injury, 4th edition

This is the 4th edition of Occupational health: recognising and preventing work related disease and injury, edited, as before, by Levy and Wegman. Four editions—1983, 1988, 1995, and now 2000—say something in itself: there must be people out there buying it in sufficient numbers for the publishers to continue the expense of a further edition. There must also be sufficient changes and updates between editions for some people to buy it again for the updates. The questions for the reader of this review must be: Is this a genuine update with additional relevant material to suit the new millennium and is the book worth the price? The short answer, on both counts, is yes.

I have read or scanned all the chapters and I can say that this is a genuine update. Many chapters have been largely rewritten, and where necessary, updated. Some—such as epidemiology—do not require such major revisions as others, when old topics have become longer in 5 years. New chapters have been added: environmental health, occupational health service, injuries, young workers, older workers, and healthcare workers.

One of the criticisms I had of earlier editions was the book’s heavy American bias: to some extent this is still true but less so. The list of contributors is truly international and many are the leading authority on their subject. In some cases—for example, worker compensation—I think the book is still missing a trick by being so United States orientated. The broad concepts of recompensing an injured worker are used worth spelling out and there is much to be gained reviewing the way different countries approach the issue. There is even now the stance taken by pan national organisations, like the European Union, to harmonise their schemes across national boundaries. What we get is the United States scene by and large.

In other areas the book has not expanded to meet the needs of the time. For example, the chapter on shift work is about shift work. Very good it is too but the issue for today is working hours, not just shift work. Much is known and agreed about the health effects of shift work. The new unanswered questions relate to long or irregular hours of work.

Still, these are relatively trivial issues to raise in relation to this splendid book. It is authoritative, well written, and ably edited. It covers the broad gamut of occupational health illness and occupational health practice. It also now has few peers among the middle sized books (a book of now 842 pages as opposed to 650—middle sized?) Last time around the 3rd edition Levy and Wegman (3rd edition) had the edge on Waldron’s Occupational Health (3rd edition). The 4th edition of Waldron’s book (Waldron and Edging) is not a true update but a supplement to the 3rd edition and has a very patchy in quality and suffers also from some poor editorial control.

So, Levy and Wegman’s 4th edition is clearly out in front. If you do not possess one or even if you do own an earlier edition, there’s enough in this new edition to warrant the modest outlay.

J M HARRINGTON

Environmental toxicants: human exposures and their health effects

This is the second edition of Lippmann’s well known book on environmental toxicants. Seven new chapters are included bringing the total to 30. Forty one authors make contributions and the book runs to almost 1000 pages. Despite this it is surprisingly slim, due to the use of fine high quality paper, and the book is pleasant to hold and read.

The editor has set out to provide in depth reviews of environmental toxicants: including air pollutants, dioxins, environmental tobacco smoke, food additives, radiation, noise, metals, and microwaves. Chapters dealing with risk and methods for reducing risks are also included. The book ends with an industrial perspective, which suggests how integration of information on the effects of chemicals into corporate policies and practices for protecting health can be achieved. The scope is thus broad although not all embracing. The first impression I got on reading this book is dealing with topics with which I am familiar was one of awe. The detailed included is extensive, facts fall like snowflakes, and hardly a line seems to lack either the science or the data from a study or experiment. This does not make for easy or rapid reading but it does make for an outstanding source of reference. Readers should look at the editor’s 70 page review of ozone that includes reference to more than 300 sources to see what a detailed review actually should be. Recent references are included throughout.

The first detailed chapter is on ambient particulate matter (this and some of the other chapters on classic air pollutants) is by the editor. This chapter is fairly short and presents a summary of most of what one needs to know. There is a trace of a bias towards the United States literature and the discussion on the setting of standards is focussed sharply on United States practice. The much discussed ultrafine hypothesis is treated lightly and the author has not dwelt on the mechanisms of free radical formation that are currently being discussed. Recent work on the effects of particles in animal models is discussed. This is followed by a longer account of asbestos and other fibres.

The evidence for effects on health reviewed
in depth, sifted, and summarised judiciously. A great deal of detail is provided—enough to make some pages hard reading. The chapter ends with a useful recapitulation of the key findings. The editor has contributed further chapters—on ozone and sulphur dioxide; these follow the same pattern: exhaustive detail, careful weighing, and balanced conclusions.

In reading other chapters from this book I wondered whether the authors could keep up to Lippmann’s standard. Mauderly has dealt with diesel exhaust, and yes, he has maintained the standard: about 40 pages and on reaching the end the reader wonders whether he needs to read more on this vexed issue. The summary of what can be learnt from the epidemiological studies should be reprinted—widely. This chapter compares very favourably with recent monographs on diesel exhaust.

As well as dealing with chemicals, noise and radiation are reviewed. I read the chapter on noise and found it useful and short. The emphasis is on the classic effects of noise and current concerns about effects on blood pressure, likelihood of myocardial infarction, and effects on children’s learning in noisy schools receive little attention. Sleep disturbance is mentioned but much more could be said of how this might be measured and of the comparative importance of mid-sleep waking and early morning waking.

Who, then, is this book for? Not for the beginner I think, but as a source of reference for the professional environmental toxicologist it is unequalled. Faults? A certain and understandable bias towards the United States perhaps but not much else that I can see. The book has been well proofed and is remarkably free from misprints. In conclusion then, an outstanding book that every environmental toxicologist should have.

Good value at £96.50.

R L MAYNARD


This is an exceptionally useful book with an odd title. The idea is that you can look up a problem—for example, poisoning by mercury—and read all you need to know about it in 5 minutes—really? Well, not quite perhaps, but almost. The authors have achieved their objective by designing a standard layout for each topic and sticking to it. Information is presented in columns: then to the page and divided up by clear subheadings.

The book is in four sections: the first “general approach” is only a few pages long; the second “patient presentations with toxicological causes”; the third “antidotes” and the fourth “chemical and biological agents”. The fourth section covers about 300 compounds or agents. In reviewing this book I looked up topics I thought I knew a good deal about and topics that I knew I didn’t know enough about. In both cases I was pleased. Take Gulf war syndrome or methaemoglobinemia, or multiple chemical sensitivity. On each a spread of two pages is provided—and you can, just, read the two pages in 5 minutes. The information provided is focused and clear—the reader is given clear information on basics, diagnosis, treatment, follow up, and pitfalls. Recommended reading is also provided. I looked up treatment for metal fume fever: beautifully clear, telling you what to do and also what not to do, listed in “not recommended therapies”. The section on individual chemicals and agents is equally good. Interesting topics—such as gila monster, marijuana, and cane snail are included as well as the better known chemical toxicants.

This is the best book I’ve seen for use in dealing with an enquiry over the telephone about a poisoning. Not as comprehensive, of course, as the books that simply list chemicals and provide a few details but wonderfully helpful in sorting out a patient management plan. At £69.95 and with 752 large pages this book is excellent value for money. It should be at the elbow of every occupational physician who is called upon to deal with poisoning and on the desk of every clinical toxicologist.

R L MAYNARD


The publishers of this 7 volume book have kindly provided me with volume 1. I have learned something of substances beginning A-B! For each compound information is provided on physical properties, occupational exposure standards, ecotoxicity, environmental fate, mammalian and avian toxicology, genotoxicity, and legislation. A section entitled “other comments” is appended, as is a useful list of references. Some entries are short—and not all these topics are covered for each. Take for example, picked at random, allyl chloroformate. This compound is not very toxic (LC50 (mouse)=2000 mg/m3), is corrosive, is classified as a toxic substance for transport purposes, is a respiratory irritant but I have no idea whether anybody has looked to see whether it is a carcinogen. We are also not told the uses of this chemical. Perhaps it is rare: the 12th edition of the Merck index does not list it at all! I then looked for amyl nitrite: not listed. I wondered whether drugs were included—yes, amylorbarbitone is included. Benzo(a)pyrene is much better treated: pages of useful data are provided.

So: this is the first volume of a reference text that is designed more for libraries than for individual purchase. At £1295.00 a set it is not cheap but free access to a web database version is provided with each paper copy. Useful? Yes, although as usual with encyclopaedias the thing you wanted to know may not be there!

R L MAYNARD
Prevalence and risk factors for latex allergy

NAESINEE CHAIEAR, IAIN FOULDS and P SHERWOOD BURGE

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