BRITISH MEDICAL JOURNAL

LONDON, SATURDAY 3 MAY 1986

What should we do about work related cancer?

The recent report of an association between nasal and bladder cancer with urban occupations raises several issues —some familiar, some new, and some still without satisfactory solutions.[1] What is the contribution of occupation to overall cancer mortality? How profitable is it for occupational physicians to think simply in terms of "occupational" carcinogens and how profitable to think of environment-host interaction?[2] What action should be taken where there is suspicion, but not unequivocal evidence, of a causal link between the suspected agent and an occupational cancer? In what circumstances should people who may have been exposed to carcinogens be put under surveillance, given that it may need to be continued for 20 years or more because of the long latency of occupational cancer? If medical surveillance is decided on how can it best be achieved?

In England and Wales about 130 000 people die every year from cancer, and in the United States some 4% of cancers are believed to be occupational (with a range of "acceptable estimates" of 2% to 8%).[3,4] If the American figures are right about 5000 deaths a year in England and Wales are attributable to occupational cancer. To what extent are they all solely attributable to work, and are all of them preventable?

Occupational physicians think of prevention under two headings—primary and secondary.[5] Primary prevention aims at removing the carcinogenic agent or at reducing exposure when removal is not feasible. Secondary prevention is directed towards the person who has been exposed with the aim of detecting a change early enough for treatment to be successful, when that is feasible.

In primary prevention the sequence of decision making[6] includes, firstly, identification of possible carcinogens by epidemiological or laboratory studies; secondly, characterisation of the risks, including the examination of relative potency, nature of exposure, and, perhaps, the range of susceptibility of individuals; and, thirdly, policy decisions on control measures. Some people may be more susceptible because of their genetic make up[2] or their lifestyle, and Lower has made the useful distinction between "causes of a cancer" (actual agents—for example, benzidine) and "causes of a cancer incidence" (including lifestyle, such as smoking, or other determinants such as individual differences in the metabolism of the actual agent).[7]

For example, for nearly 20 years smoking has been known to increase the risk of asbestos workers developing lung cancer.[8] Genetically determined variations in susceptibility to environmental agents are now being studied with the hope of identifying susceptible individuals ("ecogenetics").[9] The parts played in lung[10] and laryngeal[11] cancers by genetically controlled arylhydrocarbon hydroxylase inducibility and in bladder cancer by acetylator state[12,13] are being explored with the hope of identifying "susceptible" individuals, though evidently there is still some way to go.[14,15] If it were convincingly shown that some people could be identified as having a greater susceptibility occupational physicians might consider screening exposed workers. In the United States this potential designation of some workers as "hypersusceptible" has been criticised for being tantamount to shifting the responsibility for consequences away from the employer and diminishing the need to eliminate hazards, particularly if the susceptible workers were to be excluded. Others, however, have seen the ability to recognise "susceptible" workers as an important part of primary prevention.[9]

Secondary prevention aims at the detection of disease at a stage when it may be successfully treated. Theoretically, this means identifying those people who have been exposed to a carcinogen and putting them under medical surveillance. Some programmes have been operated successfully, but they are not always straightforward. Routine inspection of the skin of mule spinners or of automatic lathe operators led to early diagnosis and successful treatment of skin cancer because it is readily diagnosed and usually responds to early treatment. The screening programme for bladder cancer among workers in parts of the chemical and rubber industries has also been successful[16,17]—but it was acceptable because exfoliative cytology was used, whereas routine cystoscopy would have had a low uptake in the exposed population.

To look to the future, changes in cellular immunity might ultimately be used for the screening of workers at risk from carcinogens. These include changes in lymphocytic immunoreactivity to bladder cancer cells[18,19] and decreased normal killer cell activity in asbestos workers.[20] Though these developments look interesting, and may be promising, the biological mechanisms of lymphocyte-tumour interactions are not clearly understood, and they are cross sectional studies comparing groups at one point in time. Longitudinal studies in which these changes in individuals are followed up over time would greatly strengthen the argument.

Some carcinogens bind covalently to deoxyribonucleic

acid (DNA), forming adducts which are detectable by immunological techniques, so individuals, at high risk from certain carcinogens, might possibly be screened using polyclonal or monoclonal antibodies to measure carcinogen:DNA adduct levels. Furthermore, this method might be employed not only to monitor the genotoxic effect but also to assess the efficiency of DNA repair.[14 21] Nevertheless, we need to remember that if a neoplasm is not amenable to treatment (for example, mesothelioma from asbestos exposure) there is little point in regularly drawing a patient's attention to the sword of Damocles.

When early diagnosis can lead to successful treatment, however, we need to decide who should be put under surveillance—and this decision must be arbitrary. We cannot hope to trace everyone who might have been exposed throughout the long latent period of development of an occupational cancer, perhaps a lifetime. Factors that need to be considered include the length and severity of exposure to the carcinogen and possibly the lifestyle of genetically determined metabolic state of the individuals at risk. The decision requires good science, sound judgment, and common sense. The long latent period causes almost insurmountable obstacles to organisation in large as well as small enterprises. Not many workers nowadays remain with the same employer for up to 40 years. So how is long term surveillance to be organised? To bring the problem home—What personal exposure records has the National Health Service kept of nurses and pharmacists handling cytotoxic drugs? Should they be subjected to a lifetime of medical surveillance, simply on the basis of perceived risk from mutagenicity, though no increased incidence of cancer has been reported?[22] So far we have found no universal answer to these problems.

The Health and Safety Commission is concerned with prevention (including the identification and assessment of hazards) and has called for certain records of exposure to be kept for up to 50 years, but it does not appear to have considered whether some exposed workers should be identified for follow up or how this might be achieved.[23] In the rubber industry a successful programme has been operated by the British Rubber Manufacturers' Association which began by an approach to men working in the industry. They were, of course, aware of the problems and perhaps some of their friends and colleagues had developed tumours. When the Health and Safety Executive attempted to extend the scheme to men who had left the industry many years previously and who had to be traced through national registers the response rate was considerably lower (H G Parkes, personal communication), which illustrates the separation which still exists between occupational and other medical services.

We need to develop in this area, possibly using the family doctor (or more likely over a 40 year period a succession of family doctors). Theoretically, the use of central (NHS and National Insurance) registers would help, but the response by former workers may be uncertain—and apart from apathy not everyone wants a yearly reminder of a possibly remote risk to his life. Sir Herman Bondi has perceptively reminded us that the death rate in any community is one per person.[24] How far is it morally justifiable, how far is it economically justifiable, continually to pursue people late into old age with the object of making a presymptomatic diagnosis? Should we look at such questions, or is it better to continue to ignore them?

For the present a general practitioner, aware of his patient's present and past occupations, must be alert for early evidence of an occupational cancer. Many hospital clinicians, aware of the connection between the cancers with which they deal and occupation, frequently do inquire into the occupational history. But by that time the establishment of the occupational link generally serves to point the patient only towards some form of financial benefit—important and useful, but no substitute for primary and secondary prevention.

W R LEE

Professor of Occupational Health,
University of Manchester,
Manchester M13 9PT

1 Baxter PJ, McDowall ME. Occupation and cancer in London: an investigation into nasal and bladder cancer using the Cancer Atlas. *Br J Ind Med* 1986;**43**:44-9.
2 Harnden DG. Views on the aetiology of some cancers. *J R Coll Physicians Lond* 1980;**14**:106-10.
3 Doll R, Peto R. The causes of cancer: quantitative estimates of avoidable risks of cancer in the United States today. *JNCI* 1981;**66**:1194-308.
4 Roe FJC. Avoidable cancer risks with special reference to occupational factors. *Br Med J* 1981;**283**:1421-2.
5 Alderson M. Industrial cancer—whose responsibility? *Ann Occup Hyg* 1978;**21**:285-91.
6 Calkins DR, Dixon RL, Gerber CR, Zarin D, Omenn GS. Identification, characterization, and control of potential human carcinogens: a framework for federal decision making. *JNCI* 1980;**64**:169-76.
7 Lower GM. Arylamines and bladder cancer causality: application of conceptual and operational criteria. *Clin Pharmacol Ther* 1983;**34**:129-35.
8 Selikoff IJ, Hammond EC, Churg J. Asbestos exposure, smoking, and neoplasia. *JAMA* 1968;**204**:104-10.
9 Omenn GS. Advances in genetics and immunology: the importance of basic research to prevention of occupational diseases. *Arch Environ Health* 1984;**39**:173-82.
10 Emery AEH, Anand R, Danford N, Duncan W, Paton L. Aryl-hydrocarbon-hydroxylase inducibility in patients with cancer. *Lancet* 1978;i:470-2.
11 Trell E, Korsgaard R, Hood B, Kitzing P, Norden G, Simonsson BG. Aryl hydrocarbon hydroxylase inducibility and laryngeal carcinomas. *Lancet* 1976;ii:140.
12 Cartwright RA, Glashan RW, Rogers HJ, *et al*. Role of N-acetyltransferase phenotypes in bladder carcinogenesis: a pharmacogenetic epidemiological approach to bladder cancer. *Lancet* 1982;i:842-6.
13 Evans DAP, Eze LC, Whibley EJ. The association of the slow acetylator phenotype with bladder cancer. *J Med Genet* 1983;**20**:330-3.
14 Perera FP, Weinstein IB. Molecular epidemiology and carcinogen-DNA adduct detection: new approaches to studies of human cancer causation. *J Chronic Dis* 1982;**35**:581-600.
15 Arnott MS, Yamauchi T, Johnston DA. Aryl hydrocarbon hydroxylase in normal and cancer populations. In: Griffin AC, Shaw CR, eds. *Carcinogens: identification and mechanisms of action*. New York: Raven Press, 1979:145-56.
16 Fox AJ, White CG. Bladder cancer in rubber workers. *Lancet* 1976;i:1009-11.
17 Cartwright RA, Gadian T, Garland JB, Bernard SM. The influence of malignant cell cytology screening on the survival of industrial bladder cancer cases. *J Epidemiol Community Health* 1981;**35**:35-8.
18 Kumar S, Taylor G, Wilson P, Hurst W. Prognostic importance of specific immunoreactivity in occupational bladder cancer. *Br Med J* 1980;**280**:512-3.
19 Cordiali-Fei P, Natali PG, Pecci G, Pellegrino MA, Ferrone S. Levels of Ia-like antigen bearing lymphocytes in patients with solid primary tumours. *J Clin Lab Immunol* 1981;**6**:197-9.
20 Ginns LC, Ryu JH, Rogol PR, *et al*. Natural killer cell activity in cigarette smokers and asbestos workers. *Am Rev Respir Dis* 1985;**131**:831-4.
21 Shamsuddin AKM, Sinopoli NT, Hemminki K, Boesch R, Harris CC. Detection of benzo(a)pyrene:DNA adducts in human white blood cells. *Cancer Res* 1985;**45**:66-8.
22 William CJ. Handling cytotoxics. *Br Med J* 1985;**291**:1299-300.
23 Health and Safety Commission. *Control of substances hazardous to health. Draft regulations and draft approved codes of practice*. London: HMSO, 1984. (Consultative document.)
24 Bondi H. Risk in perspective. In: Cooper MG, ed. *Risk: man-made hazards to man*. Oxford: Clarendon Press, 1985:8-17.

IVF update

Twenty five centres in Britain are carrying out in vitro fertilisation (IVF). Of these only one is operated by the NHS; so this form of treatment—the only hope for many of Britain's estimated 1 in 10 infertile couples—is readily available only to those who can afford to pay between £1000 and £2500 per treatment cycle. Such fees are not surprising, for the cost in salaries and running expenses alone for a unit treating five patients a week is about £100 000. Private clinics must also cover the cost of their beds, new buildings, etc. Irrespective of the high cost the demand is there, and the private centres are flourishing. Indeed, five new centres are on the starting blocks. Waiting lists are long, many as long as four years. This is bad news for those in their late 30s for if a clinic has a policy of accepting only women under 40, and many do, today's 35 year old applicants are likely to be turned down.