Social Inequalities and Cancer
Kogevinas, M., Pearce, N., Susser, M. and Boffetta, P., eds
IARC Scientific Publications No. 138
International Agency for Research on Cancer, Lyon, 1997

Exposure to occupational carcinogens and social class differences in cancer occurrence

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It has been estimated that occupational exposures are responsible for about 4% of all human cancers in industrialized countries. These cancers are concentrated among manual workers and in the lower social classes, thus contributing to the social class gradient in cancer incidence and mortality. On the basis of the 1971 cancer mortality data from England and Wales, it was estimated that occupational cancer is responsible for about a third of the total cancer difference between high (I, II and III-NM) and low (III-M, IV and V) social classes, and for about half of the difference for lung and bladder cancer. However, direct evidence on the extent of the contribution of occupational exposure to carcinogens to social class differences is lacking, and several problems, such as the possible interaction between carcinogens and the effect of extraoccupational confounding factors, add further elements of uncertainty.

The analysis of social class differences in cancer occurrence by occupation involves aspects of circular reasoning, since in many cases people are classified by social class according to the job they hold or have held at sometime during their life (see the chapter by Berkman and Macintyre in this book), and main occupation is highly correlated with other indicators of social class, such as education and income.

Occupational exposure to carcinogens has some peculiar characteristics compared with other causes of cancer related to social class, such as tobacco smoking and alcohol drinking. First, the exposure is to a large extent involuntary. Although some aspects of personal choice exist, such as the decision not to use protective equipment, the determinants of the exposure to carcinogens in the workplace are mainly inherent in the job tasks. Second, the cancer hazard may not be known to the worker, such as in the case of complex mixtures with variable composition (for example, mineral oil mist). Third, occupational cancer can be prevented by means other than (or in addition to) changes in personal behaviour. Finally, more data are available on the interaction between specific occupational exposures and other risk factors, both occupational and extraoccupational, than in other areas of cancer epidemiology (Saracci & Boffetta, 1994).

Occupational causes of cancer

Over the last two decades, the *Monographs* programme of the International Agency for Research on Cancer (IARC) has systematically evaluated the carcinogenic risk to humans from exposure to chemical, physical and biological agents and mixtures (IARC 1972–1996), and the majority of known occupational or suspected occupational carcinogens have now been assessed*. At present, 21 chemicals, groups of chemicals or mixtures for which exposures are mostly occupational (excluding pesticides and drugs) are classified as human carcinogens (IARC Group 1; Table 1). While some agents, such as asbestos, benzene and heavy metals, are currently widely used in many countries, others are mainly of historical interest (for example, mustard gas and 2-naphthylamine). An additional 20 agents are classified as probably carcinogenic to humans (IARC Group 2A): these are mainly agents carcinogenic in experimental animals with limited evidence of carcinogenicity in humans from epidemiological studies (Table 2). Exposures to some of these agents, such as crystalline silica, formaldehyde and

*Although the IARC Monographs programme has covered most of the known or suspected causes of cancer, there are some important groups of occupational agents that have not yet been evaluated by IARC – namely ionizing radiation, and electrical and magnetic fields.

Table 1. Chemicals, groups of chemicals or mixtures for which exposures are mostly occupational, and industrial processes and occupations, evaluated in the IARC *Monographs* (Vols 1–63) as carcinogenic to humans (IARC Group 1)[a]

Agents[b]	Human target organ(s)/cancer	Main industry/use
Chemicals and groups of chemicals		
4-Aminobiphenyl [92-67-1]	Bladder	Rubber manufacture
Arsenic [7440-38-2] and arsenic compounds[c]	Lung, skin	Glass, metals, pesticides
Asbestos [1332-21-4]	Lung, pleura, peritoneum	Insulation, filter material, textiles
Benzene [71-43-2]	Leukaemia	Solvent, fuel
Benzidine [92-87-5]	Bladder	Dye/pigment manufacture, laboratory agent
Beryllium [7440-41-7] and beryllium compounds (1993)	Lung	Aerospace industry/metals
Bis(chloromethyl)ether [542-88-1] and chloromethyl methyl ether [107-30-2] (technical-grade)	Lung	Chemical intermediate, by-product
Cadmium [7440-43-9] and cadmium compounds (1993)	Lung	Dye/pigment manufacture
Chromium[VI] compounds (1990)	Nasal cavity, lung	Metal plating, dye/pigment manufacture
Coal-tar pitches [65996-93-2]	Skin, lung, bladder	Building material, electrodes
Coal-tars [8007-45-2]	Skin, lung	Fuel
Ethylene oxide [75-21-8]	Leukaemia	Chemical intermediate, sterilant
Mineral oils (untreated and mildly treated	Skin	Lubricants
Mustard gas (sulphur mustard) [505-60-2]	Pharynx, lung	War gas
2-Naphthylamine [91-59-8]	Bladder	Dye/pigment manufacture
Nickel compounds (1990)	Nasal cavity, lung	Metallurgy, alloys, catalyst
Shale-oils [68308-34-9]	Skin	Lubricants, fuels
Soots	Skin, lung	Pigments
Talc containing asbestiform fibres	Lung	Paper, paints
Vinyl chloride [75-01-4]	Liver, lung, blood vessels	Plastics, monomer
Wood dust (1994)	Nasal cavity	Wood industry
Industrial processes and occupations		
Aluminium production	Lung, bladder	
Auramine manufacture	Bladder	
Boot and shoe manufacture and repair	Nasal cavity, leukaemia	
Coal gasification	Skin, lung, bladder	
Coke production	Skin, lung, kidney	
Furniture and cabinet making	Nasal cavity	
Haematite mining (underground) with exposure to radon	Lung	
Iron and steel founding	Lung	
Isopropanol manufacture (strong-acid process)	Nasal cavity	
Magenta manufacture (1993)	Bladder	

Table 1. (Contd) Chemicals, groups of chemicals or mixtures for which exposures are mostly occupational, and industrial processes and occupations, evaluated in the IARC *Monographs* (Vols 1–63) as carcinogenic to humans (IARC Group 1)[a]

Agents[b]	Human target organ(s)/cancer	Main industry/use
Industrial processes and occupations		
Painter (occupational exposure as a) (1989)	Lung	
Rubber industry (certain occupations)	Bladder, leukaemia	
Strong-inorganic-acid mists containing sulphuric acid (occupational exposure to) (1992)	Lung, larynx	

[a]Several drugs used in cancer chemotherapy are classified as human carcinogens; occupational exposure can occur in manufacturing, pharmacies and hospitals.
[b]Year in parenthesis, year in which the evaluation was made subsequent to the 1987 Supplement 7 Working Group for agents, mixtures or exposure circumstances considered in Vols 43–63 of the *Monographs*. Number in square brackets, CAS Registry No.
[c]This evaluation applies to the group of chemicals as a whole and not necessarily to all individual chemicals within the group.

1,3-butadiene, are currently prevalent in many countries. A large number of agents are classified as possible human carcinogens (IARC Group 2B), such as acetaldehyde, DDT, inorganic lead compounds and man-made mineral fibres. For the majority of these chemicals the evidence of carcinogenicity comes from studies in experimental animals.

In addition, the IARC *Monographs* programme has evaluated the evidence of carcinogenic risk from employment in specific industries and occupations for which data existed from epidemiological studies, although the exposures responsible for the risk could not be identified with certainty. At present, 13 industries or occupations are classified as entailing a carcinogenic risk (Group 1; Table 1), and four additional industries or occupations are classified as probably entailing a risk (Group 2A; Table 2). Three points should be considered when looking at these tables. First, there is a certain degree of duplication between the list of agents and that of occupations and industries, which is partially due to historical reasons. For example, employment in certain wood industries such as furniture and cabinet making was classified in Group 1 in 1981, and at that time the data did not allow a conclusion to be made about the role of specific exposures, such as to wood dust. However, in 1994 exposure to wood dust was evaluated on the basis of additional evidence that had become available in recent years and was in turn classified in Group 1, so the early classification based on industry has now lost most of its relevance. Second, in contrast to the case for individual chemical and physical agents, there was no attempt in the *Monographs* programme to evaluate occupations and industries systematically, and the lists of these in Tables 1 and 2 are therefore by no means exhaustive (for a more complete discussion of industries and occupations entailing a carcinogenic risk, besides the *Monographs* evaluations, see Boffetta *et al.*, 1995). Finally, as the classifications are based on incomplete knowledge of exposures, such evaluations do not necessarily apply to all workers employed in a given industry, and differences (although not detectable by the evaluation) are likely to exist between time periods of employment, countries, factories, and even departments and jobs within a factory. For example, employment in the rubber industry has been classified in Group 1 on the basis of an excess risk of bladder cancer that was mainly reported in studies conducted during the 1960s and 1970s of exposures between the 1930s and the 1950s; subsequent studies from the same and other plants, however, have shown much smaller, if any, excess risk, suggesting that changes in the technological process may have greatly reduced, if not abolished, the risk (Swerdlow, 1990).

Several environmental agents are known or suspected to cause cancer in humans (Table 3), and although exposure to such agents is not primarily

Table 2. Chemicals, groups of chemicals or mixtures for which exposures are mostly occupational, and industrial processes and occupations, evaluated in the IARC *Monographs* (Vols 1–63) as probably carcinogenic to humans (IARC Group 2A)

Agents[a]	Suspected human target organ(s)/cancer	Main industry/use
Chemicals and groups of chemicals		
Acrylonitrile [107-13-1]	Lung, prostate, lymphoma	Plastics, rubber, textiles, monomer
Benzidine-based dyes	Bladder	Paper, leather, textile dyes
1,3-Butadiene [106-99-0] (1992)	Leukaemia, lymphoma	Plastics, rubber, monomer
para-Chloro-ortho-toluidine [95-69-2]	Bladder	Dye/pigment manufacture, textiles and its strong acid salts (1990)
Creosotes [8001-58-9]	Skin	Wood preservation
Diethyl sulphate [64-67-5] (1992)	–	Chemical intermediate
Dimethylcarbamoyl chloride [79-44-7]	–	Chemical intermediate
Dimethyl sulphate [77-78-1]	–	Chemical intermediate
Epichlorohydrin [106-89-8]	–	Plastics/resins monomer
Ethylene dibromide [106-93-4]	–	Chemical intermediate, fumigant, fuels
Formaldehyde [50-00-0] (1995)	Nasopharynx	Plastics, textiles, laboratory agent
4,4´-Methylene bis(2-chloroaniline) (MOCA) [101-14-4] (1993)	Bladder	Rubber manufacture
Polychlorinated biphenyls [1336-36-3]	Liver, bile ducts, leukaemia, lymphoma	Electrical components
Silica [14808-60-7], crystalline	Lung	Stone cutting, mining, glass, paper
Styrene oxide [96-09-3]	–	Plastics, chemical intermediate
Tetrachloroethylene [127-18-4] (1995)	Oesophagus, lymphoma	Solvent, dry cleaning
Trichloroethylene [79-01-6] (1995)	Liver, lymphoma	Solvent, dry cleaning, metal
Tris(2,3-dibromopropyl)phosphate [126-72-7]	–	Plastics, textiles, flame retardant
Vinyl bromide [593-60-2]	–	Plastics, textiles, monomer
Vinyl fluoride [75-02-5] (1995)	–	Chemical intermediate
Industrial processes and occupations		
Art glass, glass containers and pressed ware, manufacture of (1993)	Lung, stomach	
Hairdresser or barber (occupational exposure as a) (1993)	Bladder, lung	
Non-arsenical insecticides (occupational exposures in spraying and application of) (1991)	Lung, myeloma	
Petroleum refining (occupational exposures in) (1989)	Leukaemia, skin	

[a]Year in parenthesis, year in which the evaluation was made subsequent to the 1987 Supplement 7 Working Group for agents, mixtures or exposure circumstances considered in Vols 43–63 of the *Monographs*. Number in square brackets, CAS Registry No.

occupational, there are groups of individuals exposed to them because of their work. For example, hospital workers are exposed to hepatitis B virus, food processors are exposed to aflatoxins from contaminated foodstuff, outdoor workers are exposed to ultraviolet radiation or diesel engine exhaust, and bar staff are exposed to environmental tobacco smoke.

Occupation may exert an indirect effect on cancer risk. For example, employed women, in particular those in high social classes, may have fewer pregnancies and be older at their first pregnancy than unemployed women – two factors that are linked to risk of breast cancer.

It is important to note that the known or highly suspected occupational carcinogens exert their effects on a limited number of cancer sites – namely the organs of the respiratory tract, the urinary bladder, the liver, the skin and the lymphatic and haematopoietic system. Cancers of these organs, with the exception of the lymphatic and haematopoietic system, are among those showing the strongest social class gradients (see the chapter by Faggiano *et al.* in this book), suggesting an important role of occupation in social class differences.

Estimates of cancers due to occupational risk factors

Different estimates of cancer risk attributable to occupation vary greatly. A summary of existing estimates is shown in Table 4. The large variability in the estimates arises from the differences in the data sets used and on the assumptions applied.

Most of the published estimates of the fraction of cancers attributable to occupational risk factors are not based on accurate measures of the proportions of exposed subjects and the degree of exposure. An exception is the paper by Vineis and Simonato (1991), which provided estimates of the number of cases of lung and bladder cancer attributable to occupation derived from a detailed review of case–control studies, and demonstrated that in specific populations located in industrial areas the proportion of lung cancer due to occupational exposures may be as high as 40%; these estimates were dependent not only on the local prevailing exposures, but also to some extent on the method of defining and assessing exposure.

The most generally accepted estimates of cancers attributable to occupations, however, are those

Table 3. Environmental agents and exposures that may be encountered in occupational settings evaluated in IARC *Monographs* (Vols 1–63) as carcinogenic (IARC Group 1) or probably carcinogenic (IARC Group 2A) to humans

Agent/exposure[a]	Target organ[b]
IARC Group 1	
Aflatoxins [1402-68-2] (1993)	Liver
Chronic infection with hepatitis B virus (1993)	Liver
Chronic infection with hepatitis C virus (1993)	Liver
Erionite [66733-21-9]	Lung, pleura
Radon [10043-92-2] and its decay products (1988)	Lung
Infection with *Schistosoma haematobium* (1994)	Bladder
Solar radiation (1992)	Skin
Tobacco smoke	Lung, bladder, oral cavity, pharynx, larynx, oesophagus, pancreas
IARC Group 2A	
Benz[a]anthracene [56-55-3]	–
Benzo[a]pyrene [50-32-8]	–
Dibenz[a,h]anthracene [52-70-3]	–
Diesel engine exhaust (1989)	(Lung, bladder)
IQc (2-Amino-3-methylimidazo[4,5-f]quinoline) [76180-96-6] (1993)	–
N-Nitrosodimethylamine [62-75-9]	–
Ultraviolet radiation A (1992)	(Skin)
Ultraviolet radiation B (1992)	(Skin)
Ultraviolet radiation C (1992)	(Skin)

[a]Year in parenthesis, year in which the evaluation was made subsequent to the 1987 Supplement 7 Working Group for agents, mixtures or exposure circumstances considered in Vols 43–63 of the *Monographs*. Number in square brackets, CAS Registry No.

[b]Suspected target organs are given in parentheses.

Table 4. Estimated proportions of cancer attributable (PAR) to occupations in selected studies

Study	Population	PAR and cancer site	Comments
Higginson & Muir, 1976	Not stated	1–3% total cancer	No detailed presentation of assumptions
Doll & Peto, 1981	United States, early 1980	4% (range 2–8%) total cancer. In men: 6.8% all cancers, 4% liver, 2% larynx, 15% lung, 25% nose, 25% pleura, 4% bone, 10% skin (non-melanoma), 1% prostate, 10% bladder, 10% leukaemia. In women: 1.2% all cancers	Based on all studied cancer sites; reported as 'tentative' estimate
Hogan & Hoel, 1981	United States	3% (range 1.4–4.4%) total cancer	Risk associated with occupational asbestos exposure
Vineis & Simonato, 1991	Various	1–5% lung cancer, 16–24% bladder cancer	Calculations on the basis of data from case–control studies.

presented in a detailed review by Doll and Peto (1981) on the causes of cancer in the population of the United States of America in 1980. These authors concluded that about 4% of all deaths due to cancer may be caused by occupational carcinogens, with 'acceptable limits' (that is, still plausible in view of all the evidence at hand) of 2% and 8%. These authors also provided an estimate of this proportion for specific cancer sites (Table 4), with pleural, sinonasal and lung cancer having the highest proportions.

These proportions are dependent on how causes other than occupational exposures contribute to the development of cancers. For example, the proportion of lung cancer attributable to occupational exposures would be higher in a population of lifetime non-smokers than in a population containing the same proportion of exposed workers and a higher proportion of smokers. Furthermore, if one considered not the whole population (to which most of the estimates refer) but the segments of the adult population in which exposure to occupational carcinogens almost exclusively occur (manual workers in mining, agriculture and industry, broadly taken – who in the USA numbered 31 million out of a population aged 20 and over of 158 million), the proportion of cancer deaths attributable to occupational exposure would be substantially higher than the 4% in the overall population.

Estimates of the role of occupational cancer in social class differences in cancer occurrence

One possible approach to estimate the contribution of occupational exposure to carcinogens to differences in cancer occurrence by social class is to calculate a measure of association between social class and cancer risk after excluding those cancers that may be attributable to occupation, and to compare it with the same measure based on all cancers. In the case of the comparison between two social classes, this approach can be formalized as:

$$c = \frac{R_c - R_a}{R_c - 1} \times 100,$$

where R_c is the 'crude' measure of association, equal to the ratio of the rate of cancer in the lower class over the rate in the upper class (r_1 / r_0), R_a is the 'adjusted' measure once the contribution of occupation is accounted for ($R_a = r_1'/r_0'$), and c is the percentage of the difference explained by the adjustment. One can calculate r_1' and r_0' as follows:

$$r_1' = (r_1 p_1 - (r_1 p_1 + r_0 p_0)db)/p_1, \text{ and}$$
$$r_0' = [r_0 p_0 - (r_1 p_1 + r_0 p_0)d(1 - b)]/p_0,$$

where p_1 and p_0 are the proportion of subjects in the two classes, d is the estimate of the proportion of cancers attributable to occupation and b is the proportion of such cancers occurring in the lower social class. When $b = 1$ (that is, it is assumed that

Table 5. Ratios of cancer mortality between manual and non-manual social classes with and without excluding cancers attributable to occupational exposures (England and Wales, 1971)[a]

Cancer site	Crude rate ratio (R_c)[b]	Rate ratio for the proportion of cancers not attributable to occupation (R_a)[c]	Excess risk (%) attributable to occupation[d]
Liver	1.16	1.09	42
Larynx	1.76	1.71	5
Lung	1.71	1.37	48
Nose	1.38	0.90	100
Skin (non-melanoma)	1.77	1.55	29
Prostate	1.19	1.17	9
Bladder	1.36	1.17	52
All cancers	1.40	1.27	32

[a]Based on 25–64 years cumulative rates reported by Logan (1982). Only cancer sites that have been strongly related with occupational exposures are reported. Proportions of cancers attributable to occupation were derived from Doll & Peto (1981); all cancers related to occupation were assumed to occur among manual workers.

[b]Ratio of the rate among manual workers to the rate among non-manual workers.

[c]As crude rate ratio, after excluding cancers attributable to occupation (see text for details).

[d]Percentage of the crude rate ratio accounted for by cancers attributable to occupation, or $[(R_c - R_a)/(R_c - 1)] \times 100$.

all cancers attributable to occupation occur in the lower social class), $r_0' = r_0$. This method can be easily expanded to a comparison of more than two classes.

This approach has been applied to the 1971 cancer mortality data of England and Wales reported by Logan (1982; see the chapter by Faggiano *et al.* in this book for detailed results). Cumulative mortality rates between ages 25 and 64 were calculated for the combined social classes I, II and III-NM (r_0) and III-M, IV and V (r_1). The values for 1971 of $p_1 = 0.65$ and $p_0 = 0.35$ were also derived from Logan (1982). The proportions of cancer attributable to occupational exposures (d) proposed by Doll and Peto (1981) were used (Table 4). Table 5 shows the results among males for those cancer sites, included in the review by Doll and Peto (1981), that showed a social class gradient ($r_1 > r_0$) in the data reported by Logan (1982), assuming $b = 1$. Occupational exposures were estimated to account for about a third of the difference in total cancer mortality, for the whole difference for sinonasal cancer and for about half of the difference for lung and bladder cancer.

Key elements in these estimates are the parameters b and d. In particular, the values for d were derived from the review of Doll and Peto (1981). These authors stress that their values may represent an overestimation of the true proportion of cancers due to occupational exposures; in addition, they attempted an estimate for the United States, and this proportion in other countries may be smaller. The effect of the assumptions on the value of b and d was addressed by repeating the analysis on lung cancer with different values for these two parameters (Figure 1). Although the figure suggests the role of occupation in social class differences in cancer is small if the proportion of lung cancers attributable to occupation is below 10% or if the proportion of such cancers occurring in manual workers is below 90%, the most reliable estimates for the percentage of the social class difference due to occupation are in the range 20–50%.

Direct evidence from epidemiological studies

While in many epidemiological studies socioeconomic status has been treated as a potential confounder in the analysis of occupational cancer risk

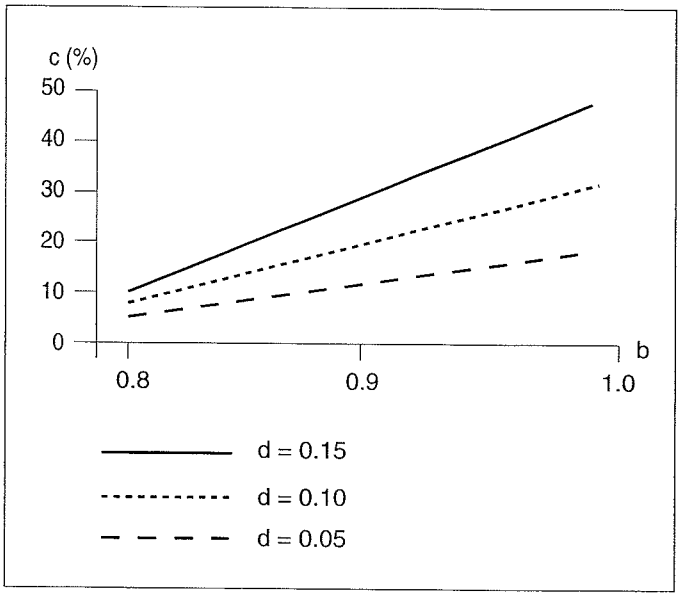

Figure 1. Percentage of difference in lung cancer between manual and non-manual workers attributable to occupational exposure (c) according to the proportion of cancers attributable to occupation occurring among manual workers (b), and the proportion of cancers attributable to occupation (d).

factors, no study has addressed this relationship from the other point of view – that is, to what extent occupational exposure confounds the association between social class and cancers. In the traditional approach, the increased cancer risk among certain occupational groups is seen as resulting from the combined effect of an 'occupational' factor, related to workplace exposures, and a 'social' factor, related to lifestyle or other determinants of cancer risk. It has therefore been proposed that the latter be adjusted to obtain an unbiased estimate of the former (Fox & Adelstein, 1978). Different methods have been proposed for such adjustment, such as comparison of cancer mortality of men and their wives (Office of Population Censuses and Surveys, 1978), standardization for social class (Fox & Adelstein, 1978; Milham 1985), and multivariate regression including a social class term in the model (Miettinen & Rossiter, 1990).

A number of studies have addressed this issue analytically. For example, Siemiatycki *et al.* (1988) have calculated the degree of confounding introduced by tobacco smoking, ethnicity (French versus other) and family income (used as an indicator of social class) in the association between lung cancer and 25 occupations in a large case–control study conducted in Montreal, Canada. The results did not suggest a large confounding effect of family income: for five of the 25 occupations, family income exerted a stronger confounding effect than either smoking or ethnicity, and only in the same number of occupations the confounding bias was greater than 1.10.

The approach of adjusting for social class when studying occupational carcinogens has been criticized, as it will lead to an underestimation of the risk if the group chosen for comparison (for example, other occupations in the same social class stratum) also has job-related carcinogenic exposures (Brisson *et al.*, 1987).

Although no direct evidence can therefore be drawn from analytical studies, it is clear that a confounding effect exists, which is likely to act in both directions, and that the difference between social groups defined by occupation (for example, manual and non-manual workers) in cancer risk cannot be viewed as indicating solely an effect of occupational exposures.

Interaction between occupational exposures and other cancer risk factors

An important aspect to take into account when considering occupational exposures as a cause of social class differences in cancer is the possibility of an interaction between these exposures and other risk factors in determining cancer risk. Although interaction between contributory factors may be a general characteristic of carcinogenesis – and the interactions between alcohol drinking and tobacco smoking in the etiology of cancer of the upper aerodigestive tract (Boyle *et al.*, 1992) and between aflatoxin intake and chronic infection with hepatitis B virus in the etiology of liver cancer (Ross *et al.*, 1992) have been extensively studied – it may be particularly important when considering occupational exposures, as it offers a particularly strong argument in favour of prevention.

Strictly speaking, interaction occurs when the combined effect of two exposures differs from the sum (additive model) or the product (multiplicative model) of the effect of each exposure, or:

$$R_{AB} \neq R_A + R_B - 1 \quad \text{(additive model), and}$$
$$R_{AB} \neq R_A \times R_B \quad \text{(multiplicative model),}$$

where R_A and R_B are the relative risk among those exposed to binary exposure variables A and B, and R_{AB} is the relative risk of those exposed to both. In

practice, however, one also speaks of interaction when $R_{AB} = R_A \times R_B$, and the example below refers to this situation.

Let us consider an example of two populations of manual and non-manual workers differing only either for exposure to tobacco smoking (with relative risk of lung cancer of 10 among smokers as compared with non-smokers) or for an occupational exposure, say asbestos (with relative risk of 5), assuming no interaction according to a multiplicative model (relative risk among those exposed to both factors of 50), and a rate of lung cancer of 1/1000 among those exposed to neither factor. If 40% of nonmanual workers smoke and no nonmanual workers are exposed to asbestos, their overall lung cancer rate would be 4.6/1000 (1/1000 $\times$ 0.6 + 10/1000 $\times$ 0.4). The rate among manual workers with a 20% higher proportion of smokers would be 6.4/1000 (1/1000 $\times$ 0.4 + 10/1000 $\times$ 0.6) while the rate with 40% smokers but 10% of the workers exposed to asbestos would be 6.44/1000 (1/1000 $\times$ 0.54 + 10/1000 $\times$ 0.36 + 5/1000 $\times$ 0.06 + 50/1000 $\times$ 0.04). Therefore, a smaller increase in the proportion of those exposed to a weaker risk factor has a similar or greater effect than a larger increase in the proportion of those exposed to a stronger risk factor, because of the very strong risk in the small group of workers exposed to both factors. Note that no association was assumed between the two exposures – that is, the proportion of smokers was considered to be the same among workers exposed and unexposed to asbestos. Had such an association been present, the results would have been even more extreme.

This example shows that when groups, such as social class groups, differ in their exposure to more than one factor, small differences in risk in one factor that interacts with other factor(s) may have unexpectedly large effects on the overall difference in risk. In most cases, however, information on the distribution of exposures and their pattern of interaction is lacking, and one can only speculate about the relative contributions of each factor and of their interaction.

A problem related to the interaction between occupational exposures and other risk factors is exposure to mixed occupational agents; this may be through work in an environment where several carcinogenic agents are present or through exposure to complex mixtures. In these situations, one should consider that, even if the exposure to each component of the mixture may have a relatively small effect on cancer risk, the exposure to the whole mixture, resulting from the sum of the individual effects and from the interactions, may be large. Again, detailed data are rarely available to evaluate the relevance of this problem both in specific situations and in global estimates such as those presented above (Vainio *et al.*, 1990).

Short-term workers

Short-term workers are particularly interesting with respect to the association between low social class, occupational exposure to carcinogens and cancer risk. In many occupational epidemiological studies, the characterization of job tasks, exposures and social class indicators for each member of the cohort is problematic, but information on duration of employment is available. A higher cancer risk has been frequently observed in short-term workers (Stewart *et al.*, 1990). Short-term workers are usually defined as those with less than six months or one year of employment and they constitute a group with high job mobility. For example, Figure 2 shows as an example the standardized mortality ratios for several types of cancer among workers producing man-made vitreous fibres, followed-up between 1950 and 1990 in seven European countries, by duration of employment. Two explanations are possible for this difference. First, short-term workers may be at increased risk of cancer because of employment in particularly hazardous or dirty jobs. Second, the fact that mortality from most cancers was higher among workers with less than one year of employment as compared with longer-term workers suggests that extraoccupational factors may play an important role. Short-term workers may differ from other workers in personal habits entailing a higher risk of cancer. In this sense, specific groups of manual workers such as short-term workers may contribute disproportionately to social class differences, even in those cancers that are not directly caused by occupational exposures.

Conclusions

The complete assessment of the confounding effect of occupational exposures on the association between social class and cancer risk is complicated by a number of factors: incomplete knowledge about occupational carcinogens; possible interaction

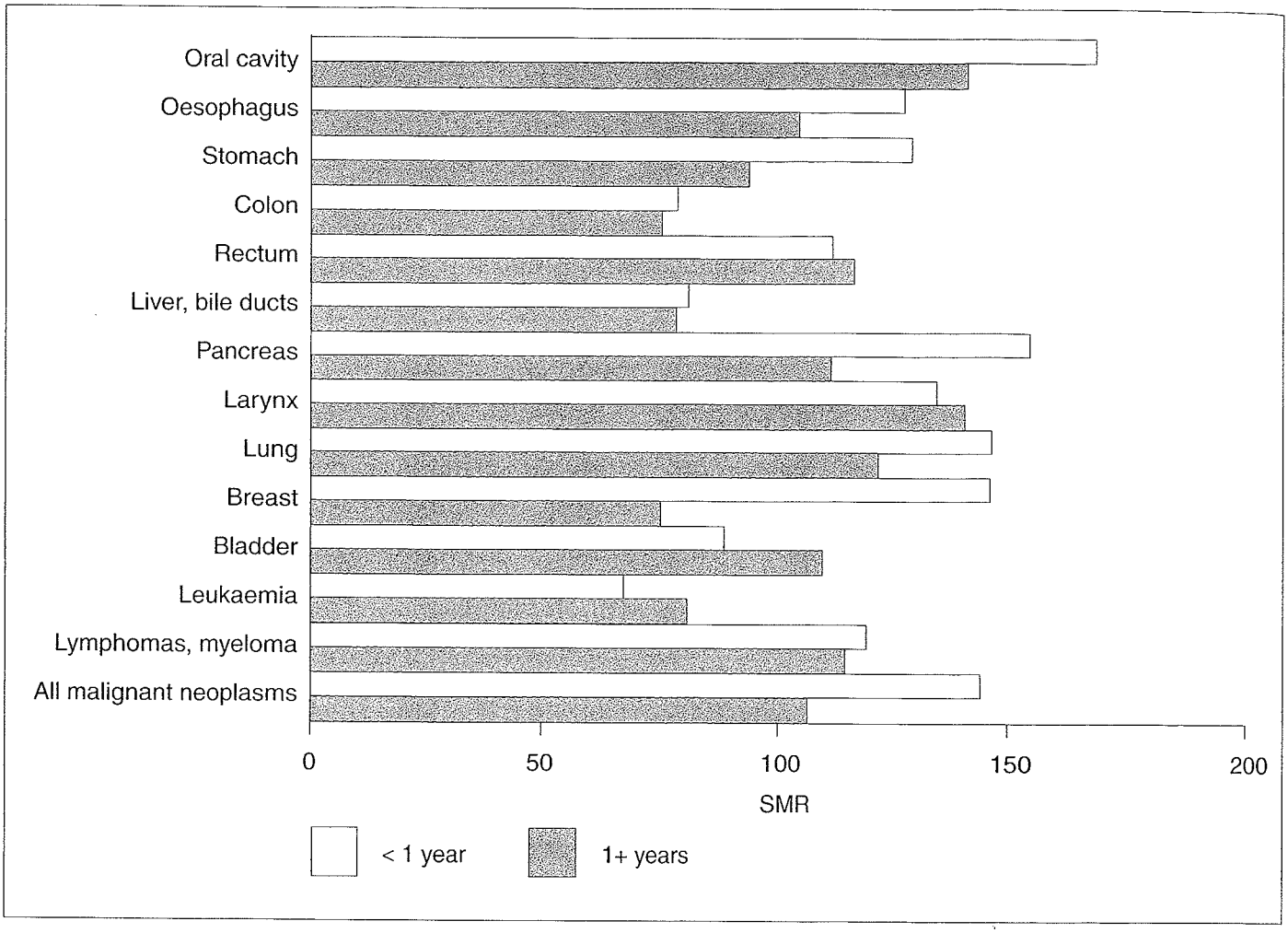

Figure 2. Standardized cancer mortality ratios (SMRs) of workers in man-made vitreous fibre production, by duration of employment.

between occupational carcinogens and other risk factors linked with social class (for example, tobacco smoking); and lack of information on the distribution of other socially determined risk factors.

A full assessment and control of confounding could be achieved only if all carcinogenic exposures (both occupational and extraoccupational) were known and measured; in practice, however, this is not possible because of both ignorance about the carcinogenicity of many agents and incomplete information on exposure to known carcinogens.

On the basis of the available evidence, occupational exposures have been estimated to be responsible, in developed countries, for approximately a third of the excess of all cancers occurring in lower social classes as compared with higher social classes, and for approximately half of this difference for important occupationally related cancers such as lung and bladder cancer. Their contribution to social differences in cancer risk in women and in people from developing countries is likely to be smaller. The figure of a third of excess cancers among men from industrialized countries in the lower social classes caused by occupational exposures may represent an overestimation as it is based on the results of epidemiological studies that investigated the effect of relatively high exposure levels occurring in the past (this argument, however, would not apply to developing countries). Other considerations suggest the possibility of an underestimation – in particular, the lack of knowledge on the interaction among different occupational exposures and between those and other cancer risk factors, and the possibility that yet undetected occupational carcinogens have operated and are still operating.

References

Boffetta, P., Kogevinas, M., Simonato, L., Wilbourn, J. & Saracci, R. (1995) Current perspectives on occupational cancer risk. *Int. J. Occup. Environ. Health,* 1, 315–325

Boyle, P., Macfarlane, G.J., Zheng, T., Maisonneuve, P., Evstifeeva, T. & Scully, C. (1992) Recent advances in epidemiology of head and neck cancer. *Curr. Opin. Oncol.*, 4, 471–477

Brisson, C., Loomis, D. & Pearce, N. (1987) Is social class standardisation appropriate in occupational studies? *J. Epidemiol. Community Health*, 41, 290–294

Doll, R. & Peto, R. (1981) *The causes of cancer. Quantitative estimates of avoidable risk of cancer in the United States today*. New York, Oxford University Press

Fox, A.J. & Adelstein, A.M. (1978) Occupational mortality: work or way of life? *J. Epidemiol. Community Health*, 32, 73–78

Higginson, J. & Muir, C.S. (1976) The role of epidemiology in elucidating the importance of environmental factors in human cancer. *Cancer Detect. Prev.*, 1, 79–105

Hogan, M.D. & Hoel, D.G. (1981) Estimated cancer risk associated with occupational asbestos exposure. *Risk Analysis*, 1, 67–76

IARC (1972–1995) *IARC monographs on the evaluation of carcinogenic risks to humans* (Vols 1–63). Lyon, International Agency for Research on Cancer

Logan, W.P.D. (1982) *Mortality from cancer in relation to occupation and social class* (IARC Scientific Publication No. 36). Lyon, International Agency for Research on Cancer

Miettinen O.S. & Rossiter, C.E. (1990) Man-made mineral fibers and lung cancer. Epidemiologic evidence regarding the causal hypothesis. *Scand. J. Work Environ. Health*, 16, 221–231

Milham, S. (1985) Improving occupational standardized proportionate mortality ratio analysis by social class stratification. *Am. J. Epidemiol.*, 121, 472–475

Office of Population Censuses and Surveys (1978) *Occupational mortality decennial supplement, 1970–1972, England and Wales*. London, Her Majesty's Stationery Office

Ross, R.K., Yuan, J.M., Yu, M.C., Wogan, G.N., Qian, G.S., Tu, J.T., Groopman, J.D., Gao, Y.T. & Henderson, B.E. (1992) Urinary aflatoxin biomarkers and risk of hepatocellular carcinoma. *Lancet*, 339, 943–946

Saracci, R. & Boffetta, P. (1994) Interactions of tobacco smoking with other causes of lung cancer. In: Samet, J.M., ed., *Epidemiology of lung cancer*. New York, Dekker. pp. 465–493

Siemiatycki, J., Wacholder, S., Dewar, R., Cardis, E., Greenwood, C. & Richardson, L. (1988) Degree of confounding bias related to smoking, ethnic group, and socioeconomic status in estimates of the associations between occupation and cancer. *J. Occup. Med.*, 30, 617–625

Stewart, P.A., Schairer, C. & Blair, A. (1990) Comparison of jobs, exposures, and mortality risks for short-term and long-term workers. *J. Occup. Med.*, 32, 703–708

Swerdlow, A.J. (1990) Effectiveness of primary prevention of occupational exposures on cancer risk. In: Hakama, M., Beral, V., Cullen, J.W. & Parkin, D.M., eds, *Evaluating effectiveness of primary prevention of cancer* (IARC Scientific Publication No. 103). Lyon, International Agency for Research on Cancer. pp. 23–56

Vainio, H., Sorsa, M. & McMichael, A.J. (1990) *Complex mixtures and cancer risk* (IARC Scientific Publication No. 104). Lyon, International Agency for Research on Cancer

Vineis, P. & Simonato, L. (1991) Proportion of lung and bladder cancers in males resulting from occupation: a systematic approach. *Arch. Environ. Health*, 46, 6–15

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