PBN as a possible bladder carcinogen

In their paper updating a previous investigation of the mortality of workers employed at a factory producing chemicals in North Wales, Sorahan, 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. In such areas, contaminated by β-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 study1 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 primary antioxidant was followed up from 1951 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). The withdrawal of BNA from production in 1949 was inevitable, but a large number of other antioxidants are still in use worldwide. The findings of his study need to be considered along with our own new findings2 in arriving at any overall evaluation. Our simplest interpretation of the new findings was that “PBN (or a chemical reagent of chemical intermediates) was 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 Veyes—namely that epidemiological findings relating to workers engaged in the manufacture of a given chemical may be quite different to those pertaining to workers engaged in other chemical. Clearly, large scale studies relating to both sets of circumstances should assist confident interpretation.

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1 Sorahan T, Hamilton L, Jackson JR. A further cohort study of workers employed at a factory manufacturing chemicals for the rubber industry, with special reference to the chemicals 2-mercaptobenzothiazole (MBT), online, phenyl-β-naphthylamine and o-toluidine. Occup Environ Med 2000;57:106–15.


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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 makes a major contribution to the exposure to benzene in some areas. Probably the burning of other fuels for heating will also contribute. Chilen are transported in cars, stay in kindergartens, schools, sports areas, shopping areas, etc., much of their days. Even studies at schools sampling shows a difference in 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 ± 1.9 µg/m³), there was almost no difference in the mean personal exposure of these children (3.4 v 4.5 µg/m³). Such misclassification of exposure leads to an underestimation of the relative risk.

The important findings of Harrison et al and other studies1 (see London Research Centre for further references) is that living in highly populated areas, with a lot of traffic, with high car density, means a higher risk of childhood leukaemia, which may be preventable. We think that as benzene is a known cause of non-lymphocytic leukaemia in adults, much more thorough studies in children before we can rule out that benzene is an important factor in childhood leukaemia.

So even if we disagree with Harrison et al about the importance of the risk, we agree that further studies are necessary. They should focus on different types of leukaemia and use much better precision in the estimates of benzene and other possible exposures.
corruption, and indeed would not be consistent with United Kingdom smoke control laws. The inventory of air pollutant emissions for the corruption 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 back ground 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.

Järnholm 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.

None of 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 Järnholm and Forsberg that this merits further investigation.

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**NOTICES**

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

**EDITOR**—The recent report by Smedley et al is useful in measuring the prevalence and risk factors for latex allergy within a United Kingdom environment, and providing an up to date review of this problem.

The paper highlights the high frequency of symptoms in healthcare staff but suggests a low frequency of confirmed type I latex allergy. Those who only read the abstract might be misled into considering that the frequency is much lower (two of 372 respondents).

The frequency among those tested with symptoms was 3% (one of 33) and one person without symptoms was positive on testing (4%; 1/26).

Within the Argyll and Clyde region health surveillance has been performed on staff working in areas with exposure to glutaraldehyde. Such staff also received gloves to protect them from blood and body fluids. A recent audit of the results of health surveillance over the past 5 years identified seven cases of type I latex allergy (confirmed by specific IgE radio allergosorbent test (RAST)) in a workforce of 226 nurses (3% prevalence). The frequency of reported skin symptoms was higher (6% at the last health surveillance) but other causes were also identified (such as rosacea, seborrheic eczema, irritant dermatitis, and type IV allergy to colophony, formaldehyde, and rubber accelerators).

The findings confirm a low frequency of type I latex allergy and support the view that highly intensive health surveillance is not justified. One of the seven healthcare workers identified noted an allergic reaction after eating a sandwich bought from the hospital canteen which had been handled by a member of the catering staff who was wearing latex gloves. Healthcare workers with type I latex allergy can be exposed to latex proteins away from their own work area by such actions or from the common use of powdered gloves in other areas. This emphasises the need for an organisational approach to this issue. Organisational action to reduce the incidence of this allergy should have priority including the use of non-powdered latex gloves where exposure to blood and body fluids is a risk for those without allergy, the provision of non-latex gloves for those identified with type I allergy and early assessment of those with symptoms related to glove use. Catering staff do not now use latex gloves in the hospital where the reaction reported here occurred.

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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.

Contact: Contemporary Forums Conference Management, 11900 Silvergate Drive, Dublin, CA 94568, USA. 001 925 828 7100, ext 0, www.clin tox.org

IEA European Regional Meeting. 24-26 August 2000. Lithuania.

Satellite Seminar, Future of Epidemiology II. 24 August 2000. Kaunas University of Medicine, Central Building, Mickevicius str 9, LT-3000 Kaunas, Lithuania.


Epidemiology is still the core discipline in preventive medicine despite recent and important achievements in biology and clinical medicine. This discipline plays a key part in public health and clinical research. This will
be true also in the next millennium. Epidemiologists have to consider how best to use the new tools provided by the biologists and how best to use methods and knowledge from demography, sociology, and philosophy.

The IEA European Regional Meeting in the year 2000 is an appropriate scene for reflection. Lithuania is an appropriate place for discussing our role in a rapidly changing Europe, which is so crucial for our common future.

The Organising Committee hereby invite you to participate at the Satellite Seminar and the Big Meeting.

Electronic registration form please find at http://www.info.kma.lt/EUROIEA2000, meeting secretariat email address: EUROIEA2000@KMA.LT

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 anesthetists. 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 530, 550 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, Fen, Cournard model has been reduced—this is perhaps disappointing. Some, although, 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 sections of earlier editions appealed, I suspect, more to anaesthetists than to physicians.

The book concludes 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 presaged by the chapter. For 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 the airways against free radical attack are complex and not clearly explained. 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, Fen, Cournard model has been reduced—this may disappoint some, although, 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 sections of earlier editions appealed, I suspect, more to anaesthetists than to physicians.

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 Siggarda-Anderson equation. The Pao2–Fio2 nomogram remains as does the invaluable Pao2–FiO2 nomogram (much photographed!).

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 catastrophes 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 rapidly 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 triad of doctorate degrees (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 write closely, and very clearly, prose to permeate and dissect multidimensional, 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 law are highlighted to 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 compensation, fraud and abuse, and the medicolegal case precedents, spawned by the law—form the subject of a third part. In a concluding part, on end of life considerations, Liang stolidly 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 suits 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 possibly 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 due to date, a relevancy 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

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LEO UZYCH
Evaluation in occupational health practice, 1st edition
Edited by: EVA MENCKEL, PETER WESTERHOLM.
ISBN: 0 7506 4303 X.

Evaluation of healthcare systems, with its significant use of qualitative data, has to date received less sympathy or 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 research questions. Calls for a greater awareness on 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 new 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 unnecessary 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 themes. Such approaches may not only be formal research but also use informed management decisions on the development and impact of occupational health services. In conclusion this book is an outstanding tool for revision or relearning immunology. Much has changed in recent years but this book will bring you rapidly up to date. At £14.95 this is essential immunology!

R. L. MAYNARD

Environmental toxicants: human exposures and their health effects
Edited by: MORTON LIPPMAN.

This is the second edition of Lippman'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 resolution 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, endomembrane baco 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 of the chapter was dealing with topics with which I am familiar was one of awe. The detail included is extensive, facts fall like snowflakes, and hardly a line seems to lack either the detail 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 focused 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 are 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 need 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 with diesel exhaust, and yes, he has maintained the standard: about 40 pages and on reaching the end the reader wonders whether he need 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.

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

The 5-minute toxicology consult

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 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 dictionary of substances and their effects

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, amylbarbitone 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!