Special Report 16 November 2007

Mobile-Source Air Toxics: A Critical Review of the Literature on Exposure and Health Effects

Polycyclic Organic Matter

For further information please contact the Health Effects Institute:
+1-617-886-9330
pubs@healtheffects.org
www.healtheffects.org

Polycyclic Organic Matter

INTRODUCTION

Polycyclic organic matter (POM) consists of a mixture of hundreds of chemicals, including polycyclic aromatic hydrocarbons (PAHs), their oxygenated products, and their nitrogen analogs (nitro-PAHs). POM compounds with five or more benzene rings are generally associated with particulate matter (PM). Those with four or fewer rings are semivolatile and are partitioned between the particulate and gaseous phase.

The mixture of compounds in POM varies from place to place and from time to time. Sources of airborne POM include various mobile-source combustion, industrial, and domestic processes. In populated areas, the principal emission source in ambient air is exhaust from the combustion of gasoline, diesel fuel, and home-heating oil. In addition, there are industrial and municipal sources that can have a significant effect on human exposure, although most POM compounds have no commercial uses. In indoor air, the principal source is usually smoke from the burning of tobacco. Food is thought to be the major source of human exposure to PAHs, owing largely to PAH formation during cooking. Another source of dietary intake is the deposition of PAH-containing particles from ambient air onto fruits, vegetables, grains, and other foods grown outdoors. For nonsmokers living in relatively low-pollution areas, dietary intake of PAHs represents a larger source of POM exposure than does inhalation (Boström et al. 2002).

The EPA definition used for POM in the National Air Toxics Assessment (NATA) included only particle-phase POM; it defined POM as a group of 16 individual PAH species that are measured by the EPA's Method 610. They are known as the 16-PAH group and include acenaphthene, acenaphthylene, anthracene, benzo[*a*]anthracene, benzo[*a*]pyrene, benzo[*b*]fluorene, benzo[*ghi*]perylene, benzo[*k*]fluoranthene, chrysene, dibenz[*a*,*h*]anthracene, fluoranthene, fluorene, indeno[1,2,3-*cd*]pyrene, naphthalene, phenanthrene, and pyrene. Seven of these—benzo[*a*]anthracene, benzo[*a*]pyrene, benzo[*b*]fluoranthene, benzo[*k*]fluoranthene, chrysene, dibenz[*a*,*h*]anthracene, and indeno[1,2,3-*cd*]pyrene—are known as the 7-PAH group and are classified as "probable human carcinogens." The structures of these compounds are included in Figure 21. Reactive bay regions and fjord regions are pointed out.

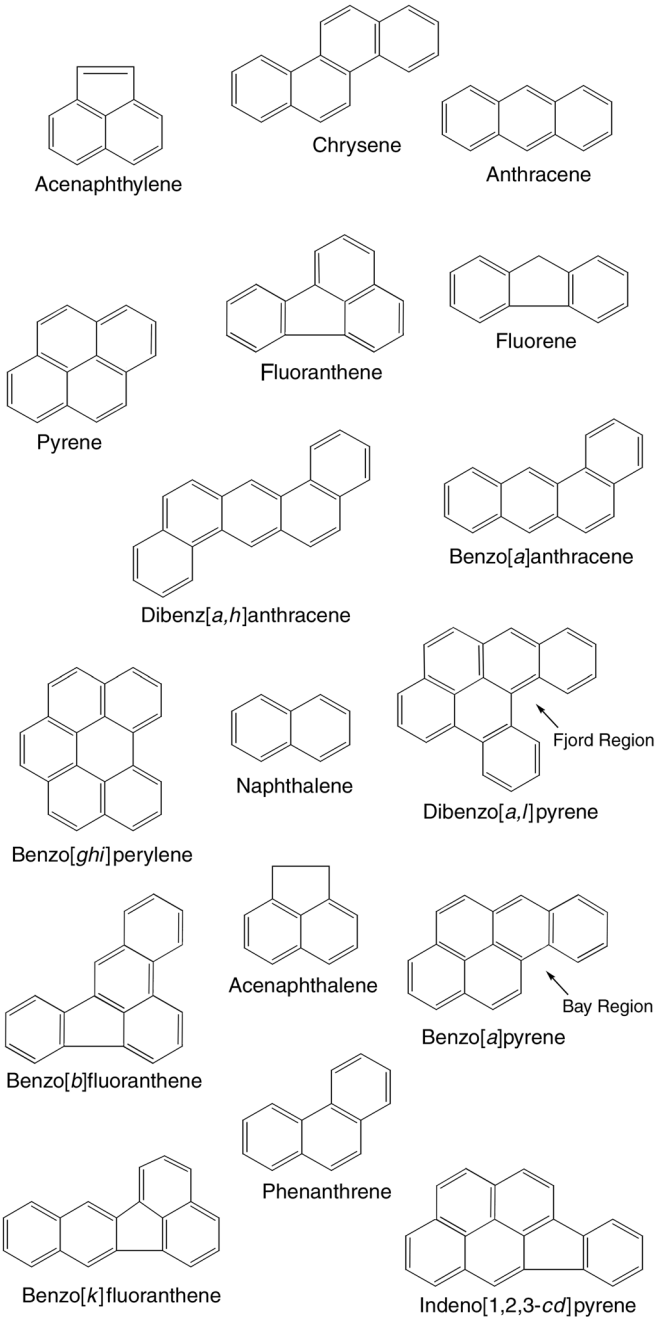

Figure 21. Structure of 17 POM compounds, with examples of bay and fjord regions indicated.

A glossary of terms appears on page 17; a list of abbreviations and other terms appears at the end of this report.

BENCHMARK LITERATURE

The following evaluation of research literature on POM is based on data and source tables listed in Appendices B–D (available on the HEI Web site) of this report as well as on key selected studies. Information on biomarkers of exposure is based on reviews in the Agency for Toxic Substances and Disease Registry (ATSDR 1995), Angerer and colleagues (1997), and Kyrtopoulos and colleagues (2001). Toxicologic information is based on reviews in the ATSDR (1995), EPA (1994b, 2000g), Rijksinstituut voor Volksgezondheid en Milieu (RIVM) (Sloof et al. 1989), and World Health Organization (WHO 1998; 2000a). Information on cancer risk is based primarily on a review for the Swedish government (Boström et al. 2002) and a risk assessment for benzo[*a*]pyrene developed by the WHO (1987). Additional information on health effects was summarized primarily from workplace studies and a limited number of community studies. In particular, sources of information central to the recent International Agency for Research on Cancer (IARC) review of PAHs (Cogliano et al. 2005) were reviewed.

EXPOSURE

SOURCES AND EMISSIONS

POM compounds result primarily from incomplete combustion and occur primarily as airborne particles. Emissions sources include vehicle-fuel combustion, cigarette smoking, road paving, roof tarring, meat grilling, and wood burning. Residential wood burning is believed to be the largest source of POM emissions, although vehicle-fuel combustion might be the largest source in urban areas (Boström et al. 2002). Nationally, however, the 1996 NATA estimates suggested that mobile sources accounted for only a small percentage of ambient exposure to the 7-PAH group in urban (2.9% on-road vehicles, 0.6% non-road vehicles) and rural counties (3.1% on-road, 0.8% non-road). Mobile-source contributions to the larger 16-PAH group accounted for less than 0.5% (EPA 2002d). Diesel vehicles generally emit more PAHs than gasoline-fueled vehicles, although different PAHs are emitted by the different types of engines. In a tunnel study, Marr and colleagues (1999) concluded that light-duty vehicles were an important source of higher molecular weight (four- and five-ring) PAHs, such as benzo[*b*+*k*]fluoranthene, benzo[*a*]pyrene, dibenz-[*a*,*h*]anthracene, and indeno[1,2,3-*cd*]pyrene, and that heavy-duty vehicles were a more important source of lower molecular weight PAHs, such as fluoranthene and pyrene. Another tunnel study also suggested that fluoranthene and pyrene are good tracers for exposure to diesel emissions (Chellam et al. 2005). In cold climates, emissions from "cold starts" might account for as much as 50% of the PAHs emitted by gasoline-fueled vehicles (Boström et al. 2002).

POM compounds are highly reactive and can be degraded in the atmosphere by photooxidation and reaction with atmospheric oxidants. Particle-bound PAHs are removed by deposition in 0.4 to 40 days (Seinfeld and Pandis 1998). PAH-particle sizes are bimodal. Fresh emissions range from 0.01 to 0.5 μm in size; urban aerosols also include an additional mode of particles that range from 0.5 to 1 μm. In the atmosphere, PAHs react with gaseous NO_2 (in the presence of HNO_3) to form mono- and di-nitro-PAHs. At 25°C, at equilibrium, benzo[*a*]pyrene, other PAHs with five or six rings, and chrysene exist predominantly in the aerosol phase. POM can be transported great distances and has been found even in locations remote from where the POM originated (Boström et al. 2002; Seinfeld and Pandis 1998).

Although recent research has begun to provide information on ambient concentrations of nitro-PAHs as well as quinones and hydroquinones (oxygenated products of PAHs) that might be important toxicologically, more information is still needed to support general conclusions about these compounds.

AMBIENT, OUTDOOR, AND INDOOR CONCENTRATIONS AND PERSONAL EXPOSURES

Ambient Air

Most measurements of POM involve collection of particles on filters and chemical analysis of the collected samples. A semicontinuous monitor is also available that measures total particle-bound PAH. This monitor was used by Levy and colleagues (2003) in a study in Roxbury, Mass. The mean total particle PAH concentration (averaged over 10 minutes) was 18 ng/m^3 (ranging from 4 to 57 ng/m^3, with a median of 8 ng/m^3). Higher concentrations were measured closer (within 20 m) to vehicle traffic. Regression models indicated an association between PAH concentrations and the numbers of nearby large diesel vehicles. The same total-PAH technique was used by Sapkota and colleagues (2005) in their study of tollbooth workers. The mean total particle PAH concentration (averaged over 3 hours) outside tollbooths was 135 ng/m^3 (ranging from 3 to 1130 ng/m^3) and correlated with the changes in traffic counts over time. The most extensive set of continuous particle-bound PAH data comes from the California Children's Environmental Health Protection Program measurements in Fresno, Calif. (California Air Resources Board 2003). Over a 1-year period, the mean concentration (averaged

over 1 hour) was 11.5 ng/m^3 (ranging from 0.4 to 291 ng/m^3).

Because of the complexity and cost of analysis, most studies of POM species include only a limited number of samples and are difficult to interpret in terms of their representativeness. Furthermore, different studies focused on different POM species and used different sampling and analytical techniques. Table 7 summarizes the range of concentrations of specific PAHs (particle phase only) measured in urban areas (including urban roadside high-traffic sites).

The NATA (EPA 2002d) reported higher modeled mean concentrations of PAHs in urban counties (108 ng/m^3) than in rural counties (21 ng/m^3). This finding was supported by data from Dachs and colleagues (2002), who reported PAH

Table 7. PAHs Measured in Ambient Air in Urban Areas

Compound	Number of Rings	Molecular Weight	Concentrations (ng/m^3) Minimum	Maximum	Citations	Notes
Benzo[*a*]anthracene	4	228	0.006	0.19	Manchester-Neesvig et al. 2003 Dachs et al. 2002 Naumova et al. 2002 Eiguren-Fernandez et al. 2004	a
Benzo[*b*]fluoranthene	5	252	0.01	0.26[b]	Sapkota et al. 2005 California Air Resources Board 2003 Naumova et al. 2002 Eiguren-Fernandez et al. 2004 Gigliotti et al. 2000	c
Benzo[*k*]fluoranthene	5	252	0.006	0.32	California Air Resources Board 2003 Manchester-Neesvig et al. 2003 Naumova et al. 2002 Eiguren-Fernandez et al. 2004 Gigliotti et al. 2000	d
Benzo[*a*]pyrene	5	252	0.009	0.28	California Air Resources Board 2003 Manchester-Neesvig et al. 2003 Dachs et al. 2002 Naumova et al. 2002 Eiguren-Fernandez et al. 2004 Gigliotti et al. 2000	e
Chrysene	4	228	0.008	0.3	Manchester-Neesvig et al. 2003 Dachs et al. 2002 Naumova et al. 2002 Eiguren-Fernandez et al. 2004 Gigliotti et al. 2000	e
Dibenz[*a,h*]anthracene	5	278	No measurements identified			
Indeno[1,2,3-*cd*]pyrene	6	276	0.003	0.59	California Air Resources Board 2003 Manchester-Neesvig et al. 2003 Dachs et al. 2002 Naumova et al. 2002 Eiguren-Fernandez et al. 2004 Gigliotti et al. 2000	f

[a] Measurements in tunnel studies as high as 10 ng/m^3 (Naumova et al. 2002; Eiguren-Fernandez et al. 2004).

[b] Maximum measurements as high as 1.1 ng/m^3 for unresolved benzo[*b*]fluoranthene + benzo[*k*]fluoranthene.

[c] Measurements in tunnel studies as high as 6.8 ng/m^3.

[d] Measurements in tunnel studies as high as 3.6 ng/m^3.

[e] Measurements in tunnel studies as high as 8.4 ng/m^3.

[f] Measurements in tunnel studies as high as 3.1 ng/m^3.

concentrations in urban Baltimore that were two to three times higher than concentrations measured over water in the Chesapeake Bay. (Their study was limited to 24 samples collected in a single month.) Gigliotti and colleagues (2000) measured similarly high concentrations in urban areas compared with rural areas in Southern California.

In Canada, data from approximately 2200 daily PAH samples collected at 35 sites between 1994 and 1997 were summarized (Environment Canada 1998). Mean PAH concentrations varied by more than three orders of magnitude from remote rural areas to industry-influenced sites (the range of means was 0.9 to 801 ng/m^3, and the range of 90th-percentile values was 4.8 to 2650 ng/m^3). For urban sites (with more than 10 sampling days of data), mean total-PAH concentrations ranged from 10 to 65 ng/m^3 and 90th-percentile concentrations ranged from 14 to 115 ng/m^3. Large population centers and sites with industrial emissions or wood-smoke sources had the highest concentrations. The most commonly measured PAH species were phenanthrene, fluoranthene, pyrene, and benzo[*b*+*k*+*j*]fluoranthene. Vapor-phase species accounted for the majority of the PAH mass. No consistent nationwide trends were observed.

As part of the Relationships of Indoor, Outdoor, and Personal Air (RIOPA) study (Weisel et al. 2005), measurements were collected outside 55 homes of nonsmoking residents in Elizabeth, N.J., Houston, Tex., and Los Angeles, Calif. (Naumova et al. 2002). In the outdoor samples, total-PAH concentrations ranged from 12 to 110 ng/m^3 in Elizabeth, 10 to 160 ng/m^3 in Houston, and 4.2 to 64 ng/m^3 in Los Angeles. In the outdoor and corresponding indoor samples, total gas-phase-PAH concentrations were highest in Elizabeth, followed by Houston and then Los Angeles. Outdoor and corresponding indoor samples were highest in Elizabeth, followed by Los Angeles and then Houston. Significantly different profiles for five- to seven-ring PAHs in the outdoor samples suggested different PAH sources in the three cities. Benzo[*ghi*]perylene and coronene were the predominant high-molecular-weight PAHs in the outdoor samples in Los Angeles. Benzo[*b*+*k*]fluoranthene predominated in Houston. Such PAH-species variability was less striking in Elizabeth. The principal source of PAHs in Los Angeles is motor-vehicle emissions; in Houston it is petrochemical-industry emissions; and in Elizabeth it is both mobile-source and industrial emissions.

Given the interest in compounds that generate reactive oxygen species, measurements of four quinones (1,2-naphthoquinone, 1,4-naphthoquinone, 9,10-phenanthraquinone, and 9,10-anthraquinone) were made in airborne PM in Los Angeles. Substantial spatial variability in concentrations was observed, with downwind measurements showing elevated concentrations of 1,4-naphthoquinone and 9,10-phenanthraquinone, which are thought to be associated with vehicle emissions (Cho et al. 2004).

In-Vehicle Exposures

Measurements in vehicles are limited to total particle-bound PAHs. Riediker and colleagues (2003) reported a mean PAH concentration of 21.5 ng/m^3 in police patrol cars. No corresponding ambient or roadside measurements were available, but comparison with other roadside measurements did not suggest that in-vehicle concentrations were substantially higher than ambient concentrations at typical traffic sites. In a school-bus study in Southern California, Fitz and colleagues (2003) measured total particle PAH concentrations ranging from 36 to 198 ng/m^3, concentrations that were much higher than those measured at roadside locations.

Indoor Exposures

Only limited information is available about indoor concentrations of PAHs in developed countries. In China, high concentrations of PAHs have been measured in indoor settings in which biomass, and especially coal, is used for residential heating (Mumford et al. 1987). In addition to the outdoor RIOPA measurements at 55 homes in three cities described above, corresponding indoor measurements were made. The profiles for the five- to seven-ring PAHs in the indoor air in each of the three cities were similar to the outdoor profiles, which suggested that indoor concentrations of these PAHs were dominated by outdoor sources. Specifically, the measurements suggested that indoor concentrations of the particle-bound five- to seven-ring PAHs (e.g., benzo[*b*+*k*]fluoranthene, benzo[*a*]pyrene, indeno[1,2,3-*cd*]-pyrene, and dibenzo[*a*,*h*]anthracene) were dominated by outdoor sources; indoor sources were important for three-ring PAHs. Indoor concentrations of total PAHs were 22 to 350 ng/m^3 in Elizabeth, 21 to 310 ng/m^3 in Houston, and 16 to 220 ng/m^3 in Los Angeles; the ranking of mean concentrations by city corresponded to those of the outdoor samples.

Dubowsky and colleagues (1999) measured total particle-bound PAH in three (nonsmoking) Boston homes with varying proximities to traffic. The mean total PAH concentration at an urban site with traffic was 31 ng/m^3, more than three times higher than at a suburban site (8 ng/m^3). A daily peak in indoor PAH concentrations coincided with the morning rush hour at all three locations; higher concentrations were measured on weekdays than on weekends. Peaks also coincided with cooking, indicating the importance of this indoor source of PAHs in indoor air (Dubowsky et al. 1999). Total particle-bound PAHs measured in a variety of indoor environments in Boston were generally low, with mean concentrations ranging from approximately 5 to

10 ng/m^3. The highest concentrations were measured in a mall and a food court (Levy et al. 2002).

Personal Exposures

Tonne and colleagues (2004) measured personal PAH exposures (48-hour samples) of pregnant women in New York City. The mean total PAH concentration (for benz[*a*]anthracene, benzo[*b*]fluoranthene, benzo[*k*]fluoranthene, benzo[*ghi*]perylene, benzo[*a*]pyrene, chrysene and isochrysene, dibenz[*a,h*]anthracene, indeno[1,2,3]pyrene, and pyrene) was 8.0 ng/m^3 (ranging from 1.5 to 127 ng/m^3; SD = 9.5 ng/m^3). Mean concentrations of individual PAHs ranged from 0.06 ng/m^3 for dibenz[*a*,*h*]anthracene to 4.1 ng/m^3 for pyrene. Maximum concentrations ranged from 0.46 ng/m^3 for dibenz[*a*,*h*]anthracene to 96 ng/m^3 for pyrene. Both ambient concentrations and personal exposures were higher in winter than in summer for virtually all PAHs; the only exception was pyrene. The study identified significant predictors of PAH exposures, including amount of time spent outdoors, amount of time residential heating systems were running (more than 50% used fuel oil), and indoor burning of incense. No variables related to traffic sources were identified.

As part of the EXPOLIS (Air Pollution Exposure Distributions of Adult Populations in Europe) study (Zmirou et al. 2000), personal exposures to particle-phase PAHs were measured for 38 nonoccupationally exposed adult residents of Grenoble, France (Zmirou et al. 2002). Mean concentrations of nine PAHs (fluoranthene, pyrene, chrysene, benzo[*a*]-anthracene, benzo[*b*+*k*]fluoranthenes, benzo[*a*]pyrene, indeno[1,2,3-*cd*]pyrene, and benzo[*ghi*]perylene) were higher in winter than in summer. Annual mean concentrations ranged from 0.13 to 1.67 ng/m^3, depending on the species; the concentrations of fluoranthene and indeno[1,2,3-*cd*]pyrene were highest (Tonne et al. 2004). In Amsterdam, personal exposures of cyclists and drivers to total PAH during 1-hour trips along inner-city routes ranged from 7.5 to 24.7 ng/m^3 (van Wijnen et al. 1995).

SEASONAL TRENDS

Seasonal differences are evident for many of the PAHs. In general, concentrations of PAHs—especially those of higher molecular weight—are higher in winter than in summer, because emissions from heating sources increase and, to a lesser extent, because PAHs in the particle form are more abundant at lower temperatures (Naumova et al. 2002; Eiguren-Fernandez et al. 2004).

AMBIENT CONCENTRATIONS IN OTHER COUNTRIES

Measured concentrations of PAHs in Canada are similar to those in the United States, as shown in Table 8.

TOXICOLOGY

The biologic properties of the majority of POM compounds are not yet fully understood. Benzo[*a*]pyrene and 7,12-dimethylbenz[*a*]anthracene are the most extensively studied PAHs. The majority of the available information on POM toxicity is related to these two compounds.

BIOCHEMISTRY AND METABOLISM

The metabolism of POM is predominantly catalyzed by cytochrome P450-dependent monooxygenases (reviewed by the WHO International Programme on Chemical Safety 1998). The 1A1 and 1B1 forms of cytochrome P450 from animals and humans have been identified as being the most involved in metabolizing various carcinogenic PAHs to DNA-reactive diol epoxides. The presence of bay and fjord regions (see Figure 21) on many of these compounds makes them particularly reactive. These two major P450 forms are enzymes that are expressed in many mammalian tissues, either upon aryl hydrocarbon receptor–mediated induction (P450 1A1) or both constitutively and upon receptor-mediated induction (P450 1B1).

Benzo[*a*]pyrene is the most studied PAH with a bay region. It is first oxidized to form epoxide groups at several sites in its ring structure. These epoxides can be hydrated by epoxide hydrolase to form dihydrodiols or spontaneously rearrange to form phenols or quinone structures. The epoxide groups can also be detoxified by conjugation with glutathione; the phenol groups can be detoxified by conjugation with glucuronic acid. Benzo[*a*]pyrene is activated to

Table 8. PAH Measured in Canada[a]

Compound	Concentration (ng/m^3)	
	Rural Sites (n = 5)	Urban Sites (n = 12)
Indeno[1,2,3-*cd*]pyrene	0.04	0.24
Benz[*a*]anthracene	0.02	0.20
Benzo[*a*]pyrene	0.02	0.15
Benzo[*k*]fluoranthene	0.02	0.14
Benzo[*b*]fluoranthene	0.07	0.49
Chrysene	0.05	0.35
Dibenz[(*a,c*)+(*a,h*)] anthracene	0.01	0.04

[a] National Air Pollution Surveillance (NAPS) Air Toxics Monitoring Program (2002–2004). Data compiled by Tom Dann, Environment Canada (data available at *www.etc-cte.ec.gc.ca/NAPS/naps_data_e.html*). The urban Jonquiere site was excluded because it was affected by an aluminum smelter.

its ultimate DNA-reactive carcinogenic metabolite through the initial formation of (+)-benzo[*a*]pyrene-7,8-epoxide and its subsequent dihydrodiol metabolite (via epoxide hydrolase). This metabolite is subsequently activated to the ultimate reactive intermediate, (+)-*anti*-benzo[*a*]pyrene-7,8-dihydrodiol-9,10-epoxide, which can covalently interact with cellular DNA. In recent years, alternative metabolism mechanisms, such as formation of the radical cation (quinone and benzylic oxidation), have been proposed as contributors to the carcinogenic effects of PAHs.

In principle, the PAHs with fjord regions undergo the same metabolic activation and inactivation reactions as PAHs with bay regions. Of these, the most-studied compound is dibenzo[*a*,*l*]pyrene. Both P450 1A1 and P450 1B1 catalyze the formation of the 11,12-dihydrodiol and subsequently the 11,12-dihydrodiol-13,14-epoxide, of which the (−)-*anti*-dihydrodiol-epoxide is the most reactive and forms DNA adducts. Recent studies indicate that rat P450s form both the reactive 11,12-dihydrodiol-13,14-epoxide and the less reactive 7,8-dihydrodiol and that the human P450s 1A1 and 1B1 preferentially form the highly reactive (−)-*anti*-dihydrodiol-epoxide (Schober et al. 2006). This suggests that humans might be more susceptible to dibenzo[*a*,*l*]pyrene-induced cancers than rats.

NONCANCER HEALTH EFFECTS

Acute Effects

In animals, little is known about the adverse health effects associated with acute inhalation exposure to any of the PAHs, although some information is available on the effects of acute oral and dermal exposures to PAHs in animals, where the skin and liver have been identified as target organs of PAH toxicity.

Recently, toxicologic studies have suggested the importance of reactive oxygen species in the health effects of PM. To investigate the ability of PM to catalyze generation of reactive oxygen species, an assay was developed based on the reduction of oxygen by dithiothreitol. When the activity of this assay was correlated with measurements of the chemical composition of PM, high correlations were found for benzo[*g*]perylene ($r^2 = 0.82$), phenanthrene ($r^2 = 0.73$), pyrene ($r^2 = 0.73$), chrysene ($r^2 = 0.60$), and benzo[*b*]fluoranthene ($r^2 = 0.56$) and lower correlations ($r^2 = 0.32$ to 0.43) for other measured PAHs (fluoranthene, benz[*a*]anthracene, benzo[*k*]fluoranthene, benzo[*a*]pyrene, and indeno[1,2,3-*cd*]pyrene) (Cho et al. 2005).

Repeated-Dose Toxicity

Animal studies of some of the PAHs have identified the skin, liver, and hematopoietic system as targets. Animal studies have also reported that oral exposure to benzo[*a*]pyrene affects the blood and liver, and acenaphthene, fluoranthene, and fluorene affect the liver and other organ systems. By contrast, no effects of anthracene were seen in the liver or any other organ system even at the highest dose of 1000 mg/kg body weight/day. Adverse skin effects have been noted in animals after application of solutions containing benzo[*a*]pyrene; skin exposure to mixtures of PAHs also caused skin disorders.

Benzo[*a*]pyrene and dimethylbenzanthracene have been found to be potent immunosuppressants. Effects have been documented on humoral immunity, cell-mediated immunity, and host resistance.

Reproductive and Developmental Effects

Oral- and parenteral-exposure studies of pregnant rodents have reported adverse effects of PAHs, including intrauterine growth retardation, fetal mortality, and teratogenesis. Toxic effects in adult rodents were often reversible, even after high exposure concentrations, but effects in fetuses and neonates were severe and persistent even at lower doses. Oral or parenteral exposure to benzo[*a*]pyrene decreased fertility and induced total sterility in F1 progeny of CD-1 mice and decreased the incidence of pregnancy in female rats. Developmental effects resulting from oral exposure to benzo[*a*]pyrene, such as reduced viability of litters and reduced mean pup weight, have also been noted.

GENOTOXICITY

The genotoxic potential of PAHs has been extensively investigated using both in vivo and in vitro assays. Most PAHs are genotoxic in bacterial and mammalian systems after the addition of an exogenous mammalian metabolic system or metabolization by P450 enzymes. It has been shown that macrophages are the primary cells capable of metabolizing PAHs; these cells generate 7,8-dihydroxy-9,10-epoxybenzo[*a*]pyrene, the reactive metabolite of benzo[*a*]pyrene. Limited genotoxicity tests conducted on urine obtained from humans exposed to PAHs have, however, been negative. The formation of benzo[*a*]pyrene–DNA adducts, as well as of benzo[*a*]pyrene–protein adducts and DNA adducts with metabolically generated reactive PAH intermediates, has been demonstrated.

Exposure to PAH might increase the risk of heritable mutations. Somers and colleagues (2004) exposed mice to ambient air in an urban-industrial area of Hamilton, Ontario, with high ambient concentrations of both PM and PAHs. Control groups were exposed to high-efficiency particulate air (HEPA)–filtered air at the same location and to air in a rural area with less pollution. HEPA filtration was

associated with a significant reduction in the heritable-mutation rate. This effect was primarily related to paternal mutations. PAHs bound to ambient air particles are the leading candidates for causing such mutations, as discussed in an editorial accompanying the Somers report (Samet et al. 2004). Whether this occurs in humans is unknown, but one study (Selevan et al. 2000) has suggested that exposure to elevated concentrations of ambient air pollution might affect sperm quality in young men. Furthermore, PAHs can be transferred across the placenta, exposing the fetus. In studies of mothers and newborns in Poland (Perera et al. 2002), PAH–DNA adducts in cord blood, determined using ^{32}P-postlabeling, were associated with the mutant frequency at the *HPRT* locus in the newborn ($\beta = 0.56$, $P = 0.03$). This suggests a possible link between exposure to PAHs in ambient air and somatic mutations in human newborns.

CARCINOGENICITY

There is a large database concerning the health effects in animals caused by exposure to complex mixtures that contain PAHs (such as crude oils, high-boiling-point distillates, petroleum products, coal tars, and creosote), and many PAHs are animal carcinogens by various routes. Studies have reported tracheal papillomas and carcinomas in hamsters from inhalation exposure to benzo[*a*]pyrene and squamous-cell tumors of the lung in rats from inhalation exposure to PAH mixtures. Leukemia and tumors in the liver, mammary gland, respiratory tract, and gastrointestinal tract were found in animals after oral exposure to benzo[*a*]pyrene, benz[*a*]anthracene, and dibenz[*a*,*h*]anthracene. The ability of inhaled benzo[*a*]pyrene to cause lung cancer can be enhanced by coexposure to other substances, such as cigarette smoke, asbestos, and (probably) airborne particles. The results of skin studies indicate that benz[*a*]anthracene, benzo[*a*]pyrene, benzo[*b*]fluoranthene, benzo[*j*]fluoranthene, benzo[*k*]fluoranthene, chrysene, dibenz[*a*,*h*]anthracene, and indeno[1,2,3-*cd*]pyrene are tumorigenic in rats and mice. Although many of these studies would be considered inadequate by current standards, the results nevertheless indicate that these PAHs can induce tumors, acting as both tumor initiators and promoters.

HUMAN HEALTH

BIOMARKERS OF EXPOSURE

The presence of PAHs and their metabolites in human urine and blood after inhalation, oral, or dermal exposures indicates that PAH absorption occurs. PAHs appear to be widely distributed in tissues after inhalation or oral exposure. The metabolism of some individual PAH compounds has been extensively studied in human- and animal-tissue homogenates, cultures, and perfused systems; information on interactions between individual components of POM is, however, insufficient.

PAHs have been identified and quantified in tissues of exposed humans, including lung, ovary, placenta, and uterine cervix, as well as leukocytes. Samples of lung tissue, for example, were obtained from 364 autopsies in Japan and analyzed for benzo[*a*]pyrene, benzo[*k*]fluoranthene, and benzo[*ghi*]perylene (Seto et al. 1993). PAH concentrations in the lung were higher in males than in females and higher in patients with lung cancer than in those without. Only benzo[*ghi*]perylene concentrations correlated with a history of smoking, and then only in males.

In general, POM (metabolized or unmetabolized) can be excreted into bile and urine as well as into breast milk. Secretion into the bile followed by elimination in the feces appears to be the major excretory route. The extent of elimination of PAHs varies among species. Tolos and colleagues (1990) measured concentrations of 1-hydroxypyrene in the urine of workers. Exposed workers had concentrations of 1-hydroxypyrene in the urine that were 17 times higher than those in unexposed controls; a history of smoking did not affect these results. In the study, ambient concentrations of pyrene were found to reflect environmental concentrations of coal tar pitch–derived PAHs.

Metabolites of POM can form adducts with DNA and proteins in tissues and blood; these can be measured in vivo. Using ^{32}P-postlabeling, Peluso and colleagues (2004) measured DNA adducts in blood lymphocytes and in bronchial and nasal brush biopsies from 55 patients undergoing diagnostic bronchoscopy. The quantity of adducts in bronchial tissue was weakly but significantly correlated with the quantity in blood lymphocytes ($r = 0.320$, $P < 0.05$) and tissue from the nasal brush biopsies ($r = 0.477$, $P < 0.01$). Specific adducts were not determined. The study suggests that nasal tissue is a potentially useful source for detecting PAH–DNA adducts. Other studies (Wiencke et al. 1995) have confirmed associations between DNA adducts in blood lymphocytes and lung tissue, although the relationship was generally weak.

Benzo[*a*]pyrene diol epoxide–DNA adducts were detected in bronchial epithelial cells in one of five lung specimens examined (Shamsuddin and Gan 1988). Smokers have higher concentrations of PAHs and DNA adducts than nonsmokers. Using the ^{32}P-postlabeling assay, Reddy and colleagues (1991) found that PAH–DNA adducts in blood leukocytes from foundry workers correlated with their exposure to benzo[*a*]pyrene, which was used as a surrogate for POM exposure.

PAH adducts were detected in placentas from live births in two regions of Bohemia in the Czech Republic—in Teplice, a polluted industrial area, and Prachatice, an agricultural area without heavy industry (Topinka et al. 1997). The quantities of adducts were higher in placentas from Teplice than from Prachatice (2.12 ± 1.46 compared with 1.48 ± 1.09 adducts per 10^8 nucleotides, respectively; $P = 0.0004$). However, little detail was provided on subject selection, ambient-air-monitoring methodology, or indoor exposure conditions, and the number of subjects was relatively small.

Using high-performance liquid chromatography and fluorescence detection, Pavanello and colleagues (1999) measured benzo[*a*]pyrene diol epoxide–DNA adducts in blood mononuclear cells from 130 people exposed to PAHs in various settings and by various routes—26 patients with psoriasis undergoing coal-tar treatment, 15 coke-oven workers, 19 chimney sweeps, 36 aluminum workers—and 34 nonexposed controls. Urinary levels of 1-pyrenol served as the biomarker of exposure. The quantities of adducts appeared to be most influenced by chronic, high-concentration respiratory exposure. No effect on the quantities of adducts was seen in patients undergoing coal-tar treatment, even though their daily dose of coal tar was 10 to 50 times higher than that of occupationally exposed workers. Eating grilled meats or smoking had no effect on the quantities of adducts. These findings suggest that the inhalation route of exposure to chronic, high concentrations of PAHs is the most important factor in adduct formation in occupational settings.

Breast milk has also been analyzed for DNA adducts following exposure to POM (Kalantzi et al. 2004). This is relevant not only with respect to determining exposure to POM, but also to the subsequent risk of breast cancer. Human mammary carcinoma cells were exposed to extracts from breast milk samples from four women in the U.K., and DNA adducts were measured using the ^{32}P-postlabeling assay. Effects were also examined when cells were exposed to breast milk extracts in combination with benzo[*a*]pyrene. Breast milk extracts increased micronuclei formation, independent of co-exposures to benzo[*a*]pyrene. All four extracts increased the percentage of p53-positive cells. One extract, when combined with benzo[*a*]pyrene, caused a 100-fold increase in benzo[*a*]pyrene–DNA adducts compared with benzo[*a*]pyrene alone. These findings suggest that environmental contaminants in breast milk other than benzo[*a*]pyrene might enhance the genotoxic effect of benzo[*a*]pyrene.

These studies illustrate that urinary concentrations of PAH metabolites, tissue concentrations of PAHs, and PAH–DNA and PAH–protein adducts in blood cells and tissue provide useful biomarkers of exposure to POM. However, because the exposures to POM in these studies are not known, the exposure–biomarker relationship is far from clear. Also unclear is the relationship between these biomarkers and the risk of cancer or noncancer health effects.

CANCER

The evidence for effects of exposure to POM on human health comes from epidemiologic studies. In general, these studies establish relationships between exposures and health outcomes but usually cannot prove causality. The exposures involve complex mixtures of POM and other gaseous and particulate pollutants and might be confounded by tobacco-smoke exposure. Therefore, human studies of POM exposure generally cannot ascribe health effects to POM alone nor to specific POM species.

Soot, coal tar, and pitch, all of which contain POM, have been known since the early 20th century to cause cancer in workers. Studies in the 1960s (Doll et al. 1972) demonstrated increased risk of mortality from lung and bladder cancers in "gasworkers" (workers exposed to coal-combustion products) in the U.K. More recent studies in occupational settings, where PAH concentrations can be one to two orders of magnitude higher than in ambient air, provided convincing evidence that POM is genotoxic and carcinogenic in humans (Kyrtopoulos et al. 2001; Mori 2002).

Armstrong and colleagues (2004) undertook a review and meta-analysis to quantify the lung-cancer risk associated with occupational exposure to benzo[*a*]pyrene. A 100 μg/m^3-years exposure to benzo[*a*]pyrene was associated with an average relative risk (RR) for lung cancer of 1.20 (CI, 1.11–1.29). The RR varied markedly with occupation; the highest risks were in the asphalt industry (RR = 17.5; CI, 4.21–72.78) and among chimney sweeps (RR = 16.2; CI, 1.64–160.7). Exposure to PM did not appear to be a confounder.

Studies in the Xuan Wei region of China provided evidence that cooking with "smoky" coal, which is high in PAHs and methylated PAHs, causes lung cancer (Mumford et al. 1987). The women in the study were virtually all nonsmokers yet, in some communes in the region, had a very high incidence of lung cancer. Lung-cancer mortality correlated closely with the use of smoky coal for cooking. In the commune of Cheng Guan, where 100% of homes used smoky coal, the lung-cancer mortality was 151.8 per 100,000 population. In the commune of Xi Ze, where no homes used smoky coal, lung-cancer mortality was 0.7 per 100,000. Tumors from 24 women who were nonsmokers showed high rates of mutations in both the *K-ras* and *P53* oncogenes, but their mutational spectra differed from those of smoking-related tumors (DeMarini et al. 2001).

These studies provided strong evidence for PAH exposure as a cause of lung cancer.

Studies of ambient exposure provided less definitive findings. Confounders included occupational exposures, indoor exposures to tobacco smoke and other sources, and dietary intake of PAHs. A series of studies have compared PAH concentrations in ambient air and PAH–DNA adducts in people living in an industrialized, highly polluted area and in a relatively clean area of Poland (Perera et al. 1998, 1992a,b, 2002; Whyatt et al. 1998). Estimated benzo[*a*]pyrene concentrations in the air of an industrialized area ranged from 0.057 μg/m^3 (in January) to 0.015 μg/m^3 (in May). The mean numbers of adducts per 10^8 nucleotides measured in subjects were 30.4×10^{-8} in winter and 4.2×10^{-8} in summer in the polluted area and 11.01×10^{-8} in winter and 3.0×10^{-8} in summer in the cleaner area. These findings suggested that variations in the amounts of PAH–DNA adducts by season and degree of pollution were related to variations in PAH concentrations in ambient air.

PAHs cause breast cancer in animals, but their role in causing breast cancer in humans is less clear. In a case–control study in Long Island, N.Y., Gammon and colleagues (2002) examined the relationship between breast cancer and blood PAH–DNA adducts (measured using an enzyme-linked immunosorbent assay [ELISA]) as a biomarker of exposure in women. Blood samples were tested from 576 women with cancer and 427 controls. The age-adjusted odds ratio (OR) for breast cancer for the highest compared with the lowest quintiles of adducts was 1.51 (CI, 1.04–2.20). However, there was no dose–response relationship and no relationship between the quantity of adducts and smoking or dietary PAH sources. The authors concluded that there might be a threshold above which additional effects are not observed. It is also possible that the ELISA lacked specificity for PAH adducts.

Taken together, these studies provided suggestive evidence that living in areas with high concentrations of ambient air pollution containing POM is genotoxic. However, the exposure–response relationship remains unclear, and the causality of POM in these relationships has not been established. Furthermore, there is little convincing evidence that the lower ambient concentrations of POM found in most Western industrialized cities are genotoxic in humans.

NONCANCER HEALTH EFFECTS

No reports of effects on human health after acute (short-term) exposure to POM were available. Epidemiologic studies of workers exposed to benzo[*a*]pyrene and PM by inhalation reported respiratory health effects. Recent studies suggest an effect of PAHs in conjunction with PM on the development of cardiovascular diseases, including atherosclerosis. Skin exposure to mixtures of PAHs might cause skin disorders or exacerbate existing lesions. Chronic exposure to benzo[*a*]pyrene has resulted in dermatitis, photosensitization, irritation of the eyes, and cataracts.

Reproductive and Neonatal Health

Only limited data were available on the effects of POM on reproduction and development in humans. Benzo[*a*]pyrene can adversely affect fertility, oocytes, and weight gain in animals. However these effects are observed at far higher concentrations than those found in ambient air. Although there are no studies directly addressing this issue in humans, the possibility exists that exposure to POM can cause noncancer health effects in humans, especially in conjunction with other exposures to PM.

Exposure to PAHs as part of ambient PM might contribute to low birth weight in infants. This possibility is supported by a study (Dejmek et al. 2000) of full-term births in two regions of Bohemia in the Czech Republic—Teplice, an area of industry and coal-burning power plants, and Prachatice, an agricultural area without heavy industry and with much lower concentrations of ambient PM than Teplice. However, both regions had similar ambient concentrations of PAHs. Data on full-term births to mothers of European origin were compared with ambient concentrations of PM and seven carcinogenic PAHs. In Teplice, for each 10-ng increase in PAH concentration, the adjusted OR for intrauterine growth retardation during the first gestational month was 1.22 ($P < 0.004$). A similar relationship was seen in Prachatice, but the data were not statistically significant.

Another study (Hertz-Picciotto et al. 2005), using the same data from these two areas, showed that ambient concentrations of both PM less than or equal to 2.5 μm in aerodynamic diameter ($PM_{2.5}$) and PAHs were significantly associated with decreases in T lymphocytes in the cord blood of newborn infants. For a 100-ng/m^3 increase in PAHs, the percentage change in CD3+ T lymphocytes was −3.3% (95% CI, −5.6% to −1.0%). This effect was more than doubled for infants from homes that burned coal for heating. The findings suggested that the mother's exposure to ambient PAHs in the two weeks before birth might affect the immune status of the newborn. However, PAH and $PM_{2.5}$ concentrations were correlated in this study (Spearman correlation coefficient = 0.56, $P < 0.0001$), and independent effects were not determined.

Recent studies have examined birth outcomes in relation to environmental exposures in susceptible populations in New York City (Perera et al. 2004, 2005a). In 214 deliveries by nonsmoking women, maternal and cord blood was analyzed

for benzo[*a*]pyrene–DNA adducts and cotinine (as a measure of environmental tobacco-smoke exposure). There was a significant relationship between birth outcomes and both the amount of adducts in cord blood and cotinine. In the group with more DNA adducts and cotinine, birth weight was reduced 6.8% and head circumference 2.9% compared with the group with fewer adducts and less cotinine (Perera et al. 2004). Data were also examined following the World Trade Center disaster of September 11, 2001 (Perera et al. 2005b). In women pregnant at the time and living within one mile of the World Trade Center site on that date, amounts of DNA adducts in cord blood were inversely correlated with distance from the site. In the newborns of mothers exposed to environmental tobacco smoke (higher cotinine concentrations), a doubling of DNA adducts in cord blood corresponded to an 8% reduction in birth weight ($P = 0.03$) and a 3% reduction in head circumference ($P = 0.04$). In a pilot study performed in New Jersey, high ambient POM exposure was associated with fetal death (OR = 1.19), premature birth (OR = 1.25), and low birth weight (OR = 1.31) (Vassilev et al. 2001).

Cardiovascular and Respiratory Effects

Burstyn and colleagues (2003) studied a retrospective cohort of 58,862 men who started working in the asphalt industry between 1919 and 1939 in Denmark, Finland, France, Germany, Israel, the Netherlands, and Norway. Exposures to PAHs were modeled, based on workplace measurements. Deaths from obstructive lung disease were significantly associated with average exposures to PAHs ($P = 0.01$) and marginally associated with cumulative exposures ($P = 0.06$). However, data on smoking were not available, and confounding could not be excluded. Deaths from ischemic heart disease were examined in 12,367 of these workers employed between 1953 and 2000, with an average follow-up of 17 years (Burstyn et al. 2005). The risk of death from ischemic heart disease was significantly associated with both the average and the cumulative benzo[*a*]pyrene exposure concentrations. The relative risk associated with exposure to benzo[*a*]pyrene concentrations of 273 ng/m^3 or higher was 1.64 (CI, 1.13–2.38). The authors estimated that, if smoking were considered as a potential confounder, the highest PAH-exposure categories would be associated with an approximately 20 to 40% excess risk of ischemic heart disease.

POM is a component of combustion-related PM, especially diesel exhaust. Diesel PM (DPM) has been associated with airway inflammation in humans as well as allergic sensitization in nasal-instillation studies. However, diesel exhaust is a complex mixture, and there is little direct evidence to implicate POM as a causative factor of these health effects. In in vitro studies, ultrafine PM has been shown to enter cells and intracellular organelles, including the nucleus and mitochondria, by way of diffusion (Geiser et al. 2005). PM can interfere with one-electron transfers in the mitochondrial internal membrane; perturbation of the mitochondrial permeability transition pore can contribute to increased generation of superoxide anions and the induction of apoptosis (Li N et al. 2003). Organic extracts from DPM and quinone compounds appear to mimic these phenomena. Although the concentrations of PM and POM used in these studies are higher than those found in ambient air, they might provide insights into plausible mechanisms by which POM associated with ambient PM could mediate noncancer health effects.

One study provided insights into how POM might enhance responses to allergen challenge. Kepley and colleagues (2003) incubated human blood basophils with PAHs and measured the release of histamine and interleukin (IL)-4 with and without antigen. Several PAHs enhanced histamine and IL-4 release in response to crosslinking of the high-affinity IgE receptor FcϵRI. For one compound, 1,6-benzo[*a*]pyrene-quinone, signaling involved tyrosine phosphorylation and production of reactive oxygen species. Thus, PAHs might enhance allergic inflammation by increasing allergen-induced mediator release from basophils and possibly from mast cells, which are key effector cells in asthma.

REGULATORY SUMMARY

No specific guideline value has been recommended by the WHO for POM in air, although there are recommendations for individual PAHs. A unit lifetime risk for benzo[*a*]pyrene as an indicator air constituent for PAHs was estimated to be 8.7×10^{-5} per ng/m^3, based on epidemiologic data from studies in coke-oven workers (WHO 2000a). The European Union has proposed a target concentration of 1 ng/m^3 of benzo[*a*]pyrene (as a surrogate for PAH) in ambient air (Commission of the European Communities 2003). If this proposal is adopted, air monitoring would be required if the target is not met. The IARC has classified benzo[*a*]pyrene as a Group 1 carcinogen ("carcinogenic to humans") and dibenz[*a*,*h*]anthracene and dibenzo[*a*,*l*]pyrene as Group 2A ("probably carcinogenic to humans"), based on sufficient evidence in animals and strong mechanistic data. Several other compounds in the 16-PAH group were classified by the IARC as Group 2B ("possibly carcinogenic to human beings"), including benz[*a*]anthracene, benzo[*b*]fluoranthene, benzo[*k*]fluoranthene, chrysene, and indeno[1,2,3-*cd*]pyrene, based on sufficient evidence in animals (Cogliano et al. 2005; IARC 2007).

The cancer potency of PAH mixtures is often calculated using relative-potency values (in this case, benzo[*a*]-pyrene-equivalency factors). A recent analysis (Schneider et al. 2002), however, showed that this use of benzo[*a*]-pyrene-equivalency factors leads to underestimations of the carcinogenic potency of PAH mixtures in most cases. The EPA (1993b) and WHO (1998) have proposed using equivalent factors to estimate the toxic potency of PAH mixtures. The relative potencies are derived relative to benzo[*a*]pyrene in increments of multiples of 10. These factors are based on cancer bioassays using various routes of exposure and assuming that all PAHs have the same mode of action. Originally the EPA had used the 7-PAH group as a surrogate for the complex mixtures of hundreds of PAHs (EPA 1993b). The list has been repeatedly adapted as the EPA has developed new cancer potencies for individual PAHs. The WHO International Programme on Chemical Safety (1998) proposed a list of 13 compounds, which includes several PAHs with fjord regions, such as dibenzo[*a,l*]pyrene. Dibenzo[*a,l*]pyrene is metabolically activated by P450 1A1 and 1B1 to highly reactive and mutagenic species (Buters et al. 2002), and its carcinogenic potency has been estimated to be 100 times greater than that of benzo[*a*]pyrene (see **Table 9**). Dibenzo[*a,h*]anthracene, dibenzo[*a,e*]fluoranthene, dibenzo[*a,e*]pyrene, and dibenzo[*a,h*]pyrene have a relative carcinogenic potency similar to that of benzo[*a*]pyrene; that of dibenzo[*a,i*]pyrene is 10 times lower (WHO 1998). More recently, anthanthrene, benzo[*b*]naphthol[2,1-*d*]thiophene, naphthalene, phenanthrene, and pyrene have been proposed for addition to the list (see Table 9) (Jacob 2004). Note that the relative-potency range of this group of PAHs varies by five orders of magnitude.

SUMMARY AND KEY CONCLUSIONS

EXPOSURES

Food is thought to be the major source of human exposure to POM, owing to the formation of PAHs during cooking and also to the deposition of PAHs on fruits, vegetables, and grains from the atmosphere. Combustion of vehicle fuels and especially home-heating oil appears to be the principal source of exposure by the inhalation route for five- to seven-ring PAHs (e.g., benzo[*b*+*k*]fluoranthene, benzo[*a*]pyrene, indeno[1,2,3-*cd*]pyrene, dibenzo[*a,h*]-anthracene) that are associated with PM. Total PAH concentrations show some relationship to traffic proximity,

Table 9. Relative Carcinogenic Potencies of PAHs

Compound	EPA 1993b[a]	WHO 1998[b]	Jacob 2004
Anthracene	—	—	0.1
Benzo[*a*]pyrene	1	1	1
Benz[*a*]anthracene	0.1	0.1	0.1
Benzo[*b*]fluoranthene	0.1	0.1	0.1
Benzo[*j*]fluoranthene	—	0.1	0.1
Benzo[*k*]fluoranthene	0.01	0.1	0.1
Benzo[*b*]naphthol[2,1-*d*]thiophene	—	—	0.01
Chrysene	0.001	0.1	0.01
Cyclopenta[*cd*]pyrene	—	0.1	0.1
Dibenzo[*a,h*]anthracene	—	1	1
Dibenzo[*a,e*]fluoranthene	—	1	—
Dibenzo[*a,h*]pyrene	1	1	1
Dibenzo[*a,i*]pyrene	—	0.1	—
Dibenzo[*a,l*]pyrene	—	100	100
Indeno[1,2,3-*cd*]pyrene	0.1	0.1	0.1
Naphthalene, phenanthrene, pyrene	—	—	0.001

[a] Environmental Protection Agency (US) 1993b.

[b] World Health Organization International Programme on Chemical Safety 1998.

although the contribution of motor-vehicle emissions appears to be relatively small compared with that of other sources. Ambient concentrations and exposures are higher in winter than in summer because of atmospheric chemistry and increased emissions from heating systems. Preliminary measurements of a number of atmospheric transformation products suggest a contribution of motor-vehicle emissions.

TOXICOLOGY

Most POM are genotoxic in both in vitro and in vivo test systems. They generally require metabolism to epoxides and diol epoxides that can interact with DNA. The presence of PAHs and their metabolites in blood and tissues (including lung, ovary, placenta, and uterine cervix) indicate that PAHs are absorbed and distributed in tissues. Both metabolized and unmetabolized compounds are excreted into bile, feces, and urine as well as into breast milk. POM can induce tumors of the lung, skin, and breast. Effects on the blood and liver have also been observed. In pregnant rodents, intrauterine growth retardation, fetal mortality, and teratogenesis have been observed.

Biomarkers of exposure to PAHs are 1-hydroxypyrene in the urine as well as adducts with DNA and protein in tissues and blood. These are clearly elevated in exposed workers. Whether there is a correlation between increased environmental exposure and quantities of these biomarkers is less clear.

HUMAN HEALTH

POM as a mixture is a human carcinogen and is associated with lung, skin, esophageal, colon, pancreatic, and breast cancer. While different POM constituents have different degrees of carcinogenic potency, most studies have used benzo[*a*]pyrene as an indicator compound. Several PAHs are estimated to have relative carcinogenic potencies more than 10 times higher than that of benzo[*a*]pyrene. Epidemiologic studies of workplace and community exposures to complex mixtures that include POM have been used in carcinogenic-risk assessment. These studies were not able to ascribe effects to specific POM constituents, nor even to POM alone, but they did suggest that air pollution containing POM is genotoxic. Similar issues exist with regard to the effects of POM on reproduction. Exposure to ambient PM containing POM is associated with low birth weight and altered immune status in newborns. Occupational-exposure studies of asphalt workers indicated an association between long-term POM exposure and mortality from chronic obstructive pulmonary disease and ischemic heart disease. Together, these studies suggested that exposure to mixtures containing POM, including mixtures at concentrations found in ambient air, are associated with carcinogenic and reproductive effects, although it is not possible specifically to implicate POM or its individual components as being causally related to these health effects. Recent evidence from occupational and epidemiologic studies indicated associations between POM and mortality from respiratory and cardiovascular effects. But it is difficult to exclude confounding by exposure to cigarette smoke, and the concentrations of POM in these studies were often higher than those found in ambient urban air.

KEY CONCLUSIONS

1. To what extent are mobile sources an important source of POM?

Food is thought to be the major source of human exposure to POM. Combustion (of home-heating oil and, to some extent, of vehicle fuels) appears to be the dominant source of the particle-bound five- to seven-ring PAHs to which people are exposed by inhalation. For other POM species, insufficient data are available to determine the extent of mobile sources as contributors to exposure.

2. Does POM affect human health?

Occupational and community studies suggest that exposure to mixtures containing POM (and specifically PAHs) is associated with carcinogenic and reproductive effects, although it is not possible specifically to implicate POM or its individual components as being causally related to these health effects. Recent evidence from occupational epidemiologic studies indicated that exposure to high concentrations of PAHs is associated with mortality from respiratory and cardiovascular effects.

3. Does POM affect human health at environmental concentrations?

While there is evidence that air pollution containing PAHs is genotoxic and has effects on reproductive health, there is no direct evidence from community studies that POM specifically, at ambient exposure concentrations, causes health effects. Because community studies involve exposures to complex mixtures, they have limited ability to address the effects of POM alone. Additional identification of relevant biomarkers of exposure is needed.

RESEARCH GAPS AND RECOMMENDATIONS

POM is a complex mixture of PAHs in both gas and particle phases. Many different PAHs and mixtures of PAHs have been evaluated in different studies, making it difficult to compare results. General research recommendations for POM include the following:

- Identify a core set of specific species of POM for further study or indicator compounds to facilitate consistent research approaches.
- Although studies have investigated the effects of individual species of POM, studies of complex POM-containing mixtures should also be undertaken.

EXPOSURE

Specific research recommendations for POM-exposure studies include the following:

- Perform studies of ambient concentrations of nitro-PAHs, quinones, and hydroquinones.
- Further research the chemical reaction products of POM under typical atmospheric conditions and the possible biologic activities of these products.
- Determine regional variability (including "hot spots") in the concentrations of specific POM and total particle-bound POM. This information might be important for understanding the distribution and determinants of personal exposure.
- Add highly potent POM containing a fjord region to the NATA list of 16 particle-bound PAH species that define POM. Of these, the compounds in the 7-PAH group (benzo[*a*]anthracene, benzo[*a*]pyrene, benzo[*b*]-fluoranthene, benzo[*k*]fluoranthene, chrysene, dibenz-[*a,h*]anthracene, and indeno[1,2,3-*cd*]pyrene) are already classified as "probable human carcinogens."

TOXICITY

Specific research recommendations for POM-toxicity studies include the following:

- Undertake studies to determine the most appropriate animal species for extrapolation to humans, taking into account the potential toxic effects of reactive metabolites in various species and at various organ sites.
- Perform studies of the toxicokinetics and bioaccumulation of inhaled POM, including the dose for target tissues and the bioavailability of particle-bound POM.
- Initiate toxicity studies of the major atmospheric transformation products of POM.

HUMAN HEALTH

Specific research recommendations for human-health studies of POM include the following:

- Identify additional biomarkers of exposure to individual species of POM to facilitate epidemiologic studies (which heretofore have invariably involved mixtures).
- Determine the relative sensitivity of DNA adducts in order to help understand possible threshold concentrations of exposure.

POM REFERENCES

Agency for Toxic Substances and Disease Registry. 1995. Toxicological Profile for Polycyclic Aromatic Hydrocarbons (PAHs). U.S. Department of Health and Human Services, Atlanta, GA. Available from *www.atsdr.cdc.gov/toxprofiles/tp69.pdf*.

Angerer J, Mannschreck C, Gundel J. 1997. Biological monitoring and biochemical effect monitoring of exposure to polycyclic aromatic hydrocarbons. Int Arch Occup Environ Health 70(6):365–77.

Armstrong B, Hutchinson E, Unwin J, Fletcher T. 2004. Lung cancer risk after exposure to polycyclic aromatic hydrocarbons: a review and meta-analysis. Environ Health Perspect 112(9):970–8.

Boström CE, Gerde P, Hanberg A, Jernstrom B, Johansson C, Kyrklund T, Rannug A, Tornqvist M, Victorin K, Westerholm R. 2002. Cancer risk assessment, indicators, and guidelines for polycyclic aromatic hydrocarbons in the ambient air. Environ Health Perspect 110 Suppl 3:451–88.

Burstyn I, Boffetta P, Heederik D, Partanen T, Kromhout H, Svane O, Langard S, Frentzel-Beyme R, Kauppinen T, Stucker I, Shaham J, Ahrens W, Cenee S, Ferro G, Heikkila P, Hooiveld M, Johansen C, Randem B G, Schill W. 2003. Mortality from obstructive lung diseases and exposure to polycyclic aromatic hydrocarbons among asphalt workers. Am J Epidemiol 158(5):468–78.

Burstyn I, Kromhout H, Partanen T, Svane O, Langard S, Ahrens W, Kauppinen T, Stucker I, Shaham J, Heederik D, Ferro G, Heikkila P, Hooiveld M, Johansen C, Randem BG, Boffetta P. 2005. Polycyclic aromatic hydrocarbons and fatal ischemic heart disease. Epidemiology 16(6):744–50.

Buters JT, Mahadevan B, Quintanilla-Martinez L, Gonzalez FJ, Greim H, Baird WM, Luch A. 2002. Cytochrome P450 1B1 determines susceptibility to dibenzo[a,l]pyrene-induced tumor formation. Chem Res Toxicol 15(9):1127–35.

California Air Resources Board. 2003. Assessment of California's Statewide Air Monitoring Network for the Children's Environmental Health Protection Act (SB 25). California Environmental Protection Agency, Sacramento, CA. Available from *www.arb.ca.gov/ch/programs/sb25/adequacyreport.pdf.*

Chellam S, Kulkarni P, Fraser MP. 2005. Emissions of organic compounds and trace metals in fine particulate matter from motor vehicles: a tunnel study in Houston, Texas. J Air Waste Manag Assoc 55(1):60–72.

Cho A, Stefano E, You Y, Rodriguez C, Schmitz D, Kumagai Y, Miguel A, Eiguren-Fernandez A, Kobayashi T, Avol E, Froines J. 2004. Determination of four quinones in diesel exhaust particles, SRM 1649a, and atmospheric $PM_{2.5}$. Aerosol Sci Technol 38(Suppl 1):68–81.

Cho AK, Sioutas C, Miguel AH, Kumagai Y, Schmitz DA, Singh M, Eiguren-Fernandez A, Froines JR. 2005. Redox activity of airborne particulate matter at different sites in the Los Angeles Basin. Environ Res 99(1):40–7.

Cogliano VJ, Grosse Y, Baan RA, Straif K, Secretan MB, El Ghissassi F. 2005. Meeting report: summary of IARC monographs on formaldehyde, 2-butoxyethanol, and 1-*tert*-butoxy-2-propanol. Environ Health Perspect 113(9): 1205–8.

Commission of the European Communities. 2003. Proposal for a Directive of the European Parliament and of the Council relating to arsenic, cadmium, mercury, nickel, and polycyclic aromatic hydrocarbons in ambient air. Commission of the European Communities, Brussels, Belgium. Available from *http://europa.eu.int/eur-lex/en/com/pdf/2003/com2003_0423en01.pdf.*

Dachs J, Glenn TR IV, Gigliotti CL, Brunciak P, Totten LA, Nelson ED, Franz TP, Eisenreich SJ. 2002. Processes driving the short-term variability of polycyclic aromatic hydrocarbons in the Baltimore and northern Chesapeake Bay atmosphere, USA. Atmos Environ 36(14):2281–2295.

Dejmek J, Solansky I, Benes I, Lenicek J, Sram RJ. 2000. The impact of polycyclic aromatic hydrocarbons and fine particles on pregnancy outcome. Environ Health Perspect 108(12):1159–64.

DeMarini DM, Landi S, Tian D, Hanley NM, Li X, Hu F, Roop BC, Mass MJ, Keohavong P, Gao W, Olivier M, Hainaut P, Mumford JL. 2001. Lung tumor KRAS and TP53 mutations in nonsmokers reflect exposure to PAH-rich coal combustion emissions. Cancer Res 61(18):6679–81.

Doll R, Vessey MP, Beasley RW, Buckley AR, Fear EC, Fisher RE, Gammon EJ, Gunn W, Hughes GO, Lee K, Norman-Smith B. 1972. Mortality of gasworkers—final report of a prospective study. Br J Ind Med 29(4):394–406.

Dubowsky SD, Wallace LA, Buckley TJ. 1999. The contribution of traffic to indoor concentrations of polycyclic aromatic hydrocarbons. J Expo Anal Environ Epidemiol 9(4):312–21.

Eiguren-Fernandez A, Miguel AH, Froines JR, Thurairatnam S, Avol EL. 2004. Seasonal and spatial variation of polycyclic aromatic hydrocarbons in vapor-phase and $PM_{2.5}$ in southern California urban and rural communities. Aerosol Sci Technol 38:447–455.

Environment Canada. 1998. Ambient Air Measurements of Polycyclic Aromatic Hydrocarbons (PAH), Polychlorinated Dibendo-*p*-Dioxins (PCDD), and Polychlorinated Dibenzofurans in Canada (1987–1997). Report Series AAQD 98-3. Environmental Technology Centre, Ottawa, Ontario, Canada. Available from *www.etcentre.org/publications/naps/pahrep.pdf.*

Environmental Protection Agency (U.S.). 1993b. Provisional Guidance for Quantitative Risk Assessment of Polycyclic Aromatic Hydrocarbons (Schoeny R, Poirier K, eds.). EPA/600/R-93/089. NTIS PB 94-116571. Environmental Criteria Assessment Office, Cincinnati, OH. Available from *www.ntis.com.*

Environmental Protection Agency (U.S.). 1994b. Integrated Risk Information System: Benzo[*a*]pyrene (CASRN 50-32-8) (last updated November 1, 1994). Available from *www.epa.gov/iris/subst/0136.htm.* Accessed January 26, 2006.

Environmental Protection Agency (U.S.). 2000g. Technology Transfer Network Air Toxics Website: Polycyclic Organic Matter. Available from *www.epa.gov/ttn/atw/hlthef/polycycl.html.* Accessed February 7, 2005.

Environmental Protection Agency (U.S.). 2002d. Technology Transfer Network: 1996 National Air Toxics Assessment Exposure and Risk Data. Available from *www.epa.gov/ttn/atw/nata/ted/exporisk.html.* Accessed June 7, 2006.

Fitz D, Winer A, Colome S, Behrentz E, Sabin L, Lee S, Wong K, Kozawa K, Pankratz D, Bumiller K, Gemmill D, Smith M. 2003. Characterizing the Range of Children's Pollutant Exposure During School Bus Commutes. California Air Resources Board, Sacramento, CA.

Gammon MD, Santella RM, Neugut AI, Eng SM, Teitelbaum SL, Paykin A, Levin B, Terry MB, Young TL, Wang LW, Wang Q, Britton A, Wolff MS, Stellman SD, Hatch M, Kabat GC, Senie R, Garbowski G, Maffeo C, Montalvan P, Berkowitz G, Kemeny M, Citron M, Schnabel F, Schuss A,

Hajdu S, Vinceguerra V. 2002. Environmental toxins and breast cancer on Long Island. I. Polycyclic aromatic hydrocarbon DNA adducts. Cancer Epidemiol Biomarkers Prev 11(8):677–85.

Geiser M, Rothen-Rutishauser B, Kapp N, Schurch S, Kreyling W, Schulz H, Semmler M, Im Hof V, Heyder J, Gehr P. 2005. Ultrafine particles cross cellular membranes by nonphagocytic mechanisms in lungs and in cultured cells. Environ Health Perspect 113(11):1555–60.

Gigliotti CA, Dachs J, Nelson ED, Brunciak PA, Eisenreich SJ. 2000. Polycyclic aromatic hydrocarbons in the New Jersey coastal atmosphere. Environ Sci Technol 34:3547–3554.

Hertz-Picciotto I, Herr CE, Yap PS, Dostal M, Shumway RH, Ashwood P, Lipsett M, Joad JP, Pinkerton KE, Sram RJ. 2005. Air pollution and lymphocyte phenotype proportions in cord blood. Environ Health Perspect 113(10): 1391–8.

International Agency for Research on Cancer. 2007. Monographs on the evaluation of carcinogenic risks to humans, volume 92, some non-heterocyclic polycyclic aromatic hydrocarbons and some related exposures. World Health Organization, Lyon, France. In press.

Jacob J (ed.). 2004. Polycyclische aromatische Kohlenwasserstoffe: Forschungsbericht. Deutsche Forshungsgemeinschaft. Wiley-VCH, Weinheim, Germany.

Kalantzi OI, Hewitt R, Ford KJ, Alcock RE, Thomas GO, Morris JA, Hewer A, Phillips DH, Jones KC, Martin FL. 2004. Inter-individual differences in the ability of human milk-fat extracts to enhance the genotoxic potential of the procarcinogen benzo[a]pyrene in MCF-7 breast cells. Environ Sci Technol 38(13):3614–22.

Kepley CL, Lauer FT, Oliver JM, Burchiel SW. 2003. Environmental polycyclic aromatic hydrocarbons, benzo(a)-pyrene (BaP) and BaP-quinones, enhance IgE-mediated histamine release and IL-4 production in human basophils. Clin Immunol 107(1):10–19.

Kyrtopoulos SA, Georgiadis P, Autrup H, Demopoulos NA, Farmer P, Haugen A, Katsouyanni K, Lambert B, Ovrebo S, Sram R, Stephanou G, Topinka J. 2001. Biomarkers of genotoxicity of urban air pollution. Overview and descriptive data from a molecular epidemiology study on populations exposed to moderate-to-low levels of polycyclic aromatic hydrocarbons: the AULIS project. Mutat Res 496(1-2):207–28.

Levy JI, Bennett DH, Melly SJ, Spengler JD. 2003. Influence of traffic patterns on particulate matter and polycyclic aromatic hydrocarbon concentrations in Roxbury, Massachusetts. J Expo Anal Environ Epidemiol 13(5):364–71.

Levy JI, Dumyahn T, Spengler JD. 2002. Particulate matter and polycyclic aromatic hydrocarbon concentrations in indoor and outdoor microenvironments in Boston, Massachusetts. J Expo Anal Environ Epidemiol 12(2):104–14.

Li N, Sioutas C, Cho A, Schmitz D, Misra C, Sempf J, Wang M, Oberley T, Froines J, Nel A. 2003. Ultrafine particulate pollutants induce oxidative stress and mitochondrial damage. Environ Health Perspect 111(4):455–60.

Manchester-Neesvig JB, Schauer JJ, Cass GR. 2003. The distribution of particle-phase organic compounds in the atmosphere and their use for source apportionment during the Southern California Children's Health Study. J Air Waste Manag Assoc 53(9):1065–79.

Marr LC, Kirchstetter TW, Harley RA, Miguel AH, Hering SV, Hammond SK. 1999. Characterization of polycyclic aromatic hydrocarbons in motor vehicle fuels and exhaust emissions. Environ Sci Technol 33(18):3091–3099.

Mori I. 2002. Cancer mortality among man-made graphite electrode manufacturing workers: results of a 38 year follow up. Occup Environ Med 59(7):473–80.

Mumford JL, He XZ, Chapman RS, Cao SR, Harris DB, Li XM, Xian YL, Jiang WZ, Xu CW, Chuang JC, et al. 1987. Lung cancer and indoor air pollution in Xuan Wei, China. Science 235(4785):217–20.

Naumova YY, Eisenreich SJ, Turpin BJ, Weisel CP, Morandi MT, Colome SD, Totten LA, Stock TH, Winer AM, Alimokhtari S, Kwon J, Shendell D, Jones J, Maberti S, Wall SJ. 2002. Polycyclic aromatic hydrocarbons in the indoor and outdoor air of three cities in the U.S. Environ Sci Technol 36(12):2552–9.

Pavanello S, Favretto D, Brugnone F, Mastrangelo G, Dal Pra G, Clonfero E. 1999. HPLC/fluorescence determination of anti-BPDE-DNA adducts in mononuclear white blood cells from PAH-exposed humans. Carcinogenesis 20(3):431–5.

Peluso M, Neri M, Margarino G, Mereu C, Munnia A, Ceppi M, Buratti M, Felletti R, Stea F, Quaglia R, Puntoni R, Taioli E, Garte S, Bonassi S. 2004. Comparison of DNA adduct levels in nasal mucosa, lymphocytes and bronchial mucosa of cigarette smokers and interaction with metabolic gene polymorphisms. Carcinogenesis 25(12):2459–65.

Perera F, Brenner D, Jeffrey A, Mayer J, Tang D, Warburton D, Young TI, Wazneh L, Latriano L, Motykiewicz G, et al. 1992a. DNA adducts and related biomarkers in populations

exposed to environmental carcinogens. Environ Health Perspect 98:133–7.

Perera FP, Hemminki K, Gryzbowska E, Motykiewicz G, Michalska J, Santella RM, Young TL, Dickey C, Brandt-Rauf P, DeVivo I, et al. 1992b. Molecular and genetic damage in humans from environmental pollution in Poland. Nature 360(6401):256–8.

Perera F, Hemminki K, Jedrychowski W, Whyatt R, Campbell U, Hsu Y, Santella R, Albertini R, O'Neill JP. 2002. In utero DNA damage from environmental pollution is associated with somatic gene mutation in newborns. Cancer Epidemiol Biomarkers Prev 11(10 Pt 1):1134–7.

Perera FP, Rauh V, Whyatt RM, Tang D, Tsai WY, Bernert T, Tu YH, Andrews H, Barr DB, Camann E, Diaz D, Dietrich J, Reyes A, Kinney PL. 2005a. A summary of recent findings on birth outcomes and developmental effects of prenatal ETS, PAH, and pesticide exposures. Neurotoxicology 26(4):573–87.

Perera FP, Rauh V, Whyatt RM, Tsai WY, Bernert JT, Tu YH, Andrews H, Ramirez J, Qu L, Tang D. 2004. Molecular evidence of an interaction between prenatal environmental exposures and birth outcomes in a multiethnic population. Environ Health Perspect 112(5):626–30.

Perera FP, Tang D, Rauh V, Lester K, Tsai WY, Tu YH, Weiss L, Hoepner L, King J, Del Priore G, Lederman SA. 2005b. Relationships among polycyclic aromatic hydrocarbon-DNA adducts, proximity to the World Trade Center, and effects on fetal growth. Environ Health Perspect 113(8):1062–7.

Perera FP, Whyatt RM, Jedrychowski W, Rauh V, Manchester D, Santella RM, Ottman R. 1998. Recent developments in molecular epidemiology: A study of the effects of environmental polycyclic aromatic hydrocarbons on birth outcomes in Poland. Am J Epidemiol 147(3):309–14.

Reddy MV, Hemminki K, Randerath K. 1991. Postlabeling analysis of polycyclic aromatic hydrocarbon-DNA adducts in white blood cells of foundry workers. J Toxicol Environ Health 34(2):177–85.

Riediker M, Williams R, Devlin R, Griggs T, Bromberg P. 2003. Exposure to particulate matter, volatile organic compounds, and other air pollutants inside patrol cars. Environ Sci Technol 37(10):2084–93.

Samet JM, DeMarini DM, Malling HV. 2004. Biomedicine. Do airborne particles induce heritable mutations? Science 304(5673):971–2.

Sapkota A, Williams D, Buckley TJ. 2005. Tollbooth workers and mobile source-related hazardous air pollutants: how protective is the indoor environment? Environ Sci Technol 39(9):2936–43.

Schneider K, Roller M, Kalberlah F, Schuhmacher-Wolz U. 2002. Cancer risk assessment for oral exposure to PAH mixtures. J Appl Toxicol 22(1):73–83.

Schober W, Luch A, Soballa VJ, Raab G, Stegeman JJ, Doehmer J, Jacob J, Seidel A. 2006. On the species-specific biotransformation of dibenzo[a,l]pyrene. Chem Biol Interact 161(1):37–48.

Seinfeld JH, Pandis SN. 1998. Atmospheric Chemistry and Physics: From Air Pollution to Climate Change. John Wiley & Sons Inc, New York, NY.

Selevan SG, Borkovec L, Slott VL, Zudova Z, Rubes J, Evenson DP, Perreault SD. 2000. Semen quality and reproductive health of young Czech men exposed to seasonal air pollution. Environ Health Perspect 108(9):887–94.

Seto H, Ohkubo T, Kanoh T, Koike M, Nakamura K, Kawahara Y. 1993. Determination of polycyclic aromatic hydrocarbons in the lung. Arch Environ Contam Toxicol 24(4):498–503.

Shamsuddin AK, Gan R. 1988. Immunocytochemical localization of benzo(a)pyrene-DNA adducts in human tissue. Hum Pathol 19(3):309–15.

Sloof W, Janus JA, Matthijsen AJCM, Montizaan GK, and Ros JPM. 1989. Integrated Criteria Document PAHs [translation]. Report 758474011. National Institute of Public Health and Environmental Protection, Bilthoven, The Netherlands. Available from *www.rivm.nl/bibliotheek/rapporten/758474011.pdf*.

Somers CM, McCarry BE, Malek F, Quinn JS. 2004. Reduction of particulate air pollution lowers the risk of heritable mutations in mice. Science 304(5673):1008–10.

Tolos WP, Shaw PB, Lowry LK, MacKenzie BA, Deng J-F, Markel HL. 1990. 1-Pyrenol: A biomarker for occupational exposure to polycyclic aromatic hydrocarbons. Appl Occup Environ Hyg 5(5):303–309.

Tonne CC, Whyatt RM, Camann DE, Perera FP, Kinney PL. 2004. Predictors of personal polycyclic aromatic hydrocarbon exposures among pregnant minority women in New York City. Environ Health Perspect 112(6):754–9.

Topinka J, Binkova B, Mrackova G, Stavkova Z, Peterka V, Benes I, Dejmek J, Lenicek J, Pilcik T, Sram RJ. 1997. Influence of GSTM1 and NAT2 genotypes on placental DNA

adducts in an environmentally exposed population. Environ Mol Mutagen 30(2):184–95.

van Wijnen JH, Verhoeff AP, Jans HW, van Bruggen M. 1995. The exposure of cyclists, car drivers and pedestrians to traffic-related air pollutants. Int Arch Occup Environ Health 67(3):187–93.

Vassilev ZP, Robson MG, Klotz JB. 2001. Outdoor exposure to airborne polycyclic organic matter and adverse reproductive outcomes: a pilot study. Am J Ind Med 40(3):255–62.

Weisel CP, Zhang J, Turpin BJ, Morandi MT, Colome S, Stock TH, Spektor DM. 2005. Relationships of Indoor, Outdoor, and Personal Air (RIOPA). Part I. Collection Methods and Descriptive Analyses. Research Report 130. Health Effects Institute, Boston, MA.

Whyatt RM, Santella RM, Jedrychowski W, Garte SJ, Bell DA, Ottman R, Gladek-Yarborough A, Cosma G, Young TL, Cooper TB, Randall MC, Manchester DK, Perera FP. 1998. Relationship between ambient air pollution and DNA damage in Polish mothers and newborns. Environ Health Perspect 106 Suppl 3:821–6.

Wiencke JK, Kelsey KT, Varkonyi A, Semey K, Wain JC, Mark E, Christiani DC. 1995. Correlation of DNA adducts in blood mononuclear cells with tobacco carcinogen-induced damage in human lung. Cancer Res 55(21):4910–4.

World Health Organization. 1987. Air Quality Guidelines: Final Unedited Draft. WHO Regional Office for Europe, Copenhagen, Denmark.

World Health Organization. 1998. International Programme on Chemical Safety. Selected Non-heterocyclic Polycyclic Aromatic Hydrocarbons. In: Environmental Health Criteria, Series 202. World Health Organization, Geneva, Switzerland.

World Health Organization. 2000a. Air Quality Guidlines for Europe. Second Edition. Who Regional Publications, European Series No. 91. WHO Regional Office for Europe, Copenhagen, Denmark.

Zmirou D, Masclet P, Boudet C, Dor F, Dechenaux J. 2000. Personal exposure to atmospheric polycyclic aromatic hydrocarbons in a general adult population and lung cancer risk assessment. J Occup Environ Med 42(2):121–126.