IN-DEPTH REVIEWS

Workplace and cancer: interactions and updates

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Occupational and environmental hazards and the potential adverse health effects arising from them are an area of increasing public interest and a topic of a large body of research within many different disciplines. Investigation involves both knowledge of the source and nature of the hazard and an understanding of the relationship of the exposure to the disease. Epidemiological studies of industrial workforces have played an important role in the identification of carcinogens and the understanding of the aetiology of cancer. A distinction is often made between conditions from which individuals may have no or only partial control and those for which some element of personal choice exists. Exposures encountered at work would tend to fall in the former category, while ‘lifestyle’ factors such as smoking, eating a high-fat diet and drinking alcohol would come in the latter. The working environment should not be a place where there is a risk of disease or injury, yet many thousands of workers worldwide are exposed to hazardous substances at work everyday. Although substances related to occupational cancer are often associated with chemical exposures, especially man-made [1], a wider definition is needed to encompass all patterns of working.

The International Agency for Research into Cancer (IARC) classifies substances into four groups according to the evidence as shown in Table 1 (http://monographs.iarc.fr/ENG/Preamble/index.php, accessed July 2008).

For human data, sufficient evidence is defined as the establishment of a causal relationship between exposure to the agent and human cancer. Limited evidence is defined as the observation of a positive association between exposure to the agent and human cancer, for which a causal interpretation is considered credible, but chance, bias or confounding could not be ruled out with reasonable confidence. Similar definitions relate to the evidence from experimental data. Since 1972, IARC has published 92 volumes as part of their monograph programme, with 400 have been classed as carcinogenic (Group 1 or 2A) or potentially carcinogenic to humans (Group 2B). In a review of the IARC monograph series through 2003 [2], and in subsequent monographs (published and unpublished), some 31 definite (IARC Group 1) and 32 probable (IARC Group 2A) human occupational carcinogens have been defined for >20 cancer sites.

The results from studies of occupational groups have many uses, for example in carrying out risk assessments for standard setting and for decisions regarding compensation. There is also an increasing interest in estimating and comparing burdens of disease generally [3] and for cancer [4,5]. Estimates can identify major risk factors and high-risk populations, support decisions on priority actions for risk reduction and provide an understanding of important contributions to health inequalities.

Nearly 30 years ago, Doll and Peto [6], in their report to the US Congress, presented a method of estimating the effects of different factors on cancer mortality in the USA; their estimate for occupational factors was 4% of all US cancer deaths with an uncertainty range of 2–8%. These figures have been used by the Health & Safety Executive (HSE) to inform their strategy for chemicals and other agents that may cause occupational cancer. Since 1981, there have been several other estimates of attributable occupational cancer burden some of which are shown for selected cancers in Table 2 [6, 12]. The second row of the table gives recent estimates by Rushton et al. [7] from an ongoing study to update the Doll and Peto figures for Great Britain (GB).

Some of the differences between the results can be explained by differences in the numbers of agents considered. For example, Steenland et al. [10] estimate the burden of lung cancer for eight occupational carcinogens compared to 19 in the British study [7]. Other differences may be due to differences between countries in the occupational situations in which exposures occur. Different methodological approaches were also used for some of the studies in the table. However, although the magnitude of the burden differs between studies, the patterns are generally similar.

These percentages can translate into considerable numbers of deaths and cancer registrations. For example, the World Health Organization estimate every year that at least 200 000 people worldwide die from cancer related to
Table 1. Carcinogenicity defined by the IARC

<table>
<thead>
<tr>
<th>Group</th>
<th>Definition</th>
<th>Used when</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>Carcinogenic to humans</td>
<td>Sufficient evidence in humans</td>
</tr>
<tr>
<td>2A</td>
<td>Probably carcinogenic to humans</td>
<td>Limited evidence in humans and sufficient evidence in experimental animals</td>
</tr>
<tr>
<td>2B</td>
<td>Possibly carcinogenic to humans</td>
<td>Limited evidence in humans and absence of sufficient evidence in experimental animals or inadequate evidence in humans or human data non-existent and sufficient evidence in experimental animals</td>
</tr>
<tr>
<td>3</td>
<td>Not classifiable as to carcinogenicity to humans</td>
<td>Inadequate or unavailable evidence in humans and inadequate or limited evidence in animals</td>
</tr>
<tr>
<td>4</td>
<td>Probably not carcinogenic to humans</td>
<td>Evidence suggests a lack of carcinogenicity in humans and in experimental animals</td>
</tr>
</tbody>
</table>

their workplace (http://www.who.int/mediacentre/news/notes/2007/np19/en/index.html). In the GB study, estimates of cancer registrations attributable to work-related carcinogens for the six cancers assessed (bladder, leukaemia, lung, mesothelioma, non-melanoma skin, sinonasal) were 13 338 (4.0%) registrations [men: 11 284 (6.7%); women 2054 (1.2%)] [7].

The methodology developed for the GB study and the data available in GB allowed a more detailed investigation of the carcinogenic agents, occupational circumstances and industry sectors than has been possible in other burden estimation studies and included consideration of the potential to be exposed to several carcinogens concurrently. For the six cancers assessed, asbestos contributed over half the occupational attributable deaths, followed by silica, diesel engine exhaust, radon, work as a painter, mineral oils in metal workers and in the printing industry, environmental tobacco smoke (non-smokers), work as a welder and dioxins. Occupational exposure to solar radiation, mineral oils and coal tars/pitches contributed 2557, 1867 and 550 skin cancer registrations, respectively. The industry sectors contributing to the burden of occupational cancer are not always those where substantial historical exposures have occurred. For example, the main occupations with substantial historical exposure to inorganic arsenic include hot copper smelting, manufacturing of arsenical pesticides and sheep dip compounds, fur handlers and vineyard workers and some miners [13,14]. In GB, the majority of exposure occurs in the non-ferrous metal basic industry and the manufacture of wood and wood and cork products. Although potential asbestos exposure occurred to large numbers of workers in the mining industry (excluding coal mining), the industry with the greatest potential for asbestos exposure now is the construction industry, occurring for example in asbestos removal or stripping.

In addition to allowing for overlapping and multiple exposures, wherever possible the GB study [7] uses risk estimates that adjust for important non-occupational risk factors, including confounders. However, cancer is a multifactorial and multistage disease that may not be due to any single sufficient cause but rather a sequence of 'hits' over a life course. For example, smoking alone may not be sufficient to cause lung cancer and those who get it are likely to have been exposed to several lung carcinogens and possess other characteristics such as some form of inherited susceptibility. The mathematical implication of this is that the sum of attributable fractions for several exposures may be >100%, with the amount exceeding 100% being partly due to synergistic interactions among the risk factors [15].

One of the substances identified as contributing considerable to the burden of lung cancer in the recent GB study was silica with ~800 lung cancer deaths in men in 2004 being attributable to silica exposure. However, there remains considerable controversy over the role of silica in the development of lung cancer. Brown [16] gives an overview of the literature on this issue and discusses the interactions between cigarette smoking and exposure to respirable crystalline silica (RCS) and their role in the development of silicosis and lung cancer; disentangling these effects still presents a considerable challenge.

Another important issue in carrying out occupational studies is assessment of all sources of an exposure and evaluation of the relative contributions of occupational and non-occupational elements. This is a particular problem in a ubiquitous exposure such as solar radiation. Young [17] reviews the literature on the effects of solar radiation on the occurrence of both melanoma and non-melanoma skin cancers and describes the efforts of researchers to estimate separately the risks due to non-occupational and occupational exposures.

For many substances, there have been general trends for a reduction in measured exposure levels over the last few decades. Cherrie et al. [18] in an analysis of the CARcinogen Exposure database and the UK National Exposure Database found considerable variation in the levels of exposure between substances and workplaces. Symanski et al. [19] analysed ~700 exposure datasets, including carcinogens, worldwide and found consistent rates of decline ranging from ~4 to 14% per year. As illustrated in the review of the effects of (RCS) by Brown [16], RCS measures in the UK silica sand industry showed a steady decline from 1978 to 2001 with 20% of the measurements between 1978 and 1985 being above the maximum exposure limit (MEL) compared to <10% by 2001.
Cherrie [20] highlights the 10 substances or occupations identified by Rushton et al. [7] as contributing most to the six cancers evaluated. Cherrie discusses control strategies for two of these: diesel engine exhaust, which occurs in a diverse range of workplaces, and work as a painter, where the exact substance causing excess cancers is uncertain. Davis and Muir [21] advocate the use of the ‘precautionary principle’ as an approach to reducing risk, even though uncertainty may still exist about the magnitude of the risks and the cellular and genetic mechanisms may not be fully understood. Logically, primary prevention of occupational carcinogens should result in lower cancer rates. The challenge facing researchers is to develop appropriate methodology and carry out suitable studies to quantify changes in future. Methodology for this is currently being developed for GB as part of the HSE funded burden of occupational cancer research programme. Comparison of forecasts from different scenarios for changes in exposure, such as gradual reduction [20], complete elimination or stepped reduction in levels through lowering of occupational limits, will facilitate the policy choices for legislators and employers.

Conflicts of interest
None declared.

References


