Editorial

Contribution of occupational exposure to cancer: recent developments

Exposures and technologies in the workplace are constantly changing and thus clearly affect both employers and employees. Mechanisation and automation have modified processes that would have required more direct contact between workers and process materials in the past but which now use machines, with an amended workforce or no workforce at all. Improvements in industrial hygiene and worker protection have resulted in lower levels of exposures to some substances that formerly would have been major hazards—but how widely are these advances and precautions heeded throughout industry to include, for example, production, manufacturing, the user industry, and the third world? Better codes of practice are being devised and implemented—but can they be adequately enforced and monitored to protect all workers? How much can the worker do himself to lower his exposure? Problems from visibly high exposures to fibres, for example, are being replaced by growing concerns about invisible exposures, high or low, such as electromagnetic fields—what do such exposures and the ever expanding and modified new processes of industry have in store for occupational cancer?

So, exposures are changing. Old high ones are being lowered, sometimes reduced by alteration of processing methods and sometimes removed by substitution with hopefully less hazardous materials. But the question of what effect occupational exposures have on cancer will remain with us regardless, through all developments or changes, as long as man spends his day or night in the workplace. To establish the picture it is necessary to have at least a wide, preferably complete, documentation of the working environment and the development of cancers in those people who have experienced that environment. Rationally it can be expected that man, or a measurable fraction of the human race, will continue to live a sizeable proportion of life in the workplace—so what adverse health effects, particularly cancer, are there now compared with the past and what of the future?

Measurement of occupational cancer

In many publications over at least the last twenty years the contribution of occupational exposures to cancer in the workforce and population has been estimated.^{1,2} This is notoriously a tricky and complex

area for many reasons. These include inadequate knowledge of carcinogenic substances in the workplace because of as yet undiscovered carcinogens, and incomplete representation of exposure response relations for known carcinogens (including interactions with other workplace, environmental, or behavioural factors). Also, a lack of suitable information on the distribution and patterns of exposure to these substances exists, either locally, regionally, nationally, or internationally; although there are moves towards improving this aspect. Further, there are some inadequacies in our understanding of non-occupational causes of cancer, such as diet, which affect any attempt to partition the overall population cancer risk into segments.

Difficulties also ensue with the commonly used method of presenting this information, which is in the form of the percentage of all cancer or cases of a specific cancer due to occupational causes. Proportions of this nature are not commonly used in epidemiological or statistical analysis, where rates or risks are preferred approaches. One simple difficulty with proportions can be seen by considering the commonly quoted estimates of about 4% of all cancers being associated with occupational origin, about 35% with diet, about 30% with cigarette smoking, and the remainder with other known and unknown factors.¹ If the smoking habit had not been invented and the tobacco cases did not exist then the base of total cancers would be 30% fewer and the percentage associated with occupation would be increased to at least 6% rather than 4%. This may not seem numerically a very large difference, but it does make the point that this widely quoted statistic is dependent upon the relative frequency of other causes of cancer, whereas the annual rate per 1000 (or whatever base) of the working population is relatively unchanged (ignoring complications such as confounding and interaction). Alternatively, if the rate of occurrence of cases of occupational cancer were to be doubled then the quoted percentage would change from 4% to near 7.5% (not quite doubled).

Another feature that makes these estimates of somewhat dubious use and generalisation is because for specific cancers and exposures—for example, bladder cancer and occupational chemicals—the relative risks are based on studies deliberately carried out on highly exposed subjects (for higher study statistical power) and hence may not be suitable for

the purpose of making estimates for the whole industry or population.³ The figures obtained from such studies may exaggerate the risk faced by most employees who may work, at least now, in cleaner conditions and may overstate the attributable number of cancer cases from the particular exposure.

New causes for old?

Many occupational links with cancer have been identified since the early years of observation and research on this topic.⁴ Some of the first recognised were scrotal cancer among chimney sweeps, bone cancer among luminous radium dial painters, nasal tumours among furniture and leather workers, lung cancer from exposure to radon decay products among uranium miners and—along with mesothelioma—from exposure to fibre among asbestos workers, and bladder cancer among workers with dyestuffs and in the rubber industry. With the recognition of occupationally related cancers steps were taken in many instances to remove or reduce exposures to the recognised or suspected hazard with the result that the numbers of associated cases have decreased. In some instances, because of the long latent period between first exposure and diagnosis of cancer, such as for asbestos and mesothelioma, the annual number of cases by calendar year has not yet reached a maximum, but a peak followed by a decline should occur over the next few years in western countries at least. Most of these well known occupational causes of cancer were discovered as a consequence of high exposures when regulation of the workplace was not as well developed as now.

New links of occupation to cancer are continually being suggested, however, despite lower exposures. Examples include leukaemia among electrical workers, lung cancer among butchers, and laryngeal cancer among workers exposed to acid mists. In some cases the evidence is not definitive and in others, although a consistent excess has been found, such as among butchers, whether the increased lung cancers are due to tobacco confounding or another occupational exposure, possibly a papilloma virus, is yet to be determined. Other suggestions of new occupational causes of cancer have come from single studies that await replication.

Leads to potential occupational hazards have come from animal studies of substances, mainly chemicals, for which there has been sufficient evidence in the laboratory of carcinogenic potential; the International Agency for Research on Cancer has a list of over 100 such agents.⁵ There is certainly a requirement to consider obtaining relevant observations on man to follow up these suggestions, but also the need to consider the appropriateness of the animal model and level of exposure to the human workplace situation. A relevant example is that of formaldehyde for which experiments in rats at higher

exposures than man could tolerate produced tumours of the nasal cavities and sinuses that have not been found in large studies of production and manufacturing workers—although sufficient doubts in various reports ensure that the situation is still under review. The role of showing carcinogenic potential regardless of dose level should be carefully considered.

Priorities in occupational cancer epidemiology

A recent review of ongoing studies in occupational cancer epidemiology indicated that a large proportion was being carried out on established workplace carcinogens, in particular asbestos.⁶ This situation should be thoughtfully assessed. It is essential, of course, to obtain as many data as are required to make reasonable judgements about effects of substances causing cancer in man. This is particularly true if these cannot be removed from the workforce or substituted (such as radon decay products in some mines) so that acceptable risks can be related to control of exposure levels using epidemiological data rather than extrapolating, with all the ensuing difficulties, from animal studies. Some debate, however, about the balance of carrying out such research relative to exploring suspected new carcinogens with limited available expertise and resources is needed.

It is evident that research and academic institutions in many countries are reliant on outside research funding for studies they undertake. It appears to be easier to obtain research funds to support a replicate study of a known carcinogen, possibly to find out more about a variant of the manufacturing process or fibre in the case of asbestos or simply to see if the knowledge already available is applicable to one's own situation, but maybe the total pool of support could be better partitioned to enable us to learn more about newer areas and exposures. An international research agenda is a possible forward move that may enhance the breadth and scope of examination of occupational causes of cancer.

The International Agency for Research on Cancer held a preliminary meeting of this nature during 1986 that resulted in a report identifying a scheme for selecting priorities for study.⁶ This was partly in response to the long list of chemicals previously mentioned where sufficient evidence exists for carcinogenicity in animals but for which no or inadequate evidence exists in man. Factors that were considered important in setting up human studies included the numbers of workers exposed, levels of exposure, quality of exposure data, trends in exposure, and size of relative risk anticipated. This scheme, perhaps with an agreed scoring system, has the potential to rank occupational exposures in order of the requirements for research priority and action.

Multicentre studies

One of the changing faces of the occupational workplace is that exposures are in general becoming lower and thus it may be expected that cancer risks will also become lower. This raises the problem that epidemiological studies will need to be larger to detect such risks than was necessary to be certain qualitatively that, for example, asbestos was a lung carcinogen. These larger numbers of exposed workers are not always going to be available in any one country for some of the rarer substances, and the need for some kind of international collaboration to tackle this situation is indicated. Such initiatives have been operated successfully in the past and are also currently under way. Examples include the setting up of a multinational study of man made mineral fibre workers to a common protocol from thirteen factories in seven European countries to assess the risk if any of this substitute for asbestos. Also, coordinated pooling projects are being conducted of data from studies with varying protocols, such as for styrene, herbicide, and radiation workers. Moreover, meta-analyses of other exposures have been and are being carried out, but these often rely on combining published results rather than collating original individual observations. All this points to the necessity of coordination and collaboration to obtain better evidence on occupational exposures in regard to possible carcinogenicity.

Notification of risks to workers

One role of identifying causes of occupational cancer is to introduce preventive measures of some nature. This will usually imply a modification to the production process or to the workplace environment to eliminate or reduce exposure, including the introduction of protective clothing or respirators for individual workers. In general this will also use worker education into the risks associated with their employment, but will mostly be limited to the current and future workforce (if potentially hazardous exposures are ongoing). Less effort or thought, however, has been invested in identifying, tracing, and counselling those past employees who would have been members of specific occupational cohort studies in which risks have been discovered or quantified.^{7,8}

Several questions arise in this area including those of whether and under what circumstances ex-worker notification of risk should proceed. Cancers typically have long latent periods from the time of initiating exposure in the workplace before their diagnosis. Therefore, many resultant tumours may occur after exposed workers have changed employment or retired. Although ethical issues (for example, the "right to know" and the potential lack of knowledge among workers that they have been in cohort studies carried out entirely by the use of records) and

limitations in risk statements that can be given on an individual basis must be considered, a consensus that such risk information should be notified to ex-workers seems to have been emerging; but that problems exist in how to do so is apparent.⁹ Specific advice may be possible in some instances—for example, screening programmes for workers previously exposed to aromatic amines who are at high risk of bladder cancer¹⁰ or antismoking advice to former amosite asbestos workers at particularly high risk of lung cancer.¹¹ It is clearly desirable that any such interventions should be evaluated where possible with appropriately conducted trials.

Cancer among family members

Information is needed on the cancer risks, if any, experienced by members of the families of exposed workers. In studies of household contacts of employees in an amosite asbestos factory raised rates of lung cancer have been reported, and there are indications that mesotheliomas have also been caused by this route of exposure—by fibrous dust brought home by workers.¹² Many studies have now been carried out investigating cancer among children of workers to search for associations with parental exposures, but without altogether concordant findings.¹³ A recent paper has reported a relation between occupational ionising radiation dose of fathers working at the Sellafield nuclear plant and leukaemia in their children.¹⁴

Limits of epidemiology

It is pertinent to point to some of the limitations of epidemiological research in this field—as well as having commented on its potential. One of the major difficulties is in identifying a possible low relative risk for a common cancer, such as lung cancer compared with a higher risk for a rare cancer, such as nasal cancer. The first will not be as easy to discern from the background of cases due, possibly, to many other causes, whereas the second will be more noticeable because it may be somewhat bizarre.¹⁵ In terms of the attributable numbers of cases that may be associated with the occupational exposure, however, the first (low relative risk) is likely to be more important than the second (high relative risk). Thus the epidemiological approach is likely to be less definitive in the future for lower exposures, except for unusual tumours. This is a difficulty only partly covered by the extension to multicentre studies, and we are in need of better epidemiological tools with better exposure banks to continue progress, including biological markers where appropriate and exposures external to the particular occupation of interest.

The future

The greater control of exposures in the workplace

may lead to lower rates of occupational cancer in the years ahead if sufficient heed is paid to the lessons of high exposure/cancer situations of the past. The emergence of possible new workplace carcinogens, however, indicates that our knowledge is as yet insufficient to have certainties about the future. Occupational physicians, industrial hygienists, toxicologists, epidemiologists, and others will need to increasingly share a network of information to expedite the identification of and action on any new hazardous exposures.

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