Benzo(a)pyrene (BaP)

TEACH Chemical Summary

U.S. EPA, Toxicity and Exposure Assessment for Children's Health

This TEACH Chemical Summary is a compilation of information derived primarily from U.S. EPA and ATSDR resources, and the TEACH Database. The TEACH Database contains summaries of research studies pertaining to developmental exposure and/or health effects for each chemical or chemical group. TEACH does not perform any evaluation of the validity or quality of these research studies. Research studies that are specific for adults are not included in the TEACH Database, and typically are not described in the TEACH Chemical Summary.

I. INTRODUCTION

Benzo(a)pyrene (BaP) is a polycyclic aromatic hydrocarbon (PAH) that is a byproduct of incomplete combustion or burning of organic (carbon-containing) items, e.g., cigarettes, gasoline, and wood (1). Pure BaP crystals are pale yellow and needlelike with a faint odor (1). BaP is commonly found with other PAHs in cigarette smoke, in grilled and broiled foods, and as a by-product of many industrial processes (1). BaP is also found in ambient (outdoor) air, indoor air, and in some water sources (1).

BaP is metabolized (chemically modified in the body) in humans and animals to form a number of metabolites that may elicit toxicity (1). BaP and BaP metabolites can bind to DNA forming a structure called BaP-DNA adducts. The formation of BaP-DNA adducts can interfere with or alter DNA replication (formation of DNA copies during cell division), and may be associated with an increased risk of several forms of cancer (1). BaP is classified as having a mutagenic mode of action (MOA) for inducing tumor formation, and is thought to require metabolic activation to become carcinogenic (2). Much of the current information pertaining to health effects following BaP exposure come from adult occupational exposure studies and experimental animal studies (1), though human developmental studies are accumulating (see Exposure and Toxicity Studies from the TEACH Database, in this Chemical Summary) (2). In experimental animal studies, effects of BaP exposure during pregnancy include increased incidence of several types of cancer in adulthood (3-7); impairments in the development and function of the immune system (8-11) (some of which persisted into adulthood (9)); and impairments in fertility in adult males and females (12, 13).

Based on what is known about effects of BaP exposure, health concerns associated with BaP exposure for children are: formation of BaP-DNA adducts which may lead to errors in DNA replication and increased risk of cancer (1, 2); also increased risk of cancer associated with BaP metabolite formation (1, 2); persistent effects on the development and function of the immune system (8-11); and reduced fertility in offspring during adulthood following BaP exposure during pregnancy (12, 13).

Concerns for BaP exposure of pregnant women and children are: ambient air contamination from mobile sources (e.g., cars) and industrial sources (e.g., coke ovens, metal processing plants); fetal exposure from maternal cigarette smoking; fetal and childhood exposure from second-hand cigarette smoke; and exposure from diet, including grilled and broiled food (1). Children may also have greater exposure than adults to contaminated soil in areas where BaP-contaminated soil from industrial contamination may be present, because of behavior patterns, particularly hand-to-mouth activity (1).

II. EXPOSURE MEDIA AND POTENTIAL FOR CHILDREN'S EXPOSURE[1]

Exposure Media	Relative Potential for Children's Exposure[2,3]	Basis[4]
Ambient Air	Higher	BaP is a ubiquitous compound in ambient (outdoor) air due to numerous releases from multiple processes, such as metal processing plants, motor vehicle emissions, wood stoves, tar and asphalt fumes, and cigarette smoke.
Indoor Air	Higher	BaP is a common indoor air pollutant, particularly in homes where people smoke. Indoor media include cigarette smoke, cooking and grilling, and smoke from burning wood or coal in heating stoves or fireplaces.
Sediment	Higher	BaP partitions strongly to sediment, but will break down when exposed to UV in sunlight.
Soil	Higher	BaP partitions strongly to soil, but will break down when exposed to UV in sunlight.
Diet	Medium	BaP is found primarily in grilled or charcoal-broiled foods.
Drinking Water	Lower	BaP has very low solubility in water, but can be found in drinking water when groundwater or surface water sources are contaminated with BaP. BaP binds to particulate matter in water, which is often removed by filtration before reaching the tap.
Surface Water	Lower	BaP has very low solubility in water, but can be found bound to particulate matter in surface water. BaP contamination can occur as a consequence of industrial pollution.
Groundwater	Lower	BaP has very low solubility in water, but can be found bound to particulate matter in groundwater. BaP does not leach to groundwater, but can be transported to groundwater as a consequence of industrial pollution.

[1] For more information about child-specific exposure factors, please refer to the Child-Specific Exposure Factors Handbook (http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=55145).

[2] The Relative Potential for Children's Exposure category reflects a judgment by the TEACH Workgroup, U.S. EPA, that incorporates potential exposure pathways, frequency of exposure, level of exposure, and current state of knowledge. Site-specific conditions may vary and influence the relative potential for exposure. For more information on how these determinations were made, go to http://www.epa.gov/teach/teachprotocols_chemsumm.html.

[3] Childhood represents a lifestage rather than a subpopulation, the distinction being that a subpopulation refers to a portion of the population, whereas a lifestage is inclusive of the entire population.

[4] Information described in this column was derived from several resources (e.g., 1, 2) including studies listed in the TEACH Database (http://www.epa.gov/teach).

III. TOXICITY SUMMARY[5, 6]

In humans, BaP has been associated with chromosomal replication (DNA copying) errors and altered DNA in gametes (sperm and eggs); BaP also forms BaP-DNA adducts in fetal, child, and adult tissues (1, 14-28). In adults, BaP exposure was associated with altered sperm morphology and decreased sperm numbers (15, 24), and decreased egg numbers (14). At high levels of acute exposure in adults, BaP has been reported to be associated with immune system suppression and red blood cell damage, which can lead to anemia (1).

In experimental animal studies, BaP exposure during pregnancy resulted in increased incidence of tumors in lung, liver, ovaries, and other organs in adult offspring (3-6, 29). BaP exposure during pregnancy resulted in increased incidence of fetal death (30-34), abnormalities (e.g., exencephaly or growth of the brain outside of the skull, and thoracoschisis or cleft in the chest wall) in offspring at birth at doses ranging from 50-300 mg/kg (32, 35-37), impaired development of T lymphocytes (8-11), and decreased antibody responses (4, 5). Reduced fertility during adulthood has been observed following BaP exposure during pregnancy (12, 13). Formation of BaP-DNA adducts have been detected in several species and in several tissues following BaP exposure during pregnancy (38-42).

Carcinogenicity Weight-of-Evidence Classification[7]: BaP is classified as having a mutagenic mode of action (MOA) for inducing tumors, and is thought to require metabolic activation to become carcinogenic (2). BaP is classified by the U.S. EPA as B2: a probable human carcinogen (1); based on numerous adult studies in several animal species (primates, rats, mice) that demonstrate BaP can increase the incidence of tumors (1). BaP is often used as a positive control in tumor formation experiments and in genotoxic assays (1) (http://www.epa.gov/iris/subst/0136.htm, II.A.1) (43); last agency verification date 12/4/91. The World Health Organization International Agency for Research on Cancer (IARC) concluded that there was sufficient evidence that BaP is carcinogenic (causes cancer) in experimental animals and that BaP is probably carcinogenic in humans (http://monographs.iarc.fr/ENG/Monographs/vol32/volume32.pdf) (44).

[5] Please refer to research article summaries listed in the TEACH Database for details about study design considerations (e.g., dose, sample size, exposure measurements).

[6] This toxicity summary is likely to include information from workplace or other studies of mature (adult) humans or experimental animals if child-specific information is lacking for the chemical of interest. Summaries of articles focusing solely on adults are not listed in the TEACH Database because the TEACH Database contains summaries of articles pertaining to developing organisms.

[7] For recent information pertaining to carcinogen risk assessment during development, consult "Guidelines for Carcinogen Risk Assessment and Supplemental Guidance on Risks from Early Life Exposure" at *http://www.epa.gov/cancerguidelines*.

IV. EXPOSURE AND TOXICITY STUDIES FROM THE TEACH DATABASE

This section provides a brief description of human and animal studies listed in the TEACH Database. For more details about study design parameters, e.g., doses and exposure information, please refer to article summaries in the TEACH Database. Any consideration should include an understanding that exposure levels in animal studies, in many cases, are greater than exposure levels normally encountered by humans.

A. *HUMAN EXPOSURE AND EFFECTS*

- Studies have measured concentrations of BaP in media that children may encounter. One study of BaP concentrations in house dust, personal air, outdoor air, and food samples was performed in a study of children's exposure to PAHs in Minnesota, and found BaP in 43-58% of different types of air samples, 19% of household dust samples, and 22% of food samples (45). One study of children in day care centers found that BaP was detected in indoor air and floor dust, and not detected in solid foods (17). Another study in Spain of BaP in diet detected BaP in foods, and children ages 4-9 years old were found to have the highest estimated daily intake of BaP, as compared to adults and adolescents (46). Another study of BaP concentrations in soil found higher concentrations in soil of homes near steel processing plants than homes further away (47).
- BaP and its metabolites have been detected in urine of pregnant women and children (18-20). BaP has been detected in placenta, cord blood, maternal blood, and human breast milk (16).
- BaP and BaP metabolites can chemically bind to DNA to form BaP-DNA adducts, which may interfere with DNA replication (see Introduction and reference 1), and have been detected in reproductive organs of adults. BaP-DNA adducts were detected in granulosa-lutein cells in ovaries of adult women who were exposed to cigarette smoke from smoking themselves or from second-hand smoke (14). Increasing amounts of BaP-DNA adducts in sperm of adult men were associated with significantly decreased sperm counts (15, 24).
- BaP-DNA adducts have been detected in multiple tissues during development (1, 14-28). The placenta can metabolize BaP, and these metabolites bound to DNA in placenta (16, 21, 22, 48) and cord blood (16, 21, 27, 28). One study detected BaP adducts in preimplantation embryos (early in prenatal development) from couples where the father and/or mother, or even the father alone, smoked cigarettes (23). BaP-DNA adducts were also detected in blood of mothers and their newborn infants (25).
- Decreased birth weight and head circumference in infants at birth were significantly associated with maternal exposure to cigarette smoke during pregnancy, as measured by the combination of cotinine and BaP-DNA adduct formation concentrations in fetal cord blood together, but not with either concentration alone (26, 49).

B. *EXPERIMENTAL ANIMAL EXPOSURE AND EFFECTS*

- Effects of BaP exposure on sperm and egg development in animals have been studied. Adult male and female mice, who were exposed to BaP during pregnancy via gavage (tube-feeding) (12) or injection (13) of their mothers during pregnancy, had reduced numbers of sperm and egg follicles respectively.
- BaP was reported to cross the placenta in mice (50, 51), rats (52), and guinea pigs (53, 54) following maternal injection (50, 53, 54), dermal (51), or inhalation (52) exposure to BaP. BaP was also found in maternal breast milk in rats following exposure via maternal ingestion of BaP, or injection of mothers with BaP during pregnancy (55).
- Effects of prenatal BaP exposure on fetal development have been investigated. Inhalation exposure of pregnant rats (30) or mice (33) to BaP (25-100 μg/L) resulted in decreased numbers of live pups at birth. Administration of BaP (50 mg/kg) by inhalation or injection to pregnant rats resulted in decreased fetal weight (31, 34) and increased fetal resorptions (death) (34). Ingestion of BaP (50-300 mg/kg) by pregnant rats resulted in an increased number of stillborn pups (32). Injection of pregnant mice with BaP also resulted in measurable changes in some enzymes in lungs (pyruvate kinase and lactic acid dehydrogenase) of exposed fetuses (56).
- Effects of BaP exposure during pregnancy on the occurrence of birth defects in offspring have been investigated. In one study, there was increased incidence of birth defects, including exencephaly (growth of the brain outside of the skull) and thoracoschisis (cleft in the chest wall), in offspring following maternal exposure during pregnancy (via injection) to some BaP metabolites, but not to BaP itself (36). In another study, pregnant mice were exposed to BaP via ingestion; the incidence of abnormalities in exposed offspring at birth varied depending on the strain of mice, suggesting that the genetic background of the mice was important (32).
- Pregnant mice showed genetic variability in the ability to metabolize BaP following maternal ingestion (37) or injection of BaP (57). The type of Ah receptor (aryl hydrocarbon receptor, or AhR) in each strain influenced the extent of toxic effects of BaP exposure; the AhR binds aromatic hydrocarbons (compounds containing rings of carbon atoms) including BaP, and is a component of the cytochrome P450 system that metabolizes BaP and other compounds (1, 32, 35). The incidence of teratogenic effects (e.g., fetal death and decreased fetal weight) (32, 37), and the time of onset of aplastic anemia following BaP exposure during pregnancy via maternal ingestion (35) varied between strains of mice that differed at the AhR locus, while numbers of tumors induced by BaP exposure did not vary (57).
- Offspring of pregnant mice, who were injected with BaP during pregnancy, had an increased incidence of tumors, predominantly in lung, liver, and ovaries, during adulthood (3-6). Significantly increased multiplicity of tumors (number of tumors that arose at each site) was seen in lungs of offspring exposed during pregnancy, and this effect persisted through five generations of unexposed offspring in one study (3). Liver tumors were more common in prenatally-exposed males than females (4, 6).

- Developing T lymphocytes of the immune system of offspring can be affected following BaP exposure during pregnancy, with some effects persisting into adulthood. Atrophy (shrinkage) of the thymus (the organ important for T lymphocyte development) was increased in offspring of pregnant mice exposed to BaP via gavage (8). Thymic glucocorticoid receptor numbers were reduced in adult rats who were exposed to BaP during pregnancy via maternal dermal exposure (9); glucocorticoid receptors play a role in broad array of physiological processes in the body (9). Reductions in the number of fetal liver T lymphocytes and some neonatal T lymphocyte subsets were also observed in offspring following maternal exposure to BaP during pregnancy via injection (10) or ingestion (11).
- Other hematological and immune system effects have been observed in mice following prenatal exposure to BaP. Decreased antibody responses were observed in offspring following maternal injection with BaP (4, 5), and the effect persisted into adulthood (5). Another study found reduced numbers of leukocytes (white blood cells) and erythrocytes (red blood cells) in fetal and newborn offspring following maternal BaP exposure via injection during pregnancy (58).
- Numerous experimental animal studies have examined BaP-DNA adduct formation following prenatal and early life BaP exposure. Maternal exposure to BaP via gavage of pregnant monkeys resulted in BaP-DNA adducts in fetal tissue that correlated with maternal BaP exposure levels (38). Several studies in mice have detected BaP-DNA adducts in fetal liver and lung tissue following maternal gavage exposure to BaP (32, 41, 42) or maternal injection with BaP (39, 40). The extent of BaP-DNA adduct formation was influenced by genetic background or strain of the mice (32, 41) and by gestational period during which exposure occurred (38, 41, 42).
- Dermal exposure of pregnant mice to BaP was also shown to result in BaP-hemoglobin adduct formation in erythrocytes of offspring (51). Increased micronuclei (unusually small nuclei that can indicate DNA damage) formation in erythrocytes was also observed in offspring following maternal exposure of mice to BaP via gavage during pregnancy (59).
- One study reported that exposure of newborn mice to a single subcutaneous injection of BaP resulted in lung adenoma (a type of tumor) formation during adulthood; treatment of BaP-exposed mice during young adulthood with Panex ginseng extract (60) or peppermint extract (61) significantly reduced the numbers and incidence of lung tumors.

V. CONSIDERATIONS FOR DECISION-MAKERS

This section contains information that may be useful to risk assessors, parents, caregivers, physicians, and other decision-makers who are interested in reducing the exposure and adverse health effects in children for this particular chemical. Information in this section focuses on ways to reduce exposure, assess possible exposure, and, for some chemicals, administer treatment.

- Although BaP-DNA adduct formation demonstrates exposure has occurred, quantitative correlation between exposure level and adduct formation currently remains unclear, and generally is not considered sufficient for use in quantitative exposure assessments (1).
- Current regulatory values exist for BaP exposure based on cancer and reproductive effects (see Toxicity section). The U.S. EPA IRIS is currently reassessing BaP reference values (http://cfpub.epa.gov/iristrac/index.cfm?fuseaction=listChemicals.showList&letter=B) (62).
- In view of the U.S. EPA Maximum Contaminant Level Goal (MCLG) of 0 for BaP (see Toxicity Summary and Reference Values in this Chemical Summary), caregivers may consider an alternate water supply where BaP contamination is impacting drinking water.
- A detailed compilation of information pertaining to exposure and health effects of BaP is available from the U.S. Centers for Disease Control Agency for Toxic Substances and Disease Registry (1).
- BaP is number 9 on the 2005 Priority List of Hazardous Substances for the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) section 104(i), as amended by the Superfund Amendments and Reauthorization Act (SARA). This is a prioritized list of concern of substances most commonly found at sites on the National Priorities List (NPL); there are currently 275 substances on this list (63). The priority of concern is determined by considering the frequency of occurrence at NPL sites, the potential hazard to human health, and the potential for human exposure (63).
- The U.S. EPA recommends that age-dependent adjustment factors (ADAFs) be used in risk assessments for carcinogens with a mutagenic mode of action, including BaP (2). The U.S. EPA concluded that “higher cancer risks typically result from a given exposure occurring early in life when compared with the same amount of exposure during adulthood” (2). Specific details are provided by the U.S. EPA for adjustments for children from birth to less than 16 years old (2).
- Consult “Child-Specific Exposure Factors Handbook,” EPA-600-P-00-002B, for factors to assess children’s ingestion and inhalation rates; a 2006 draft version is also available (64, 65).

VI. TOXICITY REFERENCE VALUES

A. Oral/Ingestion

U.S. EPA Cancer Oral Slope Factor: 7.3E+0 (or 7.3) per (mg/kg)/day (range of 4.5E+0 or 4.5, to 11.7E+0 or 11.7) per (mg/kg)/day); factor was based on forestomach squamous cell papillomas and carcinomas (types of tumors) in adult mice; and forestomach, larynx, and esophagus papillomas and carcinomas in adult rats (www.epa.gov/iris/subst/0136.htm, II.B.1) (43). Last Workgroup Verification Date 12/4/91.

U.S. EPA Cancer Drinking Water Unit Risk: 2.1E-4 (or 0.00021) per (µg/L), calculated using the extrapolation method and the geometric mean of four slope factors obtained by differing modeling procedures; derived from the combination of multiple data sets from two different reports using more than one sex and species in adults (www.epa.gov/iris/subst/0136.htm, II.B.1) (43). Last Workgroup Verification Date 12/4/91.

U.S. EPA Drinking Water Concentrations at Specified Risk Levels: 1E-4 (or 1 in 10,000), 5E-1 (or 0.5) µg/L; 1E-5 (or 1 in 100,000), 5E-2 (or 0.05) µg/L; 1E-6 (or 1 in 1,000,000), 5E-3 (or 0.005) µg/L (www.epa.gov/iris/subst/0136.htm, II.B.1) (43). Last Workgroup Verification Date 12/4/91.

U.S. EPA Maximum Contaminant Level (MCL) for Drinking Water: 0.0002 mg/L. Critical effects were reproductive difficulties and an increased risk of cancer (http://www.epa.gov/safewater/contaminants/index.html) (66). Last revised 6/02.

U.S. EPA Maximum Contaminant Level Goal (MCLG): 0 (http://www.epa.gov/safewater/contaminants/index.html) (66). Last revised 6/02.

B. Inhalation

There are currently no inhalation reference values available.

VII. U.S. FEDERAL REGULATORY INFORMATION

- BaP is regulated in public drinking water supplies (the Maximum Contaminant Level, or MCL, is 0.2 μg/L) ((http://www.epa.gov/safewater/contaminants/index.html) (66). There are currently no regulatory values for BaP in ambient or indoor air, and the U.S. EPA is currently reassessing toxicity values (http://cfpub.epa.gov/iristrac/index.cfm?fuseaction=listChemicals.showList&letter=B) (62).
- BaP is listed within a category of chemicals called "polycyclic organic matter as 7-PAH" as a Hazardous Air Pollutant (HAP) and is regulated under section 112(b) of the 1990 Clean Air Act Amendments (67).
- The U.S. EPA requires reporting of quantities of certain chemicals that exceed a defined reportable quantity, and that quantity varies for different chemicals (68). Under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), reporting releases of any quantity of BaP exceeding 1 pound is required (68). Under the Emergency Planning and Community Right-to-Know Act (EPCRA) Section 313 "Toxic Chemicals," quantities of benzo(a)pyrene greater than 25,000 pounds manufactured or processed, or greater than 10,000 pounds otherwise used, is required (68).

VIII. BACKGROUND ON CHEMICAL

A. CAS Number: 50-32-8

B. Physicochemical Properties: BaP is a polyaromatic hydrocarbon that is poorly soluble in water, and can adhere to particulate matter in water sources. Purified BaP is a yellow, crystalline substance. Search for benzo(a)pyrene at *http://chem.sis.nlm.nih.gov/chemidplus*.

C. Production: BaP and other PAHs are not used or made commercially, but result from incomplete combustion of organic (carbon-containing) materials such as cigarettes, wood, and coal (1). BaP and other PAHs are formed and released in cigarette smoke; motor vehicle exhaust; emissions from coal; oil and wood burning stoves or furnaces; coal tar and asphalt processes; incinerators; coke ovens in metal processing plants; and foods that are smoked, grilled, or charcoal-broiled (1, 69).

D. Uses: Total U.S. reported releases and disposals of PAHs, one of which is BaP, were nearly 2 million pounds in 2005 (70); total releases are likely to be greater than this estimate because not all sources of BaP releases are required to report (1, 70).

E. Environmental Fate: BaP is largely associated with particulate matter, soils, and sediment, with a half life of 2 days to 1.9 years in different soils (1, 69, 71). It is reasonably stable in the atmosphere and can be carried for long distances (1, 69, 71). In air, it may be broken down by light (photolysis) or may react with ozone or NO_2. In water, it will absorb strongly to sediment and solids in the water column, where it can be degraded by light near water surfaces, or metabolized by microorganisms in some natural water bodies (71). In soil, BaP associates with soil particles and will not leach into groundwater, though groundwater has become contaminated (71). Most organisms can metabolize BaP, so it does not readily bioaccumulate. Organisms that cannot metabolize BaP include: rainbow trout, bluegill, plankton, and oysters (71).

F. Synonyms and Trade Names: 3,4-Benz(a)pyrene, BaP, B[A]P, BP, 6,7-Benzopyrene, 3,4-Benzopyrene, Benzo[d,e,f]chrysene, 3,4-Benzpyrene, Benzpyrene, 3,4-benzylpyrene, 3,4-benz[a]pyrene, 3,4-BP, and others (for a more complete list, go to *http://chem.sis.nlm.nih.gov/chemidplus/jsp/common/ChemInfo.jsp?type=names*).

Additional information on BaP is available in the TEACH Database for BaP, and at the following Web sites:

http://www.atsdr.cdc.gov/mrls/index.html
www.epa.gov/safewater/dwh/t-soc/pahs.html
www.epa.gov/safewater/dwh/c-soc/benzopyr.html

REFERENCES

1. U.S. Centers for Disease Control Agency for Toxic Substances and Disease Registry (ATSDR). 1995. "Toxicological Profile for Polyaromatic Hydrocarbons (PAHs)." http://www.atsdr.cdc.gov/toxprofiles/tp69.html.
2. U.S. Environmental Protection Agency. 2005. "Supplemental Guidance for Assessing Cancer Susceptibility from Early-Life Exposure to Carcinogens." http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=116283.
3. Turusov, V.S., et al. 1990. "Increased multiplicity of lung adenomas in five generations of mice treated with benz(a)pyrene when pregnant." Cancer Lett. 55(3):227-231.
4. Urso, P., and N. Gengozian. 1982. "Alterations in the humoral immune response and tumor frequencies in mice exposed to benzo[a]pyrene and X-rays before or after birth." J.Toxicol.Environ.Health 10(4-5):817-835.
5. Urso, P., and N. Gengozian. 1984. "Subnormal expression of cell-mediated and humoral immune responses in progeny disposed toward a high incidence of tumors after in utero exposure to benzo[a]pyrene." J.Toxicol.Environ.Health 14(4):569-584.
6. Wislocki, P.G., et al. 1986. "Tumorigenicity of nitrated derivatives of pyrene, benz[a]anthracene, chrysene and benzo[a]pyrene in the newborn mouse assay." Carcinogenesis 7(8):1317-1322.
7. Vesselinovitch, S.D., et al. 1975. "Conditions modifying development of tumors in mice at various sites by benzo(a)pyrene." Cancer Res. 35(11 Pt 1):2948-2953.
8. Holladay, S.D., and B.J. Smith. 1994. "Fetal hematopoietic alterations after maternal exposure to benzo[a]pyrene: a cytometric evaluation." J.Toxicol.Environ.Health 42(3):259-273.
9. Csaba, G., and A. Inczefi-Gonda. 1992. "Benzpyrene exposure at 15 days of prenatal life reduces the binding capacity of thymic glucocorticoid receptors in adulthood." Gen.Pharmacol. 23(1):123-124.
10. Lummus, Z.L., and G. Henningsen. 1995. "Modulation of T-cell ontogeny by transplacental benzo(a)pyrene." Int.J.Immunopharmacol. 17(4):339-350.
11. Rodriguez, J.W., et al. 1999. "Maternal exposure to benzo[a]pyrene alters development of T lymphocytes in offspring." Immunopharmacol.Immunotoxicol. 21(2):379-396.
12. MacKenzie, K.M., and D.M. Angevine. 1981. "Infertility in mice exposed in utero to benzo(a)pyrene." Biol.Reprod. 24(1):183-191.
13. Kristensen, P., et al. 1995. "Fertility in mice after prenatal exposure to benzo[a]pyrene and inorganic lead." Environ.Health Perspect. 103(6):588-590.
14. Zenzes, M.T., et al. 1998. "Immunodetection of benzo[a]pyrene adducts in ovarian cells of women exposed to cigarette smoke." Mol.Hum.Reprod. 4(2):159-165.
15. Gaspari, L., et al. 2003. "Polycyclic aromatic hydrocarbon-DNA adducts in human sperm as a marker of DNA damage and infertility." Mutat.Res. 535(2):155-160.
16. Madhavan, N.D., and K.A. Naidu. 1995. "Polycyclic aromatic hydrocarbons in placenta, maternal blood, umbilical cord blood and milk of Indian women." Hum.Exp.Toxicol. 14(6):503-506.
17. Wilson, N.K., et al. 2001. "Levels of persistent organic pollutants in several child day care centers." J.Expo.Anal.Environ.Epidemiol. 11(6):449-458.
18. Kang, J.W., et al. 2002. "Correlation of urinary 1-hydroxypyrene and 2-naphthol with total suspended particulates in ambient air in municipal middle-school students in Korea." Arch.Environ.Health 57(4):377-382.

19. Staessen, J.A., et al. 2001. "Renal function, cytogenetic measurements, and sexual development in adolescents in relation to environmental pollutants: a feasibility study of biomarkers." Lancet 357(9269):1660-1669.
20. Ptashekas, J., et al. 1996. "Environmental and health monitoring in Lithuanian cities: exposure to heavy metals and benz(a)pyrene in Vilnius and Siauliai residents." J.Environ.Pathol.Toxicol.Oncol. 15(2-4):135-141.
21. Arnould, J.P., et al. 1997. "Detection of benzo[a]pyrene-DNA adducts in human placenta and umbilical cord blood." Hum.Exp.Toxicol. 16(12):716-721.
22. Manchester, D.K., et al. 1988. "Detection of benzo[a]pyrene diol epoxide-DNA adducts in human placenta." Proc.Natl.Acad.Sci.U.S.A 85(23):9243-9247.
23. Zenzes, M.T., et al. 1999. "Detection of benzo[a]pyrene diol epoxide-DNA adducts in embryos from smoking couples: evidence for transmission by spermatozoa." Mol.Hum.Reprod. 5(2):125-131.
24. Zenzes, M.T., et al. 1999. "Detection of benzo(a)pyrene diol epoxide-DNA adducts in sperm of men exposed to cigarette smoke." Fertil.Steril. 72(2):330-335.
25. Perera, F.P., et al. 2004. "Biomarkers in maternal and newborn blood indicate heightened fetal susceptibility to procarcinogenic DNA damage." Environ.Health Perspect. 112(10):1133-1136.
26. Perera, F.P., et al. 2004. "Molecular evidence of an interaction between prenatal environmental exposures and birth outcomes in a multiethnic population." Environ.Health Perspect. 112(5):626-630.
27. Perera, F., et al. 2005. "DNA damage from polycyclic aromatic hydrocarbons measured by benzo[a]pyrene-DNA adducts in mothers and newborns from Northern Manhattan, the World Trade Center Area, Poland, and China." Cancer Epidemiol.Biomarkers Prev. 14(3):709-714.
28. Perera, F.P., et al. 2005. "Relationships among polycyclic aromatic hydrocarbon-DNA adducts, proximity to the World Trade Center, and effects on fetal growth." Environ Health Perspect. 113(8):1062-1067.
29. Vesselinovitch, S.D., et al. 1975. "Conditions modifying development of tumors in mice at various sites by benzo(a)pyrene." Cancer Res. 35(11 Pt 1):2948-2953.
30. Archibong, A.E., et al. 2002. "Alteration of pregnancy related hormones and fetal survival in F-344 rats exposed by inhalation to benzo(a)pyrene." Reprod.Toxicol. 16(6):801-808.
31. Cervello, I., et al. 1992. "Enhanced glutathione S-transferase (GST) activity in pregnant rats treated with benzo(a)pyrene." Placenta 13(3):273-280.
32. Shum, S., et al. 1979. "The murine Ah locus: in utero toxicity and teratogenesis associated with genetic differences in benzo[a]pyrene metabolism." Teratology 20(3):365-376.
33. Wu, J., et al. 2003. "Assessment of metabolites and AhR and CYP1A1 mRNA expression subsequent to prenatal exposure to inhaled benzo(a)pyrene." Int.J.Dev.Neurosci. 21(6):333-346.
34. Bui, Q.Q., et al. 1986. "A comparative study of the reproductive effects of methadone and benzo[a]pyrene in the pregnant and pseudopregnant rat." Toxicology 42(2-3):195-204.
35. Nebert, D.W., et al. 1977. "Birth defects and aplastic anemia: differences in polycyclic hydrocarbon toxicity associated with the Ah locus." Arch.Toxicol. 39(1-2):109-132.
36. Barbieri, O., et al. 1986. "Embryotoxicity of benzo(a)pyrene and some of its synthetic derivatives in Swiss mice." Cancer Res. 46(1):94-98.
37. Legraverend, C., et al. 1984. "Importance of the route of administration for genetic differences in benzo[a]pyrene-induced in utero toxicity and teratogenicity." Teratology 29(1):35-47.
38. Lu, L.J., et al. 1993. "Persistence, gestation stage-dependent formation and interrelationship of benzo[a]pyrene-induced DNA adducts in mothers, placentae and fetuses of Erythrocebus patas monkeys." Carcinogenesis 14(9):1805-1813.
39. Bolognesi, C., et al. 1985. "Benzo[a]pyrene-induced DNA damage in mouse fetal tissues." Carcinogenesis 6(8):1091-1095.

40. Lu, L.J., et al. 1986. "32P-postlabeling assay in mice of transplacental DNA damage induced by the environmental carcinogens safrole, 4-aminobiphenyl, and benzo(a)pyrene." Cancer Res. 46(6):3046-3054.
41. Lu, L.J., and M.Y. Wang. 1990. "Modulation of benzo[a]pyrene-induced covalent DNA modifications in adult and fetal mouse tissues by gestation stage." Carcinogenesis 11(8):1367-1372.
42. Wang, M.Y., and L.J. Lu. 1990. "Differential effect of gestation stage on benzo(a)pyrene-induced micronucleus formation and/or covalent DNA modifications in mice." Cancer Res. 50(7):2146-2151.
43. U.S. Environmental Protection Agency. 1994. "Integrated Risk Information System (IRIS): Benzo[a]pyrene." http://www.epa.gov/iris/subst/0136.htm.
44. World Health Organization. 1998. "Volume 32: Polynuclear Aromatic Compounds, Part 1, Chemical, Environmental and Experimental Data." http://monographs.iarc.fr/ENG/Monographs/vol32/volume32.pdf.
45. Clayton, C.A., et al. 2003. "Distributions, associations, and partial aggregate exposure of pesticides and polynuclear aromatic hydrocarbons in the Minnesota Children's Pesticide Exposure Study (MNCPES)." J.Expo.Anal.Environ Epidemiol. 13(2):100-111.
46. Falco, G., et al. 2003. "Polycyclic aromatic hydrocarbons in foods: human exposure through the diet in Catalonia, Spain." J.Food Prot. 66(12):2325-2331.
47. Lambert, T.W., and S. Lane. 2004. "Lead, arsenic, and polycyclic aromatic hydrocarbons in soil and house dust in the communities surrounding the Sydney, Nova Scotia, tar ponds." Environ Health Perspect. 112(1):35-41.
48. Manchester, D.K., et al. 1992. "Determinants of polycyclic aromatic hydrocarbon-DNA adducts in human placenta." Cancer Res. 52(6):1499-1503.
49. Perera, F.P., et al. 2003. "Effects of Transplacental Exposure to Environmental Pollutants on Birth Outcomes in a Multiethnic Population." Environmental Health Perspectives 111:201-205.
50. McCabe, D.P., and E.J. Flynn. 1990. "Deposition of low dose benzo(a)pyrene into fetal tissue: influence of protein binding." Teratology 41(1):85-95.
51. Shugart, L., and R. Matsunami. 1985. "Adduct formation in hemoglobin of the newborn mouse exposed in utero to benzo[a]pyrene." Toxicology 37(3-4):241-245.
52. Withey, J.R., et al. 1993. "Distribution of benzo[a]pyrene in pregnant rats following inhalation exposure and a comparison with similar data obtained with pyrene." J.Appl.Toxicol. 13(3):193-202.
53. Kelman, B.J., and D.L. Springer. 1982. "Movements of benzo[a]pyrene across the hemochorial placenta of the guinea pig." Proc.Soc.Exp.Biol.Med. 169(1):58-62.
54. Kihlstrom, I. 1986. "Placental transfer of benzo(a)pyrene and its hydrophilic metabolites in the guinea pig." Acta Pharmacol.Toxicol.(Copenh) 58(4):272-276.
55. LaVoie, E.J., et al. 1987. "Transfer of the tobacco-specific carcinogens N'-nitrosonornicotine and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone and benzo[a]pyrene into the milk of lactating rats." Carcinogenesis 8(3):433-437.
56. Rady, P., et al. 1981. "Activity of pyruvate kinase and lactic acid dehydrogenase in mouse lung after transplacental exposure to carcinogenic and non-carcinogenic chemicals." Toxicol.Lett. 8(4-5):223-227.
57. Anderson, L.M., et al. 1995. "Fetal mouse susceptibility to transplacental carcinogenesis: differential influence of Ah receptor phenotype on effects of 3-methylcholanthrene, 12-dimethylbenz[a]anthracene, and benzo[a]pyrene." Pharmacogenetics 5(6):364-372.
58. Urso, P., et al. 1988. "Changes in peripheral blood cells in mice after injection with benzo(a)pyrene during pregnancy." Immunopharmacol.Immunotoxicol. 10(2):179-193.

59. Harper, B.L., et al. 1989. "Micronucleus formation by benzene, cyclophosphamide, benzo(a)pyrene, and benzidine in male, female, pregnant female, and fetal mice." Teratog.Carcinog.Mutagen. 9(4):239-252.
60. Panwar, M., et al. 2005. "Inhibition of benzo(a)pyrene induced lung adenoma by panax ginseng extract, EFLA400, in Swiss albino mice." Biol.Pharm.Bull. 28(11):2063-2067.
61. Samarth, R.M., et al. 2006. "Protective effects of Mentha piperita Linn on benzo[a]pyrene-induced lung carcinogenicity and mutagenicity in Swiss albino mice." Mutagenesis 21(1):61-66.
62. U.S. Environmental Protection Agency. 2006. "IRIS Chemical Assessment Tracking System: Benzo[a]pyrene (BaP)." http://cfpub.epa.gov/iristrac/index.cfm?fuseaction=listChemicals.showList&letter=B.
63. U.S. Environmental Protection Agency. 2005. "2005 CERCLA Priority List of Hazardous Substances." http://www.atsdr.cdc.gov/cercla/05list.html.
64. U.S. Environmental Protection Agency. 2002. "Child-Specific Exposure Factors Handbook." http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=55145.
65. U.S. Environmental Protection Agency. 2006. "Child-Specific Exposure Factors Handbook 2006 (External Review Draft)." http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=56747.
66. U.S. Environmental Protection Agency. 2003. "Drinking Water Contaminants." http://www.epa.gov/safewater/contaminants/index.html.
67. U.S. Environmental Protection Agency. 2006. "AirData: NEI Hazardous Air Pollutant Names - Page 8 of 10." http://www.epa.gov/air/data/help/hneihaps8.html.
68. U.S. Environmental Protection Agency. 2001. "Lists of Lists: Consolidated List of Chemicals Subject to the Emergency Planning and Right-to-Know Act (EPCRA) and Section 112(r) of the Clean Air Act." http://www.epa.gov/ceppo/pubs/title3.pdf.
69. World Health Organization. 1999. "International Program on Chemical Safety, Environmental Health Criteria 202: Selected Non-Herterocyclic Policyclic Aromatic Hydrocarbons." http://www.inchem.org/documents/ehc/ehc/ehc202.htm.
70. U.S. Environmental Protection Agency. 2006. "TRI Explorer: Providing Access to EPA's Toxic Release Inventory Data." http://www.epa.gov/triexplorer/.
71. U.S. Environmental Protection Agency. 2002. "Technical Factsheet on: Polycyclic Aromatic Hydrocarbons (PAHs)." http://www.epa.gov/safewater/dwh/t-soc/pahs.html.