INDOOR EMISSIONS FROM HOUSEHOLD COMBUSTION OF COAL

Indoor combustion of coal was considered by a previous IARC Working Group in 2006 (IARC, 2010a). Since that time, new data have become available, these have been incorporated into the *Monograph*, and taken into consideration in the present evaluation.

1. Exposure Data

1.1 Constituents of coal emissions from household use of coal

1.1.1 Types and forms of coal

Coal is a highly variable fuel, which ranges from high heating-value anthracite through various forms of bituminous coal to intermediates in coal formation, viz. lignite and peat. Each of these types of fuel can contain different levels of moisture, non-combustible inorganic material (ash), sulfur, and sometimes significant levels of other impurities, e.g. arsenic, fluorine, lead and mercury.

Raw coal may be used in many forms, from lumps and briquettes to fine powders. Processing of coal may be as simple as forming coal balls or cakes by hand followed by sun-drying, or it may be a sophisticated procedure, blending coal into a uniform mixture with binders to reduce sulfur and particulate emissions and formed into briquettes designed to burn efficiently and cleanly in special stoves.

1.1.2 Constituents of coal emissions

When using small and simple combustion devices such as household cooking and heating stoves, coals are difficult to burn without substantial emission of pollutants principally due to the difficulty of completely pre-mixing the fuel and air during burning. Consequently, a substantial fraction of the fuel carbon is converted to products of incomplete combustion. For example, typical household coal stoves in China and India divert between more than 10% and up to ~30% of their fuel carbon into products of incomplete combustion (Smith *et al.*, 2000; Zhang *et al.*, 2000a).

The products that are formed can be present in the gas phase, the particle phase, or both, depending on their volatility. Hence, they represent a complex mixture of particulate and gaseous chemical species, including carbon monoxide, nitrogen dioxide and particulate matter (PM). Products of incomplete combustion include polycyclic aromatic hydrocarbons (PAHs) and a large number of compounds that are precursor components of photochemical smog, such as aldehydes (Chuang *et al.*, 1992a; Tsai *et al.*, 2003). In addition, many types of coal contain intrinsic

contaminants from their mineral deposits, such as sulfur, arsenic, silica, fluorine, lead or mercury. During combustion, these contaminants are released into the air in their original or oxidized form. In households that use sulfur-rich coals, for example, sulfur dioxide is present at elevated levels. The high temperature of coal combustion leads to emission of large amounts of nitrogen oxides (Zhang *et al.*, 2000a).

The chemical constituents of coal emissions have been reported as individual chemical compounds (e.g. carbon monoxide, benzene, formaldehyde, PAHs), groups of compounds (e.g. total non-methane hydrocarbon, total organic carbon), elements (e.g. carbon, arsenic), or ions (e.g. fluoride, sulfate) (IARC, 2010a). The constituents identified to date are summarized in Table 1.1 by compound class, element and ion, respectively. Selected chemicals that are associated with carcinogenicity are discussed below.

(a) Particles and particle components

Particles emitted from coal combustion are fine and ultra-fine in size (well below 1 μm in diameter) (Kleeman *et al.*, 1999; Hays *et al.*, 2002). Fresh coal emissions contain a large number of ultra-fine particles that condense rapidly as they cool and age. The emissions may include larger particles resulting from suspension of ash and solid fuel debris. Combustion-generated particles and ash/debris particles have different chemical composition and particle size. For this reason, there has been a switch in recent studies from measuring total suspended particles (TSP) to measuring inhalable particles (< 10 μm, referred to as PM_{10}) or respirable particles (< 2.5 μm, referred to as $PM_{2.5}$).

A large number of chemical species are found in combustion-generated particles and many of these are not stable (Rogge *et al.*, 1998). Elemental carbon has a characteristic core onto which many metals and organic compounds can be readily adsorbed or absorbed.

Earlier studies also focused on different solvent extracts of particles (soot) emitted from coal combustion. For example, in Xuanwei County, China, particles released from smoky-coal combustion contained the highest amount of organic compounds extractable with dichloromethane, followed by particles released from anthracite (smokeless) coal combustion (Mumford *et al.*, 1987). Some particles carry stabilized free radicals (Tian, 2005).

Analytical techniques such as ion chromatography can measure chemicals in the extracts of combustion particles in their dissociated form (ions). The most abundant commonly identified ions in coal emissions are shown in Table 1.1.

(b) PAHs and substituted PAHs

Polycyclic aromatic hydrocarbons are formed during incomplete combustion of all carbon-based fuels and organic materials, including coal. At typical ambient temperature, lower molecular-weight PAHs (with 2–4 aromatic rings) are present predominantly in the gas phase while higher molecular-weight PAHs are present predominantly in the particle phase. Because PAHs of higher cancer potency are predominantly present in the particle phase (IARC, 2010a), combustion particles have often been subject to compositional analysis for PAHs and PAH derivatives. A detailed analysis of PAHs in dichloromethane extracts of soot deposits from coal-burning stoves in several homes of Hunan Province, China, has identified 32 individual PAHs ranging in size from three to eight fused aromatic rings. The PAHs found in the soot deposits included 20 benzenoid PAHs, six fluoranthene benzologues, one cyclopenta-fused PAH, one indene benzologue, three oxygenated PAHs and one ring-sulfur-containing aromatic compound (Table 1.1; Wornat *et al.*, 2001). Carcinogenic PAHs, methylated PAHs and nitrogen-containing heterocyclic aromatics were detected in the particles emitted from smoky coal combustion, as typically found

Table 1.1 Constituents of coal emissions, by chemical class

Compound	Species	
Inorganic compounds	CO, SO_2, NO_x	
Hydrocarbons		
Alkanes	C_1–C_{10}	
Alkenes	C_2–C_{10} (including 1,3-butadiene)	
Aromatics	Benzene, Xylene, Toluene, Styrene	
PAHs and substituted PAHs	Acenaphthene Acenaphthylene Acephenanthrylene Anthracene Benz[*a*]anthracene Benzanthrone Benzo[*b*]chrysene Benzo[*a*]coronene Benzo[*b*]fluoranthene Benzo[*k*]fluoranthene Benzo[*b*+*j*+*k*]fluorene Benzo[*a*]fluorine Benzo[*b*]naphtha[2,l-*d*]thiophene Benzo[*pqr*]naphtha[8,1,2-*bcd*]perylene Benzo[*ghi*]perylene Benzo[*a*]pyrene Benzo[*e*]pyrene Chrysene Coronene Cyclopenta[*def*]chrysene-4-one Cyclopent[*hi*]acephenanthrylene Cyclopenta[*cd*]benzo[*ghi*]perylene	Cyclopenta[*bc*]coronene Cyclopenta[*cd*]fluoranthrene Cyclopenta[*cd*]pyrene Dibenz[*a,c*]anthracene Dibenz[*a,h*]anthracene Dibenz[*a,j*]anthracene Dibenzo[*a,e*]pyrene Dibenzo[*e,l*]pyrene Dibenzo[*b,k*]fluoranthene Dicyclopenta[*cd,mn*]pyrene Dicyclopenta[*cd,jk*]pyrene Fluoranthene Fluorene Indeno[123-*cd*]pyrene Naphtho[1,2-*b*]fluoranthene Naphtho[2,1-*a*]pyrene Phenanthrene Picene Pyrene Triphenylene Tribenzo[*e,ghi,k*]perylene 4-Oxa-benzo[*cd*]pyrene-3,5-dione
Aldehydes and ketones	Acetaldehyde Acetone Acrolein Benzaldehyde Butyraldehyde Crotonaldehyde Formaldehyde Hexaldehyde	Isobutyraldehyde Isovaleraldehyde *meta,para*-Tolualdehyde *ortho*-Tolualdehyde Propionaldehyde Valeraldehyde 2-Butanone 2,4-Dimethylbenzaldehyde
Carbon	Elemental and organic	
Metals	Na, Mg, Al, K, Ca, Ti, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, Ga, As, Se, Br, Rb, Sr, Yt, Zr, Mo, Pd, Ag, In, Sn, Sb, Ba, La, Au, Hg, Tl, Pb	
Non-metals	S, P, Si, Cl, Br	
Anions	SO_4^{2-}, Cl^-, NO_3^-	
Cations	NH_4^+, K^+	

From Kauppinen & Pakkanen (1990), Chuang *et al.* (1992a), Miller *et al.* (1994), Zhang & Smith (1999), Watson *et al.* (2001), Wornat *et al.* (2001), Ross *et al.* (2002), Yan *et al.* (2002), Tsai *et al.* (2003), Chen *et al.* (2004, 2005), Ge *et al.* (2004), Lee *et al.* (2005)

in numerous households in Xuanwei County, Yunnan Province, China (Mumford *et al.*, 1987; Chuang *et al.*, 1992a). In the aromatic fraction, coal combustion particles appeared to contain high concentrations and many species of methylated PAHs (Chuang *et al.*, 1992a). However, profiles of specific PAHs and their abundance vary largely, depending on the fuel types and combustion conditions (Tian, 2005).

(c) Hydrocarbons and partially oxidized organic compounds

Hydrocarbons identified in coal emissions include alkanes with 1–10 carbons, alkenes with 2–10 carbons (including 1,3-butadiene) and aromatic compounds (e.g. benzene, xylenes, toluene, styrene) (Table 1.1). Partially oxidized organic compounds identified in coal emissions include alkanols, aldehydes and ketones (carbonyls), carboxylic acids, alkyl esters and methoxylated phenolic compounds (Rogge *et al.*, 1998).

(d) Metals

Some carcinogenic substances were found to be released during the combustion of lignites used in Shenyang City in northern China and smoky coals used in Xuanwei County, China. Lignites from a local Shenyang coal field had very high concentrations of nickel (75 ppm) and chromium (79 ppm) (Ren *et al.*, 1999, 2004) when compared with the levels reported elsewhere in the world (0.5–50 ppm for nickel and 0.5–60 ppm for chromium) (Swaine, 1990). Microfibrous quartz has been found in some smoky coals from Xuanwei County and the resulting coal emissions (Tian, 2005). In Guizhou Province of China and other areas, particles emitted from burning coal have been reported to contain high levels of chemicals like fluorine, arsenic and mercury (Gu *et al.*, 1990; Yan, 1990; Shraim *et al.*, 2003).

1.1.3 Emission factors of some carcinogens

The emission factor of a particular chemical species can be measured as the mass of the species emitted per unit mass of fuel combusted or the mass of the species emitted per unit energy produced or delivered through combustion. Few studies conducted to date have quantified emission factors of common pollutants from household stoves used in developing countries.

The available data for several known human carcinogens (benzene, 1,3-butadiene, formaldehyde and benzo[*a*]pyrene) are summarized in Table 1.2. The sum of PAHs, when ≥14 individual PAHs were measured, is also shown. The cited studies measured the PAHs that are most commonly reported in the literature: acenaphthene, acenaphthylene, anthracene, benz[*a*]anthracene, benzo[*b*]fluoranthene, benzo[*a*]pyrene, benzo[*ghi*]perylene, benzo[*k*]fluoranthene, chrysene, dibenz[*a,h*]anthracene, fluoranthene, fluorene, indeno[1,2,3-*cd*]pyrene, naphthalene, phenanthrene and pyrene.

Burning four types of household coal fuel (honeycomb coal briquette, coal briquette, coal powder and water-washed coal powder) in three different coal stoves generated a very wide range of benzene (2.71–1050 mg/kg fuel) (Tsai *et al.*, 2003) and 1,3-butadiene emission factors (Table 1.2). The range of emission factors for formaldehyde was smaller.

These patterns of emission factors measured under experimental conditions are, in general, consistent with indoor air concentration profiles measured in households using coal stoves.

1.2 Prevalence of use and exposure

1.2.1 China

(a) Use and determinants of use of coal

In China, coal accounts for 70–75% of energy consumption (Millman *et al.*, 2008).

Table 1.2 Emission factors of carcinogenic compounds from household stoves

Compound	Fuel type	Fuel source	Emission factor[a] (mg/kg fuel)	Emission factor[a, b] (mg/MJ)	Reference
Benzene	Coal (4 types)	China	2.71–1050	0.9–390	Tsai *et al.* (2003)
1,3-Butadiene	Coal (4 types)	China	ND–21.3	ND–7.9	Tsai *et al.* (2003)
Styrene	Coal (4 types)	China	ND	ND	Tsai *et al.* (2003)
Formaldehyde	Coal (3 types)	China	2–51	0.9–12	Zhang & Smith (1999)
Acetaldehyde	Coal (3 types)	China	0.8–81	0.3–20	Zhang & Smith (1999)
Naphthalene	Coal briquettes	Viet Nam	44.5		Kim Oanh *et al.* (1999)
Benzo[*a*]pyrene	Coal briquettes	Viet Nam	0.30		Kim Oanh *et al.* (1999)
Benz[*a*]anthracene	Coal briquettes	Viet Nam	0.11		Kim Oanh *et al.* (1999)
Dibenz[*a*,*h*]anthracene	Coal briquettes	Viet Nam	ND		Kim Oanh *et al.* (1999)
Sum of PAHs (≥14 individual PAHs)	Coal briquettes	Viet Nam	102	4.4	Kim Oanh *et al.* (1999)

[a] The values are ranges of the means reported in individual studies.
[b] Denotes milligrams per megajoule of energy delivered to the pot
ND, not detected (below method detection limit)

Although in-home coal use is banned in all Chinese cities, about 10% of urban households still use coal as their primary source of fuel. In 2004, this corresponded to 27 million tonnes of coal. The use of coal is associated with access to local fuel sources and household income; a greater percentage of households in rural areas tend to use coal than in urban areas. In rural regions with ample and inexpensive coal supplies, virtually all households depend upon coal as their domestic fuel. In aggregate, about 40% of all households in rural China rely on coal for heating or cooking (National Bureau of Statistics, 2005).

According to the National Bureau of Statistics (2005, 2006), household energy use from coal (raw coal, washed coal and briquettes) in China represented 21% of total energy use in urban areas, and 12.8% in rural areas. An earlier publication by the Ministry of Agriculture (EBCREY, 1999), by contrast, reported a corresponding value of 34% in rural households.

Occasionally, use of coal for heating does not equate with use of coal for cooking. For example, some households that use coal for heating may use wood for cooking. A recent survey evaluated the specific types of fuels used for cooking throughout rural China. Overall, about 30% of rural households cook with coal. This distribution varied by geographic region, with coal being used for cooking in 19% of homes in Eastern China, 38% in Central China, 27% in Western China, and 7% in North-eastern China (National Bureau of Statistics, 2008).

The use of coal varies largely by geographical conditions and socioeconomic status. Coal and other commercial fuels in generally associated with higher incomes. Where coal resources are highest – predominantly in the north – coal use is highest. In a 2003–04 winter survey of rural areas near Xi'an, 16% and 33% of the households, located in a small village, depended mainly on coal for heating and cooking, respectively (Tonooka *et al.*, 2006). In a study in Shaanxi, Hubei and Zhejiang in China, most households (64%) in Shaanxi reported that they heated with coal in winter, compared to 0.2% in Zhejiang and 28.5% in Hubei (Sinton *et al.*, 2004). Similarly, 70% of the households in Shaanxi used coal for heating, compared to 1.5% in Zhejiang and 6% in Hubei (Sinton *et al.*, 2004).

Table 1.3 Levels of indoor air pollutants from coal emissions in Chinese homes

Pollutant	Urban (mg/m^3)	Rural (mg/m^3)
TSP	0.21–2.8	0.01–20
PM_{10}	0.16–2.7	0.12–26
CO	0.58–97	0.7–87
SO_2	0.01–5.8	0.01–23
NO_x	0.01–1.8	0.01–1.7
B[*a*]P	0.3–190	5.3–19000

B[*a*]P, benzo[*a*]pyrene; PM, particulate matter; TSP, total suspended particles
From Sinton *et al.* (1995)

(b) Pollutant levels and exposures

Since the 1980s, many studies of indoor air quality in China have been published, measuring particulate matter, benzo[*a*]pyrene, sulfur dioxide, nitrogen oxide and carbon monoxide (Table 1.3). The three-province survey (Sinton *et al.*, 2004) found that in summer when stove use was dominantly for cooking, households that used coal experienced high particulate (PM_4) levels, and traditional stoves emitted higher particulate levels than improved stoves.

Kitchens may not be the sites with the highest average particulate matter levels. In the three-province study (Sinton *et al.*, 2004), those households that used coal had higher particulate levels in living rooms than in kitchens; heating, smoking and perhaps other factors can result in levels over time that are higher in living rooms than in kitchens, despite the peaks associated with cooking. In another study (Jin *et al.*, 2005), differences between rooms with and without stoves were small.

A large number of studies monitored benzo[*a*]pyrene in households in Xuanwei County, Yunnan Province, others reported measurements taken elsewhere (IARC, 2010a). Indoor levels of benzo[*a*]pyrene were in a range spanning four orders of magnitude, from 1 ng/m^3 to over 10 000 ng/m^3 in some of the studies in Xuanwei County, in which bituminous coal led to much higher indoor levels than anthracite coal. In studies performed in other parts of the country, household averages rarely exceeded 40 ng/m^3.

A recent study examined winter levels of PM_4 in households in Guizhou and Shaanxi, in areas where coal in contaminated with fluorine, and found that average levels in kitchen and living areas were from about 200 µg/m^3 to 2000 µg/m^3 (He *et al.*, 2005).

1.2.2 Ouside China

There is little literature about coal use outside China.

A few measurements of particulate size fractions have been made in households of peri-urban Gujarat (in western India) that use coal (Aggarwal *et al.*, 1982; Raiyani *et al.*, 1993). During cooking, the proportion of total suspended particulates < 9 µm in aerodynamic diameter was 92%, and 70% were particles < 2 µm in aerodynamic diameter. Particulate PAH size distributions measured in these same indoor environments showed that in houses that used coal, 76% of the PAH mass was contained in particulates < 2 µm aerodynamic diameter (Raiyani *et al.*, 1993).

In one study, conducted in winter on households in urban Santiago in Chile, levels of PM_{10} were 250 µg/m^3 in the kitchen, and 295 ppb SO_2 (Cáceres *et al.*, 2001).

2. Cancer in Humans

The Working Group evaluated studies that focused on exposure to coal emissions only without exposure to other solid fuels.

2.1 Studies in China

2.1.1 Cancer of the lung

(a) Overview of studies

Since the previous *IARC Monograph* (IARC, 2010a), two new case–control studies (Galeone *et al.*, 2008; Lan *et al.*, 2008) and a re-analysis of a previously published cohort (Hosgood *et al.*, 2008) were published.

A retrospective cohort study carried out in Xuanwei, China, evaluated the association between lung cancer risk and in-home coal use (Lan *et al.*, 2002). Among lifetime smoky coal users, households that changed to stoves with chimneys experienced a significantly decreased risk of lung cancer in both men and women compared to individuals that used fire pits. Reduction in lung cancer mortality was also observed among lifetime smoky coal users that changed to portable stoves compared to those that used fire pits, both in men and women (Hosgood *et al.*, 2008). Both analyses were adjusted for average tons of fuel used annually, years of tobacco smoking, years of cooking, history of spousal lung cancer, family history of lung cancer, as well as other potential confounders.

Several case–control studies (Koo *et al.*, 1983; Xu *et al.*, 1989; Wu-Williams *et al.*, 1990; Liu *et al.*, 1991; Huang *et al.*, 1992; Sun, 1992; Ger *et al.*, 1993; Lan *et al.*, 1993; Liu *et al.*, 1993; Dai *et al.*, 1996; Du *et al.*, 1996; Lei *et al.*, 1996; Luo *et al.*, 1996; Shen *et al.*, 1996; Wang *et al.*, 1996; Ko *et al.*, 1997; Shen *et al.*, 1998; Zhong *et al.*, 1999; Lan *et al.*, 2000; Zhou *et al.*, 2000; Le *et al.*, 2001; Kleinerman *et al.*, 2002; Galeone *et al.*, 2008; Lan *et al.*, 2008), have evaluated the association of lung cancer risk with in-home coal use in China (Table 2.1 available at http://monographs.iarc.fr/ENG/Monographs/vol100E/100E-08-Table2.1.pdf). Four evaluated the effects by histology of lung cancer (Ger *et al.*, 1993; Luo *et al.*, 1996; Shen *et al.*, 1996; Le *et al.*, 2001). While these studies assessed exposure with different questionnaires and methodologies, in the aggregate, almost every study found in-home coal use to be associated with lung cancer risk in China by some measure of exposure. Notably, lung cancer has been associated with years of coal stove use (Xu *et al.*, 1989; Wu-Williams *et al.*, 1990; Dai *et al.*, 1996), years of kang use (heated by coal) (Wu-Williams *et al.*, 1990; Dai *et al.*, 1996), years of cooking or heating with coal as the fuel source (Xu *et al.*, 1989; Wu-Williams *et al.*, 1990; He *et al.*, 1991; Liu *et al.*, 1991 Lan *et al.*, 2002; Hosgood *et al.*, 2008), amount of coal used (Lan *et al.*, 1993; Lan *et al.*, 2000; Kleinerman *et al.*, 2002; Hosgood *et al.*, 2008), and quality of ventilation in homes that use coal (Liu *et al.*, 1993; Ko *et al.*, 1997; Le *et al.*, 2001). The studies were from different areas in China, including northern, southern, Xuanwei and the rest of central China, and Taiwan, China.

(b) Exposure–response evidence

All studies reporting an exposure–response association between coal use and lung cancer controlled for tobacco smoking. Lan *et al.* (1993) reported a significant exposure–response relationship according to the amount of smoky coal used per year in Xuanwei, China (P for trend < 0.001). Duration of cooking with coal was significantly and positively associated with the risk for lung cancer among women (Lan *et al.*, 2002; Hosgood *et al.*, 2008). In Gansu, individuals who use coal as their main fuel source were also found to experience higher lung cancer risk, with a significant exposure–response relationship among men (P for trend = 0.04) (Kleinerman *et al.*, 2002) but not among women. In northern China, lung cancer risk increased in

an exposure–response manner according to the duration of use of heated kang (Xu *et al.*, 1989). Galeone *et al.* (2008) constructed an index of indoor air pollution due to solid fuel use (mainly coal) and found a significant exposure–response relationship.

(c) Type of coal

Various smoky coal types were associated with a range of lung cancer risks with substantial heterogeneity ($P < 0.001$) in Xuanwei, China (Lan *et al.*, 2008). The risk for lung cancer ranged from 24.8 (95%CI: 12.4–49.6) for using smoky coal from the Laibin mine to 0.7 (95%CI: 0.2–3.1) from the Yangliu mine, compared to use of smokeless coal or wood. In this study, indoor benzo[*a*]pyrene concentrations were highly correlated with the risk for lung cancer.

(d) Histology

In-home coal use has been associated with both adenocarcinomas and squamous-cell carcinomas of the lung (Ger *et al.*, 1993; Luo *et al.*, 1996; Shen *et al.*, 1996; Le *et al.*, 2001); however these studies are based on small sample sizes.

(e) Population characteristics

Most studies have focused on women, as they tend to spend more time at home and consequently have greater exposures to coal combustion products than men. Six studies enrolled only women (Dai *et al.*, 1996; Wang *et al.*, 1996; Ko *et al.*, 1997; Shen *et al.*, 1998; Zhong *et al.*, 1999; Zhou *et al.*, 2000), of which three (Dai *et al.* 1996; Wang *et al.*, 1996; Shen *et al.*, 1998) were also restricted to non-smokers. [Fuel type was not specified in Zhou *et al.* (2000) but both cases and controls had 'high level' of exposure to coal emissions.] In-home coal was associated with lung cancer risk in three studies (Dai *et al.*, 1996; Shen *et al.*, 1998; Zhong *et al.*, 1999). In study populations including men, the risks associated with in-home coal use was generally greater among women than among men (He *et al.*, 1991; Liu *et al.*, 1991; Liu *et al.*, 1993).

(f) Interactions

The most notable genetic interaction with in-home coal use involves the *GSTM1* null genotype. A meta-analysis found the *GSTM1* null genotype to be associated with lung cancer risk (OR, 1.64; 95%CI: 1.25–2.14; 4 studies) among studies carried out in regions of China that use coal for heating and cooking (Hosgood *et al.*, 2007).

2.2 Studies outside China

2.2.1 Indoor exposures

Two case–control studies that adequately separated the effect of coal from wood or other biomass products evaluated the association of coal use for heating or cooking and cancers of the lung, hypopharynx and larynx (Lissowska *et al.*, 2005; Sapkota *et al.*, 2008; Table 2.2 available at http://monographs.iarc.fr/ENG/Monographs/vol100E/100E-08-Table2.2.pdf).

In a multicenter study conducted in seven European countries (Czech republic, Hungary, Poland, Romania, the Russian Federation, Slovakia and the United Kingdom), Lissowska *et al.* (2005) evaluated the association of heating and cooking with solids fuels with risk of lung cancer. The study included 2861 cases and 3118 matched population-based controls. In an analysis that evaluated coal use specifically, ever use of coal (either as a cooking or heating fuel) was not significantly related to the risk of lung cancer, after adjusting for tobacco smoking and other factors.

Sapkota *et al.* (2008) conducted a multicenter hospital-based case–control study in India to investigate lifetime fuel usage as risk factors for three different cancer types (1042 hypopharyngeal/laryngeal and 635 lung) and 718 matched controls. Compared with never users, among

those who always used coal for cooking the odds ratios for cancer was 1.92 (95%CI: 0.67–5.54) for the hypopharynx, 2.42 (95%CI: 0.94–6.25) for the larynx, and 3.76 (95%CI: 1.64–8.63) for the lung after adjusting for tobacco smoking and other factors. Among never smokers, the risk for lung cancer was 7.46 (95%CI: 2.15–25.94; based on 11 cases). The risk increased with years of coal usage for cancers of the hypopharynx (*P* for trend = 0.06), larynx (*P* for trend = 0.05) and lung (*P* for trend < 0.01).

2.2.2 Ambient coal smoke exposure from ecological studies

Two ecological studies evaluated the association of coal emissions with lung cancer. A study conducted in Dublin (Kabir *et al.*, 2007) evaluated the impact of coal burning (black smoke outdoor concentration) on lung cancer mortality using data from 1981 to 2000. In 1990 the use of coal was banned in Dublin. A strong decline in black smoke was noted between the pre- and post-ban periods, from 46.4 μg/m^3 in 1981–90 (pre-ban) to 18.2 μg/m^3 in 1991–2000 (post-ban). After adjusting for age, sex and smoking, annual mean black smoke concentration was not related to annual death rates from lung cancer. [The Working Group noted that the post-ban period was too short to see any changes in lung cancer mortality.]

Another study evaluated the impact of industrial installations involving combustion of coal and other fuels on the mortality due to lung, laryngeal and bladder cancer in the population of 8073 Spanish towns in 1994–2003 (García-Pérez *et al.*, 2009). Mortality data were obtained form the National Statistics Institute and population exposure was evaluated by the distance of the centroid of the town to the closest combustion facility. Installations using coal only as the fuel source, within a vicinity of 5 km, was related to an increased risk for lung cancer overall (OR, 1.10; 95%CI: 1.02–1.18) with higher risk in men (OR, 1.13; 95%CI: 1.05–1.22), for bladder cancer overall (OR, 1.18; 95%CI: 1.01–1.37) and 1.22 (95%CI: 1.03–1.44) in men and for laryngeal cancer (OR, 1.46; 95%CI: 1.21–1.77 in men) after adjusting for smoking and sociodemographic variables. The authors noted that there was no other industry nearby that could bias the risk estimates.

2.3 Synthesis

Several case–control studies from China and a study from India have demonstrated an increased risk for lung cancer associated with exposure to emissions from coal burning, after accounting for potential confounders, including smoking and in analyses restricted to non-smokers. There were higher risks in women than men, and exposure–response relationships were found. A European case–control study did not find a significant effect of indoor coal use for cooking or heating. An ecological study from Europe provided further evidence of an increased risk for lung cancer in the vicinity of coal plants. No major effect was observed on lung cancer mortality after the ban of coal use in Dublin, probably because there was insufficient latency to see a change. Other cancer sites have been studied (larynx, bladder, hypopharynx); however there is not enough evidence to evaluate carcinogenicity with exposure to coal emissions.

In conclusion, there is convincing evidence based on multiple studies, mainly from different parts of China and one in India, that indoor emissions from household combustion of coal (used for heating and cooking) are causally linked to lung cancer in humans.

3. Cancer in Experimental Animals

Soots have been evaluated previously (IARC, 1985, 2010a).

Coal soot has been tested for carcinogenicity to mice by whole body exposure and coal emissions have been tested by inhalation in both mice and rats. Extracts of coal soot and smoke particles have also been tested by intratracheal, dermal, and subcutaneous administration to mice. A veterinary case–control study has studied sinonasal cancer in pet dogs from households with indoor use of coal.

3.1 Coal emissions and coal soot

3.1.1 Whole-body and inhalation exposure

In one study, whole-body exposure of Buffalo strain mice to coal soot mixed with bedding caused eight lung adenocarcinomas in 100 exposed mice compared to one in 50 controls [not significant] (Seeling & Benignus, 1936). In a second study, no increase in lung or skin tumours resulted from repeated exposure of mice to a 'moderate' cloud of soot in an inhalation chamber for a period of one year (Campbell, 1939).

Inhalation exposure to coal emissions for periods of 15 to 24 months caused markedly increased incidence of lung cancer in two studies in mice (Liang *et al.*, 1988; Lin *et al.*, 1995) and one study in rats (Liang *et al.*, 1988; Table 3.1). Squamous cell lung carcinomas occurred in exposed animals in one of the studies in mice and the study in rats (Liang *et al.*, 1988).

3.2 Extracts of coal soot

3.2.1 Intratracheal administration

Intratracheal administration of an aqueous detergent extract of coal soot once every 10 days for about 100 days increased lung adenocarcinoma incidence (29/72 versus 7/43, $P < 0.01$) in Kumming mice compared to controls after 18 months (Yin *et al.*, 1984).

3.2.2 Dermal application

Coal-soot extracts applied repeatedly to mouse skin increased the incidence of skin tumours including squamous cell carcinomas in four studies (Passey, 1922; Passey & Carter-Braine, 1925; Campbell, 1939; Mumford *et al.*, 1990).

Smoky coal-soot extracts applied to mouse skin followed by repeated dermal applications of the skin tumour promoter 12-*O*-tetradecanoylphorbol-13-acetate initiated skin tumours in mice in two studies (Liang & Wang, 1987; Mumford *et al.*, 1990; Table 3.2).

3.2.3 Subcutaneous injection

In one study, a low incidence (17%) of injection-site subcutaneous tumours [histology not specified] developed after 55 weeks in 30 (C57BpxCBA)F_1 male mice given five subcutaneous injections of extracts of brown coal. No tumours were observed in controls (Khesina *et al.*, 1977).

In two experiments, repeated subcutaneous injections for 10 weeks of extracts of coal soot collected from Xuanwei County, China, increased the incidence of lung cancer (adenocarcinomas, adenosquamous and squamous cell carcinomas) in Kumming mice after 10 months (Liang *et al.*, 1983, 1984; Table 3.3).

3.3 Veterinary epidemiology

A case–control study in pet dogs found that indoor use of coal was a strong risk factor for sinonasal cancers (adjusted odds ratio, 4.24; 95% confidence interval: 1.30–16.52) (Bukowski *et al.*, 1998).

Table 3.1 Carcinogenicity studies of inhalation exposure to coal emissions in experimental animals

Species, strain (sex) Duration Reference	Dosing regimen, Animals/group at start	Incidence of tumours	Significance	Comments
Mouse, Kunming (M, F) 2 yr Lin *et al.* (1995)	Control air Smoke, 60 g coal, daily Smoke, 105 g coal, daily Smoke, 160 g coal, daily 30 M + 30 F	Lung cancer, 3.6% Lung cancer, 9.4% Lung cancer, 12.8% Lung cancer, 24.3%	– NS $P < 0.05$ $P < 0.05$	Purity NR; Age at start NR (weight, 13 ± 1 g) Amounts of coal chosen to simulate normal indoor air conditions for humans in Harbin City, China Exposure assumed to be daily exposure
Mouse, Kunming (M, F) 15 mo Liang *et al.* (1988)	Control air Coal smoke 113 M + 58 F (control) 160 M + 50 F	29/171, total lung cancer (all adenocarcinomas) 188/210, total lung cancer (including: 119/210, adenocarcinoma; 45/210 adenosquamous carcinoma; 24/210 squamous-cell carcinoma)	– $P < 0.001$	Age at start NR (weight, 21 g) Total suspended particles, 0.91 mg/m^3 (control air) vs 14.38 mg/m^3 (coal smoke). B[*a*]P, 0.15 µg/m^3 (control air), 50.5 µg/m^3 (coal smoke) Bituminous coal incompletely burned to simulate normal indoor air in Xuanwei County, China
Rat, Wistar (M, F) 19 mo Liang *et al.* (1988)	Control air Coal smoke 59 M + 51 F (control) 62 M + 63 F	1/110, total lung tumours (1 adenocarcinoma) 84/125, total lung carcinomas (all squamous cell carcinomas)	– $P < 0.001$	Age at start NR (weight, 105 g) Total suspended particles, 0.91mg/m^3 (control air) vs 14.38 mg/m^3 (coal smoke). B[*a*]P, 0.15 µg/m^3 (control air), 50.5 µg/m^3 (coal smoke) Bituminous coal incompletely burned to simulate normal indoor air in Xuanwei County, China

B[*a*]P, Benzo[*a*]pyrene; F, female; M, male; mo, month or months; NR, not reported; NS, not significant; yr, year or years

Table 3.2 Carcinogenicity studies of dermal exposure to coal-soot extracts in mice

Species, strain (sex) Duration Reference	Dosing regimen, Animals/group at start	Incidence of tumours	Significance	Comments
Mouse, SENCAR (F) 77 wk Mumford *et al.* (1990)	0.2 ml, Acetone twice/wk, 52 wk (control)	No skin carcinomas at 52 wk (100% survival) or at 77 wk (78% survival)	–	Exposure to organic extracts of indoor air particles from burned smoky coal in Xuanwei County, China. B[*a*]P content, 19.3 μg/m^3 air
	1 mg smoky coal extract, twice/wk, 52 wk	38% carcinomas[a] (1.3 per tumour bearing mouse) at 52 wk (88% survival), 88%[a] (1.1 per tumour bearing mouse) at 77 wk (10% survival)	NR [significant]	
	40 animals			
Mouse, SENCAR (F) 27 wk Mumford *et al.* (1990)	Initiation with smoky coal extract, followed one wk after by promotion with TPA (2 μg/mouse in 0.2 ml acetone, twice/wk, 26 wk). Initiation doses:			Exposure to organic extracts of indoor air particles from burned smoky coal in Xuanwei County, China. B[*a*]P content, 19.3 μg/m^3 air Tumour incidence and numbers estimated from graphical presentation of data.
	0 mg	15% with skin papillomas	–	
	1 mg	80% with papillomas	NR [significant]	
	2 mg	90% with papillomas	NR [significant]	
	5 mg	> 90% with papillomas	NR [significant]	
	10 mg	> 90% with papillomas	NR [significant]	
	20 mg	100% with papillomas	NR [significant]	
	40 animals			
Mouse, Kunming (M) 26 wk Liang & Wang (1987)	Initiation with 0, 1, 5, 10, 20 mg smoky coal soot; promotion with TPA (repeated application of 2 μg/mouse)	Skin tumours: 10, 25, 54, 60, 40%	[$P < 0.05$], 5–20 mg coal soot	Age at start NR (weight, 28.7 g) Extracts of smoky coal soot from Xuanwei County, China
	40 animals			

[a] mainly squamous cell carcinomas

B[*a*]P, benzo[*a*]pyrene; F, female; M, male; NR, not reported; TPA, 12-*O*-tetradecanoylphorbol-13-acetate; wk, week or weeks

Table 3.3 Carcinogenicity studies of subcutaneous injections of coal soot extracts in mice

Species, strain (sex) Duration Reference	Dosing regimen, Animals/group at start	Incidence of tumours	Significance	Comments
		Lung cancer[a]		
Mouse, Kunming (M) 10 mo Liang *et al.* (1983)	Once/wk, 10 wk: 0 mg (control)	1/38	-	Age at start NR (weight, 18–26 g) Exposure to cyclohexane extracts of coal soot from Xuanwei County, China.
	500 mg soot extract (total dose)	44/57	$P < 0.001$	
	1000 mg soot extract (total dose)	36/56	$P < 0.001$	
	38–57 animals			
Mouse, Kunming (M) 311 d Liang *et al.* (1984)	Once/wk, 10 wk: 0 mg (control)	6/60, all adenocarcinomas	-	Age at start NR (weight, 18–22 g) Exposure to Tween 80 – saline extracts of coal soot from Xuanwei County, China.
	119 mg soot extract (total dose)	52/58	$P < 0.001$	
	400 mg soot extract (total dose)	39/59	$P < 0.001$	
	~60 animals			

[a] Lung cancers included squamous cell carcinomas, adenosquamous carcinomas, and adenocarcinomas.
d, day or days; M, male; mo, month or months; NR, not reported; wk, week or weeks

3.4 Synthesis

There is convincing evidence for the carcinogenicity of coal smoke and coal soot in experimental animals, based on the consistent induction of lung cancers in mice and rats exposed to coal emissions by inhalation, and in mice given subcutaneous injections of coal soot extract, and induction of malignant tumours of the skin in mice given repeated dermal applications of coal soot extract.

4. Other Relevant Data

4.1 Inhalable particles

The primary mechanisms for deposition of airborne particles in the respiratory tract are sedimentation, impaction and diffusion (see IARC (2010b) for a review). Deposition by sedimentation and impaction depends on the aerodynamic diameter of the particle, whereas deposition by diffusion depends on its thermodynamic diameter (ICRP, 1994). Following inhalation, particles may either deposit in the extrathoracic, tracheobronchial or pulmonary airways or remain in the air stream and be eliminated upon exhalation. The deposition of particles in the respiratory tract depends primarily on the size of the inhaled particle, the route of breathing (i.e. through the nose and/or mouth) and the breathing pattern (e.g. volume and frequency) (Bailey *et al.*, 1985; Freedman & Robinson, 1988; ICRP, 1994).

Particles are frequently aggregates or agglomerates of smaller primary particles. The aerodynamic and thermodynamic properties of these aggregates (rather than the primary particles) affect their behaviour in the air and the probability of deposition in the respiratory tract. Once deposited, properties such as the size and surface area of both the aggregate and the primary particle can potentially affect the kinetics of clearance (ICRP, 1994; Oberdörster, 1996).

The deposition and clearance of particles vary among individuals for several reasons, including age, sex, tobacco smoking status and health status. Pre-existing lung diseases or conditions such as asthma or chronic obstructive pulmonary disease can influence the efficiency and pattern of deposition within the respiratory tract. Deposition and retention determine the initial and retained dose of particles in each region of the respiratory tract and may, therefore, influence the risk for developing diseases specific to those regions of the respiratory tract (Oberdörster, 1988; ICRP, 1994).

All animal species that are routinely used in particle toxicology, as well as humans, are susceptible to impairment of clearance of poorly soluble particles from the lungs. In rats, impaired clearance is probably one of the first steps necessary to initiate a sequence of events that may lead to lung cancer. Different animal species exhibit differences in particle-induced impairment of clearance, which can result in different lung burdens (expressed as mass or surface area) following exposures to the same particle concentration (Brown *et al.*, 2005; IARC, 2010b). In cancer bioassays in rats exposed to various types of poorly soluble particles of fine or ultrafine size, the surface area of the particles may be a better predictor of lung tumours than particle mass (Oberdörster & Yu, 1990; Driscoll *et al.*, 1996).

Inhaled and deposited particles are cleared more rapidly from the normal lungs of healthy rats than from those of humans. However, at high lung burdens, macrophage-mediated clearance from the rat lung can be impaired and in time, clearance effectively ceases. This phenomenon (termed 'overload') is observed with poorly soluble particles generally considered to have low toxicity (Morrow, 1988). Several studies have shown that rats, but not mice or hamsters, develop excess incidence of lung cancer after chronic inhalation of 'overloading' doses of poorly soluble particles. Several authors have discussed this

phenomenon and the challenges it poses for the extrapolation of chronic effects in rats to humans (Morrow, 1994; Levy, 1995; Watson & Valberg, 1996; ILSI, 2000; Miller, 2000; Oberdörster 2002; Hext *et al.*, 2005; IARC, 2010b).

The events proposed to describe the biological process that starts with particle deposition on critical target cells (e.g. alveolar epithelial cells type II) or tissues within the rat lung and results in lung tumours include:

- sustained inflammation, where the cell population (dominated by activated and probably persistent polymorphonuclear neutrophils) secretes a collection of pro-/anti-inflammatory cytokines, proteases, cytotoxins, fibrogenic and other growth factors;
- production of reactive oxygen species by particle effects or intracellular formation, which may gradually deplete the antioxidant defences; damage DNA directly and potentially induce mutations, promote cell turnover and cell proliferation; events that may enhance the risk for DNA replication error and/or expand a mutated or transformed cell to initiate a tumour (Castranova, 2000; Knaapen *et al.*, 2004).

Some of these events have been demonstrated in humans exposed to poorly soluble particles, but it is not known to what extent they are operative in humans and whether humans are eventually susceptible to particle-induced lung cancer. Species differences such as breathing conditions, respiratory tract structure and pulmonary defences must be considered when extrapolating toxicological findings from rodents to humans (Castranova, 2000; Knaapen *et al.*, 2004; Brown *et al.*, 2005). Clear differences in antioxidant defence mechanisms in the lungs also exist between humans and rats, and there is evidence that humans overall are relatively deficient in some of these mechanisms compared with rats (IARC, 2010b). Studies in rats have shown that, depending on the concentration and duration of exposure, the long-term retention of particles in humans can be greater than that predicted from rodent studies that used lower concentrations or shorter durations of exposure (Morrow, 1988, 1992; ILSI, 2000).

Although the degree of sustained inflammation experienced by rats at high lung burdens is not observed in humans, humans may experience sustained inflammation under certain disease conditions, including late-stage interstitial pulmonary fibrosis. Patients who have interstitial pulmonary fibrosis have a high incidence of lung tumours (Daniels & Jett, 2005).

4.2 Polycyclic aromatic hydrocarbons

Polycyclic aromatic hydrocarbons are important components of coal emissions (see IARC (2010c) for a review). These compounds are absorbed through the respiratory tract – from where, as adsorbed particulates, they can also be swept back up and swallowed into the gastrointestinal tract and even reach the skin. Smaller molecules (2–3-ring) are absorbed more rapidly than larger ones (IARC, 2010c).

The rate and extent of absorption by the respiratory tract of PAHs from particles onto which they are adsorbed is generally dependent on particle size, which determines regional deposition in the respiratory tract and the rate of release of PAHs from the particle. Highly lipophilic PAHs released from particles deposited in the conducting and bronchial airways are largely retained for several hours and absorbed slowly by a diffusion-limited process. In contrast, PAHs that are released from particles in alveolar airways are generally absorbed within minutes (Gerde & Scott, 2001; IARC, 2010c).

Once absorbed, PAHs are distributed widely to most organs and tissues and tend to accumulate in fatty tissue (WHO, 1998; IARC, 2010c). They are metabolized rapidly to more soluble metabolites, e.g. phenols, dihydrodiols, and phenol dihydrodiols, and in some cases to more reactive species like epoxides, dihydrodiol

epoxides, quinones and tetrols. At least three main pathways of metabolism are involved:

- the cytochrome P450 (CYP) pathway, where PAHs may be (1) metabolized to their bay- and fjord-region diol epoxides with the involvement of epoxide hydrolase (Xue & Warshawsky, 2005) or (2) undergo cyclopenta-ring oxidation (IARC, 2010c).
- the cytochrome P450/peroxidase pathway, where removal of one electron from the π system by CYPs or peroxidases generates a radical cation (Cavalieri & Rogan, 1992; Xue & Warshawsky, 2005).
- the cytochrome P450/aldo-keto reductase (oxidative) pathway where, following metabolization to dihydrodiols by CYPs and epoxide hydrolase, formation of *ortho*-quinones and generation of reactive oxygen species is ensured by aldo-keto reductases (Penning *et al.*, 1999; Xue & Warshawsky, 2005; Penning & Drury, 2007).

Many of the above-mentioned metabolites are electrophilic and bind to DNA and proteins, which results in genotoxic effects — primarily through the formation of DNA adducts (Xue & Warshawsky, 2005). Beyond these phase-I metabolic pathways, PAH metabolites may be eliminated in a conjugated form with either glutathione, sulfate or glururonic acid via the phase-II metabolism (WHO, 1998; IARC, 2010c).

Ample evidence, summarized in IARC (2010c), supports a role for PAHs in lung cancer due to exposure to indoor emissions from coal combustion.

A general genotoxic mechanism has emerged in which PAHs such as benzo[*a*]pyrene are metabolized to electrophilic compounds (e.g. benzo[*a*]pyrene-7,8-diol-9,10-epoxide) that form adducts in DNA (Xue & Warshawsky, 2005; IARC, 2010c). If these adducts are not repaired, misreplication converts them primarily into G→T transversion mutations in the *TP53* gene in the lung. An over-representation of G→T transversions has been found on the non-transcribed strand of DNA in the *TP53* gene in lung tumours from smoky coal-exposed women in China, which is consistent with exogenous exposure and the lack of transcription-coupled DNA repair on that strand, resulting in mutations (DeMarini *et al.*, 2001). A preference for G→T transversions in the methylated CpG dinucleotides in human lung tumours has been found, in agreement with in-vitro studies that show the same dinucleotide as a target of benzo[*a*]pyrene diol epoxide (Casale *et al.*, 2001; DeMarini *et al.*, 2001; Hainaut & Pfeifer, 2001; Pfeifer & Hainaut, 2003).

A study by Sun *et al.* (2007) found that coal emission-exposed subjects carrying an exon-3 mutation in the microsomal epoxide hydrolase gene had a nearly 2-fold increased risk for lung cancer compared to those with the wild type version of the gene. Thus, metabolism to PAH-epoxides plays an important role in lung cancer associated with coal emissions.

A role for the aldo-keto reductase (AKR) pathway in the formation of mutagenic/carcinogenic metabolites of PAHs has also been found among smoky coal emission-exposed lung cancer patients in China. Lan *et al.* (2004) found that subjects who had the *AKR1C3-Gln/Gln* genotype had a 1.84-fold increased risk for lung cancer compared with those without the polymorphism. In subjects having the *OGG1-Cys/Cys* or the *OGG1-Ser/Cys* polymorphism, the risk for lung cancer was increased about 1.9-fold relative to *OGG1-Ser/Ser*. Indeed, AKRs convert trans-dihydrodiols to *ortho*-quinones, and Park *et al.* (2008) have used a yeast system to show that the pattern of *ortho*-quinone-induced mutations in *TP53* in this system is driven by 8-oxo-dGuo formation, whereas the spectrum of mutations is driven by biological selection for dominance. Park *et al.* (2009) have shown recently that the aryl-hydrocarbon receptor shuttles the AKR-generated *ortho*-quinones into the nucleus.

Consistent with a role for PAHs, studies in smoky coal-exposed women in China have

shown that a polymorphism in nucleotide excision repair (*ERCC2 Gln* at codon 751) reduced lung cancer risk by 60%. A similar reduction was also found for subjects with a particular haplotype in *ERCC2*. A 2-fold increased risk for lung cancer was found for subjects having 1 or 2 copies of the *RAD23B* gene with Val at codon 249 (Shen *et al.*, 2005).

In addition, accumulation of mutations in other key genes (e.g. *KRAS*; Mass *et al.*, 1993; DeMarini *et al.*, 2001; Keohavong *et al.*, 2003), production of reactive oxygen species (Xue & Warshawsky, 2005), photomutagenicity (Yan *et al.*, 2004), together with interruption of gap-junctional intercellular communication (Bláha *et al.*, 2002), cell-cycle dysregulation, increase in cell proliferation, tumour promotion (Tannheimer *et al.*, 1998, 1999; Burdick *et al.*, 2003; Oguri *et al.*, 2003; Plísková *et al.*, 2005), and induction of apoptosis (Ko *et al.*, 2004) can result in tumour formation. PAHs can also have immunosuppressive and haematological effects (Burchiel & Luster, 2001; Booker & White, 2005). Several of the above effects are partly mediated by activation of the aryl-hydrocarbon receptor to which many PAHs can bind (IARC, 2010c).

4.3 Biomarkers and mutagenicity

The available information on the mutagenicity and genotoxicity of smoky-coal emissions from Xuanwei County, China, includes a wide range of end-points that encompass mutations in *KRAS* and *TP53* genes in lung tumours from non-smokers who were exposed to smoky-coal emissions (Li *et al.*, 1997; DeMarini *et al.*, 2001; Keohavong *et al.*, 2003, 2004, 2005). In addition, studies show that such exposures result in the excretion of several PAHs and their metabolites, e.g. methylated- and hydroxyl-PAHs (Mumford *et al.*, 1995; Siwińska *et al.*, 1999) and that exposed individuals exhibit elevated levels of DNA adducts (Gallagher *et al.*, 1993; Mumford *et al.*, 1993; Xu *et al.*, 1997; Casale *et al.*, 2001) and accumulation of *TP53* protein (Feng *et al.*, 1999; Lan *et al.*, 2001). Recently, mitochondrial DNA content, which is associated with production of reactive oxygen species through oxidative phosphorylation, was found to be elevated in smoky coal-exposed subjects (Bonner *et al.*, 2009).

It was also reported that exposure to coal emissions in Guizhou Province, China, is associated with increased levels of DNA–protein cross-links, unscheduled DNA synthesis (Zhang *et al.*, 2000b), sister chromatid exchange, chromosomal aberrations, micronucleus formation (Zhang *et al.*, 2007a) and *p16* gene deletion and hypermethylation (Zhang *et al.*, 2007b) in peripheral blood lymphocytes. Mutated P53 protein was also elevated in the skin (Hu *et al.*, 2001). [Some of the observed cytogenetic damage were probably due to the elevated levels of arsenic present in this coal].

In many studies, extracts or condensates of coal emissions were found to be mutagenic in *Salmonella* with or without metabolic activation: in strain TA98 in the presence of S9 the potency for smoky-coal could reach 60000 revertants per cubic metre of air (Mumford *et al.*, 1987) and 3000 revertants per milligram of particle (Nakanishi *et al.*, 1997). Bioassay-directed fractionation studies with *Salmonella* have identified that, for smoky-coal, most of the mutagenic activity is due to PAHs and alkylated PAHs (Chuang *et al.*, 1992a, b). Evaluation of the mutation spectrum produced by smoky coal extract in *Salmonella* showed a similar percentage of GC to TA mutations (≈77–86%) as found in the *TP53* (76%) and *KRAS* (86%) genes in lung tumours from smoky coal-exposed women (Granville *et al.*, 2003).

Several studies evaluated populations who are exposed to indoor air pollution from coal for associations between polymorphisms in genes that are involved in xenobiotic metabolism and risk for lung cancer. However, multiple comparisons and generally small sample sizes could have resulted in both false-positive and false-negative findings. There is some evidence that

the *GSTM1*-null genotype was associated with increased risk for lung cancer in some studies in which at least part of the study population was definitely or probably exposed to indoor coal emissions, particularly where exposure to PAHs was suspected to be a contributing agent (Lan *et al.*, 2000; Chen *et al.*, 2006). However, results for polymorphisms in other genes are inconsistent or have been analysed in only one study. Therefore, no conclusion can be made regarding the effect of polymorphisms of genes other than possibly *GSTM1* on risk for lung cancer in these populations.

4.4 Synthesis

Chemical analyses and bioassay-directed fractionation of smoky coal emissions have identified PAHs as an important chemical class that accounts for much of their mutagenicity and carcinogenicity. The epidemiological link between exposure to smoky coal emissions and an increased risk for lung cancer is strengthened mechanistically by the fact that the mutation spectra of the *P53* tumour-suppressor gene and the *KRAS* oncogene in the lung tumours from non-smokers exposed to smoky coal esmissions reflect an exposure to PAHs and differs from the mutation spectra found in these genes in lung tumours from cigarette smokers. Thus, the mutation spectra in lung tumours from non-smokers whose cancers are linked to smoky coal emissions reflect the primary DNA damage induced by the most prominent class of mutagens/carcinogens in these emissions.

5. Evaluation

There is *sufficient evidence* in humans for the carcinogenicity of indoor emissions from household combustion of coal. Indoor emissions from household combustion of coal cause cancer of the lung.

There is *sufficient evidence* in experimental animals for the carcinogenicity of coal-derived soot extract.

There is *sufficient evidence* in experimental animals for the carcinogenicity of emissions from combustion of coal.

Indoor emissions from household combustion of coal are *carcinogenic to humans (Group 1).*

References

Aggarwal AL, Raiyani CV, Patel PD *et al.* (1982). Assessment of exposure to benzo(a)pyrene in air for various population groups in Ahmedabad. *Atmos Environ*, 16: 867–870. doi:10.1016/0004-6981(82)90405-X

Bailey MR, Fry FA, James AC (1985). Long-term retention of particles in the human respiratory tract. *J Aerosol Sci*, 16: 295–305. doi:10.1016/0021-8502(85)90037-0

Bláha L, Kapplová P, Vondrácek J *et al.* (2002). Inhibition of gap-junctional intercellular communication by environmentally occurring polycyclic aromatic hydrocarbons. *Toxicol Sci*, 65: 43–51. doi:10.1093/toxsci/65.1.43 PMID:11752684

Bonner MR, Shen M, Liu CS *et al.* (2009). Mitochondrial DNA content and lung cancer risk in Xuan Wei, China. *Lung Cancer*, 63: 331–334. doi:10.1016/j.lungcan.2008.06.012 PMID:18691788

Booker CD & White KL Jr (2005). Benzo(a)pyrene-induced anemia and splenomegaly in NZB/WF1 mice. *Food Chem Toxicol*, 43: 1423–1431. doi:10.1016/j.fct.2005.03.018 PMID:15936865

Brown JS, Wilson WE, Grant LD (2005). Dosimetric comparisons of particle deposition and retention in rats and humans. *Inhal Toxicol*, 17: 355–385. doi:10.1080/08958370590929475 PMID:16020034

Bukowski JA, Wartenberg D, Goldschmidt M (1998). Environmental causes for sinonasal cancers in pet dogs, and their usefulness as sentinels of indoor cancer risk. *J Toxicol Environ Health A*, 54: 579–591. doi:10.1080/009841098158719 PMID:9726781

Burchiel SW & Luster MI (2001). Signalling by environmental polycyclic aromatic hydrocarbons in human lymphocytes. *Clin Immunol*, 98: 2–10. doi:10.1006/clim.2000.4934 PMID:11141320

Burdick AD, Davis JW 2nd, Liu KJ *et al.* (2003). Benzo(a)pyrene quinones increase cell proliferation, generate reactive oxygen species, and transactivate the epidermal growth factor receptor in breast epithelial cells. *Cancer Res*, 63: 7825–7833. PMID:14633709

Cáceres D, Adonis L, Retarnal C *et al.* (2001). Contaminación intradomiciliaria en un sector de extrema pobreza de la comuna de La Pintana. (Indoor air pollution in a zone of extreme poverty of La Pintana, Santiago-Chile) *Rev Med Chil*, 129: 33–42. PMID:11265203

Campbell JA (1939). Carcinogenic agents present in the atmosphere and incidence of primary tumours in mice. *Br J Exp Pathol*, 20: 122–132.

Casale GP, Singhal M, Bhattacharya S *et al.* (2001). Detection and quantification of depurinated benzo[a] pyrene-adducted DNA bases in the urine of cigarette smokers and women exposed to household coal smoke. *Chem Res Toxicol*, 14: 192–201. doi:10.1021/tx000012y PMID:11258968

Castranova V (2000). From coal mine dust to quartz: Mechanisms of pulmonary pathogenicity. *Inhal Toxicol*, 12: Suppl. 37–14. doi:10.1080/08958370050164842

Cavalieri EL & Rogan EG (1992). The approach to understanding aromatic hydrocarbon carcinogenesis. The central role of radical cations in metabolic activation. *Pharmacol Ther*, 55: 183–199. doi:10.1016/0163-7258(92)90015-R PMID:1289900

Chen HC, Cao YF, Hu WX *et al.* (2006). Genetic polymorphisms of phase II metabolic enzymes and lung cancer susceptibility in a population of Central South China. *Dis Markers*, 22: 141–152. PMID:16788248

Chen Y, Bi XH, Mai B *et al.* (2004). Emission characterization of particulate/gaseous phases and size association for polycyclic aromatic hydrocarbons from residential coal combustion. *Fuel*, 83: 781–790. doi:10.1016/j.fuel.2003.11.003

Chen YJ, Sheng GY, Bi XH *et al.* (2005). Emission factors for carbonaceous particles and polycyclic aromatic hydrocarbons from residential coal combustion in China. *Environ Sci Technol*, 39: 1861–1867. doi:10.1021/es0493650 PMID:15819248

Chuang JC, Cao SR, Xian YL *et al.* (1992a). Chemical characterization of indoor air of homes from communes in Xuan Wei, China, with high lung cancer mortality rate. *Atmos Environ*, 26: 2193–2201. doi:10.1016/0960-1686(92)90408-D

Chuang JC, Wise S, Cao S, Mumford JL (1992b). Chemical characterization of mutagenic fractions of particles from indoor coal combustion - a study of lung-cancer in Xuan-Wei, China. *Environ Sci Technol*, 26: 999–1004. doi:10.1021/es00029a020

Dai XD, Lin CY, Sun XW *et al.* (1996). The etiology of lung cancer in nonsmoking females in Harbin, China. *Lung Cancer*, 14: Suppl 1S85–S91. doi:10.1016/S0169-5002(96)90213-5 PMID:8785670

Daniels CE & Jett JR (2005). Does interstitial lung disease predispose to lung cancer? *Curr Opin Pulm Med*, 11: 431–437. doi:10.1097/01.mcp.0000170521.71497.ba PMID:16093818

DeMarini DM, Landi S, Tian D *et al.* (2001). Lung tumor KRAS and TP53 mutations in nonsmokers reflect exposure to PAH-rich coal combustion emissions. *Cancer Res*, 61: 6679–6681. PMID:11559534

Driscoll KE, Carter JM, Howard BW *et al.* (1996). Pulmonary inflammatory, chemokine, and mutagenic responses in rats after subchronic inhalation of carbon black. *Toxicol Appl Pharmacol*, 136: 372–380. doi:10.1006/taap.1996.0045 PMID:8619246

Du YX, Cha Q, Chen XW *et al.* (1996). An epidemiological study of risk factors for lung cancer in Guangzhou, China. *Lung Cancer*, 14: Suppl 1S9–S37. doi:10.1016/S0169-5002(96)90208-1 PMID:8785671

EBCREY; Editorial Board of the China Rural Energy Yearbook (1999). *Zhongguo Nongcun Nengyuan Nianjian 1998–1999* [China Rural Energy Yearbook 1998–1999]. Beijing: Zhongguo Nongye Chubanshe

Feng Z, Tian D, Lan Q, Mumford JL (1999). A sensitive immunofluorescence assay for detection of p53 protein accumulation in sputum. *Anticancer Res*, 19: 5B3847–3852. PMID:10628322

Freedman AP, Robinson K (1988). *Noninvasive magnetopneumographic studies of lung dust retention and clearance in coal miners*. In: *Respirable Dust in the Mineral Industries: Health Effects, Characterization and Control.* Frantz RL, Ramani RV, editors. University Park, PA: Penn State University Press, pp. 181–186.

Galeone C, Pelucchi C, La Vecchia C *et al.* (2008). Indoor air pollution from solid fuel use, chronic lung diseases and lung cancer in Harbin, Northeast China. *Eur J Cancer Prev*, 17: 473–478. doi:10.1097/CEJ.0b013e328305a0b9 PMID:18714191

Gallagher J, Mumford J, Li X *et al.* (1993). DNA adduct profiles and levels in placenta, blood and lung in relation to cigarette smoking and smoky coal emissions. *IARC Sci Publ*, 124: 283–292. PMID:8225497

García-Pérez J, Pollán M, Boldo E *et al.* (2009). Mortality due to lung, laryngeal and bladder cancer in towns lying in the vicinity of combustion installations. *Sci Total Environ*, 407: 2593–2602. doi:10.1016/j.scitotenv.2008.12.062 PMID:19187950

Ge S, Xu X, Chow JC *et al.* (2004). Emissions of air pollutants from household stoves: honeycomb coal versus coal cake. *Environ Sci Technol*, 38: 4612–4618. doi:10.1021/es049942k PMID:15461170

Ger LP, Hsu WL, Chen KT, Chen CJ (1993). Risk factors of lung cancer by histological category in Taiwan. *Anticancer Res*, 13: 5A1491–1500. PMID:8239527

Gerde P & Scott BR (2001). A model for absorption of low-volatile toxicants by the airway mucosa. *Inhal Toxicol*, 13: 903–929. doi:10.1080/089583701752378160 PMID:11696866

Granville CA, Hanley NM, Mumford JL, DeMarini DM (2003). Mutation spectra of smoky coal combustion emissions in Salmonella reflect the TP53 and KRAS mutations in lung tumors from smoky coal-exposed individuals. *Mutat Res*, 525: 77–83. PMID:12650907

Gu SL, Ji RD, Cao SR (1990). The physical and chemical characteristics of particles in indoor air where high fluoride coal burning takes place. *Biomed Environ Sci*, 3: 384–390. PMID:2096842

Hainaut P & Pfeifer GP (2001). Patterns of p53 G–>T transversions in lung cancers reflect the primary mutagenic signature of DNA-damage by tobacco smoke. *Carcinogenesis*, 22: 367–374. doi:10.1093/carcin/22.3.367 PMID:11238174

Hays MD, Geron CD, Linna KJ *et al.* (2002). Speciation of gas-phase and fine particle emissions from burning of foliar fuels. *Environ Sci Technol*, 36: 2281–2295. doi:10.1021/es0111683 PMID:12075778

He G, Ying B, Liu J *et al.* (2005). Patterns of household concentrations of multiple indoor air pollutants in China. *Environ Sci Technol*, 39: 991–998. doi:10.1021/es049731f PMID:15773470

He XZ, Chen W, Liu ZY, Chapman RSCase–control Study on Lung Cancer and Cooking Fuel (1991). An epidemiological study of lung cancer in Xuan Wei County, China: current progress. Case–control study on lung cancer and cooking fuel. *Environ Health Perspect*, 94: 9–13. doi:10.2307/3431286 PMID:1954946

Hext PM, Tomenson JA, Thompson P (2005). Titanium dioxide: inhalation toxicology and epidemiology. *Ann Occup Hyg*, 49: 461–472. doi:10.1093/annhyg/mei012 PMID:15790613

Hosgood HD 3rd, Berndt SI, Lan Q (2007). GST genotypes and lung cancer susceptibility in Asian populations with indoor air pollution exposures: a meta-analysis. *Mutat Res*, 636: 134–143. doi:10.1016/j.mrrev.2007.02.002 PMID:17428724

Hosgood HD 3rd, Chapman R, Shen M *et al.* (2008). Portable stove use is associated with lower lung cancer mortality risk in lifetime smoky coal users. *Br J Cancer*, 99: 1934–1939. doi:10.1038/sj.bjc.6604744 PMID:19034286

Hu C, Zhang A, Huang X (2001). [Study on expression of P53mt protein in skin of patient with arseniasis caused by coal-burning] *Zhonghua Yu Fang Yi Xue Za Zhi*, 35: 23–25. PMID:11860954

Huang C, Zhang X, Qiao Z *et al.* (1992). A case–control study of dietary factors in patients with lung cancer. *Biomed Environ Sci*, 5: 257–265. PMID:1333225

IARC (1985). Polynuclear aromatic compounds, Part 4, bitumens, coal-tars and derived products, shale-oils and soots. *IARC Monogr Eval Carcinog Risk Chem Hum*, 35: 1–247. PMID:2991123

IARC (2010a). Household use of solid fuels and high-temperature frying. *IARC Monogr Eval Carcinog Risks Hum*, 95: 1–424. PMID:18756632

IARC (2010b). Carbon black, titanium dioxide, and talc. *IARC Monogr Eval Carcinog Risks Hum*, 93: 1–452. PMID:21449489.

IARC (2010c). Some non-heterocyclic polycyclic aromatic hydrocarbons and some related exposures. *IARC Monogr Eval Carcinog Risks Hum*, 92: 1–853. PMID:21141735 PMID:18756632

ICRP; International Commission on Radiological Protection (1994). *Human Respiratory Tract Model for Radiological Protection. A Report of a Task Group of the International Commission on Radiological Protection*. Oxford: Pergamon, ICRP Publication 66.

ILSI; Risk Science Institute Workshop Participants (2000). The relevance of the rat lung response to particle overload for human risk assessment: a workshop consensus report. *Inhal Toxicol*, 12: 1–17. doi:10.1080/08958370050029725 PMID:10715616

Jin Y, Zhou Z, He G *et al.* (2005). Geographical, spatial, and temporal distributions of multiple indoor air pollutants in four Chinese provinces. *Environ Sci Technol*, 39: 9431–9439. doi:10.1021/es0507517 PMID:16475318

Kabir Z, Bennett K, Clancy L (2007). Lung cancer and urban air-pollution in Dublin: a temporal association? *Ir Med J*, 100: 367–369. PMID:17432813

Kauppinen EI & Pakkanen TA (1990). Coal Combustion Aerosols - A Field-Study. *Environ Sci Technol*, 24: 1811–1818. doi:10.1021/es00082a004

Keohavong P, Gao WM, Zheng KC *et al.* (2004). Detection of K-ras and p53 mutations in sputum samples of lung cancer patients using laser capture microdissection microscope and mutation analysis. *Anal Biochem*, 324: 92–99. doi:10.1016/j.ab.2003.09.030 PMID:14654050

Keohavong P, Lan Q, Gao WM *et al.* (2003). K-ras mutations in lung carcinomas from nonsmoking women exposed to unvented coal smoke in China. *Lung Cancer*, 41: 21–27. doi:10.1016/S0169-5002(03)00125-9 PMID:12826308

Keohavong P, Lan Q, Gao WM *et al.* (2005). Detection of p53 and K-ras mutations in sputum of individuals exposed to smoky coal emissions in Xuan Wei County, China. *Carcinogenesis*, 26: 303–308. doi:10.1093/carcin/bgh328 PMID:15564291

Khesina AIa, Gaevaia TIa, Linnik AB (1977). Polycyclic aromatic hydrocarbon content and carcinogenic activity of soot extracts from the heating systems *Gig Sanit*, 8107–109. PMID:590784

Kim Oanh NT, Reutergardh LB, Dung NT (1999). Emission of polycyclic aromatic hydrocarbons and particulate matter from domestic combustion of selected fuels. *Environ Sci Technol*, 33: 2703–2709. doi:10.1021/es980853f

Kleeman MJ, Schauer JJ, Cass GR (1999). Size and composition distribution of fine particulate matter emitted from wood burning, meat charbroiling and cigarettes. *Environ Sci Technol*, 33: 3516–3523. doi:10.1021/es981277q

Kleinerman RA, Wang Z, Wang L *et al.* (2002). Lung cancer and indoor exposure to coal and biomass in rural China. *J Occup Environ Med*, 44: 338–344. doi:10.1097/00043764-200204000-00014 PMID:11977420

Knaapen AM, Borm PJ, Albrecht C, Schins RP (2004). Inhaled particles and lung cancer. Part A: Mechanisms. *Int J Cancer*, 109: 799–809. doi:10.1002/ijc.11708 PMID:15027112

Ko CB, Kim SJ, Park C *et al.* (2004). Benzo(a)pyrene-induced apoptotic death of mouse hepatoma Hepa1c1c7 cells via activation of intrinsic caspase cascade and mitochondrial dysfunction. *Toxicology*, 199: 35–46. doi:10.1016/j.tox.2004.01.039 PMID:15125997

Ko YC, Lee CH, Chen MJ *et al.* (1997). Risk factors for primary lung cancer among non-smoking women in Taiwan. *Int J Epidemiol*, 26: 24–31. doi:10.1093/ije/26.1.24 PMID:9126500

Koo LC, Lee N, Ho JH (1983). Do cooking fuels pose a risk for lung cancer? A case–control study of women in Hong Kong. *Ecol Dis*, 2: 255–265. PMID:6681156

Lan Q, Chapman RS, Schreinemachers DM *et al.* (2002). Household stove improvement and risk of lung cancer in Xuanwei, China. *J Natl Cancer Inst*, 94: 826–835. PMID:12048270

Lan Q, Chen W, Chen H, He XZ (1993). Risk factors for lung cancer in non-smokers in Xuanwei County of China. *Biomed Environ Sci*, 6: 112–118. PMID:8397894

Lan Q, Feng Z, Tian D *et al.* (2001). p53 gene expression in relation to indoor exposure to unvented coal smoke in Xuan Wei, China. *J Occup Environ Med*, 43: 226–230. doi:10.1097/00043764-200103000-00010 PMID:11285870

Lan Q, He X, Costa DJ *et al.* (2000). Indoor coal combustion emissions, GSTM1 and GSTT1 genotypes, and lung cancer risk: a case–control study in Xuan Wei, China. *Cancer Epidemiol Biomarkers Prev*, 9: 605–608. PMID:10868696

Lan Q, He X, Shen M *et al.* (2008). Variation in lung cancer risk by smoky coal subtype in Xuanwei, China. *Int J Cancer*, 123: 2164–2169. PMID:18712724

Lan Q, Mumford JL, Shen M *et al.* (2004). Oxidative damage-related genes AKR1C3 and OGG1 modulate risks for lung cancer due to exposure to PAH-rich coal combustion emissions. *Carcinogenesis*, 25: 2177–2181. doi:10.1093/carcin/bgh240 PMID:15284179

Le CH, Ko YC, Cheng LS *et al.* (2001). The heterogeneity in risk factors of lung cancer and the difference of histologic distribution between genders in Taiwan. *Cancer Causes Control*, 12: 289–300. doi:10.1023/A:1011270521900 PMID:11456224

Lee RG, Coleman P, Jones JL *et al.* (2005). Emission factors and importance of PCDD/Fs, PCBs, PCNs, PAHs and PM10 from the domestic burning of coal and wood in the U.K. *Environ Sci Technol*, 39: 1436–1447. doi:10.1021/es048745i PMID:15819195

Lei YX, Cai WC, Chen YZ, Du YX (1996). Some lifestyle factors in human lung cancer: a case–control study of 792 lung cancer cases. *Lung Cancer*, 14: Suppl 1S121–S136. doi:10.1016/S0169-5002(96)90218-4 PMID:8785658

Levy LS (1995). Review: Inhalation toxicology and human risk assessment of carbon black. *Indoor and Built Environment*, 4: 263–280. doi:10.1177/1420326X9500400504

Li J, Li X, Quan X (1997). [Studies on serum regulatory protein for cell growth in patients with lung cancer exposed to indoor coal-burning] *Zhonghua Yu Fang Yi Xue Za Zhi*, 31: 92–94. PMID:9812620

Liang CK, Guan NY, Ma F *et al.* (1983). Carcinogenicity in mice of soot extract collected from Xuan Wei County *Zhongguo Yi Xue Ke Xue Yuan Xue Bao*, 5: 307–310. PMID:6329534

Liang CK, Guan NY, Yin XR *et al.* (1984). Extracts from Xuan Wei coal and wood smoke induce lung cancer in mice. *Wei Sheng Yan Jiu*, 13: 19–23.

Liang CK, Quan NY, Cao SR *et al.* (1988). Natural inhalation exposure to coal smoke and wood smoke induces lung cancer in mice and rats. *Biomed Environ Sci*, 1: 42–50. PMID:3268107

Liang CK & Wang W (1987). Kunming mouse skin tumor-initiating activity of extracts of inhalable particles in indoor air *Zhonghua Yu Fang Yi Xue Za Zhi*, 21: 316–318. PMID:3452506

Lin C, Dai X, Sun X (1995). Expression of oncogene and anti-oncogene in mouse lung cancer induced by coal-burning smoke *Zhonghua Zhong Liu Za Zhi*, 17: 432–434. PMID:8697995

Lissowska J, Bardin-Mikolajczak A, Fletcher T *et al.* (2005). Lung cancer and indoor pollution from heating and cooking with solid fuels: the IARC international multicentre case–control study in Eastern/Central Europe and the United Kingdom. *Am J Epidemiol*, 162: 326–333. doi:10.1093/aje/kwi204 PMID:16014775

Liu Q, Sasco AJ, Riboli E, Hu MX (1993). Indoor air pollution and lung cancer in Guangzhou, People's Republic of China. *Am J Epidemiol*, 137: 145–154. PMID:8452118

Liu ZY, He XZ, Chapman RS (1991). Smoking and other risk factors for lung cancer in Xuanwei, China. *Int J Epidemiol*, 20: 26–31. doi:10.1093/ije/20.1.26 PMID:2066232

Luo RX, Wu B, Yi YN *et al.* (1996). Indoor burning coal air pollution and lung cancer–a case–control study in Fuzhou, China. *Lung Cancer*, 14: Suppl 1S113–S119. doi:10.1016/S0169-5002(96)90217-2 PMID:8785657

Mass MJ, Jeffers AJ, Ross JA *et al.* (1993). Ki-ras oncogene mutations in tumors and DNA adducts formed by benz[j]aceanthrylene and benzo[a]pyrene in the lungs of strain A/J mice. *Mol Carcinog*, 8: 186–192. doi:10.1002/mc.2940080309 PMID:8216737

Miller C, Srivastava RK, Ryan JV (1994). Emissions Of Organic Hazardous Air-Pollutants From The Combustion Of Pulverized Coal In A Small-Scale Combustor. *Environ Sci Technol*, 28: 1150–1158. doi:10.1021/es00055a028

Miller FJ (2000). Dosimetry of particles in laboratory animals and humans in relationship to issues

surrounding lung overload and human health risk assessment: a critical review. *Inhal Toxicol*, 12: 19–57. doi:10.1080/089583700196536 PMID:10715617

Millman A, Tang D, Perera FP (2008). Air pollution threatens the health of children in China. *Pediatrics*, 122: 620–628. doi:10.1542/peds.2007-3143 PMID:18762533

Morrow PE (1988). Possible mechanisms to explain dust overloading of the lungs. *Fundam Appl Toxicol*, 10: 369–384. doi:10.1016/0272-0590(88)90284-9 PMID:3286345

Morrow PE (1992). Dust overloading of the lungs: update and appraisal. *Toxicol Appl Pharmacol*, 113: 1–12. doi:10.1016/0041-008X(92)90002-A PMID:1553742

Morrow PE (1994). *Mechanisms and significance of "particle overload"*. In: *Toxic and carcinogenic effects of solid particles in the respiratory tract. [Proceedings of the 4th international inhalation symposium, March 1993]*. Mohr U, editor-in-chief. Hannover, Germany: International Life Sciences Institute Press, pp. 17–25.

Mumford JL, He XZ, Chapman RS *et al.* (1987). Lung cancer and indoor air pollution in Xuan Wei, China. *Science*, 235: 217–220. doi:10.1126/science.3798109 PMID:3798109

Mumford JL, Helmes CT, Lee XM *et al.* (1990). Mouse skin tumorigenicity studies of indoor coal and wood combustion emissions from homes of residents in Xuan Wei, China with high lung cancer mortality. *Carcinogenesis*, 11: 397–403. doi:10.1093/carcin/11.3.397 PMID:2311182

Mumford JL, Lee X, Lewtas J *et al.* (1993). DNA adducts as biomarkers for assessing exposure to polycyclic aromatic hydrocarbons in tissues from Xuan Wei women with high exposure to coal combustion emissions and high lung cancer mortality. *Environ Health Perspect*, 99: 83–87. doi:10.1289/ehp.939983 PMID:8319664

Mumford JL, Li X, Hu F *et al.* (1995). Human exposure and dosimetry of polycyclic aromatic hydrocarbons in urine from Xuan Wei, China with high lung cancer mortality associated with exposure to unvented coal smoke. *Carcinogenesis*, 16: 3031–3036. doi:10.1093/carcin/16.12.3031 PMID:8603481

Nakanishi Y, Chen S, Inutsuka S *et al.* (1997). Possible role of indoor environment and coal combustion emission in lung carcinogenesis in Fuyuan County, China. *Neoplasma*, 44: 69–72. PMID:9201284

National Bureau of Statistics (2005). *China Energy Statistical Yearbook 2005*. Beijing: China Statistics Press.

National Bureau of Statistics (2006). *China Statistical Yearbook 2006*. Beijing: China Statistics Press.

National Bureau of Statistics (2008). *The Major Statistics of the 2nd National Survey for Agriculture*. Beijing: China Statistics Press.

Oberdörster G (1988). Lung clearance of inhaled insoluble and soluble particles. *J Aerosol Med*, 1: 289–330. doi:10.1089/jam.1988.1.289

Oberdörster G (1996). Significance of particle parameters in the evaluation of exposure-dose-response relationships of inhaled particles. *Inhal Toxicol*, 8: Suppl73–89. PMID:11542496

Oberdörster G (2002). Toxicokinetics and effects of fibrous and nonfibrous particles. *Inhal Toxicol*, 14: 29–56. doi:10.1080/089583701753338622 PMID:12122559

Oberdörster G & Yu PP (1990). The carcinogenic potential of inhaled diesel exhaust: a particle effect? *J Aerosol Sci*, 21: S397–S401. doi:10.1016/0021-8502(90)90265-Y

Oguri T, Singh SV, Nemoto K, Lazo JS (2003). The carcinogen (7R,8S)-dihydroxy-(9S,10R)-epoxy-7,8,9,10-tetrahydrobenzo[a]pyrene induces Cdc25B expression in human bronchial and lung cancer cells. *Cancer Res*, 63: 771–775. PMID:12591724

Park JH, Gelhaus S, Vedantam S *et al.* (2008). The pattern of p53 mutations caused by PAH o-quinones is driven by 8-oxo-dGuo formation while the spectrum of mutations is determined by biological selection for dominance. *Chem Res Toxicol*, 21: 1039–1049. doi:10.1021/tx700404a PMID:18489080

Park JH, Mangal D, Frey AJ *et al.* (2009). Aryl hydrocarbon receptor facilitates DNA strand breaks and 8-oxo-2′-deoxyguanosine formation by the aldo-keto reductase product benzo[a]pyrene-7,8-dione. *J Biol Chem*, 284: 29725–29734. doi:10.1074/jbc.M109.042143 PMID:19726680

Passey RD (1922). Experimental soot Cancer. *BMJ*, ii: 1112–1113.

Passey RD & Carter-Braine J (1925). Experimental soot cancer. *J Pathol Bacteriol*, 28: 133–144. doi:10.1002/path.1700280202

Penning TM, Burczynski ME, Hung CF *et al.* (1999). Dihydrodiol dehydrogenases and polycyclic aromatic hydrocarbon activation: generation of reactive and redox active o-quinones. *Chem Res Toxicol*, 12: 1–18. doi:10.1021/tx980143n PMID:9894013

Penning TM & Drury JE (2007). Human aldo-keto reductases: Function, gene regulation, and single nucleotide polymorphisms. *Arch Biochem Biophys*, 464: 241–250. doi:10.1016/j.abb.2007.04.024 PMID:17537398

Pfeifer GP & Hainaut P (2003). On the origin of G –> T transversions in lung cancer. *Mutat Res*, 526: 39–43. PMID:12714181

Plísková M, Vondrácek J, Vojtesek B *et al.* (2005). Deregulation of cell proliferation by polycyclic aromatic hydrocarbons in human breast carcinoma MCF-7 cells reflects both genotoxic and nongenotoxic events. *Toxicol Sci*, 83: 246–256. doi:10.1093/toxsci/kfi040 PMID:15548639

Raiyani CV, Jani JP, Desai NM *et al.* (1993). Assessment of indoor exposure to polycyclic aromatic hydrocarbons for urban poor using various types of cooking fuels.

Bull Environ Contam Toxicol, 50: 757–763. doi:10.1007/BF00194673 PMID:8490282

Ren D, Zhao F, Wang Y *et al.* (1999). Distributions of minor and trace elements in Chinese coals. *Int J Coal Geol*, 40: 109–118. doi:10.1016/S0166-5162(98)00063-9

Ren DY, Xu DW, Zhao FH (2004). A preliminary study on the enrichment mechanism and occurrence of hazardous trace elements in the Tertiary lignite from the Shenbei coalfield, China. *Int J Coal Geol*, 57: 187–196. doi:10.1016/j.coal.2003.10.001

Rogge W, Hildemann LM, Mazurek MA, Cass GR (1998). Sources of fine organic aerosol. 9. Pine, oak and synthetic log combustion in residential fireplaces. *Environ Sci Technol*, 32: 13–22. doi:10.1021/es960930b

Ross AB, Jones JM, Chaiklangmuang S *et al.* (2002). Measurement and prediction of the emission of pollutants from the combustion of coal and biomass in a fixed bed furnace. *Fuel*, 81: 571–582. doi:10.1016/S0016-2361(01)00157-0

Sapkota A, Gajalakshmi V, Jetly DH *et al.* (2008). Indoor air pollution from solid fuels and risk of hypopharyngeal/laryngeal and lung cancers: a multicentric case–control study from India. *Int J Epidemiol*, 37: 321–328. doi:10.1093/ije/dym261 PMID:18234740

Seeling MG & Benignus EL (1936). Coal smoke soot and tumors of the lung and mice. *Am J Cancer*, 28: 96–111.

Shen M, Berndt SI, Rothman N *et al.* (2005). Polymorphisms in the DNA nucleotide excision repair genes and lung cancer risk in Xuan Wei, China. *Int J Cancer*, 116: 768–773. doi:10.1002/ijc.21117 PMID:15849729

Shen XB, Wang GX, Huang YZ *et al.* (1996). Analysis and estimates of attributable risk factors for lung cancer in Nanjing, China. *Lung Cancer*, 14: Suppl 1S107–S112. doi:10.1016/S0169-5002(96)90216-0 PMID:8785656

Shen XB, Wang GX, Zhou BS (1998). Relation of exposure to environmental tobacco smoke and pulmonary adenocarcinoma in non-smoking women: a case control study in Nanjing. *Oncol Rep*, 5: 1221–1223. PMID:9683839

Shraim A, Cui X, Li S *et al.* (2003). Arsenic speciation in the urine and hair of individuals exposed to airborne arsenic through coal-burning in Guizhou, PR China. *Toxicol Lett*, 137: 35–48. doi:10.1016/S0378-4274(02)00379-X PMID:12505431

Sinton JE, Smith KR, Hu HS, Liu JZ (1995). *Indoor Air Pollution Database for China*. WHO/EHG/95.8. Geneva: World Health Organization.

Sinton JE, Smith KR, Peabody J *et al.* (2004). An assessment of programs to promote improved household stoves in China. *Energy for sustainable development*, 8: 33–52. doi:10.1016/S0973-0826(08)60465-2

Siwińska E, Mielzyńska D, Bubak A, Smolik E (1999). The effect of coal stoves and environmental tobacco smoke on the level of urinary 1-hydroxypyrene. *Mutat Res*, 445: 147–153. PMID:10575425

Smith KR, Uma R, Kishore V *et al.* (2000). Greenhouse implications of household stoves. *Annu Rev Energy Environ*, 25: 741–763. doi:10.1146/annurev.energy.25.1.741

Sun XW (1992). Heating fuels and respiratory diseases in the risks of female lung cancer. *Zhonghua Zhong Liu Za Zhi*, 13: 413–415. PMID:1576905

Sun XW, Ma YY, Wang B *et al.* (2007). The interaction between microsomal epoxide hydrolase polymorphisms and indoor pollution in non small cell lung cancer. *Chinese*, 41: l30–34. PMID:17767854.

Swaine D (1990). *Trace Elements in Coal.* Boston, MA: Butterworth Press.

Tannheimer SL, Ethier SP, Caldwell KK, Burchiel SW (1998). Benzo[a]pyrene- and TCDD-induced alterations in tyrosine phosphorylation and insulin-like growth factor signalling pathways in the MCF-10A human mammary epithelial cell line. *Carcinogenesis*, 19: 1291–1297. doi:10.1093/carcin/19.7.1291 PMID:9683191

Tannheimer SL, Lauer FT, Lane J, Burchiel SW (1999). Factors influencing elevation of intracellular Ca2+ in the MCF-10A human mammary epithelial cell line by carcinogenic polycyclic aromatic hydrocarbons. *Mol Carcinog*, 25: 48–54. doi:10.1002/(SICI)1098-2744(199905)25:1<48::AID-MC6>3.0.CO;2-6 PMID:10331744

Tian L (2005). *Coal combustion emissions and lung cancer in Xuan Wei, China* [PhD Thesis]. Berkeley, CA: University of California.

Tonooka Y, Liu J, Kondou Y *et al.* (2006). A survey on energy consumption in rural households in the fringes of Xian city. *Energy Build*, 38: 1335–1342. doi:10.1016/j.enbuild.2006.04.011

Tsai SM, Zhang JJ, Smith KR *et al.* (2003). Characterization of non-methane hydrocarbons emitted from various cookstoves used in China. *Environ Sci Technol*, 37: 2869–2877. doi:10.1021/es026232a PMID:12875388

Wang TJ, Zhou BS, Shi JP (1996). Lung cancer in nonsmoking Chinese women: a case–control study. *Lung Cancer*, 14: Suppl 1S93–S98. doi:10.1016/S0169-5002(96)90214-7 PMID:8785672

Watson AY, Valberg PA (1996). *Particle-induced lung tumors in rats: evidence for species specificity in mechanisms.* In: *Particle overload in the rat lung and lung cancer: Implications for human risk assessment.* Taylor and Francis, editors. Washington, DC: pp. 227–257.

Watson JG, Chow JC, Houck JE (2001). PM2.5 chemical source profiles for vehicle exhaust, vegetative burning, geological material, and coal burning in Northwestern Colorado during 1995. *Chemosphere*, 43: 1141–1151. doi:10.1016/S0045-6535(00)00171-5 PMID:11368231

WHO (1998). *Selected Non-heterocyclic Polycyclic Aromatic Hydrocarbons*. Geneva: International Programme on Chemical Safety, No. Environmental Health Criteria 202.

Wornat MJ, Ledesma EB, Sandrowitz AK *et al.* (2001). Polycyclic aromatic hydrocarbons identified in soot extracts from domestic coal-burning stoves of Henan Province, China. *Environ Sci Technol*, 35: 1943–1952. doi:10.1021/es001664b PMID:11393972

Wu-Williams AH, Dai XD, Blot W *et al.* (1990). Lung cancer among women in north-east China. *Br J Cancer*, 62: 982–987. doi:10.1038/bjc.1990.421 PMID:2257230

Xu K, Li X, Hu F (1997). [A study on polycyclic aromatic hydrocarbon-DNA adduct in lung cancer patients exposed to indoor coal-burning smoke] *Zhonghua Yu Fang Yi Xue Za Zhi*, 31: 95–98. PMID:9812621

Xu ZY, Blot WJ, Xiao HP *et al.* (1989). Smoking, air pollution, and the high rates of lung cancer in Shenyang, China. *J Natl Cancer Inst*, 81: 1800–1806. doi:10.1093/jnci/81.23.1800 PMID:2555531

Xue W & Warshawsky D (2005). Metabolic activation of polycyclic and heterocyclic aromatic hydrocarbons and DNA damage: a review. *Toxicol Appl Pharmacol*, 206: 73–93. doi:10.1016/j.taap.2004.11.006 PMID:15963346

Yan J, Wang L, Fu PP, Yu H (2004). Photomutagenicity of 16 polycyclic aromatic hydrocarbons from the US EPA priority pollutant list. *Mutat Res*, 557: 99–108. PMID:14706522

Yan L (1990). [Epidemiological survey of endemic fluorosis in Xiou Shan and Bao Jing areas] *Zhonghua Liu Xing Bing Xue Za Zhi*, 11: 302–306. PMID:2261621

Yan R, Zhu H, Zheng C, Xu M (2002). Emissions of organic hazardous air pollutants during Chinese coal combustion. *Energy*, 27: 485–503. doi:10.1016/S0360-5442(02)00003-8

Yin XR, Guan N, Liang C *et al.* (1984). Study on lung cancer in mice by intra-bronchial injection of Xuan Wei coal fumes extracts. *Wei sheng Yan Jui*, 13(3): 21–25.

Zhang A, Feng H, Yang G *et al.* (2007a). Unventilated indoor coal-fired stoves in Guizhou province, China: cellular and genetic damage in villagers exposed to arsenic in food and air. *Environ Health Perspect*, 115: 653–658. doi:10.1289/ehp.9272 PMID:17450239

Zhang AH, Bin HH, Pan XL, Xi XG (2007b). Analysis of p16 gene mutation, deletion and methylation in patients with arseniasis produced by indoor unventilated-stove coal usage in Guizhou, China. *J Toxicol Environ Health A*, 70: 970–975. doi:10.1080/15287390701290808 PMID:17479413

Zhang AH, Yang GH, Li J *et al.* (2000b). The situation of DNA synthesis DNA damage and DNA repair in arsenism patients blood cells caused by coal burning. *Carcinogen Teratogen Mutagen*, 12: 76–78.

Zhang J & Smith KR (1999). Emissions of carbonyl compounds from various cookstoves in China. *Environ Sci Technol*, 33: 2311–2320. doi:10.1021/es9812406

Zhang J, Smith KR, Ma Y *et al.* (2000a). Greenhouse gases and other airborne pollutants from household stoves in China: a database for emission factors. *Atmos Environ*, 34: 4537–4549. doi:10.1016/S1352-2310(99)00450-1

Zhong L, Goldberg MS, Gao YT, Jin F (1999). Lung cancer and indoor air pollution arising from Chinese-style cooking among nonsmoking women living in Shanghai, China. *Epidemiology*, 10: 488–494. doi:10.1097/00001648-199909000-00005 PMID:10468420

Zhou BS, Wang TJ, Guan P, Wu JM (2000). Indoor air pollution and pulmonary adenocarcinoma among females: a case–control study in Shenyang, China. *Oncol Rep*, 7: 1253–1259. PMID:11032925