CORRESPONDENCE

Exposure to asphalt or bitumen fume and renal disease

Editor,—The correspondence from Dittmer and Armitage1 provides further support for a causal association between exposure to various hydrocarbons and the development of renal disease. Since 1912, some case reports,1,2 case-control studies,3 and cross sectional4 studies together with animal experiments5 have provided compelling evidence for a causative role for hydrocarbon exposure in the development of both tubular and glomerular lesions.

We now report the case of a road worker exposed to asphalt and bitumen fumes who presented in 1990 at the age of 56 with nephrotic syndrome. He was then normotensive, had proteinuria with 24 hour urinary protein concentrations of 12.2 g, showed some clinical oedema, and his renal biopsy was consistent with a diagnosis of stage 2 membranous glomerulonephritis. Later that year he presented with an unexplained deterioration in renal function. This followed several weeks of abdominal pain, and he then had haematuria without pyuria, serum creatinine of 298 compared with his previously normal value of 85 µmol/l, and a marked deterioration in his renal biopsy with 20 glomerular profiles per section and tubulointerstitial scarring occupying 40% of the biopsy.

Before developing renal disease, the patient had been employed as a road worker for more than 10 years, during which time he was repeatedly exposed to intermittent but high concentrations of asphalt or bitumen fumes. Since the diagnosis of nephrotic syndrome due to membranous glomerulonephritis, the patient stopped being exposed to asphalt and bitumen fumes. Subsequent assessments of proteinuria have shown a reduction of up to 50% from 12 to 5 g/day. However, he currently is hypertensive with serum creatinine 170 µmol/l, urea 10.4 mmol/l, serum albumin 30 mmol/l, and 24 hour urinary excretion of protein 5.0 g.

Searches of the scientific literature in 1990 and subsequently have not found any specific references to exposure to asphalt or bitumen and renal disease. We therefore investigated the issue further by means of (a) detailed fume analyses, and (b) a study of the renal health of road workers exposed to asphalt or bitumen. It was clear from the fume analyses that exposures in this industry include a wide range of aromatic and aliphatic hydrocarbons. Time weighted average exposures ranged from 0.4 to 8.9 mg/m³ measured as total organic fume (not including inorganic particulates), but short term or peak fume exposures were as high as 300–900 mg/m³. During all his years exposed to these fumes, the patient had never been provided with or worn respiratory protective equipment.

The study of renal health included 92 people regularly exposed to asphalt or bitumen fumes as road workers, 38 hard rock quarry workers not occupationally exposed to hydrocarbons, and 43 office workers also not exposed to hydrocarbons. Each participant was given a questionnaire which included questions about occupational and recreational exposures and medical history including renal disease. Urine and blood samples were collected for urinary chemistry, blood biochemistry, and microscopic analyses. Any person with an abnormal finding on blood or urine analyses were tested and examined by a nephrologist to assess the presence or otherwise of renal disease.

The criteria which determined an abnormal test result were as follows: (a) persistently raised serum creatinine >120 µmol/l; (b) persistently raised serum urea >7.5 mmol/l; (c) persistent microscopic haematuria or pyuria; (d) 24 hour urinary protein >150 mg/ day; or (e) corrected creatinine clearance <90 ml/min.

The presence of renal disease was determined as presenting or idiopathic according to the following criteria. Pre-existing renal disease: (a) family history or history of renal disease; (b) abnormal renal ultrasound. Idiopathic renal disease: (a) no known cause for abnormalities; (b) abnormal creatinine, urea, and creatinine clearance; (c) abnormal proteinuria; or (d) abnormal urinalysis—haematuria or pyuria.

The findings of the study are summarised in tables 1–3.

We concluded from this study that: (a) workers regularly exposed to asphalt or bitumen fumes were far more likely to have evidence of early stage renal disease than those working in a quarry or office; (b) workers regularly exposed to asphalt or bitumen fumes were far more likely to have at least one abnormal renal function test than those working in a quarry or office; and (c) the renal dysfunction was non-specific, but the overall findings were consistent with previous findings—such as those from the similar study done by Yaqoob et al.1

We think that chronic glomerulonephritis and chronic tubulointerstitial nephritis are renal diseases which may result from exposure to hydrocarbons—such as those experienced from asphalt or bitumen fumes generated during road making.

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2 Anderson K. Acute nephritis due to turpentine absorbed by the skin. BMJ 1912;1:861.


Authors’ reply.—The report of Douglas and Carney of a further case of renal disease associated with hydrocarbon exposure, together with their cross sectional study of those with prolonged exposure to bitumen and asphalt further strengthens the case for an association between renal disease and hydrocarbon exposure. Yaqoob et al have also convincingly shown, that in particular, proteinuria may be associated with hydrocarbon exposure.1

This highlights the need for a careful occupational and social history to be taken at the time of presentation. This case also highlights the need for performing a renal biopsy in adults presenting with unexplained proteinuria. If interstitial nephritis is found then a short course of steroids may result in a dramatic improvement in renal function as we noted in the case of our patient exposed to

**p<0.01.

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**Table 1** Age and blood pressure

<table>
<thead>
<tr>
<th>No exposure</th>
<th>Office</th>
<th>Quarry</th>
<th>Exposure to asphalt or bitumen</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean)</td>
<td>39</td>
<td>32</td>
<td>35</td>
<td>36</td>
</tr>
<tr>
<td>People (n)</td>
<td>43</td>
<td>38</td>
<td>92</td>
<td>173</td>
</tr>
<tr>
<td>BP (mean systolic)</td>
<td>133</td>
<td>131</td>
<td>133</td>
<td>133</td>
</tr>
<tr>
<td>BP (mean diastolic)</td>
<td>86</td>
<td>83</td>
<td>83</td>
<td>84</td>
</tr>
</tbody>
</table>

**Table 2** Renal disease

<table>
<thead>
<tr>
<th>No exposure</th>
<th>Office</th>
<th>Quarry</th>
<th>Exposure to asphalt or bitumen</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of people</td>
<td>43</td>
<td>38</td>
<td>92</td>
<td>173</td>
</tr>
<tr>
<td>Pre-existing renal disease (n (%)) NS</td>
<td>4 (9.3)</td>
<td>2 (5.3)</td>
<td>1.1 (1.1)</td>
<td>7.4 (0.9)</td>
</tr>
<tr>
<td>Idiopathic renal disease (%)**</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>12 (13.0)</td>
<td>12 (6.9)</td>
</tr>
</tbody>
</table>

* *p<0.01.

**Table 3** Renal function

<table>
<thead>
<tr>
<th>No exposure</th>
<th>Office</th>
<th>Quarry</th>
<th>Exposure to asphalt or bitumen</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>People (n)</td>
<td>43</td>
<td>38</td>
<td>92</td>
<td>173</td>
</tr>
<tr>
<td>Haematuria</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>0</td>
<td>0</td>
<td>17</td>
<td>17</td>
</tr>
<tr>
<td>Raised creatinine</td>
<td>0</td>
<td>0</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>At least one abnormality (n (%))**</td>
<td>4 (9.3)</td>
<td>2 (5.3)</td>
<td>24 (26.1)</td>
<td>30 (17.3)</td>
</tr>
</tbody>
</table>

**p<0.01.
Cancer risk in the rubber industry: a review of recent epidemiological evidence

EDITOR,—Although the comprehensive review of the rubber industry reported by Kogevinas et al. only considers papers published after 1982, several of these studies relate to groups of workers from much earlier eras—for example, 1940 for the German study, 1946 for the British Rubber Manufacturers Association (BRMA) study, and Veys studies.1 Considering the findings of these earlier rubber worker studies along with studies of more recent groups of workers we are getting a picture of 80 years of cancer experience in the industry, which is not the same as the situation that exists today.

It should also be borne in mind that the very large cohort study—such as the 34 000 workers in the BRMA study—have a very much greater statistical power than those of the smaller studies, in which confounding factors and the role of chance are more difficult to evaluate. This does not seem to have been fully taken into account and indeed Kogevinas et al tell us that they have not “paid much attention to statistical significance”. This is disappointing as it is the omission of a full meta-analysis of the studies, which if it had been carried out, would have added considerable weight to their conclusions.

In general, the review would seem to endorse and reflect the evaluation by the International Agency for Research on Cancer (IARC) of the industry in the 1987 monograph, supplement 7, of a moderate increase in risk of cancer at several different organ sites which are not consistently found in similar studies carried out in other parts of the world. Evidence suggests that this may reflect alternative methods of handling and processing rubber and different sources of raw materials around the world.

The reviewers seem to give less endorsement to the IARC evaluation in 1982, monograph 28, that there was “sufficient evidence for a causal association” between work in the rubber industry and developing cancer and that the issues of genotoxicity are largely resolved. Although it is interesting to look at the worldwide experience of rubber workers, from the point of view of the United Kingdom industry, domestic findings are more relevant, given that they are based on the largest and most closely researched populations of rubber workers anywhere in the world. These studies include the Health and Safety Executive study (40 000 workers), the BRMA study1 (34 000 workers), and the Veys studies1 (14 000 workers) followed up for 40 years. The analysis of this domestic epidemiology enables us to conclude, with considerable confidence, that in the United Kingdom occupational leukaemia was never a factor and that the problems of bladder cancer were largely confined to the 1940s with the discontinued use of chemicals contaminated with β-naphthylamine. These studies also showed a small but nevertheless significant excess of stomach, lung, pharyngeal, and oesophageal cancers. With more detailed analysis, however, and consideration of confounding and socioeconomic factors, the occupational importance of these excesses seems to be less clear as time goes on. Geographical and confounding factors and a lack of a clear time-dose response also lessen the possibility of occupational causes.

Having expressed our confidence in the United Kingdom findings, I re-emphasise that they are largely based on results from an earlier generation of rubber workers and that their experience may not be the same as those currently employed in a modern day rubber factory.

So that we may investigate more recent experience, the BRMA initiated a further collaborative project with Birmingham University, to carry out a new study of its members’ employees. The collection of data for this study was completed last year and it includes nearly 10 000 male and female workers with at least 12 months of employment and who were first employed between 1982 and 1991. This study involves 42 rubber factories engaged in manufacturing the full range of rubber goods. This cohort study will look at both cancer incidence and mortality and make full use of all available occupational hygiene and exposure data.

Examination of the health experience generated by the study to date will take place later this year to see if there is sufficient information for a full analysis to be carried out or whether it would be appropriate to delay this until more data are available. Kogevinas et al have given an interesting and important overview of health hazards observed in rubber workers employed during the past 80 years and I agree with him that, more relevant, modern, and comprehensive epidemiological evidence is necessary if we are to obtain a true picture of the situation today.

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Although he concurs with the use of skin prick tests as an index of sensitisation, Kendrick expresses reservations about my evidence of causality in respect of chest symptoms from u-amylase. This is understandable if I relied solely on his condensation of an already condensed text. Although my report followed from a comprehensive ongoing investigation, I had hoped I had summarised sufficient information to make my point. His reservations seem to derive from the fact that papain has been handled in the workplace, and that some of those sensitised to u-amylase were also sensitised to papain. At this factory papain and u-amylase were handled in pure form, seldom, and at different times and places. The association between handling one or other material and the development of symptoms was clear cut, and because of the short period of handling, with intervals of at least a month between these periods, there was time for symptoms to regress between exposures. I had already validated a skin prick test for papain sensitivity, and was able to use the same test with those exposed to u-amylase, and a similar one for u-amylase. Positive prick test findings seemed to confirm the specificity and likely mechanism of the typically asthmatic symptoms from each enzyme.

Hendrick points to my objectionable doubt as to causality I would not have published the warning. Happily, subsequent reports, including the excellent one by Aitkin et al., of which Hendrick is a coauthor, which included inhalation challenge tests with fungal u-amylase, have endorsed my conclusions and added further knowledge.

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Occupational asthma due to amylase


Flindt MLH, Allergy to amylase and papain. Lancet 1979;i:1407–8.


Flindt MLH, Respiratory hazards from papain. Lancet 1978;i:430–43.


Health of children born to medical radiographers


Flindt MLH, Allergy to amylase and papain. Lancet 1979;i:1407–8.


Flindt MLH, Respiratory hazards from papain. Lancet 1978;i:430–43.

of epidemiological associations, and reliance on personal memory will not provide the detailed data which allow chromosomal abnormalities to be grouped in a meaningful way when exploring possible environmental influences. The study of Roman et al. illustrates the need to confirm diagnoses reported in questionnaires whenever possible, and to obtain any additional information that may assist in the scientific evaluation of epidemiological results.

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CORRECTION

Older workers in the construction industry: results of a routine health examination and a five year follow-up by

Also corresponding headlines in tables 2 and 3 (page 688) should read age adjusted hearing loss >30 dB (not hearing loss at 2, 3, and 4 kHz >105 dB) and diastolic blood pressure >95 mm Hg (not diastolic blood pressure >95 mm Hg).

The authors deeply regret these errors, which do not alter the conclusions of the paper. We kindly ask the reader to comply with these corrections when interpreting the data presented in tables 2 and 3.

BOOK REVIEWS


As indicated by the title, this book is the eighth in a series of proceedings on inhaled particles. These international symposia, held in 1960, 1965, 1970, 1975, 1980, 1985, 1991, and 1996 at various venues in the United Kingdom, were all sponsored by the British Occupational Hygiene Society (BOHS). Since the 1975 meeting, the proceedings were also issued simultaneously as special issues of the BOHS journal *Annals of Occupational Hygiene*. These symposia and their proceedings have served as landmarks documenting the state of the art in knowledge and techniques concerning human exposures to airborne particles, their deposition and clearance within the respiratory tract, and their health effects.

The broadening depth and scope of the symposia to now include radioactive, outdoor and indoor particulate matter have put a great strain on the organisers and especially on the editors. Additional reasons resulted from the fact that the two previous proceedings did not appear until three years after the meetings. Thus, the publication of this volume only one year after the symposium is a significant accomplishment and a tribute to the dedication of its new editors. A price for this accomplishment was the restriction of the 127 papers to four to six pages each, and the elimination of external peer reviews. The reviews and editing were done by the editors alone. Also, for the first time, there were no abstracts included in the papers and the questions from the audience, and authors’ responses, that were notable features of the earlier volumes, were not included.

The quality of the papers and editing remain at a high level, and this volume should be a valuable addition to the bookshelf of all scientists, health professionals, and public health authorities who are seriously interested in the health effects of airborne particles. It must be noted that the price is high enough to limit its readership.

MORTON LIPPMANN


This book is aimed at managers and others who wish to gain an understanding of the principles of occupational safety and health in the United Kingdom. It is published by the Institution of Occupational Safety and Health (IOSH) and it is the recommended text for their safety appreciation course, *Managing Safety*.

The text is divided into four sections: safety technology, occupational health and hygiene, safety management techniques, and law. There are 68 short chapters which cover the essential factual information required by someone responsible for managing health and safety. Each chapter includes several self-assessment questions and a bullet point sum-


Airborne fibre concentrations have been evaluated by the membrane filter method for over 30 years. The original method, which was developed for use in asbestos factories, has been adapted for use with many different types of fibre in both occupational and non-occupational situations. By the 1970s it was clear that there were substantial differences between laboratories when evaluating the same samples. Much of this could be attributed to variations in the detailed methodology and this started the quest to devise a ‘standardised’ version of the membrane filter method. This book is the latest attempt to standardise the method. On this occasion to harmonise methods used for analysis of asbestos—for example, the European Reference Method (ERM) used throughout the European Union, with the previously published World Health Organisation method for man made mineral fibres (rockwool and glass wool). The new method is applicable to all fibre types, both organic and inorganic.

The method specification is contained within 17 statements which are supplemented by more detailed descriptions. It contains details of everything required from the type of filters to be used to the characteristics of the fibres to be examined. The accuracy, precision, and lower limit of measurement are also provided.

This is a specialist book which will be of limited interest to those not directly involved with measurement of exposure to fibres. However, it is clearly the authors’ intentions to influence the appropriate national authorities to incorporate this version of the method into their legislation. The accuracy, precision, and lower limit of measurement are also provided.

John W Cherry
This book, one of a series of reviews produced by the World Health Organisation in the late 1980s and early 1990s. The second and larger part provides a series of "country profiles" for each of the member states, typically of one or two pages. These list the latest available information on demographic and general health indicators, tobacco production, trade and industry, tobacco consumption, and smoking prevalence by age and sex, and national tobacco control policies and programmes.

Designed as a reference text, this is not a book to be read from cover to cover. Its strength is the near comprehensive coverage of national statistics on tobacco production and use, which are usefully summarised in part one. These may suffice for readers with an epidemiological background, among whom the adverse health effects of smoking are taken for granted. For a more general readership, however, a notable weakness of this book is the paucity of information on the health consequences of tobacco use. The relevant chapter in the first part runs to only five pages, including only four tables, and is supported by only two references, one of which is yet to be published. However, a new edition has been published (although it could have been released in 1994) as a revised edition of this work (Lancet).

The discussion of health effects is entirely focused on mortality, mainly from broad groups of causes, such as total mortality and cancer death. In marked contrast there is no mention of the disability and loss of productivity related to cardiovascular and respiratory diseases, nor is the evidence on environmental tobacco smoke. Where the health effects are assessed for individual countries in part two, figures are provided mainly for developed countries and relate principally to estimates of tobacco related deaths and ill health.

This volume provides a powerful reminder, if such is needed, that tobacco use is a global phenomenon, with one third of adults now smoking, and two thirds of these residing in developing countries. The premise upon which this report is based is that widespread tobacco consumption and public health are mutually incompatible, but readers seeking a comprehensive collation and consideration of the epidemiological evidence linking smoking and health will be disappointed. It is apparent that the WHO intends these data to be a baseline for a global programme of surveillance of smoking habits and tobacco control policies. It is well to remember that the volume compiles a comprehensive account of the effects of tobacco use on health in many countries, particularly in the developing world. A valuable addition to future editions would be evidence from countries with well developed tobacco control policies of the extent to which lowering smoking prevalence reduces death and disability. This might encourage much needed policy initiatives in many other countries where tobacco control has yet to achieve prominence on the public health agenda.

DAVID P STRACHAN


This monograph gives full details of a study conducted to test the Gardner hypothesis—namely, that childhood leukaemia and non-Hodgkin's lymphoma result from the father's...
exposures to ionising irradiation before conception. This study has also been published as a paper in the *BMJ*, but this volume goes into far greater details than is available elsewhere. This is very much a book for the concerned specialist reader who wants the technical background to the *BMJ* article.

This study is essentially a record linkage exercise. The exposed fathers (and mothers) were defined as having records with the National Registry for Radiation Workers (NRRW) held by the NRPB. This is a database of over 120,000 people and it was linked with the national register of childhood tumours, a database of over 50,000 children with all types of cancers. Two other data sources on childhood cancers were also included.

For the three sources of data on childhood tumours, controls were found in various ways to ascertain if these children had a father in the NRRW. The parental estimated doses were created from the NRRW. In all a total of 200 fathers and mothers were linked to children with cancer. Eighty two children with leukaemia or lymphoma were linked to fathers’ records at the NRRW, as were 79 control fathers. The corresponding numbers for mothers were 15 and three.

The cases in the original Gardner paper were excluded and the results for fathers showed that case fathers had a 1.77 significant excess risk over control fathers for having a child with leukaemia or lymphoma. However, the risk was associated with the lowest dosages and there were no dose responses in any of the comparisons. In this sense the Gardner hypothesis is refuted!

Furthermore, the risk in mothers was also significantly and greater in magnitude than the fathers. However, the small numbers make this result unreliable and difficult to use to extrapolate risk.

The explanation of the association found in these NRRW members exposed to low doses is not known. It could be chance, it could also be due to misuse of film badges by those in high risk industries. This explanation is unlikely in that the cancers were distributed widely across industries in the United Kingdom and were not confined, by any means, to the nuclear reprocessing or related industries. It may be due to other exposures associated with the wider radiation industries where many other hazardous substances exist as well as ionising irradiation. Finally, it could be some other, more subtle aspect, of wearing a film badge. The authors speculate that this might be associated with the mobility of the parents, thereby linking these results with the Kinlen hypothesis which is based on ideas of infectivity associated with population mixing. They do not produce evidence to suggest that film badge wearers are more mobile than other professions but the differences in behaviour may be more complex.

Further light might be shed on this association when the nuclear industry family study (NIFS) is analysed shortly. This study will answer some criticisms of the present study. For example, it is known that there are differences in behaviour of people within the nuclear industry and those outside it. The NIFS uses internal comparisons and so such differences can be accounted for.

Despite the lack of any explanation of this observation attention is now bound to be focused on other preconceptional and periconceptual exposures in both sexes and their possible links with childhood malignancies.

R A CARTWRIGHT