Prostatic cancer and radionuclides

Evidence implicates zinc-65

EDITOR,—In their paper on prostatic cancer in employees of the United Kingdom Atomic Energy Authority, Cleone Rooney and colleagues raise the possibility of localisation of zinc-65 in the prostate being an aetiological factor but state that "there are no reliable data on ^{65}Zn uptake by the human prostate."[1] Prout *et al* showed in 1959 that ^{65}Zn localises avidly in the prostate in human males, and especially in benign adenomas.[2] In 1956 Daniel *et al* showed that the ratio of the ^{65}Zn concentration in normal prostates to that in blood was over 2·5:1; one patient had a ratio of 27:1.[3] The consensus of both groups was that neoplastic prostates concentrated less zinc. The uptake of zinc by the human prostate is so high that it is technically possible to image the prostate with ^{69m}Zn.[4,5] (Unfortunately, there are no isotopes of zinc suitable for routine imaging, so this approach has not found a place in routine nuclear medicine.)

This avid uptake of zinc by the prostate must increase the probability of ^{65}Zn being a relevant factor in carcinogenesis in this population.

ANDREW HILSON

Department of Nuclear Medicine,
Royal Free Hospital,
London NW3 2QG

1 Rooney C, Beral V, Maconochie N, Fraser P, Davies G. Case-control study of prostatic cancer in employees of the United Kingdom Atomic Energy Authority. *BMJ* 1993;307:1391-7. (27 November.)
2 Prout GR Jr, Sierp M, Whitmore WF. Radioactive zinc in the prostate. Some factors influencing concentrations in dogs and men. *JAMA* 1959;169:1703-10.
3 Daniel O, Hadda F, Prout G, Whitmore WF. Some observation on the distribution of radioactive zinc in prostatic and other human tissues. *Br J Urol* 1956;28:271-8.
4 First human prostate scans reported. *JAMA* 1967;200:19-20.
5 Gold FM, Lorber SA. Radioisotope ^{69m}Zn chloride prostate gland scan I: ^{69m}Zn organ distribution studies and gamma-camera scan in canine subjects. *Invest Urol* 1970;8:231-8.

Excess of other cancers in Wales

EDITOR,—As Cleone Rooney and colleagues have shown an increased risk of prostatic cancer in men exposed to certain internally incorporated nuclides, including strontium-90, caesium-137, and caesium-134,[1] increased incidence of the disease might be expected in those countries that experienced fallout of fission products from atmospheric testing. One place where such a comparison can be made is Wales: contamination related to rainfall in Wales was more than twice that in England in 1958-65.[2]

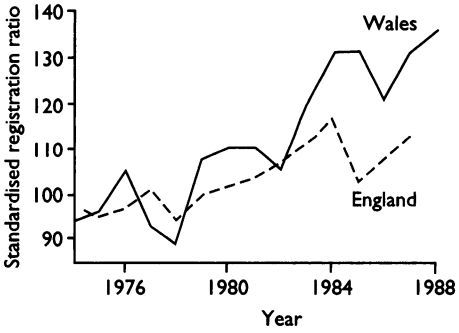
The figure compares standardised registration ratios for prostatic cancer obtained from the Office of Population Censuses and Surveys and Welsh cancer registries based on the combined rates for 1979. There is a clear increase in the differential and total incidence of the disease in line with the differences in contamination 20 years earlier.[3]

Rooney and colleagues' study may be pivotal in highlighting the fact that certain internally decaying nuclides may enhance the risk. The increase in prostatic cancer in Wales is only one aspect of a general and unexplained increase in cancer in Wales between 1975 and 1987 (the last year for which data are available).

One illuminating example is the incidence of

Advice to authors

Priority will be given to letters that are less than 400 words long and are typed with double spacing. All authors should sign the letter. Please enclose a stamped addressed envelope for acknowledgment.



Standardised registration ratios for prostatic cancer (ICD9 code 185) based on combined rates for England and Wales for 1979

bone cancer (*International Classification of Diseases* (ninth revision) code 170). This remained the same in the two countries between 1962 and 1975, when it began to increase in Wales. In 1984 the incidence in Wales peaked at 350% of that in England, which remained constant at about 1/100 000.[3] Though the American Committee on the Biological Effects of Ionizing Radiations does not accept that the prostate is radiosensitive and might have difficulty in accommodating the findings of Rooney and colleagues, it accepts a causal link between ^{90}Sr and bone cancer, though not at the low doses involved reported by Rooney and colleagues.[4] With the help of the British National Radiological Protection Board, and using published data on intake of ^{90}Sr,[2] Green Audit (Wales) has calculated that the 10 year dose to the bone surfaces of people in Wales during 1958-65 was 0·75 mSv.

On the basis of the currently accepted risk factors for radiogenic bone cancer.[4] the predicted number of fatal cancers resulting from this dose in the population of Wales (three million) is less than 1·5 for all time. If it is assumed that the excess incidence is equal to the incidence in Wales minus that in England for each year, then that yields some 425 excess bone cancers in Wales for the period 1979-87. If these cancers were caused by ^{90}Sr then there must be an error in the perception of this hazard of some 500 times.[5] A similar enhancement of effect is needed to explain Rooney and colleagues' findings.

Algorithms of risk derive mainly from data on short term external irradiation.[4] In the Hiroshima series, irradiated and control groups were both exposed to equal internal contamination and hazards from this source would have been missed.

Comparison of rates of cancer in Wales and England since the 1960s raises important questions about the radiation from internal isotopes, and such questions must surely also follow Rooney and colleagues' work.

I thank John Harrison of the National Radiological Protection Board for help with calculations of doses and risks.

CHRIS BUSBY

Green Audit (Wales),
Wales Green Party,
Aberystwyth,
Dyfed SY23 1JJ

1 Rooney C, Heral V, Maconochie N, Fraser P, Davies C. Case-control study of prostatic cancer in employees of the United Kingdom Atomic Energy Authority. *BMJ* 1993;307:1391-7. (27 November.)
2 Letcombe Radiation Laboratory, Agricultural Research Council. *Annual reports.* London: HMSO, 1958-72.
3 Office of Population Censuses and Surveys. *Cancer statistics registrations 1971-87.* London: HMSO, 1979-93. (Series MB1.)
4 Committee on the Biological Effects of Ionizing Radiations. *Health effects of low levels of ionizing radiations: BEIR V.* Washington, DC: National Academy Press, 1990.
5 Busby C. *Radiation and cancer in Wales.* Aberystwyth: Green Audit (Wales), 1994.

Cancer risk has no effect on mortality

EDITOR,—Cleone Rooney and colleagues have shown a raised risk of prostatic cancer in a particular subset of employees of AEA Technology (the trading name of the United Kingdom Atomic Energy Authority).[1] We accept their conclusions but believe that two additional points are important in interpreting the study.

Firsty, although the risks of prostatic cancer are high in workers exposed to the radionuclides tritium, chromium-51, iron-59, cobalt-60, and zinc-65, particularly in those working with heavy water reactors, the general mortality of these workers is good. The table presents standardised mortality ratios for subgroups of the workforce of

Standardised mortality ratios (observed/expected deaths) for AEA Technology's workforce†

	Cause of death (ICD codes (9th revision)		
	All causes (000-999)	Malignant neoplasms (140-209)	Prostatic cancer (185)
All employees‡	78** (6881/8861·0)	79**(1897/2387·8)	90 (104/115·8)
Radiation workers:			
All	76** (3786/4951·8)	75** (1001/1326·0)	89 (64/72·0)
Monitored for tritium	66** (203/309·4)	70* (62/88·9)	253* (11/4·3)
Monitored for other intakes§	77* (963/1257·3)	80** (282/351·3)	141 (26/18·5)
Working with heavy water reactor‖	65** (246/379·4)	63* (67/105·6)	141 (8/5·7)
At Winfrith	70** (460/656·7)	78* (143/184·0)	201* (19/9·4)
Who had worked with steam generating heavy water reactor at Winfrith	63** (53/84·4)	90 (22/24·6)	405* (5/1·2)

†Mortality is to the end of 1990, the last full year for which data are available. The underlying cause mortality stratified by age, sex, and calendar year is compared with that in the population of England and Wales: significance of difference from 100: *P < 0·05, **P < 0·001.
‡This category of employees is the cohort defined in Fraser *et al*'s study,[2] the other categories being subgroups of that cohort.
§Radiation workers monitored for nuclides other than tritium and plutonium.
‖Radiation workers identified from dose records as ever having worked with the heavy water reactors at Harwell or the steam generating heavy water reactor at Winfrith.

AEA Technology chosen to be as close as possible to those identified in the case-control study as being at high risk of prostatic cancer. It shows that, while increased mortality from prostatic cancer is detectable in subgroups related to the case-control study, the all cause mortality and all neoplasm mortality in these groups are no different from those in the generality of employees, and most are significantly lower than the national average. The results of the case-control study cannot, therefore, be interpreted as showing an increased occupational risk overall. Rather it shows a significantly increased risk for one disease which is not sufficient to detract from a considerable "healthy worker" effect when all mortality is considered.

Secondly, we have examined the dosimetric aspects of exposure to the radionuclides associated with an increased risk of prostatic cancer in the case-control study, especially zinc-65, the putative carcinogen that attracts most speculation from Rooney and colleagues. When account is taken of the enhanced concentration of zinc-65 in the prostate, the increased radiobiological effectiveness of Auger electrons, the incorporation of these radionuclides into DNA, and practical limits on employees' intake of these radionuclides, radiation doses to the prostate from conceivable levels of contamination with zinc-65 are too low by a factor of about 50—and probably by more than 1000—to account for the observed excess of cases of prostatic cancer, assuming internationally accepted models of radiation risk. This implies that the radionuclides are acting as a surrogate for some other agent. Details of our dosimetric calculations will be published elsewhere.

W D ATKINSON
M MARSHALL
B O WADE

Corporate Safety Directorate,
AEA Technology,
364 Harwell,
Didcot,
Oxfordshire OX11 0RA

1 Rooney C, Beral V, Maconochie N, Fraser P, Davies G. Case-control study of prostatic cancer in United Kingdom Atomic Energy Authority employees. *BMJ* 1993;307:1391-7.
2 Fraser P, Carpenter L, Maconochie N, Higgins C, Booth M, Beral V. Cancer mortality and morbidity in employees of the United Kingdom Atomic Energy Authority, 1946-86. *Br J Cancer* 1993;67:615-24.

Repetitive strain injury

Examine working practices

EDITOR,—The subtitle of Peter Brooks's editorial on repetitive strain injury ("Does not exist as a separate medical condition"), if not the editorial itself, risks seriously misleading the medical profession to the detriment of people doing manual work.[1] The subtitle will reinforce the prejudices of those doctors who believe that all people who attribute their ill health to their work are malingerers or potential litigants. The editorial does, however, hint at a more positive approach to preventing the panoply of muscular aches and pains that occur in working people and that, if not managed appropriately, may lead to anxiety and more chronic disablement. This approach stems from listening to the patient's views on causation and investigating the relevant work practices.

Regretably, investigation of work practices, which is essential, is beyond the competence of most doctors, who are unfamiliar with the methods taught to occupational physicians. It is therefore quite usual for workers such as musicians, laundry assistants, or hospital cleaners to develop forearm or wrist pain that is exacerbated by their continuing the tasks; to be given inappropriate treatment by a doctor or a series of doctors; and to receive conflicting prognoses from doctors, workmates, and union officials without anyone looking at the job and giving advice on its modification. Ultimately the patients will meet an orthopaedic surgeon who may well believe that the syndrome "does not exist as a separate medical condition" and alienation from the medical profession or even litigation follows.

The doctor has an important role in preventing such problems arising, and the key to this is an examination of the work done. When doctors suspect muscular syndromes related to work they should consider consulting a local occupational physician or employment medical adviser, who is probably experienced in managing such conditions. These conditions do exist and are usually quite easily managed if caught early. Moreover, the presence of symptoms in one patient is often a pointer to similar problems in several other people from the same workplace and leads to opportunities for inexpensive modifications that in turn result in reduced sickness absence and improved morale in the organisation. Doctors can have a positive role when dealing with such conditions.

ANTHONY SEATON

Environmental and Occupational Medicine,
University of Aberdeen,
Aberdeen AB9 2ZD

1 Brooks P. Repetitive strain injury. *BMJ* 1993;307:1298. (20 November.)

A real occupational illness . . .

EDITOR,—Though Peter Brooks is well known in Australia for his non-conformist views concerning repetitive strain injury (a term long discarded among medical practitioners in Australia in favour of the occupational overuse syndrome), this seems a poor reason for asking him to write an editorial in the *BMJ*.[1] I would have thought that the few, one sided references in his editorial would have alerted the editor to the possibility of it not being a useful contribution. A more balanced approach is expected of an editorial.

Although Judge Prosser's views made headlines in Australia, they did so because they were deemed bizarre. Most people who apply for compensation for the condition succeed in Australia and, I assume, in Britain. Those who fail are generally those whose complaints are not believed and those who sue for negligence on the part of the employer. This does not end the debate, but it indicates how one sided Brooks's editorial is.

The absence of abnormal histopathological findings reflects the fact that almost no biopsies have been done in this condition; when they have been a few authors have found abnormalities.[2] Moreover, histopathological abnormalities and disease are not synonymous—a fact strikingly illustrated in the sudden infant death syndrome.

Brooks is a generation younger than me. That is why he is unaware of the similar epidemic which developed in many of the labour intensive electronics component industries in the 1960s. There are peaks of occupational illness and accidents accompanying many innovations. These abate not because of brain washing but because workers and employers modify the workplace and teach their employees how to avoid the problems. This applies as much to asbestos mining as to typing.

The only factor that all patients have in common, whether they be typists, steel workers, or self employed musicians, is long periods of uninterrupted muscle contraction. That is why the muscles most affected in typists are the extensors of the wrist, which "fix" the wrist during typing, not the finger flexors. Hence isometric contraction myopathy might be a better name for the condition. It is certainly an improvement on the meaningless term "regional pain syndrome."

ARNOLD MANN

Freemasons Medical Centre,
East Melbourne,
Victoria 3002,
Australia

1 Brooks P. Repetitive strain injury. *BMJ* 1993;307:1298. (20 November.)
2 Dennett X, Fry HJH. Overuse syndrome: a muscle biopsy study. *Lancet* 1988;i:905-8.

. . . that is misunderstood and misdiagnosed

EDITOR,—Peter Brooks's editorial on repetitive strain injury[1] promotes the contemporary Australian view of this condition, which is based on the apparent reduction of the "epidemic" of the condition after the denial of its existence. Arguments have been propounded, largely on semantic grounds, that an injury does not result from repetitive use of the arm. Instead it is conceded that "pain occurs in the workplace" and "endemic work related musculoskeletal syndromes remain," yet the problem is considered to be a "complex psychosocial phenomenon."

Such obfuscation is a disservice to the medical profession. Judge Prosser's judgment that repetitive strain injury does not exist as a separate medical condition seems to have been based on the confusing medical evidence presented to him in court. Any thoughtful health service professional would surely accept that overuse conditions result from excessive musculoskeletal activity to which the body has not made a satisfactory adaptive response. "Overuse injuries" are seen commonly in sports medicine and regularly in the workplace. To suppress the recognition of the condition and therefore its assessment and appropriate management, and thereby to deny its sufferers reasonable means of redress, represents medical omnipotence based largely on diagnostic incompetence.

The answer lies in improving skill in musculoskeletal medicine, which will lead to greater understanding. Unless it is recognised that conventional techniques of orthopaedic examination can be inadequate in providing a sastisfactory diagnosis, procrastination will prevail. Until more clinicians who are consulted by patients with musculoskeletal problems are capable of assessing the cervical spine and arm (as are those with osteopathic training) and can thereby detect the more subtle signs the medical profession in general will continue to be bemused by the plethora of "unfathomable syndromes," (Has the time not come for the term syndrome to be rejected in favour of neurophysiological labels?)

Of course there are often psychosocial and socioeconomic overtones. What disease or injury is ever considered in isolation? Employers should continue to be made aware of their responsibilities, particularly with regard to providing sound ergonomic advice. If legislation exists to promote such good work practice why should appropriate enforcement procedures be criticised? The argument regarding nomenclature (repetitive strain injury; work related upper limb disorder) should be subservient to an emphasis on specialist medical assessment procedures.

MICHAEL HUTSON

Department of Accident and Orthopaedic Surgery,
Faculty of Medicine,
Nottingham University Hospital,
Nottingham NG1 6GR

1 Brooks P. Repetitive strain injury. *BMJ* 1993;307:1298. (20 November.)

Pain linked to repetitive work

EDITOR,—Peter Brooks's editorial correctly concludes that repetitive strain injury is a pain syndrome rather than a defined injury.[1] Having seen several patients with alleged repetitive strain injury for medicolegal reports, I support this position. There is, however, a relation between symptoms in this condition and degree of repetitive work. Those carrying out continuous work of