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Table 3 Kaplan-Meier log rank tests of homogeneity of survival rates of men in the high exposure category for >2 y compared with all other men

Cause of death	χ^2	P value
Lung cancer	0·04	0·85
Cancers of the digestive system	1·36	0·24
All cancer	0·10	0·75
All causes	3·21	0·07

the highest exposure did not seem to have significantly different mortalities for lung cancer, cancers of the digestive system, and all causes, compared with all the other men in the study (table 3).

Discussion

The only categories in which the number of observed deaths exceeded expected deaths (but not significantly) are lung cancer in men in the high exposure category for six months or more (three observed *v* 2·43 expected) and cancers of the digestive system in men in the low or moderate exposure category (eight observed *v* 6·54 expected). Two of the three deaths from lung cancer in men in the high exposure category were in men exposed in that category for less than two years. Only one case, however, occurred in men exposed in the high exposure category for more than two years *v* 2·11 expected. No cancers of the digestive system occurred in men with exposure in the high exposure category. No deaths occurred from nasal cancer.

A similar study in France of 140 men working at a plant producing hydrazine since 1962 reached similar conclusions (personal communication: Cordier S, Grand C, Contassot J-C). No significant excess in incidence of cancer was observed in the cohort of workers in comparison with the numbers expected from local cancer incidence. As in our study, however, an excess of digestive cancers was found in the low exposure group (three cases observed *v* 0·52 expected; P = 0·02). A significant excess of head and neck cancers (ICD-8 140-9) in the high exposure category was also found in the French study (two cases observed *v* 0·27 expected; P = 0·03), but no death from these causes was found in our study (0·49 expected). No excess of respiratory cancers was observed in the French study (we found one case *v* 1·29 expected).

Conclusions

The numbers of men exposed to hydrazine in both this and the French study were small. The results obtained are encouraging in that no obvious hazard from lung cancer or any other disease has appeared up to 46 years later. The study can confidently exclude a relative risk of lung cancer of about 3·5 or more, but the power of the study is too limited to exclude lower relative risks.

We thank Dr J Bonsall, former medical officer at FBC Limited, Hauxton, Cambridge, UK, for all his work on the study. We also thank National Aeronautics and Space Administration, Houston, Texas, for financial support for this project.

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discomfort. Whether or not these effects are precursors of musculoskeletal disorders is unclear, and not yet proved.

A research area indicated by this study is the development of finer measures (of greater generality, capacity, and sensitivity) for dimensions of exposure considered important in the scientific literature where there is disagreement or haziness of meaning. The term "postural constraint" is a case in point; ergonomists would generally agree that being unable to adopt a variety of postures is undesirable, but how to quantify this lack of flexibility is less clear. Measures of the frequency of transitions between sitting and standing have been used to describe constraint, but are not very helpful for the many industrial jobs in which workers have to be sitting or standing all of the time. Another problematic dimension of exposure is force, the use of a psychophysical rating scale allows for the measurement of whole body force, but regionally specific forces, relevant in surveys that include disorders of the hands and wrists, are more difficult to include in a simple low technology model. Lastly, the development of an appropriate measure of outcome and its link to work related musculoskeletal disorders is required; self reported pain promises the appropriate outcome measure that is required, but the range of disorders need to have better defined nodes and endpoints for further study.

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CORRESPONDENCE

Differences in the effects of two hexachlorophenols on superoxide generation by polymorphonuclear leucocytes stimulated by N-formyl-methionyl-leucyl-phenylalanine and phorbol myristate acetate

Editor—Recently Iwata *et al* presented a paper on the effects of hexachlorobiphenyls on production of the superoxide anion stimulated by agonists in polymorphonuclear leukocytes. Bearing in mind what is known about the production of the superoxide anion in this system, some additional points can be made.

The production of superoxide anion by phagocytes is stimulated by activation of the phospholipase C (PLC) to protein kinase C (PKC) signalling pathway. In this pathway, an agonist, such as N-formyl-methionyl-leucyl-phenylalanine (FMLP), acts through a receptor to activate PLC. The PLC cleaves phosphatidyl inositol (phosphatidyl inositol turnover) and results in a transient increase in the concentration of diacylglycerol (DAG). The DAG activates the PKC, which in turn phosphorylates a membrane bound NADPH oxidase that reduces molecular oxygen to superoxide anion. The DAG is removed by DAG kinase or DAG lipase. This removes the stimulus for PKC activation and so ends oxygen reduction. Thus, production of superoxide anion is a transient effect. The maximum rate of production of superoxide anion occurs in one minute followed by a decline to a lower rate. The phorbol esters, such as phorbol myristate acetate (PMA), are direct activators of superoxide production that is stimulated by PKC and PMA. The reaction is not self limiting.[1 2]

In the study of Iwata *et al*, 2,3,6,2′,3′,6′-hexachlorobiphenyl (2,3,6-HCB) does not seem to have any effect on the maximum rate of production of the superoxide anion stimulated by FMLP. This suggests that 2,3,6-HCB does not increase the number of FMLP receptors, as Iwata *et al* suggested in their discussion. An increase in the number of receptors might result in greater production of DAG that results in a higher maximum rate of production of superoxide anion. On the other hand, 2,3,6-HCB does seem to significantly alter the kinetics of the production of superoxide anion, which results in a prolonged period of maximum production of superoxide anion. As production of the superoxide anion stimulated by PMA was not affected by 2,3,6-HCB, the 2,3,6-HCB probably affects production of the superoxide anion pathway before PKC. This suggests that 2,3,6-HCB may inhibit the breakdown of DAG by inhibition of DAG kinase or DAG lipase, thus prolonging the time course of production of superoxide anion. The inhibition of DAG degradation could also explain their findings that production of the superoxide anion occurs after addition of 2,3,6-HCB in the absence of FMLP. Prolonged inhibition of the mechanisms of DAG removal may result in the build up of DAG that leads to activation of PKC and production of the superoxide anion. Alternatively, 2,3,6-HCB may prolong the activation of PLC by FMLP, which could also result in a sustained rise of DAG concentrations. As the PLC to PKC signalling pathway is ubiquitous in the body, disruption of this pathway could have serious effects on the body's homeostasis.

The results of the 3,4,5,3′,4′,5′-hexachlorobiphenyl (3,4,5-HCB) indicate that it has a different effect on phagocytic cells. Production of superoxide anion stimulated by both PMA and FMLP was inhibited by 3,4,5-HCB. This suggests that 3,4,5-HCB directly inhibits PKC or the NADPH oxidase. It is not possible to distinguish between these potential effects on the available data. Also, one cannot determine whether 3,4,5-HCB has any effect on the signalling pathway before PKC. As noted above, PKC is an important enzyme in the cell signalling pathway and any compound that affects the activity of PKC could be expected to have a profound effect on the body's homeostasis.

In conclusion, Iwata *et al* have presented evidence that 2,3,6-HCB and 3,4,5-HCB have the potential to affect an important cell signalling pathway, the PLC to PKC pathway. It is worth bearing in mind that activation of this pathway is potentially very important in the inflammatory response beyond production of the oxygen radical. For instance, activation of this pathway in macrophages results in release of interleukin I.[3] The authors are to be complemented on their interesting work and their traces of the dynamic production of superoxide anion *v* time, which offer more information than static data of production of superoxide anion *v* unit time. Additional experimental work to examine the effect of these HCBs on turnover of phosphatidyl inositol and DAG concentrations as well as on the pattern of phosphorylation of PKC stimulated by FMLP would be useful in further characterising the effects of these compounds.

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Coal mining, emphysema and compensation revisited

Editor—Wikeley's response to my comments in regard to compensation in coal miners who develop emphysema is a trifle too disingenuous. I concede that I may have overlooked the exact date the report was sent; however, I wrote that it was "perhaps coincidental", not that the timing of the IIAC was deliberately contrived so that the Secretary received the report in November 1993. The report was sent to the Secretary of State in August 1992—August 25th to be precise—but may well have not been received until September, and was not published until November 1992. Having some familiarity with bureaucratic delays, I would not be surprised if the report and its contents were not discussed by the Civil Service hierarchy and Cabinet until late October or November 1992. By that time the Government had recognised its folly and with instant opportunism decided to accept the IIAC report, regardless of its validity, as a means of partially redressing the hardship inflicted by closing down most of the coal mines. Moreover, had Wikeley read my text with an open mind, he would perhaps have noted that my barbs were in the main directed at the Government as by rapidly accepting the IIAC report they created a meretricious impression of concern.

Finally, Wikeley would do well to remember that vituperation is no form of argument and that the higher forms of life—does this term include lawyers and himself—sometimes make errors. Perhaps his disdain for journalists is related to their penchant for tracking down and revealing misbehaviour in the legal profession.

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NOTICES

National Radiological Protection Board (NRPB)

Dr John Harrison, who was the Head of the Defence Radiological Protection Service, joined the National Radiological Protection Board (NRPB), Chilton, Oxon as the Assistant Director Medical on 3 October 1994. It is anticipated that a new Medical Head of Department will be in post by April 1995. The new division will act as the focal point within the NRPB for medical matters and have responsibility for the research and support roles of the Epidemiology and Medical Dosimetry Groups. It is intended that the NRPB will provide the Department of Health, other Government Departments and all health professions engaged in radiation practices with authoritative medical advice on the full spectrum of occupational and public health issues concerning ionising and non-ionising radiation. To achieve this the division will provide the medical secretariat to the existing NRPB Advisory Committee on Non-Ionising Radiation chaired by Sir Richard Doll. The old National Registry for Radiation Workers Advisory Committee on the medical aspects of ionising radiation and the division will provide the secretariat for this committee. The new medical staff will have academic and clinical attachments with university departments and it is intended that close links be forged with the medical schools, medical postgraduate deans, the Royal Colleges, faculties, and learned societies to establish the most cost effective means of enhancing radiation protection, knowledge, and practices. The need to establish specific training for medical and emergency services personnel to deal with radiation incidents or emergencies will be explored.

XIVth World Congress on Occupational Safety and Health, 22–26 April 1996, Madrid, Spain

The organisers of the congress are the Spanish Ministry of Labour and Social Security, through the National Institute for Occupational Safety and Health (INSHT), the International Labour Office (ILO), Geneva, and the International Social Security Association (ISSA), Geneva.

The XIVth World Congress, to be held in Madrid, aims to be an open forum for all people involved in risk prevention at work, safety and health safety specialists, occupational health physicians, labour inspectors, people directly concerned with safety and health at work, including entrepreneurs and managers in enterprises, trade union representatives, manufacturers and importers, as well as heads of public administration and social security administrators.

The main focus of this congress will be on the consequences for occupational safety and health of processes of international and regional integration—for example EU, NAFTA—and of the global spread of economic relations, on an in depth analysis of chemical risks and on new proposals for cooperation and participation within enterprises. Other specific issues will also be dealt with, such as training and information, control of working conditions or new responsibilities. Special emphasis will be placed on small and medium sized enterprises and sectors facing specific problems with regard to safety and health at work, such as the construction sector and agriculture.

Also, as part of this congress, the international section "Electricity" of the ISSA will be organising the 3rd international film and video festival on occupational safety and health.

For further information, please contact: Secretaría del Congresso, Instituto Nacional de Seguridad e Higiene en el Trabajo, Calle de Torrelaguna, 73E-28027 Madrid-Spain. Telephone +34-1-404 57 36 FAX +34-1-326 78 55

XIIth International Symposium on Night and Shift work, 13–18 June 1995, Foxwoods Resort and Casino, Ledyard, Connecticut, USA.

The symposium is sponsored by: Mashantucket Pequot Tribe, Foxwoods Resort and Casino, International Commission on Occupational Health, University of Connecticut Graduate Program in Industrial and Organisational Psychology.

The Foxwoods Resort and Casino in Connecticut will be the site of the 12th International Symposium, June 13–18, 1995. This will be the first time in history that the symposium is held in the United States. By design, this meeting will follow many of the traditions of these symposia. The meeting will be held in a remote area. Participants will be selected to assure a good international mix of disciplines, ages, and experiences. The number of participants will be limited to assure easy access and promote interaction between participants. All presentations will be in English. Papers presented at the symposia will be published in a dedicated issue of a referred journal.

For further information contact: Professor Donald I Tepas, Department of Psychology, University of Connecticut, 406 Babbidge Road, Box U-20, Storrs, Connecticut 06269-1020. Fax: 203-486-2760.

Thomas L Petty Aspen Lung Conference, 38th Annual Meeting. Environmental lung disease: exposures and mechanisms. Aspen, Colorado. 7–10 June 1995.

We shall explore the common ground shared by researchers who study the basic mechanisms of occupational and environmental lung disease and who study the impact of environmental exposure on human populations. Topics will include: cellular, molecular, immunological, and genetic mechanisms involved in the response to environmental and occupational toxicants; the clinical and epidemiological relation of inhalational exposure to lung diseases of the airway and interstitium, including asthma, fibrosis, granulomatosis, and malignancy. The abstract deadline is 1 February 1995.

For abstract forms or more information, contact: Dr Lee S Newman, Box C272, University of Colorado Health Sciences Center, 4200 E. 9th Avenue, Denver, CO 80262. Telephone: (303) 270–7767; or FAX: (303) 270–5632.

Third International Symposium on Cutaneous Fungal, Bacterial, and Viral Infection and Therapy. 14–17 September 1995, Hyatt Regency, San Francisco, California.

This third international symposium explores the rapidly changing advances in diagnosis and therapy for cutaneous infections. Emphasis will be placed on molecular biology and the risk-benefit analysis of diagnostics and treatment.

The symposium is jointly chaired by Professors Raza Aly, Karl R Beutner, and Howard I Maibach from the Departments of Dermatology and Microbiology/Immunology, University of California School of Medicine, San Francisco, which is accredited by the Accreditation Council for Continuing Medical Education. This program will meet the criteria for category 1 credit.

Major topics to be covered include:

- Dermatophytoses-dermatomycoses
- Opportunistic infections in AIDS and immunocompromised patients
- Bacterial cutaneous infections
- Viral cutaneous infections
- Antimicrobial agents

For further information, please write or call the Office of Continuing Medical Education, Room MCB-630, University of California, San Francisco, California 94143–0742. Telephone: (415) 476–4251.