*Cancer Causes and Control*, 1997, 8, pp. 444-472

# Cancer risk from occupational and environmental exposure to polycyclic aromatic hydrocarbons

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Epidemiologic evidence on the relationship between polycyclic aromatic hydrocarbons (PAH) and cancer is reviewed. High occupational exposure to PAHs occurs in several industries and occupations. Covered here are aluminum production, coal gasification, coke production, iron and steel foundries, tar distillation, shale oil extraction, wood impregnation, roofing, road paving, carbon black production, carbon electrode production, chimney sweeping, and calcium carbide production. In addition, workers exposed to diesel engine exhaust in the transport industry and in related occupations are exposed to **PAHs** and nitro-PAHs. Heavy exposure to PAHs entails a substantial risk of lung, skin, and bladder cancer, which is not likely to be due to other carcinogenic exposures present in the same industries. The lung seems to be the major target organ of PAH carcinogenicity and increased risk is present in most of the industries and occupations listed above. An increased risk of skin cancer follows high dermal exposure. An increase in bladder cancer risk is found mainly in industries with high exposure to PAHs from coal tars and pitches. Increased risks have been reported for other organs, namely the larynx and the kidney; the available evidence, however, is inconclusive. The results of studies addressing environmental PAH exposure are consistent with these conclusions. ***Cancer Causes and Control* 1997, 8, 444-472**

***Key words:*** Bladder cancer, lung cancer, occupational exposures, polycyclic aromatic hydrocarbons, skin cancer.

## Introduction

Polycyclic ('polynuclear') aromatic hydrocarbons (PAH) are present ubiquitously in the environment as pollutants, often in small quantities of the order of µg/kg or ng/m$^3$. They are a family of lipophilic non-polar chemicals comprising **two** or more benzene rings, and are formed mainly as a result of pyrolytic processes, in particular the incomplete combustion of organic materials. Exposure to PAHs often entails exposure to heterocyclic aromatic compounds, such as acridine and carbazole, that are formed under similar circumstances. Several hundred PAHs have been characterized; the best known is benzo[*a*]pyrene, which is often used as a marker of PAH exposure. The chemistry and formation of PAHs is reviewed by the International Agency for Research on Cancer (IARC).'

Humans are exposed to PAHs by inhalation, ingestion, and skin contact. Non-occupational respiratory exposure is mainly from tobacco smoke and urban air, while the major sources of ingested PAHs are drinking water and cooked food. The main route of occupational exposure is, in most industries, inhalation; in many cases; however, skin exposure represents an important route.

The interpretation of the studies on cancer risk from PAH exposure in humans is complicated by several factors. PAHs occur invariably as mixtures, whose

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composition depends mainly on the raw material and the combustion circumstances. The comparison of studies conducted in the same industry is complicated therefore by qualitative, in addition to quantitative, differences in exposure. In addition, it is practically impossible for epidemiology to disentangle the risk posed by each individual PAH. PAHs in occupational environments are often adsorbed to particles. Epidemiologic data are inadequate to evaluate the possible interaction between PAHs and particles in the induction of lung cancer in humans. Finally, exposure to PAHs is ubiquitous, and many nonoccupational sources of exposure exist, mainly tobacco smoke and diet; the comparison of occupationally exposed populations and 'unexposed' reference populations therefore is biased to an unknown extent.

The evidence of carcinogenicity of several PAHs, their mixtures and related occupational settings has been evaluated by IARC within the Monograph program' (Table I).

This review focuses on several industries and occupational groups at high exposure to various mixtures of PAHs. Although, almost invariably, other carcinogens – and in particular, other lung carcinogens such as crystalline silica, metals, and asbestos – are present in these occupational settings, PAH mixtures represent the most significant exposure. The industries and occupations reviewed in detail include aluminum production, coal gasification, coke production, iron and steel foundries, and different groups of workers exposed to diesel engine exhaust, coal tars and related products, carbon blacks, and other mixtures of PAHs. The review in particular focuses on data accumulated after the Monograph evaluations (Table 1). Data on cancer risk from exposure to mineral oils (including data on workers exposed to lubricating oil, such as mule spinners in the textile industry) are reviewed elsewhere in this issue (see Tolbert).

Most available information comes from industry-based cohort and nested case-control studies; in some instances, however, community-based studies, mainly of case-control design, have provided additional relevant results. However, a systematic review of community-based studies has been conducted only for cancer of the lung, larynx, skin, kidney, and urinary bladder. Results of cohort studies also have been reviewed systematically for risk of cancer of the same organs;" dose-response relationships have been given special attention whenever data were available. It should be noted, however, that the risk of skin cancer is difficult to assess in studies based on mortality. Epidemiologic or experimental indication of risk from PAH exposure is available for other cancer sites, such as colon[3] and esophagus.[4]

[a] The only exception are studies of diesel exhaust exposed workers, for whom only data on lung and bladder cancer risk have been systematically reviewed.

A brief review of data on cancer risk from environmental exposure to PAHs is included, together with a discussion of some key issues in the interpretation of experimental studies on PAH carcinogenicity. Given the abundance of human studies, however, a detailed review of experimental studies was not considered as a priority. Apart from exposure to PAHs in tobacco smoke,' which is not reviewed in detail here, data from exposure to PAHs outside the workplace and the general environment are sparse. One exception is the use of coal tar containing ointments and pastes for the treatment of psoriasis and other dermatologic diseases and symptoms.[6] Data on cancer risk among these patients, however, are of very limited use as for carcinogenicity of coal tar.

In recent years, a number of biomarker-based studies have been published on individuals exposed to PAHs in the occupational and the general environment (see, for example, Schoket *et al*[7] and van Schooten *et al*[8]). Although these studies are useful to investigate mechanisms of toxicity (and, in particular, carcinogenicity of PAHs) and to contribute to the identification of the biological activity of specific chemicals, they have not contributed thus far to the identification and quantification of risk. These studies therefore are not reviewed in detail.

## Aluminum production

PAH exposure in the aluminum industry originates mainly from the evaporation of carbon electrode materials used in the electrolysis process, in which carbon anodes are suspended in a bath contained in a carbon-lined steel vessel.' Anodes and the lining materials usually are made from coal tar pitch and coke. PAH exposure is particularly high (typical benzo[*a*]pyrene levels in the range 1–10 mg/m$^3$)[9] in the Soderberg electrolysis department, while substantial, although lower (typical benzo[*a*]pyrene range, 0.1–1 mg/m$^3$),[9] exposure occurs in the other main type of electrolysis, prebake, and in other departments, such as the carbon plant, in which anodes are manufactured." Other potential exposures in this industry include asbestos, fluorides, sulfur dioxide, and magnetic fields.

Large epidemiologic studies of aluminum workers have been conducted in Canada, Norway, France, and the United States (Table *2*). The risk of bladder cancer was increased, in particular among Soderberg workers, in all the adequate studies that have considered it. A case-control study nested in a large Canadian cohort[21] was particularly informative: bladder cancer risk was associated with increased exposure to coal tar pitch volatiles, measured either as benzene soluble matter or as benzo[*a*]pyrene (Figure 1), the latter being a better predictor of risk in a linear model with 10 years of lag. Under this model, the risk of bladder cancer increased by 1.7

**Table 1.** Carcinogenicity of polycyclic aromatic hydrocarbons (PAH), their mixtures, and related exposure circumstances – evaluations made within the IARC Monograph program[2]

| | Evidence of carcinogenicity[a,b] | | | Year of evaluation |
|---|---|---|---|---|
| | Human[1] | Animal[1] | Overall[b] | |
| PAHs and groups of PAHs | | | | |
| Anthanthrene | ND | L | 3 | 1987 |
| Anthracene | ND | I | 3 | 1987 |
| Benz[*a*]acridine | ND | L | 3 | 1987 |
| Benz[*c*]acridine | ND | L | 3 | 1987 |
| Benz[*a*]anthracene | ND | S | 2A | 1987 |
| Benzo[*b*]fluoranthene | ND | S | 26 | 1987 |
| Benzo[*j*]fluoranthene | ND | S | 26 | 1987 |
| Benzo[*k*]fluoranthene | ND | S | 26 | 1987 |
| Benzo[*ghi*]fluoranthene | ND | I | 3 | 1987 |
| Benzo[*a*]fluorene | ND | I | 3 | 1987 |
| Benzo[*b*]fluorene | ND | I | 3 | 1987 |
| Benzo[*c*]fluorene | ND | I | 3 | 1987 |
| Benzo[*ghi*]perylene | ND | I | 3 | 1987 |
| Benzo[*c*]phenathrene | ND | I | 3 | 1987 |
| Benzo[*a*]pyrene | ND | S | 2A | 1987 |
| Benzo[*e*]pyrene | ND | I | 3 | 1987 |
| Carbazole | ND | L | 3 | 1987 |
| Carbon-black extracts | — | S | — | 1995 |
| Carbon blacks | I | S | 26 | 1995 |
| Chrysene | ND | L | 3 | 1987 |
| Coronene | ND | I | 3 | 1987 |
| Cyclopenta[*cd*]pyrene | ND | L | 3 | 1987 |
| Dibenz[*a,h*]acridine | ND | S | 26 | 1987 |
| Dibenz[*a,j*]acridine | ND | S | 26 | 1987 |
| Dibenz[a,*c*]anthracene | ND | L | 3 | 1987 |
| Dibenz[*a,h*]anthracene | ND | S | 2A | 1987 |
| Dibenz[*a,j*]anthracene | ND | L | 3 | 1987 |
| 7H-Dibenzo[*c,g*]carbazole | ND | S | 26 | 1987 |
| Dibenzo[*a,e*]fluoranthene | ND | L | 3 | 1987 |
| Dibenzo[*h,rst*]pentaphene | ND | L | 3 | 1987 |
| Dibenzo[*a,e*]pyrene | ND | S | 28 | 1987 |
| Dibenzo[*a,h*]pyrene | ND | S | 26 | 1987 |
| Dibenzo[*a,i*]pyrene | ND | S | 26 | 1987 |
| Dibenzo[*a,l*]pyrene | ND | S | 26 | 1987 |
| 1,4-Dimethylphenanthrene | ND | I | 3 | 1987 |
| 1,3-Dinitropyrene | ND | L | 3 | 1988 |
| 1,6-Dinitropyrene | ND | S | 26 | 1988 |
| 1,8-Dinitropyrene | ND | S | 26 | 1988 |
| 3,7-Dinitrofluoranthene | I | S | 26 | 1995 |
| 3,9-Dinitrofluoranthene | I | S | 26 | 1995 |
| 1,3-Dinitropyrene | ND | L | 26 | 1988 |
| 1,6-Dinitropyrene | ND | S | 3 | 1988 |
| 1,8-Dinitropyrene | ND | S | 26 | 1988 |
| Fluoranthene | ND | I | 28 | 1987 |
| Fluorene | ND | I | 3 | 1987 |
| Indeno[*1,2,3-cd*]pyrene | ND | S | 3 | 1987 |
| 1-Methylchrysene | ND | I | 26 | 1987 |

Continued

Table 1. Continued

| | Evidence of carcinogenicity[a,b] | | | Year of evaluation |
|---|---|---|---|---|
| | Human[a] | Animal[a] | Overall[b] | |
| 2-Methylchrysene | ND | L | 3 | 1987 |
| 3-Methylchrysene | ND | L | 3 | 1987 |
| 4-Methylchrysene | ND | L | 3 | 1987 |
| 5-Methylchrysene | ND | S | 2B | 1987 |
| 6-Methylchrysene | ND | L | 3 | 1987 |
| 2-Methylfluoranthene | ND | L | 3 | 1987 |
| 3-Methylfluoranthene | ND | I | 3 | 1987 |
| 1-Methylphenanthrene | ND | I | 3 | 1987 |
| 6-Nitroacenaphtane | ND | S | 2B | 1987 |
| 9-Nitroanthracene | ND | ND | 3 | 1987 |
| 7-Nitrobenz[*a*]anthracene | ND | L | 3 | 1988 |
| 6-Nitrobenzo[*a*]pyrene | ND | L | 3 | 1988 |
| 6-Nitrochrysene | ND | S | 2B | 1988 |
| 3-Nitrofluoranthene | ND | I | 3 | 1987 |
| 2-Nitrofluorene | ND | S | 2B | 1988 |
| 1-Nitronaphthalene | ND | I | 3 | 1988 |
| 2-Nitronaphthalene | ND | I | 3 | 1988 |
| 3-Nitroperylene | ND | I | 3 | 1988 |
| 1-Nitropyrene | ND | S | 2B | 1988 |
| 2-Nitropyrene | ND | I | 3 | 1988 |
| 4-Nitropyrene | ND | S | 2B | 1988 |
| Phenanthrene | ND | I | 3 | 1987 |
| Pyrene | ND | I | 3 | 1987 |
| Mixtures of PAHs | | | | |
| Bitumens | I | — | 3 | 1987 |
| Extracts of steam-refined and air-refined bitumens | — | S | 26 | 1987 |
| Steam-refined and cracking-residue bitumens | — | L | 3 | 1987 |
| Air-refined bitumens | — | I | 3 | 1987 |
| Coal-tar pitches | S | S | 1 | 1987 |
| Coal-tars | S | S | 1 | 1987 |
| Creosotes | L | S | 2A | 1987 |
| Diesel engine exhaust | L | — | 2A | 1988 |
| Whole diesel engine exhaust | — | S | — | 1988 |
| Gas-phase diesel engine exhaust (with particles removed) | — | I | — | 1988 |
| Extracts of diesel engine exhaust particles | — | S | — | 1988 |
| Engine exhaust (unspecified as from diesel or gasoline engines) | L | — | — | 1988 |
| Gasoline engine exhaust | I | — | 2B | 1988 |
| Whole gasoline engine exhaust | — | I | — | 1988 |
| Condensate/extracts of gasoline engine exhaust | — | S | — | 1988 |
| Mineral oils, untreated and mildly-treated | S | S | 1 | 1987 |
| Mineral oils, highly-refined | I | I | 3 | 1987 |
| Shale-oils | S | S | 1 | 1987 |
| soots | S | I | 1 | 1987 |
| Exposure circumstances related to PAHs: | | | | |
| Aluminum production | S | — | 1 | 1987 |
| Coal gasification | S | — | 1 | 1987 |
| Coke production | S | — | 1 | 1987 |
| Iron and steel foundry | S | — | 1 | 1987 |

[a] Abbreviations: ND = no data; I = inadequate evidence; L = limited evidence; S = sufficient evidence of carcinogenicity.
[b] 1 = carcinogenic to humans; 2A = probably carcinogenic to humans; 2B = possibly carcinogenic to humans; 3 = not classifiable as for carcinogenicity to humans (for details, see the Preamble of an IARC Monograph volume).

**Table 2.** Cohort studies of aluminum production workers

| Author (ref.) Year | Country | Period of employment | Follow-up, outcome[a] | Study population | Cancer site, process | Observed cases | RR[b] | (CI)[c] | Notes |
|---|---|---|---|---|---|---|---|---|---|
| Milham[11] 1979 | USA | 1946-62 | 1946-76 D | 2,103 M w. at 1 prebake plant | Respiratory | 35 | 1.2 | [0.8-1.6] | 3+ years empl.; excess of lymphoma; no trend in respiratory cancer risk by duration of employment |
| | | | | | Bladder | 1 | 0.4 | [0.1-2.1] | |
| | | | | | Kidney | 2 | 0.9 | [0.1-3.2] | |
| Giovanazzi & D'Andrea[12] 1981 | Italy | 1965-79 | NA, D | 494 w. at 1 Söderberg plant | Lung | 4 | [0.8] | [0.2-2.0] | |
| | | | | | Larynx | 1 | [2.5] | [0.3-14] | |
| Andersen *et al*[13] 1982 | Norway | 1953-70 | 1953-79 D,I | 7,410 M w. at 4 plants | Lung | 57 | 1.6 | [1.2-2.1] | Nonsignificant excess of leukemia. Lung cancer risk highest in processing department of two older factories |
| | | | | | Bladder | 26 | 1.2 | [0.8-1.7] | |
| | | | | | Kidney | 18 | 1.2 | [0.7-1.9] | |
| | | | | | Larynx | 7 | 1.2 | [0.5-2.5] | |
| Rockette & Arena[14] 1983 | USA | 1946-77 | 1946-77 D | 21,829 M w. at 14 plants | Lung, prebake | 161 | 1.0 | [0.8-1.1] | Increase in pancreas and kidney cancers in prebake workers. No trend of lung cancer with latency or duration |
| | | | | | Lung, Söderberg | 64 | 0.9 | [0.7-1.1] | |
| | | | | | Bladder, prebake | 11 | 0.7 | [0.4-1.3] | |
| | | | | | Bladder, Söderberg | 8 | 1.6 | [0.7-3.2] | |
| | | | | | Kidney, prebake | 19 | 1.5 | [0.9-2.3] | |
| | | | | | Kidney, Söderberg | 3 | 0.5 | [0.1-1.6] | |
| Gibbs[15] 1985 | Canada | 1950-51 | 1950-77 D | 5,406 M w. at 2 Söderberg plants | Lung | [131] | [1.3] | [1.1-1.6] | Excess of esophageal and stomach cancer. Risk of lung and bladder cancer limited to workers exposed to tar; dose-response for both neoplasms with estimated exposure to tar |
| | | | | | Bladder | [13] | [1.2] | [0.6-2.0] | |
| Mur *et al*[16] 1987 | France | 1950-76 | 1950-76 D | 6,455 M w. at 11 plants | Lung, all | 37 | 1.1 | (0.9-1.5) | No trend in lung cancer with duration of employment |
| | | | | | Lung, Söderberg | 4 | 1.4 | (0.4-3.5) | |
| | | | | | Bladder, all | 7 | 2.1 | (1.0-3.7) | |
| Spinelli *et al*[17] 1991 | Canada | 1954-85 | 1954-85 D,I | 4,213 M Söderberg w. | Lung | 37 | 1.0 | (0.7-1.3) | Nonsignificant excess of brain and testicular cancers; trend between CTPV (coal tar pitch volatiles) index and bladder cancer (weak for lung cancer) |
| | | | | | Bladder | 16 | 1.7 | (1.1-2.6) | |
| | | | | | Kidney | 7 | 1.2 | (0.6-2.3) | |
| | | | | | Larynx | 6 | 1.5 | (0.7-3.0) | |
| Carta *et al*[18] 1992 | Italy | 1971-80 | 1971-90 D | 1,148 w. at 1 plant | Lung | 3 | 0.6 | (0.2-2.0) | |
| Armstrong *et al*[19] 1994 | Canada | 1950-73 | 1950-88 D | 338 lung cancer cases, 1,138 controls | Employment in Söderberg rooms: | | | | Nested in expanded cohort studied by Gibbs[15] |
| | | | | | Lung < 1 yr. | 88 | 1.0 | Ref. | |
| | | | | | Lung 1-9 yrs. | 65 | 1.3 | (0.9-1.9) | |
| | | | | | Lung 10-19 yrs. | 35 | 1.4 | (0.9-2.2) | |
| | | | | | Lung 20+ yrs. | 74 | 2.0 | (1.4-2.9) | |
| Ronneberg *et al*[20] 1995 | Norway | 1922-75 | 1953-91 D,I | 1,137 M w. at 1 prebake plant incl. in Andersen *et al*[13] | Lung, < 3 yrs. empl. | 20 | 2.7 | (1.6-4.1) | Suggestion of a trend by estimated exposure to coal tar for bladder cancer; trend with lung cancer in 30-50 years time window. Increase of skin cancer workers < 3 years of employment |
| | | | | | Lung, 3+ yrs. empl. | 19 | 1.2 | (0.7-1.8) | |
| | | | | | Bladder, < 3 yrs. empl. | 5 | 1.3 | (0.4-3.0) | |
| | | | | | Bladder, 3+ yrs. empl. | 14 | 1.6 | (0.9-2.7) | |
| | | | | | Kidney, < 3 yrs. empl. | 2 | 0.9 | (0.1-3.3) | |
| | | | | | Kidney, 3+ yrs. empl. | 6 | 1.3 | (0.5-2.9) | |

[a] D = death; I = incidence of cancer; NA = not available; M = male; w. = workers; y. = year(s); [ ] = result derived from the data presented in the paper; Ref = reference category.
[b] RR = relative risk. [c] CI = confidence interval.

percent for each year of exposure to benzo[*a*]pyrene at a concentration of 1 μg/m$^3$.

The risk of lung cancer was increased in some of the cohort studies of aluminum workers, although the results were not consistent among studies, nor clearly linked with estimates of coal tar pitch or PAH exposure. In the most informative study, however, a case-control study nested in a large Canadian cohort," lung cancer risk was associated with employment in the Soderberg electrolysis department and in the carbon plant; a dose-response was found in this study between lung cancer risk and estimated exposure to benzene soluble matter as well as benzo[*a*]pyrene (Figure 2). Under a linear model, the estimated relative risk (RR) was 1.0034 for 1 mg/m$^3$-year of benzene soluble matter and 1.0028 for 1 ng/m$^3$-year of benzo[*a*]pyrene. However, power curve models fitted the data better than linear models, suggesting a decreasing slope at high exposures.

## Coal gasification

Exposure to PAHs was high among workers employed in the production of town gas and industrial gas from destructive distillation of coal, in particular among workers involved in coal distillation and purification using old types of gasifiers, such as horizontal, vertical and continuous vertical retorts (range of typical benzo[*a*]pyrene levels: 1-10 mg/m$^3$).[22] PAH exposure, however, also occurs in modern processes (*e.g.*, fixed-bed, fluidized-bed, and entrained-bed).[22] In the older gas-making processes, gas and tars were produced by the destructive distillation of coal; in modern gasifiers, oxygen is introduced, resulting in partial combustion of the coal: in this case, all the coal is distilled into gas and no coke is produced.

Workers employed in the destructive distillation of coal were among the occupational groups included in early studies which reported an increase in scrotal and other skin cancers linked to exposure to tar or pitch.[23-25] Early reports of increase of lung cancer among gas workers include the study by Bruusgaard from Norway.[26] The first modern epidemiologic studies on gas workers (Table 3) were conducted by Doll and colleagues[27,32,33] in eight gas boards in the United Kingdom. A twofold increased risk of lung and bladder cancer was reported among workers employed in coal carbonization, while no such excess was reported among other groups of workers. The same tumors were increased among gas workers from Hamburg, Germany,[28] although the interpretation of this study is complicated by the poor reporting. In addition to a small Danish study[29] suggesting an increased mortality from lung cancer, a small cohort from Sweden" confirmed the increased risk of bladder cancer, but not that of lung cancer. Increased risk of cancer from other sites has been reported occasionally in these studies; the evidence regarding skin cancer is weak mainly because most of the studies analyzed cancer mortality rather than incidence.

PAHs from coal tar are the most plausible explanation for the increased risk of lung and bladder cancer among coal gasification workers, in particular, those employed when the older equipment was in use. Other exposures include heavy metals, silica, and aromatic amines.

## Coke production

Substantial airborne exposure to PAHs has been measured in various occupations in coke production." Other agents, including heterocyclic and substituted aromatic compounds, also have been reported. Exposure to PAHs is highest in coke oven operations, in particular at the top of the oven. In studies done in eastern European countries, average benzo[*a*]pyrene concentrations were as high as 112 μg/m$^3$,[35] whereas measurements in western Europe and the US during the same period showed concentrations one order of magnitude lower.[36]

The most important epidemiologic study to date on coke oven workers has been conducted since the 1960s in the US and Canada." A recent update of this cohort[38] shows a twofold increased risk of lung cancer, that decreased during the follow-up (Table **4).** An analysis of lung cancer risk according to cumulative exposure to coal-tar pitch volatiles, based on measurements taken in the plants of the study in the late 1960s, showed a monotonic, significant dose-response (Figure **3).** In another large cohort study, from China," the risk of lung cancer was increased between two- and fourfold, according to the department in which the subject worked. Similar results'were obtained in two smaller studies from Italy[45] and France,[46] while the risk of lung cancer was increased only moderately (30 percent) in other studies from the Netherlands*' and Japan.[40]

In the study from the US and Canada, an excess risk of prostate and kidney cancer also was found, but not for risk for other types of tumor, including digestive cancers; excess of digestive cancers, on the other hand, were reported sporadically in other studies. No evidence of an increased risk of bladder cancer was present in any study.

## Iron and steel foundry

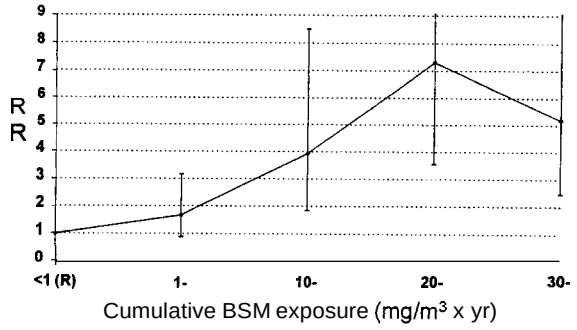
Employment in iron and steel foundries entails exposure to PAHs: concentrations of benzo[*a*]pyrene in the range 0.1-1.1 μg/m$^3$ have been reported.[47,48] PAHs are formed during thermal decomposition of organic materials in the sand; the main sources of PAHs are organic binders, coal powder and other organic additives as well as engine exhaust. In particular, use of coal tar pitch as a binder may result in high PAH exposure: in one study,[49] benzo[*a*]pyrene levels were higher in foundries using coal

**Table 3.** Cohort studies of coal gasification workers

| Year | [illegible] | Period of employment | Period of follow-up; outcome[a] | Study population | Cancer site | Observed cases | RR | (CI) | Comments |
|---|---|---|---|---|---|---|---|---|---|
| Doll et al 1972 | UK | 1933-65 | 1953-65 D | 2,449 M w., 4 companies | Lung | 99 | 1.8 | | |
| | | | | | Bladder | 10 | 2.3 | | |
| Manz[28] 1980 | Germany | 1953-77 | NA, D | 5,405 M w., 1 company | Respiratory tract | 63 | [3.7] | | |
| | | | | | Urinary tract | 6 | 6.1 | | |
| Hansen *et al*[29] 1986 | Denmark | NA | NA, D | 47 M w., 141 unexposed controls | Lung | 7 | 8.9 | | |
| Gustavsson & Reuterwall[30] 1990 | Sweden | 1965-72 | 1966-86 D,I | 295 M w., 1 company | Lung | 4 | 0.8 | (0.2-2.1) | Excess of prostate cancer |
| | | | | | Bladder | 2 | 2.9 | (0.3-10) | |
| Berger & Manz[31] 1992 | Germany | 1900-89 | 1953-89 D | 789 M furnace w., 1 company | Lung | 78 | 2.9 | (2.3-3.6) | Excess of stomach and colorectal cancers; possible overlap with Manz[28] |

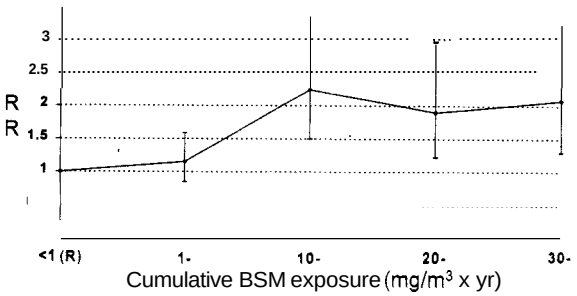
[illegible] = duration, I = incidence of cancer, NA = not available, w. = workers, [ ] = result [illegible] from the data presented in the paper; Ref = reference category. RR = relative risk. [c] CI = confidence interval.

**Figure 1.** Bladder cancer risk among aluminum workers by benzene-soluble matter (BSM) exposure[21]




R: reference category: RR: relative risk

**Figure 2.** Lung cancer risk among aluminum workers by benzene-soluble matter (BSM) exposure[19]




R reference category. RR. relative risk

**Figure 3.** Lung cancer risk among coke oven workers by PAH exposure[38]

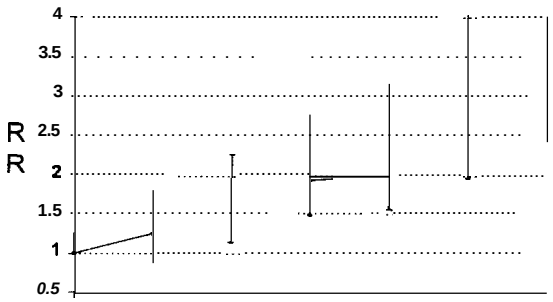


**Table 4.** Cohort studies of lung cancer among coke production workers

| Author (ref.) Year | Country | Period of employment | Follow-up, outcome[a] | Study population | Exposure category | Observed cases | RR[b] | (CI)[c] | Comments[d] |
|---|---|---|---|---|---|---|---|---|---|
| Reid & Buck[39] 1956 | UK | 1949-54 | 1950-54 D | 8,000 M w., 1 plant | Coke oven worker | 14 | 1.4 | [0.8-2.3] | Short follow-up |
| Sakabe *et al*[40] 1975 | Japan | 1949-73 | 1949-73 D | 2,178 retired M w., 11 companies | Coke oven worker | 15 | 1.3 | [0.7-2.1] | |
| Davies[41] 1977 | UK | 1954-65 | 1954-65 D | 610 M w., 2 steel plants | Coke oven worker | 8 | [0.8] | [0.4-1.6] | Excess of colorectal and urothelial cancers; possible under-ascertainment of deaths |
| Hurley *et al*[42] 1983 | UK | 1966-67 | 1966-80 D | 2,842 M w. at 14 steel plants; 3,952 M w. at 13 coking plants | All workers<br>Steel plants<br>Coking plants | 167<br>63<br>104 | 1.2<br>1.2<br>1.2 | [1.0-1.4]<br>(0.9-1.5)<br>(1.0-1.4) | Short follow-up |
| Wu[43] 1988 | China | 1930-65 | 1971-82 D | 21,995 w., 19 coking plants | All workers<br>Coking dept.<br>Preparing dept. | 93<br>53<br>12 | 2.6<br>4.4<br>2.5 | [2.1-3.1]<br>[3.3-5.8]<br>[1.3-4.3] | Highest risk in top of oven workers |
| Swaen *et al*[44] 1991 | Nether-lands | 1945-69 | 1954-84 D | 5,639 M w., 3 plants | Coke oven worker<br>By-product worker | ≤2<br>1–4 | 1.3<br>1.0 | [1.0-1.7]<br>[0.8-1.2] | Excess of larynx and liver cancers; no excess of bladder cancer |
| Franco *et al*[45] 1993 | Italy | 1960-85 | 1960-90 D | 538 M+F w., 1 plant | Coke oven worker | 19 | 1.7 | (1.0-2.7) | |
| Chau *et al*[46] 1993 | France | 1963-82 | 1963-87 D | 536 retired M ω 2 plants | Coke oven worker<br>Near ovens worker<br>Repair mainten. worker<br>Byproducts worker | 2<br>8<br>6<br>2 | 1.8<br>2.5<br>4.3<br>2.4 | [0.2-6.3]<br>[1.1-5.0]<br>[1.6-9.4]<br>[0.3-8.6] | Lung cancer risk highest among employed during old technological phase in one plant |
| Costantino *et al*[38] 1995 | USA & Canada | 1951-55 | 1951-82 D | 15,818 M w., 12 companies | Coke oven worker | 255 | 2.0 | (1.6-2.3) | Excess in prostate and kidney cancers; trend in lung cancer risk with PAH exposure index; lung cancer risk decreased during follow-up |

[a] D = death; M = male; w. = workers; y. = year(s); [ ] = result derived from the data presented in the paper; Ref = reference category.
[b] RR = relative risk.
[c] CI = confidence interval.
[d] PAH = polycyclic aromatic hydrocarbon.

tar pitch as molding sand additive than in foundries using coal powder. Iron and steel foundry workers, however, are exposed to several other classes of known and suspected carcinogens, including in particular crystalline silica and heavy metals. The contribution of PAHs to any increase in cancer risk in this group of workers is therefore particularly difficult to assess.

An increased risk of lung cancer has been reported consistently in cohort studies conducted in Europe and North America (Table 5). The overall increase in risk was rather small in most studies, with RRs in the range 1.2 to 1.5, although a suggestion of a dose-response was found in some of the studies that addressed it. Several studies analyzed the risk of lung cancer by department; however, no clear pattern has emerged. The risk of bladder cancer was increased sporadically; the fact that no results on bladder cancer was presented in several studies suggests the possibility of selective report of positive findings. Similarly, an elevated risk of stomach and prostate cancer was reported in some studies.

## Workers exposed to diesel engine exhaust

Diesel engine exhaust comprises a particulate and a gaseous phase, the former being important for a possible carcinogenic effect. Diesel particles comprise a carbon core with organic compounds adsorbed. Particulate extracts contain PAHs – in particular, nitro-PAHs such as nitro- and dinitro-pyrenes.[68] Diesel exhaust extracts are carcinogenic in experimental animals, as is whole engine exhaust in inhalation experiments (Table 1). Exposure to diesel engine emissions occurs in many occupational settings, and it is often difficult to separate this agent from other combustion fumes, notably gasoline engine emissions. Levels of **PAHs** are highest in emissions from heavy-duty diesel engines, lower (and comparable) in emissions from light-duty diesel engines and from gasoline engines without catalytic converters, and lowest in emissions from gasoline engines with catalytic converters. Diesel engines, however, emit at least 10 times more nitro-PAHs than gasoline engines.[68] Therefore, although epidemiologic studies have been conducted on groups at relatively high and pure exposure to diesel exhaust, co-exposure to other PAH-rich mixtures is invariably present. Table **6** reports the results of the industry-based studies conducted among workers exposed to diesel exhaust. Although many types of cancer have been reported sporadically at increased risk among workers exposed to diesel exhaust, this review will focus on lung and bladder cancer, for which the suspicion of an association is strongest.

Drivers are an important group of workers exposed to diesel exhaust. Results of studies on bus drivers do not consistently show an excess of lung and bladder cancer. The evidence in favor of an association, on the other hand, is strong for truck drivers; all available studies consistently showed an increased risk, which was significant in many investigations. Tobacco smoking was controlled for in several of these studies. The most informative study is the case-control study nested in a cohort of US teamsters,[11] in which a dose-response was found for duration of employment as a long-haul driver and the risk of lung cancer was highest among drivers of diesel trucks only. These findings are reinforced by a few studies conducted on unspecified and mixed drivers, in which truck drivers were the largest group, that also found positive results. The evidence regarding taxi drivers is less compelling than the one on truck drivers; most of the available studies suggest the presence of an association similar to the one found for truck drivers. In only one study, however, was tobacco smoking controlled for.

Railroad workers may be a particularly informative group since exposure to other carcinogens is more limited than in the case of other diesel exposed groups. However, these studies are limited to countries where diesel engines have been widely used. Two large studies have been conducted in Canada[85] and the US.[86-88] In the Canadian study, a small overall increase in lung cancer risk was found, and a trend with estimated level of diesel fume exposure (RR = 1.2 for possible exposure and 1.4 for probable exposure, compared with no exposure, $P < 0.01$). In the American study, the risk of lung cancer was increased significantly among workers aged less than **65** (RR for one year of exposure to diesel = 1.0, $P < 0.05$), while no association was found in older workers (RR = 1.0, $P = 0.9$). Mortality from other cancers, and notably bladder cancer, is not increased in studies of railroad workers.

Other groups of workers exposed to diesel engine exhaust, that have been studied mainly in North America and northern Europe, include heavy equipment operators, dock workers, and crane workers. In most of these studies, an increased risk of lung cancer has been found. The most informative study has been conducted on dock workers from Sweden,[92,93] where a dose-response was found according to estimated diesel exposure. Results on bladder cancer are less consistent and often not available, suggesting the possibility of report bias.

A further occupational group for which several investigations are available are garage mechanics and other maintenance workers in transport companies. Benzo[*a*]-pyrene levels in bus garages have been measured in the range of 1-20 ng/m$^3$.[68] For these workers, however, exposure to other carcinogens, such as mineral oils, is likely to occur, making the interpretation of the results problematic. In particular, one study[95] attempted to address the effect of diesel exhaust exposure among workers in five bus garages in Stockholm, Sweden. Although based

**Table 5.** Cohort studies of iron and steel foundry workers

| Author (ref.) Year | Country | Period of employment | Follow-up, outcome[a] | Study population | Cancer site | Observed cases | RR[b] | (CI)[c] | Comments[d] |
|---|---|---|---|---|---|---|---|---|---|
| Koskela *et al*[50] 1976 | Finland | 1950-72 | 1950-72 D | 1,233 M w. (5+ yrs empl.) | Lung | 10 | [2.1] | [1.0-3.8] | Higher risk of lung cancer among iron workers; case-control study on expanded series by Tola.[51] risk of lung cancer highest among molders and casters non-significant dose-response with PAH exposure |
| Gibson *et al*[52] 1977 | Canada | 1957 | 1967-77 D | 439 w., 1 company | Lung | 21 | [2.5] | [1.5-3.8] | No excess in a group of non-foundry workers from the same company; study expanded (3 companies) by Finkelstein *et al*[53-55] in a population-based case-control study: no excess for steelworkers overall but increase among foundry coke oven and pouring pit workers |
| Breslin[56] 1979 | USA | 1953 | 1953-70 D | 2,167 M w., 7 steel foundries | Lung<br>Bladder<br>Kidney | 34<br>3<br>4 | 1.0<br>[1.0]<br>[1.6] | [0.7-1.4]<br>[0.2-2.8]<br>[0.4-4.1] | Non-significant excess of prostate cancer; similar results in an expanded analysis by Redmond *et al*[57] |
| Decouflé[58] 1979 | USA | 1938-67 | 1938-67 D | 2861 M w., 1 iron foundry | Respiratory<br>Bladder<br>Kidney | 29<br>3<br>3 | [1.3]<br>[1.1]<br>[1.6] | [0.8-1.8]<br>[0.2-3.1]<br>[0.3-4.6] | Higher risk of respiratory cancer for employment 5+ years before 1938 |
| Andjelkovich *et al*[59-61] 1990, 1992, 1994 | USA | 1950-79 | 1950-84 D | 8,147 M w., 1 iron foundry | Lung<br>Bladder<br>Kidney<br>Larynx | 139<br>8<br>9<br>4 | 1.3<br>[1.0]<br>[1.1]<br>[0.7] | [1.1-1.5]<br>[0.4-2.0]<br>[0.5-2.1]<br>[0.2-1.8] | Nonsignificant excess of stomach cancer; highest risk of lung cancer in finishing and maintenance but no trend with duration of employment in these areas |
| Hansen[62] 1991 | Denmark | 1970 | 1970-80 D | 632 molders at census follow-up 1970-80 | Lung<br>Bladder | 9<br>6 | 1.4<br>9.0 | (0.6-2.6)<br>(3.3-19) | |
| Sherson *et al*[63] 1991 | Denmark | 1967-74 | 1967-85 I | 3,377 M foundry w. follow-up to 1985 | Lung<br>Bladder | 85<br>32 | 1.2<br>1.1 | (1.0-1.5)<br>(0.8-1.6) | Similar results for core room ($n = 451$) and finishing workers ($n = 1071$); unspecified foundry workers ($n = 330$) had RR = 1.5 for lung and 2.8 for bladder cancer |
| Rotini *et al*[4] 1993 | USA | 1952-85 | 1973-85 D | 5,540 M w., 1 iron foundry follow-up 1973-86 | Lung | 72 | 1.2 | (0.9-1.5) | Nonsignificant excess of prostate cancer |
| Sorahan *et al*[65] 1994 | UK | 1946-65 | 1946-90 D | 10,438 M w., 9 steel foundries | Lung<br>Bladder<br>Kidney<br>Larynx | 551<br>37<br>24<br>12 | 1.5<br>1.1<br>1.3<br>1.3 | (1.3-1.6)<br>(0.8-1.5)<br>(0.9-2.0)<br>(0.7-2.3) | Excess of stomach cancer; lung cancer risk highest in fettling and furnace workers and laborers |
| Xu *et al*[66,67] 1996 | China | NA | 1987-93 I | 610 M cases, 1 large complex | Lung cum. BaP exp. ($ng/m^3$ year)<br>< 0.85<br>0.85-1.96<br>1.97-3.20<br>> 3.20 | <br>72<br>117<br>96<br>105 | <br>1.1<br>1.6<br>1.6<br>1.8 | <br>(0.8-1.7)<br>(1.2-2.3)<br>(1.1-2.3)<br>(1.2-2.5) | Nested case-control study among workers of a large complex (ref. category: unexposed to BaP), mainly involving iron and steel workers. In PMR analysis, excess of lung cancer among foundry workers and coke oven workers. |

[a] NA = not available; D = death; I = incidence of cancer; M = male; w. = workers; y. = year(s); [ ] = result derived from the data presented in the paper.
[b] RR = relative risk. [c] CI = confidence interval. [d] PAH = polycyclic aromatic hydrocarbon; BaP = benzo[*a*]pyrene; PMR = proportional mortality ratio.

**Table 6**. Epidemiologic studies of workers exposed to diesel exhaust

| Author (ref.) Year | Study area, design[a] | Period of employment | Follow-up, outcome[b] | Study population | Cancer site | Observed cases | RR[c] | (CI)[d] | Comments |
|---|---|---|---|---|---|---|---|---|---|
| Bus drivers | | | | | | | | | |
| Waller[69] 1981 | London, UK CO | 1950-74 | 1950-74 D | 1 company | Lung | 259 | 0.7 | [0.6-0.8] | |
| Edling *et al*[70] 1987 | Southeast Sweden, CO | 1950-59 | 1951-83 D | 5 companies | Lung | 5 | [0.7] | [0.2-1.6] | |
| Balarajan & McDowall[71] 1988 | London, RL | 1950 | 1950-84 D | Drivers at 1939 census alive in 1950 | Lung<br>Bladder | 18<br>1 | [1.4]<br>[0.6] | [0.8-2.3]<br>[0.1-3.2] | |
| Paradis *et al*[72] 1989 | Montreal, Canada CO | 1957 | 1962-85 D | 2,134 drivers 5+ yrs empl.,1 company | Lung<br>Bladder | 78<br>4 | [0.9]<br>[0.5] | [0.7-1.2]<br>[0.1-1.4] | |
| Hrubec *et al*[73] 1992 | USA, CO | 1954-57 | 1954-80 D | 255 drivers among veterans | Lung<br>Bladder | 14<br>3 | 2.6<br>3.1 | (1.7-4.1)<br>(1.2-8.1) | |
| Alfredsson *et al*[74] 1993 | Sweden, CO | 1970 | 1971-86 D | 9,446 drivers at 1970 census | Lung | 64 | 1.0 | (0.8-1.3) | |
| Taxi drivers | | | | | | | | | |
| Menck & Henderson[75] 1976 | Los Angeles, CA (USA) DC | — | 1968-70 D | 3,100 estimated exposed | Lung | 23 | 3.4 | [2.2-5.2] | |
| Balarajan & McDowall[71] 1988 | London, UK RL | 1950 | 1950-84 D | Drivers at 1939 census alive in 1950 | Lung<br>Bladder | 30<br>5 | [0.9]<br>[1.2] | [0.6-1.2]<br>[0.4-2.8] | |
| Rafnsson & Gunnarsdöttir[76] 1991 | Iceland, CO | 1951 | 1951-88 D | 726 drivers | Lung<br>Bladder | 12<br>1 | 1.4<br>0.5 | (0.7-2.4)<br>(0.01-3.1) | |
| Hrubec *et al*[73] 1992 | USA, CO | 1954-57 | 1954-80 D | 397 drivers among veterans | Lung | 16 | 1.5 | (1.0-2.2) | |
| Borgia *et al*[77] 1994 | Rome, Italy CO | 1950-75 | 1965-88 D | 2,311 drivers, 65 companies | Lung<br>Bladder | 76<br>9 | [1.2]<br>[0.8] | [1.0-1.5]<br>[0.4-1.6] | |
| Truck drivers | | | | | | | | | |
| Menck & Henderson[75] 1976 | Los Angeles, CA (USA) DC | — | 1968-70 D | 34,800 estimated exposed | Lung | 109 | 1.7 | [1.4-2.0] | |
| Morton & Treyve[78] 1982 | Oregon, USA DC | — | 1968-72 D | 9,630 drivers at 1970 census | Lung | 64 | [1.8] | [1.4-2.3] | [illegible] |
| Boffetta *et al*[79] 1988 | USA, CO | 1982 | 1982-84 D | 16,208 drivers ACS volunteers | Lung | 48 | 1.2 | (0.9-1.7) | |
| Balarajan & McDowall[71] 1988 | London, UK RL | 1950 | 1950-84 D | Drivers at 1939 census alive in 1950 | Lung<br>Bladder | 280<br>19 | [1.6]<br>[1.1] | [1.4-1.8]<br>[0.6-1.7] | |
| Steenland *et al*[80] 1990 | Central USA, CC | — | 1982-83 D | 1,288 cases 1452 controls among Teamsters Union members | Lung | 609<br>121 | 1.3<br>1.3 | (0.8-1.9)<br>(0.8-2.1) | Long haul driver<br>Short haul driver<br>Dose-response with duration of long haul driving; higher risk for diesel truck driver |

*Continued*

**Table 6.** Continued

| Author (ref.) Year | Study area, design[a] | Period of employment | Follow-up, outcome[b] | Study population | Cancer site | Observed cases | RR[c] | (CI)[d] | Comments |
|---|---|---|---|---|---|---|---|---|---|
| Rafnsson & Gunnarsdöttir[76] 1991 | Iceland, CO | 1951 | 1951-88 D | 868 drivers | Lung | 24 | 2.1 | (1.4-3.2) | |
| | | | | | Bladder | 3 | 1.0 | (0.2-3.0) | |
| Hrubec *et al*[73] 1992 | USA, CO | 1954-57 | 1954-80 D | 1,453 drivers among veterans | Lung | 45 | 1.4 | (1.0-1.8) | |
| | | | | | Bladder | 6 | 1.1 | (0.5-2.1) | |
| Hansen[81] 1993 | Denmark, RL | 1970 | 1970-80 D | 14,225 drivers at census | Lung | 76 | 1.6 | (1.3-2.0) | |
| | | | | | Urinary tract | 11 | 1.0 | (0.5-1.8) | |
| Mixed drivers | | | | | | | | | |
| Gubéran *et al*[82] 1992 | Geneva, CO | 1949-61 | 1970-86 D, I | 1,726 drivers | Lung | 64 | 1.6 | (1.3-2.0) | 15 year latency analysis |
| | | | | | Bladder | 13 | 1.3 | (0.7-2.0) | |
| Costa *et al*[83] 1995 | Italy, RL | 1981 | 1981-82 D | 550,728 drivers at census | Lung | 87 | 1.4 | [1.1-1.7] | |
| | | | | | Bladder | 2 | 0.5 | [0.1-1.7] | |
| Pukkala[84] 1995 | Finland, RL | 1970 | 1970-85 I | 46,193 drivers at census | Lung | 717 | 1.1 | (1.1-1.2) | |
| | | | | | Bladder | 98 | 1.0 | (0.8-1.2) | |
| Railroad workers | | | | | | | | | |
| Howe *et al*[85] 1983 | Canada CO | < 1965 | 1965-77 D | 43,826 retirees, 1 company | Lung | 933 | 1.1 | (1.0-1.1) | Dose-response of lung cancer by level of diesel exhaust exposure |
| | | | | | Bladder | 175 | 1.0 | (0.9-1.2) | |
| Boffetta *et al*[79] 1988 | USA, CO | 1982 | 1982-84 D | 2,973 w. ACS volunteers | Lung | 14 | 1.6 | (0.9-2.7) | |
| Schenker *et al*[86] 1984 | USA, CO CC | 1959 | 1959-80 D, I | 55,407 w., 1,256 cases, 2,385 controls | Lung | 43 | 0.8 | (0.6-1.1) | |
| | | | | | Bladder | 3 | 0.8 | (0.1-2.2) | |
| Garshick *et al*[87-88] 1987, 1988 | | | | | Lung | 35 | 1.4 | (1.1-1.9) | < 65 yrs (20+ diesel yrs) |
| | | | | | (case-control analysis) | 3 | 0.9 | (0.7-1.2) | 65+ yrs (20+ diesel yrs) |
| Hrubec *et al*[89] 1995 | USA, CO | 1954-57 | 1954-80 D | 7,068 railroad w. among veterans | Lung | 250 | 1.4 | (1.2-1.5) | |
| | | | | | Bladder | 39 | 0.9 | (0.7-1.2) | |
| Nokso-Koivisto & Pukkala[90] 1994 | Finland, CO | 1953-91 | 1953-91 I | 8,391 locomotive driver union members | Lung | 236 | 0.9 | (0.7-1.0) | Partial overlap with Pukkala[84] |
| | | | | | Bladder | 48 | 1.1 | (0.8-1.4) | |
| Costa *et al*[83] 1995 | Italy, RL | 1981 | 1981-82 D | 693,776 railroad drivers at census | Lung | 13 | 1.5 | [0.8-2.5] | |
| Pukkala[84] 1995 | Finland, RL | 1970 | 1970-85 I | 5,328 w. at census | Lung | 72 | 0.6 | (0.5-0.8) | |
| | | | | | Bladder | 22 | 1.3 | (0.9-2.1) | |
| Heavy equipment operators | | | | | | | | | |
| Wong *et al*[91] 1984 | Western USA, CO | 1964-78 | 1964-78 D | 34,156 union members | Lung | 309 | 1.0 | (0.9-1.1) | |
| | | | | | Bladder | 27 | 1.2 | (0.8-1.7) | |
| Boffetta *et al*[79] 1988 | USA, CO | 1982 | 1982-84 D | 855 operators ACS volunteers | Lung | 5 | 2.6 | (1.1-6.1) | |
| Hrubec *et al*[73] 1992 | USA, CO | 1954-57 | 1954-80 D | 110 operators among veterans | Lung | 5 | 1.6 | NA | |
| Pukkala[84] 1995 | Finland, RL | 1970 | 1970-85 I | 8,199 machine operators at census | Lung | 137 | 1.3 | (1.1-1.6) | |
| | | | | | Bladder | 18 | 1.2 | (0.7-1.8) | |

*Continued*

**Table 6**. Continued

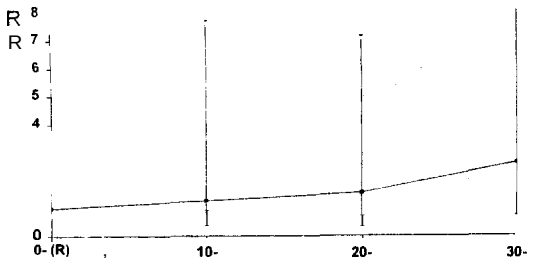
| Author (ref.) Year | Study area, design[a] | Period of employment | Follow-up, outcome[b] | Study population | Cancer site | Observed cases | RR[c] | (CI)[d] | Comments |
|---|---|---|---|---|---|---|---|---|---|
| Dock workers | | | | | | | | | |
| Gustafsson *et al*[92] 1986 | Sweden, CO | 1961-81 | 1961-81 D, I | 6,071 w. | Lung | 70 | 1.3 | (1.0-1.6) | |
| | | | | | Urogenital tract | 61 | 1.1 | (0.9-1.4) | |
| Steenland *et al*[80] 1990 | Central USA, CC | — | 1982-83 D | 1,288 cases,1,452 controls among Teamsters Union members | Lung | 70 | 0.9 | (0.5-1.5) | |
| Emmelin *et al*[93] 1993 | Sweden, CC | 1960-82 | 1960-82 I | 6,573 w., 50 cases, 154 controls | Lung | 12 | 1.0 | Ref. | Low diesel exposure |
| | | | | | | 19 | 1.6 | (0.5-5.1) | Medium exposure |
| | | | | | | 19 | 2.9 | (0.8-10.7) | High exposure |
| | | | | | | | | | Substantial overlap with Gustafsson *et al*[92] |
| Pukkala[84] 1995 | Finland, RL | 1970 | 1970-85 I | 3,298 dockers at census | Lung | 93 | 1.3 | (1.0-1.6) | |
| | | | | | Bladder | 7 | 0.7 | (0.3-1.5) | |
| | | | | | Lung | | | | |
| Crane operators | | | | | | | | | |
| Hrubec *et al*[73] 1992 | USA, CO | 1954-57 | 1954-80 D | 119 cranemen among veterans | Lung | 2 | 0.7 | NA | |
| Costa *et al*[83] 1995 | Italy, RL | 1981 | 1981-82 D | 33,582 operators at census | Lung | 5 | 1.3 | [0.4-3.0] | |
| Pukkala[84] 1995 | Finland, RL | 1970 | 1970-85 I | 1,848 operators at census | | 23 | 1.0 | (0.6-1.5) | |
| Garage and maintenance workers, mechanics | | | | | | | | | |
| Rushton *et al*[94] 1983 | London, CO | 1967-75 | 1967-75 D | 8,684 w., 1 company | Lung | 102 | 1.0 | [0.8-1.2] | Maintenance workers |
| | | | | | Bladder | 12 | 1.4 | [0.7-2.4] | |
| Gustavsson *et al*[95] 1990 | Stockholm, CO | 1945-70 | 1958-84 D, I | 695 w. at 5 garages | Lung | 17 | 1.6 | (0.9-2.6) | Dose-response of lung cancer by cumulative exposure |
| | | | | | Bladder | 4 | 0.7 | (0.2-1.7) | |
| Steenland *et al*[80] 1990 | Central USA, CC | — | 1982-83 D | 1,288 cases, 1,452 controls among Teamsters Union members | Lung | 50 | 1.7 | (0.9-3.1) | Truck mechanics. No trend with duration of employment |
| Hrubec *et al*[73] 1992 | USA, CO | 1954-57 | 1954-80 D | 192 railroad and car mechanics among veterans | Lung | 5 | 1.6 | NA | |
| Mixed categories | | | | | | | | | |
| Boffetta *et al*[79] 1988 | USA, CO | 1982 | 1982-84 D | 62,800 exposed ACS volunteers | Lung | 174 | 1.2 | (1.0-1.4) | Diesel exhaust exposure based on occupation |
| | | | | | Bladder | 13 | 1.0 | [0.6-1.8] | |
| Van den Eeden & Friedman[96] 1993 | Northern California, CO | 1964-72 | 1964-88 I | 7,049 exposed check-up clinic attenders | Lung | NA | 1.0 | (0.8-1.3) | Self-reported exposure |
| | | | | | Bladder | NA | 1.2 | (0.8-1.7) | |

[a] [illegible] study; RL = record linkage study; DC = death certificate study; CC = case-control study.

[b] D = death; I = incidence of cancer; y. = year(s); ACS = American Cancer Society; w. = workers; [ ] = result derived from the data presented in the paper; NA = not available; Ref = reference category.

[c] RR = relative risk. [d] CI = ( interval

**Figure 4.** Lung cancer risk by cumulative exposure to diesel exhaust among bus garage workers[96]




R referencecategory; RR· relative risk

* Based on score (0, 1, 1.5. 2.25 3.38, 5.06) x years of exposure

on relatively few deaths, a dose-response was found with estimated cumulative diesel-exhaust exposure (Figure 4).

In conclusion, different occupational groups at high exposure to diesel exhaust have been studied. An increased risk of lung cancer has been found quite consistently and the results were more consistent among studies conducted on workers with the highest exposure; the overall RR is in the order of 1.5 to 2.0, and dose-response analyses, in most cases, have shown a positive trend. Although a final conclusion cannot be reached, the increased risk does not seem to be due to tobacco smoking (which was controlled for in a number of the available investigations), nor to other extra-occupational confounders. The groups studied experienced exposures to other agents, including known or suspected carcinogens such as asbestos and mineral oils; however, different exposures occurred in the different industries, and a cautious interpretation of the body of evidence would identify diesel engine exhaust as the most likely cause of the increase. No pattern of excess of bladder cancer risk emerges from cohort studies of workers exposed to diesel engine exhaust.

## Workers exposed to coal tars and related products

Exposure to coal tars, coal tar pitches, and related products occurs in a number of occupational environments. Groups of workers have been studied, for whom PAH exposure is mainly to coal tar and related products. They include workers in tar distillation, shale oil extraction, and workers exposed to creosotes, mainly during wood impregnation. In addition, workers exposed to bitumen in roofing, road paving, and related industries may have substantial exposure to coal tar. Results of relevant cohort studies are summarized in Table 7.

## Tar distillation

Crude coal tar is one of the main by-products of coal carbonization for coke production. Distillation is aimed to produce, from the different fractions of coal tar, different products such as creosote oils, fluxing oils, carbon black oils, and road tars.[6] Tar distillation workers from the UK were found at higher risk of bladder cancer in a early mortality study.'" Results of two cohort studies are available, from the UK[97] and France[98] (Table 7). An increase was found in lung and bladder cancer mortality in the UK but not in the French study.

## Shale oil extraction

Shale oil is the product of thermal processing of raw oil shale; on average, crude shale oils have higher PAH content than crude petroleum oils. Shale oils have been used in the past as fuels and chemical plant feedstocks. They are used currently in only a few countries. Workers in shale oil extraction are exposed to PAHs in gas and vapor, as well as to crude and spent shale oil through dermal contact.[105] (See Tolbert, this issue.)

The carcinogenicity of shale oil was shown in the 1920s among workers from Scotland who experienced a high number of skin and, in particular, scrotal cancers.[106] Cohort studies conducted in this industry are summarized in Table 7. Excesses of skin cancer were confirmed in a study from Estonia[99] and Scotland (only for workers employed before 1953), but not in a US study of 325 workers employed during 1948-69.[107] No increased risk of lung cancer was present in these investigations, nor in a population-based case-control study[108] conducted in seven parishes from an area in central Sweden where shale oil extraction used to be a major industry.

## Creosote exposed workers

Creosotes are one of the main distillate fractions of coal tars and coal tar pitches. PAHs, mostly unsubstituted, generally account for at least 75 percent of creosotes. They have been used extensively as wood preservatives.[6]

As for shale oil, during the first decades of the century, there were reports of skin cancer and, in particular, scrotal cancer among workers exposed to creosotes;[23,109] these reports were confirmed by a mortality analysis of brick-makers from the UK.[24] A study of wood impregnators exposed to creosotes from Norway'"' in which an increased incidence of lip and skin cancer – but no excess of lung cancer – was reported, is summarized in Table 7. A small study from Swedish wood impregnators reported no excess of lung cancer.'"' Creosote exposure was associated with increased risk of multiple myeloma in a case-control study from Sweden.'" (See Dich *et al*, this issue.)

**Table 7.** Cohort studies of workers employed in various industries entailing exposure to coal tar and related products

| Author (ref.) Year | Country | Period of employment | Follow-up, outcome[a] | Study population | Cancer site | Observed cases | RR[b] | (CI)[c] | Comments |
|---|---|---|---|---|---|---|---|---|---|
| Tar distillation workers | | | | | | | | | |
| Maclaren & Hurley[97] 1987 | UK | 1967 | 1967-83 D | 255 M w., 4 plants | Lung | 12 | 1.6 | [0.8-2.8] | |
| | | | | | Bladder | 3 | 4.3 | [0.9-12.5] | |
| Moulin *et al*[98] 1988 | France | 1970-84 | 1970-84 D | 963 w., 1 plant | Lung | 5 | 0.7 | (0.2-1.6) | Excess of oral, pharyngeal and esophageal cancer |
| | | | | | Bladder | 0 | 0.0 | (0.0-4.6) | |
| | | | | | Larynx | 0 | 0.0 | (0.0-1.5) | |
| Shale oil extraction | | | | | | | | | |
| Bogovski[99] 1981 | Estonia | NA | NA, I | 2,003 w. | Lung | NA | < 1.0 | $P > 0.05$ | Excess of skin cancer |
| Miller *et al*[100] 1986 | UK | 1950-62 | 1950-82 D | 6,064 M w. | Lung | 84 | 0.9 | (0.7-1.1) | Excess of skin cancer mortality in workers employed before 1953 |
| | | | | | Bladder | 8 | 0.8 | (0.4-1.7) | |
| | | | | | Kidney | 4 | 1.0 | (0.4-2.7) | |
| Creosote exposed workers | | | | | | | | | |
| Karlehagen *et al*[101] 1992 | Norway | 1950-75 | 1953-87 I | 922 M wood impregnators, 13 plants | Lung | 13 | 0.8 | (0.4-1.3) | Excess of skin cancer incidence |
| | | | | | Bladder | 10 | 1.1 | (0.5-2.0) | |
| Roofers and asphalt workers | | | | | | | | | |
| Hammond *et al*[102] 1976 | USA | 1960 | 1960-71 D | 5,939 M roofer union members | Lung | 99 | 1.6 | [1.3-1.9] | 20+ years union membership; no excess for shorter duration |
| | | | | | Bladder | 13 | 1.7 | [0.9-2.9] | |
| Hansen[103] 1989 | Denmark | 1959-80 | 1959-84 I | 679 mastic asphalt w. | Lung | 27 | 3.4 | (2.3-5.0) | High overall cancer incidence |
| | | | | | Bladder | 5 | 1.6 | (0.5-3.6) | |
| | | | | | Larynx | 3 | 4.4 | (0.9-13) | |

[a] NA = not available; D = death; I = incidence of cancer; M = male; w. = workers; [ ] = result derived from the data presented in the paper.
[b] RR = relative risk. [c] CI = confidence interval.

## Roofers and asphalt workers

Roofers and asphalt workers are exposed to **PAHs** from fumes formed during heating of bitumen.''' Groups of workers exposed to bitumen fumes include roofers, road pavers, asphalt mastic workers, highway maintenance workers, and other miscellaneous and unspecified groups. For example, roofers are exposed to PAH levels in the range 1-100 mg/m$^3$.[112] Table 7 reports the results of two cohort studies of roofers and asphalt workers; other studies have been published based on routine statistics and record linkage studies. The risk of cancer in these occupational groups has recently been reviewed;[113] an increased risk of lung (aggregated RR = **1.2,** 95 percent confidence interval [CI] = **1.1-1.3)** and skin cancer (RR = 1.7, CI = **1.1-2.7)** emerges from such studies, while the risk of bladder cancer is less consistent (RR = **1.2,** CI = **0.9-1.5).** Roofers had, in general, higher cancer risk than other asphalt workers. It is not possible, however, on the basis of available studies, to disentangle the contribution of coal tar fumes from that of tar-free bitumen fumes.

## Carbon black manufacture

Carbon black is a commercial product of fine particulate soot which is manufactured mainly by gas combustion and principally used for printing inks, rubber.products, paints, and in photocopying machines. Carbon black is lower in content of PAHs than soot generated by combustion of fossil fuels or wood. Although most workers exposed to carbon blacks are in the application industries, levels of exposure are higher in the production industry. In this industry, earlier dust levels have been high, and sometimes very high.'''

Cohort studies of carbon black workers are summarized in Table 8. A study of carbon black workers in the US'''.''' showed no increased risk of death from respiratory cancer, but the study has some methodologic problems.[114] A nested case-referent study of cancer cases within the cohort[118] did not show an association between cancer risk and exposure to carbon black. A small excess of lung cancers of borderline statistical significance and an excess of bladder cancer based on few deaths was reported among carbon-black production workers at five factories in the UK.'''

## Carbon and graphite electrode manufacture

Electrodes of carbon or graphite are used in the metal industry. Graphite is composed of crystalline carbon, which occurs naturally, and also is produced industrially from coke and pitch. Graphite dust is low in PAHs since the production process involves heating up to 2,800°C, but workers are exposed to considerable amounts of PAHs during the manufacturing.[120]

Cohort studies of carbon and graphite electrode workers are summarized in Table S. **A** study at 11 US plants showed no excess of lung cancer that could be attributed to **PAHs** or carbon products.''') There was no indication of an increased lung cancer risk at two French graphite and carbon electrode plants. However, a relatively large proportion (around 10 percent) of the cohort was lost to follow-up.[120] **A** small study of Swedish graphite electrode workers''' showed no clear excess of respiratory cancer,, but included few cancer cases. No conclusion therefore can be drawn at present on the presence of an increased risk of lung cancer in this industry. Results on bladder cancer risk are also inconclusive.

## Chimney sweeps

Chimney sweeps are exposed to chimney soot that is rich in PAHs as well as metals such as arsenic, chromium, and nickel. They also may be exposed to asbestos, combustion gases such as sulphur dioxide and carbon monoxide, and to organic solvents used for degreasing. Industrial hygiene measures have been applied to a less extent to this group compared with other workers.

Although cancer risk among chimney sweeps has a distinct place in the history of occupational epidemiology because of the report of scrotal cancer in this group of workers by Pott,[124] relatively few modern epidemiologic studies have been conducted to quantify the risk among currently employed workers. The most informative study,, from Sweden,''' is summarized in Table **8.** An increased risk of cancer of the lung, esophagus, liver, prostate,, kidney, and skin was found. Smaller studies have been conducted in Denmark''' and former Yugoslavia;[126] in both, lung cancer risk was increased, although based on small numbers.

## Calcium carbide production

Calcium carbide is used in the production of acetylene and of calcium cyanamide, used as fertilizer, and in the pyrotechnics industry. Its production involves electrothermal reduction in arc furnaces with Soderberg electrodes. Elevated **PAH** exposure may occur intermittently in several jobs. Workers from one Norwegian plant have been studied[123] (Table **8).** No excess of lung cancer was shown.

## Community-based studies

Exposure to PAHs has been examined in detail in a case-control study conducted during **1982-87** in Montreal, Canada.''' **A** total of **3,730** cases of cancer from 20 sites were administered a detailed occupational questionnaire;

**Table 8**. Cohort studies of workers employed in various industries entailing exposure to soots and other mixtures of polycyclic aromatic hydrocarbons (PAHs)

| Author (ref.) Year | Country | Period of employment | Follow-up, outcome[a] | Study population | Cancer site | Observed cases | RR[b] | (CI)[c] | Notes |
|---|---|---|---|---|---|---|---|---|---|
| Carbon black production | | | | | | | | | |
| Hodgson & Jones[115] 1985 | UK | 1947-80 | 1947-80 D | 1,422 M w., 5 plants | Lung<br>Bladder | 25<br>3 | 1.5<br>2.5 | [1.0-2.2]<br>[0.5-7.3] | No trend in lung cancer with duration of employment |
| Robertson & Inman[116] 1996 | USA | 1935-74 | 1935-94 D | 5 plants (Number of w. not available) | Respiratory | 34 | 0.8 | (0.6-1.1) | Expands the study by Robertson & Ingalls[117,118] |
| Manufacture of carbon electrodes | | | | | | | | | |
| Teta *et al*[119] 1987 | USA | 1974 | 1974-83 D | 2,219 M w. (10+ y) at 11 plants | Respiratory<br>Urinary | 29<br>4 | 0.9<br>[0.9] | (0.6-1.2)<br>[0.3-2.4] | Production of electrodes and other carbon products; non-sign. excess of lymphoma and leukemia; short follow-up |
| Moulin *et al*[120] 1989 | France | 1975 | 1975-85 D | 1,302 M w., 1 plant | Lung<br>Bladder | 7<br>0 | 0.8<br>0 | (0.3-1.6)<br>(0-1.9) | Short follow-up; excess of testicular cancer; higher risk of lung cancer among workers exposed to PAHs. |
| Moulin *et al*[120] 1989 | France | 1957 | 1957-84 D | 1,115 M w., 1 plant | Lung<br>Bladder | 13<br>3 | 1.2<br>1.9 | (0.6-2.0)<br>(0.4-5.7) | No higher risk of lung cancer among workers exposed to PAHs |
| Gustavsson *et al*[121] 1995 | Sweden | 1968-88 | 1969-89 D, I | 901 M w., 1 plant | Respiratory | 3 | 2.5 | [0.5-7.2] | Short latency |
| Chimney sweeps | | | | | | | | | |
| Evanoff *et al*[122] 1993 | Sweden | 1918-80 | 1951-90 D, I | 5,542 M w. | Lung<br>Bladder<br>Kidney | 53<br>4<br>6 | 2.1<br>1.0<br>0.8 | (1.5-2.7)<br>(0.3-2.6)<br>(0.3-1.8) | Excess of esophagus, liver, and prostate cancer; trend of lung cancer risk by duration and latency |
| Calcium carbide production | | | | | | | | | |
| Kjuus *et al*[123] 1986 | Norway | 1953-70 | 1953-83 I | 790 M w. 1 plant | Lung<br>Bladder<br>Kidney | 10<br>7<br>4 | 1.1<br>1.6<br>1.5 | (0.6-2.1)<br>(0.7-3.4)<br>(0.4-3.8) | Excess of colon and prostate cancer |

[a] D = death; I = incidence of cancer; M = male; w. = workers; y. = year(s); [ ] = result derived from the data presented in the paper.
[b] RR = relative risk. [c] CI = confidence interval.

their workplace exposure to 293 agents then was assessed by a team of chemists and industrial hygienists. The method resulted in a rather high proportion of study subjects being assessed as exposed to PAHs. In the analysis, cases of each cancer were compared with cases of all other cancers. Among the agents considered, there were several mixtures of PAHs (Table 9): the risk of lung cancer was increased among subjects exposed to PAHs from wood combustion but not to other groups of **PAHs;** results on bladder and kidney cancer did not show any pattern of risk. Exposure to carbon black in this study was analyzed more in detail.[128] A nonsignificant risk of lung cancer was found among individuals with a high cumulative exposure to carbon black.

Other community-based studies that have reported results for PAH exposure or employment in industries and occupations with high exposure are summarized in Tables 10 (lung cancer), 11 (bladder cancer), and 12 (laryngeal, skin, and renal cancers). In general, results on occupations entailing exposure to diesel exhaust (*e.g.*, bus and truck drivers) have been reported more often than results on other occupations (*e.g.*, steel foundry workers). This fact probably is due to a higher prevalence of employment in the transport industry in the populations where the studies have been conducted. The possibility of publication bias (*i.e.*, selective reporting of positive or significant results) has to be considered seriously in the case of industries and occupations for which results were presented in few studies. On the other hand, the low prevalence of exposure contributes to the lack of statistical significance reached by many studies addressing rare occupations.

Results on lung cancer (Table 10) are similar to those found in cohort studies of corresponding groups of workers: adjustment for smoking did not modify substantially the results of most studies, suggesting that confounding by tobacco smoking is not an important confounder in cohort studies. In only one study – in addition to the one from Montreal described above – was PAH exposure estimated *via* a job-exposure matrix:''' this study suggested a small increase in lung cancer risk only in the highest exposure group.

Case-control studies of bladder cancer (Table 11) tend to report positive results for exposure to PAHs, although statistical significance is rarely reached, given the small number of cases in the different exposure categories. In the two studies that addressed PAH exposure from any occupational source,[162,167] after controlling for aromatic amine exposure, an increased risk was found in the highest category of exposure. Results from case-control studies of laryngeal, skin, and renal cancer (Table **12)** are sparse, and the few strongly positive results reported should be considered with care given the possibility of reporting bias.

## Environmental exposure

Urban air pollution is a complex mixture of chemical compounds, partly adsorbed to particles. **PAHs** in urban air occur both in the gaseous and particle phase, and originate mainly from residential heating and vehicle fuels. Indoor air sources of **PAH** exposure include environmental tobacco smoke, fumes from open fires, kerosene heaters, and cooking.[176] Exposure to environmental tobacco smoke is associated with an increased **risk**

**Table 9.** Results **of** the Montreal (Canada) multisite case-control study on polycyclic aromatic hydrocarbon (PAH) exposure by Siemiatycki[127]

| Exposure | % Exp | Lung cancer | | | Bladder cancer | | | Kidney cancer | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Exp cases | OR | (90% CI) | Exp cases | OR | (90% CI) | Exp cases | OR | (90% CI) |
| Carbon black | 5 | 5 | 1.7 | (0.5-5.7) | 3 | 1.1 | (0.4-3.2) | 1 | 0.9 | (0.2-4.9) |
| Diesel engine emission | 15 | 73 | 1.2 | (0.9-1.7) | 32 | 1.0 | (0.7-1.4) | 14 | 1.3 | (0.8-2.0) |
| Coal comb. products | 5 | 19 | 1.1 | (0.6-1.9) | 4 | 0.3 | (0.1-0.8) | 3 | 1.1 | (0.4-2.9) |
| Wood comb. products | 4 | 15 | 1.9 | (1.0-3.9) | 8 | 1.3 | (0.7-2.7) | 0 | 0 | (0.0-1.7) |
| soot | 9 | 27 | 1.6 | (0.9-2.6) | 4 | 0.4 | (0.2-1.0) | 3 | 1.1 | (0.4-3.1) |
| Cutting fluids, pre-1955 | 7 | 20 | 1.0 | (0.6-1.6) | 13 | 1.3 | (0.8-2.3) | 4 | 1.1 | (0.5-2.7) |
| Asphalt | 3 | 13 | 0.7 | (0.4-1.4) | 8 | 1.1 | (0.5-2.1) | 1 | 0.4 | (0.1-2.2) |
| Coal tar, pitch | 2 | 12 | 0.7 | (0.4-1.5) | 6 | 1.6 | (0.7-3.7) | 1 | 0.6 | (0.1-3.5) |
| PAH from coal | 8 | 35 | 1.0 | (0.7-1.5) | 12 | 0.7 | (0.4-1.1) | 5 | 1.0 | (0.4-2.1) |
| PAH from petroleum | 62 | 394 | 1.1 | (0.9-1.3) | 190 | 0.9 | (0.8-1.1) | 68 | 1.1 | (0.8-1.5) |
| PAH from wood | 4 | 15 | 1.9 | (1.0-3.9) | 8 | 1.3 | (0.7-2.7) | 0 | 0 | (0.0-1.7) |
| PAH from other sources | 20 | 74 | 0.9 | (0.7-1.1) | 46 | 1.1 | (0.8-1.5) | 15 | 1.0 | (0.6-1.6) |
| PAH from any source | 64 | 79 | 1.1 | (0.8-1.4) | 29 | 0.7 | (0.5-1.1) | 8 | 0.8 | (0.4-1.4) |
| Benzo[a]pyrene | 22 | 39 | 1.0 | (0.7-1.5) | 9 | 0.5 | (0.3-0.9) | 7 | 1.3 | (0.7-2.6) |

Abbreviations: Exp = exposed; OR = odds ratio; CI = confidence interval.

**Table 10**. Case-control studies of lung cancer and exposure to polycyclic aromatic hydrocarbons (PAHs)

| Author (ref.) Year | Country, period, gender | No. cases/controls, type of case[a] | Source of controls[b] | Exposure | Exposed cases | OR[c] | (CI)[d] | Notes |
|---|---|---|---|---|---|---|---|---|
| Williams *et al*[129] 1977 | USA, NA, M | 432/1741, I | P (c) | Truck drivers | 22 | 1.5 | $P > 0.05$ | |
| Decouflé *et al*[130] 1977 | USA, 1956-65, M | NA, I | H | Bus drivers | 8 | 1.8 | NA | All categories $P > 0.05$ |
| | | | | Truck drivers | 56 | 1.1 | — | |
| | | | | Car drivers | 8 | 0.8 | — | |
| | | | | Heavy equipment operators | 6 | 0.9 | — | |
| | | | | Cranemen | 7 | 1.1 | — | |
| | | | | Locomotive workers | 12 | 1.0 | — | |
| Blot *et al*[131] 1983 | USA, 1974-77, M | 335/332, D | DC | Steel industry | 80 | 2.2 | (1.5-3.3) | Highest risk for foundry workers and mold makers |
| Milne *et al*[132] 1983 | USA, 1958-62, M | 747/3130, D | DC | Bus drivers | 4 | 3.5 | $P < 0.05$ | |
| | | | | Truck drivers | 23 | 1.6 | $P < 0.05$ | |
| | | | | Taxi drivers | 2 | 1.2 | $P > 0.05$ | |
| | | | | Heavy equipment operators | 15 | 2.1 | $P < 0.05$ | |
| Coggon *et al*[133] 1984 | UK, 1975-79, M | 598/1180, D | DC | Diesel exhaust | 172 | 1.3 | (1.0-1.6) | Based on a job-exposure matrix |
| Damber & Larsson[134] 1985 | Sweden, 1972-77, M | 467/934, D | P, D | Truck drivers | 3 | 5.4 | (0.8-27) | Nonsmokers |
| | | | | | 32 | 6.8 | (3.9-11.6) | Smokers |
| Buiatti *et al*[135] 1985 | Italy, 1981-83, M | 340/817, I | H | Ta i drivers | 20 | 1.8 | (1.0-3.4) | Only positive results reported |
| Coggon *et al*[136] 1986 | UK, 1975-80, M | 312/1221, I | H (c) | Furnace, foundry workers | 22 | 1.6 | $P > 0.05$ | Low response rate |
| Schoenberg *et al*[137] 1987 | USA, 1967-76, M | 763/900, I | ꝑ | Roofers | 13 | 1.7 | (0.7-4.4) | No excess for iron and steel workers or truck drivers |
| | | | | Car drivers | 34 | 1.5 | (0.9-2.5) | |
| Hayes *et al*[138] 1989 | USA, 1976-83, M | 2291/2570, I | ꝑ | Truck drivers | 147 | 1.5 | (1.1-1.9) | 10+ years of employment; including data from Blot *et al*,[139] Correa *et al*,[140] Schoenberg *et al*[137] |
| | | | | Bus drivers | 38 | 1.6 | (0.9-2.8) | |
| | | | | Car drivers | 16 | 1.2 | (0.5-2.6) | |
| | | | | Heavy equipment operators | 14 | 1.3 | (0.6-3.1) | |
| Lerchen *et al*[141] 1987 | USA, 1980-82, M | 333/499, I | ꝑ | Diesel exhaust | 7 | 0.6 | (0.2-1.6) | Diesel exhaust exposure estimated from job-exposure matrix |
| | | | | Diesel mechanics | 5 | 0.6 | (0.2-2.0) | |
| | | | | Roofers | 2 | 0.5 | (0.1-2.7) | |
| Benhamou *et al*[142] 1988 | France, 1976-80, M | 1260/2084, I | H | Motor vehicle drivers | 128 | 1.4 | (1.1-1.9) | |
| Ronco *et al*[143] 1988 | Italy, 1976-80, M | 126/384, D | D | Foundry workers | 18 | 1.1 | (0.6-2.1) | Asphalt workers: no cases, 2 controls |
| Zahm *et al*[144] 1989 | USA, 1980-85, M | 4431/11326, I | ꝑ (c) | Motor vehicle drivers | 186 | 1.5 | (1.2-1.8) | |
| | | | | Mechanics | 106 | 1.3 | (1.0-1.7) | |

*Continued*

**Table 10.** Continued

| Author (ref.) Year | Country, period, ge | der | No. cases/controls, type of case[a] | Source of controls[b] | Exposure | Exposed cases | OR[c] | (CI)[d] | Notes |
|---|---|---|---|---|---|---|---|---|---|
| Boffetta *et al*[145] 1990 | USA, 1969-88, | M | 2584/5099, I | H | Probable diesel exhaust | 210 | 0.9 | (0.8-1.1) | |
| Spinelli *et al*[146] 1990 | Canada, 1950-75, | M | 1687/4702, I | H | Railroad workers<br>Motor transport | 10<br>6 | 0.5<br>1.5 | (0.2-1.0)<br>(1.1-2.1) | Based on routine medical records |
| Burns & Swanson[147] 1991 | USA, 1973 )0, M+F | | 5935/3956, | CR | Drivers<br>Railroad workers<br>Iron foundry | 38<br>14<br>52 | 1.9<br>1.3<br>2.4 | (1.4-2.6)<br>(0.5-3.5)<br>(1.6-3.8) | OR 2.3 for drivers of heavy trucks |
| Yamaguchi *et al*[148] 1992 | Japan, 1989-90 | M+F | 144/6 | H | Steel workers | 2 | 0.9 | (0.5-1.6) | |
| Morabia *et al*[149] 1992 | USA, 1980-89, | M | 739/3228, I | H | Roofers<br>Car drivers | 7<br>7 | 2<br>1 | (0.7-6.2)<br>(0.5-4.1) | Partial overlap with Boffetta *et al*[145] |
| Jockel *et al*[150] 1992 | Germany, period not stated, | M+F | 194/194, I | P | High PAH exposure | 7 | 1.4 | (0.5-4.2) | No risk in intermediate PAH exposure category |
| Notani *et al*[151] 1993 | India, 1986-90, | M | 246/212, I | H | Motor vehicle workers | 18 | 1.5 | (0.7-3.6) | |
| Brownson *et al*[152] 1993 | USA, 1986-91 | | 2 1 21 I | | Ir n t l work m | 3 | 0.6 | (0.2 ) | N m r s d ex-smo rs |
| Keller & Howe[153] 1993 | USA, 1985-87, | M | 252/780, I | Co-c | Motor vehicle drivers | 2 | 1.2 | NA | Nonsmokers |
| Wu-Williams *et al*[154] 1993 | China, 1985-87, | F | 965/959, I | P | Foundry workers<br>Coke oven | 39<br>51 | 1.5<br>1.5 | (0.9-2.6)<br>(0.9-2.5) | |
| Bovenzi *et al*[155] 1993 | Italy, 1979-86, | M | 756/756, D | D | Gas workers<br>Dock workers | 7<br>32 | 1.4<br>2.1 | (0.5-4.5)<br>(1.1-4.0) | |

[a] ca = cases; co = controls; M = male; F = fem le; D = deceased cases/controls; I = incident cases.
[b] P = population controls; (c) = cancer controls H = hospital controls; DC = death certificate controls; CR = cancer registry controls; Co-c = Colon cancer controls.
[c] OR = odds ratio. [d] CI = 95% confidence inte val.

**Table 11**. Case-control studies of bladder cancer and exposure to polycyclic aromatic hydrocarbons (PAH)

| Author (ref.) Year | Country, period, gender | No. cases/controls, type of case[a] | Source of controls[b] | Exposure | Exposed cases | OR[c] | (CI)[d] | Notes |
|---|---|---|---|---|---|---|---|---|
| Williams *et al*[129] 1977 | USA, NA, M | 1≤9/2◎04, I | P (c) | Truck drivers | 3 | 0.8 | $P > 0.05$ | |
| Decouflé *et al*[130] 1977 | USA, 1956-65, M | NA, I | H | Dri e◎ | ≈2 | 1.3 | $P >$ ◎◎3 | |
| Vineis & Masgnani[156] 1985 | Italy, 1978-83, M | 512/596, I | H | Foundry workers | 15 | 0.7 | (0.4-1.3) | |
| | | | | Truck drivers | 16 | 1.2 | (0.6-2.5) | |
| Baxter & McDowall[157] 1986 | UK, 1968-78, M | 1080/2116, D | DC | Gas workers | 11 | 0.8 | $P > 0.05$ | |
| Coggon *et al*[158] 1986 | UK, 1975-80, M | 179/1354, I | H (c) | Furnace, foundry workers | 18 | 1.1 | $P > 0.05$ | Low re◎ ◎e rate |
| Steenland *et al*[159] 1987 | USA, 1960-82, M | 648/1275, I | P | Foundry workers | 7 | 3.5 | NA | Exposure information from city directories; |
| | | | | Drivers | 26 | 0.6 | NA | trend with duration of employment as truck driver |
| Risch *et al*[160] 1988 | Canada, 1979-82, M+F | 826/792, I | P | Aluminum smelting | NA | 1.9 | (0.6-6.4) | OR 5.9 for 10+ years duration |
| | | | | Tar, asphalt | | 1.4 | (0.8-2.7) | OR 2.1 for 10+ years duration |
| Schumacher *et al*[161] 1989 | USA, 1977-83, M+F | 332/685, I | P | Coal tar, pitch | 92 | 1.1 | (0.8-1.5) | |
| Bonassi *et al*[162] 1989 | Italy, 1972-82, M | 121/342, I | P | Truck drivers | 3 | 1.9 | (0.4-8.0) | Adjustment for aromatic amine exposure; |
| | | | | Definite PAH exposure | 25 | 2.1 | (0.8-5.6) | no risk for possible PAH exposure |
| Steineck *et al*[163] 1990 | Sweden, 1990, M | 320/363, I | P | Carbon black | 14 | 2.0 | (0.8-4.9) | Urothelial cancer cases |
| | | | | Coal tar | 26 | 1.0 | (0.6-1.8) | |
| | | | | Coal combustion gas | 27 | 0.8 | (0.5-1.4) | N◎ t◻ d ⊢ith d e |
| | | | | Oil combustion gas | 10 | 0.9 | (0.4-2.3) | |
| | | | | Wood combustion gas | 23 | 1.2 | (0.6-2.3) | |
| | | | | Diesel exhaust | 25 | 1.7 | (0.9-3.3) | Trend with dose |
| | | | | Coal soot | 20 | 0.8 | (0.4-1.5) | |
| | | | | Oil soot | 12 | 0.6 | (0.3-1.9) | |
| | | | | Wood soot | 14 | 0.8 | (0.4-1.7) | |
| Burns & Swanson[164] 1991 | USA, 1973-90, M+F | 2,160/3,979, I | CR | Roofers | 5 | 1.4 | (0.3-5.9) | |
| | | | | Furnace workers | 18 | 1.5 | (0.8-3.2) | |
| | | | | Drivers | 48 | 0.7 | (0.5-1.0) | |
| | | | | Iron foundries | 47 | 1.3 | (0.8-2.1) | |
| Dolin & Cook-Mozaffari[165] 1992 | UK, 1965-80, M | 2,457 | | | | | | |
| Kunze *et al*[166] 1992 | Germany, 1977-85, M | 531/531, I | H | Coal tar | 49 | 1.4 | (0.9-2.3) | |
| | | | | Gas workers | 6 | 6.0 | (0.9-3.9) | |
| | | | | Truck drivers | 51 | 1.8 | (1.1-2.8) | Trend with duration of employment |
| | | | | Foundry workers | 26 | 1.6 | (0.8-2.9) | No trend with duration of employment |
| Notani *et al*[151] 1993 | India, 1986-90, M | 153/212, I | H | Motor vehicle workers | 8 | 1.5 | (0.5-4.5) | |
| Clavel *et al*[167] 1994 | France, 1984-87, M | 658/658, I | H | PAH exposure | 231 | 1.3 | (1.0-1.7) | Trend by average, maximum and cumulative PAH exposure; similar results after exclusion of subjects exposed to aromatic amines, higher risk for smokers |

[a] ca = cases; co = controls; M = male; F = female; D = deceased cases/controls; I = incident cases.
[b] P = population controls; (c) = cancer controls; H = hospital controls; DC = death certificate controls; CR = cancer registry controls; ◎o-c = ◎olon ◎ncer controls.

**Table 12.** Case-control studies of laryngeal, skin and renal cancer and exposure to polycyclic aromatic hydrocarbons (PAH)

| Author (ref.) Year | Country, period, gender | No. cases/controls, type of case[b] | Source of controls[c] | Exposure | Exposed cases | OR[d] | (CI)[e] | Not e |
|---|---|---|---|---|---|---|---|---|
| Laryngeal cancer | | | | | | | | |
| Coggon *et al*[136] 1986 | UK, 1975-80, M | 32/1,501, I | H (c) | Furnace, foundry workers | 3 | 1.3 | $P > 0.05$ | Low response rate |
| Ahrens *et al*[168] 1991 | Germany, 1986-87 | 100/100, I | H | Coal tar, bitumen | NA | 0.6 | (0.2-1.9) | |
| Skin cancer | | | | | | | | |
| Kubasiewicz *et al*[169-170] 1989, 1991 | Poland, 1983-88, M | 376/752, I | H, P | Mineral oils | 99 | 1.5 | (1.1-2.1) | OR for 30+ years of exposure to any PAH 1.6 (1.0-2.6) |
| | | | | Tar | 28 | 1.1 | $P < 0.05$ | |
| | | | | Pitch | 15 | 0.9 | $P < 0.05$ | |
| | | | | Soot | 29 | 1.2 | $P < 0.05$ | |
| | | | | Coke | 32 | 1.3 | $P < 0.05$ | |
| | | | | Any PAH | 216 | 1.1 | $P < 0.05$ | |
| Gallagher *et al*[171] 1996 | Canada, 1983-84, M | 226 (BCC) 180 (SCC)/ 406, I | P | Tar, pitch (BCC) | 32 | 1.2 | (0.7-2.1) | |
| | | | | Tar, pitch (SCC) | 27 | 0.9 | (0.5-1.7) | |
| Renal cancer | | | | | | | | |
| Jensen *et al*[172] 1988 | Denmark, 1979-82, M | 60/180, I | P | Asphalt, tar | 9 | 5.5 | (1.6-20) | |
| | | | | Coke, coal | 8 | 4.0 | (1.2-14) | |
| Sharpe *et al*[173] 1989 | Canada, 1982-87, M+F | 164/161, I | H | Tar, pitch | 9 | 9.3 | (1.2-74) | Low response rate; trend with intensity of exposure to burning coal |
| Partanen *et al*[174] 1991 | Finland, 1977-78, M+F | 338/484, I | P | PAH | 7 | 1.1 | (0.4-3.1) | |
| Mandel *et al*[175] 1995 | 5 countries[a] 1989-91, M+F | 1,732/2,309, I | P | Iron and steel | 113 | 1.6 | (1.2-2.2) | No trend with duration of employment |

[a] USA, Denmark, Sweden, Germany, Australia.
[b] ca = cases; co = controls; I = incident cases.
[c] H = hospital controls; (c) = cancer controls; P = population controls; BCC = basal cell carcinoma; SCC = squamous cell carcinoma; NA = not available.
[d] OR = odds ratio. [e] CI = 95% confidence interval.

Table 13. Estimates, from selected studies, of lung cancer risk following lifelong exposure to 1 ng/m$^3$ of benzo[*a*]pyrene

| Author (ref.) Year | Country | Risk of lung cancer/100,000 | Notes |
|---|---|---|---|
| WHO[195] 1987 | Europe | 9 | Based on results of study of coke oven workers from the USA by Redmond,[197] assuming 0.71% benzo[*a*]pyrene in benzene soluble coke oven emissions |
| Pott[198] 1985 | Germany | 5 | Based on exposure to benzo[*a*]pyrene of German coke oven workers |
| EPA[199] 1984 | USA | 0.1-1.4 | Based on different models on results of studies of coke oven workers |
| Armstrong et *al*[19] 1994 | Canada | 1.0 | Based on risk among aluminum workers |

of lung cancer,'" and PAHs are likely to be among the agents responsible for it.

There are a number of cohort and case referent studies showing an increased lung cancer risk in urban areas; they have been reviewed recently by Pershagen and Simonato[178] and by Hemminki and Pershagen.'" Tobacco smoking has been accounted for either by direct or indirect data. A recent and large cohort study of 151 US metropolitan areas indicated that the lung cancer risk correlated with sulfate levels but not with levels of medium fine particles.'" Sulfates make up a large proportion of particles in the submicron range.

The relevance of these findings in relation to PAH carcinogenicity is debatable. Findings from animal inhalation studies indicate that particles in the submicron range are potent in inducing lung cancer, and that adsorbed PAHs play little role for the carcinogenic effect.[181,182] It is not known if this also pertains to lung cancer development in humans. Epidemiologic data are inadequate to separate the effects of particles and PAHs since both occur concurrently in most situations.

In Xuan Wei county in China, the lung cancer rate among women is among the highest in the country. Three types of cooking and heating fuels are used in this area: smoky coal, smokeless coal, and wood. The excess of lung cancer was correlated strongly with the use of smoky coal.[183] The levels of combustion products, including PAHs, in homes using smoky coal are high, of the same magnitude as in highly polluted occupational environments."* Investigations from China also suggest that fumes from cooking, particularly from rape seed oil, may contribute to an increased risk of lung cancer.[185-187] A case-referent study of risk factors for lung cancer among women in Los Angeles, California (US),""showed a positive association with coal burning in the home during childhood. For a review of cancer risk from indoor air pollution, see Simonato and Pershagen.[189]

Residential wood combustion accounts for a large part of PAHs emitted to the environment in the US, but only for a minor part of the calculated carcinogenic activity, while motor exhausts play a major role.[190-192]

In conclusion, exposure to urban airpollution, of which PAHs are one constituent, seems to be associated with an increased risk of lung cancer in humans. It is not known to what extent this excess can be attributed to exposure to PAHs, to related heterocyclic compounds, to other organic or inorganic compounds, to fine particles, or to a combination of these. Very high levels of PAHs have been demonstrated from burning of smoky coal in Chinese homes. These studies add to the evidence that combustion products from burning of fossil fuels is associated with an increased cancer risk but cannot be used for evaluation of effects of PAHs, neither as a group nor for specific PAHs.

## Animal experimental data

Historical observations of increased risk of skin cancer among chimney sweeps and workers exposed to shale oil and tar pitch were reported already in the 18th and 19th centuries. The first instance in which cancer was induced in experimental animals was in 1912 when Yamagiwa and Ichikawa[193] demonstrated development of skin cancer in rabbits after repeated applications of coal tar. Later, a number of experiments were performed, demonstrating development of skin cancer in mice after dermal application of coal tar products.' Subsequent work was aimed at identifying the chemical composition of coal tar and which substances might be involved in the carcinogenic process. In the beginning of the 1930s, Cook and colleagues demonstrated a carcinogenic activity of a specific constituent of coal tar, benzo[*a*]pyrene.[194] Subsequent research was focused on benzo[*a*]pyrene, but it later was found to be only one of several carcinogenic PAHs in coal tar and that it was a poor indicator of the carcinogenic activity of coal tar, soot, and combustion products.[102,195] A number of specific PAHs have been tested in animal experimental systems, as well as in short-term mutagenicity tests. The evidence for carcinogenicity of individual PAHs from animal experiments is summarized in Table 1.

## Conclusions

Heavy occupational exposure to mixtures of PAHs entails a substantial risk of lung, skin, or bladder cancer. The lung is the major target site of the carcinogenic effect of PAH mixtures and an increased risk of lung cancer is present in most of the industries and occupations reviewed here. The increased risk of skin cancer is restricted to settings entailing substantial dermal exposure. The increase in bladder cancer risk is less consistent, although a pattern may be identified, pointing toward positive results in industries with high PAH exposure from coal tar and pitch, such as aluminum production, coal gasification, and tar distillation. In addition, truck drivers are likely to be at increased risk of bladder cancer. Results on laryngeal and renal cancer are likely to suffer from reporting bias; however, a risk of the latter type of cancer is present in some studies.

A number of PAH mixtures and of industries in which PAH exposure in the past has been high have been classified by IARC as human carcinogens (Table 1). Recent papers on the effects on workers exposed to high levels in the past have provided useful information on the quantification of the risk.[19,21,196] Various estimates of risk of lung, bladder, and total cancers have been proposed. They usually are based on linear non-threshold models and quantify the risk of lifetime exposure (*i.e.*, 40 years' workplace exposure, 40 h per week) to 1 ng/m$^3$ benzo[*a*]pyrene or 1 µg/m$^3$ of benzene soluble compounds and are based on the results of studies on occupationally exposed populations. An important assumption is, therefore, that benzo[*a*]pyrene or benzene soluble compounds are regarded as an index of exposure to PAH mixtures, which may be valid in some situations (*e.g.*, coke oven emissions) but not in others (*e.g.*, diesel engine exhaust). Table 13 summarizes some risk estimates from exposure to 1 ng/m$^3$ benzo[*a*]pyrene: these estimates fall within a range of two orders of magnitude and should be interpreted with caution given the strong dependence on the assumptions on which different models are based. The same populations of workers studied for cancer risk may provide useful data on biomarker-based studies on mechanisms of PAH carcinogenesis in humans.[200]

From the public health perspective, whenever a carcinogenic risk attributable to PAHs has been shown, exposure to this class of compounds should be carefully controlled; and this still may not be the case, in particular in developing countries.[201] The most important current research question, however, is the identification and the quantification of the risk – mainly of lung cancer – from mixtures with relatively low PAH content, such as bitumen fumes and diesel engine exhaust.[192] In these instances, the available epidemiologic evidence is not able to identify with certainty, nor to quantify, a carcinogenic risk, which in any case is expected to be rather low. Future epidemiologic studies need to be larger and less prone to exposure misclassification. The large number of individuals exposed both occupationally and environmentally to such mixtures gives high priority to the investigation of these mixtures.

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