

KIDNEY CANCER

IARC SUPPLEMENT 7

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WORLD HEALTH ORGANIZATION

INTERNATIONAL AGENCY FOR RESEARCH ON CANCER

IARC MONOGRAPHS
ON THE
EVALUATION OF THE CARCINOGENIC
RISKS TO HUMANS

Overall Evaluations of Carcinogenicity: An Updating
of *IARC Monographs Volumes 1 to 42*

SUPPLEMENT 7

LYON, FRANCE

1987

for the first six years of observation (SMR, 438; 180-870). An increase in mortality from respiratory cancer in the exposed group was also evident (SMR, 253; 100-500)¹⁶.

A few case reports of cancer other than hepatocellular in aflatoxin-exposed workers have been published^{1,17-19}.

[B. Evidence for carcinogenicity to animals (*sufficient*)

Aflatoxins produce liver tumours in mice, rats, fish, ducks, marmosets, tree shrews and monkeys after administration by several routes, including the mouth. In rats, cancers of the colon and kidney were also seen¹. Recent studies have extended these findings. In hamsters, aflatoxin B₁ produced cholangiocellular but not hepatocellular tumours²⁰. In mice, aflatoxin B₁ administered orally or intraperitoneally resulted in an increased incidence of lung adenomas^{1,21}. All rats fed 5 mg/kg of diet aflatoxin B₁ for six weeks developed hepatocellular carcinomas²²; neoplastic hepatic nodules were produced in rats by oral administration of a single dose of 5 mg/kg bw aflatoxin B₁²³; rats fed peanut oil containing 5-7 µg/kg aflatoxin B₁ developed parenchymal liver damage but no liver-cell tumour²⁴. Aflatoxin B₁ can induce liver tumours in monkeys^{25,26}; osteogenic sarcoma, adenocarcinoma of the gall-bladder or bile duct and carcinomas of the pancreas were also observed²⁶. Aflatoxin B₁ also induced liver tumours in the subhuman primate tree shrew, *Tupaia glis*²⁷. Intraperitoneal administration of aflatoxin B₁ to pregnant rats induced liver and other tumours in the mothers and in the progeny²⁸. Aflatoxin M₁, a hydroxy metabolite of aflatoxin B₁, produced fewer hepatocellular carcinomas following its oral administration to rats than aflatoxin B₁ given at the same dose level and by the same route²⁹.

C. Other relevant data

In one study, aflatoxin B₁-DNA adducts were excreted in human urine. No data were available on the genetic and related effects of aflatoxins B₂, G₁, G₂ or M₁ in humans³⁰.

Aflatoxin B₁ has been tested extensively for genetic effects in a wide variety of tests *in vivo* and *in vitro*, giving consistently positive results. It induced chromosomal aberrations, micronuclei, sister chromatid exchanges, unscheduled DNA synthesis and DNA strand breaks, and bound covalently to DNA in cells of rodents treated *in vivo*; it was reported to be weakly active in a dominant-lethal mutation assay in mice. In human cells *in vitro*, it induced chromosomal aberrations, micronuclei, sister chromatid exchanges and unscheduled DNA synthesis and bound covalently to DNA. It induced cell transformation in several test systems, and induced chromosomal aberrations, sister chromatid exchanges, mutation, unscheduled DNA synthesis and DNA strand breaks in rodent cells *in vitro*. It induced sex-linked recessive lethal mutations and somatic mutation and recombination in *Drosophila*. In fungi, aflatoxin B₁ was mutagenic and induced gene conversion and mitotic recombination. It was mutagenic and induced DNA damage in bacteria and bound covalently to isolated DNA³⁰.

Aflatoxin B₂ bound covalently to DNA in hepatocytes of rats treated *in vivo*. It transformed Syrian hamster embryo cells and induced sister chromatid exchanges in Chinese hamster cells *in vitro* and induced unscheduled DNA synthesis in rat hepatocytes,

* [Excess risk of kidney cancer has been repeatedly associated with work in coke plants] In one study in the USA, a seven-fold increase in risk was seen for workers employed for five years or more at coke ovens. In single studies, excess risks were reported for cancers of the large intestine and pancreas¹.

The largest study was conducted on a cohort of some 59 000 steel workers in the Pittsburgh area (USA)¹. The study has recently been extended up to 1975 and the dose-response analysis of exposure to coal-tar pitch volatiles and lung cancer reviewed. Coke-oven workers (both white and nonwhite) exhibited a large, statistically significant increase in lung cancer mortality that was strongly associated with duration of exposure to coke-oven fumes and intensity of exposure, as documented by comparing topside- with side-oven experience. [Significantly elevated mortality from prostatic and kidney cancer was also noted, but without clear evidence of an exposure-response relationship. Non-oven workers had no excess of lung cancer but a significantly increased mortality from cancer of the large intestine and pancreas. Cumulative exposure indices of exposure to coal-tar pitch volatiles were calculated and increasing lung cancer risk with increasing estimated exposure was found^{2,3}. A possible causative agent is coal-tar fumes.

B. Other relevant data

An increase in the incidence of sister chromatid exchanges was observed in cultured peripheral blood lymphocytes from 12 nonsmoking coke-oven workers in a steel plant, when they were compared to a group of age-matched controls. Urine samples from nonsmoking coke-plant workers were mutagenic to *Salmonella typhimurium* in the presence of an exogenous metabolic system. In a second study of coke-plant workers, the mutagenic activity in *S. typhimurium* of extracts of urine samples collected after work was not statistically different from that of samples taken before work. Antigenicity against benzo[a]pyrene diol epoxide-DNA adducts has been demonstrated in peripheral blood lymphocytes of coke-oven workers⁴.

References

- ¹IARC Monographs, 34, 101-131, 1984
- ²Redmond, C.K. (1983) Cancer mortality among coke oven workers. *Environ. Health Perspect.*, 52, 67-73
- ³Rockette, H.E. & Redmond, C.K. (1985) Selection, follow-up, and analysis in the coke oven study. *Natl Cancer Inst. Monogr.*, 67, 89-94
- ⁴IARC Monographs, Suppl. 6, 187, 1987

CREOSOTES (Group 2A)

A. Evidence for carcinogenicity to humans (limited)

In a number of case reports, the development of skin cancer in workers exposed to creosotes is described. One study involved a review of 3753 cases of cutaneous epithelioma

★ **[LEAD AND LEAD COMPOUNDS:]****LEAD AND INORGANIC LEAD COMPOUNDS (Group 2B)
ORGANOLEAD COMPOUNDS (Group 3)****A. Evidence for carcinogenicity to humans (*inadequate*)**

Three epidemiological studies of workers exposed to lead and lead compounds were reviewed previously¹: one on smelters and battery workers in the USA, one on workers exposed to tetraethyllead in the USA, and one on copper smelters in the USA; data on the first of these populations have been updated². A study on battery workers in the UK³ is now available, and studies of a US lead smelter⁴ and of a Swedish copper smelter⁵ have also been reported. A statistically significant excess of cancers of the digestive system (21 observed, 12.6 expected) was found in the study of battery workers in the UK, spanning 1925-1976, although the excess was confined to the years 1963-1966³. Significant excesses of stomach cancer (34 observed, 20.2 expected) and of respiratory cancers (116 observed, 93.5 expected) were seen in the study of US battery plant workers², although there was a downward trend in standardized mortality ratio by number of years of employment; in the lead production facilities, the excesses noted for stomach and respiratory cancers were not significant². A nonsignificant excess of respiratory cancer (41 observed, 36.9 expected) was reported in one of the studies of smelters⁴, with 28 observed and 25.7 expected in the group with high exposure to lead. Excesses were also noted in this study for kidney cancer (6 observed, 2.9 expected) and bladder cancer (6 observed, 4.2 expected)⁴. A small study of workers at a Swedish smelter⁵ with long-term exposure to lead demonstrated a nonsignificant excess of lung cancers (8 observed, 5 expected). Two cases of kidney cancer in lead smelter workers have also been reported^{6,7}.

The excesses of respiratory cancer in these studies were relatively small, showed no clear-cut trend with length or degree of exposure, and could have been confounded by factors such as smoking or exposure to arsenic (see p. 100).

A study of workers manufacturing tetraethyllead revealed excesses of respiratory cancer (15 observed, 11.2 expected) and brain cancer (3 observed, 1.6 expected)⁸.

B. Evidence for carcinogenicity to animals (*sufficient* for inorganic lead compounds; *inadequate* for organolead compounds)

Lead acetate and lead subacetate were tested for carcinogenicity by oral, subcutaneous and intraperitoneal administration in rats, lead phosphate was tested by subcutaneous and intraperitoneal administration in rats, and lead subacetate was tested by oral administration in mice. Renal tumours were produced in animals of each species by each route of administration. Rats given lead acetate or lead subacetate orally developed gliomas. Lead subacetate also produced an increased incidence of lung adenomas in mice after its intraperitoneal administration¹. Oral administration of lead dimethyldithiocarbamate (ledate) increased the incidence of reticulum-cell sarcomas in male mice of one strain⁹ but was not carcinogenic to mice or rats in another experiment¹⁰.



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results were due to clusters of workers employed in petroleum refining. The four melanoma cases so employed had the following occupations reported on their death certificates: process worker/blender, engineer, security officer and clerk of works. The odds ratio for brain cancer was significantly elevated among men employed in petroleum refining (odds ratio, 2.9; 95% CI, 1.2–7.0), and four of the seven cases had worked as process operators.

Several studies on parental occupation involving exposure to hydrocarbons and cancer risks in children are reviewed in the monograph on gasoline. One of the studies, described more fully in that monograph, looked specifically at petrochemical occupations and industries and included 499 Texas children who had died from intracranial and spinal cord tumours and 998 controls (Johnson *et al.*, 1987). On the basis of information on paternal occupation extracted from the birth certificate, an odds ratio of 2.0 (95% CI, 0.6–6.2) for children of petroleum refinery workers was observed.

(c) Correlation studies

A survey by county of the average annual age-adjusted lung cancer mortality rates for the years 1950–69 among white men in the USA indicated higher than expected lung cancer rates (1.32 per 100 000), when compared with total US rates, in counties where at least 1% of the population was employed in the petroleum industry (Blot & Fraumeni, 1976). A second survey examined cancer mortality rates in 39 US counties where at least 100 persons were employed in the petroleum industry and the estimated number of workers comprised at least 1% of the county population (Blot *et al.*, 1977). White male residents of the petroleum industry counties had significantly higher average age-adjusted mortality rates for cancers of the lung (rate ratio, 1.15), nasal cavity and sinuses (rate ratio, 1.48), stomach (rate ratio, 1.09), rectum (rate ratio, 1.07), testis (rate ratio, 1.10) and skin (rate ratio, 1.10) than those of control counties with similar demographic characteristics.

Average annual age-adjusted cancer incidence rates for the period 1971–77 among Kaiser Health Foundation plan members living near petroleum and chemical plants in the San Francisco Bay area of the USA were compared with those among other San Francisco Bay area residents who did not live near the plants (Hearey *et al.*, 1980). Site-specific rates for cancer were not elevated for members living near the petroleum and chemical plants.

Average annual age-adjusted cancer incidence rates for the period 1969–77 in Contra Costa County, CA, USA, were examined to determine whether there was any correlation with levels of air emissions from petroleum and chemical plants (Kaldor *et al.*, 1984). The county was divided into four exposure areas, from low to high, based on air levels of sulfur dioxide, hydrocarbons and nitrogen oxides. Among men, significantly increasing incidence rates by level of exposure were found for cancers of the buccal cavity and pharynx, of the stomach, trachea, bronchus and lung, of the prostate and of the kidney. For all cancer sites combined, rates increased by exposure level, and the trend was significant. Among women, significantly increasing trends were noted only for cancers of the buccal cavity and pharynx.

Average annual age-adjusted mortality rates for multiple myeloma by state economic area in the USA were calculated for the period 1950–75 for each sex and race (Blattner *et al.*, 1981). A multiple regression model was used to examine the relationship between the

pattern of increasing mortality was seen by time since first employment or duration of employment for brain tumours among laboratory workers or leukaemia among pipe fitters and boiler makers.

[In a cohort study at the Gulf Port Arthur, TX, refinery, all 15 095 men employed for more than one day between 1 January 1937 and 1 January 1978 were followed for vital status on 1 January 1978. Of these, 972 (6.4%) were lost to follow-up; death certificates were not available for 277 (6.5%) of the 4269 male decedents. The average follow-up was 24.7 years. Expected mortality was determined from rates in the US general population, adjusted for age, race and calendar period. Excesses were seen for cancers of the bone, skin, kidney, Hodgkin's disease, leukaemia and cancer of 'other lymphatic tissue'. Only the result for cancer of the bone was significant. When white, blue-collar employees were evaluated separately, SMRs greater than 1 were observed for cancers of the pancreas, lung, bone, skin, prostate, eye and kidney, and for Hodgkin's disease and leukaemia; however, only the SMR for cancer of the bone was significant (Wen *et al.*, 1983). [The Working Group noted that the ICD8 code cited to describe the category 'cancer of other lymphatic tissue' is probably in error and should have been reported as 202-203, 208.]

SMRs for kidney cancer were examined in a separate publication by time since first employment and duration employed; no trend was observed (Wen *et al.*, 1984a).

A separate analysis with regard to employment status (retired, terminated before retirement age, actively employed) was performed on the white men in this cohort. The number of such employees was 12 526; 730 (5.8%) were lost to follow-up, 724 of whom were in the terminated group in which 88% were followed-up successfully (Wen *et al.*, 1984b). Among those who had been actively employed, nonsignificant excess mortality was observed for cancers of bone and kidney and for leukaemia. Among white men who had terminated their employment at the refinery prior to retirement, there was excess mortality from cancers of the lung, bone, skin (ICD8 172, 173) and prostate and from Hodgkin's disease. Mortality among retired men was elevated for cancers of the lung, bone, skin (ICD8 172, 173), prostate, kidney and brain, leukaemia and cancer of 'other lymphatic tissues' (ICD8 202-203, 208). None of the results was significant. Data were not shown by duration of employment, but retirees were assumed to have worked a minimum of 15 years.

In an interim report on 15 698 male and 1823 female workers employed on 15 June 1935 and followed until 31 December 1979 (4766 deaths; 87% follow-up), nonsignificant excess mortality from brain tumours (malignant, benign and unspecified combined) was observed among men who had been employed for 20 or more years (Wen *et al.*, 1982). No variation in SMR was reported for specific cancer sites by calendar period of employment (Wen *et al.*, 1986). [The Working Group noted that the 882 employees at refinery B in the study of Thomas *et al.* (1980, 1982a,b, 1984) who had died between 1947 and 1977 were included in the studies of Wen *et al.*]

Mortality among 1008 men who had worked at any time between 15 June 1935 and 1 January 1978 in the lubricating oil department at the Gulf Port Arthur, TX, refinery was examined separately (Wen *et al.*, 1985). In this department, lubricating oil was manufactured, and wax was separated from the product using a solvent dewaxing process. A mixture

about two million male employees aged 20–64 years, and the observed number of pancreatic cancer cases in certain occupational groups was compared with corresponding expected numbers based on cumulative incidence in the total cohort. Particular attention was paid to employment in the wood and paper industry, and to occupations involving potential exposure to metals or petroleum products. The observed number of cases was similar to those expected for the occupational groups studied, although a moderate excess in the incidence of pancreatic cancer was noted among gasoline station workers (SMR, 1.6; 90% confidence interval (CI), 1.1–2.3).

[The Working Group noted the lack of detailed exposure data and lack of control of potentially important confounding factors, which render the interpretation of these studies difficult.]

Information on occupation and cause of death from death records of a total of 429 926 men in Washington State, USA, from 1950–79 were used in a proportionate mortality ratio (PMR) analysis standardized for age and year of death (Milham, 1983). Three occupational groups in which exposure to gasoline may occur were studied: service station and garage owners and attendants; fuel oil dealers/workers and motor vehicle mechanics/repairmen. Considering all age groups during the total observation period, increased PMRs ($p < 0.05$) were found for cancer of the oesophagus, bronchus and lung and for non-Hodgkin's lymphomas in motor vehicle mechanics/repairmen. When specific decades were considered, elevated PMRs were also found for lymphatic leukaemia in motor vehicle mechanics/repairmen (1960–69; 8 cases; PMR, 2.8) and bladder cancer in service station and garage owners and attendants (1950–59; 9 cases; PMR, 2.2; and 1960–69; 11 cases; PMR, 1.9).

A PMR analysis was conducted of all white male deaths (37 426) occurring in the state of New Hampshire, USA, between 1975 and 1985 (Schwartz, 1987). Information on occupation, industry and cause of death was abstracted from death certificates, and expected numbers were calculated from the US general population. Total numbers of 453 and 134 deaths were recorded among motor vehicle mechanics and workers in the gasoline service industry, respectively. No significantly elevated PMR was noted for malignant neoplasms among motor vehicle mechanics, although there was a slight increase for leukaemias and aleukaemias (PMR, 1.8). For workers in service stations, the increase in PMR for leukaemia and aleukaemia was significant (PMR, 3.3; $p < 0.05$). Among nine cases of leukaemia observed, five were myeloid, two were lymphoid and two were unspecified.

[The Working Group noted the limitations inherent in PMR analysis. Furthermore, crude exposure information and lack of control for potentially important confounding factors weaken the possibility of causal interpretations.]

(b) Case-control studies

(i) Kidney

In a population-based case-control study, risk factors for renal-cell carcinoma, including occupational exposures, were investigated (McLaughlin *et al.*, 1984). A total of 506 cases diagnosed between 1974 and 1979 were identified from hospitals in the

Minneapolis/St Paul area of Minnesota, USA. An age- and sex-stratified sample of 714 population controls was taken from the same area. In addition, 495 deceased controls were frequency-matched on age at death and year of death to cases who were either deceased (237) or too ill to be interviewed directly (14). Information on smoking, diet and drug use as well as on medical, occupational and residential history was obtained from interviews of study subjects or next of kin. The response rate was 98%. Positive dose-response relationships were noted for smoking and some other exposures. In men, an elevated odds ratio adjusted for age and smoking was associated with occupational exposure to 'petroleum, tar, and pitch products' (1.7; 95% CI, 1.0–2.9). In a subsequent, more detailed analysis of this material (McLaughlin *et al.*, 1985), no clear association with petroleum-related occupations or with employment as a service station attendant was found, although a nonsignificant upward trend in risk with duration of employment was seen in the latter category.

A study was carried out of 92 white men, aged 30–89, with histologically confirmed renal-cell carcinoma and 1588 controls selected from among patients admitted to the same hospital in Buffalo, NY, USA, from 1957 to 1965 (Domiano *et al.*, 1985). Patients with neoplastic disease or with circulatory, respiratory, mental or urogenital disorders were excluded from the control group. Information on smoking habits, diet, occupational history and other variables had been obtained by interview at the time of admission. The age-adjusted odds ratio for the group exposed to gasoline was 0.53, based on four cases. The age-adjusted odds ratio associated with employment in service stations among men with over 20 pack-years of smoking was 1.6 [95% CI, 0.48–5.3].

A case-control study of cancer at many sites was performed in Montréal, Canada, to generate hypotheses on potential occupational carcinogens (Siemiatycki *et al.*, 1987a,b). Each cancer type constituted a case series. About 20 types of cancer were included and, for each cancer site analysed, controls were selected from among cases with cancer at other sites. Job histories and information on possible confounders were obtained by interview from 3726 men aged 35–70 years with cancer diagnosed at one of 19 participating hospitals between 1979 and 1985. The response rate was 82%. Each job was translated into a series of potential exposures by a team of chemists and hygienists using a check-list of 300 of the most common occupational exposures in Montréal. A separate analysis of risks associated with exposure to different petroleum-derived liquids was performed. Cumulative indices of exposure were estimated for a number of occupational exposures. Exposure below the median was considered to be 'nonsubstantial' and that above the median to be 'substantial'.

Among men exposed to aviation gasoline, an increased risk was seen for kidney cancer only (adjusted odds ratio, 3.1; 90% CI, 1.5–6.5). Among subjects classified as having substantial exposure, the odds ratio was 3.9 (1.7–8.8) using a logistic regression analysis taking confounding factors detected in a preliminary analysis into consideration. There was overlap between groups exposed to aviation gasoline and groups exposed to jet fuel resulting from combined exposures (see also monograph on jet fuel).

(ii) *Lower urinary tract*

All residents, aged 20–89 years, of an area in eastern Massachusetts, USA, with newly diagnosed, histologically confirmed transitional- or squamous-cell malignancy of the lower

urinary tract, including the renal pelvis, ureter, bladder or urethra, were ascertained for an 18-month period (Cole *et al.*, 1972). Occupational risk factors were investigated for 461 of the patients with neoplasms and for 485 population controls living in the same area. Of the cases, 94% had a bladder tumour. Data on smoking and occupational histories were obtained by interview. Among men, an age- and smoking-adjusted odds ratio of 1.0 (95% CI, 0.75–1.3) was associated with employment in occupations with suspected exposure to 'petroleum products'; 81% of controls in this exposure category were 'machinists and mechanics'. Specific data on occupations with exposure to gasoline were not provided.

A Danish case-control study of bladder cancer and occupational risk factors consisted of 212 patients (165 men and 47 women), diagnosed in 1977–79 for men and 1979–80 for women at a hospital department serving a predominantly rural area, and 259 population controls (Mommsen *et al.*, 1982, 1983; Mommsen & Aagaard, 1984). Controls were individually matched to cases (men, 1:1; women, 2:1) for sex, age, geographic area and degree of urbanization. Occupational histories were obtained by hospital interviews for cases and by telephone or by mailed questionnaire for controls. The authors compiled a list of occupations thought to involve exposure to oil or gasoline. An odds ratio of 2.7 (95% CI, 1.2–6.2), restricted to men, associated with 'oil or gasoline' work was estimated by logistic regression analysis, without adjustment for potential confounders. Among the exposed men, there were five mechanics, four 'semiskilled workers', three blacksmiths, two printers, two engineers and four workers in other occupations. [An odds ratio of 1.8 was estimated by the Working Group for work as a blacksmith or mechanic, adjusting for smoking habits, nocturia and previous venereal disease. The Working Group noted that information on exposure was obtained differently for cases and controls.]

In a population-based case-control study investigating risk factors for cancers of the renal pelvis, including occupational exposures, a total of 74 cases diagnosed between 1974 and 1979 were identified from hospitals in the Minneapolis/St Paul area of Minnesota, USA (McLaughlin *et al.*, 1983). An age- and sex-stratified sample of 697 population controls was taken from the same area. Information on smoking, diet, drug use and occupational and residential history was obtained by interview with study subjects or next of kin. An age- and smoking-adjusted odds ratio of 2.4 (95% CI, 0.9–6.1) was associated with occupational exposure to 'petroleum, tar, or pitch products'. No further specification was given about exposures or occupations in this group.

As part of the US National Bladder Cancer Study, a population-based case-control study was carried out on occupation and cancer of the lower urinary tract in men in Detroit, MI, USA (Silverman *et al.*, 1983). The cases were diagnosed in 1977–78, and 95% had urinary bladder specified as the primary site. Controls were selected from the general population of the study area in such a way that the age distribution corresponded to that of the case series. Following exclusion of non-whites, of subjects who had never held jobs during at least six months and of refusals, a total of 303 cases and 296 controls remained for analysis. Information on smoking, diet, occupation, residence and other items was obtained by home interviews. Workers in the gasoline service industry had a crude odds ratio of 1.6 (95% CI, 0.8–3.5); after adjustment for smoking, the odds ratio was 1.3. Mechanics and repairmen had an odds ratio of 1.0 (0.6–1.4).

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IARC Monographs on the Evaluation of Carcinogenic Risks to Humans

VOLUME 98

**Painting, Firefighting, and
Shiftwork**

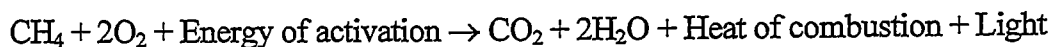


Lyon, France
2000

1.2 Composition of fire smoke

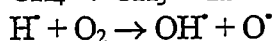
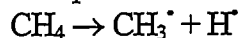
1.2.1 Fire chemistry

Smoke from fires comprises suspended liquid and solid particulate matter, gases and vapours that result from the combustion or pyrolysis of material. There is a very large number of toxic components in smoke (for reviews, see Tuve, 1985; Meyer, 1989; DiNenno *et al.*, 2002; Côté, 2003). The basic form of the overall combustion reaction of organic (carbon-containing) compounds is illustrated by the burning of methane:



Given the appropriate ratio of fuel (wood, solvent, plastic, rubber), oxygen, and combustion temperature, the products of combustion should be only water and carbon dioxide (CO_2).

Complete combustion is approached only under carefully controlled conditions. Uncontrolled or unintentional combustion tends to be “fuel rich” and therefore incomplete. The combustion of methane (CH_4) illustrates the formation of free radicals in an 11-step chain reaction, the first two of which are:



The free radicals formed during combustion are very reactive and side reactions are propagated to yield hundreds of chemical products, and smoke.

Most polymers found in buildings will burn or thermally degrade to simpler monomers. Thermal degradation products include methane, ethane, ethylene, benzene, toluene, and ethylbenzene in addition to the following monomers: ethylene, vinyl chloride, acrylonitrile, tetrafluoroethylene, styrene, methyl methacrylate, ethylene glycol, terephthalic acid, phenol, formaldehyde, hexamethylenediamine, adipic acid, propene, vinyl chloride, vinyl acetate, vinylidene chloride, chloroprene, 1,3-butadiene, ethyl acrylate, ethylene oxide, methylacrylate, urea, phenol, and isoprene.

The burning of plastics typically produces voluminous amounts of soot, together with higher levels of hydrogen cyanide (HCN), hydrochloric acid (HCl) and acrolein ($\text{CH}_2=\text{CHCHO}$) than the burning of materials such as wood, and fossil fuels. More smoke evolves from fires involving aromatic polymers, such as polystyrene, compared to aliphatic polymers, such as polyethylene.

In addition to the chemical agents described above, particulate matter is produced under conditions of incomplete combustion. The particulate matter is an aerosol consisting of condensed phase components of the products of combustion and finely divided carbon particulates that have not undergone combustion but remain suspended in the air. Although the particles themselves are microscopic in size (0.3–1.6 μm), they

rapidly coalesce and thereby become visible. These particles are also adsorbents (similar to activated charcoal) and are an additional vehicle for the transport and inhalation of toxic combustion products. Smouldering yields a substantially higher conversion of fuel to toxic compounds than does flaming, although it occurs more slowly (Ohlemiller, 2002).

1.2.2 *Modern versus pre-modern fires*

[All types of fire release toxic and carcinogenic substances, including benzene, 1,3-butadiene, and formaldehyde.] The focus has generally been on substances having short-term acute effects: carbon monoxide (CO), carbon dioxide, hydrogen cyanide, nitrogen oxides (NO_x), sulfur dioxide (SO₂) and hydrogen chloride. With the increasing use of polymers in building construction and furnishings, there is concern that the burning of these new materials might release large quantities of other highly toxic substances (Austin *et al.*, 2001b).

Combustion and pyrolysis products from newer building materials and furnishings were believed to be more toxic than smoke from fires in buildings built before these materials became commonplace, and more toxic than smoke from wildland fires (Betol *et al.*, 1983; Alarie, 1985). However, many of the carcinogenic products of combustion identified are volatile organic compounds and are common to most burning materials. In a more recent study, no new or unusual non-polar volatile organic compounds (VOCs) were observed in current structural fires compared to the combustion of wood (Austin *et al.*, 2001b, 2001c). Adding polyvinyl chloride (PVC) to the fire load at simulated apartment fires was observed to significantly increase levels of polychlorinated phenols (IARC Group 2B), while polycyclic aromatic hydrocarbon (PAH) levels remained essentially unchanged (Ruokojärvi *et al.*, 2000). The increases in levels of polychlorinated biphenyls (PCBs, 0.021 to 0.031 mg/m³), polychlorinated benzenes (0.002 to 0.010 mg/m³) and I-TEQs [or PCDD/F] (3.5 to 5.4 ng/m³) as products of combustion were not significant [possibly due to the small sample size]. In another study, proportionately higher levels of ethyl benzene (IARC Group 2B) were found at an electronics factory fire when compared to levels at residential and mixed occupancy fires (Austin *et al.*, 2001b).

The emission of combustion products (in mg per kg of material burned) for the same material varies greatly depending on combustion conditions such as ventilation (oxygen supply), temperature, and heating rate. Nonetheless, the relative amounts of the various non-polar VOCs found in smoke at municipal structural fires have been found to be remarkably similar from fire to fire, namely with the same 14 of 144 target compounds, dominated by benzene (IARC Group 1), toluene and naphthalene (IARC Group 2B) (Austin *et al.*, 2001b, 2001c).

1.2.3 *Carcinogens found in smoke at fires*

Table 1.1 lists the agents in Groups 1, 2A, and 2B that have been detected at fires in one or more studies, together with corresponding IARC evaluations, human and animal evidence of carcinogenicity, and for the agents in Group 1, the cancer sites in humans.

Table 1.1. IARC evaluations and cancer sites in humans of chemicals measured at fires

Chemicals measured at fires	Overall evaluation	Human evidence	Animal evidence	Volume	Cancer sites in humans (For Group 1 agents only)
Acetaldehyde	2B	Inadequate	Sufficient	36, Suppl. 7, 71	
Arsenic	1	Sufficient	Limited	23, Suppl. 7	Skin, lung, liver (angiosarcoma)
Asbestos	1	Sufficient	Sufficient	14, Suppl. 7	Lung, mesothelioma, larynx, gastrointestinal tract
Benz[<i>a</i>]anthracene	2B	Inadequate	Sufficient	32, Suppl. 7, 92	
Benzene	1	Sufficient	Limited	29, Suppl. 7	Leukaemia
Benzo[<i>b</i>]fluoranthene	2B	No data	Sufficient	32, Suppl. 7, 92	
Benzo[<i>k</i>]fluoranthene	2B	No data	Sufficient	32, Suppl. 7, 92	
Benzofuran (coumarone)	2B	No data	Sufficient	63	
Benzo[<i>a</i>]pyrene	1	No data	Sufficient	32, Suppl. 7, 92	Lung, bladder, skin
1,3-Butadiene	1	Sufficient	Sufficient	71, 97	Lymphohaematopoietic system
Cadmium	1	Sufficient	Sufficient	58	Lung
Carbon black (total)	2B	Inadequate	Sufficient	65, 93	
Chrysene	2B	Inadequate	Sufficient	3, 32, Suppl. 7, 92	
Dibenz[<i>a,h</i>]anthracene	2A	Inadequate	Sufficient	32, Suppl. 7, 92	
Dichloromethane (methylene chloride)	2B	Inadequate	Sufficient	71	
Ethylbenzene	2B	Inadequate	Sufficient	77	
Formaldehyde	1	Sufficient	Sufficient	88	Nasopharynx; (nasal sinuses and leukaemia, suggested)
Furan	2B	Inadequate	Sufficient	63	

Deschamps *et al.* (1995) investigated all professional male members of the Brigade des Sapeurs-Pompiers de Paris ($n = 830$) who served for a minimum of 5 years as of January 1st, 1977. They were monitored for a 14-year period, with follow-up terminating on January 1st, 1991. Cause-specific mortality rates in these firefighters were compared with national mortality data provided by the Institut National de la Santé et de la Recherche Médicale. To assess the occupational exposure as a firefighter, data were collected on duration of employment as an active duty firefighter (as opposed to office work). These 830 firefighters accrued a total of 11 414 person-years of follow-up. Follow-up appears to have been 100% complete. There were 32 deaths in the cohort during the 14-year period of follow-up. When compared to the average French male, they were found to have a far lower overall mortality (SMR, 0.52 [95% CI: 0.35–0.75]). None of the cause-specific SMRs was significant. However, a greater number of deaths than expected was observed for genito-urinary cancer (SMR, 3.29) [based on one bladder cancer, and one testicular cancer], and digestive cancer (SMR, 1.14).

{ [Baris *et al.* (2001)] conducted a retrospective cohort mortality study among 7789 firefighters in Philadelphia, Pennsylvania, USA, on males employed during 1925–1986. Vital status was ascertained up until 1986. SMRs and 95% CI were calculated with expected numbers of deaths in the United States white male population, as the overwhelming majority of firefighters were white. Occupational exposure histories were abstracted from detailed records maintained by the Philadelphia Fire Department, and a job-exposure matrix was created for each firefighter. To estimate exposure-response relationships, the study used this matrix to compare mortality among groups of firefighters defined by the estimated number of career runs. There were 2220 deaths and a total of 6.2% of the cohort was lost to follow-up. In comparison with white males in the United States, firefighters had a similar mortality from all causes of death combined (SMR, 0.96), and all cancers (SMR, 1.10). Statistically significant excess risks were observed for colon cancer (SMR, 1.51). [The risks of mortality from colon cancer (SMR, 1.68), kidney cancer (SMR, 2.20), non-Hodgkin lymphoma (SMR, 1.72), multiple myeloma (SMR, 2.31), and benign neoplasms (SMR, 2.54) were increased in firefighters with at least 20 years of service.]

{ Bates *et al.* (2001) conducted a historical cohort study of mortality and cancer incidence in all remunerated New Zealand firefighters, who served during 1977–1995. Ascertainment of employment was through a registry maintained by the United Fire Brigades Association of New Zealand. The final cohort comprised 4221 male firefighters. To assess the occupational exposure as a firefighter, data were collected on duration of employment. The 4221 male firefighters in this cohort accrued a total of 58 709 person-years of follow-up. Follow-up was successful in tracing 93.5%. There were 117 deaths up until 1995. Cancer incidence was ascertained during 1977–1996. The SIR for all cancers was 0.95. For most sites, no excesses were observed. The only cancer for which this study provided evidence of an increased risk was

Hansen (1990) performed a study of Danish firefighters employed at the time of the 1970 national census. An analysis was then conducted of 57 deaths (21 from cancer) during 1970–1980 occurring among 886 males who had reported employment as firefighter. Men employed in similar occupations were used as the reference group, and an excess of lung cancer among firefighters over the age of 60 was reported, based on small numbers.

Ma *et al.* (1998) conducted a further analysis of a data set collected by Burnett *et al.* (1994) with additional years of follow-up using 1984–1993 death certificate data from 24 states in the USA. A total of 6607 deaths and 1883 cancer deaths among firefighters were identified based on the occupational titles on death certificates. Race-specific cancer mortality odds ratios (MORs) were calculated with all non-cancer deaths as the reference group. Analyses were adjusted for age and year of death. [Among caucasian male firefighters, significant excesses were observed for cancers of the lip, pancreas, lung, prostate, kidney, and soft-tissue sarcoma and non-Hodgkin lymphoma. Among black male firefighters, significant excesses were observed for cancers of the nasopharynx, colon, prostate, and brain.]

2.3.2 *Descriptive studies with firefighter results.*

There is a large body of descriptive epidemiology carried out for the purpose of occupational cancer and mortality surveillance. The results of these studies are summarized in Table 2.8.

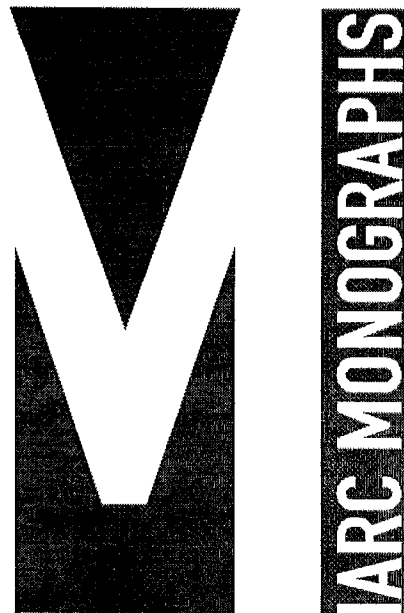
Berg & Howell (1975) examined the risk of colorectal cancer by occupation using death certificate data from the USA and the United Kingdom and observed an excess among firefighters. [The Working Group noted that there was an overlap between the United Kingdom data included in this study and the meta-analysis by Dubrow & Wegman, 1983].

Williams *et al.* (1977) observed excesses of oral cancer, lung cancer, bladder cancer, and non-Hodgkin lymphoma based on the small number of cancers among firefighters that were included in the Third National Cancer Survey, USA. [The Working Group noted that Williams *et al.* (1977) was included in the meta-analysis conducted by Dubrow & Wegman (1983), but was unique in that occupation was ascertained by interview.]

Dubrow & Wegman (1983) summarized the results of ten early USA and United Kingdom studies and reported the results that appeared to be most consistent between the studies. Among those studies that reported results for firefighters, large intestine cancer and multiple myeloma were significantly elevated.

Morton & Marjanovic (1984) examined the incidence of leukaemia by occupation in the Portland–Vancouver metropolitan area in North-western USA, and excesses were observed among firefighters based on very small numbers.

Mortality among a cohort of 293 958 United States military veterans was examined by occupation and industry (Blair *et al.*, 1985). Usual occupation and industry as well as smoking information was determined from questionnaires



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TO HUMANS

International Agency for Research on Cancer



World Health
Organization

synthesis gas (Shadle et al., 2002; Crelling et al., 2005).

The moving-bed gasifiers produce tars, oils, phenols and heavy hydrocarbons, and the concentrations in the gas product are controlled by quenching and water scrubbing. Fluidized-bed gasifiers produce significantly smaller amounts of these compounds because of higher operating temperatures. Entrained-flow gasifiers that operate at even higher temperatures (in excess of 1650 °C) can achieve carbon conversions of more than 99.5%, while generating essentially no organic compounds heavier than methane (Shadle et al., 2002).

In addition to PAHs, workers in coal gasification may be exposed to many compounds, including asbestos, silica, amines, arsenic, cadmium, lead, nickel, vanadium, hydrocarbons, sulfur dioxide, sulfuric acid and aldehydes (IARC, 1984).

2. Cancer in Humans

2.1 Cohort studies of coal-gasification workers

[Occupational exposure during coal gasification was evaluated in *IARC Monograph Volume 92* (IARC, 2010).] There was *sufficient evidence* in epidemiological studies for the carcinogenicity of occupational exposure during coal gasification. [The main body of evidence came from two cohort studies of coal-gasification workers in the United Kingdom (Doll et al., 1972) and Germany (Berger & Manz, 1992), and a case-control study nested within a cohort of French gas- and electricity-production workers (Martin et al., 2000; see Table 2.1, available at <http://monographs.iarc.fr/ENG/Monographs/vol100F/100F-10-Table2.1.pdf>). In all studies an excess of lung cancer in association with coal gasification was found, which was not likely to be explained by

confounding from tobacco smoking. There was evidence supporting a lung-cancer excess in a historical record-linkage study from the United Kingdom (Kennaway & Kennaway, 1947), in two smaller cohorts (Kawai et al., 1967; Hansen et al., 1986), and a large but inadequately reported Chinese study (Wu, 1988).

[In addition to lung cancer, the study from the United Kingdom (Doll et al., 1972) showed an excess of bladder cancer, and the German study (Berger & Manz, 1992) showed an excess of cancers of the stomach and colon-rectum.]

No epidemiological studies of coal-gasification workers have been published since the previous evaluation (IARC, 2010).

2.2 Synthesis

In three large studies, a consistent excess of lung cancer was found in association with occupational exposure during coal gasification. This excess was not likely to be explained by tobacco smoking.

3. Cancer in Experimental Animals

Coal-tars from gas works were previously evaluated in *IARC Monograph Volume 34* (IARC, 1984). As early as 1923 and in subsequent decades, crude coal-tars from gas-works were tested for carcinogenicity by skin application in six studies in mice and two studies in rabbits. These tars induced a high number of skin papillomas and carcinomas in all studies in mice (Deelman, 1923; Kennaway, 1925; Hieger, 1929; Woglom & Herly, 1929; Berenblum & Schoental, 1947; Grigorev, 1960) and in both studies in rabbits (Berenblum & Schoental, 1947; Grigorev, 1960). No new studies have been published since the previous evaluation.

Manufactured gas plant residues (MGP) were previously evaluated in *IARC Monograph*

sweeps: the 1-hydroxypyrene concentrations were in the same wide range as those reported for the chimney sweeps in Germany and Poland (Letzel *et al.*, 1999).

Increased concentrations of polychlorinated dibenzo-*p*-dioxins and polychlorinated dibenzofurans were found in blood lipids of 227 chimney sweeps from Bavaria (Wrbitzky *et al.*, 2001).

2. Cancer in Humans

In IARC Monograph Volume 92 (IARC, 2010), epidemiological studies of cancer in humans were considered to provide *sufficient evidence* for the carcinogenicity of occupational exposure as a chimney sweep. The evidence partly came from a large series of reports on cases of scrotal skin cancer in this occupational group. Soot was first noted as a cause of scrotal cancer in humans by Pott (1775). Many case reports of scrotal and other skin cancers among chimney sweeps appeared subsequently in several different countries (e.g. Earle, 1808; Butlin, 1892; Henry & Irvine, 1936; Henry, 1937, 1946, 1947). A total of 1487 cases of scrotal cancer were reported to the Registrar General for England and Wales from 1911–1935 (Henry, 1937). Of these, 6.9% had occurred in chimney sweeps; the estimated proportion of chimney sweeps in England and Wales in 1921 and 1931 was about 0.06% of all adult males, indicating a large excess of scrotal cancer among workers in this profession.

Evanoff *et al.* (1993) conducted large cohort study of Swedish chimney sweeps and found an excess of cancer of the lung, bladder, oesophagus and haematolymphatic organs; a study from Finland corroborated these findings (Pukkala, 1995). These studies did not include individual adjustments for tobacco smoking, but in the Swedish study an adjustment was made for smoking at the group level, whereas in the Finnish study adjustment was for social class. Both

analyses indicated that confounding from tobacco smoking did not explain the findings regarding lung cancer. In two Danish cohort studies an excess of total cancer was found, but the studies were too small to evaluate individual cancer sites (Hansen *et al.*, 1982; Hansen, 1983; see Table 2.1, available at <http://monographs.iarc.fr/ENG/Monographs/vol100F/100F-16-Table2.1.pdf>).

Pukkala *et al.* (2009) reported on a record-linkage study from the Nordic countries encompassing 15 million people aged 30–64 identified from the censuses in 1960, 1970, 1980/81, and 1990, and followed for cancer in the national cancer registries until 2005. A total of 5498 male chimney sweeps from Denmark, Finland, Norway and Sweden were identified in the cohort. Statistically significant excesses of cancers of the lung, oesophagus, pharynx, bladder, and colon were found. There was no excess of non-melanoma skin cancer. There was not a large heterogeneity in risk between countries, and no adjustment for smoking was made.

The above-mentioned study by Pukkala *et al.* (2009) – which included information from the earlier study (Pukkala, 1995) – adds to the previous evidence of an excess of cancer of the lung, bladder and oesophagus among chimney sweeps. Despite the classical risk for scrotal cancer in chimney sweeps, studies of this occupational group under modern working conditions show no such excesses.

Overall, considering a consistently observed increased lung-cancer risk in several studies, and on the basis of a large cohort study that demonstrated an internal dose–response after group-level adjustment for smoking, there is evidence from human epidemiological studies that lung cancer is causally associated with occupational exposure during work as a chimney sweep. No internal dose–response was observed for bladder cancer in the large Swedish study, and the evidence for an excess bladder cancer among chimney sweeps must be considered as