# ASSOCIATION OF 143 FACTORS OTHER THAN SMOKING WITH LUNG CANCER

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Contents

INTRODUCTION

In July 1991, P.N. Lee prepared a first report on the role of confounding variables in the relationship between ETS and lung cancer. That report, inter alia, listed a number of factors known or thought to be a cause of lung cancer, subdividing them into those considered, definite, probable and possible causes of lung cancer and those considered probably not a cause of lung cancer. That review only gave relatively cursory supportive evidence for this belief.

While not intended as a full and comprehensive review of the evidence for each factor, this report considers each factor in rather more detail. The intent was to prepare, for each factor, a brief summary of the key evidence, giving enough detail for the reader to be able to gain an insight into the consistency and strength of the evidence and the likely magnitude of any association with lung cancer. No attempt has been made to do a full literature search for evidence on each risk factor. Major sources of information have been the IARC Monographs and P.N. Lee's quite extensive files on lung cancer risk factors accumulated over many years. When reading available papers revealed the files missed important other papers, copies of these were obtained and considered. However, no claims are made that all relevant papers have been considered.

The major part of the work was carried out by A.J. Thornton who is leaving epidemiology for ecology at the end of June 1994. Her impending departure has meant a few risk factors could not be covered in the planned style. Nevertheless, the report should prove a valuable reference work.

THE RISK FACTORS

1. Acrylonitrile

Table 1 details the studies found which attempted to relate lung cancer risk to exposure to acrylonitrile. The six standardized mortality ratios calculated ranged from 100-400, with four of them being raised.

The main drawback of the studies is that none of them appeared to have taken any objective measurements of the levels of acrylonitrile the subjects were exposed to. It is obvious, therefore, that inaccuracies may have been introduced. Not surprisingly, in view of this lack of information, IARC considered the evidence for the carcinogenicity of acrylonitrile to humans to be "limited" [2].

Table 1: Estimates of standardized incidence ratio for exposure to acrylonitrile

| Study | Population | Standardized mortality ratio |
|---|---|---|
| US Dept of Labor (1978)[1] | US male textile fibre plant workers | 400[2] |
| Waxweiler et al (1981)[3] | US rubber workers | 100 |
| Werner and Carter (1981)[3] | UK male polymerization workers | 118[2,4] |
| Delzell and Monson (1982)[3] | US rubber workers | 153[2] |
| O'Berg et al (1985)[3] | US male textile fibre plant workers | 139[2] |
| Chen et al (1987)[3] | US textile fibre plant workers | 100 |

1 From International Agency for Research on Cancer (1979)

2 Estimated from data given

3 From International Agency for Research on Cancer (1987)

4 Tumours of the respiratory system

References

1. International Agency for Research on Cancer (1979) Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 19: Some monomers, plastics and synthetic elastomers, and acrolein, 73-113. IARC, Lyon.

2. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42, 79-80. IARC, Lyon.

## 2. Adverse life situations

Table 2 gives details of those studies found which attempted to relate the risk of lung cancer to having previously suffered from an adverse life experience, such as divorce, bereavement, unhappy home or similar situations. One relative risk was estimated, of 2.73, along with two standardized incidence ratios, of 176 and 214. One study reported that adverse life situations, both in childhood and adulthood, occurred more frequently in lung cancer cases than in controls, while another reported that smokers with lung cancer were more likely to have been severely shocked by war experiences than smokers without lung cancer. Finally, one study observed an increasing gradient in lung cancer mortality across groups of single, married, widowed and divorced men.

However, it should be noted that some inconsistencies were found. For example, in the studies by Kissen childhood parental bereavement appeared to be associated with lung cancer risk, while sibling bereavement and adult bereavement of a close relative were not. Thus, while the findings of the studies are suggestive of an influence of adverse life situations on the risk of lung cancer, the evidence is not particularly strong.

Table 2: Estimates of relative risk for adverse life situations

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Smith (1966)[1] | Scottish men aged 55-64 | Gradient in lung cancer mortality increased across single, married, widowed and divorced men |
| Kissen (1967)/ Kissen (1969) | Male patients aged 55-64 | Adverse life situations occurred more frequently in lung cancer cases than in control group |
| | As above | Adverse life situations in childhood occurred twice as frequently in lung cancer cases than in control group |
| Blohmke et al (1981) | German men | Smokers with lung cancer had more frequently been severely shocked by war experiences than smokers in control group |

Table 2 continued

| | | |
|---|---|---|
| Jones et al (1984) | UK residents | Standardized incidence ratio of 176 (62-350) estimated for subjects widowed before 1966 |
| | As above | Standardized incidence ratio of 214 (38-533) estimated for subjects widowed between 1966-68 |
| Liu et al (1993) | Chinese residents | Relative risk of 2.73(1.34-5.64) found for those suffering "serious psychic trauma" |

1 From Kissen (1969)

References

1. Blohmke M, Engelhardt BV and Stelzer O (1981) Investigations on the personality of patients with pulmonary carcinomas compared to a control group. Med Biol Environ, 9, 67-75.

3. Jones DR, Goldblatt PO and Leon DA (1984) Bereavement and cancer: some data on deaths of spouses from the longitudinal study of Office of Population Censuses and Surveys. Br Med J, 289, 461-464.

4. Kissen DM (1967) Psychosocial factors, personality and lung cancer in men aged 55-64. Br J Med Psychol, 40, 29-43.

5. Kissen DM (1969) The present status of psychosomatic cancer research. Geriatrics, 24, 129-137.

6. Liu J-Z, Hu H-S, Hu Y-H, Lu P and Hao L-Y (1993) A study on the relation between indoor exhaust and lung cancer. Proc Indoor Air, 1, 489-492.

## 3. Air pollution

Although many studies have attempted to estimate potential risks between lung cancer and specific pollutants, several have also considered general air pollution, and details of these are given in Table 3. Thirty-six relative risks were presented from cohort studies, ranging from 0.95-2.50. Only four risk estimates did not exceed 1.00. Estimates of the percentage relative differences in mortality or morbidity between various populations were also presented by some of the studies, and these ranged between 0-405%. Additionally, one study estimated that up to 40% of lung cancers were caused by urban factors other than smoking. For the case-control studies the estimates of relative risk ranged from 1.00-4.0, with 18 out of 19 being raised.

The major drawback with these studies is that only seven [5-8,12,14,16] made objective measurements of air pollution levels, with four others [1,3,4,13] relying instead on markers such as place of residence, and the remainder failing to give any details. Thus, it is obvious that inaccuracies may have been introduced. Additionally, as air pollution is a complex mix of chemicals, the actual exposures will differ from study to study, depending on the source of the pollution, and it will be impossible to separate out the effects of any one compound.

There is also the further problem of confounding by the effects of tobacco smoking, as it has been suggested that differences exist between the smoking habits of urban and rural dwellers [1,3,6,9,10,12-15]. Although most of the studies gathered data on the respondents' smoking habits, and carried out some type of adjustment during their analyses, two studies (Ehrenberg, Ponka) did not, and, in a further 10 studies (Pershagen and Simonato, Clemmesen and Nielsen, Hoffman and Gilliam, Griswold, Mancuso, Eastcott, Dean 1959, Levin, Mills, Xu) it was not possible to tell whether adjustment had been carried out due to insufficient information being given.

Therefore, although some of the studies do appear to show a higher risk of lung cancer in urban populations, it is not clear how much of this effect is due to air pollution. It has been stated that "urban air contains carcinogenic compounds, but the relatively small excess risk to men occupationally exposed to large concentrations of these compounds raises doubt about the relevance to lung cancer of the much lower levels

found in the air of even the most polluted city" [11]. It is not altogether surprising, then, that the possibility of a link between air air pollution and cancer has been described as "questionable", with any risk, if it does exist, "likely to be extremely small" [2].

Table 3: Estimates of relative risk for exposure to air pollution

| Study | Location | Relative risk (95% limits) Male | Female |
|---|---|---|---|
| Cohort studies: | | | |
| Clemmesen and Nielsen (1952)[1] | Denmark | 405[2] | 40 |
| Hoffman and Gilliam (1954)[1] | USA | 81[3] | 29 |
| Griswold et al (1955)[1] | Connecticut, USA, 1941-46 | 68[2] | 41 |
| | 1947-51 | 75[2] | 24 |
| Mancuso et al (1955)[1] | Ohio, USA | 78[3] | - |
| Eastcott (1956)[1] | New Zealand | --51[3]-- | |
| Hammond and Horn (1958)[4] | USA | 1.33 | - |
| Dean (1959)[1] | South Africa | --16[3]-- | |
| Levin et al (1960)[1] | New York State, USA | 92[2] | 33 |
| Mills (1960)[1] | Cincinnati, USA | 177[3] | 0 |
| Hammond (1962) | USA | 1.36 | - |
| Buell et al (1967)[4] | California, USA | 1.30 | - |
| Cederlof et al (1975)[4] | Sweden - city dwellers | 1.60 | Similar |
| | Town dwellers | 1.20 | trend |
| Lloyd (1978) | Scotland | 2.5 ($p<0.001$) | - |
| Hammond and Garfinkel (1980) | USA, large metropolitan area | 1.11[5] | - |
| | Small metropolitan area | 1.10[5] | - |
| | Non-metropolitan area | 0.95[5] | - |
| Doll and Peto (1981)[4] | UK | --1.00-- | |
| Ehrenberg et al (1985)[4] | Sweden | 40%[6] | 20% |

Table 3 continued

| | | | |
|---|---|---|---|
| Xiao and Xu (1985) | Shen Yang, China | --1.47(p <0.05)-- | |
| Tenkanen and Teppo (1987)[4] | Finland | 1.20 | - |
| Pershagen and Simonato (1990) | Miyagi, Japan | 1.1 | 1.1 |
| | Slovakia, Czechoslovakia | 1.0 | 1.4 |
| | Saarland, FRG | 1.2 | 1.3 |
| | Calvados, France | 1.2 | 1.2 |
| | Doubs, France | 1.4 | 1.7 |
| | Szabolcs, Hungary | 1.2 | 1.7 |
| | Norway | 1.6 | 1.9 |
| | Cluj County, Romania | 1.0 | 1.4 |
| | Vaud, Switzerland | 1.1 | 1.6 |
| | England and Wales | 1.3 | 1.3 |
| | New South Wales, Australia | 1.2 | 1.5 |
| Ponka et al (1993) | Helsinki, Finland | 1.08[5] | 1.86 |
| Case-control studies: | | | |
| Stocks and Campbell (1955)[4] | North Wales/Liverpool | --1.1-3.4-- | |
| Haenszel et al (1962)[4] | USA | 1.43 | - |
| Haenszel and Taeuber (1964)[4] | USA | - | 1.27 |
| Dean (1966) | Northern Ireland | 3.52[5] | - |
| Hitosugi (1968)[4] | Osaka, Japan | --1.2-1.8-- | |
| Dean et al (1977)[4] | North-east England | 1.70 | 1.60 |
| Dean et al (1978)[4] | North-east England | 2.30 | 1.40 |
| Vena (1982) | Erie County, USA | 1.09 (0.66-2.20) | - |
| Ulmer (1982) | Ruhr, Germany | --1.57 (p<0.05)-- | |
| Samet et al (1987)[4] | New Mexico, USA | --1.00-- | |
| Xu et al (1989) | Shen Yang, China | 2.3 (1.7-2.9) | 2.5 (1.8-3.5) |
| He et al (1990) | Xuan Wei, China | 4.0 | 3.7 |
| Jedrychowski et al(1990) | Cracow, Poland | 1.48 (1.08-2.01) | 1.17 (0.7-1.96) |
| Katsouyanni et al (1991) | Athens, Greece | - | 2.13[5] (0.92-4.91) |

Footnote to Table 3

1 From Wynder and Hammond (1962)

2 Percentage relative difference in morbidity between study populations

3 Percentage relative difference in mortality between study populations

4 From Pershagen (1989)

5 Estimated from data given

6 Percentages of cancers due to "urban factors"

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References

1. Dean G (1966) Lung cancer and bronchitis in Northern Ireland. Br Med J, 1, 1506-1514.

2. Godlee F (1991) Air pollution: II - road traffic and modern industry. Brit Med J, 303, 1539-43.

3. Hammond EC (1962) Air pollution, smoking, and health. Texas J Med, 58, 639-647.

4. Hammond EC and Garfinkel L (1980) General air pollution and cancer in the United States. Prev Med, 9, 206-211.

5. He X, Chapman RS, Yang R, Cao S, Mumford JL and Liang C (1990) Lung cancer and indoor air pollution in Xuan Wei, China: current progress. In: Kasuga H (ed.) Indoor Air Quality, 435-441. Springer-Verlag.

6. Jedrychowski W, Becher H, Wahrendorf J and Basa-Cierpialek Z (1990) A case-control study of lung cancer with special reference to the effect of air pollution in Poland. J Epidemiol Comm Health, 44, 114-120.

7. Katsouyanni K, Trichopoulos D, Kalandidi A, Tomos P and Riboli E (1991) A case-control study of air pollution and tobacco smoking in lung cancer among women in Athens. Prev Med, 20, 271-278.

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9. Pershagen G (1989) Air pollution and cancer. Published in IARC Monograph series?

10. Pershagen G and Simonato L (1990) Epidemiological evidence on air pollution and cancer. In: Tomatis L (ed.) Air pollution and human cancer, 63-74. Springer-Verlag.

11. Pike MC, Gordon RJ, Henderson BE, Menck HR and SooHoo J (19??) Air pollution. In: Fraumeni (ed.) High risk groups and cancer, 225-238. (Incomplete reference)

12. Ponka A, Pukkala E and Hakulinen T (1993) Lung cancer and ambient air pollution in Helsinki. Environ Int, 19, 221-231.

13. Ulmer WT (1982) Bronchial cancer in cities and rural districts in relation to smoking habits: epidemiological study on the city of Bochum. Inn Med, 9, 410-416.

14. Vena JE (1982) Air pollution as a risk factor in lung cancer. Am J Epidemiol, 116, 42-56.

15. Wynder EL and Hammond EC (1962) A study of air pollution carcinogenesis I: analysis of epidemiological evidence. Cancer, 15, 79-92.

16. Xiao H-P and Xu Z-Y (1985) Air pollution and lung cancer in Liaoning Province, People's Republic of China. Natl Cancer Inst Monogr, 69, 53-58.

17. Xu et al (1989) No reference given.

4. Alcohol

Although lack of time meant that a full evaluation of the possible association between lung cancer risk and alcohol drinking could not be presented in this document, the subject was reviewed by IARC in 1988 [1]. Their evaluation was based on fifteen cohort studies of alcoholics, of persons with higher than average consumption of alcoholic beverages and of the general population, and five case-control studies. The cohort studies yielded inconsistent results on the association between the drinking of alcoholic beverages and the risk for lung cancer, and smoking was only taken into account in five of the studies, while no association between alcohol consumption and lung cancer risk was seen in the case-control studies. In view of these results, IARC felt that there was "no indication that drinking of alcoholic beverages has a causal role in lung cancer".

References

1. International Agency for Research on Cancer (1988) Monographs on the evaluation of carcinogenic risks to humans. Volume 44: Alcohol drinking. IARC, Lyon.

## 5. Aluminium production

Table 5 gives details of the studies which investigated a possible association between working in aluminium production and the risk of lung cancer. The six standardized mortality ratios (SMR) given ranged from 114-174, with another study also finding a raised SMR but failing to give detailed results. Additionally, two estimates of relative risk were presented, both of which were above 1.00.

Workers in aluminium production are exposed to a wide variety of substances, frequently including aluminium compounds, carbon monoxide, chlorine and hydrogen chloride, coke, cryolite, fluorides, hydrogen fluoride, oil mists, pitch coal-tar and petroleum, polynuclear aromatic compounds, sulphur dioxide, and, less commonly, ammonia, asbestos, copper and copper oxide, cyanides, ozone, phosphine, silica, sodium hydroxide and welding fumes [1]. Information on measurements of benzo(a)pyrene concentrations was given by two studies (Konstantinov and Kuz'minykh, Spinelli et al), but apart from this no other data was available on the type of exposures experienced by the subjects in any of the studies. Thus, it is very difficult to determine which substances the workers were actually exposed to, and the effects of any one substance also remain unclear.

It has also been suggested that some of the studies (Gibbs, Rockette and Arena, Andersen) may be flawed due to an inappropriate choice of reference population, and that if a more suitable group had been selected the associations reported would have been reduced [3].

Despite these drawbacks, the consistency of the results from the various studies suggests that there may be an association between employment in aluminium production and the risk of lung cancer. In 1984, IARC classified aluminium production as "probably" carcinogenic to humans [1], but with the availability of results from further studies the evidence for carcinogenicity was later considered "sufficient" [2].

Table 5: Estimates of relative risk/standardized mortality ratio for aluminium production

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Konstantinov and Kuz'minykh (1971)[1] | USSR Soderberg process workers | >1.00 |
| Konstantinov et al (1974)[1] | USSR Soderberg process workers | >100* |
| Milham (1979)[1] | Prebake plant workers | 117* |
| Giovanazzi and D'Andrea (1981)[1] | Soderberg process plant workers | 174(p>0.05)* |
| Andersen et al (1982)[2] | Norwegian aluminium workers | 159(p<0.05)*[3] |
| Rockette and Arena (1983)[1] | White US horizontal-stud Soderberg process workers | 162(p<0.05)* |
| Gibbs (1985)[2] | Canadian Soderberg/prebake workers | 140(p<0.05)* |
| Mur et al (1987)[2] | French aluminium workers | 114*[3] |
| Spinelli et al (1991)[2] | Canadian Soderberg process workers | 1.10 |

* Standardized mortality ratio

1 From IARC (1984)

2 From Ronneberg and Langmark (1992)

3 Estimated from data given

References

1. International Agency for Research on Cancer (1984) Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 34: Polynuclear aromatic compounds, part 3, industrial exposures in aluminium production, coal gasification, coke production, and iron and steel founding, 37-64. IARC, Lyon.

2. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: an updating of IARC monographs volumes 1 to 42, 89-91. IARC, Lyon.

3. Ronneberg A and Langmark F (1992) Epidemiologic evidence of cancer in aluminum reduction plant workers. Am J Ind Med, 22, 573-590.

## 6. Antimony

Table 6 gives details of the only study found which gave data relevant to an investigation of the possible association between lung cancer risk and exposure to antimony. A standardized incidence ratio of 128 was calculated.

The main drawback of this study was that no objective measurements of exposure had been made. Therefore, it was impossible to determine the level of exposure to antimony, and to which other substances the workers had been exposed. Possible confounding exposures were noted to include arsenic, asbestos, cadmium, trivalent chromium, copper, lead, manganese, nickel oxide, zinc selenite, and sulphuric and hydrofluoric acids [1]. As several of these are thought to be potential carcinogens failure to record exposure to them may have introduced bias into the study results. Also, with only one study giving relevant results it is not really possible to evaluate the carcinogenicity of antimony to humans at this point.

Table 6: Estimate of standardized incidence ratio for exposure to antimony

| Study | Population | Standardized incidence ratio |
|---|---|---|
| Sankila et al (1990) | Finnish glass factory workers | 128(99-162)[1] |

### References

1. Sankila R, Karjalainen S, Pukkala E et al (1990) Cancer risk among glass factory workers: An excess of lung cancer? Br J Ind Med, 47, 815-818.

## 7. Arsenic

A number of studies were found which contained information on the possible association between exposure to arsenic and risk of lung cancer. Table 7 summarizes the relevant details. Seventeen relative risks were presented, ranging from 1.00-10.00, 14 of which were above 1.00. Ten standardized mortality ratios, of between 110-1189, were also given. Additionally, one study estimated an incidence rate of lung cancer of 205.6/100 000 per year when compared to the general male population, one reported 7% of deaths in smelter workers being due to lung cancer compared to 2.2-2.7% of deaths in workers in other areas, and one study simply stated that no excess in mortality from lung cancer was seen, but did not give any detailed results.

All of the studies for which the original papers were available had attempted to measure arsenic exposure, either by categorizing various jobs according to exposure [3-5], or by relying on indices such as length length of time of exposure [6]. However, the accounts of studies reported reported in the publications by IARC did not contain enough information to ascertain whether or not measurement of exposure had taken place.

Additionally, it has been suggested that, depending on the nature of their work, subjects exposed to arsenic may also be exposed to various other substances which may themselves be potential carcinogens. These include sulphur dioxide, chromium, nickel, iron, cadmium, radon, polyaromatic hydrocarbons such as benzpyrene, and various ore dusts [3-6]. As few of the studies measured for the possible occurrence of these other substances the exact nature of the subjects' exposures cannot be determined and it is difficult to separate out the effects of any one potential carcinogen.

Despite these drawbacks, when evaluating the data concerning the possible association between exposure to arsenic and risk of lung cancer, IARC considered the evidence for human carcinogenicity to be "sufficient" [1,2].

Table 7: Estimates of relative risk/standardized mortality ratio for exposure to arsenic

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Thiers et al (1967)[1] | French vineyard workers | >1.00 |
| Pinto et al (1968)[2] | Male copper smelter workers | 305*[3] |
| Lee and Fraumeni (1969) | US smelter workers | 329($p<0.01$)*[3] |
| Osburn (1969)[2] | Rhodesian gold miners | 205.6[4] |
| Nelson et al (1973)[2] | Residents in apple-growing area | No excess mortality seen |
| Milham and Strong (1974)[2] | Copper smelter workers | 222($p<0.001$)*[3] |
| Ott et al (1974)[2] | Insecticide packers | 3.2(2.0-5.0)[3,5] |
| Blot and Fraumeni (1975)[2] | US males living near copper, lead or zinc industries | 112* |
| | Females | 110* |
| Tokudome and Kuratsune (1976)[2] | Japanese copper smelter workers | 1189* |
| Pershagen et al (1977)[2] | Swedish males living near smelter | 250($p=0.002$)*[3] |
| Rencher et al (1977)[2] | Copper corporation workers | 7% of deaths in smelter workers due to neoplasm of respiratory tract compared to 2.2-2.7% in workers in other areas ($p<0.05$). |
| Axelson et al (1978)[2] | Swedish copper smelter workers | 4.6(2.2-9.6) |
| Mabuchi et al (1979)[2] | Male pesticide workers | 168* |
| Enterline and Marsh (1980,1982)[1] | US copper smelter workers | >1.00 |
| Mabuchi et al (1980) | US pesticide workers - males | 265($p<0.05$)* |
| | Females | 168($p<0.05$)* |

Table 7 continued

| | | |
|---|---|---|
| Matanoski et al (1980)[2] | US residents near pesticide plant - males | 4.00 |
| | Females | 1.00 |
| Wall (1980)[1] | Swedish smelter workers | 6.00-8.00 |
| Greaves et al (1981)[1] | Residents near smelter | 1.00 |
| Matanoski et al (1981,1983)[1] | Residents near smelters and pesticide plants | 2.0-2.5 |
| Pershagen et al (1981) | Swedish copper smelter workers | 2.9(1.4-5.7) |
| Rom et al (1982)[1] | Residents near smelter | 1.00 |
| Luchtrath (1983)[1] | German vineyard workers | >1.00 |
| Buiatti et al (1985)[1] | Italian hat makers | >1.00 |
| Chen et al (1985,1986)[1] | Taiwanese residents | >1.00 |
| Wingren and Axelson (1985)[1] | Swedish glass blowers | 2.00 |
| Lee-Feldstein (1986)[1] | Copper smelter workers | 10.00 |
| Wu et al (1989) | Chinese tin miners | 3.7 |

* Standardized mortality ratio

1 From International Agency for Research on Cancer (1987)

2 From International Agency for Research on Cancer (1980)

3 Tumours of respiratory system (ICD 6th rev. codes 160-164)

4 Incidence rate per 100 000 per year

5 Estimated from data given

References

1. International Agency for Research on Cancer (1980) Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 23: Some metals and metallic compounds, 39-142. IARC, Lyon.

2. International Agency for Research on Cancer (1987) Monographs on the evaluation of the carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42, 100-106. IARC, Lyon.

3. Lee AM and Fraumeni JF (1969) Arsenic and respiratory cancer in man: An occupational study. JNCI, 42, 1045-1052.

4. Mabuchi K, Lilienfeld AM and Snell LM (1980) Cancer and occupational exposure to arsenic: A study of pesticide workers. Prev Med, 9, 51-77.

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6. Wu K-G, Fu H, Mo C-Z, and Y L-Z (1989) Smelting, underground mining, smoking, and lung cancer: A case-control study in a tin mine area. Biomed Environ Sci, 2, 98-105.

## 8. Aryl hydrocarbon hydroxylase activity

Six studies were found which attempted to relate lung cancer risk to aryl hydrocarbon hydroxylase (AHH) activity, and details of these are given in Table 8. A relative risk of 6.0 was found for men with high AHH compared to those with low activity by one study, while another reported that 81% of lung cancer cases showed high AHH activity compared to only 31% of controls. Two other studies also noted increased AHH activity in lung cancer patients but did not give any results, while the remaining two found no differences between cases and controls.

It was suggested that AHH activity can be induced by the polycyclic hydrocarbons in tobacco smoke, thereby converting the hydrocarbons into carcinogenic metabolites [1-6], which may have accounted for the results observed by the studies. However, it is also possible the higher levels of AHH activity may somehow be caused by the development of lung cancer [5]. As all of the studies were of a case-control design, and collected data after the cases had been diagnosed with cancer, it is not clear whether this is so. Therefore, although the evidence presented in the table is suggestive of a positive relationship between lung cancer risk and high AHH activity, data from more studies are needed before more definite conclusions can be drawn.

Table 8: Estimates of relative risk for aryl hydrocarbon hydroxylase activity

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Kellerman et al (1973) | US residents | Increased AHH activity in cases compared to controls ($p<0.001$) |
| McLemore et al (1981) | US hospital patients | 81% cases and 31% controls showed high AHH activity ($p<0.001$) |
| Kouri et al (1982) | US hospital patients | Tendency for cases to show higher AHH activity than controls |
| Korsgaard et al (1984) | Swedish men | Relative risk of 6.0($p<0.05$) found for high AHH activity compared to low activity |

Table 8 continued

| | | |
|---|---|---|
| Karki et al (1987) | Finnish residents | AHH activity similar in cases and controls |
| Bartsch et al (1992) | Italian men | No difference in AHH activity found between cases and controls |

References

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2. Karki NT, Pokela R, Nuutinen L and Pelkonen O (1987) Aryl hydrocarbon hydroxylase in lymphocytes and lung tissue from lung cancer patients and controls. Int J Cancer, 39, 565-570.

3. Kellerman G, Shaw CR and Lutyen-Kellerman M (1973) Aryl hydrocarbon hydroxylase inducibility and bronchogenic carcinoma. N Engl J Med, 289, 934-937.

4. Korsgaard R, Trell E, Simonsson BG et al (1984) Aryl hydrocarbon hydroxylase induction levels in patients with malignant tumors associated with smoking. J Cancer Res Clin Oncol, 108, 286-289.

5. Kouri RE, McKinney CE, Slomiany DJ et al (1982) Positive correlation between high aryl hydrocarbon hydroxylase activity and primary lung cancer as analyzed in cryopreserved lymphocytes. Cancer Res, 42, 5030-5037.

6. McLemore TL, Martin RR, Wray NP, Cantrell ET and Busbee DL (1981) Reassessment of the relationship between aryl hydrocarbon hydroxylase and lung cancer. Cancer, 48, 1438-1443.

## 9. Asbestos

A brief review of the literature concerning asbestos exposure and the risk of lung cancer (as distinct from mesothelioma) revealed 22 studies on the subject, although this is far from exhaustive. Some relevant details of the studies are given in Table 9. For the cohort studies the estimates of relative risk ranged from 0.85-10.17, with 14 out of 15 being above 1.00, and the standardized mortality ratios calculated were between 105 and 210. Estimates of relative risk from the five case-control studies ranged from 0.97-3.29, with all but one of them being above 1.00.

Many of the studies included measurements of the levels of asbestos dust or fibre concentrations workers in the various industries were exposed to. However, two studies [16,22] did not measure the intensity of exposure, relying instead on years of employment as an index. Additionally, several of the studies [3,4,7,9,21,23] failed to make any objective measurement of the level of asbestos exposure, simply categorizing the respondents as to whether exposure had taken place or not. A failure to adequately measure exposure levels could obviously introduce inaccuracy into these studies.

Despite this limitation, the results of the studies were remarkably consistent, both for specific types of asbestos, and for those studies in which the type was not specified. This is reflected by IARC's description of the data relating asbestos exposure to risk of cancer in humans as "sufficient" (Group 1). It was also noted that there may be a synergistic effect with smoking, with the most likely model appearing to be multiplicative [11].

Table 9: Estimates of relative risk/standardized mortality ratio for asbestos exposure in men

| Study | Population | Asbestos type | Relative risk (95% limits) |
|---|---|---|---|
| Cohort studies: | | | |
| Selikoff (1964) | New York/New Jersey insulation workers | NS | 6.81[1] |
| Knox et al (1968) | Rochdale factory workers | CH, CR | 10.17($p < 0.001$)[1] |
| McDonald et al (1971) | Quebec miners and millers | CH | 9.9[2] |
| Gillam et al (1976) | South Dakota gold miners | AM | 2.70 ($p < 0.05$)[3] |
| Hammond et al (1979) | US/Canadian insulation workers | NS | 4.86 ($p < 0.001$) |
| Selikoff et al (1980) | New Jersey factory workers | AM | 5.94[1] |
| Clemmesen and Hjalgrim-Jensen (1981) | Aalborg factory workers | NS | 1.72[1] |
| McDonald et al (1982) | Pennsylvanian factory workers | CH, AM,CR | 105.0*[3] |
| McDonald et al (1983) | South Carolina factory workers | CH | 199.5*[3] |
| Acheson et al (1984) | London factory workers | AM | 210 ($p < 0.01$)* |
| Newhouse et al (1985) | London factory workers | CR, | 2.56[1] |
| | | AM,CH | 8.23[1,4] |
| | Laggers | | 3.6 ($p < 0.001$) |
| Albin et al (1990) | Swedish cement workers | CH, CR,AM | 1.80(0.90-3.70) |
| Neuberger and Kundi (1990) | Vocklabruck cement workers | CH, CR | 1.72(1.21-2.57) |
| Piolatto et al (1990) | Balangero asbestos miners | CH | 1.10 ($p > 0.05$) |
| Hughes and Weill (1991) | New Orleans cement workers | NS | 169 ($p < 0.01$)* |
| Sanden et al (1992) | Gothenburg shipyard workers | CH | 0.85(0.53-1.30) |
| Raffn et al (1993) | Aalborg cement workers | CH, CR,AM | 1.82(1.48-2.20) |

Table 9 continued

| | | | |
|---|---|---|---|
| Case-control studies: | | | |
| Blot et al (1980) | Virginian males not employed in shipyards | NS | 2.20(1.10-4.60) |
| Blot et al (1982) | US shipyard workers | NS | 3.17(0.87-11.5)[1] |
| | US construction workers | | 3.29(1.07-10.1)[1] |
| Garshick et al (1987) | US railroad workers | NS | 0.97(0.83-1.14) |
| De Klerk et al (1991) | Wittenoom asbestos miners | CR | 2.77(1.37-5.57)[1] |
| Minowa et al (1991) | Yokusuka shipyard workers | NS | 2.54($p < 0.05$) |

AM = Amosite; CH = Chrysotile; CR = Crocidolite; NS = Not specified

* Standardized mortality ratio

1 Estimated from data given

2 Death rate per 1000 men

3 Respiratory cancers (ICD codes 160-4)

4 Females only

References

1. Acheson ED, Gardner MJ, Winter PD and Bennett C (1984) Cancer in a factory using amosite asbestos. Int J Epidemiol, 13, 3-10.

2. Albin M, Jakobsson K, Attewell R, Johansson L and Welinder H (1990) Mortality and cancer morbidity in cohorts of asbestos cement workers and referents. Brit J Ind Med, 47, 602-610.

3. Blot WJ, Davies JE, Brown LM et al (1982) Occupation and the high risk of lung cancer in northeast Florida. Cancer, 50, 364-371.

4. Blot WJ, Morris LE, Stroube R, Tagnon I and Fraumeni JF (1980) Lung and laryngeal cancers in relation to shipyard employment in costal Virginia. JNCI, 65, 571-575.

5. Clemmesen J and Hjalgrim-Jensen S (1981) Cancer incidence among 5686 asbestos-cement workers followed from 1943 through 1976. Ecotoxicol Environ Safety, 5, 15-23.

6. De Klerk NH, Musk AW, Armstrong BK and Hobbs MST (1991) Smoking, exposure to crocidolite, and the incidence of lung cancer and asbestosis. Brit J Ind Med, 48, 412-417.

7. Garshick E, Schenker MB, Munoz A et al (1987) A case-control study of lung cancer and diesel exhaust exposure in railroad workers. Am Rev Respir Dis, 135, 1242-1248.

8. Gillam JD, Dement JM, Lemen RA, Wagoner JK, Archer VE and Blejer HP (1976) Mortality patterns among hard rock gold miners exposed to an asbestiform mineral. Ann N Y Acad Sci, 271, 336-344.

9. Hammond EC, Selikoff IJ and Seidman H (1979) Asbestos exposure, cigarette smoking and death rates. Ann N Y Acad Sci, 330, 473-490.

10. Hughes JM and Weill H (1991) Asbestosis as a precursor of asbestos related lung cancer: results of a prospective mortality study. Brit J Ind Med, 48, 229-233.

11. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogencity: an updating of IARC Monographs Volumes 1 to 42, 106-116. IARC, Lyon.

12. Knox JF, Holmes S, Doll R and Hill ID (1968) Mortality from lung cancer and other causes among workers in an asbestos textile factory. Brit J Ind Med, 25, 293-303.

13. McDonald AD, Fry JS, Woolley AJ and McDonald JC (1982) Dust exposure and mortality in an American factory using chrysotile, amosite, and crocidolite in mainly textile manufacture. Brit J Ind Med, 39, 368-374.

14. McDonald AD, Fry JS, Woolley AJ and McDonald J (1983) Dust exposure and mortality in an American chrysotile textile plant. Brit J Ind Med, 40, 361-367.

15. McDonald JC, McDonald AD, Gibbs GW, Siemiatycki J and Rossiter CE (1971) Mortality in the chrysotile asbestos mines and mills of Quebec. Arch Environ Health, 22, 677-686.

16. Minowa M, Hatano S, Ashizawa M et al (1991) A case-control study of lung cancer with special reference to asbestos exposure. Environ Health Perspec, 94, 39-42.

17. Neuberger M and Kundi M (1990) Individual asbestos exposure: smoking and mortality - a cohort study in the asbestos cement industry. Brit J Ind Med, 47, 615-620.

18. Newhouse ML, Berry G and Wagner JC (1985) Mortality of factory workers in east London 1933-80. Brit J Ind Med, 42, 4-11.

19. Piolatto G, Negri E, La Vecchia C, Pira E, Decarli A and Peto J (1990) An update of cancer mortality among chrysotile asbestos miners in Balangero, northern Italy. Brit J Ind Med, 47, 810-814.

20. Raffn E, Lynge E and Korsgaard B (1993) Incidence of lung cancer by histological type among asbestos cement workers in Denmark. Brit J Ind Med, 50, 85-89.

21. Sanden A, Jarvholm B, Larsson S and Thiringer G (1992) The risk of lung cancer and mesothelioma after cessation of asbestos exposure: a prospective cohort study of shipyard workers. Eur Respir J, 5, 281-285.

22. Selikoff IJ (1964) Asbestos exposure and neoplasia. JAMA, 188, 22-26.

23. Selikoff IJ, Seidman H and Hammond EC (1980) Mortality effects of cigarette smoking among amosite asbestos factory workers. JNCI, 65, 507-513.

## 10. Atomic bomb explosions

Only two studies were found which gave information relevant to an investigation of lung cancer risk in relation to exposure to atomic bomb explosions, and details of these are shown in Table 10. One study estimated a relative risk of 3.55 while the other calculated a standardized mortality ratio of 21. Neither study gave any information on the significance of their findings.

With so few studies reporting it is not possible to fully evaluate the potential carcinogenicity of exposure to atomic bomb explosions.

Table 10: Estimates of relative risk/standardized mortality ratio for exposure to atomic bomb explosions

| Study | Population | Relative risk |
|---|---|---|
| Knox et al (1983) | British servicemen | 21*[1] |
| Prentice et al (1983) | Japanese residents | 3.55 |

* Standardized mortality ratio

1 Tumours of respiratory system

References

1. Knox EG, Sorahan T and Stewart A (1983) Cancer following nuclear weapons tests. The Lancet, 815.

2. Prentice RL, Yoshimoto Y and Mason MW (1983) Relationship of cigarette smoking and radiation exposure to cancer mortality in Hiroshima and Nagasaki. JNCI, 70, 611-622.

## 11. Bakers/pastry cooks

Only two studies were found which looked at the possible association between employment as a baker/pastry cook and the risk of lung cancer, and these are shown in Table 11. Two standardized mortality ratios, of 87 and 131, were given, along with a mortality rate of 3.2 per 1000 per year, although it was not stated what reference group this rate was based on.

No information was available on the length of time the subjects had spent employed as bakers/pastry cooks, nor were any data on possible exposures presented. Furthermore, it was suggested that the raised mortality ratio calculated from the data presented by OPCS represented at best a weak association, but was more likely to be due to chance [2].

Table 11: Estimates of standardized mortality ratio for employment as a baker/pastry cook

| Study | Population | Standardized mortality ratio |
|---|---|---|
| Boucot et al (1972) | US bakers/pastry cooks/chefs/cooks | 3.2[1] |
| OPCS (1986) | UK foreman bakers/flour confectioners | 87 |
| | Bakers/flour confectioners | 131($p<0.05$) |

1 Per 1000 per year

### References

1. Boucot KR, Weiss W, Seidman H, Carnahan W and Cooper DA (1972) The Philadelphia pulmonary neoplasm research project: basic risk factors of lung cancer in older men. Am J Epidemiol, 95, 4-16.

2. Office of Population Censuses and Surveys (1986) Occupational mortality: The Registrar General's decennial supplement for Great Britain, 1979-80, 1982-83. HMSO, London.

## 12. Barbers and hairdressers

Details of the studies which attempted to relate lung cancer risk to working as a barber, hairdresser or related occupation are given in Table 12. Eighteen relative risks were estimated, ranging from 0.5-6.0, with 16 being above 1.00. Ten standardized mortality ratios, of between 90-266, were also calculated, of which seven were raised. One study presented a standardized incidence ratio of 200, while another gave a proportional incidence ratio of 144.

Hairdressers may be exposed to over 5000 different chemicals, used in the formulation of hair colouring preparations, cleansing and conditioning products, preparations for hair styling, permanent waving and hair straightening, nail and skin products, and other products. However, none of the studies had made objective measurements of the subjects' exposures, and only the study by Guberan gave some limited details of products and chemicals respondents may have been exposed to. Thus, it is not possible to determine which chemicals the subjects were exposed to or the potential carcinogenicity of any one of them.

Therefore, IARC felt that there was "limited" evidence that occupation as a hairdresser or barber entails exposures that are carcinogenic [1].

Table 12: Estimates of relative risk/standardized mortality ratio for working as a barber/hairdresser

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Registrar General (1958)[1] | UK male barbers/hairdressers | 115* |
| | Female hairdressers/manicurists | 200* |
| Garfinkel et al (1977)[1] | US female beauticians | 6.0(p=0.06) |
| Menck et al (1977)[1] | US female beauticians | 200(p<0.05)[2] |
| Alderson (1980)[1] | UK male hairdressers | 1.02 |
| Dubrow and Wegman (1982, 1983,1984)[1] | US male barbers | 1.34 |
| Logan (1982) | UK male hairdressers 1931 | 90* |
| | 1951 | 115* |
| | 1961 | 96* |
| | 1971 | 115* |
| | Married women[3] 1951 | 90* |
| | 1961 | 107* |
| | 1971 | 111* |
| Kono et al (1983)[1] | Japanese female beauticians | 1.21 |
| Teta et al (1984)[1] | US female cosmetologists | 1.41(p<0.05) |
| Guberan et al (1985)[1] | Swiss female hairdressers | 1.9 |
| | Male hairdressers | 0.78 |
| OPCS (1986)[1] | UK male barbers | 266*[4] |
| Osorio et al (1986)[1] | US female cosmetologists | 144[5] |
| Pearce and Howard (1986)[1] | New Zealand men | 2.54 |
| Malker et al (1987)[1]/Skov et al (1990)[1] | Swedish male hairdressers | 1.5(1.2-1.8) |
| | Female hairdressers | 1.6(1.1-2.2) |
| Lynge and Thygesen (1988)[1]/ Skov et al (1990)[1]/Skov and Lynge (1991)[1] | Danish female hairdressers | 1.1 |
| | Male hairdressers/barbers | 1.1 |
| Skov et al (1990)[1] | Norwegian female hairdressers | 1.4 |
| | Male hairdressers | 1.6(p<0.05) |
| | Finnish female hairdressers | 0.5 |
| | Male hairdressers/barbers | 1.5 |

Table 12 continued

| | | |
|---|---|---|
| Hrubec et al (1992)[1] | US male barbers/beauticians/ manicurists | 1.6($p<0.05$) |
| Pukkala et al (1992)[1] | Finnish female hairdressers | 1.72 |

* Standardized mortality ratio

1 From International Agency for Research on Cancer (1993)

2 Standardized incidence ratio

3 According to husband's occupation

4 Estimated from data given

5 Proportional incidence ratio

References

1. International Agency for Research on Cancer (1993) Monographs on the evaluation of carcinogenic risks to humans. Volume 57: Occupational exposures of hairdressers and barbers and personal use of hair colourants; some hair dyes, cosmetic colourants, industrial dyestuffs and aromatic amines, 43-118. IARC, Lyon.

2. Logan WPD (1982) Cancer mortality by occupation and social class 1851-1971. IARC, Lyon and OPCS, London.

13. Barbiturates

Only three studies could be found which contained data on a possible association between lung cancer and exposure to barbiturates, and details of these are given in Table 13. Two relative risks, of 1.3 and 1.4, and one standardized mortality ratio, of 173, were given.

While the study by Friedman recorded the use of three barbiturates, pentobarbital sodium, phenobarbital and secobarbital, separately, the other two studies appear to have only considered phenobarbital, and no details of exposures to other medication have been given. Therefore, it is possible that the subjects in these studies may be exposed to other drugs which may themselves have a carcinogenic effect.

Not surprisingly, IARC considered the evidence for the carcinogenicity of phenobarbital to humans to be "inadequate" [2]. Evaluations of the carcinogenicity of pentobarbital sodium and secobarbital were not made.

Table 13: Estimates of relative risk/standardized mortality ratio for exposure to barbiturates

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| White et al (1979)[1] | Epileptics | 1.4(0.9-2.1) |
| Clemmesen and Hjalgrim-Jensen (1981)[1] | Epileptics | 1.3(1.0-1.6) |
| Friedman (1981) | San Francisco outpatients | 173($p<0.002$)* |

* Standardized mortality ratio

1 From International Agency for Research on Cancer (1987)

References

1. Friedman GD (1981) Barbiturates and lung cancer in humans. JNCI, 67, 291-5.

2. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: an updating of IARC Monographs Volumes 1 to 42, 313-316. IARC, Lyon.

14. Barmen

The two studies found which attempted to relate lung cancer risk to employment as a barman are detailed in Table 14. Five standardized mortality ratios were calculated, lying in the range 100-194, of which four were raised. Two proportional mortality ratios, of 98 and 114, were also given, along with two proportional registration ratios, of 132 and 148.

Although the data presented in the table is consistent with an increased risk of lung cancer in barmen, it should be remembered that the data come from just two studies, both of which were based on mortality/morbidity statistics and no information on possible exposures, such as to alcohol and tobacco, is available. Elsewhere it has been suggested that barmen may be more exposed to tobacco than the general population, partly through environmental tobacco smoke exposure during their work, and partly through their own smoking habits [1]. However, the lack of data available makes it impossible to comment further on this theory.

Table 14: Estimates of standardized mortality ratio for employment as a barman

| Study | Population | Standardized mortality ratio |
|---|---|---|
| OPCS (1978) | English/Welsh men, aged 15-64 | 114* |
| | Aged 65-74 | 98* |
| | Incidence 1966-7 | 148($p<0.01$)[1] |
| | 1968-9 | 132($p<0.05$)[1] |
| Logan (1982) | English/Welsh men, 1951 | 117 |
| | 1961 | 137 |
| | 1971 | 165 |
| | Married women[2], 1961 | 100 |
| | 1971 | 194 |

Footnote to Table 14

* Proportional mortality ratio

1 Proportional registration ratio

2 According to husband's occupation

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References

1. Kjaerheim K and Andersen A (1993) Incidence of cancer among male waiters and cooks: Two Norwegian cohorts. Cancer Causes and Control, 4, 419-426.

2. Logan WPD (1982) Cancer mortality by occupation and social class 1851-1971. HMSO, London and IARC, Lyon.

3. Office of Population Censuses and Surveys (1978) Occupational mortality: The Registrar General's decennial supplement for England and Wales, 1970-72. HMSO, London.

15. BCME/CMME

Only seven studies were found which looked at the risks of lung cancer after exposure to chloromethyl methyl ether (CCME) and/or bischloromethyl ether (BCME), and details of these are given in Table 15. The relative risks presented were all above 1.00, and ranged from 2.02-7.27.

Although the studies were concerned with workers exposed to CMME, the technical grade of this chemical, as used in the factories under observation, is nearly always contaminated with about 1-8% of BCME [1-4,6-11], so that workers will almost certainly have been exposed to both substances. Most of the studies recorded the length of exposure and made a subjective ranking of the amount of exposure, but as objective measurements of workroom air concentrations were taken by only one of the studies [4], the exact nature of the workers' exposure is mostly unknown.

Animal studies have suggested that the carcinogenic properties of BCME are far stronger than those of CMME [1,4,6,7] and one laboratory remarked that it was "one of the most potent carcinogens ever tested" [2]. It is not altogether surprising, then, that IARC felt there was "sufficient" evidence of the carcinogenic effects of BCME/CMME in humans, although the effects of the two compounds were not discussed separately [5].

Table 15: Estimates of relative risk for BCME/CMME exposure

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Weiss et al (1979) | Philadelphia male factory workers | 3.50 (1.82-6.75) |
| Weiss (1982) | Philadelphia male factory workers | 2.91 (0.62-13.5) |
| McCallum et al (1983) | UK male factory workers | 2.02 (0.83-4.90) |
| Zagraniski (1983) | Connecticut males | 7.27 ($p > 0.05$) |
| Collingwood et al (1987) | US chemical workers | 2.08 (1.36-3.16) |
| Maher and DeFonso (1987) | Philadelphia male factory workers | 3.80 (2.24-6.46) |
| Gowers et al (1993) | French male factory workers | 5.00 (2.00-12.3) |

References

1. Collingwood KW, Pasternack BS and Shore RE (1987) An industry-wide study of respiratory cancer in chemical workers exposed to chloromethyl ethers. JNCI, 78, 1127-36.

2. Epstein SE (19??) The politics of cancer, 113-122. Sierra Club Books. (Incomplete reference)

3. Figueroa WG, Raszkowski R and Weiss W (1973) Lung cancer in chloromethyl methyl ether workers. N Engl J Med, 288, 1096-1097.

4. Gowers DS, DeFonso LR, Schaffer P et al (1993) Incidence of respiratory cancer among workers exposed to choromethyl-ethers. Am J Epidemiol, 137, 31-42.

5. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: an updating of IARC monographs volumes 1 to 42, 131-133. IARC, Lyon.

6. Maher KV and DeFonso LR (1987) Respiratory cancer among chloromethyl ether workers. JNCI, 78, 839-43.

7. McCallum RI, Woolley v and Petrie A (1983) Lung cancer associated with chloromethyl methyl ether manufacture: an investigation at two factories in the United Kingdom. Brit J Ind Med, 40, 384-9.

8. Travenius SZM (1982) Formation and occurrence of bis(chloromethyl)ether and its prevention in the chemical industry. Scand J Work Environ Health, 8 (Suppl 3), 1-86.

9. Weiss W (1976) Chloromethyl ethers, cigarettes, cough and cancer. J Occup Med, 18, 194-199.

10. Weiss W (1982) Epidemic curve of respiratory cancer due to chloromethyl ethers. JNCI, 69, 1265-70.

11. Weiss W, Moser RL and Auerbach O (1979) Lung cancer in chloromethyl ether workers. Am Rev Resp Dis, 120, 1031-7.

12. Zagraniski RT (1983) The role of occupation in the etiology of laryngeal carcinoma: a case-controlled study. Dis Abstr Int, 43, 3933.

16. Benzo(a)pyrene

It has been suggested that benzo(a)pyrene, a polycyclic aromatic hydrocarbon, may be responsible for the carcinogenic effects of soots, tars and oils observed in workers occupationally exposed to coal-soot, coal-tars and pitches, coal-tar fumes and some impure mineral oils, for whom excesses of lung cancer have been reported. In animal experiments benzo(a)pyrene has been shown to cause lung tumours, but assessment of the risk to humans is more difficult because subjects are also exposed to mixtures of other compounds, including other polycyclic aromatic hydrocarbons. Therefore, although several studies have measured benzo(a)pyrene exposure as an indication of exposure to soots, tars and oils, IARC considered the epidemiological data inadequate to evaluate the carcinogenicity to humans of benzo(a)pyrene itself [1,2].

References

1. International Agency for Research on Cancer (1973) Monographs on the evaluation of carcinogenic risk of chemicals to humans. Volume 3: Certain polycyclic aromatic hydrocarbons and heterocyclic compounds. IARC, Lyon.

2. International Agency for Research on Cancer (1974) Monographs on the evaluation of carcinogenic risk of chemicals to humans. Volume 4: Some aromatic amines, hydrazine and related substances, N-nitroso compounds and miscellaneous alkylating agents. IARC, Lyon.

## 17. Beryllium

Only six studies were found which provided data on a possible association between exposure to beryllium and the risk of lung cancer, and details of them are given in Table 17. Five standardized mortality ratios, of between 137 and 212 were given, along with two estimates of relative risk, of 2.00 and 1.26.

Several of the studies indicated that beryllium may show a carcinogenic effect after a short exposure period and a long latent period [1], and it was suggested that one explanation of this finding is that past short exposures, particularly those up to about 1950, may have entailed much higher accumulated doses than did long exposures in more recent periods, when airborne levels of beryllium became much lower [2]. However, as no objective measurements of beryllium exposure were available the total dose of beryllium received by the study subjects cannot be ascertained.

More importantly, when evaluating the evidence for carcinogenicity of beryllium and beryllium compounds, it was noted that two beryllium plants provided the database for all four of the studies cited by IARC [1]. Furthermore, the study by Ward et al also draws data from these two plants, along with five other plants, and as the study by Steenland and Ward is a continuation of that by Infante et al, it can be said that none of the studies is totally independent.

Not surprisingly then, IARC considered the evidence for the carcinogenicity of beryllium in humans to be "limited", although it was stated that "beryllium should be considered suspect of being carcinogenic to humans" [1].

Table 17: Estimates of relative risk/standardized mortality ratio for exposure to beryllium

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Infante et al (1980)[1] | US registry data | 212* |
| Mancuso (1980a)[1] | US beryllium workers - Ohio | 199($p<0.01$)* |
| | Pennsylvania | 137* |
| Mancuso (1980b)[1] | US beryllium workers | 140($p<0.01$)* |
| Wagoner et al (1980)[1] | US beryllium workers | 137($p<0.05$)* |
| Steenland and Ward (1991) | US registry data | 2.00(1.33-2.89) |
| Ward et al (1992) | US beryllium workers | 1.26(1.12-1.42) |

* Standardized mortality ratio

1 From International Agency for Research on Cancer (1980)

References

1. International Agency for Research on Cancer (1980) Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 23: Some metals and metallic compounds, 143-204. IARC, Lyon.

2. Saracci R (1991) Beryllium and lung cancer: adding another piece to the puzzle of epidemiologic evidence. JNCI, 83, 1362-1363.

3. Steenland K and Ward E (1991) Lung cancer incidence among patients with beryllium disease: A cohort mortality study. JNCI, 83, 1380-1385.

4. Ward E, Okun A, Ruder A, Fingerhut M and Steenland K (1992) A mortality study of workers at seven beryllium processing plants. Am J Ind Med, 22, 885-904.

18. Bitumens

Only three studies attempted to relate lung cancer risk to exposure to bitumens, and details of these are given in Table 18. Five standardized mortality ratios, ranging from 92-496, were calculated, of which four were raised. In addition, one study presented a proportional mortality ratio of 161.

It was noted that in the USA most roofers work with both bitumens and coal tar pitches [1], but as no information was available from the studies on the exposures the workers were subjected to it is not possible to attribute the excess cancer risk to either one or the other substance. Therefore, IARC classified the evidence for the carcinogenicity of bitumens to humans as "inadequate" [2].

Table 18: Estimates of standardized mortality ratio for exposure to bitumens

| Study | Population | Standardized mortality ratio |
|---|---|---|
| Hammond et al (1976)[1] | US roofers, 9-19 years union membership | 92 |
| | 20-29 years | 152 |
| | 30-39 years | 150 |
| | 40+ years | 247 |
| Menck and Henderson (1976)[1] | US roofers | 496 |
| Milham (1982)[1] | US roofers and slaters | 161[2] |

1 From International Agency for Research on Cancer (1985)

2 Proportional mortality ratio

References

1. International Agency for Research on Cancer (1985) Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 35: Polynuclear aromatic compounds, part 4, bitumens, coal-tars and derived products, shale-oils and soots, 39-81. IARC, Lyon.

2. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42, 133-134. IARC, Lyon.

19. Body height

Five studies provided data relevant to an investigation of the possible association between lung cancer risk and body height, and details of them are given in Table 19. Seven relative risks were estimated, ranging from 0.99-3.7, of which five were above 1.00. Incidence rates of between 8.8 and 19.0 per 1000 men were presented by one study. Finally, one study reported no apparent association between lung cancer risk and body height, but did not give any detailed results.

From the data presented in the table it can be seen that there is little consistent evidence of an association between lung cancer and body height, and therefore any risk, if it does exist, is probably very small.

Table 19: Estimates of relative risk for tall compared to short body height

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Cochrane and Moore (1983) | UK men | No association seen between height and lung cancer risk |
| Lee and Kolonel (1983) | Hawaiian male smokers, highest tertile of height | 3.7(1.2-11.5) |
| | Male non-smokers | 2.9(0.6-13.0) |
| | Female smokers | 1.8(0.6-5.2) |
| | Female non-smokers | 3.4(0.5-24.1) |
| Nomura et al (1983) | Hawaiian men of Japanese descent, 140-57cm | 14.0[1] |
| | 160cm | 8.8[1] |
| | 163cm | 14.7[1] |
| | 165-68cm | 13.4[1] |
| | 170-88cm | 19.0[1] |

Table 19 continued

| | | |
|---|---|---|
| Wynder and Goodman (1983) | White men | Relative risk of 1.00(0.98-1.01) found for height in multiple regression |
| | Women | Relative risk of 0.99(0.97-1.02) found for height in multiple regression |
| Knekt et al (1991) | Finnish men, >178cm tall compared to ≤169cm tall | 1.2(0.6-2.1) |

1 Incidence per 1000 men

References

1. Cochrane AL and Moore F (1983) Body height and lung cancer risk. Lancet, May 21, 1162 (Letter).

2. Knekt P, Seppanen R, Jarvinen R et al (1991) Dietary cholesterol, fatty acids, and the risk of lung cancer among men. Nutr Cancer, 16, 267-275.

3. Lee J and Kolonel LN (1983) Body height and lung cancer risk. Lancet, April 16, 877 (Letter).

4. Nomura A, Heilbrun LK and Stemmerman GN (1983) Body height and lung cancer risk. Lancet, May 21, 1162 (Letter).

5. Wynder EL and Goodman MT (1983) Body height and lung cancer risk. Lancet, May 21, 1162-1163 (Letter).

20. Body mass index

Three studies attempted to relate the risk of lung cancer to body mass index, and details of them are given in Table 20. For low body mass index three relative risks, ranging from 1.7-2.3, were given. The one study which used low body mass index as the baseline estimated a relative risk of 0.5 for those with a high body mass index.

It is well known that the development of cancer often leads to a drop in body weight so that any observed association between lung cancer and low body mass index may be due to, rather than a cause of, the disease. The study by Kabat tried to get round this problem by asking respondents about their weight five years prior to diagnosis. However, it is not certain how accurate such self-reported estimates of weight will be. The studies by Knekt, which were of a prospective design, collected information on weight at the start of the follow-up period.

While the evidence presented in the table suggests an association between lung cancer risk and low body mass index, with so few studies reporting it is not really possible to evaluate the relationship properly.

Table 20: Estimates of relative risk for body mass index

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Low body mass index: | | |
| Kabat (1991) | US men, lowest compared to highest quartile | 1.7(1.4-2.1) |
| | Women | 2.3(1.8-3.2) |
| Knekt et al (1991a) | Finnish men, lowest compared to highest quartile | 1.8 |
| High body mass index: | | |
| Knekt et al (1991b) | Finnish men, highest compared to lowest quartile | 0.5(0.3-0.9) |

References

1. Kabat GC (1991) Body mass index and lung cancer risk. Am J Epidemiol, 134, 725 (Abstract).

2. Knekt P, Heliovaara M, Rissanen A et al (1991a) Leanness and lung cancer risk. Int J Cancer, 49, 208-213.

3. Knekt P, Seppanen R, Jarvinen R et al (1991b) Dietary cholesterol, fatty acids, and the risk of lung cancer among men. Nutr Cancer, 16, 267-275.

## 21. Brewers

Only two studies were found which gave any information on the possible association between lung cancer risk and brewers, and details are given in Table 21. Four standardized mortality ratios were presented, ranging from 108-149.

No data was available on possible exposures brewers might be subjected to, and no hypotheses were put forward to explain the observed increase in lung cancer risk. With so little information available, it is not really possible to evaluate the potential carcinogenicity of employment as a brewer.

Table 21: Estimates of standardized mortality ratio for brewers

| Study | Population | Standardized mortality ratio |
|---|---|---|
| OPCS (1978) | English/Welsh brewers/wine makers | 119 |
| Logan (1982) | English/Welsh male brewers, 1951 | 149 |
| | 1961 | 108 |
| | 1971 | 142 |

## References

1. Logan WPD (1982) Cancer mortality by occupation and social class 1851-1971. HMSO, London and IARC, Lyon.

2. Office of Population Censuses and Surveys (1978) Occupational mortality: The Registrar General's decennial supplement for England and Wales, 1970-72. HMSO, London.

22. Bricklayers

Table 22 gives details of the four studies found which investigated a possible association between lung cancer risk and employment as a bricklayer. Seven standardized mortality ratios ranging from 96-147 were calculated, of which six were raised. Two proportional mortality ratios, of 111 and 113, were also presented, along with two proportional registration ratios, of 125 and 128, and one standardized mortality odds ratio of 143. One study estimated a relative risk of 2.1.

Although it was suggested that workers in the construction industry may be potentially exposed to asbestos [1,3], no attempts were made by the studies to measure the levels of this or any other possible carcinogen that the workers may have been subjected to. Thus, it is not possible to identify the agent or agents responsible for the increased risk of lung cancer observed.

Table 22: *Estimates of standardized mortality ratio/relative risk for bricklayers*

| Study | Population | Standardized mortality ratio |
|---|---|---|
| OPCS (1978) | E/W male bricklayers/tile setters aged 15-64 | 111($p<0.05$)[1] |
| | Aged 65-74 | 113($p<0.05$)[1] |
| | Incidence 1966-7 | 125($p<0.01$)[2] |
| | 1968-9 | 128($p<0.01$)[2] |
| Logan (1982) | E/W male bricklayers - 1931 | 104 |
| | 1951 | 113 |
| | 1961 | 136 |
| | 1971 | 147 |
| | Married women[3] - 1951 | 100 |
| | 1961 | 96 |
| | 1971 | 123 |
| Milne et al (1983) | US brickmasons | 2.1* |
| Dubrow and Wegman (1984) | US brickmasons/stonemasons/tile setters | 143($p<0.05$)[4] |

Footnote to Table 22

E/W = English/Welsh

* Relative risk

1 Proportional mortality ratio

2 Proportional registration ratio

3 According to husband's occupation

4 Standardized mortality odds ratio

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References

1. Dubrow R and Wegman DH (1984) Cancer and occupation in Massachusetts: A death certificate study. Am J Ind Med, 6, 207-230.

2. Logan WPD (1982) Cancer mortality by occupation and social class 1851-1971. HMSO, London.

3. Milne KL, Sandler DP, Everson RB and Brown SM (1983) Lung cancer and occupation in Alameda County: A death certificate case-control study. Am J Ind Med, 4, 565-575.

4. Office of Population Censuses and Surveys (1978) Occupational mortality: The Registrar General's decennial supplement for England and Wales, 1970-72. HMSO, London.

## 23. Building labourers

Table 23 gives details of the studies found which investigated a possible association between lung cancer and employment as a building labourer. Eleven standardized mortality ratios were calculated, ranging from 97-175, of which 10 were raised. Four proportional mortality ratios were also presented, lying in the range 109-118, along with four proportional registration ratios, ranging from 82-122, of which three were raised. Seven relative risks were estimated, ranging from 1.18-2.5.

Although it was suggested by one of the studies that exposure to asbestos may be responsible for the increase in lung cancer risk observed among building labourers [4], no attempt was made by this, or any of the other studies to measure the workers' potential exposures. Thus, no evidence is available to either support or refute this hypothesis. Indeed, with such little information available it is difficult to interpret the results, but from the table it can be seen that any increase in risk, if it does exist, is probably not very large.

Table 23: Estimates of standardized mortality/relative risk ratio for building labourers

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Blot et al (1978)[1] | US general construction workers | 2.0 |
| OPCS (1978) | E/W male building/contracting labourers aged 15-64 | 113($p<0.05$)[2] |
| | Aged 65-74 | 116($p<0.05$)[2] |
| | Incidence 1966-7 | 82[3] |
| | 1968-9 | 122($p<0.01$)[3] |
| | Male general construction workers aged 15-64 | 118($p<0.05$)[2] |
| | Aged 65-74 | 109($p<0.05$)[2] |
| | Incidence 1966-7 | 114($p<0.01$)[3] |
| | 1968-9 | 119($p<0.01$)[3] |
| Gottlieb et al (1979)[1] | US general construction workers | 1.3($p>0.05$) |

Table 23 continued

| | | |
|---|---|---|
| Blot et al (1982)[1] | US general construction workers | 1.4 |
| Logan (1982) | E/W men - 1931 | 153* |
| | 1951 | 175* |
| | 1961 | 124* |
| | 1971 | 97* |
| | Married women[4] - 1951 | 163* |
| | 1961 | 105* |
| | 1971 | 135* |
| Blot et al (1983)[1] | US general construction workers | 1.4(p>0.05) |
| Milne et al (1983) | US male construction labourers | 1.9(p<0.05) |
| OPCS (1986) | UK male building/construction workers | 131(p<0.01)* |
| | Married women[4] | 134(p<0.01)* |
| | Male civil engineering/craftsmen's mates/other building labourers | 135(p<0.01)* |
| | Married women[4] | 131(p<0.05)* |
| Alavanja et al (1990) | US female housing construction workers | 2.5(0.4-15.1) |
| Keller and Howe (1993) | US general construction workers | 1.18(1.02-1.36) |

E/W = English/Welsh

* Standardized mortality ratio

1 From Williams Pickle

2 Proportional mortality ratio

3 Proportional registration ratio

4 According to husband's occupation

References

1. Alavanja MCR, Brownson R and Boice JD (1990) Risk factors for lung cancer among nonsmoking women. Society for Epidemiologic Research, Snowbird, Utah, USA.

2. Keller JE and Howe HL (1993) Cancer in Illinois construction workers: A study. Am J Ind Med, 24, 223-230.

3. Logan WPD (1982) Cancer mortality by occupation and social class 1851-1971. HMSO, London.

4. Milne KL, Sandler DP, Everson RB and Brown SM (1983) Lung cancer and occupation in Alameda County: A death certificate case-control study. Am J Ind Med, 4, 565-575.

5. Office of Population Censuses and Surveys (1978) Occupational mortality: The Registrar General's decennial supplement for England and Wales, 1970-72. HMSO, London.

6. Office of Population Censuses and Surveys (1986) Occupational mortality: The Registrar General's decennial supplement for Great Britain, 1979-80, 1982-83. HMSO, London.

7. Williams Pickle L, Correa P and Fontham E (1984) Recent case-control studies of lung cancer in the United States. In: Lung cancer: Causes and prevention, 101-115. Verlag Chemie International Inc.

24. Butchers

Table 24 summarizes the available evidence on lung cancer risk for individuals employed as butchers, or in associated jobs in the meat industry. Seventeen standardized mortality ratios were presented, ranging from 85-331, with 14 being above 100. Three standardized incidence ratios, ranging between 120-178, were also given, along with one proportional mortality ratio of 154 and one relative risk estimate, of 1.17. Additionally, one study reported finding 36 cases of lung cancer in butchers compared to only 15 cases in a comparison population of bakers.

The consistent excess of lung cancer amongst butchers and those working in related jobs in the meat industry suggests that there may indeed be some risk involved, but no plausible mechanism has yet been suggested. One theory is that butchers and workers in slaughterhouses are exposed to various animal viruses, such as the bovine leukaemia virus, the avian leukosis viruses and Marek's disease virus, which are known to cause cancer in cows and chickens, and may also increase the risk of cancer in humans [4]. Another possibility, stemming from the observation of an unusually high prevalence of viral warts in butchers, is that human wart viruses may also be capable of producing malignant changes, and thus may be responsible for the excess of lung cancers in butchers [8]. It has also been suggested that risks in more recently exposed workers could be related to new exposures in the meat industry such as fumes from heated polymer wraps [9]. One further possibility, not discussed by any of the studies, is that butchers may consume more red meat than average and thus have a higher intake of dietary fat, and this may have a contributory role in the risk of developing lung cancer.

Table 24: Estimates of standardized mortality ratio/relative risk for butchers

| Study | Population | Standardized mortality ratio |
|---|---|---|
| Doerken and Rehpenning (1982) | German butchers | 36 lung cancer cases in butchers compared to 15 in bakers ($p<0.01$) |
| Fox et al (1982) | English/Welsh male butchers | 116 |
| | Male butchers 1966-67 | 127 ($p<0.01$)[1] |
| | Male butchers 1968-70 | 120 ($p<0.01$)[1] |
| | Danish butchers in slaughterhouses | 253 |
| | Butchers working elsewhere | 165 |
| | Unskilled workers in slaughterhouses | 85 |
| | Swedish butchers in slaughterhouses | 178[1] |
| | Butchers working elsewhere | 130 |
| | Other employees in slaughterhouses | 148 |
| Griffith (1982) | English/Welsh butchers | 127 |
| | Meat and fish curers and smokers | 200 |
| | Slaughterhouse workers | 131 |
| | Proprietors of retail businesses for sale of foods, including meat | 151 |
| Johnson and Fischman (1982) | US butchers | 154[2] |
| Milham (1982) | US butchers | 99 |
| Vena et al (1982) | US employees in meat industry | 1.17(0.67-2.05)* |
| Lynge et al (1983) | Danish self-employed butcher's shop employees | 169 |
| | Skilled butcher's shop employees | 148 |
| | Skilled slaughterhouse workers | 159 |
| | Unskilled slaughterhouse workers | 100 |
| OPCS (1986) | Great Britain - foreman butchers | 331 ($p < 0.01$) |
| | butchers | 176 ($p < 0.01$) |

Footnote to Table 24

* Relative risk

1 Standardized incidence ratio

2 Proportional mortality ratio

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References

1. Doerken H and Rehpenning W (1982) Lung cancer in butchers. The Lancet, Mar 6, 561. (Letter)

2. Fox AJ, Lynge E, Malker H (1982) Lung cancer in butchers. The Lancet, Jan 16, 165-166. (Letter)

3. Griffith GW (1982) Lung cancer in butchers. The Lancet, Feb 13, 399. (Letter)

4. Johnson ES and Fischman HR (1982) Cancer mortality among butchers and slaughterhouse workers. The Lancet, Apr 17, 913-914. (Letter)

5. Lynge E, Andersen O and Kristensen TS (1983) Lung cancer in Danish butchers. The Lancet, Mar 5, 527-528. (Letter)

6. Milham S (1982) Lung cancer in butchers. The Lancet, Mar 20, 690. (Letter)

7. Office of Population Censuses and Surveys (1986) Occupational mortality: the Registrar General's decennial supplement for Great Britain, 1979-80, 1982-83, 81-82. HMSO, London.

8. Pegum JS (1982) Lung cancer in butchers. The Lancet, Mar 6, 561. (Letter)

9. Vena JE, Byers T, Swanson M and Cookfair D (1982) Lung cancer in butchers? The Lancet, 2, 713. (Letter)

25. Cadmium

Ten studies were found which gave information relevant to an investigation of the possible association between lung cancer risk and exposure to cadmium, and details are given in Table 25. The relative risks estimated ranged from 0.26-17.0, with 10 out of 12 being above 1.00.

Seven studies (Ding, Elinder, Holden, Kjellstrom, Lemen, Sorahan, Stayner) took objective measurements of the levels of cadmium workers were exposed to, while the study by Kazantzis et al grouped respondents by estimated exposure level. Additionally, four studies (Ding, Lemen, Kazantzis, Sorahan) recorded the duration of exposure. However, it was noted that in some studies workers may also have been exposed to other substances, particularly nickel compounds, but also arsenic, beryllium, chromium, indium, lead, thallium and emissions from a variety of heated mineral oils [3,4], although no measurements of these appear to have been taken. Therefore, it is possible that exposure to one or more of these substances may have produced the observed results.

When initially evaluating the carcinogenicity of cadmium to humans in 1976, IARC felt the evidence to be "limited" [3], while a review of occupational exposures by Blot described cadmium as only a "possible" carcinogen [1]. However, by 1993, IARC concluded there was "sufficient" evidence that cadmium and cadmium compounds "are carcinogenic to humans" [4].

Table 25: Estimates of relative risk for cadmium exposure

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Lemen et al (1976)[1] | US smelter workers | 2.35[2] |
| Kjellstrom et al (1979)[3] | Swedish battery workers | 1.48(0.17-5.35) |
| Kazantzis et al (1992)[3]/ Kazantzis and Blanks (1992)[3] | UK cadmium workers | 1.12(1.00-1.24) |
| Elinder et al (1985)[3] | Swedish battery workers | 1.33(0.57-2.62) |
| Kipling and Waterhouse (1967)[3] | UK battery workers | 1.14(0.37-2.65) |
| Sorahan (1987)[3] | UK battery workers | 1.30(1.07-1.57) |
| Holden (1980)[3] | UK copper-cadmium alloy factory workers, urban | 1.78(0.77-3.50) |
| | Rural | 0.26(0.03-0.92) |
| Stayner et al (1992)[3] | US cadmium recovery workers | 1.49(0.95-2.21) |
| Ding et al (1987)[3] | Chinese smelter workers, cadmium shop | 6.65 |
| | Sintering shop | 17.0 |
| Siemiatycki (1991)[3] | Canadian men | 1.00 |

1 From International Agency for Research on Cancer (1976)

2 Estimated from data given

3 From International Agency for Research on Cancer (1993)

References

1. Blot WJ (1984) Lung cancer and occupational exposures. In: Lung cancer: Causes and prevention, 47-64. Verlag Chemie International Inc.

2. International Agency for Research on Cancer (1976) Monographs on the evaluation of carcinogenic risk of chemicals to man. Volume 11: Cadmium, nickel, some epoxides, miscellaneous industrial chemicals and general considerations on volatile anaesthetics, 39-74. IARC, Lyon.

3. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42, 139-142.

4. International Agency for Research on Cancer (1993) Monographs on the evaluation of carcinogenic risks to humans. Volume 58: Beryllium, cadmium, mercury, and exposures in the glass manufacturing industry, 119-237. IARC, Lyon.

26. Carbon-blacks

Table 26 gives details of the 25 studies found which investigated the risk of lung cancer in workers potentially exposed to carbon-blacks. The standardized mortality ratios calculated ranged from 47-434, with 17 out of 25 being raised. Five relative risks were also estimated, ranging from 1.4-2.3. Additionally, one study reported a mortality rate of 1.07 per 1000 per year, while another calculated a standardized incidence ratio of 126.

Exposure to carbon-blacks occurs mostly in the rubber and printing industries, and such workers are likely to be exposed to a variety of other chemicals, many of which have been shown experimentally to be mutagenic or carcinogenic. These include mineral oils, curing fumes, some monomers, solvents, nitroso compounds and aromatic amines, thiurams and dithiocarbamate compounds, ethylenethiourea, di(2-ethylhexyl)phthalate, di(2-ethylhexyl)adipate and hydrogen peroxide [2]. However, due to a lack of historical industrial hygiene data none of the studies could accurately ascertain exposure, although some of the studies of rubber workers (Baxter and Werner, Delzell, Fox, McMichael 1976, Monson and Fine, Monson and Nakano 1976b, Parkes, Zhang) did attempt to classify workers into particular job categories as a substitute for exposure categories. Thus, attempting to evaluate the potential carcinogenicity of any one compound will be extremely difficult.

Therefore, IARC's evaluation of the evidence for the carcinogenicity to humans of carbon-blacks as "inadequate" [3,4] appears to be justified.

Table 26: Estimates of standardized mortality ratio/relative risk for exposure to carbon-blacks

| Study | Population | Standardized mortality ratio |
|---|---|---|
| Goldstein et al (1970)[1] | US newspaper plant workers | 1.07[2] |
| Greenberg (1972)[1] | UK newspaper printers | 133($p<0.01$)[3] |
| Moss et al (1972)[1]/Moss (1973)[1] | UK newspaper workers | 134($p<0.01$)[3] |
| Fox et al (1974) | British rubber workers | 118 |
| McMichael et al (1974)[4] | US rubber workers | 83 |
| Andjelkovich et al (1976)[4] | US rubber workers | 83 |
| Fox and Collier (1976)[4] | British rubber workers | 127 |
| McMichael et al (1976a,b)[4] | US Receivers/shippers | 1.9*[5] |
| | Compounders/mixers | 1.4*[5] |
| | Mill-mixers | 2.1*[5] |
| | Extruders | 1.4*[5] |
| | Reclaimers | 2.3*[5] |
| Menck and Henderson (1976)[1] | US newspaper printers | 98 |
| Monson and Nakano (1976a)[4] | US rubber workers | 92 |
| Monson and Nakano (1976b)[4] | US female non-tyre rubber workers | 333 |
| Andjelkovich et al (1977)[4] | US workers exposed to synthetic latex | 434 |
| Lloyd et al (1977)[1] | US newspaper pressmen | 112[3] |
| Andjelkovich et al (1978)[4] | US female rubber workers | 191[3] |
| Monson and Fine (1978)[4] | US tyre curers | 220[3] |
| | Tyre moulders | 200[3] |
| | Fuel cell/deicer manufacturers | 158[3] |
| Baxter and Werner (1980)[4] | British rubber workers | 115[3] |
| Bovet and Lob (1980)[4] | Swiss rubber workers | 47 |
| Paganini-Hill et al (1980)[1] | US newspaper pressmen | 149[3] |
| Robertson and Ingalls (1980)[1] | US carbon black workers | 88[3] |
| Delzell and Monson (1981)[4] | US rubber workers | 84 |
| Kilpikari et al (1981)[4] | Finnish rubber workers | 150[5] |

Table 26 continued

| | | |
|---|---|---|
| Delzell et al (1982)[4] | US tyre workers - mortality | 99 |
| | Incidence | 126[6] |
| Parkes et al (1982)[4] | British rubber workers | 122 |
| Hodgson and Jones (1985)[7] | UK carbon black workers | >100 |
| Zhang et al (1989) | Chinese rubber workers | 133 |

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* Relative risk

1 From International Agency for Research on Cancer (1984)

2 Per 1000 per year

3 Estimated from data given

4 From IARC (1982)

5 Tumours of respiratory system

6 Standardized incidence ratio

7 From International Agency for Research on Cancer (1987)

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References

1. Fox AJ, Lindars DC and Owen R (1974) A survey of occupational cancer in the rubber and cablemaking industries: Results of five-year analysis, 1967-71. Br J Ind Med, 31, 140-151.

2. International Agency for Research on Cancer (1982) Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 28: The rubber industry. IARC, Lyon.

3. International Agency for Research on Cancer (1984) Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 33: Polynuclear aromatic compounds, part 2, carbon blacks, mineral oils and some nitroarenes, 35-168. IARC, Lyon.

4. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42, 142-143 and 332-334. IARC, Lyon.

5. Zhang Z-F, Yu S-Z, Li W-X and Choi BCK (1989) Smoking, occupational exposure to rubber, and lung cancer. Br J Ind Med, 46, 12-15.

27. Carcinoid syndrome

Table 27 details the studies found which gave information relevant to an investigation of lung cancer risk in relation to the carcinoid syndrome. A total of 29 cases of bronchial carcinoma with the carcinoid syndrome have been described.

With such little information it is not possible to evaluate the possible association between lung cancer risk and the carcinoid syndrome.

Table 27: Observations for the carcinoid syndrome

| Study | Population | Observations |
|---|---|---|
| Stanford et al (1958) | US female | 1 case of bronchial carcinoma with the carcinoid syndrome described |
| Goodner et al (1961) | US residents | 27 cases of bronchial carcinoma with the carcinoid syndrome reported |
| Calvert et al (1963) | Spanish male | 1 case of bronchial carcinoma with the carcinoid syndrome reported |

References

1. Calvert HT, Karlish AJ and Wells RS (1963) Bronchial adenoma with the carcinoid syndrome presenting with unusual skin changes. Postgrad Med J, 39, 547-550.

2. Goodner JT, Berg JW and Watson WL (1961) The nonbenign nature of bronchial carcinoids and cylindromas. Cancer, 14, 539-546.

3. Stanford WR, Davis JE, Gunter JU and Hobart SG (1958) Bronchial adenoma (carcinoid type) with solitary metastasis and associated functioning carcinoid syndrome. Sth Med J, 51, 449-454.

28. Cardiac anomalies

Details of the only study which attempted to relate the risk of lung cancer to cardiac anomalies are given in Table 28. A relative risk of 2.5 was estimated.

Although the findings of this study are suggestive of a positive association between lung cancer risk and cardiac anomalies, evidence from further studies is needed before such a relationship can be confirmed.

Table 28: Estimate of relative risk for cardiac anomalies

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Tenkanen et al (1987) | Finnish men | 2.5 (1.7-3.7) |

References

1. Tenkanen L, Teppo L and Hakulinen T (1987) Smoking and cardiac symptoms as predictors of lung cancer. J Chron Dis, 40, 1121-1128.

## 29. Chemical workers

There are numerous studies which have attempted to relate the risk of lung cancer to exposure to a single chemical, and these are discussed elsewhere in separate reports for each specific exposure. The purpose of this report is to consider those studies which investigated a possible association between lung cancer and employment in the chemical industry in general terms, rather than those which restricted themselves to one or two exposures. Eight studies were found which examined lung cancer risk among chemical workers, and details of these are given in Table 29. Ten standardized mortality ratios are presented, lying in the range 91-211, with nine being raised. Four relative risks of between 1.4 and 1.5 were estimated.

The exposures of chemical workers will obviously vary depending on the nature of their work and most will probably be exposed to several potentially carcinogenic compounds. For example, the workers in these studies were exposed to chlorinated hydrocarbons, mining chemicals, methionine, inorganic chemicals, chlorpyridines, antimicrobials, chloralkali and latex [1], as well as chemicals associated with the production of herbicides, particularly 2,4,5-trichlorophenoxyacetic acid, lindane, hexachlorocyclohexane, dichlorobromophenol, trichlorophenol, opioids, and 2,3,7,8-tetrachlorodibenxo-p-dioxin [4]. One of the studies also collected information on previous occupations which may have led to exposure to potentially carcinogenic substances [1].

The evidence presented in the table suggests that there may indeed be an increased risk of lung cancer associated with employment in the chemical industry. However, it is not possible to identify the agent responsible, and in any case it is likely that workers will be exposed to several potential carcinogens.

Table 29: Estimates of relative risk/standardized mortality ratio for workers in the chemical industry

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Li et al (1969) | US chemists | 116*[1] |
| Blot et al (1978)[2] | US chemical workers, including painters | 1.5(p>0.05) |
| Gottlieb et al (1979)[2] | US chemical workers | 1.4(p<0.05) |
| Logan (1982) | UK male chemical workers - 1951 | 105* |
| | 1961 | 103* |
| | 1971 | 118* |
| | Married women - 1951 | 140* |
| | 1961 | 105* |
| | 1971 | 131* |
| Blot et al (1983)[2] | US chemical workers | 1.4(p<0.05) |
| OPCS (1986) | UK male chemical/gas/petroleum process plant operators | 179(p<0.01)* |
| | Married women[3] | 211(p<0.01)* |
| Manz et al (1991) | German chemical plant workers | 1.41(0.95-2.01) |
| Burchfiel et al (1992) | US chemical workers | 91(66-122)* |

* Standardized mortality ratio

1 Estimated from data given

2 From Williams Pickle et al (1984)

3 According to husband's occupation

References

1. Burchfiel CM, Cartmill JB, Axe FD and Bond GG (1992) General mortality and respiratory cancer among a cohort of male chemical workers in California. Am J Ind Med, 22, 69-83.

2. Li FP, Fraumeni JF, Mantel N and Miller RW (1969) Cancer mortality among chemists. JNCI, 43, 1159-1164.

3. Logan WPD (1982) Cancer mortality by occupation and social class 1851-1971. HMSO, London.

4. Manz A, Berger J, Dwyer JH et al (1991) Cancer mortality among workers in chemical plant contaminated with dioxin. The Lancet, 338, 959-964.

5. Office of Population Censuses and Surveys (1986) Occupational mortality: The Registrar General's decennial supplement for Great Britain, 1979-80, 1982-83. HMSO, London.

6. Williams Pickle L, Correa P and Fontham E (1984) Recent case-control studies of lung cancer in the United States. In: Lung cancer: Causes and prevention. Verlag Chemie International Inc.

30. Chlorophenols/chlorophenoxy herbicides

Only three studies were found which looked at exposure to chlorophenols and/or chlorophenoxy herbicides in relation to lung cancer risk, one of which combined the results from 20 cohorts collected from several occupational groups in various countries. From the details given in Table 30, it can be seen that the standardized mortality ratios calculated ranged from 102-208.

It was noted by IARC, in 1986, that the study by Riihimaki et al was of limited usefulness due to the small size of the cohort, the brief follow-up period and the low exposures of the subject. As only three studies were found which considered the possible association between lung cancer risk and exposure to chlorophenols and/or chlorophenoxy herbicides it is not really surprising that the evidence for carcinogenicity in humans was felt to be "limited" [1].

Table 30: Estimates of standardized mortality ratio for exposure to chlorophenols and/or chlorophenoxy herbicides

| Study | Population | Standardized mortality ratio |
|---|---|---|
| Riihimaki et al (1982,1983)[1] | Finnish brush control workers | 108(56-189) |
| Lynge (1984,1985)[1] | Danish chemical plant workers | 208($p<0.05$)[2] |
| Saracci et al (1991)[3] | Herbicide workers | 102(87-118) |

1 From IARC (1986)

2 Estimated from data given

3 Combined results from 20 cohorts

References

1. International Agency for Research on Cancer (1986) Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 41: Some halogenated hydrocarbons and pesticide exposures, 319-408. IARC, Lyon.

2. Saracci R, Kogevinas M, Bertazzi P-A et al (1991) Cancer mortality in workers exposed to chlorophenoxy herbicides and chlorophenols. The Lancet, 338, 1027-1032.

## 31. Chromium compounds

The possible association between exposure to chromium compounds and lung cancer risk was considered by numerous studies, details of which are given in Table 31. Studies restricted to workers in chromate-producing industries presented five standardized mortality ratios, ranging between 102 and 943. Six estimates of relative risk, of 2.00-80.00, were also given. One study reported that while 11 cases had been exposed to chromium compounds, none of the controls had, and another observed that some 24% of deaths in a cohort were due to respiratory cancer. Finally, one study presented a crude death rate of 369.7/100 000 per year, but no independent reference group was available for comparison. Studies of workers in chromate-pigment producing industries estimated relative risks of 0.7-42.9, with four out of five being above 1.00. One standardized mortality ratio, of 102, was also given. Three estimates of relative risk were produced by studies restricted to workers in chromium-plating industries, and these ranged from <1.00-1.8, with two being raised. Relative risks of <1.00-6.6 were estimated from studies of workers in ferrochromium industries, again with two out of three being above 1.00. Finally, studies of workers in other industries with exposure to chromium compounds produced two estimates of relative risk, of 1.7 and 4.4.

However, some important limitations of the studies which may have led to inaccuracies should be highlighted. Firstly, there were differences between the studies in the amount of time that subjects were required to have spent in a particular job in order to have been classified as "exposed". Furthermore, although chromium exists as many different compounds, with potentially differing toxic effects, only nine studies (Alderson, Axelsson, Davies, Davies et al, Hayes, Kano, Langard and Norseth, Langard et al, Pokrovskaya and Shabynina) made any attempt to identify the compounds the subjects were exposed to, so that the contribution to cancer risk by any one compound would be very difficult to determine. Likewise, only nine studies made any assessment of the dosage received by the respondents, either by taking objective measurements (Axelsson, Langard and Norseth, Langard et al, Mancuso 1975), estimating the degree of exposure (Alderson, Davies), or by using length of employment as an index of exposure (Davies et al, Hayes, Kano).

In 1980, IARC stated that "although the available epidemiological evidence does not permit a clear distinction between the relative carcinogenicity of chromium compounds of different oxidation states or solubilities, it appears that exposure to a mixture of chromium [VI] compounds of different solubilities (as found in the chromate production industry) carries the greatest risk to humans" [4]. Thus, while the evidence for the carcinogenicity of hexavalent chromium compounds was classified as "sufficient", it was felt that the evidence for chromium metal and trivalent chromium compounds was "inadequate" [5].

Table 31: Estimates of relative risk/standardized mortality ratio for exposure to chromium compounds

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Workers in chromate-producing industries: | | |
| Machle and Gregorous (1948)[1] | US chromate workers | 25.00 |
| Baetjer (1950)[1] | US chromium workers | 11 cases and no controls exposed to chromium |
| Mancuso (1951)[2] | Chromate workers | 24% deaths due to respiratory cancer |
| Mancuso and Hueper (1951)[1] | US chromate workers | 15.00[3] |
| Gafafer (1953)[1] | US chromate workers - whites | 14.3($p<0.05$) |
| | Blacks | 80.0 |
| Bidstrup and Case (1956)[2] | British chromate workers | 364($p<0.05$)* |
| Taylor (1966)[1] | US chromate workers | 8.5($p<0.05$)[3] |
| Enterline (1974) | US chromate workers | 943* |
| Mancuso (1975)[1] | US chromate workers | 369.7[4] |
| Hayes et al (1979)[1] | US chromate workers | 2.00($p<0.05$) |
| Alderson et al (1981) | UK chromate factory workers | 240($p<0.001$)* |

Table 31 continued

| | | |
|---|---|---|
| Davies et al (1991) | UK chromate factory workers early/prechange | 197($p<0.05$)* |
| | Postchange | 102(56-171)* |
| Workers in chromate-pigment industries: | | |
| Langard and Norseth (1975)[1] | Norwegian pigment producers | 38.00($p<0.05$) |
| Davies (1978,1979)[1] | UK lead/zinc chromate workers | 2.2($p<0.05$) |
| | UK lead/zinc chromate workers | 5.0($p<0.05$) |
| | UK lead chromate workers | 0.7 |
| Langard and Vigander (1983)[5] | Norwegian pigment producers | 42.9[6] |
| Kano et al (1993) | Japanese pigment workers | 102(21-298)* |
| Workers in chromium-plating industries: | | |
| Royle (1975a,b)[1] | UK chromium-plating workers | 1.8($p>0.05$)[3] |
| Waterhouse (1975)[1] | UK chromium-plating workers | 1.4($p<0.05$) |
| Okubo and Tsuchiya (1977)[1] | Japanese chromium-plating workers | <1.00[3] |
| Workers in ferrochromium industries: | | |
| Pokrovskaya and Shabynina (1973)[1] | Soviet ferrochromium alloy workers | 4.4-6.6($p<0.05$) |
| Axelsson et al (1980)[1] | Swedish ferrochromium workers | <1.00[3] |
| Langard et al (1980)[1] | Norwegian ferrochromium and ferrosilicon workers | 2.3($p>0.05$) |
| Workers in other industries with chromium exposure: | | |
| Sjogren (1980)[5] | Stainless steel welders | 4.4 |
| Becker et al (1985)[5] | Stainless steel welders | 1.7 |

Footnote to Table 31

* Standardized mortality ratio

1 From International Agency for Research on Cancer (1980)

2 From Enterline (1974)

3 Tumours of respiratory system (ICD codes 160-164)

4 Crude death rate per 100 000 per year

5 From International Agency for Research on Cancer (1987)

6 Estimated from data given

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References

1. Alderson MR, Rattan NS and Bidstrup L (1981) Health of workmen in the chromate-producing industry in Britain. Brit J Ind Med, 38, 117-124.

2. Davies JM, Easton DF and Bidstrup PL (1991) Mortality from respiratory cancer and other causes in United Kingdom chromate production workers. Brit J Ind Med, 48, 299-313.

3. Enterline PE (1974) Respiratory cancer among chromate workers. J Occup Med, 16, 523-526.

4. International Agency for Research on Cancer (1980) Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 23: Some metals and metallic compounds, 205-324. IARC, Lyon.

5. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: an updating of IARC monographs volumes 1 to 42, 165-168. IARC, Lyon.

6. Kano K, Horikawa M, Utsunomiya T et al (1993) Lung cancer mortality among a cohort of male chromate pigment workers in Japan. Int J Epidemiol, 22, 16-22.

## 32. Coal gasification

Table 32 gives details of the available evidence for a possible association between the risk of lung cancer and exposure to coal gasification. Seventeen standardized mortality ratios were calculated, all of them raised and they ranged from 112-571. Additionally, one study reported observing significantly more cancers of the respiratory tract than expected, but did not give any detailed results.

Workers in coal gasification processes may be exposed to any of a number of chemicals, including alcohols, aldehydes, amines, ammonia, arsenic compounds, asbestos, bauxite, cadmium compounds, carbon compounds, glycols, hydrogen compounds, lead compounds, mercaptans, nickel compounds, nitrogen heterocyclics and oxides, oxygen heterocyclics, phenols, polynuclear aromatic hydrocarbons, silica, sulphur compounds, thiocyanates, and vanadium compounds. However, none of the studies made any objective measurements of workplace exposures, and thus it is very difficult to tell which, if any, of these substances the workers were exposed to, and at what level.

Despite this, IARC still felt that there was "sufficient" evidence for the carcinogenicity of coal gasification to humans. It was suggested that working in retort houses in older gasification processes may carry the highest risk, and the most likely agent of carcinogenicity was thought to be coal-tar fumes [3].

Table 32: Estimates of standardized mortality ratio for exposure to coal gasification

| Study | Population | Standardized mortality ratio |
|---|---|---|
| Kennaway and Kennaway (1936, 1947)[1] | E/W patent-fuel workers | 571 |
| | Gas stokers/coke oven chargers | 284 |
| | Gas-works engine drivers/foremen/ producers/fitters | 138-202 |
| Doll (1952)[1] | British gas workers | 240($p<0.001$)[2] |
| | Employees inside works | 198($p<0.02$)[2] |
| | Employees outside works | 154[2] |
| Bruusgaard (1959)[1] | Gas workers | Significantly more cancers of respiratory tract than expected |
| Doll et al (1965) | E/W Coal-carbonization process workers | 169[2] |
| | Intermittent exposure in coal-carbonization plant | 112[2] |
| Doll et al (1972) | E/W coal-carbonization process workers | 134[2] |
| | Intermittent exposure in coal-carbonization plant | 172[2] |
| OPCS (1978) | E/W coal gas/coke oven furnacemen | 180[2] |
| Logan (1982) | UK men making coal/gas/coke - 1931 | 367 |
| | 1951 | 129 |
| | 1961 | 152 |
| | 1971 | 178 |
| OPCS (1986) | British chemical/gas/petroleum process plant operators - men | 179 |
| | Married women[3] | 211 |

Footnote to Table 32

E/W = English/Welsh

1 From IARC (1984)

2 Estimated from data given

3 Classified according to husband's occupation

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References

1. Doll R, Fisher REW, Gammon EJ et al (1965) Mortality of gasworkers with special reference to cancers of the lung and bladder, chronic bronchitis, and pneumoconiosis. Br J Ind Med, 22, 1-12.

2. Doll R, Vessey MP, Beasley RWR et al (1972) Mortality of gasworkers - final report of a prospective study. Br J Ind Med, 29, 394-406.

3. International Agency for Research on Cancer (1984) Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 34: Polynuclear aromatic compounds, part 3, industrial exposures in aluminium production, coal gasification, coke production, and iron and steel founding, 65-99. IARC, Lyon.

4. Logan WPD (1982) Cancer mortality by occupation and social class 1851-1971. HMSO, London and IARC, Lyon.

5. Office of Population Censuses and Surveys (1978) Occupational mortality: The Registrar General's decennial supplement for England and Wales, 1970-72. HMSO, London.

6. Office of Population Censuses and Surveys (1986) Occupational mortality: The Registrar General's decennial supplement for Great Britain, 1979-80, 1982-83. HMSO, London.

33. Coal-tars and coal-tar pitches

Table 33 gives details of the studies which investigated the possible association between lung cancer risk and exposure to coal-tars and/or coal-tar pitches. Thirty standardized mortality ratios (SMR) were calculated, ranging from 92-571, of which 29 were raised. Nine relative risks were estimated, lying in the range 1.00-44.0, with all but one being above 1.00. Two studies calculated proportional mortality ratios, of 149 and 161. Four studies failed to give detailed results, with one reporting 12 lung cancers in exposed workers compared to none in non-exposed workers, one observing significantly more respiratory tract cancers than expected, one reporting an excess of lung cancer deaths among workers exposed to coal-tars and/or coal-tar pitches, and one reporting no difference in SMR between groups of exposed and non-exposed workers.

It has previously been reported that roofers are often exposed to bitumens as well as pitches [4], while workers in the coal gasification and coke production industries may be exposed to numerous chemicals, among them alcohols, aldehydes, amines, ammonia, arsenic compounds, asbestos, bauxite, cadmium compounds, carbon compounds, glycols, hydrogen compounds, lead compounds, mercaptans, nickel compounds, nitrogen heterocyclics and oxides, oxygen heterocyclics, phenols, polynuclear aromatic hydrocarbons, silica, sulphur compounds, thiocyanates, and vanadium compounds [3]. As only one study (Mazumdar) took objective measurements, and then only of benzene concentrations in the workplace, the exact nature of the subjects' exposures is impossible to ascertain, and the excess lung cancer risk cannot be attributed to any one chemical.

Several other potential problems were noted in some of the studies. The design of the study by Reid and Buck, in which the SMRs are based on a working population with only a short period of follow-up during which death might have occurred, may have led to a serious underestimation of the risk involved. Conversely, the use of a "precision factor" to weight the relative risks from various different plants in the study by Redmond et al (1972) increased the SMR over that calculated directly. Problems were also noted in the study by Radford, due to under-identification of deaths, loss of terminated workers, and lack of age corrections, and a difficulty in assessing how the reported excesses relate to coke-oven

workers. Other potential sources of inaccuracy noted in some of the studies included small numbers of subjects, possible selection factors, imprecise work histories obtained from next-of-kin respondents, and differences in the source of information on occupation for cases and controls [3].

Despite these drawbacks, IARC considered the evidence for the carcinogenicity to humans of both coal-tars and coal-tar pitches to be "sufficient" [5].

Table 33: Estimates of standardized mortality ratio/relative risk for exposure to coal-tars and coal-tar pitches

| Study | Population | Standardized mortality ratio |
|---|---|---|
| Kennaway and Kennaway (1936,1947)[1] | E/W patent-fuel workers | 571 |
| | Gas stokers/coke oven chargers | 284 |
| | Gas works engine drivers/gas works foremen/gas producers/gas fitters | 138-202 |
| Kuroda (1937)[1] | Japanese gas-generator workers | 12 lung cancers compared to none in workers in other areas |
| Doll (1952)[1] | British gas workers | 240($p<0.001$)[2] |
| | Employees inside works | 198($p<0.02$)[2] |
| | Employees outside works | 154[2] |
| Reid and Buck (1956)[1] | English coking plant workers | 140 |
| Bruusgaard (1959)[1] | Gas workers | Signif. more cancers of respiratory tract than expected |

Table 33 continued

| | | |
|---|---|---|
| Doll et al (1965) | E/W Coal-carbonization process workers | 169[2] |
| | Intermittent exposure in coal-carbonization plant | 112[2] |
| Kawai et al (1967)[1] | Japanese gas-generator workers | 44.0* |
| Lloyd and Ciocco (1969)[1] | US non-white coke plant workers | 342[3] |
| Lloyd (1971)[1] | US coke-oven workers | 248[3] |
| Doll et al (1972) | E/W coal-carbonization process workers | 134[2] |
| | Intermittent exposure in coal-carbonization plant | 172[2] |
| Redmond et al (1972)[1] | US/Canadian coke-oven workers | 2.85($p<0.05$)* |
| Mazumdar et al (1975)[1] | US/Canadian coke-oven workers | 13.65* |
| Sakabe et al (1975)[1] | Japanese coke-oven workers | 128 |
| Hammond et al (1976)[4] | US roofers, 9-19 years union membership | 92 |
| | 20-29 years | 152 |
| | 30-39 years | 150 |
| | 40+ years | 247 |
| Menck and Henderson (1976)[4] | US roofers | 496 |
| Radford (1976)[1] | US steel company workers | 149[5] |
| Davies (1977)[1] | Welsh coke-oven workers | 1.00* |
| OPCS (1978) | E/W coal gas/coke oven furnacemen | 180[2] |
| Axelson et al (1979)[1] | Swedish coke-oven workers | >1.00($p<0.05$)* |
| Gibbs and Horowitz (1979)[1] | Canadian aluminium workers | SMRs same in exposed and non-exposed groups |
| Lloyd (1980)[1] | US coke-oven workers | 6.94($p<0.05$)* |
| Manz (1980)[1] | German gas/water plant workers | Lung cancer deaths higher in exposed than non-exposed group |
| Redmond et al (1981)[1] | US coke-oven workers | 2.63($p<0.05$)* |

Table 33 continued

| | | |
|---|---|---|
| Logan (1982) | UK men making coal/gas/coke, 1931 | 367 |
| | 1951 | 129 |
| | 1961 | 152 |
| | 1971 | 178 |
| Milham (1982)[4] | US roofers and slaters | 161[5] ($p<0.01$) |
| Blot et al (1983)[1] | US coke-oven workers | 1.2 |
| Hurley et al (1983)[1] | British coke-oven workers | 117 |
| Redmond (1983)[6]/Rockette and Redmond (1985)[6] | US coke-oven workers | >1.00 ($p<0.05$)* |
| Silverstein et al (1985)[6] | Millwrights/welders | >100 ($p<0.05$) |
| Kjuus et al (1986)[6] | Furnace/maintenance workers | >100 |
| OPCS (1986) | British chemical/gas/petroleum process plant operators - men | 179 |
| | Married women[7] | 211 |

E/W = English/Welsh

* Relative risk

1 From International Agency for Research on Cancer (1984)

2 Estimated from data given

3 Cancers of respiratory tract

4 From International Agency for Research on Cancer (1985)

5 Proportional mortality ratio

6 From International Agency for Research on Cancer (1987)

7 According to husband's occupation

References

1. Doll R, Fisher REW, Gammon EJ et al (1965) Mortality of gasworkers with special reference to cancers of the lung and bladder, chronic bronchitis, and pneumoconiosis. Br J Ind Med, 22, 1-12.

2. Doll R, Vessey MP, Beasley RWR et al (1972) Mortality of gasworkers - final report of a prospective study. Br J Ind Med, 29, 394-406.

3. International Agency for Research on Cancer (1984) Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 34: Polynuclear aromatic compounds, part 3, industrial exposures in aluminium production, coal gasification, coke production, and iron and steel founding, 37-131. IARC, Lyon.

4. International Agency for Research on Cancer (1985) Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 35: Polynuclear aromatic compounds, part 4, bitumens, coal-tars and derived products, shale-oils and soots, 83-159. IARC, Lyon.

5. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42, 174-177. IARC, Lyon.

6. Logan WPD (1982) Cancer mortality by occupation and social class 1851-1971. HMSO, London and IARC, Lyon.

7. Office of Population Censuses and Surveys (1978) Occupational mortality: The Registrar General's decennial supplement for England and Wales, 1970-72. HMSO, London.

8. Office of Population Censuses and Surveys (1986) Occupational mortality: The Registrar General's decennial supplement for Great Britain, 1979-80, 1982-83. HMSO, London.

## 34. Coffee drinking

Details of the six studies found which gave information on the risk of lung cancer in relation to coffee drinking are shown in Table 34. Five relative risks, ranging from 0.8-7.0, were given, of which four were above 1.00. One study reported that bronchial cancer cases drank more coffee than controls but did not give detailed results. Finally, one study compared non-coffee drinkers to coffee drinkers, rather than vice versa, and estimated relative risks of 2.07 for men and 1.38 for women who did not drink coffee.

With the exception of the study by Dean, no account appeared to have been taken of consumption of other hot beverages, such as tea. Thus, it is possible that in these studies non-drinkers of coffee could in fact have been consumers of other hot drinks, which may have led to inaccuracies.

Not surprisingly then, IARC described the evidence for the carcinogenicity of coffee drinking to humans as "inadequate" [3].

Table 34: Estimates of relative risk for coffee drinking

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Denoix et al (1958) | French men | Bronchial cancer cases drank more coffee than controls |
| Heuch et al (1983)[1]/ Jacobsen et al (1986)[1] | Norwegian residents | 1.8 |
| Schuman (1985)[2] | US men | 7.0 |
| Nomura et al (1986)[1] | Japanese men | 1.4 |
| Dean et al (1987) | UK male non-coffee drinkers | 2.07 |
| | Female non-coffee drinkers | 1.38 |
| Mettlin (1989)[1] | US residents, caffeinated coffee | 1.3(0.9-1.8) |
| | Decaffeinated coffee | 0.8(0.5-1.3) |

Footnote to Table 34

1 From International Agency for Research on Cancer (1991)

2 From Rowland (1985)

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References

1. Dean G, Lee PN, Todd GF and Wicken AJ (1977) Tobacco Research Council research paper 14.

2. Denoix PF, Schwartz D and Anguera G (1958) French investigation into the etiology of broncho-pulmonary cancer. Detailed analysis. Bull Assoc Franc pour l'etude du Cancer, 49: 1-37.

3. International Agency for Research on Cancer (1991) Monographs on the evaluation of carcinogenic risks to humans. Volume 51: Coffee, tea, mate, methylxanthines and methylgloyoxal, 41-197. IARC, Lyon.

4. Rowland WD (1985) Personal communication

35. Coke production

Several studies have concerned themselves with the potential risks between coke production and lung cancer, and details of them are given in Table 35. Eleven standardized mortality ratios (SMR) were calculated, and these ranged from 117 to 367. Nine studies gave estimates of relative risk from 1.00-44.00, with all but one being above 1.00. One proportional mortality ratio of 149 was also given, while the remaining study simply stated that 12 lung cancers were observed in gas-generator workers compared to none in workers in other areas.

When making an assessment of the possible risk of working in the coke production industry, several potential problems in the design of some of the studies should be borne in mind. Workers in coke production plants may be exposed to many substances to a varying degree, including aldehydes, amines, ammonia, arsenic compounds, asbestos, carbon compounds, hydrocarbons, hydrogen compounds, mercaptans, nitrogen heterocyclics, oxygen heterocyclics, phenols, polynuclear aromatic hydrocarbons, silica, sulphur compounds and thiocyanates. As only one study (Mazumdar) took objective measurements, of benzene concentrations, in the workplace, the exact nature of the subjects' exposures is impossible to ascertain.

The design of the study by Reid and Buck, in which the SMRs are based on a working population with only a short period of follow-up during which death might have occurred, may have led to a serious underestimation of the risk involved. Conversely, the use of a "precision factor" to weight the relative risks from various different plants in the study by Redmond et al (1972) increased the SMR over that calculated directly. Problems were also noted in the study by Radford, due to under-identification of deaths, loss of terminated workers, and lack of age corrections, and a difficulty in assessing how the reported excesses relate to coke-oven workers. Other potential sources of inaccuracy noted in some of the studies included small numbers of subjects, possible selection factors, imprecise work histories obtained from next-of-kin respondents, and differences in the source of information on occupation for cases and controls [1].

Despite these drawbacks, IARC stated that there was "sufficient" evidence for the carcinogenicity of certain exposures in the coke production industry to humans, and suggested that a possible causative agent may be coal-tar fumes [1,2].

Table 35: Estimates of relative risk/standardized mortality ratio for workers in coke production

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Kennaway and Kennaway (1936, 1947)[1] | E/W gas stokers/coke-oven chargers | 284* |
| Kuroda (1937)[1] | Japanese gas-generator workers | 12 lung cancers compared to none in workers in other areas |
| Reid and Buck (1956)[1] | English coking plant workers | 140* |
| Kawai et al (1967)[1] | Japanese gas-generator workers | 44.0 |
| Lloyd and Ciocco (1969)[1] | US non-white coke plant workers | 342*[2] |
| Lloyd (1971)[1] | US coke-oven workers | 248*[2] |
| Redmond et al (1972)[1] | US/Canadian coke-oven workers | 2.85($p<0.05$) |
| Mazumdar et al (1975)[1] | US/Canadian coke-oven workers | 13.65 |
| Sakabe et al (1975)[1] | Japanese coke-oven workers | 128* |
| Radford (1976)[1] | US steel company workers | 149[3] |
| Davies (1977)[1] | Welsh coke-oven workers | 1.00 |
| OPCS (1978) | E/W coal gas/coke oven furnacemen | 180*[4] |
| Axelson et al (1979)[1] | Swedish coke-oven workers | >1.00($p<0.05$) |
| Lloyd (1980)[1] | US coke-oven workers | 6.94($p<0.05$) |
| Redmond et al (1981)[1] | US coke-oven workers | 2.63($p<0.05$) |
| Logan (1982) | UK men making coal/gas/coke - 1931 | 367* |
| | 1951 | 129* |
| | 1961 | 152* |
| | 1971 | 178* |

Table 35 continued

| | | |
|---|---|---|
| Blot et al (1983)[1] | US coke-oven workers | 1.2 |
| Hurley et al (1983)[1] | British coke-oven workers | 117* |
| Redmond (1983)[5]/Rockette and Redmond (1985)[5] | US coke-oven workers | >1.00($p<0.05$) |

E/W = English/Welsh

* Standardized mortality ratio

1 From International Agency for Research on Cancer (1984)

2 Cancers of respiratory tract

3 Proportional mortality ratio

4 Estimated from data given

5 From International Agency for Research on Cancer (1987)

References

1. International Agency for Research on Cancer (1984) Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 34: Polynuclear aromatic compounds, part 3, industrial exposures in aluminium production, coal gasification, coke production, and iron and steel founding, 101-132. IARC, Lyon.

2. International Agency for Research on Cancer (1984) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42, 176-177. IARC, Lyon.

3. Logan WPD (1982) Cancer mortality by occupation and social class 1851-1971. HMSO, London.

4. Office of Population Censuses and Surveys (1978) Occupational mortality: The Registrar General's decennial supplement for England and Wales, 1970-72. HMSO, London.

36. Cooking over coal-fired stove

Only two studies could be found which gave data relevant to an investigation of the possible association between lung cancer risk and the use of a coal-fired stove for cooking, and details of these are given in Table 36. One study estimated a relative risk of 1.88, and while the other reported a positive association, no detailed results were presented.

Therefore, while the evidence shown in the table appears to suggest a positive relationship between lung cancer and cooking over a coal-fired stove, with so little available data it is not really clear whether such an association does exist.

Table 36: Estimates of relative risk for cooking over a coal-fired stove

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Chen et al (1990) | Chinese residents | Positive association |
| Liu et al (1993) | Chinese residents | 1.88(1.12-3.15) |

References

1. Chen BH, Hong CJ, Pandey MR and Smith KR (1990) Indoor air pollution in developing countries. Wld Hlth Statist Quart, 43, 127-138.

2. Liu J-Z, Hu H-S, Hu Y-H, Lu P and Hao L-Y (1993) A study on the relation between indoor exhaust and lung cancer. Proc Indoor Air, 1, 489-492.

37. Cooking with wok

Table 37 gives details of the only study found which attempted to relate lung cancer risk to cooking with a wok. Six relative risks were estimated for various indices of wok cooking, and these ranged from 1.4-2.8.

Although the findings of this study are suggestive of an association between lung cancer risk and cooking with a wok, results from more studies are needed before the relationship can be confirmed.

Table 37: Estimates of relative risk for cooking with a wok

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Gao et al (1987) | Chinese women reporting frequent eye irritation | 1.4(0.9-2.3)[1] |
| | | 2.8(1.8-4.3)[2] |
| | Some/frequent eye irritation and some/considerable household smokiness | 2.6(1.8-3.7) |
| | Stir frying 30+ dishes per week | 2.6(1.3-5.0) |
| | Deep frying 3+ dishes per week | 1.9(0.5-6.8) |
| | Boiling 12+ dishes per week | 2.2(1.3-3.7) |

1 Users of soybean oil
2 Users of rapeseed oil

References

1. Gao Y-T, Blot WJ, Zheng W et al (1987) Lung cancer among Chinese women. Int J Cancer, 40, 604-609.

38. Cooking with wood/straw

Table 38 gives details of the only study found which attempted to relate lung cancer risk to the use of wood or straw as a fuel for cooking. A relative risk of 1.77 was estimated.

With only one study reporting it is not really possible to evaluate the potential carcinogenicity of wood or straw used as a cooking fuel.

Table 38: Estimate of relative risk for cooking with wood/straw

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Sobue (1990) | Japanese women | 1.77(1.08-2.91) |

References

1. Sobue T (1990) Association of indoor air pollution and lifestyle with lung cancer in Osaka, Japan. Int J Epidemiol, 19, S62-S66.

39. Cooks

Only four studies were found which gave data relevant to an investigation of the possible association between employment as a cook and the risk of lung cancer, and these are detailed in Table 39. Two relative risks, of 0.7 and 1.82, were estimated, along with two proportional mortality ratios, of 100 and 103, and two proportional registration ratios, of 124 and 130. One study observed a mortality rate of 3.2 per 1000 per year.

It has been suggested that the excess of lung cancers seen in cooks may be caused by the fumes generated during cooking, particularly frying [2,3], and also that frequent tasting of hot food may cause thermal irritation of the upper aerogastric tract [3]. However, the evidence for a possible association between lung cancer risk and employment as a cook presented here is hardly conclusive, and even if a risk does exist, it does not appear to be very large.

Table 39: Estimates of relative risk/mortality ratio for employment as a cook

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Boucot et al (1972) | US male bakers/pastry cooks/ chefs/cooks | 3.2[1] |
| OPCS (1978) | E/W male cooks - aged 15-64 | 100[2] |
| | Aged 65-74 | 103[2] |
| | Registrations, 1966-7 | 130($p<0.01$)[3] |
| | 1968-9 | 124($p<0.05$)[3] |
| Coggon and Wield (1993) | UK army cooks | 1.82(1.25-2.57) |
| Kjaerheim and Andersen (1993) | Norwegian male cooks | 0.7(0.2-1.7)[4] |

Table 39 continued

E/W = English/Welsh

1 Per 1000 per year

2 Proportional mortality ratio

3 Proportional registration ratio

4 Standardized incidence ratio

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References

1. Boucot KR, Weiss W, Seidman H, Carnahan W and Cooper DA (1972) The Philadelphia pulmonary neoplasm research project: basic risk factors of lung cancer in older men. Am J Epidemiol, 95, 4-16.

2. Coggon D and Wield G (1993) Mortality of army cooks. Scand J Work Environ Health, 19, 85-88.

3. Kjaerheim K and Andersen A (1993) Incidence of cancer among male waiters and cooks: Two Norwegian cohorts. Cancer Causes and Control, 4, 419-426.

4. Office of Population Censuses and Surveys (1978) Occupational mortality: The Registrar General's decennial supplement for England and Wales, 1970-72. HMSO, London.

## 40. Cushing's syndrome

Table 40 gives details of the three studies which attempted to relate the risk of lung cancer to Cushing's syndrome, a disorder due to the excessive secretion of corticosteroid hormones by the adrenal cortex. A total of 24 cases of lung cancer were associated with the syndrome.

It was suggested that the association of the two conditions might arise from secretion of hormones by the tumour, or that both conditions may be due to pituitary-hypothalamic or adrenal over-activity. However, in the absence of any risk estimates it is not possible to determine the relationship between lung cancer and Cushing's syndrome, or the cause of any such association if it does exist.

Table 40: Observations for Cushing's syndrome

| Study | Population | Observations |
|---|---|---|
| Allott and Skelton (1960) | Hospital patients | 18 lung cancer cases associated with Cushing's syndrome |
| Vogel et al (1961) | Hospital patients | 5 lung cancer cases associated with Cushing's syndrome |
| Marks et al (1963) | US male | 1 lung cancer case associated with Cushing's syndrome |

References

1. Allott EN and Skelton MO (1960) Increased adrenocortical activity associated with malignant disease. Lancet, ii, 278-283.

2. Marks LJ, Russfield AB and Rosenbaum DL (1963) Corticotropin-secreting carcinoma. JAMA, 183, 115-117.

3. Vogel MD, Keating FR and Bahn RC (1961) Acute Cushing's syndrome associated with bronchogenic carcinoma. Proc Mayo Clinic, 36, 387-393.

41. DDT

Table 41 gives details of the studies which investigated the possible association between lung cancer risk and exposure to DDT. Five relative risks were estimated, ranging from 0.91-1.8, of which all but one were above 1.00. Two standardized mortality ratios, of 156 and 180, were also calculated. Additionally, one study reported five cases of lung cancer associated with inhalation of DDT among a group of patients with granulomatous disease of the lungs.

Only the study by Austin took objective measurements of exposure to DDT, by measuring serum levels of the chemical. Two other studies (Blair, Ditraglia) did at least attempt to quantify exposure by recording the length of time workers were exposed to DDT. However, no information on the level of exposure was available from the other studies. Thus, inaccuracies could have been introduced into them. Furthermore, several of the studies (Bartel, Blair, Wang and MacMahon, Wong) stated that workers were exposed to other substances, usually other pesticides, in addition to DDT, making an analysis of the effects of DDT alone very difficult.

Therefore, IARC felt there was "inadequate" evidence for the carcinogenicity of DDT to humans [1], and in a later review, described it as only "possibly carcinogenic" [2].

Table 41: Estimates of relative risk/standardized mortality ratio for exposure to DDT

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Pimentel and Menezes (1979)[1] | Patients with granulomatous disease of the lungs | Five lung cancer cases reported |
| Wang and MacMahon (1979)[1] | Pesticide applicators | >1.00 |
| Bartel (1981)[1] | Agricultural workers | 180(140-240)* |
| Ditraglia et al (1981)[2] | US DDT manufacturing workers | 1.3(0.34-3.2) |
| Blair et al (1983)[1] | Pesticide applicators | >1.00 |
| Wong et al (1984)[1] | Male DDT manufacturing workers | 156(74-286)*[3] |
| Wicklund et al (1988)[2] | US orchard workers | 0.91(0.4-2.1)[3] |
| Austin et al (1989)[2] | US adults | 1.8(0.5-6.2)[3] |

Footnote to Table 41

* Standardized mortality ratio

1 From International Agency for Reseach on Cancer (1987)

2 From International Agency for Reseach on Cancer (1991)

3 Tumours of respiratory system

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References

1. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42, 186-189. IARC, Lyon.

2. International Agency for Research on Cancer (1991) Monographs on the evaluation of carcinogenic risks to humans. Volume 53: Occupational exposures in insecticide application, and some pesticides, 179-249. IARC, Lyon.

## 42. Debrisoquine metabolism

Six studies were found which attempted to relate lung cancer risk to debrisoquine metabolism, and Table 42 gives details of them. Two estimates of relative risk were given, one of 0.61 for poor debrisoquine metabolizers and one of 6.1 for extensive metabolizers. One study reported that 78.8% of cases were extensive metabolizers compared to only 27.8% of controls, while another noted that 1.9% of cases were poor metabolizers compared to some 8.7% of the control group. Two studies failed to find any differences between cases and controls in the proportions of the metabolic types.

All of the studies were of a case-control design, and most assessed debrisoquine metabolism by administering the drug to respondents and classifying them phenotypically according to the rate of metabolism. However, it is possible that debrisoquine metabolism may be affected by the disease status of the subject [5], and in these studies it is not clear whether the observed differences in metabolic type were a cause or an effect of lung cancer. Only the study by Smith measured debrisoquine metabolism genotypically, thus avoiding this problem. In the light of this drawback, it is difficult to properly evaluate the possible association between lung cancer risk and debrisoquine metabolism suggested by the evidence presented in the table.

Table 42: Estimates of relative risk for debrisoquine metabolism

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Ayesh et al (1984) | UK residents | 78.8% of cases extensive metabolizers compared to 27.8% of controls |
| Roots et al (1988) | German residents | 0.61(0.31-1.15)[1] |
| Law et al (1989) | UK residents | 1.9% cases poor metabolizers compared to 8.7% of controls |
| Caporaso et al (1990) | US residents | 6.1(2.2-17.1)[2] |
| Spiers et al (1990) | UK residents | No difference in proportion of poor metabolizers between cases and controls |

Table 42 continued

| | | |
|---|---|---|
| Smith et al (1992) | UK residents | No difference in proportion of poor metabolizers between cases and controls |

1 Relative risk estimate for poor metabolizers
2 Relative risk estimate for extensive metabolizers

References


1. Ayesh R, Idle JR, Ritchie JC, Crothers MJ and Hetzel MR (1984) Metabolic oxidation phenotypes as markers for susceptibility to lung cancer. Nature, 312, 169-170.

2. Caporaso NE, Tucker MA, Hoover RN et al (1990) Lung cancer and the debrisoquine metabolic phenotype. JNCI, 82, 1264-1272.

3. Law MR, Hetzel MR and Idle JR (1989) Debrisoquine metabolism and genetic predisposition to lung cancer. Br J Cancer, 59, 686-687.

4. Roots I, Drakoulis N, Ploch M et al (1988) Debrisoquine hydroxylation phenotype, acetylation phenotype, and ABO blood groups as genetic host factors of lung cancer risk. Klin Wochenschr, 66, 87-97.

5. Smith CAD, Moss JE, Gough AC, Spurr NK and Wolf CR (1992) Molecular genetic analysis of the cytochrome P450-debrisoquine hydroxylase locus and association with cancer susceptibility. Environ Health Perspec, 98, 107-112.

6. Speirs CJ, Murray S, Davies DS, Biola Mabadeje AF and Boobis AR (1990) Debrisoquine oxidation phenotype and susceptibility to lung cancer. Br J Clin Pharmac, 29, 101-109.

## 43. Dental mechanics

Details of the only study found which attempted to relate the risk of lung cancer to employment as a dental mechanic are given in Table 43. Three cases of lung cancer among men working as dental mechanics were reported, as was an increased risk of lung cancer found in two previous surveys, details of which were not available.

It was noted by the authors of the study that dental mechanics may be exposed to several potentially carcinogenic materials, including solvents, fumes, dust from abrasives and asbestos paper. It is therefore possible that any one of these may have caused the observed increase in lung cancer, but with no further information available it is not possible to determine which one, if any. Thus, the relationship between lung cancer risk and employment as a dental mechanic remains unclear.

Table 43: Observations for dental mechanics

| Study | Population | Observations |
|---|---|---|
| Coggon et al (1986) | UK men | Three lung cancer cases worked as dental mechanics |

### References

1. Coggon D, Pannett B, Osmond C and Acheson ED (1986) A survey of cancer and occupation in young and middle aged men. I Cancers of the respiratory tract. Br J Ind Med, 43, 332-338.

## 44. Dermatomyositis

Table 44 gives details of the only study found which attempted to investigate lung cancer risk in relation to dermatomyositis. It was reported that 14 cases of lung cancer were associated with dermatomyositis.

With so little information available it is not possible to evaluate the relationship between lung cancer and dermatomyositis, but it was thought unlikely that such an association existed [1].

Table 1: Observations for dermatomyositis

| Study | Population | Observations |
|---|---|---|
| Williams (1959) | Hospital patients | 14 cases of lung cancer associated with dermatomyositis |

### References

1. Roe FJC and Walters MA (1965) Some unsolved problems in lung cancer etiology. Progr Exp Tumor Res, 6, 126-227.

2. Williams RC (1959) Dermatomyositis and malignancy: A review of the literature. Ann Intern Med, 50, 1174-1181.

## 45. 1,2-Dibromo-3-chloropropane

Only two studies could be found which gave any data relevant to an investigation of the possible association between lung cancer risk and exposure to 1,2-dibromo-3-chloropropane, and details of these are given in Table 45. One standardized mortality ratio, of 146, was calculated, while the other study stated that the increase in mortality observed was due mainly to an excess of respiratory cancers.

However, several drawbacks were noted with these studies. Workers in the study by Hearn had been exposed to arsenicals as well as 1,2-dibromo-3-chloropropane, but no information on the extent of exposure to either substance was given. Workers in the study by Wong were exposed to several brominated chemicals, but again no details of exposure were given.

In view of the numbers involved and the lack of control of confounding factors, IARC considered these studies to be "inadequate", as was the evidence for the carcinogenicity of 1,2-dibromo-3-chloropropane to humans [1].

Table 45: Estimates of standardized mortality ratio for exposure to 1,2-dibromo-3-chloropropane

| Study | Population | Standardized mortality ratio |
|---|---|---|
| Hearn et al (1984)[1] | Chemical workers | Observed increase in mortality due mainly to excess of respiratory cancers |
| Wong et al (1984)[1] | US workers | 146[2] |

1 From International Agency for Research on Cancer (1987)

2 Estimated from data given

References

1. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: an updating of IARC monographs volumes 1 to 42, 191-192. IARC, Lyon.

46. Diesel engine exhausts

Table 46 lists the 30 studies found which gave details of a possible association between exposure to diesel engine exhausts and lung cancer. For cohort studies the estimates of relative risk ranged from 0.88-2.67, and standardized mortality ratios calculated were between 99 and 226, with 20 of the 26 reported results showing a positive association. The case-control studies showed a similar pattern, with relative risk estimates ranging from 0.60-2.70, with 21 out of 25 being above 1.00.

However, when considering these results, some important limitations in the design of the studies must be borne in mind. None of the studies included measurements of diesel exhaust concentrations during the actual exposure of the study population, relying instead on surrogate indices such as contemporary measurement of diesel soot in work environments similar to those used to classify past exposure, job history from interview, employment records or death certificates, and membership in a trade union. Additionally, further inaccuracies will be introduced due to the variable amount of time that subjects in different studies were required to have spent in a particular job or occupation in order to have been considered "exposed". Finally, many respondents exposed to diesel engine exhausts will have been exposed to other pollutants, particularly gasoline engine exhausts.

Not surprisingly then, a review by the US EPA [29] concluded that, due to methodological drawbacks, the evidence of carcinogenicity in humans was considered to be limited for diesel exhaust exposure. A more recent review [21] described the evidence of an association between exposure to diesel engine exhausts and lung cancer as "largely circumstantial", although it was felt that "taken in aggregate...the weight of the epidemiological evidence is convincing for a small positive effect." This is reflected by the categorization given by IARC, who describe diesel engine exhausts as "probably carcinogenic" (Group 2A) [17].

Table 46: Estimates of relative risk/standardized mortality ratio for diesel engine exhausts

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Cohort studies: | | |
| Raffle (1957) | London transport employees | 1.42 |
| Kaplan (1959) | Baltimore/Ohio railroad workers | 0.88 |
| Waxweiler et al (1973) | US potash miners | No association |
| Leupker and Smith (1978) | US Teamsters Union Cohort | 1.21($p > 0.05$) |
| Ahlberg et al (1981) | Swedish male truck drivers | 1.33(1.10-1.60) |
| Stern et al (1981) | New Jersey vehicle examiners | 1.02 |
| Waller (1981) | London transport employees | 0.90($p > 0.05$) |
| Howe et al (1983) | Canadian railroad workers | 1.40(1.20-1.50) |
| Rushton et al (1983) | London bus maintenance workers | 101 (82-122)* |
| Wong et al (1985) | US heavy equipment operators | 99 (88-110)* |
| Gustafsson et al (1986) | Swedish dock workers | 132 (105-166)* |
| Steenland (1986) | US teamsters - mechanics | 226 (162-309)* |
| | truck drivers | 154 (144-166)* |
| | dock workers | 132 (99-175)* |
| | other | 116 (95-142)* |
| Edling et al (1987) | Swedish bus company employees | <1.00 |
| Boffetta et al (1988) | US males - miners | 2.67(1.63-4.37) |
| | Heavy equipment operators | 2.60(1.12-6.06) |
| | Railroad workers | 1.59(0.94-2.69) |
| | Truck drivers | 1.24(0.93-1.66) |
| Garshick et al (1988) | US railroad workers - age 40-44 | 1.45(1.11-1.89) |
| | age 45-49 | 1.33(1.03-1.73) |
| | age 50-54 | 1.20($p > 0.05$) |
| | age 55-59 | 1.18($p > 0.05$) |
| | age 60-64 | 0.99($p > 0.05$) |
| Grandjean et al (1991) | Danish filling station attendants | 1.58(1.25-2.00) |

Table 46 continued

| | | |
|---|---|---|
| Case-control studies: | | |
| Menck and Henderson (1976) | LA County truck drivers | 1.65($p < 0.05$) |
| Decoufle et al (1977) | US truck/bus/taxi drivers | 0.92($p > 0.05$) |
| | US train engineers and firemen | 0.94($p > 0.05$) |
| Williams et al (1977) | US male truck drivers | 1.52($p > 0.05$) |
| Coggon et al (1984) | English/Welsh populations | 1.30(1.10-1.60) |
| Hall and Wynder (1984) | US males | 2.00(1.20-3.20) |
| | Heavy equipment repair/operators | 1.90($p > 0.05$) |
| Buiatti et al (1985) | Italian male taxi drivers | 1.80(1.00-3.40) |
| Damber and Larsson (1987) | Swedish professional drivers | 1.20(0.90-2.60) |
| | Underground miners | 2.70(1.20-6.00) |
| Garshick et al (1987) | US railroad workers | 1.39(1.05-1.83) |
| Lerchen et al (1987) | New Mexicans exposed to diesel | 0.60(0.20-1.60) |
| Benhamou et al (1988) | French motor vehicle drivers | 1.42(1.07-1.89) |
| | Transport equipment operators | 1.35(1.05-1.75) |
| | Miners and quarrymen | 2.10(1.10-4.30) |
| Siemiatycki et al (1988) | Montreal males | 1.20($p > 0.05$) |
| Hayes et al (1989) | US truck drivers > 10 years | 1.50(1.10-1.90) |
| | All except truck drivers | 1.30(1.00-1.70) |
| | Taxi drivers/chauffeurs <10 years | 2.50(1.40-4.80) |
| | Taxi drivers/chauffeurs >10 years | 1.20(0.50-2.60) |
| | Heavy equipment operators | 2.10(0.60-7.10) |
| Boffetta et al (1990) | US males "probably exposed" | 0.92(0.75-1.12) |
| | Self-reported exposure | 1.26($p > 0.05$) |
| Steenland et al (1990) | US truck mechanics | 1.69($p > 0.05$) |
| | Diesel truck drivers | 1.42($p > 0.05$) |

* Standardized mortality ratio

References

1. Ahlberg J, Ahlbom A, Lipping H, Norell S and Osterblom L (1981) Cancer among professional drivers - a problem-oriented register-based study [Swed.] Lakartidningen, 78, 1545-46.

2. Benhamou S, Benhamou E and Flamant R (1988) Occupational risk factors of lung cancer in a French case-control study. Br J Ind Med, 454, 231-233.

3. Boffetta P, Stellman SD and Garfinkel L (1988) Diesel exhaust exposure and mortality among males in the American Cancer Society prospective study. Am J Ind Med, 14, 403-415.

4. Boffetta P, Harris RE and Wynder EL (1990) Case-control study on occupational exposure to diesel exhaust and lung cancer risk. Am J Ind Med, 15, 577-591.

5. Buiatti E, Kriebel D, Geddes M, Santucci M and Pucci N (1985) A case-control study of lung cancer in Florence, Italy. I. Occupational risk factors. J Epidemiol Commun Health, 39, 244-250.

6. Coggon D, Pannett B and Acheson ED (1984) Use of job-exposure matrix in an occupational analysis of lung and bladder cancers on the basis of death certificates. JNCI, 72, 61-66.

7. Damber LA and Larsson LG (1987) Occupation and male lung cancer: a case-control study in northern Sweden. Br J Ind Med, 44, 446-453.

8. Decoufle P, Stanislawczyk K, Houten L, Bross JDJ and Viadana E (1977) A retrospective survey of cancer in relation to occupation. DHEW (NIOSH) Publ. No. 77-178. US Department of Health, Education and Welfare.

9. Edling C, Anjou C-G, Axelson O and Kling H (1987) Mortality among personnel exposed to diesel exhaust. Int Arch Occup Environ Health, 59, 559-565.

10. Garshick E, Schenker MB, Munoz A et al (1987) A case-control study of lung cancer and diesel exhaust exposure in railroad workers. Am Rev Respir Dis, 135, 1242-1248.

11. Garshick E, Schenker MB, Munoz A et al (1988) A retrospective cohort study of lung cancer and diesel exhaust exposure in railroad workers. Am Rev Respir Dis, 137, 820-825.

12. Grandjean P and Andersen O (1991) Lung cancer in filling station attendants. Am J Ind Med, 20, 763-768.

13. Gustafsson L, Wall S, Larsson L-G and Skog B (1986) Mortality and cancer incidence among Swedish dock workers - a retrospective cohort study. Scand J Work Environ Health, 12, 22-26.

14. Hall NEL and Wynder EL (1984) Diesel exhaust exposure and lung cancer: a case-control study. Environ Res, 34, 77-86.

15. Hayes RB, Thomas T, Silverman DT et al (1989) Lung cancer in motor exhaust occupations. Am J Ind Med, 16, 685-695.

16. Howe GR, Fraser D, Lindsay J, Presnal B and Yu SZ (1983) Cancer mortality (1965-1977) in relation to diesel fume and coal exposure in a cohort of retired railway workers. JNCI, 70, 1015-1019.

17. International Agency for Research on Cancer (1989) Monographs on the evaluation of carcinogenic risks to humans. Volume 46: Diesel and gasoline engine exhausts and some nitroarenes, 132-185. IARC, Lyon.

18. Kaplan I (1959) Relationship of noxious gases to carcinoma of the lung in railroad workers. JAMA, 171, 97-101.

19. Lerchen ML, Wiggins CL and Samet JM (1987) Lung cancer and occupation in New Mexico. JNCI, 79, 639-45.

20. Leupker RV and Smith ML (1978) Mortality in unionized truck drivers. J Occup Med, 20, 677-682.

21. Mauderly JL (1992) Diesel Exhaust. In: Environmental toxicants: human exposures and their health effects. 119-162. Van Nos, New York.

22. Menck HR and Henderson BE (1976) Occupational differences in rates of lung cancer. J Occup Med, 18, 797-801.

23. Raffle PAB (1957) The health of the worker. Br J Ind Med, 14, 73-80.

24. Rushton L, Alderson MR and Nagarajah CR (1983) Epidemiological survey of maintenance workers in London Transport executive bus garages and Chiswick works. Br J Ind Med, 40, 340-345.

25. Siemiatycki J, Gerin M, Stewart P, Nadon L, Dewar R and Richardson L (1988) Associations between several sites of cancer and ten types of exhaust and combustion products: results from a case-referent study in Montreal. Scand J Work Environ Health, 14, 79-90.

26. Steenland K (1986) Lung cancer and diesel exhaust: a review. Am J Ind Med, 10, 177-189.

27. Steenland NK, Silverman DT and Hornung RW (1990) Case-control study of lung cancer and truck driving in the Teamsters' Union. Am J Publ Health, 80, 670-674.

28. Stern FB, Curtis RA and Lemen RA (1981) Exposure of motor vehicle examiners to carbon monoxide: a historical perspective mortality study. Arch Environ Health, 36, 59-66.

29. United States Environmental Protection Agency (1990) Health assessment document for diesel emissions. EPA.

30. Waller RE (1981) Trends in lung cancer in London in relation to exposure to diesel fumes. Environ Int, 5, 479-483.

31. Waxweiler RJ, Wagoner JK and Archer VE (1973) Mortality of potash workers. J Occup Med, 15, 486-489.

32. Williams RR, Stegens NL and Goldsmith JR (1977) Associations of cancer site and type with occupation and industry from the Third National Cancer Survey interview. JNCI, 59, 1147-1185.

33. Wong D, Mitchell CE, Wolff RK, Mauderly JL and Jeffrey AM (1986) Mortality among members of a heavy construction equipment operators union with potential exposure to diesel emissions. Br J Ind Med, 42, 435-438.

47. Dietary fat/cholesterol and serum cholesterol

Table 47a gives details of the studies which considered dietary fat or cholesterol as a risk factor for lung cancer. It can be seen from this table that, of the 4 risk factors presented for low dietary intake, 2 are below 1.00 and 2 above, with the estimates of relative risk ranging from 0.60-2.70. For the studies which looked at high dietary intake the relative risk estimates ranged from 0.30-3.50, with 24 out of 32 being above 1.00, and only 8 risk estimates being 1.00 or below. Additionally, one study presented highly significant partial regression coefficients of 6.30 and 16.2, for age groups of 55-64 and 65-74 years respectively. However, as on the whole few confidence intervals were given, it is difficult to interpret the significance of these findings.

Table 47b lists the four prospective studies which attempted to measure serum cholesterol levels in relation to lung cancer risk. Two studies found some evidence of an increased risk in individuals with low serum cholesterol, although the results were only significant in one. However, the other two studies appeared to find a positive association between serum cholesterol level and lung cancer risk, with respondents in the lower cholesterol categories having a reduced risk.

However, several points should be considered when trying to interpret these results. Table 19a shows the wide variety of indices used to measure dietary fat intake, and it is not clear how accurately these may have measured fat intake. Additionally, most of the studies limited their subjects to men only, and so few results are available for women. Therefore, if any differences exist between the sexes they will be very difficult to spot.

Unlike nutrients such as vitamins A and C, it is well known that serum cholesterol is not highly correlated with dietary cholesterol, but rather with intake of saturated fat. Therefore, while the results from studies looking at dietary and at serum cholesterol may show few similarities, there should be some comparability in the findings of those studies measuring dietary fat intake and those measuring serum cholesterol. As discussed above, while most of the relative risks for high fat intake were above 1.00, the evidence for high serum cholesterol was less convincing.

Finally, the onset of cancer may affect appetite and metabolism, so that patients may appear to have different levels of dietary and serum nutrients than non-sufferers. It has been suggested that the early stages of cancer cause a drop in serum cholesterol levels [7,8,10,14,15], so that subjects with lower levels may have a cancer that has not yet been detected. This is obviously a problem in case-control studies, and may also be so in prospective studies if the period of follow-up is not very long.

Table 47a: Estimates of relative risk for dietary cholesterol/fat intake

| Study | Study type | Location | Index of fat intake | Relative risk (95% limits) |
|---|---|---|---|---|
| Low dietary intake: | | | | |
| Mettlin et al (1979) | C-C | USA | Milk | 1.60[1] |
| Wu et al (1985) | C-C | USA | Dairy products/ eggs | 2.70[2] |
| Byers et al (1987) | C-C | USA | Total fat | 0.60[3] |
| | | | Cholesterol | 0.90[3] |
| High dietary intake: | | | | |
| Hinds et al (1983) | C-C | USA | Cholesterol | 1.75[3] |
| | | | Cholesterol | 3.50(1.70-7.21)[1] |
| Kvale et al (1983) | PR | Norway | Milk | 0.30[1] |
| | | | Meat | 1.00[1] |
| | | | Eggs | 0.90[1] |
| Heilbrun et al (1984) | PR | USA | Cholesterol | 1.00[1] |
| Wynder et al (1987) | EC | 43 countries | Total fat | >1.00(p <0.0001)[1] |
| | | | | >1.00(p = 0.006)[2] |
| Goodman et al (1988) | C-C | USA | Total cholesterol | 1.77(1.12-2.80)[3] |
| | | | Eggs | 1.36(0.89-2.09)[3] |
| | | | Other sources | 1.99(1.25-3.15)[3] |
| Mettlin (1989) | C-C | USA | Animal fat | 1.50 |
| | | | Whole milk | 2.10 |
| | | | Pork chops | 2.40 |

Table 47a continued

| | | | | |
|---|---|---|---|---|
| Jain et al (1990) | C-C | Canada | Cholesterol | 1.55[3] |
| | | | Total fat | 1.30 |
| Fraser et al (1991) | PR | USA | Meat/fish/poultry | 1.31(0.52-3.28) |
| | | | Milk | 0.88(0.37-2.12) |
| Kesteloot et al (1991) | EC | 34 countries | Dairy fat/lard | >1.00($p < 0.01$)[1] |
| | | | | No association[2] |
| Knekt et al (1991) | PR | Finland | Cholesterol | 1.03(0.58-1.85)[1] |
| | | | Total fat | 1.55(0.78-3.10)[1] |
| | | | Saturated fat | 1.64(0.84-3.19)[1] |
| | | | Monounsat. fat | 1.07(0.56-2.05)[1] |
| | | | Polyunsat. fat | 0.87(0.50-1.52)[1] |
| | | | P/S ratio | 0.71(0.44-1.12)[1] |
| Shekelle et al (1991) | PR | USA | Cholesterol | 1.94[1] |
| Xie et al (1991) | EC | 29 countries | Animal fat | 6.30(1.86-10.7)[5,6] |
| | | | | 16.2(9.19-23.2)[5,7] |
| Goodman et al (1992) | C-C | USA | Dairy products | 2.19(1.40-3.43)[3] |
| | | | Processed meats | 2.35(1.83-3.01)[3] |
| | | | Eggs | 1.31(0.85-2.03)[3] |
| | | | Desserts | 2.12(1.40-3.20)[3] |
| | | | Fried foods | 1.42(0.89-2.29)[3] |

C-C = Case-control; EC = Ecological; PR = Prospective; P/S = ratio of polyunsaturated to saturated fat

1 Males only

2 Females only

3 Estimated from data for males and females separately

4 Data from 43 countries

5 Partial regression coefficient

6 Age group 55-64 years only

7 Age group 65-74 years only

Table 47b: Measurements of serum cholesterol levels in lung cancer patients and controls (Males only unless otherwise indicated)

| Study | Location | Average cholesterol difference between cases and controls | Significance of difference |
|---|---|---|---|
| Kagan et al (1981) | USA | -20.30 mg/dl | $p < 0.01$ |
| Law and Thompson (1991) | Various[1] | -0.181 mmol/l | $p > 0.05$[2] |
| | | -0.041 mmol/l | $p > 0.05$[3] |
| | | -0.106 mmol/l | $p > 0.05$[2,4] |
| | | -0.032 mmol/l | $p > 0.05$[3,4] |
| | | Cholesterol level | Relative risk (95% limits) |
| Knekt et al (1991) | Finland | 215-248 mg/dl | 0.80(0.40-1.50) |
| | | 249-285 mg/dl | 1.10(0.60-1.80) |
| | | >285 mg/dl | 1.30(0.80-2.20) |
| Shekelle et al (1992) | USA | <5.53 mmol/l | 0.90($p > 0.05$) |
| | | 5.53-6.13 mmol/l | 0.70($p > 0.05$) |
| | | 6.14-6.90 mmol/l | 1.00($p > 0.05$) |
| | | ≥6.91 mmol/l | 1.00($p > 0.05$) |

1 Combined results from 33 prospective studies

2 Short term studies (cancers presenting in first 5 years in mortality studies or first 2 years in incidence studies)

3 Long term studies (cancer presenting after 5 years in mortality studies or after 2 years in incidence studies)

4 Females only

References

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48. Dimethyl sulphate

No epidemiological studies concerning the risk of lung cancer in relation to exposure to dimethyl sulphate could be found, but two case reports of cancers following such exposure are shown in Table 48. A total of five cases of cancer of the lung and bronchus have been reported in workers occupationally exposed to dimethyl sulphate.

No objective measurements of the level of exposure of the cases were reported. In addition, it was stated that the case in the study by Bettendorf was also exposed to bis(chloromethyl)ether and chloromethyl methyl ether, both potent carcinogens, in higher concentrations than the exposure to dimethyl sulphate. It is clearly possible, then, that the observed pulmonary cancer could have been caused by exposure to substances other than dimethyl sulphate.

Although IARC stated that there was "some suspicion as to the possible carcinogenicity of dimethyl sulphate in man" [1], the evidence to support this was felt to be "inadequate" [2].

Table 48: Case reports following exposure to dimethyl sulphate

| Study | Observation |
|---|---|
| Druckrey et al (1966)[1] | 4 cases of bronchial carcinoma observed among chemical factory workers exposed to dimethyl sulphate. |
| Bettendorf (1977)[2] | 1 case of pulmonary carcinoma after exposure to 'small amounts' of dimethyl sulphate. |

1 From International Agency for Research on Cancer (1974)

2 From International Agency for Research on Cancer (1987)

References

1. International Agency for Research on Cancer (1976) Monographs on the evaluation of carcinogenic risk of chemicals to man. Volume 4: Some aromatic amines, hydrazine and related substances, N-nitroso compounds and miscellaneous alkylating agents, 271-276. IARC, Lyon.

2. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42, 200-201. IARC, Lyon.

## 49. Dock workers

Only four studies were found which attempted to relate the risk of lung cancer to employment as a dock worker, and details of these are given in Table 49. Nine standardized mortality ratios were given, lying in the range 127-246, along with three proportional registration ratios, of between 122 and 143. Additionally, one proportional mortality ratio of 117 was presented, while another study estimated a relative risk of 1.46.

It was suggested that exposure to diesel exhaust may be an important factor in the development of lung cancer among dock workers [1]. However, only the study by Emmelin et al gave any information on the level of the workers' exposure, and this was not based on objective measurements but on an index of exposure, namely annual diesel fuel consumption. Therefore, it is difficult to assess lung cancer risk in terms of diesel exhaust exposure. Furthermore, it is likely that dock workers are exposed to other, potentially carcinogenic, substances such as asbestos [1], but as no measurements of workplace exposures were taken it is impossible to determine whether or not this is so.

The evidence presented in the table is consistent with an increased risk of lung cancer in dock workers. However, this information comes from a small number of studies and does not provide sufficient data to determine the nature of the subjects' exposures, nor the agent or agents responsible for the observed increase in risk.

Table 49: Estimates of standardized mortality ratio/relative risk for dock workers

| Study | Location | Subset | Standardized mortality ratio |
|---|---|---|---|
| OPCS (1978) | England | Men, 1970-72 | 117($p<0.05$)[1] |
| | and | 1966-67 | 122($p<0.01$)[2] |
| | Wales | 1968-69 | 125($p<0.01$)[2] |
| Logan (1982) | England | Men, 1931 | 183 |
| | and | 1951 | 149 |
| | Wales | 1961 | 169 |
| | | 1971 | 182 |
| | | Married women[3], 1951 | 132 |
| | | 1961 | 246 |
| | | 1971 | 213 |
| OPCS (1986) | Great | Men | 136($p<0.01$) |
| | Britain | Married women[3] | 127($p<0.01$) |
| | | Men | 143[2] |
| Emmelin et al (1993) | Sweden | Men | 1.46(0.93-2.29)* |

* Relative risk (95% limits)

1 Proportional mortality ratio

2 Proportional registration ratio

3 According to husband's occupation

References

1. Emmelin A, Nystrom L and Wall S (1993) Diesel exhaust exposure and smoking: A case-referent study of lung cancer among Swedish dock workers. Epidemiol, 4, 237-44.

2. Logan WPD (1982) Cancer mortality by occupation and social class 1851-1971. HMSO, London and IARC, Lyon.

3. Office of Population Censuses and Surveys (1978) Occupational mortality: the Registrar General's decennial supplement for England and Wales, 1970-72. HMSO, London.

4. Office of Population Censuses and Surveys (1986) Occupational mortality: the Registrar General's decennial supplement for Great Britain, 1979-80, 1982-83. HMSO, London.

## 50. Epichlorohydrin

Only three studies were found which attempted to relate the risk of lung cancer to exposure to epichlorohydrin, and details of these are given in Table 50. Two standardized mortality ratios, of 80 and 137, were calculated, along with one relative risk of 2.4.

The main problem with these studies was the lack of information on the workers' exposures. Although the study by Barbone attempted to classify potential exposures this was based on interviews with the respondents and not on objective measurements. Additionally, no attempt was made to separate out the effects of epicholorohydrin and anthraquinone dye in those workers who had been exposed to both. Similar problems were noted in the study by Enterline, in which some workers had previously been exposed to isopropyl alcohol, and in the study by Tassignon, in which it was stated that workers had been exposed to a variety of chemicals but no data was available on which ones.

Therefore, with so few studies reporting, and noting the drawbacks mentioned above, it is difficult to reach any conclusions about the carcinogenicity of epicholorohydrin to humans. Not surprisingly then, IARC [2] classified the evidence as "inadequate".

Table 50: Estimates of standardized mortality ratio/relative risk for exposure to epichlorohydrin

| Study | Population | Standardized mortality ratio |
|---|---|---|
| Enterline (1982)[1] | US factory workers | 137*[2] |
| Tassignon et al (1983)[1] | European factory workers | 80*[2] |
| Barbone et al (1992) | US dye/resin factory workers | 2.4(1.1-5.2)* |

* Relative risk

1 From International Agency for Research on Cancer (1987)

2 Estimated from data given

References

1. Barbone F, Delzell E, Austin H and Cole P (1992) A case-control study of lung cancer at a dye and resin manufacturing plant. Am J Ind Med, 22, 835-849.

2. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42, 202-203. IARC, Lyon.

## 51. Family history of lung cancer/mendelian inheritance

Table 51 gives details of the studies which attempted to investigate lung cancer risk in relation to a family history of lung cancer. Fourteen relative risks were estimated, lying in the range 0.31-5.31, of which 12 were above 1.00. Two studies reported a 2.5- and a 3-fold excess of lung cancer among the relatives of cases, while another noted a family history of lung cancer among 9.3% of cases, compared to 4.8% of controls. One study found 21% of patients with primary lung cancer to have a family history of the disease, compared to only 6% of patients with secondary lung cancer and 6% of controls, and pairs of probands in which both members had lung cancer were found significantly more frequently than expected by one study. Case reports of lung cancer in close relatives were made by three studies, who noted the disease in four out of eight siblings over the age of 50, in two identical twins, and a total of 12 cases in two different families. Finally, one study reported findings compatible with a hypothesis of mendelian codominant inheritance of a rare autosomal gene producing an earlier age of onset of lung cancer in carriers.

It should be noted that bias arising from a variety of sources could have been introduced into the studies, and a more detailed discussion of this is given elsewhere [7]. Briefly, however, it was not thought that the results of the studies could be explained by confounding due to differences in age, smoking habits, family size or other variables, between the cases and controls, and recall bias was also not considered to be of great importance.

Therefore, there does appear to be evidence of an increased risk of lung cancer among subjects who have had a relative suffer from the same disease.

Table 51: Estimates of relative risk for family history of lung cancer

| Study | Location | Relative risk |
|---|---|---|
| Tokuhata and Lilienfeld (1963a) | US residents | 2.5-fold excess of lung cancer among case relatives compared to controls |
| Tokuhata and Lilienfeld (1963b) | US residents | 3-fold excess of lung cancer among case relatives compared to controls |
| Brisman et al (1967) | US residents | All four of eight siblings aged over 50 developed lung cancer |
| Joishy et al (1977) | US men | Identical twins developed lung cancers with similar time of onset, histochemistry and site of metastasis |
| Goffman et al (1982) | US residents | 5 cases of lung cancer reported in one family and 7 cases reported in another |
| Alderson et al (1985)[1] | UK residents | 1.28(0.93-1.78) |
| Ooi et al (1986) | US residents | 3.07(1.1-8.7) |
| Samet et al (1986) | US residents | 5.31(2.21-12.76) |
| Gao et al (1987) | Chinese women | 1.1(0.6-2.3)[2]<br>3.0(0.7-12.5)[3] |
| Tsugane et al (1987) | Japanese men<br>Women | 1.67($p>0.05$)<br>0.31($p>0.05$) |
| Horwitz et al (1988) | US women | 2.8(1.02-7.7) |
| McDuffie et al (1989) | Canadian residents | 9.3% of cases had family history of lung cancer compared to 4.8% of controls ($p<0.005$) |
| Sellers et al (1990) | US residents | Results indicated compatibility of data with mendelian codominant inheritance of rare autosomal gene producing earlier age of onset of cancer |
| McDuffie (1991) | Canadian residents | 1.99(1.18-3.37) |

Table 51 continued

| | | |
|---|---|---|
| Murata et al (1991) | Japanese women | Pairs of probands in which both members had lung cancer occurred significantly more frequently than expected |
| Osann (1991) | US women | 1.9(0.7-5.6) |
| Shaw et al (1991) | US residents | 2.8(1.2-6.6) |
| Sellers et al (1992) | US residents | 1.9(0.9-4.1)[4] |
| Ambrosone et al (1993) | US residents, 0-20 years smoking | 3.01(1.38-6.63)[5] |
| | 21+ years | 0.85(0.62-1.16)[5] |
| Pavlakou et al (1993) | Greek women | 21% of primary lung cancer patients had family history of lung cancer compared to 6% of secondary lung cancer patients and 6% of controls |

1 From Lee (1993)

2 Lung cancer in parents

3 Lung cancer in siblings

4 Small cell lung cancer compared to non-small cell lung cancer

5 Squamous cell/small cell cancers compared to large cell/adenocarcinomas

References

1. Ambrosone CB, Rao U, Michalek AM, Cummings MK and Mettlin CJ (1993) Lung cancer histologic types and family history of cancer. Cancer, 72, 1192-1198.

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3. Gao Y-T, Blot WJ, Zheng W et al (1987) Lung cancer among Chinese women. Int J Cancer, 40, 604-609.

4. Goffman T, Hassinger D and Mulvihill J (1982) Familial respiratory tract cancer: Opportunities for research and prevention. JAMA, 247, 1020-1023.

5. Horwitz RI, Smaldone LF and Viscoli CM (1988) An ecogenetic hypothesis for lung cancer in women. Arch Intern Med, 148, 2609-2612.

6. Joishy SK, Cooper RA and Rowley PT (1977) Alveolar cell carcinoma in identical twins: Similarity in time of onset, histochemistry and site of metastasis. Ann Internal Med, 87, 447-450.

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11. Ooi WL, Elston RC, Chen VW, Bailey-Wilson JE and Rothschild H (1986) Increased familial risk for lung cancer. JNCI, 76, 217-222.

12. Osann KE (1991) Lung cancer in women: The importance of smoking, family history of cancer, and medical history of respiratory disease. Cancer Res, 51, 4893-4897.

13. Pavlakou G, Tsarouha A, Koza T et al (1993) Primary and secondary lung cancer in women: Association of histological type with personal and family history. Eur Respir J, 6 (Supplement), 291S (Abstract).

14. Samet JM, Humble CG and Pathak DR (1986) Personal and family history of respiratory disease and lung cancer risk. Am Rev Respir Dis, 134, 466-470.

15. Sellers TA, Bailey-Wilson JE, Elston RC et al (1990) Evidence for mendelian inheritance in the pathogenesis of lung cancer. JNCI, 82, 1272-1279.

16. Sellers TA, Elston RC, Atwood LR and Rothschild H (1992) Lung cancer histologic type and family history of cancer. Cancer, 69, 86-91.

17. Shaw GL, Falk RT, Pickle LW, Mason TJ and Buffler PA (1991) Lung cancer risk associated with cancer in relatives. J Clin Epidemiol, 44, 429-437.

18. Tokuhata GK and Lilienfeld AM (1963a) Familial aggregation of lung cancer among hospital patients. Pub Health Report, 78, 277-283.

19. Tokuhata GK and Lilienfeld AM (1963b) Familial aggregation of lung cancer in humans. JNCI, 30, 289-312.

20. Tsugane S, Watanabe S, Sugimura H et al (1987) Smoking, occupation and family history in lung cancer patients under fifty years of age. Jpn J Clin Oncol, 17, 309-317.

52. Farmers/agricultural workers

Table 52 gives details of the studies which attempted to relate lung cancer risk to employment in the agricultural industry. Twenty-two standardized mortality ratios were calculated, ranging from 31-132, with 18 being below 100. In addition, five relative risks were estimated, ranging from 0.5-1.24, of which three were below 1.00. One proportional mortality ratio of 61 was also presented, along with a standardized mortality odds ratio of 929. These results are consistent with farmers and agricultural workers having a lower risk of lung cancer than workers in other industries.

One study put forward the theory that the lower incidence of lung cancer in farmers and farm workers is due to exposure to endotoxins which bring about a protective effect by stimulating macrophages to produce tumour necrosis factor, thus augmenting the body's defences against tumours. It was also suggested that exposure to tobacco smoke at low levels may have a similar effect, and that as farmers tend to smoke less than the general population this may be sufficient to explain their lower risk of lung cancer [8]. As little information was available from the studies on smoking habits it is not really possible to determine which of these explanations, if either, is the more likely.

In contrast, Benhamou et al suggested that the increased risk of lung cancer observed among farmers in their study could be explained by the use of arsenical insecticides [1]. Again, as none of the studies had collected information on such exposures, this hypothesis cannot be evaluated.

Overall, then, from the evidence presented in the table it can be seen that farmers and agricultural workers appear to have a decreased risk of lung cancer, but, as yet, no satisfactory explanations for this observation have been put forward.

Table 52: Estimates of standardized mortality ratio/relative risk for farmers/agricultural workers

| Study | Population | Standardized mortality ratio |
|---|---|---|
| OPCS (1978) | E/W male farmers/farm managers/ market gardeners | 84[1] |
| | Agricultural workers | 86 |
| Logan (1982) | UK male farmers - 1931 | 35 |
| | 1951 | 46 |
| | 1961 | 59 |
| | 1971 | 57 |
| | Married women - 1931 | 50 |
| | 1951 | 69 |
| | 1961 | 70 |
| | 1971 | 74 |
| | UK male agricultural workers, 1931 | 31 |
| | 1951 | 51 |
| | 1961 | 77 |
| | 1971 | 105 |
| | Married women[2] - 1931 | 29 |
| | 1951 | 74 |
| | 1961 | 88 |
| | 1971 | 118 |
| Blot et al (1983) | US male agricultural workers | 1.0(0.4-2.3)* |
| Milne et al (1983) | US male farmers | 0.5($p<0.05$)* |
| | Farmers/farm labourers | 0.8* |
| Dubrow and Wegman (1984) | US agricultural scientists | 929($p<0.001$)[3] |
| OPCS (1986) | UK male farmers/horticulturists/ farm managers | 47($p<0.01$) |
| | Married women[2] | 57($p<0.01$) |
| | UK male farm workers | 117($p<0.01$) |
| | Married women[2] | 132 |
| Benhamou et al (1988) | French farmers | 1.24(0.94-1.62)* |
| Rylander (1990) | US male wheat/grain farmers | 61($p<0.05$)[4] |
| Zappa et al (1993) | Italian agricultural workers | 0.77(0.5-1.1)* |

Footnote to Table 52

E/W = English/Welsh

* Relative risk

1 Estimated from data given

2 According to husband's occupation

3 Standardized mortality odds ratio

4 Proportional mortality ratio

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References

1. Benhamou S, Benhamou E and Flamant R (1988) Occupational risk factors of lung cancer in a French case-control study. Br J Ind Med, 45, 231-233.

2. Blot WJ, Brown LM, Pottern LM, Stone BJ and Fraumeni JF (1983) Lung cancer among long-term steel workers. Am J Epidemiol, 117, 706-16.

3. Dubrow R and Wegman DH (1984) Cancer and occupation in Massachusetts: A death certificate study. Am J Ind Med, 6, 207-230.

4. Logan WPD (1982) Cancer mortality by occupation and social class 1851-1971. HMSO, London and IARC, Lyon.

5. Milne KL, Sandler DP, Everson RB and Brown SM (1983) Lung cancer and occupation in Alameda County: A death certificate case-control study. Am J Ind Med, 4, 565-575.

6. Office of Population Censuses and Surveys (1978) Occupational mortality: The Registrar General's decennial supplement for England and Wales, 1970-72. HMSO, London.

7. Office of Population Censuses and Surveys (1986) Occupational mortality: The Registrar General's decennial supplement for Great Britain, 1979-80, 1982-83. HMSO, London.

8. Rylander R (1990) Environmental exposures with decreased risks for lung cancer? Int J Epidemiol, 19 (Suppl 1), S67-S72.

9. Zappa M, Paci E, Seniori Costantini A and Kriebel D (1993) Lung cancer among textile workers in the Prato area of Italy. Scand J Work Environ Health, 19, 16-20.

53. Fishermen

The five studies found which investigated a possible association between lung cancer risk and employment as a fisherman are detailed in Table 53. Three relative risks were estimated, ranging from 1.0-3.2, with two being above 1.00. Two proportional mortality ratios, of 125 and 144, were also given, along with one standardized mortality ratio of 205.

It can be seen, then, that there is a fairly consistent increase in the risk of lung cancer among fishermen, but as yet no plausible mechanism for this observation has been put forward. One study suggested that the excess of lung cancers was probably more a reflection of the way way of life of fishermen, particularly their drinking and smoking habits, than a direct consequence of the occupation [2]. However, elsewhere it was felt that the persistence of the raised PMR after the removal of other causes of death individually large enough to seriously affect it added support to the hypothesis that fishermen are at excess risk of lung cancer [3]. Unfortunately, there is not really sufficient data for a full evaluation to be made.

Table 53: Estimates of relative risk/standardized mortality ratio for fishermen

| Study | Location | Subset | Relative risk(95% limits) |
|---|---|---|---|
| OPCS (1978) | England/Wales | | 205*[1] |
| Gottlieb et al (1979)[2] | US | | 1.8 |
| Blot et al (1982)[2] | US | | 3.2 |
| Howe and Lindsay (1983)[3] | Canada | | 1.00 |
| OPCS (1986) | UK | Aged 15-64 | 144[4] |
| | | Aged 65-74 | 125[4] |

Footnote to Table 53

* Standardized mortality ratio

1 Estimated from data given

2 From Williams Pickle (1984)

3 From Blot (1984)

4 Proportional mortality ratio

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References

1. Blot WJ (1984) Lung cancer and occupational exposures. In: Lung cancer: Causes and prevention, 47-64. Verlag Chemie International Inc.

2. Office of Population Censuses and Surveys (1978) Occupational mortality: The Registrar General's decennial supplement for England and Wales, 1970-72. HMSO, London.

3. Office of Population Censuses and Surveys (1986) Occupational mortality: The Registrar General's decennial supplement for Great Britain, 1979-80, 1982-83. HMSO, London.

4. Williams Pickle L, Correa P and Fontham E (1984) Recent case-control studies of lung cancer in the United States. In: Lung cancer: Causes and prevention, 101-115. Verlag Chemie International Inc.

## 54. Fishmongers/poultry dressers

Table 54 gives details of the only study which attempted to investigate the possible association between lung cancer risk and working as a fishmonger or poultry dresser. A standardized mortality ratio of 273 was calculated. Separate findings for the two occupations were not presented.

It was suggested that, as with butchers, the excess of lung cancers observed may have arisen from the handling of raw flesh, but with only one study reporting it is not possible to properly evaluate this hypothesis, or determine if there is a relationship between lung cancer risk and employment as a fishmonger or poultry dresser.

Table 54: Estimate of standardized mortality ratio for fishmongers/ poultry dressers

| Study | Population | Standardized mortality ratio |
|---|---|---|
| OPCS (1986) | UK men | 273 |

### References

1. Office of Population Censuses and Surveys (1986) Occupational mortality: The Registrar General's decennial supplement for Great Britain, 1979-80, 1982-83. HMSO, London.

55. Formaldehyde

Table 55 presents details of the studies which gave data relevant to an investigation of the possible association between lung cancer risk and exposure to formaldehyde. The seven relative risks which were estimated ranged from 0.34-1.11, with only one being above 1.00. Two standardized mortality ratios, of 97 and 136, were also presented, along with one proportional mortality ratio of 102.

From the table it can be seen that subjects drawn from the medical professions show a consistent decrease in lung cancer risk, an observation which has been noted elsewhere, and it has been suggested that this deficit might be explained by the lower prevalence of tobacco use in these occupational groups [2]. However, insufficient data on the subjects' smoking habits was given by the studies to determine whether or not this was the case. Little information was also given about the level of exposure of the subjects, with only the study by Partanen giving broad categories of exposure, while only the study by Wong had attempted to identify other substances the subjects may have been exposed to. These include oxygenated hydrocarbons other than formaldehyde, benzene, asbestos, and inorganic and organic pigments. Embalming fluid also contains a variety of chemicals apart from formaldehyde [1]. Thus, it is possible that workers were exposed to other substances which were themselves potentially carcinogenic, and this may have introduced bias into the results.

While those working in the medical professions appear to show a decreased risk of lung cancer in relation to formaldehyde exposure, studies of workers manufacturing or using formaldehyde have given less conclusive results. This led IARC to classify the evidence for the carcinogenicity of formaldehyde to humans as "limited" [2].

Table 55: Estimates of relative risk/standardized mortality ratio for exposure to formaldehyde

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Doll and Peto (1976)[1] | British doctors | 1.00 |
| Doll and Peto (1977)[1] | UK male scientific researchers/ pathologists/biochemists | <1.00 |
| OPCS (1978) | E/W qualified medical practitioners | <1.00 |
| Jensen and Andersen (1982) | Danish doctors ever employed in pathology, forensic medicine or anatomy | 1.0(0.4-2.4) |
| Walrath and Fraumeni (1982)[1] | US embalmers | 102[2,3] |
| Wong (1982)[1] | US male chemical factory workers | 97*[3,4] |
| Bertazzi et al (1986)[5] | Italian formaldehyde-resin plant workers | 136* |
| Partanen (1993) | Anatomists, pathologists, forensic medicine specialists | 0.34(0.26-0.44)[6] |
| | Funeral directors, embalmers, undertakers, drug users | 0.98(0.89-1.07)[6] |
| | Industrial workers | 1.11(1.03-1.19)[6] |

* Standardized mortality ratio

1 From International Agency for Research on Cancer (1982)

2 Proportional mortality ratio

3 Tumours of respiratory system

4 Estimated from data given

5 From International Agency for Research on Cancer (1987)

6 Combined results from 9 studies

References

1. International Agency for Research on Cancer (1982) Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 29: Some industrial chemicals and dyestuffs, 345-389. IARC, Lyon.

2. International Agency for Research on Cancer (1987) Monographs on the evaluation of the carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42, 211-216. IARC, Lyon.

3. Jensen OM and Andersen SK (1982) Lung cancer risk from formaldehyde. The Lancet, Apr 17, 913. (Letter)

4. Office of Population Censuses and Surveys (1978) Occupational mortality: The Registrar General's decennial supplement for England and Wales, 1970-72. HMSO, London.

5. Partanen T (1993) Formaldehyde exposure and respiratory cancer - a meta-analysis of the epidemiological evidence. Scand J Work Environ Health, 19, 8-15.

56. Fruits and vegetables

Lack of time meant that a full evaluation of the possible association between lung cancer risk and fruit and/or vegetable consumption could not be presented in this document. However, the studies dealing with this area have been included, where relevant, in the sections for vitamins A and C. All presented evidence suggestive of a protective effect of fruit and/or vegetable intake on lung cancer risk.

As with other dietary variables, it is possible that the development of cancer may affect appetite and thus lead to changes in fruit and/or vegetable consumption which are a result of the disease rather than a cause of it. Thus, findings from prospective studies may be more reliable than those from case-control studies. It is also possible that a high intake of fruit and/or vegetables may be correlated with some other dietary variable which is itself protective for lung cancer, or there may be an inverse correlation with a dietary factor, such as fat, which is thought to be positively associated with lung cancer risk.

Overall, the evidence for a protective effect of fruit and/or vegetable intake is more consistent than that for any one particular nutrient, although the mechanism responsible for this effect remains unclear.

57. Fuel oils

Only five studies were found which gave data relevant to an investigation of the possible association between lung cancer risk and exposure to fuel oils and details of these are given in Table 57. Five relative risks, ranging from 1.4-2.7, were calculated. One study reported that while 91% of the case group had used kerosene stoves, only 36% of the controls had done so.

None of the studies appeared to have taken objective measurements of the exposures the respondents were subjected to, although the studies by Koo and Siematycki did attempt to classify exposure levels. Furthermore, subjects in the study by Tsuchiya were exposed to several substances, including kerosene, diesel oil, crude petroleum and mineral oil, while those in the studies by Chan, Leung and Koo were more likely to have been exposed to the combustion products of kerosene rather than to kerosene itself. Exposure to cooking oil may also have contributed to the observed effects in these studies. Finally, problems in the statistical analysis of the study by Tsuchiya were noted [1].

Thus, IARC stated that while residual (heavy) fuel oils were "possibly carcinogenic to humans", distillate (light) fuel oils were "not classifiable as to their carcinogenicity". Overall, it was felt that there was "inadequate" evidence for the carcinogenicity of fuel oils to humans [1].

Table 57: Estimates of relative risk for exposure to fuel oils

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Tsuchiya (1965)[1] | Japanese workers | 2.7(1.4-5.3) |
| Siematycki et al (1987)[1] | Canadian men | 1.7(1.2-3.4) |
| Leung (1977)[1] | Hong Kong women | Kerosene stoves used by 91% cases and 36% controls |
| Chan et al (1979)[1] | Hong Kong women | 1.6(0.99-2.6) |
| Koo et al (1983)[1] | Hong Kong women, smokers | 2.5(1.2-5.4) |
| | Non-smokers | 1.4(1.1-1.9) |

Footnote to Table 57

1 From International Agency for Research on Cancer (1989)

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References

1. International Agency for Research on Cancer (1989) Monographs on the evaluation of carcinogenic risks to humans. Volume 45: Occupational exposures in petroleum refining; crude oil and major petroleum fuels, 239-270. IARC, Lyon.

58. Gasoline engine exhaust

The five studies which gave data relevant to an investigation of the possible association between lung cancer risk and exposure to gasoline engine exhaust are detailed in Table 58. Six relative risks were estimated, and they ranged between 1.2 and 1.8.

A number of potential problems were identified in the studies. Firstly, since exposure to engine exhaust is nearly ubiquitous in urban areas 'unexposed' reference groups are likely to contain a large number of individuals who are in fact exposed non-occupationally. Secondly, the studies assessed the subjects' exposure indirectly, as no measurements of exposure level appeared to have been taken. In fact, all of the studies except the one by Siemiatycki relied on job title as a surrogate for exposure to gasoline engine exhaust. This may obviously have introduced inaccuracies into these studies. Lastly, some of the study subjects may have been exposed to other potentially carcinogenic substances, particularly diesel engine exhausts, and again this may have affected the results.

Therefore, IARC considered that gasoline engine exhaust could only be described as "possibly carcinogenic to humans [2].

Table 58: Estimates of relative risk for exposure to gasoline engine exhaust

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Buiatti et al (1985)[1] | Italian taxi drivers | 1.8(1.0-3.4) |
| Damber and Larsson (1987)[1] | Swedish professional drivers, dead controls | 1.5(0.9-2.6) |
| | Live controls | 1.7(0.9-3.2) |
| Benhamou et al (1988)[1] | French motor vehicle drivers | 1.4(1.1-1.9) |
| Siemiatycki et al (1988)[1] | Canadian men aged 35-70 years | 1.2(1.0-1.4)[2] |
| Grandjean and Andersen (1991) | Danish filling station attendants | 1.58(1.25-2.0) |

Footnote to Table 58

1 From International Agency for Research on Cancer (1989)

2 90% confidence interval

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References

1. Grandjean P and Andersen O (1991) Lung cancer in filling station attendants. Am J Ind Med, 20, 763-768.

2. International Agency for Research on Cancer (1989) Monographs on the evaluation of carcinogenic risks to humans. Volume 46: Diesel and gasoline engine exhausts and some nitroarenes, 41-185. IARC, Lyon.

59. General labourers

Four studies were found which investigated the possible association between lung cancer risk and employment as a general labourer and details of these are given in Table 59. Ten standardized mortality ratios, lying in the range 84-270, were calculated, of which eight were raised. In addition, two proportional mortality ratios, of 106 and 109, were presented, along with two proportional registration ratios, of 115 and 119, and one relative risk estimate of 0.9.

None of the studies gave any information on the possible exposures of the subjects, and no hypotheses were put forward to explain the increase in lung cancer risk observed. Thus, although the evidence presented in the table appears to suggest a slightly higher risk of lung cancer among general labourers, it is not possible to identify any potentially carcinogenic agents which may have been responsible for this increase.

Table 59: Estimates of standardized mortality ratio/relative risk for general labourers

| Study | Population | Standardized mortality ratio |
|---|---|---|
| OPCS (1978) | E/W male labourers/unskilled workers aged 15-64 | 109($p<0.01$)[1] |
| | Aged 65-74 | 106($p<0.01$)[1] |
| | Incidence 1966-7 | 115($p<0.01$)[2] |
| | 1968-9 | 119($p<0.01$)[2] |
| Logan (1982) | E/W male labourers - 1931 | 96 |
| | 1951 | 169 |
| | 1961 | 161 |
| | 1971 | 199 |
| | Married women[3] - 1931 | 84 |
| | 1951 | 106 |
| | 1961 | 147 |
| | 1971 | 193 |

Table 59 continued

| | | |
|---|---|---|
| Milne et al (1983) | US male general labourers | 0.9* |
| OPCS (1986) | British male labourers | 246($p<0.01$) |
| | Married women[3] | 270($p<0.01$) |

E/W = English/Welsh

* Relative risk

1 Proportional mortality ratio

2 Proportional registration ratio

3 According to husband's occupation

References

1. Logan WPD (1982) Cancer mortality by occupation and social class 1851-1971. HMSO, London.

2. Milne KL, Sandler DP, Everson RB and Brown SM (1983) Lung cancer and occupation in Alameda County: A death certificate case-control study. Am J Ind Med, 4, 565-575.

3. Office of Population Censuses and Surveys (1978) Occupational mortality: The Registrar General's decennial supplement for England and Wales, 1970-72. HMSO, London.

4. Office of Population Censuses and Surveys (1986) Occupational mortality: The Registrar General's decennial supplement for Great Britain, 1979-80, 1982-83. HMSO, London.

60. Glass workers

Only three studies were found which contained data relevant to an investigation of the possible association between lung cancer risk and working in the glass manufacturing industry and details of these are given in Table 60. Two relative risks, of 2.0 and 2.2, were estimated, and one standardized incidence ratio of 128 was also presented.

Glass workers may be exposed to various potentially carcinogenic substances, including arsenic, metals and asbestos [1,3]. However, none of the studies made any attempt to measure the workers' exposures and thus it is difficult to identify the agent or agents responsible for producing the observed increase in lung cancer risk among glass workers. In any case, from the evidence presented in the table it can be seen that any increase in risk, if it does exist, is not likely to be particularly large.

Table 60: Estimates of relative risk/standardized incidence ratio for glass workers

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Milne et al (1983) | US glass manufacturing workers | 2.2($p<0.05$) |
| Wingren and Axelson (1985)[1] | Swedish glass blowers | 2.00 |
| Sankila et al (1990) | Finnish glass factory workers | 128(99-162) |

* Standardized incidence ratio

1 From International Agency for Research on Cancer (1987)

References

1. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42, 100-106. IARC, Lyon.

2. Milne KL, Sandler DP, Everson RB and Brown SM (1983) Lung cancer and occupation in Alameda County: A death certificate case-control study. Am J Ind Med, 4, 565-575.

3. Sankila R, Karjalainen S, Pukkala E et al (1990) Cancer risk among glass factory workers: An excess of lung cancer? Br J Ind Med, 47, 815-818.

61. Gold mining

Details of the five studies found which presented data relevant to the investigation of a possible association between lung cancer and gold mining are given in Table 61. Four relative risks were estimated, ranging from 1.4-7.9, along with one standardized mortality ratio of 100. Finally, one study calculated an annual incidence rate of 205.6/100 000, compared to the general male population.

Gold miners are thought to have potential exposure to several substances which may be carcinogenic, and those which have been discussed include arsenic, asbestos, chromium, nickel, radon and silica [1-5]. However, only two of the studies [1,2] attempted to make any objective measurements of workers' exposures and, with the exception of asbestos [2], all of the above-named substances were found only in very low concentrations, below levels which are thought to pose any risk. Thus, the possible role of any individual exposure is very hard to ascertain.

Although the data presented in the table is consistent with an increase in lung cancer risk among gold miners, the lack of information on exposures such workers are subjected to makes it very difficult to identify the agent or agents responsible. One study which found high levels of asbestos but negligible levels of arsenic, chromium, nickel and radon felt that this was sufficient evidence for the excess of respiratory disease observed to be attributed to asbestos exposure [2]. However, no data was available from the other studies to back this up.

Table 61: Estimates of relative risk/standardized mortality ratio for gold miners

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Osburn (1957)[1] | Rhodesian gold miners | 205.6[2] |
| Gillam et al (1976) | South Dakota gold miners | 2.70($p<0.05$)[3] |
| Armstrong et al (1979) | Australian gold miners | 1.4($p<0.01$)[3] |
| Katsnelson and Mokronosova (1979)[4] | Russian gold miners - underground | 7.9($p<0.001$) |
| | Surface | 1.6 |
| Brown et al (1986)[5] | US gold miners | 100* |

Footnote to Table 61

* Standardized mortality ratio

1 From International Agency for Research on Cancer (1980)

2 Incidence rate per 100 000 per year

3 Tumours of respiratory system

4 From Goldsmith et al (1982)

5 From International Agency for Research on Cancer (1987)

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References

1. Armstrong BK, McNulty JC, Levitt LJ, Williams KA and Hobbs MST (1979) Mortality in gold and coal miners in Western Australia with special reference to lung cancer. Br J Ind Med, 36, 199-205.

2. Gillam JD, Dement JM, Lemen RA et al (1979) Mortality patterns among hard rock gold miners exposed to an asbestiform mineral. Ann N Y Acad Sci, 271, 336-344.

3. Goldsmith DF, Guidotti TL and Johnston DR (1982) Does occupational exposure to silica cause lung cancer? Am J Ind Med, 3, 423-440.

4. International Agency for Research on Cancer (1980) Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 23: Some metals and metallic compounds, 39-142. IARC, Lyon.

5. International Agency for Research on Cancer (1987) Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 42: Silica and some silicates, 39-144. IARC, Lyon.

62. Haematite and iron oxide

Table 62 gives details of the studies which attempted to relate the risk of lung cancer to exposure to haematite and iron oxide. Ten studies calculated standardized mortality ratios, ranging from 100-176, of which half were raised, while another study reported a raised standardized incidence ratio but did not give details of the results. One study observed a lung cancer incidence 10.7 times higher among iron ore miners than among non-miners, while another reported bronchial cancer to be 2.29 times higher in such workers. Three other studies observed lung cancer incidence of 9.4% in haematite miners compared to 2.0% in controls, bronchogenic carcinoma incidence of 3.3% in iron ore miners compared to 1.5% in controls, and a lung cancer mortality rate of 6.6 per 10,000 compared to the national rate of 4 per 10,000. A further three studies reported that lung cancer mortality was higher in the population of interest than in the controls, but did not give any further details. A total of seven lung or bronchial cancers were observed in the remaining three studies.

No information was available from the studies on the level of exposure to haematite and iron oxide, as none appeared to have attempted to quantify exposure in any way. Thus, it is obviously possible that inaccuracies could have been introduced into the results. Furthermore, the study subjects came from a range of occupations, some of which entail exposure to other substances which may themselves be potentially carcinogenic. For example, miners may be exposed to silica and radon, while welding involves exposure to many metals, particularly zinc. Boiler scalers may be exposed to both silica and soot. In the absence of exposure data it is not possible to determine which, if any, of these substances subjects may have come into contact with, or the potential carcinogenicity of any one material.

Therefore, IARC appear to be justified in their classification of the evidence for the carcinogenicity of haematite and iron oxide to humans as "inadequate". However, the evidence for underground haematite mining with exposure to radon was considered "sufficient" [4].

Table 62: Estimates of standardized mortality ratio for exposure to haematite and iron oxide

| Study | Population | Standardized mortality ratio |
|---|---|---|
| Stewart and Faulds (1934)[1] | Haematite miners | 1 bronchial cancer observed |
| Vorwald and Karr (1937,1938)[1] | Haematite miners | 3 lung cancers observed |
| Turner and Grace (1938)[1] | UK foundry workers/ metal grinders | Lung cancer mortality higher than in other occupations |
| McLaughlin et al (1945)[1] | Silver finishers | 100 |
| Barrie and Harding (1947)[1] | Silver finishers | 100 |
| Kennaway and Kennaway (1947)[1] | UK metal grinders | 176 |
| Harding (1948)[1] | Silver finishers | 100 |
| McLaughlin et al (1950)[1]/ McLaughlin and Harding (1956)[1] | UK iron/steel foundry workers | >100[2] |
| Harding and Massie (1951)[1] | Boiler scalers | 3 lung cancers observed |
| Wynder and Graham (1951)[1] | Welders/hot metal workers | Lung cancer cases more often hot metal workers than other diseases |
| Doll (1953)[1] | Welders/hot metal workers | 100 |
| Breslow et al (1954)[1] | Welders/hot metal workers | Lung cancer cases more often hot metal workers than other diseases |
| Faulds and Stewart (1956) | UK haematite miners | Lung cancer incidence 9.4% vs. 2.0% controls |
| Podhrazsky (1957)[1] | Czech steel plant workers | Mortality rate 6.6[3] vs. 4 nationally |
| Braun et al (1960)[1] | French iron-ore miners | Bronchogenic carcinoma incidence 3.3% vs. 1.5% in controls (p=0.01) |

Table 62 continued

| | | |
|---|---|---|
| Monlibert and Roubille (1960)[1] | French iron-ore miners | Bronchial cancer incidence 2.29 times higher than in controls |
| Gurevich (1967)[1] | USSR iron-ore miners | Lung cancer mortality 10.7 times higher than among non-miners |
| Boyd et al (1970) | UK haematite miners | 168[4] |
| Anthoine et al (1979)[5] | French iron ore miners | >100 |
| Axelson and Sjoberg (1979)[5] | Iron foundry workers | 100 |
| Tola et al (1979)[5] | Iron foundry workers | >100 |
| Lawler et al (1985)[5] | US iron ore miners | 100 |

1 From International Agency for Research on Cancer (1972)

2 Standardized incidence ratio

3 Per 10,000

4 Estimated from data given

5 From International Agency for Research on Cancer (1987)

References

1. Boyd JT, Doll R, Faulds JS and Leiper J (1970) Cancer of the lung in iron ore (haematite) miners. Br J Ind Med, 27, 97-105.

2. Faulds JS and Stewart MJ (1956) Carcinoma of the lung in haematite miners. J Path Bacteriol, 72, 353-366.

3. International Agency for Research on Cancer (1972) Monographs on the evaluation of carcinogenic risk of chemicals to man. Volume 1, 29-39. IARC, Lyon.

4. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42, 216-219. IARC, Lyon.

## 63. Hairiness of 2nd phalanx

Table 63 gives details of the only study found which attempted to relate lung cancer risk to hairiness of the 2nd phalanx. It was reported that 3.1% of cancer cases had a hairy 2nd phalanx compared to only 2.1% of controls.

The authors themselves stated that multiple comparisons result in some apparent association due to chance alone, and that the observed relationship between lung cancer risk and hairiness of the 2nd phalanx may be a case in point.

Table 63: Observations on hairiness of 2nd phalanx

| Study | Population | Observations |
|---|---|---|
| Denoix et al (1958) | French men | 3.1% bronchial cancer cases had hairy 2nd phalanx compared to 2.1% controls |

* Standardized mortality ratio

References

1. Denoix PF, Schwartz D and Anguera G (1958) French investigation into the etiology of broncho-pulmonary cancer. Detailed analysis. Bull Assoc Franc pour l'etude du cancer, 49: 1-37.

## 64. Hashimoto's thyroiditis

Table 64 gives details of the only study found which presented data relevant to an investigation of the possible association between lung cancer risk and Hashimoto's thyroiditis. A standardized mortality ratio of 209 was calculated.

With so little information available it is not possible to evaluate the relationship between lung cancer and Hashimoto's thyroiditis.

Table 64: Estimate of standardized mortality ratio for Hashimoto's thyroiditis

| Study | Population | Standardized mortality ratio |
|---|---|---|
| Yamashita et al (1979) | Japanese women | 209($p<0.05$)[1] |

1 Estimated from data given

### References

1. Yamashita N, Maruchi N and Mori W (1979) Hashimoto's thyroiditis: A possible risk factor for lung cancer among Japanese women. Cancer Letters, 7, 9-13.

65. Hexachlorocyclohexanes

Table 65 gives details of the only study found which investigated the possible association between lung cancer risk and exposure to hexachlorocyclohexanes (HCH). A standardized mortality ratio of 180 was calculated.

However, it should be noted that the workers in this study received their exposure through the application of various pesticides, and thus exposure could be to compounds other than HCH, or in addition to HCH. Therefore, IARC felt that it was not possible to evaluate the carcinogenicity of HCH to humans on the basis of this study [1] and classified the evidence as "inadequate" [2].

Table 65: Estimate of standardized mortality ratio for exposure to hexachlorocyclohexanes

| Study | Population | Standardized mortality ratio (95% limits) |
|---|---|---|
| Barthel (1976)[1] | Agricultural workers | 180(140-240) |

1 From International Agency for Research on Cancer (1987)

References

1. International Agency for Research on Cancer (1979) Monographs on the evaluation of carcinogenic risk of chemicals to humans. Volume 20: Some halogenated hydrocarbons, 195-223. IARC, Lyon.

2. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: an updating of IARC monographs volumes 1 to 42, 220-222. IARC, Lyon.

66. History of lung disease

Details of the studies which investigated the possible association between lung cancer risk and a history of previous lung disease are given in Table 66. Relative risks ranging between 0.76-29.82 were estimated, with 55 out of 62 being above 1.00. Two standardized proportionate mortality ratios, both of 1.50, were also estimated. In addition, one study reported a positive association but did not give any detailed results, while two others stated that tuberculosis patients and pneumonia patients were 20 and 100 times more likely to develop lung cancer than the general population respectively, and one study reported that 10.0% of male and 8.2% of female lung cancer cases had a history of tuberculosis infection. Finally, one study reported finding a correlation between lung cancer mortality in adulthood and tuberculosis mortality in the period corresponding to the childhood of the lung cancer cases.

Most of the studies gathered information on history of lung disease from registers or medical records, or followed-up groups of patients with lung diseases, but several (Alavanja, Campbell, Campbell and Hughes, Wu, Wynder, Wynder and Fairchild) appeared to have based their data on information elicited at interviews with the subjects or their next-of-kin. It is obvious that this could have led to inaccuracies due to mistakes in recalling disease status, particularly in those studies which collected health data from a surrogate respondent. Additionally, no details were given at all on how the data on tuberculosis infection were collected in the study by Zheng.

Although results for several diseases were presented in the table, apart from tuberculosis, and to a lesser extent pneumonia, very few studies reported on each disease. Thus, with the exception of tuberculosis, an unequivocal relationship was not seen for any of the diseases considered. The data presented in the table suggest a positive association between lung cancer risk and a history of tuberculosis infection, but on the whole the estimates of relative risk are not particularly large, and therefore the relationship does not appear to be very strong. Furthermore, a recent review of lung cancer and tuberculosis stated that although patients with active pulmonary tuberculosis had a higher than normal risk of dying from lung cancer, there was "little biological evidence of TB lesions themselves, or TB bacilli *per se*,

having major roles to play in the carcinogenesis of lung cancer at the moment" [2].

Table 66: Estimates of relative risk for history of lung disease

| Study | Population | Dis-ease | Relative risk (95% limits) |
|---|---|---|---|
| Wynder et al (1956)[1] | Women | PNEU | 1.00 |
| | | TB | 1.00 |
| Campbell and Hughes (1960)[1] | Not stated | TB | Lung cancer occurred 20 times more frequently in TB patients than general population |
| Campbell (1961)[1] | Not stated | TB | Positive association |
| Steinitz (1965)[2] | Israeli residents | TB | 10.0% male and 8.2% female lung cancer cases had history of TB |
| Wynder and Fairchild (1966) | US men | ANY | 4.28(2.79-6.56)[3] |
| | | ASTH | 3.93(1.18-13.1)[3] |
| | | EMPH | 0.93(0.09-9.24)[3] |
| | | INJ | 0.76(0.20-2.88)[3] |
| | | PLEU | 2.49(1.29-4.80)[3] |
| | | PNEU | 1.70(0.99-2.93)[3] |
| | | TB | 0.84(0.22-3.21)[3] |
| Simecek and Simeckova (1967)[2] | Czech residents | TB | 4.2 |
| Aoki et al (1969)[2] | US white men | TB | 6.7(4.0-9.6) |
| | Non-white men | TB | 8.6(4.0-13.7) |
| | US white men active | TB | 10.5 |
| | Non-white men " | TB | 20.6 |
| | White men, inactive | TB | 4.5 |
| | Non-white men " | TB | 2.3 |
| | US residents, 1962-3 | TB | 3.6(1.9-5.3) |
| | 1963-4 | TB | 1.7(0.4-3.0) |
| | Japanese men | TB | 2.75 |
| | Women | TB | 5.48 |

Table 66 continued

| | | | |
|---|---|---|---|
| Aoki et al (1969)[2]/ Ipsen (1967)[2] | US men | TB | 3.1 |
| Campbell and Guilfoyle (1970)[2] | Australian men | TB | 2.06 |
| Kreus et al (1970)[2] | Finnish residents | TB | 2.2 |
| Aoki and Ohtani (1971)[2] | Japanese men, 1964-68 | TB | 1.41[4] |
| | | | 1.23[5] |
| | Women | TB | 1.33[4] |
| | | | 1.54[5] |
| | Men, 1974-82 | TB | 4.21[4] |
| | | | 2.13[6] |
| | Women, | TB | 3.87[4] |
| | | | 2.16[6] |
| Watanabe and Kurashima (1977)[2] | Japanese residents | TB | 3.56 |
| | Japanese residents | TB | 6.93 |
| Clemmensen and Hjalgrim-Nelson (1979)[2] | Danish men, INH+ | TB | 3.36 |
| | INH- | TB | 2.58 |
| | Women, INH+ | TB | 4.55 |
| Howe et al (1979)[2] | Canadian men | TB | 1.50(1.21-1.47)[7] |
| | Women | TB | 1.50(1.11-1.98)[7] |
| Hongo et al (1981)[2] | Japanese men | TB | 4.88 |
| | Women | TB | 9.69 |
| Komatsu et al (1981)[2] | Japanese men | TB | 2.58 |
| | Women | TB | 19.6 |
| Mercer (1981) | English residents | TB | Correlation between lung cancer mortality in adulthood and TB mortality in time period corresponding to childhood |
| Hinds et al (1982) | Hawaiian women | TB | 1.0(0.2-5.5) |
| | Japanese women | TB | 2.0(0.4-10.3) |
| | Chinese women | TB | 2.1(0.3-16.1) |
| Aoki (1985)[2] | Japanese men | TB | 12.0 |
| | Women | TB | 5.0 |

Table 66 continued

| | | | |
|---|---|---|---|
| Takatorige et al (1985)[2] | Japanese residents, -1 year follow-up | TB | 29.82 |
| | 1-2 years | TB | 6.36 |
| | 2-3 years | TB | 5.00 |
| | 3-4 years | TB | 4.35 |
| | 4-5 years | TB | 1.27 |
| | 5+ years | TB | 1.27 |
| Zheng et al (1987)[2] | Chinese residents | TB | 1.5(1.2-1.8) |
| Wu et al (1988) | Not stated | TB | 10.0(1.1-90.1) |
| Sakurai et al (1989)[2] | Japanese women | TB | 6.4 |
| Gao et al (1991)[2] | Chinese men | TB | 1.72(1.11-2.53) |
| | Women | TB | 2.79(1.79-4.14) |
| Alavanja et al (1992) | US female residents | ANY | 1.2(1.0-1.5) |
| | | ASTH | 1.3(0.8-2.1) |
| | | EMPH | 2.6(1.5-4.7) |
| | | PLEU | 0.9(0.7-1.3) |
| | | PNEU | 1.2(1.0-1.6) |
| | | TB | 2.0(1.0-4.1) |
| Ohtsuka et al (19??) | Japanese men | PNEU | Pneumonia sufferers 100 times more likely to develop lung cancer than general population |

ANY = any previous lung disease; ASTH = asthma; EMPH = emphysema; INH = Isoniazid treatment; INJ = lung injury; PLEU = pleurisy; PNEU = pneumonia; TB = tuberculosis

1 From Roe and Walters (1965)

2 From Aoki (1993)

3 Estimated from data given

4 Cardiovascular disease controls

5 Gastric cancer controls

6 Ischaemic heart disease controls

7 Standardized proportionate mortality ratio

References

1. Alavanja MCR, Brownson RC, Boice JD and Hock E (1992) Preexisting lung disease and lung cancer among nonsmoking women. Am J Epidemiol, 136, 623-632.

2. Aoki K (1993) Excess incidence of lung cancer among pulmonary tuberculosis patients. Jpn J Clin Oncol, 23, 205-220.

3. Hinds MW, Cohen HI and Kolonel LN (1982) Tuberculosis and lung cancer risk in nonsmoking women. Am Rev Resp Dis, 125, 776-778.

4. Mercer AJ (1981) Risk of dying from tuberculosis or cancer: Further aspects of a possible association. Int J Epidemiol, 10, 377-380.

5. Ohtsuka Y, Tanimura K, Munakata M et al (19??) Idiopathic interstitial pneumonia(IIP) as a risk factor for a lung cancer - a prospective study. Incomplete reference.

6. Roe FJC and Walters MA (1965) Some unsolved problems in lung cancer etiology. Progr Exp Tumor Res, 6, 126-227.

7. Wu AH, Yu MC, Thomas DC, Pike MC and Henderson BE (1988) Cancer Res, 48, 7279-7284.

8. Wynder EL and Fairchild EP (1966) The role of a history of persistent cough in the epidemiology of lung cancer. Am Rev Resp Dis, 94, 709-720.

67. Hormone therapy in women

Details of the only study found which presented data relevant to an investigation of lung cancer risk in women in relation to having received hormone therapy are given in Table 67. A relative risk of 1.26 was estimated.

With only one study reporting it is not possible to properly evaluate the relationship between lung cancer risk and hormone therapy in women.

Table 67: Estimate of relative risk for hormone therapy in women

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Adami et al (1989) | Swedish women | 1.26(0.92-1.68) |

References

1. Adami H-O, Persson I, Hoover R, Schairer C and Bergkvist L (1989) Risk of cancer in women receiving hormone replacement therapy. Int J Cancer, 44, 833-839.

68. Hydrazine and derivatives

The five studies found which attempted to relate the risk of lung cancer to exposure to hydrazine and its derivatives are detailed in Table 68. One study looked at exposure to hydrazine itself, while the other four considered isonicotinic acid hydrazide (INH). Seven relative risks were estimated overall, of between 1.10 and 4.6.

None of the studies gave any information on the level of exposure to hydrazine or INH, simply stating whether or not exposure had taken place. In fact, in the study by Hammond, it was stated that only 10% of one of the groups of patients had been exposed to INH. Thus, a raised relative risk was observed among a group of patients who were predominately not exposed to INH.

Not surprisingly, IARC felt there was "inadequate" evidence for the carcinogenicity to humans of both hydrazine and INH [2].

Table 68: Estimates of relative risk for exposure to hydrazine and its derivatives

| Study | Population | Exposure | Relative risk (95% limits) |
|---|---|---|---|
| Hammond et al (1967)[1] | TB patients | INH | 1.23(p>0.05)[2] |
| | TB patients | INH | 1.59(p>0.05)[2] |
| Campbell and Guilfoyle (1970)[1] | Male TB patients | INH | 1.10(p>0.05)[2] |
| Stott et al (1976)[3] | TB patients | INH | 1.6(1.2-2.1) |
| Clemmensen and Hjalgrim-Jensen (1979)[3] | Male TB patients | INH | 3.4 |
| | Female TB patients | INH | 4.6 |
| Wald et al (1984)[3] | Male factory workers | HYD | 1.2(0.2-4.5) |

HYD = hydrazine; INH = isonicotinic acid hydrazide

1 From International Agency for Research on Cancer (1974)

2 Estimated from data given

3 From International Agency for Research on Cancer (1987)

References

1. International Agency for Research on Cancer (1976) Monographs on the evaluation of carcinogenic risk of chemicals to man. Volume 4: Some aromatic amines, hydrazine and related substances, N-nitroso compounds and miscellaneous alkylating agents, 159-172. IARC, Lyon.

2. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42, 223-224 and 227-228. IARC, Lyon.

69. Hypercalcaemia

Table 69 gives details of the only two studies found which attempted to relate the risk of lung cancer to the presence of hypercalcaemia. A total of 6 lung cancers were observed in association with hypercalcaemia.

With so few studies reporting, and in the absence of any estimates of risk, it is not possible to properly evaluate the relationship between lung cancer and hypercalcaemia.

Table 69: Observations for hypercalcaemia

| Study | Population | Observations |
|---|---|---|
| Connor et al (1956) | US men | 2 cases reported in which hypercalcaemia disappeared after removal of lung tumour |
| Tashjian (1963) | US residents | 4 cases of lung cancer associated with hypercalcaemia |

References

1. Connor TB, Thomas WC and Howard JE (1956) The etiology of hypercalcemia associated with lung carcinoma. Am Soc Clin Invest, 35, 697-698.

2. Tashjian AH (1963) Case records of the Massachusetts General Hospital. N Engl J Med, 269, 801-813.

## 70. Hypertrophic pulmonary osteoarthropathy

Only two studies were found which gave information relevant to an investigation of the possible association between lung cancer risk and hypertrophic pulmonary osteoarthropathy (HOA), and details of these are presented in Table 70. One study reported that 3-4% of lung cancer cases were also suffering from HOA, while the other noted that 13 of the 14 cases of lung cancer associated with HOA arose from peripherally located tumours, rather than centrally located ones.

Various explanations of the association between the two conditions were put forward, but with so few studies reporting it is not possible to evaluate the relationship between lung cancer and HOA.

Table 70: Observations for hypertrophic pulmonary osteoarthropathy

| Study | Population | Observations |
|---|---|---|
| Ray and Fisher (1953) | US residents | 13 out of 14 cases of HOA associated with lung cancer arose from peripherally located tumours |
| Coury (1960) | French residents | 3-4% lung cancer cases also have HOA |

References

1. Coury C (1960) Hippocratic fingers and hypertrophic osteoarthropathy: A study of 350 cases. Br J Dis Chest, 54, 202-209.

2. Ray ES and Fisher HP (1953) Hypertrophic osteoarthropathy in pulmonary malignancies. Ann Intern Med, 38, 239-246.

71. Iron/steel founding

Table 71 details the numerous studies found which gave some data on the risk of lung cancer in those employed in iron and steel founding and allied occupations. Standardized mortality ratios (SMR) in the range 129-233 were presented by those studies which concentrated on mortality statistics. Three studies gave proportional mortality ratios (PMR), of 123, 170 and 186. The cohort studies showed a similar pattern, with the 25 SMRs presented lying in the range 0-714, with all but one being raised. Two PMRs, of 144 and 147, were also given. Additionally, seven studies produced estimates of relative risk of between 0.96 and 1.39, five of which were above 1.00. Finally, three case-control studies presented eight relative risks of between 1.20 and 7.10. Detailed results were not available from the fourth case-control study, which simply stated that cases were more often floor moulders, coremakers, casters and fettlers than controls.

Iron and steel workers may be exposed to a variety of potentially hazardous substances, including airborne crystalline silica from quartz sand used in moulding and coremaking, metallic fumes present during melting, pouring, welding and flame-cutting, metal dusts associated with abrasive grinding operations, carbon monoxide emitted from the cupola and casting operations, phenol, formaldehyde, furfuryl alcohol, isocyanates and amines used as ingredients of organic binders in mould and core sands, and pyrolysis products, such as polynuclear aromatic compounds, formed as a result of the contact between molten metal and carbonaceous materials during pouring [2]. No information was available from any of the studies as to the actual exposures of the workers, and therefore it is not possible to separate out the effects of any one substance, or even to say which substances the subjects were exposed to.

Despite this drawback, the consistent excess of lung cancer deaths seen in iron and steel foundry workers suggests that certain occupational exposures may be risk factors, and this is reflected in the ratings given by IARC, which stated that such exposures were "probably" carcinogenic [2], although it was later felt that the evidence for carcinogenicity to humans was "sufficient" [3].

Table 71: Estimates of relative risk/standardized mortality ratio for iron/steel founding

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Mortality statistics: | | |
| Turner and Grace (1938)[1] | Foundry/furnace workers, smiths | 233*[2] |
| Swantson (1950)[1] | Furnace men, rollers and assistants | 160* |
| | Metal moulders and diecasters | 193* |
| | Iron foundry furnacemen and labourers | 188* |
| Morrison (1957)[1] | Scottish moulders | 162*[2] |
| | Foundry workers | 161*[2] |
| Enterline and McKiever (1963)[1] | US metal moulders | 227* |
| | | 170[3] |
| Adelstein (1972)[1] | E/W furnace/forge/foundry rolling mill workers | 123($p < 0.05$)[3] |
| Milham (1976)[1] | US metal moulders | 135*[2] |
| OPCS (1978)[1] | E/W Moulders | 184*($p < 0.05$) |
| | Fettlers | 129* |
| | Metal furnacemen | 155* |
| Petersen and Milham (1980)[1] | US metal moulders | 186[3] |
| Logan (1982)[1] | E/W Furnace/forge/foundry rolling mill workers - 1961 | 140* |
| | 1971 | 155* |
| Cohort studies: | | |
| Lerer et al (1974)[1] | US foundrymen | 1.11 |
| Koskela et al (1976)[1] | Finnish iron/steel/non-ferrous foundry workers | 151* |
| | Iron foundry workers | 270*($p < 0.05$) |
| | Steel foundry workers | 0* |
| | Non-ferrous foundry workers | 143*[4] |
| | Moulders, coremakers | 231*[4] |
| | Casters, furnacemen | 238*[4] |
| | Fettlers | 111*[4] |
| | Labourers | 139*[4] |

Table 71 continued

| | | |
|---|---|---|
| Gibson et al (1977)[1] | Canadian steel casters | 250*($p < 0.05$) |
| | Crane operators | 714*($p < 0.05$) |
| | Finishers | 314* |
| | Moulding | 255* |
| | Coremaking | 208* |
| Breslin (1979)[1] | US foundrymen - cohort A | 1.34 |
| | Cohort B | 0.96 |
| | Cohort C | 1.23 |
| Decoufle and Wood (1979)[1] | US grey iron foundrymen working > 5 years | 128*[4] |
| Egan et al (1979)[1] | US foundry workers | 147($p < 0.05$)[3] |
| Tola et al (1979)[1] | Finnish iron foundrymen | 144($p < 0.05$)[3] |
| Egan-Baum et al (1981)[1] | US white foundry workers | 144*($p < 0.05$) |
| | Black workers | 176*($p < 0.05$) |
| Redmond et al (1981)[1] | US foundry workers - cohort A | 1.39 |
| | Cohort B | 0.99 |
| | Cohort C | 1.30 |
| Fletcher and Ades (1984)[1] | E/W steel foundrymen | 137*[4] |
| | Foundry workers per se | 142*($p < 0.05$) |
| | Fettling shop workers | 173*($p < 0.05$) |
| | Other workers | 110* |
| | Furnace repairmen | 203*($p < 0.05$) |
| | Labourers | 139* |
| | Fettlers | 195*($p < 0.05$) |
| | Heat treatment workers | 356*($p < 0.05$) |
| | Maintenance fitter's mate | 225*($p < 0.05$) |
| Case-control studies: | | |
| Tola et al (1979)[1] | Iron foundry workers | Cases more often floor moulders, core makers, casters and fettlers than controls. |
| Egen-Baum et al (1981)[1] | Iron foundry workers | 2.36(1.01-5.53) |
| Neuberger et al (1982)[1] | Dust-exposed workers[5] | 1.29(1.01-1.65) |

Table 71 continued

| | | |
|---|---|---|
| Blot et al (1983) | Crane operators, chainmen | 1.40(0.60-3.50) |
| | Furnace workers | 2.60(1.20-5.80) |
| | Machinists | 1.60(0.70-4.00) |
| | Coke worker | 1.20(0.20-6.90) |
| | Foundry worker, coremaker | 7.10(1.20-42.3) |
| | General maintenance workers | 1.80(0.80-4.30) |

E/W = England and Wales

* Standardized mortality ratio

1 From International Agency for Research on Cancer (1984)

2 Cancers of respiratory system

3 Proportional mortality ratio

4 Estimated from data given

5 Results for iron foundry workers, who formed the largest proportion, were similar to those shown for whole group

References

1. Blot WJ, Brown LM, Pottern LM, Stone BJ and Fraumeni JF (1983) Lung cancer among long-term steel workers. Am J Epidemiol, 117, 706-16.

2. International Agency for Research on Cancer (1984) Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 34: Polynuclear aromatic compounds, part 3, industrial exposures in aluminium production, coal gasification, coke production, and iron and steel founding, 133-192. IARC, Lyon.

3. International Agency for Research on Cancer (1987) Monographs on the evaluation of the carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: an updating of IARC monographs volumes 1 to 42, 224-225. IARC, Lyon.

## 72. Keeping pet birds

Three studies investigated the possible association between lung cancer risk and keeping pet birds, and details of these are given in Table 72. Relative risks ranging from 1.29-6.7 were estimated.

The data presented in the table suggest an association between lung cancer risk and the keeping of pet birds, but with only three studies reporting such a relationship cannot yet be considered proven.

Table 72: Estimates of relative risk for keeping pet birds

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Holst et al (1988)/Holst (1988) | Dutch residents | 6.7(2.2-20) |
| Gardiner et al (1992) | Scottish residents | 1.29(0.79-2.12) |
| Kohlmeier et al (1992) | German residents | 2.14(1.35-3.40) |

* Standardized mortality ratio

References

1. Gardiner AJS, Forey BA and Lee PN (1992) Avian exposure and bronchogenic carcinoma. Br Med J, 305, 989-992.

2. Holst PAJ (1988) Bird keeping as a source of lung cancer and other human disease. A need for higher hygienic standards. Springer-Verlag, Heidelberg.

3. Holst PAJ, Kromhout D and Brand R (1988) Pet birds as an independent risk for lung cancer. Br Med J, 297, 1319-1321.

4. Kohlmeier L et al (1992) Pet birds as an independent risk factor for lung cancer: Case-control study. Br Med J, 305, 986-989.

73. Lead and lead compounds

Details of studies which gave information relevant to an investigation of the possible association between lung cancer risk and exposure to lead and lead compounds are given in Table 73. Nine standardized mortality ratios, ranging from 110-300, were calculated along with one standardized incidence ratio of 128. In addition, one study reported that levels of lead found in the lungs of patients who had died of lung cancer were similar to those in patients who had died of other causes.

Only two of the studies appeared to have taken objective measurements of the workers' exposure to lead, by analyzing levels in the lungs (Jecklin) or blood and urine (Cooper and Gaffey). No information on exposure was available from the other studies, which could therefore contain inaccuracies. Additionally, workers in at least three of the studies (Blot and Fraumeni, Rencher, Sankila) were exposed to other substances, including antimony, arsenic, cadmium, chromium, copper, manganese, nickel oxide, sulphur dioxide and zinc selenite, which may themselves be potentially carcinogenic. As workers were probably exposed to one or more of these chemicals concurrently with their exposure to lead, it is not really possible to ascertain the potential contribution of any one of these substances to the lung cancer excesses observed. Furthermore, Blot and Fraumeni stated that the increased mortality found in their study was probably caused by exposure to inorganic arsenic, and not by lead or lead compounds.

In the light of these problems, it is not altogether surprising that IARC described the evidence for the carcinogenicity of lead and lead compounds to humans as "inadequate" [5].

Table 73: Estimates of standardized mortality ratio for exposure to lead and lead compounds

| Study | Population | Standardized mortality ratio (95% limits) |
|---|---|---|
| Jecklin (1956)[1] | No data | Lead levels similar in cases and controls |
| Blot and Fraumeni (1975)[2] | US men living near lead/zinc/ copper industries | 112 |
| | Women | 110 |
| Cooper and Gaffey (1975)[3] | US lead smelter workers | 139[4] |
| | Battery plant workers | 123[4] |
| Rencher et al (1977)[2] | US copper smelter workers | 300 |
| Costello (1982)[5] | US lead/zinc miners | 130($p<0.05$) |
| Selevan et al (1985)[6] | US lead smelter workers | 111($p>0.05$)[4] |
| Gerhardsson et al (1986)[6] | Swedish lead smelter workers | 160($p>0.05$)[4] |
| Sweeney et al (1986)[6] | US chemical plant workers | 134[4] |
| Sankila et al (1990) | Finnish glass factory workers | 128(99-162)[7] |

1 From International Agency for Research on Cancer (1972)

2 From International Agency for Research on Cancer (1980)

3 From Blot (1984)

4 Estimated from data given

5 From Goldsmith et al (1982)

6 From International Agency for Research on Cancer (1987)

7 Standardized incidence ratio

References

1. Blot WJ (1984) Lung cancer and occupational exposures. In: Lung cancer: Causes and prevention, 47-64. Verlag Chemie International Inc.

2. Goldsmith DF, Guidotti TL and Johnston DR (1982) Does occupational exposure to silica cause lung cancer? Am J Ind Med, 3, 423-440.

3. International Agency for Research on Cancer (1972) Monographs on the evaluation of carcinogenic risk of chemicals to man. Volume 1, 40-50. IARC, Lyon.

4. International Agency for Research on Cancer (1980) Monographs on the evaluation of carcinogenic risk of chemicals to man. Volume 23: Some metals and metallic compounds, 104 and 325-415. IARC, Lyon.

5. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42, 230-232. IARC, Lyon.

6. Sankila R, Karjalainen S, Pukkala E et al (1990) Cancer risk among glass factory workers: an excess of lung cancer? Br J Ind Med, 47, 815-818.

74. Leather industries

The studies which attempted to relate the risk of lung cancer to employment in the leather industry are detailed in Table 74. Eight standardized mortality ratios were calculated, ranging from 50 to 158, of which five were raised. Five relative risks were estimated, all of which were above 1.00, with the highest given as 4.2. Two proportional mortality ratios, of 98 and 104, were also presented, along with two proportional registration ratios, of 131 and 136.

Workers in the leather industry may be exposed to many compounds, depending on their specific occupation. The exposures of workers in leather tanning and processing industries include dusts, solvents and other chemicals used during the processes of preservation, defestation and disinfection, beamhouse process, tanning, neutralizing, retanning, bleaching, colouring or dyeing, fat liquoring, drying, pasting, and finishing. Boot and shoe manufacturers and repairers may also be exposed to dust, but the main chemical exposures come from the application of cleaners, adhesives and finishes. One study (Walker) took measurements of toluene, methyl ethyl ketone, acetone and hexane levels in the plants under study, but for all four chemicals the concentrations were found to be less than threshold levels. No data were available for other compounds, although it was noted that several others had been used by the workers. None of the other studies gave any information on the subjects' exposures.

Not surprisingly then, IARC felt that due to the design of many of the studies the evidence for a possible association between lung cancer and employment in the leather industry could not be evaluated [1]. From the evidence presented here it can be seen that if a risk does exist it does not appear to be very large.

Table 74: Estimates of relative risk/standardized mortality ratio for employment in leather industries

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Kennaway and Kennaway (1947)[1] | E/W tanners/leather dressers/ curriers | 141* |
| Menck and Henderson (1949)[1] | US shoe repairers | 2.33(p<0.05) |
| OPCS (1978) | Male shoemakers/repairers, aged 15-64 | 104[2] |
| | Aged 65-74 | 98[2] |
| | Incidence, 1966-7 | 136(p<0.05)[3] |
| | 1968-9 | 131(p<0.05)[3] |
| Logan (1982) | UK male shoemakers - 1931 | 50* |
| | 1951 | 158* |
| | 1961 | 154* |
| | 1971 | 143* |
| | Married women[4] - 1951 | 100* |
| | 1961 | 100* |
| Garabrant and Wegman (1984)[5] | US tannery workers | 4.2(p<0.05) |
| Puntoni et al (1984)[5] | Italian tannery workers | >1.00 |
| Sweeney et al (1985)[5] | US fur tanners | >1.00(p<0.05) |
| Coggon et al (1986)[5] | UK tannery workers | >1.00 |
| Walker (1993) | US shoe factory workers | 147(120-180)* |

* Standardized mortality ratio

1 From International Agency for Research on Cancer (1981)

2 Proportional mortality ratio

3 Proportional registration ratio

4 According to husband's occupation

5 From International Agency for Research on Cancer (1987)

References

1. International Agency for Research on Cancer (1981) Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 25: Wood, leather and some associated industries, 201-292. IARC, Lyon.

2. International Agency for Research on Cancer (1981) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42, 232-237. IARC, Lyon.

3. Logan WPD (1982) Cancer mortality by occupation and social class 1851-1971. HMSO, London and IARC, Lyon.

4. Office of Population Censuses and Surveys (1978) Occupational mortality: The Registrar General's decennial supplement for England and Wales, 1970-72. HMSO, London.

5. Walker JT, Bloom TF, Stern FB et al (1993) Mortality of workers employed in shoe manufacturing. Scand J Work Environ Health, 19, 89-95.

75. Length of menstrual cycle

Only one study presented data relevant to an investigation of the possible association between lung cancer risk in women and the length of the menstrual cycle, and details of it are given in Table 75. Relative risks of 1.6, 1.6 and 2.2 were estimated for women with a menstrual cycle of 30-33 days, 26-29 days and less than 26 days respectively.

Although the data presented in the table are suggestive of an association between lung cancer risk and length of the menstrual cycle, with only one study reporting it is not really possible to make a proper evaluation.

Table 75: Estimates of relative risk for length of menstrual cycle

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Gao et al (1987) | Chinese women with menstrual cycle length 30-33 days | 1.6(1.0-2.6) |
| | 26-29 days | 1.6(1.0-2.7) |
| | <26 days | 2.2(1.3-3.7) |

* Standardized mortality ratio

References

1. Gao Y-T, Blot WJ, Zheng W et al (1987) Lung cancer among Chinese women. Int J Cancer, 40, 604-609.

## 76. Leukocyte count

Only one study was found which presented data relevant to an investigation of the possible relationship between lung cancer risk and leukocyte count, and details of it are given in Table 76. A relative risk of 1.46 was estimated for every 2000/$\mu$l increase in leukocyte count.

However, with no other studies providing data it is not possible to determine if this observed increase in risk represents a true association between lung cancer and leukocyte count.

Table 76: Estimate of relative risk for leukocyte count

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Phillips et al (1992) | US men at high risk of heart disease/UK residents | 1.46($p<0.0001$)[1] |

1 Per 2000/$\mu$l increase in leukocyte count

References

1. Phillips AN, Neaton JD, Cook DG, Grimm RH and Shaper AG (1992) The leukocyte count and risk of lung cancer. Cancer, 69, 680-684.

77. Long-lasting hopelessness/depression

The three studies found which gave data relevant to an investigation of the possible association between lung cancer risk and depression or long-lasting hopelessness are detailed in Table 77. Six relative risks, ranging from 1.58-18.47, were estimated. Additionally, one study reported that 23.1% of bronchogenic carcinoma cases suffered from psychological depression.

Although it has been reported elsewhere that depressed subjects are less likely to quit smoking [1,2], only one of the two studies which presented data on smoking prevalence found evidence that respondents with depression were more likely to be smokers than respondents not affected in this way [5]. Depressed and non-depressed subjects in the study by Shekelle were similar to each other in their smoking habits.

Another possible explanation for the findings presented in the table is that depression may lead to immune suppression, which in turn leads to an increased rate of cancer at a variety of sites [3,4,6]. However, with so little information available it is not really possible to verify this hypothesis, or to fully evaluate the association between lung cancer and long-lasting hopelessness and depression.

Table 77: Estimates of relative risk for long-lasting hopelessness and depression

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Shekelle et al (1981) | US men | 23.1% of bronchogenic carcinoma cases had psychological depression |
| Grossarth-Maticek et al (1985) | Yugoslavian residents | 1.58[1] |
| Linkins and Comstock (1990) | US residents, ex-smokers | 2.52(0.31-20.50)[2] |
| | Smokers of 1-14 cigs/day | 5.80(0.71-47.19)[2] |
| | 15-24 cigs/day | 3.77(0.46-31.19)[2] |
| | 25+ cigs/day | 18.47(4.58-74.41)[2] |
| | Unknown smoking status | 3.17(0.39-25.85)[2] |

Footnote to Table 77

1 Estimated from data given

2 Cancer sites associated with smoking (buccal cavity and pharynx, pancreas, larynx, bronchus and lung, cervix, bladder, kidney)

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References

1. Anda RF, Williamson DF, Escobedo LG et al (1990) Depression and the dynamics of smoking: A national perspective. JAMA, 264, 1541-1545.

2. Covey LS, Glassman AH and Dalack GW (1991) Re: Depressed mood and development of cancer. Am J Epidemiol, 134, 324-325 (Letter).

3. Grossarth-Maticek R, Bastiaans J and Kanazir DT (1985) Psychosocial factors as strong predictors of mortality from cancer, ischaemic heart disease and stroke: The Yugoslav prospective study. J Psychosomatic Res, 29, 167-176.

4. Linkins RW and Comstock GW (1990) Depressed mood and development of cancer. Am J Epidemiol, 132, 962-972.

5. Linkins RW and Comstock GW (1991) Re: Depressed mood and development of cancer. Am J Epidemiol, 134, 325 (Letter).

6. Shekelle RB, Raynor WJ, Ostfeld AM et al (1981) Psychological depression and 17-year risk of death from cancer. Psychosomatic Med, 43, 117-125.

78. Loss of teeth

Details of the only study found which gave information relevant to an investigation of the possible association between lung cancer risk and loss of teeth are given in Table 78. It was reported that cases had lost an average of 15.9 teeth compared to only 12.6 in controls.

Notably, the authors of this study stated that "bad teeth...are, on their own, not able to cause cancer of the lungs". Until other evidence to contradict this is found, it would appear that the possible relationship between lung cancer risk and loss of teeth is in some doubt.

Table 78: Observations of number of teeth lost

| Study | Population | Observations |
|---|---|---|
| Denoix et al (1958) | French men | Average number of teeth lost 15.9 in bronchial cancer cases and 12.6 in controls |

References

1. Denoix PF, Schwartz D and Anguera G (1958) French investigation into the etiology of broncho-pulmonary cancer. Detailed analysis. Bull Assoc Franc pour l'etude du cancer, 49: 1-37.

79. Low forced expiratory volume

Details of the two studies which attempted to relate the risk of lung cancer to low forced expiratory volume in one second ($FEV_1$) are given in Table 79. Four estimates of relative risk in relation to low $FEV_1$ were estimated, ranging from 1.3-2.1, while a relative risk of 0.7 was estimated for those whose lung function was better than average.

The evidence presented in the table suggests a positive association between lung cancer risk and low $FEV_1$, but with only two studies providing data such a relationship is far from proven.

Table 79: Estimates of relative risk for low forced expiratory volume

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Peto et al (1983) | UK men, $FEV_1$ better than average | 0.7 |
| | 0-1 SD below average | 1.5 |
| | 1-2 SD below average | 1.4 |
| | 2+ SD below average | 1.3 |
| Vestbo et al (1991) | Danish men | 2.1(1.3-3.4)[1] |

SD = standard deviations

1 Per litre under the expected $FEV_1$ for height

References

1. Peto R, Speizer FE, Cochrane AL et al (1983) The relevance in adults of air-flow obstruction, but not of mucus hypersecretion, to mortality from chronic lung disease. Am Rev Respir Dis, 128, 491-500.

2. Vestbo J, Knudsen KM and Rasmussen FV (1991) Are respiratory symptoms and chronic airflow limitation really associated with an increased risk of respiratory cancer? Int J Epidemiol, 20, 375-378.

80. Low-level radiation

Table 80 gives details of the studies which presented data relevant to an investigation of the possible association between lung cancer risk and exposure to low-level radiation. Eight standardized mortality ratios were calculated and these ranged from 69-218, with only two being raised. Two relative risks, of 1.2 and 3.7, were also estimated. Additionally, one study estimated a risk of 25-50 per million person-rems of exposure, while another estimated a decrease in risk of 1.6% for every 10mSv of exposure.

Three studies (Darby, Mole, Petersen) gave dosimetric data based on actual measurements of the radiation exposure of respondents, while three others (Jablon and Bailar, Smith and Doll 1981, Smith and Doll 1982) attempted to estimate exposure. However, it is possible that in those studies where exposure data was not based on objective measurements, and also in the study by Kabat where no information on exposure was given at all, inaccuracies may have been introduced. Other problems to note include a possible overlap in the studies by Darby, Mole and Petersen, as these were all based on respondents from the same US plant. Finally, in the study by Kabat there was a high correlation between a history of a reproductive primary and a history of radiotherapy, and it was not possible to estimate the effect of one exposure independent of the other.

Overall, then, there is little convincing evidence of an association between lung cancer risk and exposure to low-level radiation.

Table 80: Estimates of standardized mortality ratio/relative risk for exposure to low-level radiation

| Study | Population | Standardized mortality ratio (95% limits) |
|---|---|---|
| Jablon and Bailar (1980) | US residents | 25-50[1] |
| Darby and Reissland (1981) | US nuclear plant workers | 75[2] |
| Smith and Doll (1981) | UK male radiologists entering study before 1921 | 218(p<0.05) |
| | Entering study 1921-1954 | 97 |
| Smith and Doll (1982) | UK ankylosing spondylitis patients | 142(p<0.001) |
| Mole (1987) | UK radiation workers | 69(p<0.01) |
| | UK radiation workers | 87(p<0.05) |
| | US radiation workers | 78 |
| | US radiation workers | 75(p<0.05) |
| Petersen et al (1990) | US radiation workers | -1.6%(<0-5.6%)[3] |
| Kabat (1993) | US male radiotherapy patients | 1.2(0.2-6.4)* |
| | Females | 3.7(1.2-10.9)* |

* Relative risk

1 Risk per million person-rems

2 Tumours of respiratory system

3 Estimated increase in relative risk per 10 mSv

References

1. Darby SC and Reissland JA (1981) Low levels of ionizing radiation and cancer - are we underestimating the risk? J R Statist Soc, 144, 298-331.

2. Jablon S and Bailar JC (1980) The contribution of ionizing radiation to cancer mortality in the United States. Prev Med, 9, 219-226.

3. Kabat GC (1993) Previous cancer and radiotherapy as risk factors for lung cancer in lifetime nonsmokers. Cancer Causes and Control, 4, 489-495.

4. Mole RH (1987) Radiation, cancer risk, and the new dosimetry. The Lancet, Dec 12, 1403-1404.

5. Petersen GR, Gilbert ES, Buchanan JA and Stevens RG (1990) A case-cohort study of lung cancer, ionizing radiation, and tobacco smoking among males at the Hanford site. Health Phys, 58, 3-11.

6. Smith PG and Doll R (1981) Mortality from cancer and all causes among British radiologists. Brit J Radiol, 54, 187-94.

7. Smith PG and Doll R (1982) Mortality among patients with ankylosing spondylitis after a single treatment course with x rays. Brit Med J, 284, 449-60.

81. Lung scars

Four studies attempted to investigate the possible relationship between lung cancer risk and lung scarring, and details of these are given in Table 81. A total of 36 cases of lung cancer associated with lung scarring were reported.

However, from the data given it was not possible to calculate any estimates of risk of lung cancer in individuals with lung scarring, and so it is difficult to properly evaluate the evidence.

Table 81: Observations on lung cancer associated with lung scarring

| Study | Population | Observations |
|---|---|---|
| Carroll (1962) | UK residents | 13 of 109 lung cancers associated with lung scarring |
| Raeburn and Spencer (1957) | UK residents | 15 lung cancers associated with lung scarring reported |
| Strauss et al (1963) | US/UK/French/German residents | 11 lung cancers associated with embedded foreign bodies reported |
| Yokoo and Suckow (1961) | US residents | 7 out of 41 lung cancers associated with lung scarring |

References

1. Carroll R (1962) The influence of lung scars on primary lung cancer. J Path Bacteriol, 83, 293-297.

2. Raeburn C and Spencer J (1957) Lung scar cancers. Brit J Tuberc, 51, 237-245.

3. Strauss FH, Dordal E and Kappas A (1963) The problems of pulmonary scar tumors: A case report and brief review. Arch Path, 76, 693-699.

4. Yokoo H and Suckow EE (1961) Peripheral lung cancers arising in scars. Cancer, 14, 1205-1215.

82. Man-made mineral fibres

Details of the studies which gave information relevant to an investigation of the possible association between lung cancer risk and exposure to man-made mineral fibres are given in Table 82. Ten standardized mortality ratios were calculated and these ranged from 68-200, with nine being raised. Additionally, two studies reported standardized incidence ratios, of 74 and 91, while another found that four cases and no controls had worked in a glasswool plant.

Four studies (Enterline, Gustavsson, Saracci, Shannon) had made objective measurements of the level of man-made mineral fibres respondents were exposed to, while the study by Simonato had attempted to quantify exposure by length of employment. However, no information on the workers' exposure was available from the other studies, which may therefore contain inaccuracies. Furthermore, it was stated that in the study by Engholm respondents were exposed to asbestos in addition to man-made mineral fibres, although, surprisingly, this study reported a decrease in lung cancer incidence.

While IARC felt that there was "limited" evidence of the carcinogenicity of rock/slagwool to humans, that for glasswool and glass filaments was classified as "inadequate" [2]. A review by Lippmann described the risk of lung cancer following exposure to man-made mineral fibres as "virtually nil" [3].

Table 82: Estimates of standardized mortality ratio for exposure to man-made mineral fibres

| Study | Population | Standardized mortality ratio (95% limits) |
|---|---|---|
| Bayliss et al (1976)[1] | US glasswool plant workers | Four cases and no controls worked in plant |
| Morgan et al (1984)[1] | US fibrous glass plant workers | 136[3] |
| Saracci et al (1984)[2] | 7 European countries | 200 |
| Moulin et al (1986)[1] | French glass-fibre production workers | 74(24-172)[4] |
| Engholm et al (1987)[1] | Swedish construction workers | 91(83-100)[4] |
| Enterline et al (1987)[1] | US small diameter fibre workers | 133[3] |
| | Glass filament workers | 95[3] |
| | Rock/slagwool workers | 148[3] |
| Shannon et al (1987)[1] | Canadian wool plant workers | 199($p<0.05$) |
| Simonato et al (1987)[1] | European glasswool plant workers | 127($p<0.05$) |
| | Glass filament workers | 120 |
| | Rock/slagwool workers | 124(98-154) |
| Gustavsson et al (1992) | Swedish factory workers | 68(37-113) |

1 From International Agency for Research on Cancer (1988)

2 From Lippmann (1992)

4 Standardized incidence ratio

3 Tumours of respiratory system

References

1. Gustavsson P, Plato N, Axelson O et al (1992) Lung cancer risk among workers exposed to man-made mineral fibers (MMMF) in the Swedish prefabricated house industry. Am J Ind Med, 21, 825-834.

2. International Agency for Research on Cancer (1988) Monographs on the evaluation of carcinogenic risks to humans. Volume 43: Man-made mineral fibres and radon, 39-171. IARC, Lyon.

3. Lippmann M (1992) Asbestos and other mineral fibers. In: Environmental Toxicants: Human Exposures and Their Health Effects. (Incomplete reference)

83. Marine diesel fuels

Table 83 gives details of the only study which attempted to relate the risk of lung cancer to exposure to marine diesel fuels. A relative risk of 1.6 was estimated.

It was noted that no attempt was made in the study to separate the effects of exposure to the combustion products of marine diesel fuels from those of exposure to the liquid itself, and thus it is possible that the observed excess of lung cancers could have been caused by a constituent of the fuel. In the light of this, and with only one study reporting, IARC justifiably classified the evidence for the carcinogenicity of marine diesel fuels to humans as "inadequate" [1].

Table 83: Estimate of relative risk for marine diesel fuels

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Siemiatycki et al (1987)[1] | Canadian men | 1.6(1.0-2.6) |

1 From International Agency for Research on Cancer (1989)

References

1. International Agency for Research on Cancer (1989) Monographs on the evaluation of carcinogenic risks to humans. Volume 45: Occupational exposures in petroleum refining; crude oil and major petroleum fuels, 219-237. IARC, Lyon.

## 84. Maternal age at birth

Only one study attempted to relate the risk of lung cancer to the age of the mother at the time of the subject's birth, and details of it are given in Table 84. It was reported that the average maternal age for cases was 28.629 years, compared to 27.420 years for controls.

With only one study reporting it is not possible to determine if there is an effect of maternal age at birth on subsequent lung cancer risk in the offspring or whether the reported association arose simply by chance.

Table 84: Observations for maternal age at birth

| Study | Population | Observations |
|---|---|---|
| Abelin and Tokuhata (1965) | US residents | Average age for cases 28.629 years compared to 27.420 for controls |

References

1. Abelin T and Tokuhata GK (1965) Maternal age at birth and susceptibility to lung cancer. Lancet, Nov 25, 1121-1123.

85. Meat consumption

Table 85 gives details of the three studies found which presented data relevant to an investigation of the possible association between lung cancer risk and frequent meat consumption. Three relative risks were estimated, ranging from 1.29-1.53.

Although the evidence presented in the table is indicative of an association between lung cancer risk and the frequent consumption of meat, data from further studies is needed before this relationship can be confirmed.

Table 85: Estimates of relative risk for frequent meat consumption

| Study | Population | Relative risk |
|---|---|---|
| Hirayama (1974) | Japanese men | 1.53 |
| Fraser et al (1991) | US Seventh-day Adventists | 1.31(0.52-3.28) |
| Alavanja et al (1993) | US women | 1.29 |

References

1. Alavanja MCR, Brown CC, Swanson C and Brownson RC (1993) Saturated fat intake and lung cancer risk among nonsmoking women in Missouri. JNCI, 85, 1906-1916.

2. Fraser GE, Beeson WL and Phillips RL (1991) Diet and lung cancer in California Seventh-day Adventists. Am J Epidemiol, 133, 683-93.

3. Hirayama T (1974) Prospective studies on cancer epidemiology based on census population in Japan. Proc 11th International Cancer Congress, 3, 26-35.

86. Mercury and mercury compounds

Table 86 gives details of the 11 studies which considered lung cancer risk in relation to exposure to mercury and mercury compounds. Four relative risks were estimated, ranging from 1.00-4.00, and two were above 1.00. Four standardized mortality ratios, of between 134-1400, were calculated, along with two standardized incidence ratios, of 166 and 180, and one proportional mortality ratio of 105. In addition, one study found that six cases and no controls had ever been employed as hat makers.

Only three studies (Barregard, Cragle, Ellingsen) took objective measurements of exposure to mercury, by recording mercury levels in the subjects' urine. Thus, in the other studies, inaccuracies due to exposure misclassification could have been introduced. Additionally, some of the studies reported that subjects had been exposed to various other substances which may themselves be potential carcinogens, including asbestos and static magnetic fields (Barregard), arsenic and other chemicals (Buiatti), radon (Amandus and Costello) and silica (Amandus and Costello, Costello). It is therefore possible that the observed associations in these studies may have been caused by exposure to a substance other than mercury. In addition, Cragle et al suggested that the excess of lung cancer observed in their study may be due to lifestyle factors or some factor other than mercury.

Thus, when evaluating the evidence for the carcinogenicity of mercury and mercury compounds to humans, IARC gave it a classification of "inadequate" [3].

Table 86: Estimates of relative risk/standardized mortality ratio for exposure to mercury and mercury compounds

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Milham (1976)[1] | US dentists | 105(88-125)[2] |
| Costello (1982)[3] | US mercury miners | 355($p<0.05$)* |
| Cragle (1984)[4] | US workers in nuclear weapons factory | 134(100-180)* |
| Buiatti et al (1985)[4] | Italian residents | 6 cases and no controls ever employed as hat makers ($p<0.01$) |
| Walrath et al (1985)[4] | US dentists | 1.00 |
| Tamashiro et al (1986)[1] | Japanese fishermen and families | 1.52(0.79-2.65) |
| Gallagher et al (1989)[4] | Canadian dentists | 1.00 |
| Barregard et al (1990)[4] | Swedish chloralkali workers | 180(90-300)[5] |
| Amandus and Costello (1991)[4] | US mercury miners - silicotics | 1400(289-4100)* |
| | Nonsilicotics | 266(115-524)* |
| Ellingsen et al (1991)[4] | Norwegian chloralkali workers | 166(100-260)[5] |
| Siemiatycki (1991)[4] | Canadian residents | 4.0(1.2-13.0) |

* Standardized mortality ratio

1 From International Agency for Reseach on Cancer (1993)

2 Proportional mortality ratio

3 From Goldsmith et al (1982)

4 From Boffetta et al (1993)

5 Standardized incidence ratio

References

1. Boffetta P, Merler E and Vainio H (1993) Carcinogenicity of mercury and mercury compounds. Scand J Work Environ Health, 19, 1-7.

2. Goldsmith DF, Guidotti TL and Johnston DR (1982) Does occupational exposure to silica cause lung cancer? Am J Ind Med, 3, 423-440.

3. International Agency for Research on Cancer (1993) Monographs on the evaluation of carcinogenic risks to humans. Volume 58: Beryllium, cadmium, mercury, and exposures in the glass manufacturing industry, 239-345. IARC, Lyon.

87. Metal workers

Only four studies were found which attempted to relate the risk of lung cancer to employment in the metal working trades, and these are detailed in Table 87. Four standardized mortality ratios were calculated, ranging from 115-170. Six proportional mortality ratios were presented, and these lay in the range 105-113. Six proportional registration ratios, of between 117 and 134, were also given. Two studies estimated relative risks, of 1.26 and 1.3.

Previous studies of metal workers have observed associations between cancer of various sites and a number of compounds, including nitrosable amines and nitrites from cutting oils, water based cutting oils, straight oils, polycyclic aromatic hydrocarbons suspended in oil mists, chlorinated hydrocarbon solvents used for degreasing metal parts, and metal dust resulting from machining and grinding operations [1]. However, as only the study by Acquavella attempted to classify the substances the subjects were exposed to it is not really possible to identify the potential carcinogenicity of any one compound.

The data presented in the table is suggestive of an increased risk of lung cancer among metal workers, but due to a lack of information the agent or agents responsible for this increase cannot be identified. It should also be remembered that the evidence is based on results from only four studies.

Table 87: Estimates of relative risk/standardized mortality ratio for metal workers

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| OPCS (1978) | E/W male sheet metal workers, aged 15-64 | 110[1] |
| | Aged 65-74 | 106[1] |
| | Incidence, 1966-7 | 128(p<0.01)[2] |
| | 1968-9 | 122(p<0.01)[2] |
| | Male metal plate workers/riveters, aged 15-64 | 113[1] |
| | Aged 65-74 | 105[1] |
| | Incidence, 1966-7 | 131(p<0.01)[2] |
| | 1968-9 | 134(p<0.01)[2] |
| | Male other metal making/working/jewellery electrical production process workers, aged 15-64 | 110(p<0.05)[1] |
| | Aged 65-74 | 108[1] |
| | Incidence, 1966-7 | 117(p<0.01)[2] |
| | 1968-9 | 117(p<0.01)[2] |
| OPCS (1986) | UK male sheet metal workers/platers/ shipwrights/riveters | 170(p<0.01)* |
| | Married women[3] | 142(p<0.01)* |
| | Male metal working production fitters and fitter/machinists | 115(p<0.01)* |
| | Married women[3] | 124(p<0.01)* |
| Acquavella et al (1993) | Metal components workers | 1.3(0.9-1.8) |
| Keller and Howe (1993) | US construction metal workers | 1.26(0.67-2.35) |

* Standardized mortality ratio

1 Proportional mortality ratio

2 Proportional registration ratio

3 According to husband's occupation

References

1. Acquavella J, Leet T and Johnson G (1993) Occupational experience and mortality among a cohort of metal components manufacturing workers. Epidemiol, 4, 428-434.

2. Keller JE and Howe HL (1993) Cancer in Illinois construction workers: A study. Am J Ind Med, 24, 223-230.

3. Office of Population Censuses and Surveys (1978) Occupational mortality: The Registrar General's decennial supplement for England and Wales, 1970-72. HMSO, London.

4. Office of Population Censuses and Surveys (1986) Occupational mortality: The Registrar General's decennial supplement for Great Britain, 1979-80, 1982-83. HMSO, London.

## 88. Metronidazole

Only two studies were found which presented data relevant to an investigation of the possible association between lung cancer risk and exposure to metronidazole, and details of these are given in Table 88. Two standardized mortality ratios, of 77 and 667, were calculated.

With so few studies reporting, it is difficult to evaluate the carcinogenicity of metronidazole. Furthermore, additional follow-up and analysis of the data from the study by Beard suggested that the excess of lung cancer observed could be explained entirely by confounding with smoking. Thus, IARC concluded there was "inadequate" evidence for the carcinogenicity of metronidazole to humans [1].

Table 88: Estimates of standardized mortality ratio for exposure to metronidazole

| Study | Population | Standardized mortality ratio |
|---|---|---|
| Beard et al (1979)[1] | Female trichomoniasis patients | 667[2] |
| Friedman (1980)[1] | Female trichomoniasis patients | 77[2] |

1 From International Agency for Reseach on Cancer (1987)
2 Estimated from data given

## References

1. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42, 250-252. IARC, Lyon.

89. Mineral oils

Details of the 13 studies which attempted to relate the risk of lung cancer to exposure to mineral oils are given in Table 89. Eight standardized mortality ratios were calculated, ranging from 56-149, of which five were raised. Two relative risks were also estimated, at 1.73 and 3.76. Additionally, one study calculated an annual mortality rate of 1.07 per 1000, while one reported excesses of lung cancer among workers in occupations in which exposure to mineral oils was likely. Finally, one study observed 2.9% of deaths due to lung cancer among the exposed group compared to 3.2% in the control group.

Exposure to mineral oils occurs in a variety of industries, and it is highly likely that workers are also exposed to other substances which may themselves be potentially carcinogenic. For example, printing pressmen are exposed to oil mist containing carbon blacks, pitch, other pigments and additives, while the sandblasters in the study by Puntoni were noted to have been exposed to many solvents, naphtha, and silica sand. In addition, insufficient information was given by the studies to allow an assessment of the class of mineral oil, which exists in many forms, workers were exposed to. Therefore, it is difficult to determine the carcinogenic potential of any one substance.

Despite these drawbacks, IARC [2,3] felt that although there was "sufficient" evidence for the carcinogenicity to humans of untreated and mildly treated mineral oils, that for highly refined oils was "inadequate". However, these evaluations were based mainly on studies of skin cancer.

Table 89: Estimates of standardized mortality ratio/relative risk for exposure to mineral oils

| Study | Population | Standardized mortality ratio |
|---|---|---|
| Ely et al (1970)[1] | US metalworkers | 2.9% deaths from resp. system cancer against 3.2% in controls |
| Goldstein et al (1970)[1] | US newspaper plant workers | 1.07[2] |
| Greenberg (1972)[1] | UK newspaper printers | 133($p<0.01$)[3] |
| Moss et al (1972)[1]/Moss (1973)[1] | UK newspaper workers | 134($p<0.01$)[3] |
| Decoufle (1976)[1] | US metalworkers | 99[3,4] |
| Menck and Henderson (1976)[1] | US newspaper printers | 98 |
| Milham (1976)[1] | US mechanics/repairmen, tool/die makers/setters, oilers/greaser, pressmen/ plate printers | Excesses of lung cancer reported |
| Lloyd et al (1977)[1] | US newspaper pressmen | 112[3] |
| OPCS (1978)[1] | UK machine-tool setters/ setter operators, motor mechanics/auto engineers, fitters, machine erectors | >100 |
| Puntoni et al (1979)[5] | Italian sandblasters | 3.76($p<0.05$)* |
| Paganini-Hill et al (1980)[1] | US newspaper pressmen | 149[3] |
| Jarvholm et al (1981)[1] | Swedish metalworkers | 56[3] |
| Zappa et al (1993) | Italian weavers | 1.73(1.1-2.7)* |

* Relative risk

1 From International Agency for Research on Cancer (1984)

2 Per 1000 per year

3 Estimated from data given

4 Tumours of respiratory system

5 From Goldsmith et al (1982)

References

1. Goldsmith DF, Guidotti TL and Johnston DR (1982) Does occupational exposure to silica cause lung cancer? Am J Ind Med, 3, 423-440.

2. International Agency for Research on Cancer (1984) Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 33: Polynuclear aromatic compounds, part 2, carbon blacks, mineral oils and some nitroarenes, 87-168. IARC, Lyon.

3. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42, 252-254. IARC, Lyon.

4. Zappa M, Paci E, Costantini AS and Kriebel D (1993) Lung cancer among textile workers in the Prato area of Italy. Scand J Work Environ Health, 19, 16-20.

90. Month of birth

In 1963, Dijkstra first suggested that there may be a higher risk of lung cancer in people born in late winter, following the observation of an excess of lung cancer deaths in patients born in March in a series of 330 deaths occurring between 1950 and 1960 in the Netherlands. A further 8 studies were found which also attempted to relate lung cancer risk and month of birth in this way, and the results of these 8 studies are given in Table 90. From the table it can be seen that in three of the studies there does appear to be an excess of births in March, and an excess of births in the winter months is also seen in one other study. However, due to the failure of most of the studies to give any estimates of the number of births which would be expected in any one month it is difficult to assess the significance of any differences in the actual numbers of births observed.

It is hardly likely that month of birth in itself is a risk factor for lung cancer, and so it is more probably a marker for some other factor. One suggestion is that the excess of lung cancer deaths in those born in late winter can be explained by the absence of vitamin A at birth, causing irreversible metaplasia in the lungs. This leaves the tissue unable to cope with the normal stimuli of life and predisposes the individual to various pulmonary diseases, including cancer [2,6]. Although this may be a possible explanation, the evidence for an association between month of birth and lung cancer as presented here is hardly compelling.

Table 90: Relationship between lung cancer and month of birth

| | Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Dijkstra (1963): | | | | | | | | | | | | |
| O | 23 | 36 | 50 | 29 | 19 | 22 | 21 | 20 | 26 | 28 | 29 | 27 |
| E | 28.67 | 27.81 | 29.68 | 28.04 | 27.71 | 25.58 | 26.45 | 27.65 | 27.52 | 27.37 | 26.03 | 27.51 |
| Jones (1963)[1]: | | | | | | | | | | | | |
| O | --14-- | | --17-- | | --21-- | | --15-- | | --15-- | | --13-- | |
| Loxton (1963)[1]: | | | | | | | | | | | | |
| O | --116-- | | --113-- | | --115-- | | --144-- | | --138-- | | --115-- | |
| Baas and Strackee (1964)[1]: | | | | | | | | | | | | |
| O | 124 | 113 | 132 | 118 | 87 | 103 | 106 | 114 | 123 | 118 | 106 | 102 |
| Davies (1964)[1]: | | | | | | | | | | | | |
| O | 170 | 169 | 173 | 173 | 162 | 158 | 158 | 189 | 185 | 165 | 172 | 168 |
| De Sauvage Nolting (1964): | | | | | | | | | | | | |
| O | --- Higher than overall rate --- | | | | --- Lower than overall rate --- | | | | -- Not reported -- | | As Jan-Apr | |
| MacSween and Miller (1964): | | | | | | | | | | | | |
| Ca | 22 | 9 | 9 | 22 | 19 | 19 | 20 | 21 | 14 | 13 | 18 | 14 |
| Co | 18 | 16 | 24 | 17 | 20 | 19 | 13 | 16 | 11 | 15 | 12 | 19 |
| Palmer (1964): | | | | | | | | | | | | |
| O | 3352 | 3193 | 3426 | 3230 | 3360 | 3226 | 3280 | 3363 | 3267 | 3338 | 3223 | 3392 |
| Van der Wal et al (1964)[1]: | | | | | | | | | | | | |
| O | 10 | 15 | 17 | 9 | 9 | 10 | 13 | 18 | 15 | 13 | 11 | 10 |

Ca = Cases; Co = Controls; E = Expected; O = Observed

1 From Allan (1964)

References

1. Allan TM (1964) Lung cancer and month of birth. The Lancet, Feb 22, 439-440.

2. Anon (1963) Lung cancer and month of birth. The Lancet, Dec 7, 1210-1211.

3. Cochrane AL and Palmer JW (1964) Lung cancer and date of birth. The Lancet, Dec 5, 1246 (Letter).

4. Davies J (Incomplete reference)

5. De Sauvage Nolting WJJ (1964) Lung cancer and month of birth. The Lancet, Sep 5, 531 (Letter).

6. Dijkstra BKS (1963) Origin of carcinoma of the bronchus. JNCI, 31, 511-519.

7. MacSween RNM and Miller SEP (1964) Lung cancer and month of birth. The Lancet, Apr 4, 767-768 (Letter).

8. Palmer JW (1964) Lung cancer and month of birth. The Lancet, Nov 7, 1013 (Letter).

91. Mustard gas

Details of the four studies which investigated the possible association between lung cancer risk and exposure to mustard gas are given in Table 91. Four standardized mortality ratios were calculated, ranging from 147-3667.

Only the study by Wada contained any information on the level of exposure to mustard gas, giving objective measurements of workplace concentrations. Thus, there may have been inaccuracies in the other studies due to misclassification of exposure. Additionally, workers in the study by Weiss and Weiss were also exposed to nitrogen mustard, bromoacetone, phosgene, chloropicrine and organic arsenicals. It is possible that the increased lung cancer risk observed in this study may have been caused by one or more of these substances. Interestingly, Case and Lea concluded that the increased risk of lung cancer observed in their study could not be attributed to mustard gas poisoning but was in fact associated in some way with chronic bronchitis.

Despite this, IARC felt there was "sufficient" evidence for the carcinogenicity of mustard gas to humans [3], and a review by Blot described it as a "known" occupational lung carcinogen [1].

Table 91: Estimates of standardized mortality ratio for exposure to mustard gas

| Study | Population | Standardized mortality ratio |
|---|---|---|
| Case and Lea (1955)[1] | War pensioners | 207[2] |
| Beebe (1960)[1] | American soldiers | 147[3] |
| Wada et al (1968)[4] | Japanese mustard gas workers | 3667[2] |
| Weiss and Weiss (1975)[1] | German mustard gas workers | 280[2,5] |

Footnote to Table 91

1 From International Agency for Research on Cancer (1975)

2 Estimated from data given

3 Tumours of respiratory system

4 From Blot (1984)

5 Bronchial carcinoma

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References

1. Blot WJ (1984) Lung cancer and occupational exposures. In: Lung cancer: Causes and prevention, 47-64. Verlag Chemie International Inc.

2. International Agency for Research on Cancer (1975) Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 9: Some aziridines, N-, S- and O-mustards and selenium, 181-192. IARC, Lyon.

3. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42, 322-326. IARC, Lyon.

92. Neuropathy/myopathy

Table 92 gives details of the studies found which investigated lung cancer in relation to neuropathies and myopathies. One relative risk of 12.51 was estimated from one study, while a total of 28 cases of lung cancer associated with various neurological disorders were reported from the other studies.

With so few estimates of risk, it is difficult to assess the possible association between lung cancer and neuropathies and myopathies. Howeve, one author felt that it was unlikely that the neurological changes were due to any general toxic effect of the tumour, but were more likely to be due to some exceptional factor either in relation to the tumour or in the subject's reaction to it [1].

Table 92: Estimates of relative risk for neuropathy/myopathy

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Denny-Brown (1948) | UK men | 2 cases of lung cancer with sensory neuropathy |
| Wyburn-Mason (1948) | UK male | 1 case of lung cancer with sensory neuropathy |
| Lennox and Prichard (1950) | UK men | 5 cases of peripheral neuritis among 299 bronchial carcinoma cases |
| Brain et al (1951) | UK residents | 2 cases of bronchial carcinoma associated with subacute cortical cerebellar degeneration |
| Henson et al (1954) | UK residents | 17 cases of bronchial carcinoma associated with various neurological disorders |
| Croft (1958) | UK female | 1 case of lung cancer associated with neuropathy |
| Croft and Wilkinson (1963) | UK residents | 12.51(3.81-41.08)[1] |

1 Estimated from data given

References

1. Brain WR (1963) The neurological complications of neoplasms. Lancet, 1, 179-184.

2. Brain WR, Daniel PM and Greenfield JG (1951) Subacute cortical cerebellar degeneration and its relation to carcinoma. J Neurol Neurosurg Psychiat, 14, 59-75.

3. Croft PB (1958) Abnormal responses to muscle relaxants in carcinomatous neuropathy. Br Med J, 1, 181-187.

4. Croft PB and Wilkinson M (1963) Carcinomatous neuromyopathy: Its incidence in patients with carcinoma of the lung and carcinoma of the breast. Lancet, 1, 184-188.

5. Denny-Brown D (1948) Primary sensory neuropathy with muscular changes associated with carcinoma. J Neurol Neurosurg, 11, 73-87.

6. Henson RA, Russell DS and Wilkinson M (1954) Carcinomatous neuropathy and myopathy: A clinical and pathological study. Brain, 77, 82-121.

7. Lennox B and Prichard S (1950) The association of bronchial carcinoma and peripheral neuritis. Quart J Med, 19, 97-109.

8. Wyburn-Mason R (1948) Bronchial carcinoma presenting as polyneuritis. Lancet, i, 203-206.

93. Neuroticism

Table 93 gives details of the four studies found which attempted to relate lung cancer risk to measures of neuroticism. One study calculated mortality rates per 100,000 men of 296, 108 and 56 for neuroticism scores of 0-2, 3-8 and 9+ respectively. The other three studies reported that lung cancer cases had lower neuroticism scores than the control groups, but did not give details of their results.

It should be noted that all of the studies were of a retrospective design and therefore collected information from the cases after they had developed cancer, although they may still have been unaware of their diagnosis at that stage. However, it is possible that their disease status may have affected their personality in some way, thus introducing bias into the results. Studies of prospective design would not have suffered from this particular problem. Therefore, although the findings presented in the table provide some evidence of a possible association between lung cancer risk and a low level of neuroticism, with only four studies reporting, such a relationship is far from proven.

Table 93: Estimates of mortality rates for neuroticism

| Study | Population | Mortality rate |
|---|---|---|
| Kissen and Eysenck (1962)/Kissen (1963) | Scottish men | Lung cancer patients had lower neuroticism scores than controls |
| Kissen (1964) | Scottish men, neuroticism score 0-2 | 296[1] |
| | Score 3-8 | 108[1] |
| | Score 9+ | 56[1] |
| Kissen (1967) | Scottish men, aged 55-64 | Lung cancer patients with and without, and controls without, history of adverse life events had lower neuroticism scores than controls with history of adverse life events |

Table 93 continued

| | | |
|---|---|---|
| Blohmke et al (1981) | German men | Lung cancer patients had lower neuroticism scores than healthy smokers |

1 Mortality rate per 100,000 men

References

1. Blohmke M, Engelhardt BV and Stelzer O (1981) Investigations on the personality of patients with pulmonary carcinomas compared to a control group. Med Biol Environ, 9, 67-75.

2. Kissen DM and Eysenck HJ (1962) personality in male lung cancer patients. J Psychosomatic Res, 6, 123-127.

3. Kissen DM (1963) Aspects of personality of men with lung cancer. Acta Psychother, 11, 200-210.

4. Kissen DM (1964) Personality and lung cancer. Lancet, 1, 216-217.

5. Kissen DM (1967) Psychosocial factors, personality and lung cancer in men aged 55-64. Br J Med Psychol, 40, 29-43.

## 94. Nickel and nickel compounds

Table 94 given details of the studies which investigated the possible risk of lung cancer following exposure to nickel and/or nickel compounds. Relative risks of between 1.00 and 3.1 were estimated, with six out of seven being above 1.00. Seventeen standardized mortality ratios, of 54-400, were also presented, with 14 of these being raised. Three studies presented proportional mortality ratios between 97-191, of which two were raised, while one reported a standardized incidence ratio of 83. The two remaining studies simply gave the number of cases of lung cancer reported during the period of follow-up, with one finding three cases in two years, and the other some 92 cases in 20 years.

Little information was available from the studies about the nature of the exposures of the subjects. Only four studies (Andersson, Bernacki, ICNCM, Sorahan) made any attempt to estimate the level of exposure to nickel, although two of these used historical rather than contemporary measurements (Bernacki, ICNCM), and one estimated exposures rather than carrying out objective measurements (Andersson). Equally scant data were available on the substances the subjects were exposed to, with only four studies attempting to identify these (ICNCM, Roberts, Saknyn, Silverstein). Therefore, as nickel exists in many compound, it is difficult to separate out the potential effects of any one of them.

Although in 1987 IARC commented that it is "still not possible to state with certainty which specific nickel compounds are human carcinogens, and which are not", at that time it was felt that the overall evidence for the carcinogenicity of nickel was "sufficient", and it was suggested that the early stages of nickel refining, which involve exposure to respirable particles of nickel subsulphide and nickel oxide, and nickel carbonyl vapour, may carry the most risk [1,2]. This view was reaffirmed in 1990, when, in an updated evaluation of the carcinogenicity of nickel and nickel compounds, IARC classified the evidence for nickel sulphate, nickel sulphides and nickel oxides as "sufficient", whilst that for metallic nickel and nickel alloys was felt to be "inadequate" [3].

Table 94: Estimates of relative risk/standardized mortality ratio for exposure to nickel and/or nickel compounds

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Loken (1950)[1] | Norwegian nickel refinery workers | 3 cases of lung cancer between 1948-1950 |
| Rockstroh (1958)[1]/ Konetzke (1974a,b)[1] | German Democratic Republic nickel refinery workers | >1.00($p<0.05$) |
| Znamenskii (1963)[1]/ Tatarskaya (1965,1967)[1] | USSR nickel refinery workers | >1.00($p<0.05$) |
| Tsuchiya (1965)[1] | Japanese nickel refinery workers | >1.00($p<0.05$) |
| Mastromatteo (1967)[1]/ Virtue (1972)[1]/ CMBEEP (1975)[1] | Canadian nickel refinery workers | 92 cases of lung cancer between 1948-1968 |
| Saknyn and Shabynina (1970,1973)[2] | USSR nickel smelter workers A | 200* |
| | B | 280* |
| | C | 380* |
| | D | 400* |
| Bernacki et al (1978)[4] | Aircraft-engine factory workers | 1.00 |
| Lessard et al (1978)[4]/ Langer et al (1982)[4]/ Meininger et al (1982)[4] | New Caledonian nickel smelting workers | >1.00 |
| Silverstein et al (1981)[2] | US die-casting/electroplating plant workers | 191(127-276)[5] |
| Olejar et al (1982)[4] | Slovakian nickel smelting workers | >1.00 |
| Andersson et al (1984)[2] | Swedish nickel-cadmium battery factory workers | 120(44-261)* |
| Cornell (1984)[2] | US stainless steel/low-nickel alloy plant workers | 97(85-111)[5] |
| Cornell and Landis (1984)[2] | US nickel-chromium alloy foundry workers | 105(80-135)[5] |

Table 94 continued

| | | |
|---|---|---|
| Egedahl and Rice (1984)[2] | Canadian nickel refinery workers | 83(10-301)[6] |
| Gerin et al (1984)[2] | Canadian patients | 3.1(1.9-5.0) |
| Redmond (1984)[2] | US high-nickel alloy workers | 109(98-122)* |
| Roberts et al (1984)[2] | US/Canadian nickel refinery workers | 261(220-306)* |
| Sorahan (1987)[2] | UK nickel-cadmium battery factory workers | 130(107-157)* |
| | UK nickel-chromium plating factory workers | 150(117-189)* |
| ICNCM (1990)[2] | Canadian nickel miners and smelters | 135(111-162)* |
| | Welsh nickel refinery workers | 393(336-456)* |
| | Norwegian nickel refinery workers | 262(207-327)* |
| | US nickel miners and smelters with <1 year exposure | 265(107-546)* |
| | ≥1 year exposure | 127(77-196)* |
| | US high-nickel alloy workers | 97(80-121)* |
| | UK high-nickel alloy workers | 98(57-121)* |
| | US gaseous diffusion plant workers | 54(25-103)* |

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* Standardized mortality ratio

1 From International Agency for Research on Cancer (1976)

2 From International Agency for Research on Cancer (1990)

3 Estimated from data given

4 From International Agency for Research on Cancer (1987)

5 Proportional mortality ratio

6 Standardized incidence ratio

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References

1. International Agency for Research on Cancer (1976) Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 11: Cadmium, nickel, some epoxides, miscellaneous industrial chemicals and general considerations on volatile anaesthetics, 75-114. IARC, Lyon.

2. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogencity: An updating of IARC monographs volumes 1 to 42, 264-269. IARC, Lyon.

3. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Volume 49: Chromium, nickel and welding, 257-446. IARC, Lyon.

## 95. Overnutrition

Table 95 gives details of the only study found which investigated the possible association between lung cancer risk and overnutrition. A relative risk of 1.16 was estimated for subjects in the highest category of energy intake.

Although other studies [1,2,4] have reported decreased risks of lung cancer in animals following dietary restriction, with only one study presenting data for humans it is not possible to make a proper evaluation.

Table 95: Estimate of relative risk for overnutrition

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Knekt et al (1991) | Finnish men | 1.16(0.73-1.82) |

References

1. Doll R (1978) Nutrition and cancer: a review. Nutr Cancer, 1, 35-45.

2. Editorial (1982) Obesity: The cancer connection. Lancet, 1, 1223-1224.

3. Knekt P, Seppanen R, Jarvinen R et al (1991) Dietary cholesterol, fatty acids, and the risk of lung cancer among men. Nutr Cancer, 16, 267-275.

4. Roe FJC (1979) Food and cancer. J Human Nutr, 33, 405-415.

96. Painters

Numerous studies have attempted to relate the risk of lung cancer to employment as a painter or related trade, and details of these studies are given in Table 96. Twenty-one standardized mortality ratios were calculated, ranging from 63-334, with 17 of them being raised. Fourteen relative risks, of between 0.7 and 4.2 were estimated, with all but one being above 1.00. Six studies gave proportional mortality ratios, lying in the range 112-184. Additionally, two proportional registration ratios, of 128 and 129, were given, along with a standardized proportional incidence ratio of 149, a standardized incidence ratio of 199, and a mortality rate of 2.5 per 1000 per year, although no details about the comparison group this was based on were given.

Although several of the studies attempted to classify the subjects' exposures by using indices such as length of employment or estimated level of exposure (Bertazzi, Chiazze, Dalager, Engholm and Englund, Levin, Lundberg, Morgan, Viadana et al), none appear to have made objective measurements. A wide range of potential occupational health hazards is present in relation to the manufacture and use of paints, varnishes and lacquers. It has been reported that over 3000 individual paint components are used worldwide, which can be broadly classified as organic solvents, organic and inorganic pigments, extenders, resins and additives such as catalysts, surfactants, driers, plasticizers and biocides [3]. Only three studies (Bertazzi, Siemiatycki, Stockwell and Matanoski) made any attempt to identify the substances workers were exposed to, but these were limited to asbestos (Bertazzi, Stockwell and Matanoski), chromate (Bertazzi) and white spirit (Siemiatycki). Additionally, Blot (1984) suggested that the increased lung cancer death rate reported in the study by Dalager may be associated with the use of zinc chromate primer paints [1]. It is likely that workers are exposed to many potentially carcinogenic compounds, and separating out the effects of any one of them will be very difficult. Differences between the studies in the length of employment as a painter necessary to be classified as "exposed" introduced further inaccuracies.

Despite these possible problems, the results presented here do seem to be consistent with an increase in lung cancer risk among those employed as painters, or in allied industries. Indeed, IARC classified

the evidence for painters as "sufficient", although felt that the evidence for a carcinogenic effect of paint manufacture was "inadequate" [3].

Table 96: Estimates of relative risk/standardized mortality ratio for painters

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Breslow et al (1954)[1] | US construction/maintenance painters | 1.9(0.93-3.8) |
| OPCS (1958)[1] | UK male painters/decorators | 149($p<0.01$)* |
| Guralnick (1963)[1] | US male painters/plasterers | 155($p<0.01$)* |
| Dunn and Weir (1965)[1] | US painters/decorators | 129* |
| Boucot et al (1972) | US painters/plasterers/ paperhangers | 2.5[2] |
| OPCS (1972)[1] | UK male painters/decorators | 143($p<0.01$)* |
| Menck and Henderson (1976)[1] | US painters | 158($p<0.01$)* |
| Viadana et al (1976)[1]/ Decoufle et al (1977)[1]/ Houten et al (1977)[1] | US painters | 1.7($p=0.02$) |
| Williams et al (1977)[1] | US painters/construction workers/paperhangers/pattern and model makers | 4.2($p<0.01$) |
| OPCS (1978) | E/W male painters/decorators aged 15-64 | 112($p<0.01$)[3] |
| | Aged 65-74 | 118($p<0.01$)[3] |
| | Incidence 1966-7 | 128($p<0.01$)[4] |
| | 1968-9 | 129($p<0.01$)[4] |
| Chiazze et al (1980)[1] | US male spray painters | 141[3] |
| Dalager et al (1980)[1] | US male spray painters | 184($p<0.05$)[3] |
| Englund (1980)[1]/Engholm and Englund (1982)[1] | Swedish painters union members | 127($p<0.01$)* |
| Petersen and Milham (1980)[1] | US male painters | >100[3] |

Table 96 continued

| | | |
|---|---|---|
| Bertazzi et al (1981)[1] | Italian paint manufacturers | 334(106-434)* |
| Morgan et al (1981)[1] | US male workers in paint/ coating manufacture | 98*[5] |
| Logan (1982) | UK male painters/decorators,1931 | 117* |
| | 1951 | 149* |
| | 1961 | 145* |
| | 1971 | 136* |
| | Married women[6] - 1931 | 82* |
| | 1951 | 90* |
| | 1961 | 114* |
| | 1971 | 142* |
| Milham (1983)[1] | US painters/paperhangers/ decorators | 140($p<0.05$)[3] |
| Milne et al (1983)[1] | US male painters | 1.7($p<0.05$) |
| | Workers in paint manufacturing | 0.7 |
| Whorton et al (1983)[1] | US painters | 199(112-330)[7] |
| Dubrow and Wegman (1984)[1] | US male painters | 131* |
| Stockwell and Matanoski (1985)[1] | Usual occupation painter | 2.8(1.5-5.2) |
| | Ever worked as painter | 2.6(1.3-4.9) |
| Kjuus et al (1986)[1] | Norwegian painters/paperhangers | 1.7(0.4-7.3) |
| | Exposure to paint/glue/lacquer | 1.2(0.6-2.6) |
| Lundberg (1986)[1] | Swedish male workers in paint manufacture | 63(12-184)* |
| Matanoski et al (1986)[1] | US painters | 118(106-132)* |
| OPCS (1986) | UK male painters/decorators/ french polishers | 144($p<0.01$)* |
| | Married women[6] | 151($p<0.01$)* |
| Lerchen et al (1987)[1] | US construction painters | 2.7(0.8-8.9) |
| Olsen and Jensen (1987)[1] | Danish construction painters | 149(119-185)[8] |
| Siemiatycki et al (1987a,b)[1] | Canadian construction painters | 1.4 |
| Levin et al (1988)[1] | Chinese male painters | 1.4(0.5-3.5) |
| Ronco et al (1988)[1] | Italian male painters | 1.3(0.43-4.1) |
| Keller and Howe (1993) | US construction workers | 1.35(0.78-2.34) |

Footnote to Table 96

* Standardized mortality ratio

1 From International Agency for Research on Cancer (1989)

2 Per 1000 per year

3 Proportional mortality ratio

4 Proportional registration ratio

5 Tumours of respiratory tract

6 According to husband's occupation

7 Standardized incidence ratio

8 Standardized proportional incidence ratio

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References

1. Blot WJ (1984) Lung cancer and occupational exposures. In: Lung cancer: Causes and prevention, 47-64. Verlag Chemie International Inc.

2. Boucot KR, Weiss W, Seidman H, Carnahan W and Cooper DA (1972) The Philadelphia pulmonary neoplasm research project: basic risk factors of lung cancer in older men. Am J Epidemiol, 95, 4-16.

3. International Agency for Research on Cancer (1989) Monographs on the evaluation of carcinogenic risks to humans. Volume 47: Some organic solvents, resin monomers and related compounds, pigments and occupational exposures in paint manufacture and painting, 329-443. IARC, Lyon.

4. Keller JE and Howe HL (1993) Cancer in Illinois construction workers: A study. Am J Ind Med, 24, 223-230.

5. Logan WPD (1982) Cancer mortality by occupation and social class 1851-1971. HMSO, London and IARC, Lyon.

6. Office of Population Censuses and Surveys (1978) Occupational mortality: The Registrar General's decennial supplement for England and Wales, 1970-72. HMSO, London.

7. Office of Population Censuses and Surveys (1986) Occupational mortality: The Registrar General's decennial supplement for Great Britain, 1979-80, 1982-83. HMSO, London.

## 97. Palmar keratoses

Table 97 gives details of the only study found which attempted to relate the risk of lung cancer to the presence of palmar keratoses. A relative risk of 4.19 was estimated.

With so few studies reporting, it is not possible to determine whether the observed excess of lung cancer really does indicate an association with the presence of palmar keratoses. However, the p value for this study must be very small, so it is unlikely that the results arose simply by chance.

Table 97: Estimate of relative risk for palmar keratoses

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Cuzick et al (1984) | UK hospital patients | 4.19(2.16-8.13) |

References

1. Cuzick J, Harris R and Mortimer PS (1984) Palmar keratoses and cancers of the bladder and lung. Lancet, 1, 530-533.

98. Petroleum refining

Table 98 gives details of the 14 studies which attempted to relate lung cancer risk to occupational exposures in petroleum refining. Nine standardized mortality ratios were calculated, and these ranged from 78-190, with six of them being raised. Eight relative risks were also estimated, of between 0.42-2.00, and five of these were above 1.00. Additionally, one study reported a higher percentage of coal and petroleum workers among lung cancer cases.

There was a general lack of information on the exposures of the subjects, with most of the studies failing to make any objective measurements of workplace conditions. Only the studies by Bingham and Kaldor attempted to quantify exposure to petroleum and its products, the first by recording the duration of exposure, and the level of hydrocarbons workers were exposed to, and the second by estimating levels of air emissions. It is obvious then that inaccuracies in exposure classification could have been introduced into the other studies. Furthermore, workers in the petroleum refining industry are exposed to a number of substances, including ortho-anisidine, para-anisidine, arsenic compounds, asbestos, benzene, bitumens, 1,3-butadiene, carbazole, chlorinated hydrocarbons, chromium and chromium compounds, 1,2-dibromoethane, 1,2-dichloroethane, hydrazine, lead and lead compounds, mineral oils, nickel and nickel compounds, para-phenylenediamine, polycyclic aromatic compounds and silica. However, without accurate exposure data it is not possible to attribute the observed increases in lung cancer to any one chemical. Other problems noted in the studies refer to overlap of cohorts and short duration of follow-up [2].

Several of the studies observed a decrease in lung cancer risk among the exposed subjects, and two reasons for this were suggested. Firstly, it is well known that occupational cohorts tend to have a lower mortality experience than the general population, due to the "healthy worker" effect, and it was felt that the deficit in cancer mortality observed in refinery workers is compatible with this effect [2]. Alternatively, restrictions on workplace smoking in certain occupations may have lead to

a decrease in lung cancer mortality in such workers. Additional evidence for this hypothesis comes from the decreased mortality from non-malignant respiratory disease observed in some of the studies [1].

When evaluating the carcinogenicity to humans of occupational exposures in petroleum refining, IARC [2] described the evidence as "limited" for skin cancer and leukaemia, and "inadequate" for all other sites. A review of lung cancer risk factors by Blot [1] classified petroleum refining exposures only as "possible" carcinogens.

Table 98: Estimates of relative risk/standardized mortality ratio for workers in petroleum refining

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Blot and Fraumeni (1976)[1] | US residents of petroleum industry counties | 1.15 |
| Menck and Henderson (1976)[2] | US men | Higher % of coal/petroleum workers among cases |
| Wigle (1977)[1] | Canadian petroleum refining workers | 0.42(0.2-1.0) |
| Gottlieb et al (1979)[3] | US petroleum refining workers | 1.3(0.88-1.8) |
| | Crude petroleum workers | 1.6($p<0.05$) |
| Hanis et al (1979)[1] | Canadian refinery employees | 120* |
| | Exposed to petroleum or products | 190($p<0.05$)* |
| Bingham et al (1980)[2] | US refinery workers | 1.00 |
| | Canadian oil refinery workers | 1.00 |
| | Canadian oil company workers | 2.00 |
| Thomas et al (1980)[1] | US petroleum refinery/chemical plant workers | 130($p<0.05$)*[4] |
| Rushton and Alderson (1981)[2] | UK refinery workers | 78*[5] |
| Hanis et al (1982)[2] | US refinery workers | 91*[5] |
| Thomas et al (1982)[2] | US refinery workers | 110-145[6] |

Table 98 continued

| | | |
|---|---|---|
| Waxweiler et al (1983)[2] | US petrochemical manufacturing plant workers | 78*[5] |
| Wen et al (1983)[1] | US white blue-collar oil company workers | 110* |
| Kaldor et al (1984)[1] | US men exposed to petroleum/ chemical plant emissions | >1.00 |
| Hanis et al (1985)[1] | US refinery/chemical plant workers | 120* |

* Standardized mortality ratio

1 From International Agency for Research on Cancer (1989)

2 From Blot et al (1984)

3 From Pickle et al (1984)

4 Tumours of respiratory system

5 Estimated from data given

6 Proportional mortality ratio

References

1. Blot WJ (1984) Lung cancer and occupational exposures. In: Lung cancer: Causes and prevention, 47-64. Verlag Chemie International Inc.

2. International Agency for Research on Cancer (1989) Monographs on the evaluation of carcinogenic risks to humans. Volume 45: Occupational exposures in petroleum refining; crude oil and major petroleum fuels, 39-117. IARC, Lyon.

3. Pickle LW, Correa P and Fontham E (1984) Recent case-control studies of lung cancer in the United States. In: Lung cancer: Causes and prevention, 101-115. Verlag Chemie International Inc.

99. Phosphates

Details of the only study found which investigated a possible association between lung cancer risk and exposure to phosphates are given in Table 99. A relative risk of 1.20 was estimated from data given in the study.

No measurements were made of the levels of phosphates the study subjects were exposed to and without this information it is difficult to interpret the findings of the study. Results from more studies will be needed before an evaluation of the carcinogenicity of exposure to phosphates can be made.

Table 99: Estimate of relative risk for exposure to phosphates

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Stockwell et al (1988) | Florida phosphate mining area residents | 1.20(1.07-1.35)[1] |

1 Estimated from data given

References

1. Stockwell HG, Lyman GH, Waltz J and Peters JT (1988) Lung cancer in Florida: Risks associated with residence in the central Florida phosphate mining region. Am J Epidemiol, 128, 78-84.

## 100. Physical inactivity

Table 100 gives details of the two studies which attempted to investigate the possible association between lung cancer risk and lack of physical exercise. Three relative risks, ranging from 0.9-2.0, were estimated of which two were above 1.00.

Although beneficial effects of physical activity on cardiovascular disease have previously been reported [1], the relationship with lung cancer risk is still far from clear.

Table 100: Estimates of relative risk for physical inactivity

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Albanes et al (1989) | US males taking little nonrecreational activity | 2.0(1.2-3.5) |
| | Taking little recreational exercise | 0.9(0.6-1.5) |
| Dosemeci et al (1993) | Turkish workers in sedentary jobs | 1.1(0.9-1.3) |

References

1. Albanes D, Blair A and Taylor PR (1989) Physical activity and risk of cancer in the NHANES I population. Am J Public Health, 79, 744-750.

2. Dosemeci M, Hayes RB, Vetter R et al (1993) Occupational physical activity, socioeconomic status, and risks of 15 cancer sites in Turkey. Cancer Causes and Control, 4, 313-321.

101. Plumbers

The three studies which attempted to relate lung cancer risk to employment as a plumber are detailed in Table 101. Standardized mortality ratios of between 67 and 144 were calculated, with eight out of nine being raised. Additionally, two proportional mortality ratios of 103 and 106 and two proportional registration ratios of 123 and 131 were also presented.

None of the studies gave any information on possible exposures plumbers might be subjected to, and no hypotheses were put forward to explain the observed increase in lung cancer risk. Therefore, it is not really possible to properly evaluate the potential risk of employment as a plumber, but from the evidence presented in the table it appears that if a risk does exist it is probably not very large.

Table 101: Estimates of standardized mortality ratio for employment as a plumber

| Study | Population | Standardized mortality ratio |
|---|---|---|
| OPCS (1978) | English/Welsh plumbers/gas fitters/lead burners, aged 15-64 | 106* |
| | Aged 65-74 | 103* |
| | Incidence 1966-7 | 123($p<0.01$)[1] |
| | 1968-9 | 131($p<0.01$)[1] |
| Logan (1982) | English/Welsh men, 1931 | 67 |
| | 1951 | 125 |
| | 1961 | 124 |
| | 1971 | 126 |
| | Married women[2], 1951 | 144 |
| | 1961 | 109 |
| | 1971 | 135 |
| OPCS (1986) | UK male plumbers/heating/ventilation/gas fitters | 142($p<0.01$) |
| | Married women[2] | 120 |

Footnote to Table 101

* Proportional mortality ratio

1 Proportional registration ratio

2 According to husband's occupation

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References

1. Logan WPD (1982) Cancer mortality by occupation and social class 1851-1971. HMSO, London and IARC, Lyon.

2. Office of Population Censuses and Surveys (1978) Occupational mortality: The Registrar General's decennial supplement for England and Wales, 1970-72. HMSO, London.

3. Office of Population Censuses and Surveys (1986) Occupational mortality: The Registrar General's decennial supplement for Great Britain, 1979-80, 1982-83. HMSO, London.

102. Pneumonia

Table 102 gives details of the studies found which gave data relevant to an investigation of the possible association between lung cancer risk and pneumonia. Three relative risks were estimated, ranging from 1.00-1.70, with two being above 1.00. In addition, one study reported that pneumonia sufferers were 100 times more likely than the general population to develop lung cancer.

With the exception of the study by Ohtsuka, in which a group of pneumonia patients were followed-up in order to determine their lung cancer incidence, none of the studies appeared to have used medical records to determine the disease history of the subjects, relying instead on information supplied at interview by the respondents, or next-of-kin. It is obvious that this could have lead to inaccuracies due to mistakes in recalling disease status, particularly in those studies which collected health data from a surrogate respondent.

This fact, combined with the small number of studies providing data, makes it difficult to properly evaluate the possible association between lung cancer risk and pneumonia.

Table 102: Estimates of relative risk for history of pneumonia

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Wynder et al (1956) | US women | 1.00 |
| Wynder and Fairchild (1966) | US men | 1.70(0.99-2.93)[1] |
| Alavanja et al (1992) | US female residents | 1.2(1.0-1.6) |
| Ohtsuka et al (19??) | Japanese men | Pneumonia sufferers 100 times more likely to develop lung cancer than general population |

1 Estimated from data given

References

1. Alavanja MCR, Brownson RC, Boice JD and Hock E (1992) Preexisting lung disease and lung cancer among nonsmoking women. Am J Epidemiol, 136, 623-632.

2. Ohtsuka Y, Tanimura K, Munakata M et al (19??) Idiopathic interstitial pneumonia(IIP) as a risk factor for a lung cancer - a prospective study. Incomplete reference.

3. Wynder EL, Bross IJ, Cornfield J and O'Donnell WE (1956) Lung cancer in women: A study of environmental factors. N Engl J Med, 255, 1111-1121.

4. Wynder EL and Fairchild EP (1966) The role of a history of persistent cough in the epidemiology of lung cancer. Am Rev Resp Dis, 94, 709-720.

## 103. Polychlorinated biphenyls

Table 103 details the two studies found which attempted to relate lung cancer risk to exposure to polychlorinated biphenyls (PCBs). One standardized mortality ratio, of 320, was calculated, while the other study reported two cases of lung cancer among exposed subjects.

It was reported that the subjects in these studies were not exposed to PCBs alone, but that the contaminated rice oil to which they were exposed also contained polychlorinated quaterphenyls and polychlorinated dibenzofurans. It is possible that one or both of these substances was responsible for the excess of lung cancers observed.

Because of the lack of knowledge of the role of these contaminants, IARC described the evidence for the carcinogenicity of PCBs to humans as "limited" [2].

Table 103: Estimates of standardized mortality ratio for exposure to polychlorinated biphenyls

| Study | Population | Standardized mortality ratio |
|---|---|---|
| Urabe (1974)[1]/Kuratsune (1976)[1] | Japanese Yusho patients | 2 lung cancers observed |
| Kuratsune et al (1986)[2] | Japanese male Yusho patients | 320[3] |

1 From International Agency for Reseach on Cancer (1978)
2 From International Agency for Reseach on Cancer (1987)
3 Estimated from data given

References

1. International Agency for Research on Cancer (1978) Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 18: Polychlorinated biphenyls and polybrominated biphenyls, 43-103. IARC, Lyon.

2. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42, 322-326. IARC, Lyon.

104. Postmen

Table 104 gives details of the studies which investigated a possible association between lung cancer risk and employment as a postman. Nine standardized mortality ratios, lying in the range 96-123, were calculated with all but one being raised. Two proportional mortality ratios, of 99 and 102, were given along with two proportional registration ratios of 111 and 118.

Although the data in the table appear to show a higher risk of lung cancer among postmen, the increase in risk does not appear to be very large. No data was available on possible exposures postmen might be subjected to, and there was no attempt by any of the studies to explain the observed increase in lung cancer risk. It should also be remembered that the data came from very few studies. Therefore, due to a lack of information it is not really possible to draw any firm conclusions about the risk of lung cancer among postmen.

Table 104: Estimates of standardized mortality ratio for employment as a postman

| Study | Population | Standardized mortality ratio |
|---|---|---|
| OPCS (1978) | English/Welsh postmen/mail sorters, aged 15-64 | 99* |
| | Aged 65-74 | 102* |
| | Incidence 1966-7 | 118($p<0.01$)[1] |
| | 1968-9 | 111[1] |
| Logan (1982) | English/Welsh postmen, 1931 | 110 |
| | 1951 | 113 |
| | 1961 | 117 |
| | 1971 | 96 |
| | Married women[2], 1951 | 121 |
| | 1961 | 123 |
| | 1971 | 111 |
| OPCS (1986) | UK male postmen/mail sorters/messengers | 104 |
| | Married women[2] | 116 |

Footnote to Table 104

* Proportional mortality ratio

1 Proportional registration ratio

2 According to husband's occupation

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References

1. Logan WPD (1982) Cancer mortality by occupation and social class 1851-1971. HMSO, London and IARC, Lyon.

2. Office of Population Censuses and Surveys (1978) Occupational mortality: The Registrar General's decennial supplement for England and Wales, 1970-72. HMSO, London.

3. Office of Population Censuses and Surveys (1986) Occupational mortality: The Registrar General's decennial supplement for Great Britain, 1979-80, 1982-83. HMSO, London.

105. Printers

Only two studies were found which attempted to relate the risk of lung cancer to employment in the printing industry, and details of these are given in Table 105. Four standardized mortality ratios between 91 and 141 were presented, of which three were raised.

Neither study attempted to explain their findings, and indeed one of them stated that their survey did not "provide any evidence about the cause of the overall small excess of deaths from lung cancer, which might or might not be occupational" [1]. With so few studies reporting, it is difficult to draw any firm conclusions about the carcinogenicity of exposures associated with the printing industry, but it is likely that if a risk does exist it is not very large.

Table 105: Estimates of standardized mortality ratio for workers in the printing industry

| Study | Population | Standardized mortality ratio |
|---|---|---|
| Moss et al (1972) | UK male printing trade workers - London | 132($p<0.01$) |
| | Manchester | 141($p<0.01$) |
| OPCS (1986) | UK male printing workers/screen/block printers | 106 |
| | Married women[1] | 91 |

1 According to husband's occupation

References

1. Moss E, Scott TS and Atherley GRC (1972) Mortality of newspaper workers from lung cancer and bronchitis 1952-66. Br J Ind Med, 29, 1-14.

2. Office of Population Censuses and Surveys (1986) Occupational mortality: The Registrar General's decennial supplement for Great Britain, 1979-80, 1982-83. HMSO, London.

106. Publicans

Table 106 gives details of the two studies which gave information relevant to an investigation of the possible association between lung cancer and employment as a publican. Seven standardized mortality ratios of between 104 and 197 were presented. Two proportional mortality ratios of 101 and 105 were given, along with two proportional registration ratios of 118 and 122.

No data was available on possible exposures of publicans, and there was no attempt to explain the observed increase in lung cancer risk. Although the evidence suggests an increased risk of lung cancer among publicans, with so little information available it is difficult to properly evaluate the potential carcinogenicity of such employment.

Table 106: Estimates of standardized mortality ratio for publicans

| Study | Population | Standardized mortality ratio |
|---|---|---|
| OPCS (1978) | E/W male publicans/innkeepers, aged 15-64 | 105* |
| | Aged 65-74 | 101* |
| | Incidence 1966-7 | 118($p<0.05$)[1] |
| | 1968-9 | 122($p<0.01$)[1] |
| Logan (1982) | E/W men, 1931 | 146 |
| | 1951 | 144 |
| | 1961 | 142 |
| | 1971 | 153 |
| | Married women[2], 1951 | 104 |
| | 1961 | 197 |
| | 1971 | 156 |

E/W = English/Welsh

* Proportional mortality ratio

1 Proportional registration ratio

2 According to husband's occupation

References

1. Logan WPD (1982) Cancer mortality by occupation and social class 1851-1971. HMSO, London and IARC, Lyon.

2. Office of Population Censuses and Surveys (1978) Occupational mortality: The Registrar General's decennial supplement for England and Wales, 1970-72. HMSO, London.

107. Radiotherapy

Table 107 gives details of the two studies found which attempted to relate lung cancer risk to exposure to radiotherapy. Two relative risks, of 1.2 and 3.7, were estimated, along with a standardized mortality ratio of 142.

Only the study by Smith and Doll gave information on the doses of radiation received by respondents. Thus, in the study by Kabat inaccuracies could have been introduced due to misclassification of exposure. Furthermore, in this study there was a high correlation between a history of a reproductive primary and a history of radiotherapy, and it was not possible to estimate the effect of one exposure independent of the other.

In any case, with only two studies reporting it is difficult to evaluate the potential carcinogenicity of radiotherapy to humans.

Table 107: Estimates of relative risk/standardized mortality ratio for exposure to radiotherapy

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Doll (1981)/Smith and Doll (1982) | UK ankylosing spondylitis patients | 142($p<0.001$)* |
| Kabat (1993) | US male radiotherapy patients | 1.2(0.2-6.4) |
| | Females | 3.7(1.2-10.9) |

* Standardized mortality ratio

References

1. Doll R (1981) Radiation hazards: 25 years of collaborative research. Brit J Radiol, 54, 179-186.

2. Kabat GC (1993) Previous cancer and radiotherapy as risk factors for lung cancer in lifetime nonsmokers. Cancer Causes and Control, 4, 489-495.

3. Smith PG and Doll R (1982) Mortality among patients with ankylosing spondylitis after a single treatment course with x rays. Brit Med J, 284, 449-60.

108. Radon

Lack of time meant that a full evaluation of the evidence relating lung cancer risk to radon exposure could not be made. However, both IARC and the National Research Council reviewed this area in 1988 [1,2]. Although radon is ubiquitous, concentrations to which humans may be exposed in enclosed areas, such as underground mines and in buildings, are elevated compared to levels in outdoor air. Evidence for an increased risk of lung cancer following exposure to radon comes from a number of cohort and case-control studies of underground miners, including particularly uranium miners, but also iron-ore and other metal miners, and one group of fluorspar miners. Evidence for dose-response relationships has been obtained from several of these studies. Additionally, a higher risk of lung cancer among individuals living in houses known or presumed to have higher levels of radon than among those with lower presumed exposure has been suggested by several case-control studies, although these have been based on small numbers of subjects. There is also some evidence that the interaction of radon and its decay products with cigarette smoking with regard to lung cancer may follow a multiplicative or submultiplicative model [1,2].

Overall, IARC felt that there was "sufficient" evidence of the carcinogenicity of radon and its decay products to humans [1].

References

1. International Agency for Research on Cancer (1988) Monographs on the evaluation of carcinogenic risks to humans. Volume 43: Man-made mineral fibres and radon, 173-259. IARC, Lyon.

2. National Research Council (1988) Health risks of radon and other internally deposited alpha-emitters: BEIR IV. National Academy Press, Washington DC.

109. Rail workers

Only three studies were found which investigated a possible association between the risk of lung cancer and rail workers, and details of these are given in Table 109. The nine standardized mortality ratios presented ranged from 83-115, with five of them being raised.

It has been suggested that rail workers may be exposed to a number of compounds which may be carcinogenic, particularly asbestos [1,2]. The study by Howe attempted to relate the risk of lung cancer in rail workers to exposure to diesel fumes and coal dust, but estimates of the level of exposure were used in place of objective measurements. Apart from this, no information was available on the subjects' exposures, so it is not possible to determine the substances to which they may have been exposed, or the possible role of any one substance in the development of lung cancer.

Thus, it is very difficult to evaluate the evidence for the carcinogenicity of exposures of rail workers but from the data presented in the table a clear pattern of increased risk does not really emerge and therefore any risk, if it does exist, is probably not very large.

Table 109: Estimates of standardized mortality ratio for rail workers

| Study | Population | Standardized mortality ratio |
|---|---|---|
| Logan (1982) | English/Welsh male railway porters - 1931 | 100 |
| | 1951 | 108 |
| | 1961 | 106 |
| | 1971 | 115 |
| | Married women[1] - 1961 | 95 |
| | 1971 | 115 |
| Howe et al (1983) | Canadian male rail workers | 106 |
| OPCS (1986) | UK male rail transport operating staff | 87 |
| | Married women[1] | 83 |

1 According to husband's occupation

References

1. Garshick E, Schenker MB, Munoz A et al (1987) A case-control study of lung cancer and diesel exhaust exposure in railroad workers. Am Rev Respir Dis, 135, 1242-1248.

2. Howe GR, Fraser D, Lindsay J, Presnal B and Yu SZ (1983) Cancer mortality (1965-1977) in relation to diesel fume and coal exposure in a cohort of retired railway workers. JNCI, 70, 1015-1019.

3. Logan WPD (1982) Cancer mortality by occupation and social class 1851-1971. HMSO, London and IARC, Lyon.

4. Office of Population Censuses and Surveys (1986) Occupational mortality: The Registrar General's decennial supplement for Great Britain, 1979-80, 1982-83. HMSO, London.

110. Rationality/antiemotionality

Only two studies were found which attempted to relate lung cancer risk to measures of rationality and antiemotionality, and details of these are given in Table 110. One study reported that all 38 lung cancer cases occurred in those scoring highly for rationality and antiemotionality, compared to 11.62 expected, giving a standardized mortality ratio of 3.27, while the other reported that lung cancer patients showed higher prevalences of traits associated with rationality and antiemotionality than controls.

The study by Grossarth-Maticek has attracted much criticism since it was published, and the results are generally considered to be seriously flawed due to drawbacks in the study design and the method of recruiting respondents. Thus, with only one other study reporting it is not possible to evaluate the relationship between lung cancer risk and rationality and antiemotionality.

Table 110: Estimates of standardized mortality ratio for rationality/ antiemotionality

| Study | Population | Standardized mortality ratio (95% limits) |
|---|---|---|
| Blohmke et al (1984) | German/Austrian residents | Lung cancer patients showed lack of nervousness, high social conformity and strong external control compared to controls |
| Grossarth-Maticek et al (1985) | Yugoslavian residents | 3.27($p<0.001$) |

References

1. Blohmke M, von Engelhardt B and Stelzer O (1984) Psychosocial factors and smoking as risk factors in lung carcinoma. J Psychosomatic Res, 28, 221-229.

2. Grossarth-Maticek R, Bastiaans J and Kanazir DT (1985) Psychosocial factors as strong predictors of mortality from cancer, ischaemic heart disease and stroke: The Yugoslav prospective study. J Psychosomatic Res, 29, 167-176.

111. Respiratory symptoms

Details of studies which attempted to relate the risk of lung cancer to the presence of respiratory symptoms are shown in Table 111. Relative risks ranging from 0.8-3.23 were estimated, with thirteen out of fourteen being above 1.00.

Due to the reported associations between cigarette smoking, respiratory symptoms and lung cancer, all of the studies collected information on the respondents' smoking habits. However, as noted by Wynder and Fairchild, due to the strong correlation in this study between cigarette smoking and lung cancer and cigarette smoking and persistent cough, it was difficult to properly evaluate the correlation of cough to lung cancer, independent of cigarette smoking.

Therefore, despite the evidence presented in the table suggesting a possible association between the presence of respiratory symptoms and lung cancer risk, such a relationship cannot be regarded as established.

Table 111: Estimates of relative risk for respiratory symptoms

| Study | Population | Symptoms | Relative risk (95% limits) |
|---|---|---|---|
| Denoix et al (1958) | French men | BRON | 2.00(0.95-4.22)[1] |
| Wynder and Fairchild (1965) | US men | BRON | 3.23(1.61-6.48)[1] |
| | | COU | 2.76[1](p<0.001) |
| | | FLU | 1.24(0.71-2.16)[1] |
| | | PND | 1.87(1.09-3.20)[1] |
| | | SINU | 1.85(1.05-3.26)[1] |
| Tenkanen et al (1987) | Finnish men | PHL | 2.0(p<0.001) |
| | | SOB | 2.2(p<0.001) |
| | | WHE | 2.0(p<0.001) |
| Vestbo et al (1991) | Danish men | BRON | 0.8(0.3-2.7)[2] |
| | | COU | 2.5(1.3-5.0)[2] |
| | | PHL | 1.5(0.7-3.2)[2] |
| | | PHLC | 1.2(0.5-3.0)[2] |
| | | SOB | 2.2(1.0-4.9)[2] |

Footnote to Table 111

BRON = bronchitis; COU = cough; FLU = influenza; PHL = phlegm; PHLC = chronic phlegm; PND = postnasal drip; SINU = sinusitis; SOB = shortness of breath; WHE = wheezing

1 Estimated from data given

2 Tumours of respiratory system

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References

1. Denoix PF, Schwartz D and Anguera G (1958) French investigation into the etiology of broncho-pulmonary cancer. Detailed analysis. Bull Assoc Franc pour l'etude du cancer, 49: 1-37.

2. Tenkanen L, Hakulinen T and Teppo L (1987) The joint effect of smoking and respiratory symptoms on risk of lung cancer. Int J Epidemiol, 16, 509-515.

3. Vestbo J, Knudsen KM and Rasmussen FV (1991) Are respiratory symptoms and chronic airflow limitation really associated with an increased risk of respiratory cancer? Int J Epidemiol, 20, 375-378.

4. Wynder EL and Fairchild EP (1965) The role of a history of persistent cough in the epidemiology of lung cancer. Am Rev Resp Dis, 94, 709-720.

112. The rubber industry

Details of the studies which investigated lung cancer risk amongst workers in the rubber industry are given in Table 112. Eighteen standardized mortality ratios, ranging between 47 and 434, were given, with 12 being raised. Five relative risks, of 1.4-2.3, were estimated, and one study also gave an incidence ratio of 126.

Workers in the rubber industry are likely to be exposed to a combination of chemicals, in the form of dusts, vapours, condensed volatiles, solvents and gases, which will vary depending on the stage of the manufacturing process. Many of the materials which occur in rubber factories have been shown experimentally to be mutagenic or carcinogenic, and these include mineral oils, carbon black (extracts), curing fumes, some monomers, solvents, nitroso compounds and aromatic amines, thiurams and dithiocarbamate compounds, ethylenethiourea, di(2-ethylhexyl) phthalate, di(2-ethylhexyl) adipate and hydrogen peroxide [2]. However, due to a lack of historical industrial hygiene data none of the studies could accurately ascertain exposure, although some (Baxter and Werner, Delzell, Fox, McMichael 1976, Monson and Fine, Monson and Nakano 1976b, Parkes, Zhang) did attempt to classify workers into particular job categories as a substitute for exposure categories. Thus, attempting to evaluate the potential carcinogenicity of any one compound will be extremely difficult.

In their assessment of the rubber industry in 1982, IARC stated that "the combination of chemical exposures that occurs in the rubber industry is probably more relevant to the cancer pattern observed than are single compounds or groups of compounds. The variety of exposures increases the likelihood that there are interactive effects between two or more such agents" [2]. It was felt that there was "sufficient" evidence for the carcinogenicity in humans of exposures associated with the rubber industry [2,3].

Table 112: Estimates of relative risk/standardized mortality ratio for workers in the rubber industry

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Fox et al (1974) | British rubber workers | 118* |
| McMichael et al (1974)[1] | US rubber workers | 83* |
| Andjelkovich et al (1976)[1] | US rubber workers | 83* |
| Fox and Collier (1976)[1] | British rubber workers | 127* |
| McMichael et al (1976a,b)[1] | US Receivers/shippers | 1.9[2] |
| | Compounders/mixers | 1.4[2] |
| | Mill-mixers | 2.1[2] |
| | Extruders | 1.4[2] |
| | Reclaimers | 2.3[2] |
| Monson and Nakano (1976a)[1] | US rubber workers | 92* |
| Monson and Nakano (1976b)[1] | US female non-tyre rubber workers | 333* |
| Andjelkovich et al (1977)[1] | US workers exposed to synthetic latex | 434* |
| Andjelkovich et al (1978)[1] | US female rubber workers | 191*[3] |
| Monson and Fine (1978)[1] | US tyre curers | 220*[3] |
| | Tyre moulders | 200*[3] |
| | Fuel cell/deicer manufacturers | 158*[3] |
| Baxter and Werner (1980)[1] | British rubber workers | 115*[3] |
| Bovet and Lob (1980)[1] | Swiss rubber workers | 47* |
| Delzell and Monson (1981)[1] | US rubber workers | 84* |
| Kilpikari et al (1981)[1] | Finnish rubber workers | 150*[2] |
| Delzell et al (1982)[1] | US tyre workers - mortality | 99* |
| | Incidence | 126 |
| Parkes et al (1982)[1] | British rubber workers | 122* |
| Zhang et al (1989) | Chinese rubber workers | 133* |

* Standardized mortality ratio

1 From IARC (1982)

2 Tumours of respiratory system

3 Estimated from data given

References

1. Fox AJ, Lindars DC and Owen R (1974) A survey of occupational cancer in the rubber and cablemaking industries: Results of five-year analysis, 1967-71. Br J Ind Med, 31, 140-151.

2. International Agency for Research on Cancer (1982) Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 28: The rubber industry. IARC, Lyon.

3. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogencity: An updating of IARC monographs volumes 1 to 42, 332-334. IARC, Lyon.

4. Zhang Z-F, Yu S-Z, Li W-X and Choi BCK (1989) Smoking, occupational exposure to rubber, and lung cancer. Br J Ind Med, 46, 12-15.

113. Schizophrenia

Table 113 gives details of the three studies which investigated the risk of lung cancer in relation to schizophrenia. A relative risk of 0.33 was given for lung cancer incidence, while the other two studies reported that lung cancer mortality among schizophrenics was either equal to or lower than that of other populations.

One author (Mortensen) felt that the lower risk of lung cancer observed could be due to a reduced exposure to carcinogens such as cigarette smoke among schizophrenic patients. However, the other two commented on the fact that the patients in their studies showed a high prevalence of smoking, of up to 90%. In the light of this, the reduced incidence of lung cancer seems even more surprising.

While the evidence presented in the table appears to suggest a reduced risk of lung cancer among schizophrenic patients, with only three studies reporting it is difficult to make a full evaluation.

Table 113: Estimates of relative risk for schizophrenic patients

| Study | Location | Relative risk (95% limits) |
|---|---|---|
| Anon (1986) | USA | Schizophrenic patients had lower lung cancer mortality than controls |
| Gopalaswamy and Morgan (1986) | Not stated | Schizophrenics' lung cancer mortality no higher than general population |
| Mortensen (1989) | Denmark | 0.33($p<0.001$)[1] |

1 Incidence

References

1. Anon (1986) Br Med J, 293, 700.

2. Gopalaswamy AK and Morgan R (1986) Smoking in chronic schizophrenia. Br J Psych, 149, 523.

3. Mortensen PB (1989) The incidence of cancer in schizophrenic patients. J Epidemiol Community Health, 43, 43-47.

## 114. Selenium

Table 114 gives details of the five studies which investigated the possible association between lung cancer risk and selenium levels.

A correlation study found evidence of lower lung cancer mortality rates in areas with higher selenium levels in forage crops, with mortality rates per 100,000 of 32.37, 33.25 and 40.06 for men in high, medium and low selenium areas respectively, and 5.45, 5.73 and 6.33 respectively for women.

Two of the studies measuring dietary selenium intake used high intake as a baseline. One of these studies estimated a relative risk of 6.00 for low selenium intake in one population considered, but failed to find an association, or to give detailed results for the other. The other study found lower selenium levels in lung cancer cases in three populations studied, but higher levels in cases in two populations. Again, detailed results were not presented.

A study of Dutch subjects, in which those with a high dietary intake of selenium were compared to those with a low intake, estimated a relative risk of 0.50.

Finally, a study of occupational selenium exposure found lower levels in the lung tissue of lung cancer cases than in that of two control groups.

The major drawback with the studies which investigated dietary selenium intake is that it is well known that selenium cannot be measured accurately by a dietary questionnaire alone, since the level in the food is dependent on the level in the soil in which it was grown. The study by van den Brandt measured selenium levels in the respondents' toenail clippings as well as administering a dietary questionnaire, thus providing a more objective measure of selenium. However, the studies by Comstock and Fontham did not appear to have taken any such measurements.

Another problem is that the development of cancer may affect appetite or the way in which food is metabolized, either of which could affect selenium levels measurable in the body. Therefore, the study by Fontham, using a case-control design in which information on selenium levels was collected after the subject had developed cancer may have introduced bias into the results. Similar problems may have occurred in the study by Gerhardsson.

Therefore, despite the findings presented in the table suggesting a possible protective effect of selenium against lung cancer, the relationship is far from proven. Indeed, after a recent review of the data IARC concluded that the evidence for such an effect was "not convincing" [3].

Table 114: Estimates of relative risk/mortality rate for selenium

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Correlation study: | | |
| Shamberger et al (1976) | US men, high selenium area | 32.27[1] |
| | Medium selenium area | 33.25[1] |
| | Low selenium area | 40.06[1] |
| | Women, high selenium area | 5.45[1] |
| | Medium selenium area | 5.73[1] |
| | Low selenium area | 6.33[1] |
| Low dietary selenium: | | |
| Fontham (1990) | Not stated | No association reported |
| | Finnish residents | 6.00 |
| Comstock et al (1992) | Finnish males | Serum selenium levels lower in cases than controls ($p>0.05$) |
| | Finnish females | Serum selenium levels lower in cases than controls ($p>0.05$) |
| | US residents | Serum selenium levels lower in cases than controls ($p<0.05$) |
| | Hawaiian residents | Serum selenium levels higher in cases than controls ($p>0.05$) |
| | US residents | Serum selenium levels higher in cases than controls ($p>0.05$) |

Table 114 continued

| | | |
|---|---|---|
| High dietary selenium: | | |
| Van den Brandt et al (1993a,1993b) | Dutch residents | 0.50(0.30-0.81) |
| Occupational exposure: | | |
| Gerhardsson et al (1985) | Swedish smelter workers | Selenium level in lung tissue 71ppb in cases compared to 110ppb and 136ppb in controls |

1 Mortality rate per 100,000

References


1. Comstock GW, Bush TL and Helzlsouer K (1992) Serum retinol, beta-carotene, vitamin E, and selenium as related to subsequent cancer of specific sites. Am J Epidemiol, 135, 115-121.

2. Fontham ETH (1990) Protective dietary factors and lung cancer. Int J Epidemiol, 19 (Suppl 1), S32-S42.

3. Gerhardsson L, Brune D, Nordberg GF and Wester PO (1985) Protective effect of selenium on lung cancer in smelter workers. Br J Ind Med, 42, 617-626.

4. International Agency for Research on Cancer (1975) Monographs on the evaluation of carcinogenic risk of chemicals to man. Volume 9: Some aziridines, N-, S- and O-mustards and selenium, 245-260. IARC, Lyon.

5. Van den Brandt PA, Goldbohm RA, van't Veer P et al (1993a) Toenail selenium and the risk of lung, gastrointestinal, and breast cancer: A prospective study. Am J Epidemiol, 138, 626-627 (Abstract).

6. Van den Brandt PA, Goldbohm RA, van't Veer P et al (1993b) A prospective cohort study on selenium status and the risk of lung cancer. Cancer Res, 53, 4860-4865.

115. Shellfish/crustaceae

Details of the only study found which attempted to relate the risk of lung cancer to consumption of shellfish and crustaceae are given in Table 115. It was reported that 36% of cases and 26% controls consumed cooked shellfish, while 16% of cases and 10% controls were consumers of crustaceae.

With only one study reporting it is not really possible to evaluate the potential carcinogenicity to humans of shellfish or crustaceae.

Table 115: Frequency of consumption of shellfish/crustaceae

| Study | Population | Observations |
|---|---|---|
| Denoix et al (1958) | French men | 36% bronchial cancer cases consumed cooked shellfish compared to 26% controls ($p<0.001$); 16% bronchial cancer cases consumed crustaceae compared to 10% controls ($p<0.01$) |

References

1. Denoix PF, Schwartz D and Anguera G (1958) French investigation into the etiology of broncho-pulmonary cancer. Detailed analysis. Bull Assoc Franc pour l'etude du cancer, 49: 1-37.

116. Silica

The numerous studies found which contained some data relevant to an investigation of the possible association between exposure to silica and the risk of lung cancer are detailed in Table 116. From the table, it can be seen that, of the 40 estimates of relative risk given ranging from 0.2-7.9, some 34 were above 1.00. The 26 standardized mortality ratios calculated lay in the range 84-590, with 22 of them being raised. Fourteen proportional mortality ratios were given, of between 75 and 348, of which 13 were raised. Additionally, one study gave an mortality odds ratio of 1.5.

From the table it can be seen that the study subjects came from many different occupational backgrounds. It is likely that the respondents were exposed to substances other than silica, which may themselves be potential carcinogens, in the course of their work and the nature of these exposures will vary from job to job. Data on the level of exposure to silica were only available from 13 of the studies (Davis, Gibson, Hessel and Sluis-Cremer, Hessel et al, Higgins, Kjuus, Koskela 1976, Lawler, McLaughlin, Meijers, Sherson and Iversen, Silverstein, Thomas and Stewart), and even fewer measurements of exposures to other substances were made. Therefore it is difficult to draw any firm conclusions about the role of silica in the development of lung cancer. Furthermore, all of the studies concentrated on the effects of crystalline silica, with none presenting results for amorphous silica.

Lastly, as IARC noted, there are some potential problems in the design of some of the studies. In particular there was some doubt as to the comparability of reference groups in several of the studies (Chiyotani, Costello and Graham, Davis, Pham, Vutuc, Westerholm 1986, Zambon), and the comprehensiveness with which some studies had taken into account the effects of possible confounding variables (Brown, Finkelstein 1982, Katsnelson and Mokronosova, Lawler, Muller, Neuberger, Selikoff, Thomas). Other problems which may have introduced inaccuracies into the studies, particularly those based on silicosis sufferers, included differences between countries in the definition of compensable silicosis, potential differences in disease detection methods, and unorthodox methods of calculating results [1,5].

Therefore, it was felt that the evidence for the carcinogenicity to humans of crystalline silica was "limited", while that for amorphous silica was "inadequate" [5,6].

Table 116: Estimates of relative risk/standardized mortality ratio for exposure to silica

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Redmond (1975)[1] | US masons | 2.12($p<0.01$) |
| | Foundrymen | 1.62 |
| | Blacksmiths | 2.42($p<0.05$) |
| Koskela et al (1976)[1] | Finnish foundry workers | 151* |
| Milham (1976)[1] | US metal moulders | 312[2] |
| | Mine operatives/labourers | 179($p<0.05$)[2] |
| Gibson et al (1977)[1] | Canadian foundrymen | 5.0($p<0.0005$) |
| Selikoff (1978)[3] | US tunnel workers | 160* |
| Armstrong et al (1979)[3] | Australian gold miners | 140($p<0.05$)* |
| Decoufle and Wood (1979)[1] | Iron foundry workers | 200* |
| Egan et al (1979)[1] | US moulders - whites | 147($p<0.01$)[2] |
| | Blacks | 180[2] |
| Katsnelson and Mokronosova (1979)[1] | Gold miners - underground | 7.9($p<0.001$) |
| | Surface miners | 1.6 |
| | Firebrick plant workers | 2.0($p<0.05$) |
| Puntoni et al (1979)[1] | Italian sandblasters | 3.8($p<0.05$) |
| Tola et al (1979)[1] | Finnish foundry workers | 144($p<0.05$)[2] |
| Peterson and Milham (1980)[1] | US metal moulders | 192($p<0.05$)[2,4] |
| | Mine operatives/labourers | 138($p<0.05$)[2] |
| Westerholm (1980)[3] | Swedish miners/quarrymen/ tunnellers with silicosis diagnosed 1931-48 | 590($p<0.01$)* |
| | Diagnosed 1949-69 | 380($p<0.01$)* |
| | Iron/steel workers with silicosis diagnosed 1949-69 | 220($p<0.05$)* |
| Egan-Baum et al (1981)[1] | Iron foundry workers | 2.4(1.01-5.3) |

Table 116 continued

| | | |
|---|---|---|
| Redmond et al (1981)[1] | US blacksmiths | 1.89($p<0.05$) |
| Costello (1982)[1] | Metal ore miners | 127($p<0.01$)* |
| Finkelstein et al (1982)[1] | Canadian miners | 198($p<0.01$)* |
| Fletcher (1982)[1] | English foundrymen | 147(120-180)* |
| Milham (1982)[1] | Sandblasters | 348($p<0.01$)[2] |
| Thomas (1982)[1] | US pottery workers | 180($p<0.01$)[2] |
| Davis et al (1983)[3] | US granite workers | 118*[5] |
| Higgins et al (1983)[3] | US taconite miners | 84* |
| Lawler et al (1983)[3] | US haematite miners - surface | 88* |
| | Underground | 100* |
| Muller et al (1983)[3] | Canadian miners | 145($p<0.001$)* |
| Pham et al (1983)[3] | French iron miners | 3.5(1.9-6.0) |
| Vutuc (1983)[3] | Austrian stone workers | 2.0($p<0.01$) |
| Gudbergsson et al (1984)[3] | Finnish silicotics | 3.0(1.5-5.3) |
| Chiyotani (1984)[3] | Japanese silicotics | 653 |
| Puntoni et al (1985)[3] | Italian refractory plant workers with silicosis | 167* |
| | Non-silicotics | 208* |
| Rubino et al (1985)[3] | Italian silicotics | 1.36($p<0.05$) |
| Brown et al (1986)[3] | US gold miners | 100* |
| Costello and Graham (1986)[3] | US granite workers | 1.00 |
| Finkelstein et al (1986)[3] | Canadian ceramic/pottery/ granite/quarry workers, silica brickmakers, sand-blasters with silicosis | 302($p<0.01$)* |
| Fletcher (1986)[3] | UK foundry workers | 149($p<0.001$)* |
| | Skilled moulders | 125($p<0.05$)[2] |
| | Semiskilled moulders | 154($p<0.05$)[2] |
| | Dressers | 75[2] |
| | Labourers | 106[2] |
| Forastiere et al (1986)[3] | Italian pottery workers | 2.0(1.1-3.5) |
| Hessel and Sluis-Cremer (1986)[3] | South African miners | 1.1 |
| Kjuus et al (1986)[3] | Norwegian ferroalloy workers | 1.00 |
| Kurppa et al (1986)[3] | Finnish silicotics | 312(230-414)* |

Table 116 continued

| | | |
|---|---|---|
| Lynge et al (1986)[6] | Finnish/Danish stone cutters | >1.00 |
| | Swedish/Norwegian stone cutters | 1.00 |
| | Finnish excavation workers | >1.00 |
| | Danish glass workers | >1.00 |
| | Nordic ceramics workers | 1.00 |
| | Nordic metal miners | 1.0-5.0 |
| | Nordic foundry workers | >1.00 |
| Neuberger et al (1986)[3] | Austrian silicotics | 148($p<0.001$)* |
| Schuler and Ruttner (1986)[3] | Swiss silicotics | 2.41($p<0.05$) |
| Sherson and Iversen (1986)[3] | Danish foundry workers | 115* |
| Silverstein et al (1986)[3] | US iron foundry workers | 148[2] |
| Steenland and Beaumont (1986)[3] | US members of Granite Cutters Union | 1.19(0.97-1.5) |
| Westerholm et al (1986)[3] | Miners/quarrymen/tunnellers | 4.1($p<0.05$) |
| | Iron/steel workers | 1.8 |
| Zambon et al (1986)[3] | Italian silicotics | 228($p<0.05$)* |
| Koskela et al (1987)[6] | Finnish granite workers | 129*[5] |
| Thomas and Stewart (1987)[6] | US pottery workers | 137* |
| Mastrangelo et al (1988)[7] | Silicotics | 1.9($p<0.05$) |
| Forastiere et al (1989)[7] | Silicotics | 1.5($p<0.05$)[8] |
| Infante-Rivard et al (1989) | Canadian silicotics | 3.47(3.11-3.90) |
| Amandus and Costello (1990)[7] | Miners with silicosis | 2.0($p<0.05$) |
| Hessel et al (1990) | South African gold miners | Cases and controls comparable for silica dust exposure |
| Meijers et al (1990) | Dutch ceramics workers | 1.11(0.77-1.6) |
| Ng et al (1990)[7] | Silicotics | 2.0($p<0.05$) |
| Amandus et al (1991) | Workers in US dusty trades industry | 2.3(1.5-3.4) |
| McLaughlin et al (1992) | Pottery workers | 2.2(0.8-6.3)[5] |
| | Tungsten miners | 0.5(0.3-1.0) |
| | Iron-copper miners | 0.2(0.1-0.5) |
| | Tin miners | 2.5(1.3-4.8) |

Footnote to Table 116

* Standardized mortality ratio

1 From Goldsmith (1982)

2 Proportional mortality ratio

3 From International Agency for Research on Cancer (1987a)

4 Tumours of respiratory system

5 Estimated from data given

6 From International Agency for Research on Cancer (1987b)

7 From Amandus (1991)

8 Mortality odds ratio

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References

1. Amandus HE, Shy C, Wing S, Blair A and Heineman EF (1991) Silicosis and lung cancer in North Carolina dusty trades workers. Am J Ind Med, 20, 57-70.

2. Goldsmith DF, Guidotti TL and Johnston DR (1982) Does occupational exposure to silica cause lung cancer? Am J Ind Med, 3, 423-440.

3. Hessel PA, Sluis-Cremer GK and Hnizdo E (1990) Silica exposure, silicosis, and lung cancer: a necropsy study. Br J Ind Med, 47, 4-9.

4. Infante-Rivard C, Armstrong B, Petitclerc M, Cloutier L-G and Theriault G (1989) Lung cancer mortality and silicosis in Quebec, 1938-85. The Lancet, Dec 23/30, 1504-1507.

5. International Agency for Research on Cancer (1987a) Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 42: Silica and some silicates, 39-144. IARC, Lyon.

6. International Agency for Research on Cancer (1987b) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC mongraphs volumes 1 to 42, 341-343. IARC, Lyon.

7. McLaughlin JK, Chen J-Q, Dosemeci M et al (1992) A nested case-control study of lung cancer among silica exposed workers in China. Br J Ind Med, 49, 167-171.

8. Meijers JMM, Swaen GMH, Volovics A, Slangen JJM and Van Vliet K (1990) Silica exposure and lung cancer in ceramic workers: A case-control study. Int J Epidemiol, 19, 19-25.

117. Smoked/salted/cured/pickled food

Only one study could be found which attempted to relate lung cancer risk to frequent consumption of foods which were smoked, salted, cured or pickled, and details of it are given in Table 117. Three relative risks, ranging from 0.92-1.60, were estimated for various food items.

It can be seen from the evidence presented in the table that there is no convincing relationship between lung cancer risk and frequent consumption of smoked, salted, cured or pickled foods.

Table 117: Estimates of relative risk for frequent consumption of smoked/salted/cured/pickled food

| Study | Population | Food item | Relative risk (95% limits |
|---|---|---|---|
| Koo (1988) | Hong Kong women | Dried/salted fish | 0.95 |
| | | Smoked/cured meat/poultry | 0.92 |
| | | Pickled vegetables | 1.60 |

References

1. Koo LC (1988) Dietary habits and lung cancer risk among Chinese females in Hong Kong who never smoked. Nutr Cancer, 11, 155-172.

118. Smoky coal

Details of the only study which presented data relevant to an investigation of the possible association between lung cancer risk and use of smoky coal are given in Table 118. Two relative risks were estimated, 4.0 for men and 3.7 for women. In addition, evidence of an association between smoky coal use and lung cancer mortality rate per 100,000 population was presented, with rates ranging from 174.21 in an area where 100.0% of households burned smoky coal, down to 3.81 and 2.08 in two areas where no households did.

The data presented in the table provide quite strong evidence of an association between lung cancer risk and use of smoky coal, and it was suggested by the authors that in areas where smoking prevalence is low the burning of smoky coal may be the prime determinant of lung cancer [1]. However, it should be borne in mind that the data has been taken from one study only, and results from further studies are needed before definite conclusions can be reached.

Table 118: Estimates of relative risk/mortality rate for smoky coal

| Study | Population | % Households burning smoky coal | Relative risk (95% limits) |
|---|---|---|---|
| He et al (1990) | Chinese men | - | 4.0 |
| | Women | - | 3.7 |
| | Chinese residents | 100.0 | 174.21[1] |
| | | 89.7 | 128.31[1] |
| | | 81.9 | 104.09[1] |
| | | 78.0 | 22.96[1] |
| | | 76.1 | 39.46[1] |
| | | 49.7 | 13.48[1] |
| | | 35.2 | 7.49[1] |
| | | 34.0 | 19.03[1] |
| | | 2.7 | 9.55[1] |
| | | 0.0 | 3.81[1] |
| | | 0.0 | 2.08[1] |

Footnote to Table 118

1 Mortality rate per 100,000 population

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References

1. He X, Chapman RS, Yang R et al (1990) Lung cancer and indoor air pollution in Xuan Wei, China: Current progress. In: Kasuga H (ed.) Indoor air quality, 435-441. Springer-Verlag.

119. Social class

Table 119 gives details of the available data relevant to an investigation of the possible association between lung cancer risk and social class, according to the index of social class used.

For education, both of the studies using this index of social class found evidence of an increasing risk of lung cancer with decreasing educational level.

Respondents were classified according to their income in eight studies, with four finding an inverse relationship with lung cancer risk and another reporting a very weak relationship in this direction. Two studies actually observed a decrease in risk in lower income groups, although both of these studies divided the respondents into two groups only, while the remaining study failed to find any relationship between income and lung cancer risk.

None of the six studies which used occupational group as an index of social class found unequivocal evidence of an inverse relationship with lung cancer risk, although four did show that subjects in some of the "lower" occupational groups had an increased risk of lung cancer compared to those in "higher" groups.

Four studies grouped subjects according to the average rent in their area of residence, but although all found some evidence of an increasing risk of lung cancer with decreasing rent paid, in none was it a smooth relationship.

Of the 21 studies which classified respondents by their social class, as used in censuses and similar surveys, only two found a convincing inverse relationship with lung cancer risk. However, nine other studies presented some evidence that those in lower social classes have a higher risk of lung cancer than those in higher social classes.

Finally, socio-economic status was used to group respondents by seven studies, of which three found an inverse relationship with lung cancer risk, and two others found at least some evidence of such a relationship.

It can be seen from the table that a variety of indices were used to measure the respondents' social class, with some being more satisfactory than others. While occupational group and educational level are reasonably reliable, as they are based on data relating to the actual

subject, socio-economic level, income and rent may be less so. This is because for these indices classification was often based on the average for the area of residence, rather than on that pertaining to the subject specifically. Thus, such measures could be somewhat inaccurate if the subject was not average in these respects.

Although there does appear to be some evidence that those in higher social classes are at less risk of lung cancer than those of lower social class, such a relationship is far from proved.

Table 119: Estimates of relative risk/standardized mortality ratio for low social class

| Population | Standardized mortality ratios | | | | |
|---|---|---|---|---|---|
| Education level: | | | | | |
| | College | High school | Elementary school | <8 years education | |
| US white men, 1960 | 61 | 95 | 114 | 118 | |
| US white women, 1960 | 90 | 94 | 96 | 123 | |
| Income level: | | | | | |
| | High | | | | Low |
| US men, 1959-67 | 79 | 93 | 107 | 84 | 104[1] |
| US white men, 1947 | 67 | 78 | 99 | 118 | 134[1] |
| US white women, 1947 | 98 | 88 | 98 | 99 | 126[1] |
| US non-white men, 1947 | - | - | 45 | 114 | 127[1] |
| US white men, 35-54, 1959-61 | 23.0 | 25.2 | 36.8 | 48.0 | 60.8[2] |
| US white men, 55+ 1959-61 | 87.0 | 178.7 | 202.0 | 255.0 | 331.7[2] |
| US white women, 35-54 1959-61 | | 6.5 | | 4.5[2] | |
| US white women, 55+ 1959-61 | | 29.9 | | 18.1[2] | |

Table 119 continued

Occupation groups:

| | Pro-fess-ional | Mana-gerial | Cler-ical | Sales | Crafts-men | Oper-atives | Serv-ices | Labs. exc. farm | Farm-ers |
|---|---|---|---|---|---|---|---|---|---|
| US men, 1950 | 83 | 94 | 95 | 103 | 130 | 107 | 123 | 127 | 54 |

| | Outdoor workers | | Indoor workers | | |
|---|---|---|---|---|---|
| | Agri-culture | Construct-ive | Industry | Trans-port | Office, etc |
| German men, 1958-63 | 58 | 56 | 176 | 192 | 135[2] |

| | Independent | | Employees | | | | SW | UW | Unoccupied | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Rural | Urban | I | II | III | IV | | | Inc HW | Exc HW |
| Danish men, 1970-5 | 44 | 107 | 51 | 68 | 107 | 116 | 135 | 113 | 181 | - |
| Danish women 1970-5 | - | 107 | - | - | 101 | 102 | - | 115 | 115 | 99 |

| | Pro-fess-ional | Mana-gerial | Sales | Cler-ical | Crafts-men | Oper-atives | Lab-orers | Serv-ices |
|---|---|---|---|---|---|---|---|---|
| US white men, 1972-5 | 83 | 113 | 91 | 101 | 111 | 102 | 113 | 117[1] |
| US white women, 1972-5 | 103 | 213 | 73 | 104 | 92 | 62 | 177 | 95[1] |

Table 119 continued

Rent level:

| | High | | | | Low |
|---|---|---|---|---|---|
| Danish men, 1943-7 | 66 | 99 | 90 | 97 | 116[1] |
| Danish women, 1943-7 | 50 | 90 | 79 | 100 | 131[1] |
| US white men, 1948-52 | 35.8 | 31.1 | 44.8 | | 57.9[3] |
| US white women, 1948-52 | 5.0 | 6.3 | 5.0 | | 7.4[3] |

Social class:

| | I | II | III | IV | V | Farmers | Farm workers |
|---|---|---|---|---|---|---|---|
| US men, 1949-51 | 85 | 77 | 112 | 108 | 112 | 94 | 54 |

| | I | II | III | IV | V |
|---|---|---|---|---|---|
| UK men, 1911 | 94 | 106 | 106 | 83 | 111 |
| UK men, 1921 | 100 | 109 | 97 | 79 | 124 |
| UK men, 1931 | 107 | 96 | 101 | 91 | 112 |
| UK married women[4], 1931 | 100 | 100 | 110 | 82 | 91 |
| Scottish men, 1949-53 | 104 | 81 | 115 | 86 | 109[5] |
| UK men, 1951 | 81 | 82 | 107 | 91 | 118 |
| UK married women[4], 1951 | 119 | 95 | 102 | 98 | 96 |
| UK single women, 1951 | 75 | 101 | 112 | 100 | 91 |
| Scottish men, 1959-63 | 61 | 70 | 104 | 98 | 151[5] |
| Scottish married women[4], 1959-63 | 59 | 81 | 78 | 85 | 138[5] |
| Scottish single women, 1959-63 | 130 | 73 | 110 | 174 | 149[5] |
| UK men, 1961 | 53 | 72 | 107 | 104 | 148 |
| UK married women[4], 1961 | 83 | 89 | 102 | 101 | 131 |
| UK single women, 1961 | 108 | 118 | 110 | 106 | 127 |
| Finnish men, 1969-72 | 53 | 89 | 124 | 153 | 82[6] |
| Finnish married women[7], 1969-72 | 88 | 105 | 123 | 123 | 60[6] |

Table 119 continued

| | | | | | |
|---|---|---|---|---|---|
| Norwegians, 1970-73 | 81 | 113 | 74 | 122 | 40 |
| UK men, 1971 | 53 | 68 | 110 | 123 | 143 |
| UK married women[4], 1971 | 73 | 82 | 112 | 125 | 134 |
| UK single women, 1971 | 82 | 92 | 123 | 129 | 114 |

Socio-economic level:

| | High | | Low |
|---|---|---|---|
| US men, 1935-49 | 88 | 84 | 116[1] |
| US women, 1935-49 | 82 | 66 | 139[1] |
| US white men, 1949-51 | 35.1 | 43.2 | 47.3[8] |
| US white women, 1949-51 | 5.6 | 6.6 | 7.3[8] |
| Australian men, 1971 | 41 | | 52[8] |
| Australian women, 1971 | 9 | | 8[8] |
| Turkish men, 1979-84* | 1.0 | 1.0(0.7-1.4) | 0.9(0.7-1.3)[9] |

HW = housewives; SW = skilled workers; UW = unskilled workers

* From Dosemeci et al (1993); all other studies from Logan (1982)

1 Standardized incidence ratio

2 Death rate per 100,000

3 Standardized incidence rate per 100,000

4 According to husband's occupation

5 Tumours of respiratory system

6 Comparative mortality factor

7 According to own or husband's occupation

8 Standardized death rate per 100,000

9 Relative risk

References

1. Dosemeci M, Hayes RB, Vetter R (1993) Occupational physical activity, socioeconomic status, and risks of 15 cancer sites in Turkey. Cancer Causes and Control, 4, 313-321.

2. Logan WPD (1982) Cancer mortality by occupation and social class 1851-1971. HMSO, London and IARC, Lyon.

120. Soots/chimney sweeps

Although exposure to soots may occur amongst heating-unit service personnel, brick masons and helpers, building demolition personnel, insulators and firemen, chimney sweeps are the principal workers receiving occupational exposure to soots. It was thus decided to combine the reports for soots and chimney sweeps to avoid unnecessary repetition. The studies which investigated the potential risks of soot exposure and employment as a chimney sweep and lung cancer are detailed in Table 120. Thirteen standardized mortality ratios were given, lying in the range 86-313, of which 11 were raised. Additionally, two proportional registration ratios, of 128 and 134, were also given.

Little information was available from the studies on the exposures of the subjects, although one study did attempt to classify cumulative exposure to soots from the number of years spent working as a chimney sweep [1]. Soot is a complex mixture produced by the combustion of coal, coke, oils, wood, paper, rubber, plastics, and resins, and has been shown to contain potentially carcinogenic metals such as arsenic, chromium, cadmium and nickel, as well as sulphur dioxide, carbon monoxide, asbestos and organic solvents [1,2]. Additionally, the character of the sweeping duties may vary considerably and this will affect the exposure of the subject. For example, an hour's climb in chimney ducts may give an exposure to particulate dust 100 to 1000 times higher than that in other duties. Therefore, it will be very difficult to estimate the exposures of the study subjects, or the effects of any one component of soot.

Even so, IARC still felt that there was "sufficient" evidence for the carcinogenicity of soots to humans [2], although no attempt was made to identify particular causative agents from among the constituent substances in soots. It would appear that employment as a chimney sweep should also be viewed as an occupation which carries a potential carcinogenic risk.

Table 120: Estimates of standardized mortality ratio for exposure to soot/employment as a chimney sweep

| Study | Location | Subset | Standardized mortality ratio |
|---|---|---|---|
| Kennaway and Kennaway (1936, 1947)[1] | E/W | 1921-1932 | 169($p<0.05$)[2] |
| | | 1933-1938 | 90($p<0.05$)[2] |
| Kupetz (1966)[1] | GDR | | >100 |
| OPCS (1978) | E/W | Men aged 15-64[3], 1970-2 | 109 |
| | | Aged 65-74, 1970-2 | 116 |
| | | Aged 15-74, 1966-7 | 134($p<0.01$)[4] |
| | | Aged 15-74, 1968-9 | 128($p<0.01$)[4] |
| Hogstedt et al (1982)[1] | Sweden | | 232($p<0.05$)[2] |
| Logan (1982) | UK | Men, 1951 | 164 |
| | | 1961 | 123 |
| | | 1971 | 109 |
| | | Married women[5] - 1971 | 86 |
| Hansen (1983)[1] | Denmark | | 313($p<0.05$)[2] |
| Hogstedt et al (1983)[1] | Sweden | | 277($p<0.05$)[2] |
| Evanoff et al (1993) | Sweden | | 206(154-269) |

E/W = England/Wales; GDR = German Democratic Republic

1 From International Agency for Research on Cancer (1985)

2 Estimated from data given

3 Includes charwomen, office cleaners, window cleaners, chimney sweeps

4 Proportional registration ratio

5 According to husband's occupation

References

1. Evanoff BA, Gustavsson P and Hogstedt C (1993) Mortality and incidence of cancer in a cohort of Swedish chimney sweeps: An extended follow up study. Br J Ind Med, 50, 450-459.

2. International Agency for Research on Cancer (1985) Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 35: Polynuclear aromatic compounds, part 4, bitumens, coal-tars and derived products, shale-oils and soots, 219-241. IARC, Lyon.

3. Logan WPD (1982) Cancer mortality by occupation and social class 1851-1971. HMSO, London.

4. Office of Population Censuses and Surveys (1978) Occupational mortality: The Registrar General's decennial supplement for England and Wales, 1970-72. HMSO, London.

121. Spices

Only one study could be found which attempted to relate the risk of lung cancer to consumption of spices and it is detailed in Table 121. It was reported that bronchial cancer cases used less spices than controls.

With so little data, it is not possible to determine whether a protective effect of spices exists regarding lung cancer risk.

Table 121: Observations for spice consumption

| Study | Population | Observations |
|---|---|---|
| Denoix et al (1958) | French men | Bronchial cancer cases consumed less spices than controls |

References

1. Denoix PF, Schwartz D and Anguera G (1958) French investigation into the etiology of broncho-pulmonary cancer. Detailed analysis. Bull Assoc Franc pour l'etude du cancer, 49: 1-37.

122. Sugar

Details of the only study found which investigated the possible relationship between lung cancer risk and sugar consumption are given in Table 122. It was observed that cancer cases consumed more sugar than controls.

In the absence of other supporting evidence it is not possible to evaluate the potential carcinogenicity of sugar to humans.

Table 122: Observations on sugar consumption

| Study | Population | Observations |
|---|---|---|
| Denoix et al (1958) | French men | Bronchial cancer cases consumed more sugar than controls |

References

1. Denoix PF, Schwartz D and Anguera G (1958) French investigation into the etiology of broncho-pulmonary cancer. Detailed analysis. Bull Assoc Franc pour l'etude du cancer, 49: 1-37.

123. Sugarcane farmers

Table 123 gives details of the only study found which contained data relevant to the investigation of lung cancer risk among sugarcane farmers. A relative risk of 2.4 was estimated.

The occurrence of cases of mesothelioma among the study population led to the suggestion that exposure to fibrous cane dust may be responsible for the increased rates of lung disease observed [1], but no objective measures of the level of such dust were made by the study. Results from more studies will be needed before the carcinogenicity of exposures associated with sugarcane farming can be evaluated.

Table 123: Estimate of relative risk for sugarcane farmers

| Study | Location | Relative risk (95% limits) |
|---|---|---|
| Rothschild and Mulvey (1982)[1] | USA | 2.4 |

1 From Williams Pickle (1984)

References

1. Blot WJ (1984) Lung cancer and occupational exposures. In: Lung cancer: Causes and prevention, 47-64. Verlag Chemie International Inc.

2. Williams Pickle L, Correa P and Fontham E (1984) Recent case-control studies of lung cancer in the United States. In: Lung cancer: Causes and prevention, 101-115. Verlag Chemie International Inc.

124. Taking saunas

Table 124 gives details of the only study found which attempted to relate lung cancer risk to sauna usage. A relative risk of 1.7 was found for men who were heavy smokers.

It was suggested that the increase in lung cancer risk observed may be due to the production of polycyclic aromatic hydrocarbons during the wood heating, and to asbestos, used as insulation, in the ambient air. However, in the absence of any other data, it is not really possible to evaluate the potential carcinogenicity of saunas.

Table 124: Estimate of relative risk for taking saunas

| Study | Population | Relative risk |
|---|---|---|
| Tenkanen et al (1985) | Finnish male heavy smokers | 1.7 |

References

1. Tenkanen L, Hakulinen T, Hakama M and Saxen E (1985) Sauna, dust and migration as risk factors in lung cancer among smoking and non-smoking males in Finland. Int J Cancer, 35, 637-642.

125. Talc

Table 125 details the seven studies which attempted to relate lung cancer risk to exposure to talc. Five standardized mortality ratios were calculated, and these ranged from 46-290, with all but one being raised. Two relative risks, of 1.00 and 3.24, were also estimated.

Only two studies (Kleinfeld, Selevan) provided objective data on levels of exposure to talc, although these were estimated in the study by Selevan. It is possible that inaccuracies due to misclassification of exposure could have occurred in the other studies. In addition, talc deposits contain various other minerals, including carbonates, free silica, serpentines (including chrysotile) and amphibole minerals (asbestiform and non-asbestiform), which may be potential carcinogens themselves. All of the studies appeared to have considered this to some extent, and gave information on the content of other minerals, although three studies noted that there was no exposure to asbestos (Leophonte, Rubino, Selevan). However, as most of the exposures to other minerals occurred in conjunction with exposure to talc, it was not possible to analyze the effects of talc alone. Therefore, the observed associations may have been brought about by exposure to one of these other minerals.

When evaluating the carcinogenicity of talc to humans, IARC felt that the evidence for talc not containing asbestiform fibres was "inadequate", while that for talc containing asbestiform fibres was "adequate" [2,3]. Meanwhile, a review of lung cancer and occupational exposures described talc as only a "possible" carcinogen, although no attempt was made to classify talc containing and not containing asbestiform fibres separately [1].

Table 125: Estimates of standardized mortality ratio/relative risk for exposure to talc

| Study | Population | Standardized mortality ratio |
|---|---|---|
| Kleinfeld et al (1974)[1] | US talc miners/millers | 3.24*[2] |
| Rubino et al (1976)[1] | Italian talc miners/millers | 46[2] |
| Brown et al (1979)[1]/Dement et al (1980)[1] | US talc miners/millers | 290($p<0.05$)[3] |
| Selevan et al (1979)[1] | US talc miners/millers | 163($p>0.05$)[2] |
| Stille and Tabershaw (1982)[1] | US talc miners/millers | 157 |
| Leophonte et al (1983)[1] | French talc workers | 1.00* |
| Thomas and Stewart (1987)[4] | Pottery workers | 143 |

* Relative risk

1 From International Agency for Reseach on Cancer (1987a)

2 Estimated from data given

3 Tumours of respiratory system

4 From International Agency for Reseach on Cancer (1987b)

References

1. Blot WJ (1984) Lung cancer and occupational exposures. In: Lung cancer: Causes and prevention, 47-64. Verlag Chemie International Inc.

2. International Agency for Research on Cancer (1987a) Monographs on the evaluation of carcinogenic risks to humans. Volume 42: Silica and some silicates, 185-224. IARC, Lyon.

3. International Agency for Research on Cancer (1987b) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42, 349-350. IARC, Lyon.

126. Tea drinking

Table 126 gives details of the six studies which attempted to relate the risk of lung cancer to tea consumption. Seven relative risks were estimated, ranging from 0.84-2.74, of which five were above 1.00. In addition, two studies reported finding a positive correlation between lung cancer mortality, or incidence, and tea consumption.

Over 400 volatile compounds have been identified in black teas, compared to some 200 in green teas, but with the exception of the study by Tewes et al, no attempt was made to distinguish between the different types. Furthermore, information on the consumption of other hot beverages was not given by any of the studies. Therefore, non-drinkers of tea could be drinkers of other hot beverages, such as coffee.

In the conclusions of their study, Tewes et al described tea as a "low risk agent" for lung cancer in humans [3], while IARC felt there was "inadequate evidence" for the carcinogenicity to humans of tea drinking [2].

Table 126: Estimates of relative risk for tea drinking

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Stocks (1970) | Women in 20 countries | Positive correlation between lung cancer mortality and tea consumption |
| Hirayama (1974) | Japanese men | 0.84 |
| Armstrong and Doll (1975)[1] | Women in 23 countries | Positive correlation between lung cancer incidence and tea consumption |
| Dean et al (1977)[2] | UK men | 1.22($p<0.01$) |
| | Women | 1.65($p<0.01$) |
| Kinlen et al (1988) | UK men | 1.4 |

Table 126 continued

| | | |
|---|---|---|
| Tewes et al (1990) | Hong Kong women - black tea | 1.43(0.88-2.33) |
| | Green tea | 2.74(1.10-6.80) |
| Oguni et al (1992)[3] | Japanese residents | <1.00 |

1 From International Agency for Research on Cancer (1991)

2 From Tewes et al (1990)

3 From Yang and Wang (1993)

References

1. Hirayama T (1974) Prospective studies on cancer epidemiology based on census population in Japan. Proc 11th International Cancer Congress, 3, 26-35.

2. International Agency for Research on Cancer (1991) Monographs on the evaluation of carcinogenic risks to humans. Volume 51: Coffee, tea, mate, methylxanthines and methylgloyoxal, 41-197. IARC, Lyon.

3. Kinlen LJ, Willows AN, Goldblatt P et al (1988) Tea consumption and cancer. Br J Cancer, 58, 397-401.

4. Stocks P (1970) Cancer mortality in relation to national consumption of cigarettes, solid fuel, tea and coffee. Br J Cancer, 24, 215-225.

5. Tewes FJ, Koo LC, Meisgen TJ and Rylander R (1990) Lung cancer risk and mutagenicity of tea. Environ Res, 52, 23-33.

6. Yang CS and Wang Z-Y (1993) Tea and Cancer. JNCI, 85: 1038-1049.

## 127. Tetrachloroethylene

Only two studies attempted to relate the risk of lung cancer to exposure to tetrachloroethylene, and details of these are given in Table 127. Both reported an excess of lung cancers but detailed results were not given for either study.

It should be noted that laundry and dry-cleaning workers may also be exposed to other solvents, especially trichloroethylene, and petroleum solvents. However, neither study gave any information on the workers' exposures. Therefore, IARC's classification of the evidence for the carcinogenicity of tetrachloroethylene to humans as "inadequate" is not really surprising [1].

Table 127: Estimates of standardized mortality ratio for exposure to tetrachloroethylene

| Study | Population | Standardized mortality ratio |
|---|---|---|
| Blair et al (1979)[1] | Laundry/dry-cleaning workers | >100[2] |
| Duh and Asal (1984)[1] | US laundry/dry-cleaning workers | >100[2] |

1 From International Agency for Research on Cancer (1987)
2 No details of results given

## References

1. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: an updating of IARC monographs volumes 1 to 42, 355-357. IARC, Lyon.

128. 2,3,7,8-Tetrachlorodibenzo-para-dioxin

Table 128 gives details of the five studies which attempted to relate the risk of lung cancer to exposure to 2,3,7,8-tetrachlorodibenzo-para- dioxin (TCDD). One study estimated a relative risk of 1.41, while another calculated a standardized mortality ratio of 111. A total of five cases of lung or bronchogenic cancer were observed in the other three studies.

Two of the studies appeared to have taken objective measurements of exposure to TCDD. In the study by Manz, TCDD concentrations in samples of precursor materials, products, waste and soil from the grounds of the plant, and in the adipose tissue of volunteers were measured, while Fingerhut analyzed serum levels of TCDD. However, these measurements only appeared to provide information on current or very recent exposure to TCDD, and historical exposure data were not available from any of the studies. It is possible, then, that inaccuracies could have been introduced due to misclassification of exposure.

While IARC classified the evidence for the carcinogenicity of TCDD to humans as "inadequate" [3], Manz et al considered the results of their study and that by Fingerhut to be supportive of the hypothesis that TCDD is a human carcinogen [4].

Table 128: Estimates of relative risk/standardized mortality ratio for exposure to 2,3,7,8-tetrachlorodibenzo-para-dioxin

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Jirasek et al (1973,1974)[1] | Czech workers | 2 bronchogenic cancers observed |
| Thiess and Goldman (1977)[1] | German factory workers | 1 lung cancer observed |
| Pazderova-Vejlupkova et al (1981)[2] | Chloracne patients | 2 lung cancers observed |
| Fingerhut et al (1991) | US chemical plant workers | 111(89-137)* |
| Manz et al (1991) | German chemical plant workers | 1.41(0.95-2.01) |

Footnote to Table 128

* Standardized mortality ratio

1 From International Agency for Research on Cancer (1977)

2 From International Agency for Research on Cancer (1987)

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References

1. Fingerhut MA, Halperin WE, Marlow DA et al (1991) Cancer mortality in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. N Engl J Med, 324, 212-218.

2. International Agency for Research on Cancer (1977) Monographs on the evaluation of the carcinogenic risk of chemicals to man. Volume 15: Some fumigants, the herbicides 2,4-D and 2,4,5-T, chlorinated dibenzodioxins and miscellaneous industrial chemicals, 41-102. IARC, Lyon.

3. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42, 350-354. IARC, Lyon.

4. Manz A, Berger J, Dwyer JH et al (1991) Cancer mortality among workers in chemical plant contaminated with dioxin. The Lancet, 338, 959-964.

129. Textile manufacturing

Table 129 gives details of the numerous studies which attempted to relate exposures in the textile manufacturing industry to the risk of lung cancer.

For general textile workers, eleven relative risks were estimated, ranging between 0.3 and 4.8, with seven of them being above 1.00. Six standardized mortality ratios (SMR) were calculated, lying in the range of 87-192, with three of these being raised. Another six studies gave proportional mortality ratios, of between 43 and 130, again with three being raised. Finally, four standardized proportional incidence ratios were given, ranging from 75-91. It can be seen that these results are somewhat equivocal, with no obvious pattern of increasing or decreasing risk being apparent.

Several of the studies gave results restricted to workers in the cotton-textile industry only. From these studies five estimates of relative risk, of 0.3-0.8, were estimated along with 15 SMRs, ranging from 27.3-117, of which only two were raised. These results are consistent with a decrease in the risk of lung cancer among respondents whose work exposes them to cotton-textiles only.

A wide variety of occupational health hazards are present in the textile industry, of which the most common is organic dust, particularly cotton dust. Other exposures include sizing agents and spinning oils used during spinning and weaving, bacteria, desiccants and defoliants found in raw cotton, pesticide residues found in raw wool, and a variety of bleaching, scouring, singeing and mercerizing agents used during fabric preparation. Chemicals are also widely used during dyeing, printing and finishing, and exposures may be highly complex [3]. It was suggested by one of the studies [7] where an increased mortality was observed that it may have been due to exposure to asbestos and mineral oils, but as little information was available from any of the studies about the nature of the subjects' exposures, it is difficult to ascertain the level of exposure, or to estimate the effects of any one substance. Also, as an increase in the risk of lung cancer was not generally seen in the evidence for textile workers it is possible that the results of the study by Zappa may have been due to chance alone.

A number of hypotheses have been put forward to try to explain the apparent decrease in mortality in workers in the cotton-textile industry. Firstly, it has been suggested that cotton-textile workers have a lower rate of smoking than the general population, due in part to the fact that for many years such employees were not permitted to smoke at work because of an explosion hazard associated with vegetable dusts [2]. However, it has been reported that the level of smoking among cotton-textile workers is comparable to that of respondents in other occupations [2,6]. The second possible explanation is that exposure to cotton dust may stimulate stimulate mucus production, which might protect against carcinogens such as cigarette smoke [2,3,6]. A third hypothesis is based on evidence that endotoxins, whilst toxic in high concentrations, may be potent anticancer agents at the levels at which they are found in airborne cotton dust [2,3,6].

IARC [3] classify as "limited" the evidence that exposures in the textile industry as a whole increase the risk of cancer, and indeed the pattern of results reported is unimpressive. However, the possibility of a protective effect for workers in cotton-textiles appears to be much better supported.

Table 129: Estimates of relative risk/standardized mortality ratio for textile workers

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| General textile workers: | | |
| Versluys (1949)[1] | Dutch male weavers/woollens workers | 43[2] |
| Guralnik (1963)[1] | US male textile mill products labourers | 192* |
| Ashley (1967)[1] | UK wool producing boroughs | 87* |
| Menck and Henderson (1976)[1] | US male textile workers | 119(p>0.05)* |
| Williams et al (1977)[1] | US male textile mill products workers | 2.6 |

Table 129 continued

| | | |
|---|---|---|
| Decoufle et al (1978)[1] | US male textile mill operatives | 1.5(p>0.05) |
| Harrington et al (1978)[1] | US male textile workers | 0.88 |
| Newhouse (1978)[1] | UK male dyers/bleachers/textile workers | 94*[3] |
| Buiatti et al (1979)[1] | Italian textile workers - male | 2.0(1.4-2.7) |
| | Females | 4.8(0.9-14.0) |
| Delzell and Grufferman (1983)[1] | US female textile workers | 90[2] |
| Milne et al (1983)[1] | US male textile manufacturers | 1.9 |
| Coggon et al (1986)[1] | UK male textile workers | 0.3 |
| OPCS (1986) | British textile workers - male | 94* |
| | Married women[4] | 115* |
| Siemiatycki et al (1986)[1] | Wool workers | 0.5(0.3-1.0) |
| | Synthetics workers | 0.5(0.2-1.1) |
| Olsen and Jensen (1987)[1] | Danish male textile workers | 88(70-111)[5] |
| | Females | 82(56-120)[5] |
| | Male spinners/weavers/finishers | 91(66-125)[5] |
| | Females | 75(39-143)[5] |
| Paci et al (1987)[1] | Italian male nonasbestos textile workers | 1.5(0.98-2.3) |
| Dubrow and Gute (1988)[1] | US male textile workers | <100[2] |
| | Service workers | 130(p>0.05)[2] |
| | Synthetics/silk only workers | 130(p>0.05)[2] |
| O'Brien and Decoufle (1988)[1] | US male carpet/textile workers | 100(90-110)[2] |
| Zappa et al (1993) | Italian residents | 1.45(1.0-2.1) |
| | | |
| Cotton-textile workers: | | |
| Kennaway and Kennaway (1936)[1] | E/W male cotton spinners/piecers | 0.3 |
| | Cotton strippers/grinders/card-room jobbers | 0.3 |
| | Cotton weavers | 0.5 |
| Enterline (1965)[6] | Male cotton-textile workers | 27.3*[7] |
| Ashley (1967)[1] | UK cotton-textile producing towns | 89* |
| Registrar General (1971)[8] | UK cotton-textile workers - men | 85(p<0.05)* |
| | Single women | 78* |
| | Married women[4] | 81(p<0.05)* |

Table 129 continued

| | | |
|---|---|---|
| Henderson and Enterline (1973)[6] | Male cotton-textile workers | 54.8*[7] |
| Daum et al (1975) | US male cotton-textile workers | 93* |
| | Females | 96*[3] |
| Merchant and Ortmeyer (1981)[6] | Male cotton-textile workers | 40*[7] |
| Logan (1982) | UK male cotton spinners - 1931 | 117* |
| | 1951 | 57* |
| | 1961 | 66* |
| | 1971 | 109* |
| | Married women[4] - 1961 | 91* |
| Siemiatycki et al (1986)[1] | Canadian cotton workers | 0.8(0.4-1.3) |
| Levin et al (1987)[1] | Chinese cotton-textile workers | 0.7(0.6-0.9) |
| Hodgson and Jones (1990)[8] | British cotton workers | 76(54-102)* |

* Standardized mortality ratio

1 From International Agency for Research on Cancer (1990)

2 Proportional mortality ratio

3 Estimated from data given

4 According to husband's occupation

5 Standardized proportional incidence ratio

6 From Enterline et al (1985)

7 Tumours of respiratory system

8 From Rylander (1990)

References

1. Daum SM, Seidman H, Hammond EC and Selikoff IJ (1975) Mortality experience of a cohort of cotton textile workers. Presented at the XVIII International Congress on Occupational Health, Brighton, England, September 16th.

2. Enterline PE, Sykora JL, Keleti G and Lange JH (1985) Endotoxins, cotton dust, and cancer. The Lancet, Oct 26, 934-935.

3. International Agency for Research on Cancer (1990) Monographs on the evaluation of carcinogenic risks to humans. Volume 48: Some flame retardants and textile chemicals, and exposures in the textile manufacturing industry, 215-278. IARC, Lyon.

4. Logan WPD (1982) Cancer mortality by occupation and social class 1851-1971. HMSO, London and IARC, Lyon.

5. Office of Population Censuses and Surveys (1986) Occupational mortality: The Registrar General's decennial supplement for Great Britain, 1979-80, 1982-83. HMSO, London.

6. Rylander R (1990) Environmental exposures with decreased risks for lung cancer? Int J Epidemiol, 19 (Suppl 1), S67-S72.

7. Zappa M, Paci E, Seniori Constantini A and Kriebel D (1993) Lung cancer among textile workers in the Prato area of Italy. Scand J Work Environ Health, 19, 16-20.

130. Tin miners

Three studies were found which attempted to relate lung cancer risk to employment as a tin miner, and details of these are given in Table 130. Two relative risks, of 1.01 and 2.4, were estimated and one standardized mortality ratio of 157.7 was calculated.

It was suggested that underground tin miners may be exposed to various substances, including arsenic, silica, radon and polycyclic aromatic hydrocarbons (PAHs) [1-3]. The study by Hodgson and Jones used contemporary measurements of radon to estimate historical levels, and also recorded exposure to arsenic among the subjects. McLaughlin et al measured silica concentrations as well as gathering limited information on exposure to radon, arsenic, PAHs, asbestos, nickel, talc and cadmium. The study by Wu et al measured radon levels, and dust concentrations of arsenic, iron, chromium, cadmium and nickel. However, as little information was available on lung cancer risk in relation to such exposures, and with so few studies reporting, the exact carcinogen(s) responsible for the observed increases in lung cancer risk remain unclear.

Table 130: Estimates of relative risk/standardized mortality ratio for tin miners

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Wu et al (1989) | Chinese tin miners | 2.4 |
| Hodgson and Jones (1990) | English tin miners | 157.7($p<0.01$)* |
| McLaughlin et al (1992) | Chinese tin miners | 1.01(0.77-1.33)[1] |

* Standardized mortality ratio

1 Estimated from data given

References

1. Hodgson JT and Jones RD (1990) Mortality of a cohort of tin miners 1941-86. Br J Ind Med, 47, 665-676.

2. McLaughlin JK, Chen J-Q, Dosemeci M et al (1992) A nested case-control study of lung cancer among silica exposed workers in China. Br J Ind Med, 49, 167-171.

3. Wu K-G, Fu H, Mo C-Z, and Y L-Z (1989) Smelting, underground mining, smoking, and lung cancer: A case-control study in a tin mine area. Biomed Environ Sci, 2, 98-105.

131. Tobacco workers

Four studies were found which gave data relevant to an investigation of a possible association between lung cancer risk and tobacco work, and details of them are presented in Table 131. Standardized mortality ratios ranging from 87-147 were calculated, with three out of five being raised. Four proportional mortality ratios were also presented, and these ranged from 112-325. Lastly, one study estimated a relative risk of 15.1.

Before interpreting these results, one potential problem in the design of the study by Blair should be noted. The subjects were selected from obituary listings of the Tobacco Workers' International Union, and a failure to include workers who dropped their Union membership before death or retirement may have biased the findings.

Tobacco workers may be exposed to various chemicals during the processing of tobacco from leaf to finished product, including residues of pesticides and barn fumigants such as phosphine gas, dichlorovinyl dimethylphosphate or carbon tetrachloride, and silica and leaf dusts from processes such as stemming, tipping and redrying [1]. However, no measurements of any of these exposures were attempted by any of the studies. Workers in the study by Talcott et al were exposed to crocidolite asbestos, but no objective measurements of the level of exposure were available.

Thus, although the evidence in the table suggests that there may be an increased risk of lung cancer among tobacco workers, no clear explanation for this observation has been put forward.

Table 131: Estimates of relative risk/standardized mortality ratio for tobacco workers

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| OPCS (1978) | UK male tobacco preparers and product makers, aged 15-64 | 87* |
| | Aged 65-74 | 142[1] |
| | Married women[2] aged 65-74 | 325[1] |
| | Unmarried women aged 15-64 | 144* |
| | Aged 65-74 | 243[1] |
| Logan (1982) | UK male tobacco workers - 1951 | 140* |
| | 1961 | 147* |
| | 1971 | 87* |
| Blair et al (1983) | US tobacco workers | 112[1] |
| Talcott et al (1989) | US cigarette filter factory workers | 15.1(7.5-27.0)[3] |

* Standardized mortality ratio

1 Proportional mortality ratio

2 According to husband's occupation

3 Incidence

References

1. Blair A, Berney BW, Heid MF and White DW (1983) Causes of death among workers in the tobacco industry. Arch Environ Health, 38, 223-228.

2. Logan WPD (1982) Cancer mortality by occupation and social class 1851-1971. HMSO, London and IARC, Lyon.

3. Office of Population Censuses and Surveys (1978) Occupational mortality: The Registrar General's decennial supplement for England and Wales, 1970-72. HMSO, London.

4. Talcott JA, Thurber WA, Arlene RN et al (1989) Asbestos-associated diseases in a cohort of cigarette-filter workers. N Engl J Med, 321, 1220-1223.

132. Toluenes

Only three studies were found which attempted to investigate a possible association between lung cancer risk and exposure to toluenes, and details of these are given in Table 132. Two standardized mortality ratios, of 147 and 278, were calculated, while one study simply stated that six cases of respiratory cancer were observed.

Only the study by Walker made objective measurements of the concentrations of toluene the workers were exposed to, and none of the studies gave any information which would have allowed an estimation of the differential risk for individual toluenes. It is not really surprising then that IARC considered the evidence for the carcinogenicity of toluenes to humans to be "inadequate" [1].

Table 132: Estimates of relative risk/standardized mortality ratio for exposure to toluenes

| Study | Population | Standardized mortality ratio |
|---|---|---|
| Sakabe et al (1976)[1]/ Sakabe and Fukuda (1977)[1] | Japanese workers | Six cases of respiratory cancer observed |
| Sorahan et al (1983)[1] | UK workers | 278*[2] |
| Walker et al (1993) | US shoe factory workers | 147(120-180)* |

1 From International Agency for Research on Cancer (1987)

2 Estimated from data given

References

1. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42, 148-149. IARC, Lyon.

2. Walker JT, Bloom TF, Stern FB et al (1993) Mortality of workers employed in shoe manufacturing. Scand J Work Environ Health, 19, 89-95.

133. Tuberculosis

Table 133 details the studies which attempted to relate lung cancer risk to ever having suffered from tuberculosis. Fifty relative risks were estimated, ranging from 0.84-29.82, of which 47 were above 1.00. Two standardized proportionate mortality ratios, both of 1.50, were also estimated. In addition, one study reported a positive association between lung cancer and tuberculosis but did not provide any detailed results, another observed that lung cancer occurred 20 times more frequently in those who had suffered from tuberculosis than in the general population, and one study reported that 10.0% of male and 8.2% of female lung cancer cases had a history of tuberculosis infection. Finally, one study reported finding a correlation between lung cancer mortality in adulthood and tuberculosis mortality in the period corresponding to the childhood of the lung cancer cases.

Although many of the studies gathered information on tuberculosis infection from registers or medical records, or followed-up groups of tuberculosis patients, several studies (Alavanja, Campbell, Campbell and Hughes, Wu, Wynder, Wynder and Fairchild) appeared to based their data on information elicited at interviews with the subjects. Also, it was not clear how the data on tuberculosis infection were collected in the study by Zheng. Therefore, it is possible that these studies may contain inaccuracies due to misclassification of disease status.

The data presented in the table suggest a positive association between lung cancer risk and a history of tuberculosis infection, but on the whole the estimates of relative risk are not particularly large, and therefore the relationship does not appear to be very strong. A recent review by Aoki [2] stated that although patients with active pulmonary tuberculosis had a higher than normal risk of dying from lung cancer, there was "little biological evidence of TB lesions themselves, or TB bacilli per se, having major roles to play in the carcinogenesis of lung cancer at the moment".

Table 133: Estimates of relative risk for history of tuberculosis

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Wynder et al (1956)[1] | Women | 1.00 |
| Campbell and Hughes (1960)[1] | Not stated | Lung cancer occurred 20 times more frequently in TB patients than in general population |
| Campbell (1961)[1] | Not stated | Positive association |
| Steinitz (1965)[3] | Israeli residents | 10.0% male and 8.2% female lung cancer cases had history of TB |
| Wynder and Fairchild (1966) | US men | 0.84(0.22-3.21)[2] |
| Simecek and Simeckova (1967)[3] | Czech residents | 4.2 |
| Aoki et al (1969)[3] | US white men | 6.7(4.0-9.6) |
| | Non-white men | 8.6(4.0-13.7) |
| | US white men, active TB | 10.5 |
| | Non-white men | 20.6 |
| | White men, inactive TB | 4.5 |
| | Non-white men | 2.3 |
| | US residents, 1962-3 | 3.6(1.9-5.3) |
| | 1963-4 | 1.7(0.4-3.0) |
| | Japanese men | 2.75 |
| | Women | 5.48 |
| Aoki et al (1969)[3]/ Ipsen (1967)[3] | US men | 3.1 |
| Campbell and Guilfoyle (1970)[3] | Australian men | 2.06 |
| Kreus et al (1970)[3] | Finnish residents | 2.2 |

Table 133 continued

| | | |
|---|---|---|
| Aoki and Ohtani (1971)[3] | Japanese men, 1964-68, CVD controls | 1.41 |
| | Gastric cancer controls | 1.23 |
| | Women, CVD controls | 1.33 |
| | Gastric cancer controls | 1.54 |
| | Men, 1974-82, CVD controls | 4.21 |
| | IHD controls | 2.13 |
| | Women, CVD controls | 3.87 |
| | IHD controls | 2.16 |
| Watanabe and Kurashima (1977)[3] | Japanese residents | 3.56 |
| | Japanese residents | 6.93 |
| Clemmensen and Hjalgrim-Nelson (1979)[3] | Danish men, INH+ | 3.36 |
| | INH- | 2.58 |
| | Women, INH+ | 4.55 |
| Howe et al (1979)[3] | Canadian men | 1.50(1.21-1.47)[4] |
| | Women | 1.50(1.11-1.98)[4] |
| Hongo et al (1981)[3] | Japanese men | 4.88 |
| | Women | 9.69 |
| Komatsu et al (1981)[3] | Japanese men | 2.58 |
| | Women | 19.6 |
| Mercer (1981) | English residents | Correlation between lung cancer mortality in adulthood and TB mortality in time period relating to childhood |
| Hinds et al (1982) | Hawaiian women | 1.0(0.2-5.5) |
| | Japanese women | 2.0(0.4-10.3) |
| | Chinese women | 2.1(0.3-16.1) |
| Aoki (1985)[3] | Japanese men | 12.0 |
| | Women | 5.0 |
| Takatorige et al (1985)[3] | Japanese residents, -1 year follow-up | 29.82 |
| | 1-2 years | 6.36 |
| | 2-3 years | 5.00 |
| | 3-4 years | 4.35 |
| | 4-5 years | 1.27 |
| | 5+ years | 1.27 |

Table 133 continued

| | | |
|---|---|---|
| Zheng et al (1987)[3] | Chinese residents | 1.5(1.2-1.8) |
| Wu et al (1988) | Not stated | 10.0(1.1-90.1) |
| Sakurai et al (1989)[3] | Japanese women | 6.4 |
| Gao et al (1991)[3] | Chinese men | 1.72(1.11-2.53) |
| | Women | 2.79(1.79-4.14) |
| Alavanja et al (1992) | US female residents | 2.0(1.0-4.1) |

CVD = cardiovascular disease; IHD = ischaemic heart disease; INH = Isoniazid treatment

1 From Roe and Walters (1965)

2 Estimated from data given

3 From Aoki (1993)

4 Standardized proportionate mortality ratio

References

1. Alavanja MCR, Brownson RC, Boice JD and Hock E (1992) Preexisting lung disease and lung cancer among nonsmoking women. Am J Epidemiol, 136, 623-632.

2. Aoki K (1993) Excess incidence of lung cancer among pulmonary tuberculosis patients. Jpn J Clin Oncol, 23, 205-220.

3. Hinds MW, Cohen HI and Kolonel LN (1982) Tuberculosis and lung cancer risk in nonsmoking women. Am Rev Resp Dis, 125, 776-778.

4. Mercer AJ (1981) Risk of dying from tuberculosis or cancer: Further aspects of a possible association. Int J Epidemiol, 10, 377-380.

5. Roe FJC and Walters MA (1965) Some unsolved problems in lung cancer etiology. Progr Exp Tumor Res, 6, 126-227.

6. Wu AH, Yu MC, Thomas DC, Pike MC and Henderson BE (1988) Cancer Res, 48, 7279-7284.

7. Wynder EL and Fairchild EP (1966) The role of a history of persistent cough in the epidemiology of lung cancer. Am Rev Resp Dis, 94, 709-720.

## 134. Typhoid infection

Only one study could be found which attempted to relate the risk of lung cancer to typhoid, and details of it are given in Table 134. A relative risk of 2.5 was estimated.

This excess risk was only seen in chronic typhoid and paratyphoid carriers, and not in a group of people who had suffered from the acute disease but not gone on to become carriers. It was therefore suggested by the authors that an increased lung cancer risk is only associated with chronic carriers, but with only one study reporting there is no other evidence to support this view, or indeed that typhoid in any form is a risk factor for lung cancer.

Table 134: Estimates of relative risk for typhoid infection

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Caygill et al (1994) | Scottish residents | 2.5(0.82-5.89) |

### References

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135. Uranium compounds

Table 135 gives details of the studies found which provided data relevant to an investigation of the possible association between lung cancer risk and exposure to uranium compounds. Fifteen standardized mortality ratios were calculated, ranging from 82-482, with 12 being raised. One study estimated relative risks of between 0.943 and 1.027 per centigray increase in the cumulative lung dose of uranium, while two others stated that excesses of lung cancer had been observed, but failed to give any detailed results.

Various drawbacks were noted in some of the studies, which should be highlighted before an evaluation of the evidence is made. The standardized mortality ratio presented by Archer was calculated on the basis of nonwhite rates of lung cancer, and it was stated that this would have produced an overestimate of the expected number of lung cancers in the study population. It was also noted that there was a degree of overlap in the studies by Chovil, Ham and Muller, which cannot therefore be considered as completely independent of each other. Other potential problems include possible incomplete ascertainment of cases in the studies by Chovil and Kunz.

It was noted in the study by Kusiak that many of the miners were also exposed to arsenic, nickel, copper and gold, and that there was a difference in risk particularly for those miners who had also been exposed to arsenic and gold. Additionally, it is highly likely that most of the subjects in these studies were exposed to radiation, and it is possible that this is a more important factor in the observed increase in in lung cancer than the uranium itself. In fact, the National Research Council stated that "the dominant source of radiation damage to the respiratory system in miners is generally considered to be the inhalation of radon daughters, rather than the uranium content of the ore". Therefore, it is difficult to properly determine the carcinogenicity of uranium and its compounds to humans, although the evidence presented in the table is suggestive of a positive association.

Table 135: Estimates of standardized mortality ratio/relative risk for uranium compounds

| Study | Population | Standardized mortality ratio (95% limits) |
|---|---|---|
| Archer et al (1976)[1] | American Indian uranium miners | 423($p>0.01$) |
| Ham (1976)[1] | Canadian uranium miners | 180[2] |
| Kunz et al (1979)[1] | Czech uranium miners | Excess lung cancer observed for all levels of cumulative exposure and exposure duration |
| Chovil (1981)[1] | Canadian uranium miners | Excess of lung cancer observed |
| Muller et al (1981, 1983,1985)[1] | Canadian uranium miners | 181($p<0.05$) |
| Waxweiler et al (1981)[1] | US white uranium miners | 482(lower 95% limit 425) |
| Waxweiler et al (1983)[3] | US uranium workers never employed in mining | 83(54-121) |
| Tirmarche et al (1984)[1] | French uranium miners | 191[2] |
| Nair et al (1985)[3] | Canadian uranium miners | 184 |
| | Uranium refinery workers | 82 |
| | Surface uranium miners | 175 |
| | Underground uranium miners | 375 |
| | Other uranium workers | 110 |
| Howe et al (1986)[1] | Canadian uranium miners | 190[2] |
| Polednak and Frome (1986)[3] | US uranium processing workers employed less than 1 year | 92 |
| | Employed 1 year or more | 106 |
| Dupree et al (1993) | US uranium processing workers | 0.943-1.027[4] |
| Kusiak et al (1993) | Canadian uranium miners | 225(191-264) |

Footnote to Table 135

1 From International Agency for Research on Cancer (1988)

2 Estimated from data given

3 From National Research Council (1988)

4 Relative risk per centigray increase in cumulative lung dose

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References

1. Dupree E, Watkins J, Ingle J et al (1993) Risk of lung cancer among uranium processing workers. Am J Epidemiol, 138, 640 (Abstract).

2. International Agency for Research on Cancer (1988) Monographs on the evaluation of carcinogenic risks to humans. Volume 43: Man-made mineral fibres and radon, 173-259. IARC, Lyon.

3. Kusiak RA, Ritchie AC, Muller J and Springer J (1993) Mortality from lung cancer in Ontario uranium miners. Br J Ind Med, 50, 920-928.

4. National Research Council (1988) Health risks of radon and other internally deposited alpha-emitters: BEIR IV. National Academy Press, Washington DC.

## 136. Vegetarianism

Table 136 gives details of the two studies which investigated lung cancer risk in relation to a vegetarian diet. Three standardized mortality ratios, ranging from 8-89, were calculated.

While these results are indicative of a protective effect of vegetarianism, data from more studies is needed before such a relationship can be confirmed.

Table 136: Estimates of standardized mortality ratio for vegetarianism

| Study | Population | Standardized mortality ratio |
|---|---|---|
| Kinlen (1982) | UK female members of religious orders | 45 |
| Chang-Claude and Frentzel-Beyme (1993) | German men | 8 |
| | Women | 89 |

References

1. Chang-Claude J and Frentzel-Beyme R (1993) Dietary and lifestyle determinants of mortality among German vegetarians. Int J Epidemiol, 22, 228-236.

2. Kinlen LJ (1982) Meat and fat consumption and cancer mortality: A study of strict religious orders in Britain. Lancet, 1, 946-949.

137. Vinyl chloride

Although most of the studies which have investigated the potential effects of exposure to vinyl chloride have concentrated on liver cancer, a few studies were found which had also looked for a possible association with lung cancer, and details of these are given in Table 137. Few detailed results were available, but it can be seen from the table that of the 10 estimates of relative risk given, all but 1 were raised. Additionally, one standardized mortality ratio, of 194, was presented.

It is not clear how extensive the exposures of the subjects were, as objective measurements of vinyl chloride concentrations in the workplace do not appear to have been made by any of the studies. It is also possible that some workers may have been exposed to other chemicals which may themselves be potential carcinogens. Lastly, there are differences between the studies in the length of time a subject had to be employed for before being considered as "exposed", which may also introduce inaccuracies.

Additionally, the findings by Monson can be questioned, on the grounds that not all of the deaths studied had occurred in workers in activities directly related to vinyl chloride production or polymerization and that the study failed to include deaths among workers who had terminated employment prior to retirement or death [1].

Despite these drawbacks, IARC considered there to be "sufficient" evidence for the carcinogenicity of vinyl chloride to humans [1,2].

Table 137: Estimates of relative risk/standardized mortality ratio for exposure to vinyl chloride

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Monson et al (1974)[1] | US vinyl chloride workers | >1.00 |
| Tabershaw and Gaffey (1974)[1] | US vinyl chloride workers | >1.00[2] |
| Byren et al (1976)[1] | Swedish vinyl chloride/polyvinyl chloride workers | >1.00(p>0.05) |
| Fox and Collier (1976)[1] | Workers exposed to vinyl chloride for <15 years | 1.56 |
| Saric et al (1976)[1] | Yugoslavian vinyl/polyvinyl chloride workers | 1.00 |
| Waxweiller et al (1976)[1] | US vinyl chloride/polyvinyl chloride workers | 194*[2] |
| Von Reinl et al (1977)[1] | German vinyl chloride workers | >1.00 |
| Buffler et al (1979)[3] | Vinyl chloride workers | >1.00 |
| Waxweiler et al (1981)[3] | Synthetic chemical plant workers | >1.00 |
| Fedotova (1983)[3] | Vinyl chloride/polyvinyl chloride workers | >1.00 |
| Heldaas et al (1984)[3] | Vinyl chloride/polyvinyl chloride workers | >1.00 |

* Standardized mortality ratio

1 From International Agency for Research on Cancer (1979)

2 Tumours of respiratory system

3 From International Agency for Research on Cancer (1987)

References

1. International Agency for Research on Cancer (1979) Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 19: Some monomers, plastics and synthetic elastomers, and acrolein, 377-438. IARC, Lyon.

2. International Agency for Research on Cancer (1979) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42, 373-376. IARC, Lyon.

138. Vitamin A

There has recently been much interest in the relationship between diet and the risk of cancer, and several studies have attempted to investigate the possible association between vitamin A intake and the risk of lung cancer. The results of these studies are detailed in Table 138, which also includes two overall estimates of relative risk, based on 3 and 24 studies respectively. For those studies which divided the respondents into multiple categories of vitamin A intake only the relative risk estimate for the highest, or lowest, intake category has been given, as appropriate. For the studies which used a high intake of vitamin A as the reference category, 11 out of 13 estimates of relative risk were above 1.00, ranging from 1.13-3.00. The other two studies failed to find an association, but did not report their results in detail. All of the 7 relative risks presented from the studies which compared a high intake of vitamin A to a base category of low intake were reduced, lying in the range of 0.31-0.91.

It can be seen from the table that the index of vitamin A used varied widely. A number of studies took measurements from blood samples, recording serum levels of vitamin A or beta-carotene. Most of the remaining studies concentrated on dietary intake, calculating indices of vitamin A or beta-carotene intake from the amount of certain foods eaten, although three studies simply used total consumption of vegetables, or fruits and vegetables, as an index of vitamin A intake. It is not clear how reliable indices of vitamin A intake based on dietary assessment are, especially where the frequency of consumption rather than the actual amount eaten is measured. Additionally, there may be important sources of vitamin A, such as vitamin supplements, which are not included in dietary questionnaires.

Another point to consider is the fact that vitamin A is taken into the body in two forms; as pre-formed vitamin A and as beta-carotene, from which the body is able to manufacture the vitamin as required. Therefore, it is difficult to tell whether it is the vitamin itself or the provitamin which is providing the protective effect. One further problem lies in the fact that foods are rarely a source for just one vitamin but

usually contain several. A high intake of vitamin A, therefore, could correlate with a high intake of some other component of the diet which may itself be the protective factor, rather than the vitamin.

Finally, the development of cancer may affect appetite and change the way the body metabolizes food. As a result, cancer patients may appear to have different levels of serum and dietary vitamins than those not suffering from cancer, but these could be as a result of the disease rather than a cause of it. Therefore, case-control studies of the relationship between diet and cancer should be viewed with some caution, while cohort studies, which measure vitamin levels or dietary intake before the onset of disease, may provide more reliable results.

Bearing all these potential problems in mind, the results obtained from the various studies are remarkably consistent, suggesting that there may indeed be some protective effect, although whether this is from vitamin A or beta-carotene is not clear.

Table 138: Estimates of relative risk for vitamin A intake

| Study | Study type | Location | Vitamin A index | Relative risk (95% limits) |
|---|---|---|---|---|
| Highest intake as reference category: | | | | |
| MacLennan et al (1977) | C-C | Singapore | VEG | 2.23(1.49-3.33) |
| Hankin et al (1984) | C-C | USA | DVA | 1.39(0.89-2.15) |
| Seigel (1984) | C-C[1] | USA/Switzerland | SVA | No association |
| Menkes et al (1986) | PR | USA | SVA | 1.13 |
| | | | SBC | 2.20 |
| Humble et al (1987) | C-C | USA | DVA | 1.29(0.91-1.83) |
| | | | DBC | 1.35(0.96-1.90) |
| Kok et al (1987) | PR | Netherlands | SVA | No association |
| Orentreich et al (1991) | C-C | USA | SVA | 1.5 |
| | | | SBC | 3.0 |
| Block et al (1992) | CO[2] | Various | FVI | 2.20(1.20-7.00) |
| Forman et al (1992) | C-C | China | FVI | 1.22(0.76-1.94) |
| Dorgan et al (1993) | C-C | USA | DCA | 1.27(1.03-1.56) |

Table 138 continued

| | | | | |
|---|---|---|---|---|
| Lowest intake as reference category: | | | | |
| Bjelke (1975) | PR | Norway | DVA | 0.31 ($p < 0.01$) |
| Wald et al (1988) | PR | England | SBC | 0.81(0.37-1.78) |
| Chow et al (1992) | PR | USA | DVA | 0.80(0.50-1.20) |
| | | | DBC | 0.80(0.50-1.20) |
| Huang et al (1992) | C-C | China | DBC | 0.91(0.85-0.99) |
| Shibata et al (1992) | PR | USA | DBC | 0.81(0.49-1.33) |
| Steinmetz et al (1993) | PR | USA | DBC | 0.83(0.52-1.32) |

C-C = Case-control; CO = Combined; DBC = Dietary beta-carotene; DCA = Dietary carotenoids; DVA= Dietary vitamin A; FVI = Fruit and vegetable intake; PR = Prospective; SBC = Serum beta-carotene; SVA = serum vitamin A; VEG = Vegetable intake;

1 Combined results from 3 studies

2 Combined results from 24 studies

References

1. Bjelke E (1975) Dietary vitamin A and human lung cancer. Int J Cancer, 15, 561-565.

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3. Dorgan JF, Ziegler RG, Schoenberg JB et al (1993) Race and sex differences in associations of vegetables, fruits, and carotenoids with lung cancer risk in New Jersey (United States). Cancer Causes and Control, 4, 273-281.

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13. Shibata A, Paganini-Hill A, Ross RK, Yu MC and Henderson BE (1992) Dietary $\beta$-carotene, cigarette smoking, and lung cancer in men. Cancer Causes and Control, 3, 207-214.

14. Steinmetz KA, Potter JD and Folsom AR (1993) Vegetables, fruit, and lung cancer in the Iowa Women's Health Study. Cancer Res, 53, 536-543.

139. Vitamin C

Details of some 14 studies which have attempted to investigate the possible association between vitamin C intake and the risk of lung cancer are given in Table 139, along with the key findings. Where the respondents were divided into multiple categories of vitamin C intake only the relative risk estimate for the highest, or lowest, category has been given, as appropriate. Thirteen out of the 17 estimates of relative risk presented from studies which used a high intake of vitamin C as the reference category showed a positive association, with risks ranging from 1.28-4.30, although several studies did not give details of their results. The remaining four studies failed to find an association. All of the 4 relative risks presented from the studies which compared a high intake of vitamin C to a base category of low intake were reduced, lying in the range of 0.26-0.94.

The table shows the indices of vitamin C intake used by the studies, and it can be seen that these varied widely. Only one study took measurements of serum vitamin C levels. The others measured dietary intake, calculating indices of vitamin C intake from the amount of certain foods eaten, although three studies also looked at total consumption of fruit or green salads. The reliability of nutrient indices based on dietary assessment is unclear, especially where only the frequency of consumption is measured, rather than the actual amount eaten. Additionally, as only three studies recorded usage of vitamin supplements intake of vitamin C from this source will probably not have been included by many of the studies.

One further problem lies in the fact that foods are rarely a source for just one vitamin but usually contain several. A high intake of vitamin C, therefore, could correlate with a high intake of some other component of the diet which may itself be the protective factor. In particular, foods high in vitamin C are also often high in carotenoids, for which there is some evidence of a protective effect [1]. Alternatively, a high intake of foods containing vitamin C may correlate with a low intake of foods containing nutrients, such as fat, which are believed to be positively associated with the risk of cancer.

Finally, due to the fact that the development of cancer might affect appetite and change the way the body metabolizes food, cancer patients

may appear to have different levels of serum and dietary vitamins than those not suffering from cancer, as a result of the disease rather than as a cause of it. For this reason, cohort studies which measure vitamin levels or dietary intake before the onset of disease may provide more reliable results than studies of a case-control design.

Despite these problems the results obtained are fairly consistent over the various studies, suggesting that vitamin C may indeed have a protective effect. However, due to the failure of several of the studies to present their results in detail, it is difficult to estimate the strength of such an effect if it does exist.

Table 139: Estimates of relative risk for vitamin C intake

| Study | Study type | Location | Vitamin C index | Relative risk (95% limits) |
|---|---|---|---|---|
| Low vitamin C levels: | | | | |
| Mettlin et al (1979) | C-C | USA | DVC | 1.00 |
| Shekelle et al (1981)* | PR | Not given | DVC | >1.00 (p >0.05) |
| Kvale et al (1983) | PR | Norway | DVC | 1.00 |
| Hinds et al (1984) | C-C | USA | DIS | 1.60 (p >0.05)[1] |
| Kolonel et al (1985) | C-C | USA | DIS | 1.28(0.69-2.38)[2] |
| Byers et al (1987) | C-C | USA | DVC | 1.00 |
| Kromhout (1987)* | PR | Not given | DVC | 2.80 (p <0.01) |
| | | | FRU | >1.00 (p <0.05) |
| Stahelin et al (1987)* | PR | Not given | SVC | >1.00 (p >0.05) |
| Fontham et al (1988) | C-C | USA | DVC | 1.50(p <0.001) |
| Holst et al (1988) | C-C | Netherlands | DVC | 4.30 |
| Koo (1988) | C-C | Hong Kong | FRU | 2.19(1.22-5.55) |
| | | | DVC | 1.96(1.15-4.76) |
| Le Marchand et al (1989) | C-C | USA | DIS | >1.00[1] |
| | | | DVC | >1.00[1] |
| | | | DIS | 1.00[3] |
| | | | DVC | >1.00 (p >0.05)[3] |

Table 139 continued

| | | | | |
|---|---|---|---|---|
| High vitamin C levels: | | | | |
| Fraser et al (1991) | PR | USA | FRU | 0.26(0.10-0.70) |
| | | | SAL | 0.65(0.29-1.47) |
| Enstrom et al (1992) | PR | USA | DIS | 0.94(0.52-1.71)[2] |
| | | | DVC | 0.73(0.51-1.04)[2] |

* Taken from Block (1991)

1 Males only

2 Estimated from data for males and females separately

3 Females only

C-C = Case-control; DIS = Dietary vitamin C, including supplements; DVC = Dietary vitamin C; FRU = Fruit intake; PR = Prospective; SAL = Green salads; SVC = Serum vitamin C

References

1. Block G (1991) Vitamin C and cancer prevention: the epidemiologic evidence. Am J Clin Nutr, 53, 270S-282S.

2. Byers T, Vena J, Mettlin C, Swanson M and Graham S (1984) Dietary vitamin A and lung cancer risk: an analysis by histological subtypes. Am J Epidemiol, 120, 769-776.

3. Enstrom JE, Kanim LE and Klein MA (1992) Vitamin C intake and mortality among a sample of the United States population. Epidemiol, 3, 194-202.

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15. Stahelin HB, Gey KF and Brubacher G (1987) Plasma vitamin C and cancer death: the Prospective Basel Study. Ann NY Acad Sci, 498, 124-131.

140. Vitamin E

Details of three studies, reporting on ten populations, which attempted to relate lung cancer risk to vitamin E levels are given in Table 140. A relative risk of 1.47 was estimated by one of the studies. In addition, in five of the study groups serum vitamin E levels were lower in cases than controls, while in two groups the reverse was true. No association was reported for the other two populations.

It has been suggested that vitamin E may inhibit the formation of nitrosamines, and therefore carcinogenesis [3], but data from more studies is needed before a protective effect can be confirmed.

Table 140: Estimates of relative risk for high vitamin E intake

| Study | Population | Relative risk |
|---|---|---|
| Fontham (1990) | Not stated | Serum vitamin E lower in cases than controls ($p<0.05$) |
| | Not stated | No association reported |
| | Hawaiians of Japanese ancestry | No association reported |
| Comstock et al (1992) | US residents | Serum vitamin E lower in cases than controls ($p<0.05$) |
| | Swiss residents | Serum vitamin E lower in cases than controls ($p<0.05$) |
| | US residents | Serum vitamin E lower in cases than controls ($p>0.05$) |
| | Finnish men | Serum vitamin E lower in cases than controls ($p>0.05$) |
| | Finnish women | Serum vitamin E higher in cases than controls ($p>0.05$) |
| | Hawaiian residents | Serum vitamin E higher in cases than controls ($p>0.05$) |
| Alavanja et al (1993) | US white women | 1.47 |

References

1. Alavanja MCR, Brown CC, Swanson C and Brownson RC (1993) Saturated fat intake and lung cancer risk among nonsmoking women in Missouri. JNCI, 85, 1906-1916.

2. Comstock GW, Bush TL and Helzlsouer K (1992) Serum retinol, beta-carotene, vitamin E, and selenium as related to subsequent cancer of specific sites. Am J Epidemiol, 135, 115-121.

3. Fontham ETH (1990) Protective dietary factors and lung cancer. Int J Epidemiol, 19 (Suppl 1), S32-S42.

141. Waiters

Details of the two studies found which looked for a possible association between lung cancer risk and employment as a waiter/waitress are given in Table 141. One study gave a standardized mortality ratio of 156, while the other presented a standardized incidence ratio of 2.0.

It was suggested that the increase in lung cancer among waiters may be explained by their lifestyle, particularly their smoking and drinking habits [1]. However, with so few studies reporting it is difficult to reach any firm conclusions.

Table 141: Estimates of standardized mortality/incidence ratio for working as a waiter/waitress

| Study | Population | Standardized mortality ratio |
|---|---|---|
| Logan (1982) | UK unmarried female waitresses, 1961 | 156 |
| Kjaerheim and Andersen (1993) | Norwegian male waiters | 2.0(1.3-2.9)[1] |

1 Standardized incidence ratio

References

1. Kjaerheim K and Andersen A (1993) Incidence of cancer among male waiters and cooks: Two Norwegian cohorts. Cancer Causes and Control, 4, 419-426.

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142. Welding fumes

Table 142 gives details of the studies which investigated a possible association between lung cancer risk and exposure to welding fumes. For studies based on mortality/morbidity statistics, eight standardized mortality ratios (SMR) were given ranging from 92-151, of which seven were raised. Three proportional mortality ratios (PMR), of 100-145, were also presented, with two of these being raised. Three studies estimated relative risks (RR) which ranged from 0.85-3.5, of which two were above 1.00. Additionally, one study calculated an incidence rate of 125.8 per 100 000 per year, compared to the general male population. Eight SMRs were calculated from cohort studies and they ranged from 95-249, with seven being raised. The four RRs estimated lay in the range 1.25-4.4, while the two calculations of standardized incidence ratio were of 115 and 142. One study calculated a PMR of 104. Finally, 13 estimates of RR were made by case-control studies, and these ranged from 0.7-13.2, of which 11 were above 1.00.

Before an evaluation of the carcinogenicity of exposure to welding fumes is made, several potential drawbacks in the design of some of the studies should be pointed out. Firstly, the case-control studies suffer from the problem that although many of them investigated a long list of occupations and exposures most only reported those with which positive associations were found. Thus, the possibility of a publication bias in in favour of positive associations must be taken into account when reviewing these studies. Problems were also noted with some of the cohort studies. The study by Dunn et al/Dunn and Weir appeared to have incompletely followed up its subjects, while selection bias cannot be ruled out of the study by Becker et al, due to the inclusion of only those subjects who had undergone a technical examination.

Welding can be performed under a wide variety of industrial settings and therefore welders are potentially exposed to a great number of substances, derived from the welding process itself or from other industrial activities being performed in the immediate vicinity. Compounds which have been reported in welding fumes include chromium, nickel, fluoride, lead, aluminium, barium, and various gases and organic constituents [2]. However, as little information is available from the studies about the subjects' exposures it is not possible to separate out

the effects of any one compound. Furthermore, it was suggested that subjects in several of the studies (Becker, Dunn, McMillan and Pethybridge, Puntoni) may have been exposed to asbestos from sources other than welding, which could have biased the results [2].

Taking all this into account, it is not entirely surprising that IARC classified the evidence for the carcinogenicity of welding fumes as "limited" [2].

Table 142: Estimates of relative risk/standardized mortality ratio for exposure to welding fumes

| Study | Population | Relative risk (95% limits) |
|---|---|---|
| Mortality/morbidity statistics: | | |
| Guralnick (1963)[1] | US welders/flame cutters | 92(64-129)* |
| Menck and Henderson (1976)[1] | US welders | 137(101-182)* |
| Milham (1976)[1] | US welders/flame cutters | 104(92-118)[2] |
| Decoufle et al (1977)[1] | US welders/flame cutters | 0.85 |
| Gottlieb (1980)[1] | US welders | 3.5 |
| Petersen and Milham (1980)[1] | US welders/flame cutters | 100[2] |
| Logan (1982) | UK male welders - 1951 | 118* |
| | 1961 | 122* |
| | 1971 | 151* |
| | Married women[3] - 1961 | 132* |
| | 1971 | 107* |
| Morton and Treyve (1982)[1] | US welders/burners | 125.8[4] |
| Milne et al (1983)[1] | US welders | 1.2 |
| Gallagher and Threlfall (1983)[1] | Canadian welders | 145(115-183)[2] |
| OPCS (1986)[1] | UK male welders | 146* |
| Cohort studies: | | |
| Dunn et al (1960)[1]/Dunn and Weir (1965,1968)[1] | US welders/burners | 105(78-139)* |
| Puntoni et al (1979)[1] | Italian oxyacetylene welders | 1.25(0.34-3.20) |
| | Electric arc welders | 1.60(0.33-4.66) |

Table 142 continued

| | | |
|---|---|---|
| Beaumont and Weiss (1980, 1981)[1] | US welders | 132(98-174)* |
| Sjogren (1980)[5] | Swedish stainless steel welders | 4.4 |
| Polednak (1981)[1] | US welders | 150(87-240)* |
| Fletcher and Ades (1984)[1] | UK welders | 146(62-288)* |
| McMillan and Pethybridge (1984)[1] | UK welders | 104(34-243)[2,6] |
| Becker et al (1985)[1] | German stainless steel welders | 95(35-207)* |
| Newhouse et al (1985)[1] | UK welders | 191* |
| Sjogren and Carstensen (1986)[1] | Swedish welders/gas cutters | 1.3 |
| Sjogren et al (1987)[1] | Swedish stainless-steel welders | 249(80-581)* |
| Tola et al (1988)[1] | Finnish shipyard welders | 115(76-167)[7] |
| | Machine shop welders | 142(77-237)[7] |
| IARC (1989)[1] | European welders | 134(110-160)* |
| Case-control studies: | | |
| Breslow et al (1954)[1] | US welders/sheet metal workers doing welding | 7.2(1.9-44.3) |
| Blot et al (1978)[1] | US welders/burners | 0.7 |
| Blot et al (1980)[1] | US welders/burners | 0.9(0.4-2.3) |
| Buiatti et al (1985)[1] | Italian male welders | 2.8(0.9-8.5) |
| Silverstein et al (1985)[1] | US welders/millwrights | 13.2(1.1-154.9) |
| Gerin et al (1986)[1] | Canadian welders | 2.4(1.0-5.4) |
| Kjuus et al (1986)[1] | Norwegian welders | 1.9(0.9-3.7) |
| Lerchen et al (1987)[1] | US welders | 3.2(1.4-7.4) |
| Schoenberg et al (1987)[1] | US welders/flame cutters | 1.2(0.8-1.9) |
| Benhamou et al (1988)[1] | French welders/flame cutters | 1.4(0.79-2.9) |
| Rinsky et al (1988)[1] | US shipyard workers with probable exposure to welding fumes | 1.1(0.8-1.7) |
| Ronco et al (1988)[1] | Italian welders | 2.9(0.87-9.8) |
| Keller and Howe (1993) | US construction workers | 1.68(1.03-2.76) |

Footnote to Table 142

* Standardized mortality ratio

1 From International Agency for Research on Cancer (1990)

2 Proportional mortality ratio

3 According to husband's occupation

4 Incidence per 100 000 per year

5 From International Agency for Research on Cancer (1987)

6 Tumours of respiratory system

7 Standardized incidence ratio

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143. Wood industries

Although several studies have reported an increased risk of nasal cancer in workers in wood industries, the data concerning a possible association with lung cancer is somewhat more sparse. Details of those studies which have provided information are given in Table 143.

For workers in unspecified occupations within the wood industry two relative risks, of 1.0 and 3.3, were estimated, along with three standardized mortality ratios (SMR) ranging from 104-113, and a proportional mortality ratio (PMR) of 87.

Results were also presented according to the specific occupations of the subjects. The relative risks estimated for lumber/sawmill workers appeared to show some evidence of an increase in risk, ranging from <1.0-1.7, with two of them being above 1.00. However, the two SMRs calculated, of 33 and <80, did not.

For furniture/cabinet makers two standardized mortality ratios were given, of 96 and 110. In addition two relative risks, of 0.87 and 6.0, were presented. With so few studies reporting, it is difficult to see a clear pattern of increased or decreased risk.

Four SMRs were calculated for carpenters, ranging from 96-120, with three being raised. In addition, two PMRs, of 104 and 107 were given, along with two proportional registration ratios, of 111 and 115, and one relative risk of 0.87. These results provide limited evidence of a small increase in the risk of lung cancer among carpenters/joiners.

Lastly, the six relative risks estimated for pulp/paper workers lay in the range 1.0-2.2, with four being raised. Three SMRs were given, of between 69 and 91, along with one PMR of 100. Additionally, one study stated that the lung cancer rate was 9% higher among pulp/paper workers, although no details of the comparison population were given. It can be seen that no clear pattern of increased or decreased risk emerged.

Employees in the wood industry may be exposed to various substances, depending on the nature of their occupation and the processes it involves, which may vary from country to country. The most important exposures are wood dust, solvents and biological factors such as insects and fungal spores in untreated wood. Exhaust gases and oil mists associated with sawblade lubrication are an additional hazard for workers in sawmills, while pulp/paper workers may be exposed to numerous chemicals including gaseous sulphur compounds, chlorine and chlorine dioxide, turpentine, sodium hydroxide mist, methanol, ethanol, sulphuric

acid, furfural, hydroxymethylfurfural, cymene, acetic acid, formic acid, gluconic acid, aldonic acid and hydrogen peroxide, dusts consisting of lime, sodium sulphate, and compounds used for the control of slime and algae [1,7]. However, little information was available from the studies on the subjects' exposures, and in some of the studies there was a possibility that workers may have been employed in more than one area of the wood industry. Additionally, exposures in the various occupations within the industry are quite different, and therefore it may not be appropriate to classify workers from different occupations together, as some of the studies did.

Although IARC has classified the evidence for the association between nasal cancer and employment in furniture/cabinet-making as "sufficient", it was felt that there was not enough data available to make an evaluation of the possible association between lung cancer and employment in specific occupations within the wood industry [1].

Table 143: Estimates of relative risk/standardized mortality ratio for employment in the wood industry

| Study | Population | Relative risk(95% limits) |
|---|---|---|
| General woodworkers: | | |
| Harrington et al (1978)[1] | US wood/paper workers - urban | 1.00 |
| | Rural | 3.3 |
| OPCS (1978) | English/Welsh male woodworkers | 113* |
| OPCS (1986) | UK male woodworkers, pattern makers | 104* |
| | Married women[2] | 105* |
| Rylander (1990) | US male mill/furniture/match/shingle/ weaver workers | 87[3] |
| Lumber/sawmill workers: | | |
| Milham (1974)[1] | US lumber/sawmill workers/millmen | <80* |
| Blot and Fraumeni (1976)[1] | US counties with lumber industries | <1.00 |
| Harrington et al (1978)[1] | US sawmill/lumber/forestry workers | >1.00 |
| Edling and Granstam (1980)[4] | Swedish lumberjacks | 33* |
| Blot et al (1982)[5] | US lumber/wood workers | 1.7 |

Table 143 continued

| | | |
|---|---|---|
| Furniture/cabinet makers: | | |
| Brinton et al (1976)[1] | US furniture/fixture makers | 0.87 |
| Olsen and Sabroe (1979)[4] | Danish male carpenters/cabinet makers, aged 20-64 | 96(68-114)* |
| | Aged 65-84 | 110(92-127)* |
| Esping and Axelson (1980)[1] | Swedish furniture makers | 6.0 |
| Carpenters/joiners: | | |
| Milham (1974)[1] | US carpenters/joiners | 106.7* |
| Decoufle et al (1977)[1]/ Bross et al (1978)[1] | US carpenters | 0.87 |
| Harrington et al (1978)[1] | US carpenters | >1.00 |
| OPCS (1978) | E/W male carpenters/joiners, aged 15-64 | 107[3] |
| | Aged 65-74 | 104[3] |
| | Incidence 1966-7 | 111($p<0.05$)[6] |
| | 1968-9 | 115($p<0.01$)[6] |
| Olson and Sabroe (1979)[4] | Danish male carpenters/cabinet makers, aged 20-64 | 96(68-114)* |
| | Aged 65-84 | 110(92-127)* |
| Stellman and Garfinkel (1984)[4] | Male carpenters/joiners | 120($p<0.05$)* |
| Paper workers: | | |
| Blot and Fraumeni (1976)[1] | US southern/eastern counties with pulp/paper industries - males | Lung cancer rate 9% higher ($p<0.05$) |
| Menck and Henderson (1976)[1] | US paper manufacturing/sales workers | 1.71($p<0.01$) |
| Blot et al (1978)[1] | US paper mill workers | 1.0 |
| Gottlieb et al (1979)[1] | US paper industry workers | 1.05(0.79-1.40) |
| Logan (1982) | UK male paper makers - 1951 | 69* |
| | 1961 | 84* |
| | 1971 | 91* |
| Milham and Demers (1974)[4] | US pulp/paper workers | 100[3] |
| Nurminen and Hernberg (1984)[4] | Pulp/paper workers | 2.2(0.7-6.7) |

Table 143 continued

| | | |
|---|---|---|
| Robinson et al (1986)[4] | US pulp/paper workers | 1.00 |
| Toren et al (1991) | Swedish paper mill workers | 1.1(0.3-1.3) |

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* Standardized mortality ratio

1 From International Agency for Research on Cancer (1981)

2 According to husband's occupation

3 Proportional mortality ratio

4 From International Agency for Research on Cancer (1987)

5 From Williams Pickle (1984)

6 Proportional registration ratio

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