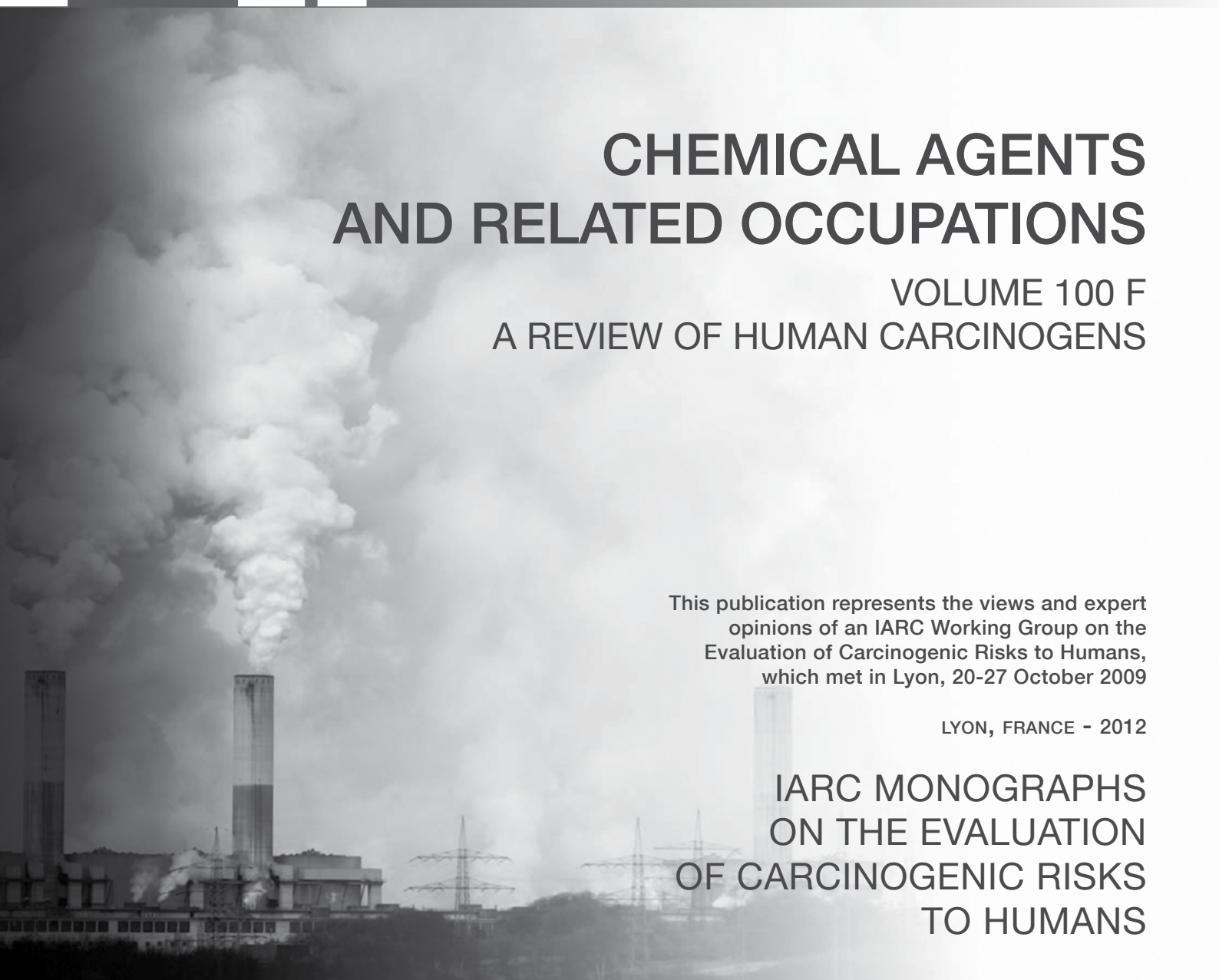
IARC MONOGRAPHS



CHEMICAL AGENTS AND RELATED OCCUPATIONS

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A REVIEW OF HUMAN CARCINOGENS

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IARC MONOGRAPHS ON THE EVALUATION OF CARCINOGENIC RISKS TO HUMANS

International Agency for Research on Cancer
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SOOT, AS FOUND IN OCCUPATIONAL EXPOSURE OF CHIMNEY SWEEPS

Soot was considered by previous IARC Working Groups in 1972, 1984, and 1987 (IARC, 1973, 1985, 1987). Chimney sweeping and other exposures to soot were evaluated in 2005 (IARC, 2010). Since that time new data have become available, which have been incorporated in this *Monograph*, and taken into consideration in the present evaluation.

1. Exposure Data

For hundreds of years, chimneys have been swept with long steel brushes inserted manually into the chimney from the top and from the bottom. Chimney sweeps are exposed to soot, with concurrent exposure to sulfur dioxide and arsenic (Bagchi & Zimmerman, 1980).

Soot is black particulate matter that is formed as a by-product of combustion or pyrolysis of organic (carbon-containing) materials, such as coal, wood, fuel oil, waste oil, paper, plastics and household refuse. The chemical composition and properties of soots are highly variable and depend on the type of starting material and the conditions of combustion. Soots vary considerably with respect to their relative content of carbon, their particle type, size and shape, and the types of organic and inorganic compounds adsorbed onto the particles. In general, soots have a total carbon content of up to 60%, a high content of inorganic material, and a soluble organic fraction. The latter is extractable with organic solvents and consists largely of PAHs and their derivatives. Inorganic constituents may include oxides, salts, metals, sulfur and nitrogen compounds, water, and other adsorbed liquids and gases (IARC, 1985; Watson & Valberg, 2001).

Table 1.1 summarizes several recent studies that investigated exposure of chimney sweeps to PAHs. Knecht *et al.* (1989) assessed exposures in the breathing zone of chimney sweeps during so-called 'dirty' or 'black work' on 11 working days. Samples were taken per 'job category', based on the type of fuel fired: oil fuel, oil/solid or solid fuels. Twenty PAHs were quantified in a total of 115 samples. Higher concentrations were seen in soots that originated from burning of solid fuels. A bio-monitoring study carried out in Germany (n = 93) and Poland (n = 7) in 1995 reported 1-hydroxypyrene concentrations in the urine ranging from below the detection limit (0.1 µg/L) up to 12.8 µg/L (Letzel *et al.*, 1999). Urinary concentrations in the samples from Poland were on average five times higher, most probably due to the fact that coal and wood are used more often as fuels in Poland. The concentrations in urine samples from workers in Germany were relatively low. The use of personal protective devices among this group of 100 chimney sweeps was not mentioned. In an Italian study, Pavanello *et al.* (2000) analysed the urine of 27 chimney

Table 1.1 Concentrations of PAHs in the ambient air and in urine of chimney sweeps

Reference Country Year of study	Job/task	No. of subjects	No. of samples	No. of smokers	PAH	Air levels (μg/m³)		Urinary levels (μmol/mol creatinine)	
						Mean	Range	Median	Range
Knecht *et al.* (1989) Germany NR	Chimney sweeps	NR							
	Oil fuel		37		Benzo[*a*]pyrene	0.36			
	Oil/solid fuel		34			0.83			
	Solid fuel		44			0.82			
Göen *et al.* (1995) Germany	Chimney sweeps	27						0.36	0.05–1.40
Letzel *et al.* (1999) Germany, Poland 1995	Chimney sweeps	100	100	42	1-Hydroxypyrene			[0.25]*	[0.04–4.5]*
	Apprentices, journeymen	79	79	NR				[0.28]*	
	District master	21	21	NR				[0.11]*	
	From Germany	93	93	38				[0.14–0.32]*	
	From Poland	7	7	4				[1.23]*	
	Smokers	42	42	42				[0.39]*	
	Non-smokers, ex-smokers	58	58	0				[0.19]*	
Pavanello *et al.* (2000) Italy NR	Chimney sweeps	27	27	0				Mean	
					1-Hydroxypyrene			0.56	0.04–2.34

* Originally reported in μg/L. Conversion factor: 1 μmol/mol creat. = 1.93 μg/g creat. = 0.013 μmol/L = 2.84 μg/L

NR, not reported

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

limited. The incidence of oesophageal cancer is highly correlated with smoking and alcohol consumption, and in the absence of control for these two factors, the evidence of an association with occupational exposure as a chimney sweep is inadequate. From historical case reports there is sufficient evidence of an increased risk for (scrotal) skin cancer among chimney sweeps.

3. Cancer in Experimental Animals

Coal soot was tested in two experiments in mice by whole-body exposure, but these studies were inadequate for evaluation. Coal-soot extracts applied to the skin of mice produced skin tumours in two studies (IARC, 1985).

In limited studies, subcutaneous implants of wood soot in female rats produced a few local sarcomas. Similar implants in the scrotal sac of rats did not produce tumours. One study of wood-soot extract applied to the skin of mice was uninformative (IARC, 1985).

One study of an extract of fuel-oil soot applied to the skin of mice was uninformative. Extracts of soot from the combustion of oil shale produced skin tumours in mice after dermal application and lung tumours in rats after intratracheal instillation (IARC, 1985).

Extracts of soot from the combustion of heating oil produced from shale oil produced skin tumours in mice in two skin-application experiments (IARC, 1985).

4. Other Relevant Data

4.1 Mechanistic evidence relevant to the carcinogenic hazards from occupational exposure as a chimney sweep

4.1.1 Experimental systems

Experimental studies on soots have been evaluated in *IARC Monograph* Volume 35 and in Supplement 7 (IARC, 1985, 1987). In one study, extracts of soot samples from domestic sources were mutagenic in *Salmonella typhimurium*, both in the presence and absence of an exogenous metabolic system. Extracts of an experimentally-derived soot were mutagenic in forward-mutation assays in *S. typhimurium* and in cultured human lymphoblasts in the presence of metabolic activation (IARC, 1985). Extracts of particulate emissions from wood-combustion induced sister chromatid exchange in Chinese hamster ovary cells, transformation of Syrian hamster embryo cells, and mutation in *S. typhimurium*. An experimentally prepared, intact particulate soot and an extract of this material were both mutagenic in a human lymphoblastoid cell line (IARC, 1987).

Chemical analyses of chimney-soot extracts have identified several polycyclic aromatic hydrocarbons that are genotoxic and carcinogenic in experimental studies. These include benz[*a*]anthracene, benzo[*c*]phenanthrene, benzo[*a*]pyrene, dibenz[*a,h*]anthracene, chrysene, and indeno[1,2,3-*cd*]pyrene (IARC, 1983, 1985, 2010). These polycyclic aromatic hydrocarbons may contribute to the genotoxic and tumorigenic activities of soots.

4.1.2 Humans

The frequency of micronuclei in peripheral B- or T-lymphocytes was studied in 71 Swedish chimney sweeps. Genetic polymorphisms in enzymes involved in metabolic activation were

investigated to explain some of the variation in micronucleus formation. The sweeps did not have higher frequencies of micronuclei in either cell type when the results were adjusted for age and smoking, and there was no association between years of work and micronucleus formation (Carstensen *et al.*, 1993).

The same group of workers was studied for the presence of aromatic DNA adducts and micronuclei, and also genotyped for *CYP1A1* and *GST1*. While no specific DNA adducts were identified, the sweeps had higher total DNA-adduct levels in white blood cells, but the increase was not statistically significant. There were no systematic differences in DNA-adduct patterns between the sweeps and the controls. DNA adducts in sweeps were moderately but statistically significantly correlated with micronuclei in both T- and B-lymphocytes. The correlation between adduct-levels and micronuclei was most marked in T-lymphocytes of individuals lacking the *GST1* gene (Ichiba *et al.*, 1994).

Groups of 45 Swedish chimney sweeps and 49 controls were investigated for micronucleus formation in blood lymphocytes stimulated by phytohaemagglutinin or pokeweed mitogen, and by analysis of lymphocyte subgroups and neutrophilic leukocytes. There were higher frequencies of micronuclei among sweeps than in controls, with both methods of stimulation. The effect on micronucleus formation in lymphocytes was more significant in cells stimulated with pokeweed mitogen, suggesting that the T4 lymphocytes were preferentially damaged by the occupational exposure (Holmén *et al.*, 1994).

Analysis of *anti*-benzo[*a*]pyrene-7,8-diol-9,10-oxide-DNA adducts in a group of 19 chimney sweeps showed that four of them (21%) had adduct levels exceeding the 95 percentile control-subject value (Pavanello *et al.*, 1999a). These higher levels were associated with the lack of GSTM1 activity: three of the chimney sweeps had the *GSTM1* *0/*0 genotype (Pavanello *et al.*, 1999b).

4.2 Synthesis

Extracts of soots contain carcinogenic polycyclic aromatic hydrocarbons and are genotoxic. Based on a small number of genotoxicity studies in exposed humans, there is moderate evidence of a genotoxic mode of action for the carcinogenic hazards associated with occupational exposures as a chimney sweep. The detection of *anti*-benzo[*a*]pyrene-7,8-diol-9,10-epoxide-DNA adducts in the peripheral blood lymphocytes of chimney sweeps suggests involvement of benzo[*a*]pyrene in the genotoxic effect of this exposure in humans.

5. Evaluation

There is *sufficient evidence* in humans for the carcinogenicity of soot as found in occupational exposure of chimney sweeps. Soot, as found in occupational exposure of chimney sweeps, causes cancer of the skin (observed in the scrotum), and of the lung.

Also, a positive association has been observed between exposure to soot as found in occupational exposure of chimney sweeps and cancer of the bladder.

There is *inadequate* evidence in experimental animals for the carcinogenicity of soot.

There is *sufficient evidence* in experimental animals for the carcinogenicity of soot extracts.

Extracts of soots contain carcinogenic polycyclic aromatic hydrocarbons and are genotoxic. Based on a small number of genotoxicity studies in humans there is moderate evidence for a genotoxic mechanism for occupational exposures as a chimney sweep.

Soot as found in occupational exposure of chimney sweeps is *carcinogenic to humans (Group 1)*.

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