ENVIRONMENTAL TOBACCO SMOKE

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30.1 INTRODUCTION

Extensive toxicological, experimental, and epidemiologic data, collected largely since the 1950s, have established that active cigarette smoking is the major preventable cause of morbidity and mortality in the United States (USDHEW 1979; USDHHS 1989). More recently, since the 1960s, involuntary exposure to tobacco smoke has been investigated as a risk factor for disease and also found to be a cause of preventable morbidity and mortality in nonsmokers. This chapter summarizes the converging and now extensive evidence on the health effects of involuntary exposure to tobacco smoke. The initial research on involuntary smoking addressed respiratory effects primarily; more recent investigations have examined associations with diverse health effects including nonrespiratory cancers, ischemic heart disease, age at menopause, sudden infant death syndrome (SIDS), and birth weight. The evidence on involuntary exposure to tobacco smoke is now voluminous; consequently, this chapter is selective in its citations. The most recent compilation of the evidence can be found in a 1997 report of the California Environmental Protection Agency (Cal EPA 1997). Prior key reviews include the 1986 reports of the U.S. Surgeon General (USDHHS 1986), the National Research Council (NRC 1986), and the 1992 report of the U.S. Environmental Protection Agency (USEPA 1992).

Respiratory effects of passive smoking have also been covered in a series of systematic reviews published in *Thorax* (Strachan and Cook 1997; Anderson and Cook 1997; Cook and Strachan 1997; Strachan and Cook 1998*a*, 1998*b*) and in the *British Medical Journal* (Hackshaw et al. 1997, Law and Hackshaw 1997). These reviews provide the

basis for conclusions on passive smoking in a 1998 report from the United Kingdom (Scientific Committee on Tobacco and Health, HSMO 1998).

30.2 EXPOSURE TO ENVIRONMENTAL TOBACCO SMOKE

Characteristics of Environmental Tobacco Smoke (ETS)

Nonsmokers inhale ETS, the combination of the sidestream smoke that is released from the cigarette's burning end and the mainstream smoke exhaled by the active smoker (First 1985). The inhalation of ETS is generally referred to as *passive* or *involuntary* smoking. The exposures of involuntary and active smoking differ quantitatively and, to some extent, qualitatively (USDHHS 1984, 1986; NRC 1981, 1986; USEPA 1992; Guerin et al. 1992). Because of the lower temperature in the burning cone of the smoldering cigarette, most partial-pyrolysis products are enriched in sidestream as compared to mainstream smoke. Consequently, sidestream smoke has higher concentrations of some toxic and carcinogenic substances than does mainstream smoke; however, dilution by room air markedly reduces the concentrations inhaled by the involuntary smoker in comparison to those inhaled by the active smoker. Nevertheless, involuntary smoking is accompanied by exposure to toxic agents generated by tobacco combustion (USDHHS 1984, 1986; NRC 1981, 1986; USEPA 1992).

Environmental Tobacco Smoke Concentrations

Tobacco smoke is a complex mixture of gases and particles that contains myriad chemical species (USDHEW 1979, USDHHS 1984, Guerin et al. 1992). Not surprisingly, tobacco smoking in indoor environments increases levels of respirable particles, nicotine, polycyclic aromatic hydrocarbons, carbon monoxide (CO), acrolein, nitrogen dioxide (NO_2), and many other substances; concentrations of some of these have been measured as ETS markers. Recent data from work environments (Table 30.1) and homes (Table 30.2) show that nicotine can be detected in locations with smoking. The extent of the increase in concentrations of these markers varies with the number of smokers, the intensity of smoking, the rate of exchange between the indoor airspace and with the outdoor air, and the use of air-cleaning devices. Ott (1999) has used mass-balance models to characterize factors influencing concentrations of tobacco smoke indoors, confirming the roles of these factors in determining ETS concentrations and offering an approach to predict concentrations.

Several components of cigarette smoke have been measured in indoor environments as markers of the contribution of tobacco combustion to indoor air pollution. Particles have been measured most often because both sidestream and mainstream smoke contain high concentrations of particles in the respirable size range (USDHHS 1986, NRC 1986). Particles are a nonspecific marker of tobacco smoke contamination, however, because numerous sources other than tobacco combustion add particles to indoor air. Other, more specific markers have also been measured, including nicotine, solanesol, and ultraviolet light (UV) absorption of particulate matter (Guerin et al. 1992). Nicotine, a highly specific marker present in the vapor phase of ETS, can be measured with active sampling methods and also using passive diffusion badges (Guerin et al. 1992, Leaderer and Hammond 1991). Studies of levels of ETS components have been conducted largely in public buildings; fewer studies have been conducted in homes and offices (USDHHS 1986, NRC 1986).

The contribution of various environments to personal exposure to tobacco smoke varies with the time-activity pattern. Time-activity patterns may heavily influence exposures in

TABLE 30.1 Occupational ETS Exposures in Non-Office Settings (Nonsmokers only)

Company type	Year sampled	Number of samples	Concentration of nicotine, $\mu g/m^3$						
			Mean	Standard deviation	Geometric mean	Minimum	Median	Maximum samples
Smoking allowed								
Specialty chemicals	1991/92	8	0.60	0.91	0.24	<0.05	0.46	2.78
Railroad workers (personal)	1983/84	152	0.80	3.30	0.18	<0.1	0.10	38.10
Tool manufacturing	1991/92	13	1.59	1.05	1.16	0.15	1.85	3.40
Textile finishing B	1991/92	11	1.74	1.69	1.10	0.31	0.93	5.09
Labels and paper products	1991/92	1	2.31				2.31	
Die manufacturer	1991/92	12	2.70	1.27	2.46	1.23	2.41	5.42
Sintering metal	1991/92	12	2.88	2.59	2.11	0.62	2.24	9.72
Newspaper B	1991/92	5	2.96	1.37	2.68	1.23	2.78	4.63
Miscellaneous	<1990	282	4.30	11.80	1.70	<1.6	<1.6	126.00
Textile finishing, A	1991/92	11	4.33	8.82	1.77	0.46	1.39	30.71
Flight attendants (personal)	1988	16	4.70	4.00	2.32	0.10	4.20	10.50
Firefighters A*	1991/92	16	5.39	3.81	4.08	1.20	4.84	13.42
Firefighters B	1991/92	24	5.83	6.77	3.83	0.71	3.65	27.50
Barber shop (personal)	1986/87	2	8.80	—	—	4.00	—	13.70
Hospital (personal)	1986/87	5	24.80	22.80	16.80	6.30	10.00	53.20
Smoking restricted								
Work clothing	1991/92	9	0.17	0.32	0.06	<0.05	<0.05	0.93
Filtration products	1991/92	10	0.32	0.87	0.08	<0.05	<0.05	2.78
Film and imaging	1991/92	6	0.82	0.83	0.39	<0.05	0.70	2.16
Fiberoptics	1991/92	13	1.34	2.79	0.63	0.20	0.64	10.57
Newspaper A	1991/92	4	4.86	6.65	2.62	0.93	1.85	14.81
Valve manufacturer	1991/92	10	5.80	7.85	3.62	1.16	3.26	27.31
Rubber products	1991/92	2	5.85	5.36	4.18	2.06	5.85	9.64
Smoking prohibited								
Infrared and imaging systems	1991/92	1	<0.05	—	—	—	<0.05	—
Hospital products	1991/92	5	0.08	0.17	<0.05	<0.05	<0.05	0.39
Weapons systems	1991/92	12	0.08	0.20	<0.05	<0.05	<0.05	0.63
Aircraft components	1991/92	12	0.20	0.18	0.13	<0.05	0.21	0.61
Radar communication components	1991/92	13	0.31	0.36	0.14	<0.05	0.26	1.08
Computer chip equipment	1991/92	10	0.51	0.33	0.41	0.15	0.39	1.08

*Omits one data point, 101 $\mu g/m^3$.
Source: Hammond (1999).

TABLE 30.2 Nicotine Concentrations in Homes

	Year sampled	Samples, N	Concentration of nicotine, $\mu g/m^3$				
			Mean	Standard deviation	Minimum	Median	Maximum
North Carolina homes (weekly)	1988	13	1.50	1.10	1.00	1.40	4.40
Personal (each sampled 3 times)	1988	15	—	—	—	—	—
Males (personal)* (16 h)	1993/94	86	2.13	—	—	1.29	>8.08†
New York homes (weekly)	1986	47	2.20	—	0.10	1.00	9.40
Females (personal)* (16 h)	1993/94	220	2.93	—	—	1.14	>7.81†
North Carolina homes (14 h) (5 P.M.–7 A.M.)	1986	13	3.74	—	—	~3.3‡	6.5
Minnesota homes (weekly)	~1989–‡	25	5.80	—	0.10	3.00	28.60

*16-h average; "away from work."
†95th percentile, as given in paper.
‡Assumed 16-h exposure.
Source: Hammond (1999).

particular environments for certain groups of individuals. For example, exposure in the home predominates for infants who do not attend day care (Harlos et al. 1987). For adults residing with nonsmokers, the workplace may be the principal location where exposure takes place (Cal EPA 1997). A recent nationwide study assessed exposures of nonsmokers in 16 metropolitan areas of the United States (Jenkins et al. 1996). This study, involving 100 persons in each location, was directed at workplace exposure and included measurements of respirable particulate matter and other markers. The results showed that in 1993/94 average exposures to ETS in the home were generally much greater than those in workplaces where smoking took place.

The contribution of smoking in the home to indoor air pollution has been demonstrated by studies using personal monitoring and monitoring of homes for respirable particles. In one of the early studies, Spengler et al. (1981) monitored homes in six U.S. cities for respirable particle concentrations over several years and found that an individual who smoked one pack of cigarettes daily contributed about 20 $\mu g/m^3$ to 24-h indoor particle concentrations. Because cigarettes are not smoked uniformly over the day, higher peak concentrations must occur when cigarettes are actually smoked. Spengler et al. (1985) measured the personal exposures to respirable particles sustained by nonsmoking adults in two rural Tennessee communities. The mean 24-h exposures were substantially higher for those exposed to smoke at home: 64 $\mu g/m^3$ for those exposed versus 36 $\mu g/m^3$ for those not exposed.

In several studies, small numbers of homes have been monitored for nicotine (Table 30.2). In a study of ETS exposure of daycare children, average nicotine concentration during the time that the ETS-exposed children were at home was 3.7 $\mu g/m^3$; in homes without smoking, the average was 0.3 $\mu g/m^3$ (Henderson et al. 1989). Coultas and colleagues (1990) measured 24-h nicotine and respirable particle concentrations in 10 homes on alternate days for a week and then on 5 more days during alternate weeks. The mean levels of nicotine were comparable to those in the study by Henderson et al. (1989), but some 24-h values were as high as 20 $\mu g/m^3$. Nicotine and respirable particle concentrations varied widely in the homes.

The Total Exposure Assessment Methodology (TEAM) study conducted by the U.S. Environmental Protection Agency, provided extensive data on concentrations of 20 volatile organic compounds in a sample of homes in several communities (Wallace and Pellizzari 1987). Indoor monitoring showed increased concentrations of benzene, xylenes, ethylbenzene, and styrene in homes with smokers compared to homes without smokers. This study indicated that cigarette smoking is a substantial contributor to benzene exposure for the population.

More extensive information is available on levels of ETS components in public buildings and workplaces of various types (Guerin et al. 1992, Hammond et al. 1995) (Table 30.1). Monitoring in locations where smoking may be intense, such as bars and restaurants, has generally revealed elevations of particles and other markers of smoke pollution where smoking is taking place (USDHHS 1986, NRC 1986). For example, Repace and Lowrey (1980) used a portable piezobalance to sample aerosols in restaurants, bars, and other locations. In the places sampled, respirable particulate levels ranged up to 700 $\mu g/m^3$, and the levels varied with the intensity of smoking. Similar data have been reported for the office environment (Cal EPA 1997, USDHHS 1986, NRC 1986, Guerin et al. 1992). More recent studies indicate low concentrations in many workplace settings, reflecting declining smoking prevalence and changing practices of smoking in the workplace. Using passive nicotine samplers, Hammond and colleagues (Hammond et al. 1995) showed that worksite smoking policies can sharply reduce ETS exposure. Transportation environments may also be polluted by cigarette smoking, although smoking is now banned in all domestic air flights and many international flights.

Biological Markers of Exposure

Biological markers, measurements of exposure indicators made in biologic materials, can be used to describe the prevalence of exposure to environmental tobacco smoke, to investigate the dosimetry of involuntary smoking, and to validate questionnaire-based measures of exposure. In both active and involuntary smokers, detection of tobacco smoke components or their metabolites in body fluids or alveolar air provides evidence of exposure to tobacco smoke, and levels of these markers can be used to gauge the intensity of exposure and to estimate risk.

At present, the most sensitive and specific markers for tobacco smoke exposure are nicotine and its metabolite, cotinine (NRC 1986, Jarvis and Russell 1984, USDHHS 1988). Nicotine or cotinine is seldom present in body fluids in the absence of exposure to tobacco smoke, although unusually large intakes of some foods could produce measurable levels of nicotine and cotinine (Idle 1990). Cotinine, formed by oxidation of nicotine, is one of several primary metabolites of nicotine (USDHHS 1988). Cotinine itself is extensively metabolized, and only about 17 percent of cotinine is excreted unchanged in the urine.

Because the circulating half-life of nicotine is generally shorter than 2 h (Rosenberg et al. 1980), nicotine concentrations in body fluids reflect very recent exposures. In contrast, cotinine has a half-life in the blood or plasma of nonsmokers of about 20 h (USDHHS 1988, Kyerematen et al. 1982, Benowitz et al. 1983); hence, cotinine levels provide information about more chronic exposure to tobacco smoke in involuntary smokers. Cotinine can be measured in plasma, saliva, and urine using either radioimmunoassay or chromatography. Concerns about nonspecificity of cotinine, arising from eating nicotine-containing foods, have been set aside (Benowitz 1996). Thiocyanate concentration in body fluids, concentration of carbon monoxide in expired air, and carboxyhemoglobin level distinguish active smokers from nonsmokers but are not as sensitive and specific as cotinine for assessing involuntary exposure to tobacco smoke (Jarvis and Russell 1984, Hoffman et al. 1984).

Cotinine levels have been measured in adult nonsmokers and children (Table 30.3) (Benowitz 1996). In the studies of adult nonsmokers, exposures at home, in the workplace, and in other settings determined cotinine concentrations in urine and saliva. The cotinine levels in involuntary smokers ranged from less than 1 percent to about 8 percent of cotinine levels measured in active smokers. Smoking by parents was the predominant determinant of the cotinine levels in their children. For example, Greenberg et al. (1984) found significantly higher concentrations of cotinine in the urine and saliva of infants exposed to cigarette smoke in their homes than in unexposed controls. Urinary cotinine levels in the infants increased with the number of cigarettes smoked during the previous 24 h by the mother. In a study of schoolchildren in England, salivary cotinine levels rose with the number of smoking parents in the home (Jarvis et al. 1985). In a study of a national sample of participants in the Third National Health and Nutrition Examination Survey, 1988–1991, 88 percent of nonsmokers had a detectable level of serum cotinine using liquid chromatography–mass spectrometry as the assay method (Pirkle et al. 1996). Cotinine levels in this national sample increased with the number of smokers in the household and the hours exposed in the workplace.

The results of studies on biological markers add to the biological plausibility of associations between involuntary smoking and disease documented in epidemiologic studies (Benowitz 1996). The data on marker levels provide ample evidence that involuntary exposure leads to absorption, circulation, and excretion of tobacco smoke components. The studies of biological markers also confirm the high prevalence of involuntary smoking, as ascertained by questionnaire (Pirkle et al. 1996, Coultas et al. 1987). Comparisons of levels of biological markers in smokers and nonsmokers have been made to estimate the relative intensities of active and involuntary smoking and thereby infer risk of ETS exposure. However, proportionality cannot be assumed between the ratio of the levels of markers in passive and active smokers and the relative doses of other tobacco smoke components.

TABLE 30.3 Cotinine Concentrations in Nonsmokers and Smokers (Selected Studies)

Study	Year	Subjects, *N*	Smoking status	Exposure level	Plasma or serum cotinine, ng/mL	Urine cotinine, ng/mL
Jarvis and Russell	1984	46	Nonsmokers	No exposure	0.8	1.5
		54	Nonsmokers	Exposed	2.0	7.7
Wald and Ritchie	1984	101	Nonsmokers	Wife nonsmoker		8.5 (SE* ± 1.3, median 5.0)
		20	Nonsmokers	Wife smoker		25.2 (SE ± 14.8, median 9.0)
Wald et al.	1984	43	Nonsmokers	0–1.5 h ETS* exposure/week		1.8
		47	Nonsmokers	1.5–4.5 h ETS exposure/week		3.4
		43	Nonsmokers	4.5–8.6 h ETS exposure/week		5.3
		43	Nonsmokers	8.6–29 h ETS exposure/week		14.7
		45	Nonsmokers	20–80 h ETS exposure/week		29.6
Jarvis et al.	1985	269	Nonsmokers, children	Neither parent smoked		
		96	Nonsmokers, children	Father smoked		
		76	Nonsmokers, children	Mother smoked		
		128	Nonsmokers, children	Both parents smoked		
Coultas et al.	1986	68	Nonsmokers aged <5 years	No smoker in home		
		41	Nonsmokers aged <5 years	1 smoker in home		
		21	Nonsmokers aged <5 years	2 or more smokers in home		
		200	Nonsmokers aged 5–17 years	No smoker in home		
		96	Nonsmokers aged 5–17 years	1 smoker in home		
		25	Nonsmokers aged 5–17 years	2 or more smokers in home		
		316	Nonsmokers aged >17 years	No smoker in home		
		60	Nonsmokers aged >17 years	1 smoker in home		
		12	Nonsmokers aged >17 years	2 or more smokers in home		
Strachan et al.	1989	405	Nonsmokers, age 7 years	No smokers in home		
		241	Nonsmokers, age 7 years	1 smoker in home		
		124	Nonsmokers, age 7 years	2 or more smokers in home		
Thompson et al.	1990	158	Nonsmokers	Lives alone or with nonsmoker		4.4 (geometric mean) (95% CI* 3.6–5.4)
		26	Nonsmokers	Lives with smoker		11.4 (geometric mean) (95% CI 6.9–18.9)

TABLE 30.3 Cotinine Concentrations in Nonsmokers and Smokers (Selected Studies) (*Continued*)

Cummings et al.	1990	162	Nonsmokers	No exposure past 4 days		6.2 (mean)	
		208	Nonsmokers	1–2 exposures past 4 days		7.8 (mean)	
		152	Nonsmokers	3–5 exposures past 4 days		9.8 (mean)	
		141	Nonsmokers	6 or more exposures		12.5 (mean)	
Tunstall-Pedoe et al.	1991	1873	Nonsmokers, male		0.68 (median)		
		1940	Smokers, male		240 (median)		
		2270	Nonsmokers, female		0.10 (median)		
Cook et al.	1994	1260	Nonsmokers, aged 5–7 years	No smokers in home			0.29 (geometric mean) (95% CI 0.28–0.31)
		293	Nonsmokers, aged 5–7 years	Mother smoker			2.2 (geometric mean) (95% CI 1.9–2.5)
		521	Nonsmokers, aged 5–7 years	Father smoker			1.2 (geometric mean) (95% CI 1.1–1.3)
		553	Nonsmokers, aged 5–7 years	Mother and father smokers			4.0 (geometric mean) (95% CI 3.7–4.4)
		629	Nonsmokers, females from 10 countries	No home or work ETS exposure		2.7 ng/mg creatinine	
Riboli et al.	1990	210	Nonsmokers, females from 10 countries	Exposure at work but not at home		4.8 ng/mg creatinine	
		359	Nonsmokers, females from 10 countries	Exposure at home but not at work		9.0 ng/mg creatinine	
		124	Nonsmokers, females from 10 countries	Exposure at home and at work		10.0 ng/mg creatinine	
		1071	Nonsmokers, aged 4–11 years	No home ETS exposure	0.12 (geometric mean) (95% CI 0.10–0.14)		
Pirkle et al.	1996	713	Nonsmokers, aged 4–11 years	Home ETS exposure only	1.13 (geometric mean) (95% CI 0.98–1.34)		
		379	Nonsmokers, aged 12–16 years	No home ETS exposure	0.11 (geometric mean) (95% CI 0.10–0.15)		
		268	Nonsmokers, aged 12–16 years	Home ETS exposure only	0.81 (geometric mean) (95% CI 0.62–1.04)		
		3154	Nonsmokers, aged ≥ 17 years	No home or work ETS exposure	0.12 (geometric mean) (95% CI 0.11–0.14)		
		1332	Nonsmokers, workers aged ≥ 17 years	No home or work ETS exposure	0.13 (geometric mean) (95% CI 0.12–0.15)		
		779	Nonsmokers, workers aged ≥ 17 years	Work ETS exposure only	0.32 (geometric mean) (95% CI 0.28–0.36)		
		315	Nonsmokers, workers aged ≥ 17 years	Home ETS exposure only	0.65 (geometric mean) (95% CI 0.52–0.81)		
		246	Nonsmokers, workers aged ≥ 17 years	Home and work ETS exposure	0.93 (geometric mean) (95% CI 0.76–1.13)		

Source: Benowitz (1996).

30.3 HEALTH EFFECTS OF INVOLUNTARY SMOKING IN CHILDREN

Fetal Effects

Researchers have demonstrated that active smoking by mothers results in a variety of adverse health effects in children. Some of the health effects result predominantly from transplacental exposure of the fetus to tobacco smoke components. Studies have also investigated and demonstrated associations between adverse health effects in children and maternal exposure to ETS. For example, paternal smoking in the presence of a pregnant mother may lead to perinatal health effects manifested on birth of the baby, and either maternal or paternal smoking in the presence of a newborn child may lead to postnatal health effects in the developing child.

Health effects on the fetus resulting from maternal smoking during pregnancy include fetal growth effects (decreased birthweight, growth retardation, or prematurity), fetal loss (spontaneous abortion and perinatal mortality), and congenital malformations. ETS exposure of nonsmoking mothers is associated with reduced birthweight as well, although the extent of the reduction is far less than for active maternal smoking during pregnancy. Health effects on the child postnatally, resulting from either ETS exposure to the fetus or to the newborn child, include sudden infant death syndrome and adverse effects on neuropsychological development and physical growth. Possible longer-term health effects of fetal ETS exposure include childhood cancers of the brain, leukemia, and lymphomas, among others.

There are a number of components of ETS that may produce these effects. Fetal exposure to carbon monoxide and nicotine due to ETS may increase risk for perinatal health effects. Carbon monoxide in ETS may contribute to increased concentrations of carbon monoxide and carboxyhemoglobin in the fetus, thereby reducing oxygen delivery, and the fetus may not be able to physiologically compensate (USDHHS 1980), leading to fetal hypoxia. Exposure to nicotine found in ETS can also alter an infant's catecholamine metabolism and response to hypoxia (Milerad and Sundell 1993). Furthermore, nicotine crossing the placenta may lead to decreased in utero placental perfusion, affecting the fetal cardiovascular system, gastrointestinal system, and central nervous system (Stillman et al. 1986). Other constituents of cigarette smoke have also been demonstrated to adversely affect fetal growth (Office of Environmental Health Hazard Assessment 1996). Association between ETS and childhood cancers is biologically plausible in the presence of carcinogenic tobacco smoke components or metabolites, such as benzene, nitrosamines, urethane, and radioactive compounds, at organ sites of the cancers.

Perinatal Health Effects

Fetal Growth. These health effects include reduced fetal growth, growth retardation, and congenital abnormalities. In most studies, paternal smoking has been used as the exposure measure to assess the association between ETS exposure and these nonfatal perinatal health effects. Low birthweight was first reported in 1957 to be associated with maternal smoking (USDHHS 1980) and maternal cigarette smoking during pregnancy is considered to be causally associated with low birthweight (USDHHS 1989). Other studies report lower birthweight for infants of nonsmoking women passively exposed to tobacco smoke during pregnancy (Martin and Bracken 1986, Rubin et al. 1986). For example, Haddow and colleagues (1988) used cotinine as a biomarker to measure exposure to ETS and found a decrease of 100 g in birthweight for fetuses exposed to ETS, defined as a cotinine level of 1.1 to 9.9 ng/mL in the fetus. The most recent biomarker studies (Eskenazi and Bergmann 1995, Eskenazi and Trupin 1995, Rebagliato et al. 1995) support the findings of Haddow et al. (1988). Other epidemiologic studies assessed ETS exposure from multiple sources through questionnaire (Mainous and Hueston 1994, Roquer et al. 1995, Rebagliato et al. 1995) and still demonstrated decreases of 20 to 40 g in mean birthweights after adjustment for potential confounding factors.

Other nonfatal perinatal health effects possibly associated with ETS exposure are growth retardation and congenital malformations. Martin and Bracken (1986) demonstrated a strong association with growth retardation in their 1986 study, and several more recent studies provide support (Mainous and Hueston 1994, Roquer et al. 1995). The few studies (Zhang et al. 1992, Savitz et al. 1991, Seidman et al. 1990) conducted to assess the association between paternal smoking and congenital malformations have demonstrated risks ranging from 1.2 to 2.6 for exposed compared to nonexposed.

ETS exposure to the fetus during its development has been associated in some studies with fatal perinatal health effects such as spontaneous abortion and perinatal mortality. Very few studies have examined the association between ETS exposure and perinatal death, with a few supporting an increase in risk (Comstock and Lundin 1967, Mau and Netter 1974, Lindbohm et al. 1991, Ahlborg and Bodin 1991).

Postnatal Health Effects

ETS exposure due to maternal or paternal smoking may lead to postnatal health effects including increased risk for SIDS, reduced physical development, decrements in cognition and behavior, and increased risk for childhood cancers. For cognition and behavior, evidence is limited and is not considered in this chapter.

SIDS. *Sudden infant death syndrome* refers to the sudden death of seemingly healthy infants while asleep. To date 10 studies have been directed at the association between SIDS and postnatal ETS exposure; six studies have addressed the association between paternal smoking and SIDS, and four studies have assessed household smoke exposure and SIDS (Table 30.4). While maternal smoking during pregnancy has been associated with SIDS, these studies measured maternal smoking after pregnancy, along with paternal smoking and household smoking generally.

Mitchell and colleagues (1993) demonstrated a significant association [odds ratio (OR) = 1.7] between postnatal maternal smoking and SIDS; this association remained significant after adjustment for potential confounders. In an updated study, Mitchell and colleagues (1995) concluded that the elimination of postnatal maternal smoking did not reduce the risk of SIDS and that prenatal exposure was still the more important risk factor. In a larger study, Klonoff-Cohen and colleagues (1995) found an adjusted odds ratio of 2.3 for SIDS and postnatal ETS exposure. Three more studies assessing maternal smoking after pregnancy (Bergman and Wiesner 1976, McGlashan 1989, Mitchell et al. 1991) could not assess a possible independent relationship between postnatal smoking and SIDS due to extensive overlap between maternal smoking during and after pregnancy.

Of the six studies conducted to assess the association between paternal smoking and SIDS, four (Mitchell et al. 1993, Klonoff-Cohen et al. 1995, Nicholl 1992, Blair et al. 1996) demonstrated elevated risks for SIDS while accounting for maternal smoking either by study design or through analyses, with odds ratios of 1.6, 1.4, 3.5, and 2.5, respectively. Two other studies (Bergman and Wiesner 1976, McGlashan 1989) demonstrated elevated risks but did not adjust for maternal smoking. Four studies assessed general household smoke exposure and SIDS. Dose-response relationships were observed by Blair and colleagues (1996), Mitchell and colleagues (1993), and Klonoff-Cohen and colleagues (1995).

TABLE 30.4 Studies Investigating the Association between ETS and SIDS

TABLE 30.4 Studies Investigating the Association between ETS and SIDS

Study	Location	Outcome assessed	Exposure	Exposure ascertainment	Participants	Odds ratio	Odds ratio adjusted for:
Berman and Wiesner (1976)	United States (King County, Washington)	SIDS	Maternal smoking after pregnancy	Mailed questionnaire	56 cases 86 controls	2.4 (1.2, 4.8)	Matched on date of birth, sex, and race Not adjusted for maternal smokin
			Paternal smoking			1.5 (0.7, 3.2)	
McGlashan (1989)	Tasmania	SIDS	Maternal smoking during and after pregnancy	Interviewed parents	167 cases 334 controls	1.9 (1.2, 2.9)	Matched on sex
			Paternal smoking			"significantly increased"	
Mitchell et al. (1991)	New Zealand	SIDS	Maternal smoking after pregnancy	Interview with parents or from medical records	128 cases 503 controls	1.8 (1.0, 3.3)	Demographic factors, social factors, breastfeeding, season, sleeping position
Nicholl and O'Cathain (1992)	United Kingdom	SIDS	Paternal smoking		242 cases 251 controls	1.4 (0.8, 2.4)	Spousal smoking matched for date and place of birth
Schoendorf and Kiely (1992)	United States (U.S. National Maternal and Infant Health Survey)	SIDS	Maternal smoking after pregnancy	Interview	435 cases 6000 controls	Whites 1.8 (1.0, 3.0); blacks 2.3 (1.5, 3.7)	Maternal age, education, marital status
Mitchell et al. (1993)	New Zealand	SIDS	Maternal smoking after pregnancy	Interview with parents or from medical records	485 cases 1800 controls	1.7 (1.2, 2.3)	Region Season Breastfeeding
			Paternal smoking			1.4 (1.0, 1.8)	Bed sharing Mother's marital status SES Age Smoking during pregnancy Infant's age Sex Birthweight Race Sleeping position Smoking by mother Smoking by father Smoking by other
Klonoff-Cohen et al. (1995)	United States (southern California)	SIDS	Maternal smoking after pregnancy		200 cases 200 controls	2.5 (1.0, 5.0)	Routine sleep position Medical conditions at birth Prenatal care
			Same-room maternal smoking after pregnancy			4.6 (1.8, 11.8)	Breastfeeding Maternal smoking during pregnancy
			Paternal smoking			3.5 (1.9, 6.8)	
			Same-room paternal smoking			5.0 (2.4, 11.0)	
Blair et al. (1996)	United Kingdom	SIDS	Paternal smoking Maternal smoking		195 cases 780 controls	2.5 (1.5, 4.2)	Marital Status Maternal age SES Maternal smoking Drug and alcohol use Gestational age Sleeping position Breastfeeding Matched by age and region

Klonoff-Cohen and colleagues (1995) reported adjusted odds ratios for 1 to 10, 11 to 20, and ≥21 cigarettes/day of 2.4, 3.6, and 22.7, respectively. Schoendorf and Kiely (1992) demonstrated increased risk of SIDS only in white infants.

Cancers

ETS exposure has been evaluated as a risk factor for the major childhood cancers. The evidence is limited and does not yet support conclusions as to the causal nature of the observed associations. Four studies have shown associations between paternal smoking and risk of brain tumors (Preston-Martin et al. 1982, Howe et al. 1989, John et al. 1991, McCredie et al. 1994), with odds ratios ranging from 1.4 to 2.2, with statistically significant results in two of the studies (McCredie et al. 1994, Preston-Martin et al. 1982). In animal studies, leukemia can be induced by transplacentally acting carcinogens found in tobacco smoke, and benzene, a component of ETS, is a leukemogen. The eight studies (John et al. 1991, Pershagen et al. 1992, van Steensel-Moll et al. 1985, Stjernfeldt et al. 1986, McKinney et al. 1987, Buckley et al. 1986, Magnani et al. 1990, Severson et al. 1993) on parental smoking and the risk of leukemia in children are conflicting. Six studies (John et al. 1991, Pershagen et al. 1992, Stjernfeldt et al. 1986, McKinney et al. 1987, Buckley et al. 1986, Magnani et al. 1990) have been conducted on ETS exposure and the risk of lymphomas and non-Hodgkin's lymphomas. While small increases in risk were observed, the data do not support a conclusion at this time.

ETS exposure has also been assessed as a risk factor for other common childhood cancers including neuroblastoma, germ cell tumors, bone and soft-tissue sarcomas, and Wilm's tumor of the kidney. A small increase in relative risk for neuroblastoma associated with paternal smoking during pregnancy has been demonstrated in one study (Kramer et al. 1987). Several studies have also attempted to assess associations between ETS and germ cell tumors (McKinney et al. 1987), bone and soft-tissue sarcomas (McKinney et al. 1987, Magnani et al. 1990, Grufferman et al. 1982, Hartley et al. 1988). Finally, active smoking is an established risk factor for cancers of the kidney and renal pelvis in adults, and animal studies have suggested that nitrosamines may have an etiologic role in these cancers. However, conclusive studies associating ETS with Wilm's tumor of the kidney in children have not yet been conducted.

Lower Respiratory Tract Illnesses in Childhood

Lower respiratory tract illness are extremely common during childhood. Studies of involuntary smoking and lower respiratory illnesses in childhood, including the more severe episodes of bronchitis and pneumonia, provided some of the earliest evidence on adverse effects of ETS (Harlap and Davies 1974, Colley et al. 1974). Presumably this association represents an increase in frequency or severity of illnesses that are infectious in etiology and not a direct response of the lung to toxic components of ETS. Investigations conducted throughout the world have demonstrated an increased risk of lower respiratory tract illness in infants with smoking parents (Strachan and Cook 1997). These studies indicate a significantly increased frequency of bronchitis and pneumonia during the first year of life of children with smoking parents. Strachan and Cook (1997) report a quantitative review of this information, combining data from 39 studies. Overall, there was an approximate 50 percent increase in illness risk if either parent smoked; the odds ratio for maternal smoking was somewhat higher at 1.72 [95% confidence interval (CI) = 1.55, 1.91]. Although the health outcome measures have varied somewhat among the studies, the relative risks associated with involuntary smoking were similar, and dose-response relationships with extent of parental smoking were demonstrable. Although most of the studies have shown that maternal smoking rather than paternal smoking underlies the increased risk of parental smoking, studies from China show that paternal smoking alone can increase incidence of lower respiratory illness (Strachan and Cook 1997, Yue Chen et al. 1986). In these studies, an effect of passive smoking has not been readily identified after the first year of life. During the first year of life, the strength of its effect may reflect higher exposures consequent to the time-activity patterns of young infants, which place them in close proximity to cigarettes smoked by their mothers.

Respiratory Symptoms and Illness in Children

Data from numerous surveys demonstrate a greater frequency of the most common respiratory symptoms: cough, phlegm, and wheeze in the children of smokers (Cal EPA 1997, USDHHS 1986, Cook and Strachan 1997). In these studies the subjects have generally been schoolchildren, and the effects of parental smoking have been examined. Thus, the less prominent effects of passive smoking, in comparison with the studies of lower respiratory illness in infants, may reflect lower exposures to ETS by older children who spend less time with their parents.

By the mid-1980s, results from several large studies provided convincing evidence that involuntary exposure to ETS increases the occurrence of cough and phlegm in the children of smokers, although earlier data from smaller studies had been ambiguous. For example, in a study of 10,000 schoolchildren in six U.S. communities, smoking by parents increased the frequency of persistent cough in their children by about 30 percent (Gold et al. 1994). The effect of parental smoking was derived primarily from smoking by the mother. For the symptom of chronic wheeze, the preponderance of the early evidence also indicated an excess associated with involuntary smoking. In a survey of 650 schoolchildren in Boston, one of the first studies on this association, persistent wheezing, was the most frequent symptom (Weiss et al. 1980); the prevalence of persistent wheezing increased significantly as the number of smoking parents increased. In the large study of children in six U.S. communities, the prevalence of persistent wheezing during the previous year was significantly increased if the mother smoked (Gold et al. 1994).

Cook and Strachan (1997) conducted a quantitative summary of the relevant studies, including 41 of wheeze, 34 of chronic cough, 7 of chronic phlegm, and 6 of breathlessness. Overall, this synthesis indicates increased risk for respiratory symptoms for children whose parents smoke (Cook and Strachan 1997). There was even increased risk for breathlessness (OR = 1.31, 95 percent CI = 1.08, 1.59). Having both parents smoke was associated with the highest levels of risk.

Childhood Asthma

Exposure to ETS might cause asthma as a long-term consequence of the increased occurrence of lower respiratory infection in early childhood or through other pathophysiological mechanisms including inflammation of the respiratory epithelium (Samet et al. 1983, Tager 1988). The effect of ETS may also reflect, in part, the consequences of in utero exposure. Assessment of airways responsiveness shortly after birth has shown that infants whose mothers smoke during pregnancy have increased airways responsiveness, a characteristic of asthma, compared with those whose mothers do not smoke (Young et al. 1991). Maternal smoking during pregnancy also reduced ventilatory function measured shortly after birth (Hanrahan et al. 1992). These observations suggest that in utero exposures from maternal smoking may affect lung development, and increased risk for asthma.

While the underlying mechanisms remain to be identified, the epidemiologic evidence linking ETS exposure and childhood asthma is mounting (Cal EPA 1997, Cook and

Strachan 1997). The synthesis by Cook and Strachan (1997) shows a significant excess of childhood asthma if both parents or the mother smoke.

Evidence also indicates that involuntary smoking worsens the status of those with asthma. For example, Murray and Morrison (1986, 1989) evaluated asthmatic children followed in a clinic. Level of lung function, symptom frequency, and responsiveness to inhaled histamines were adversely affected by maternal smoking. Population studies have also shown increased airway responsiveness for ETS-exposed children with asthma (O'Connor et al. 1987, Martinez et al. 1988). The increased level of airway responsiveness associated with ETS exposure would be expected to increase the clinical severity of asthma. In this regard, exposure to smoking in the home has been shown to increase the number of emergency room visits made by asthmatic children (Evans et al. 1987). Asthmatic children with smoking mothers are more likely to use asthma medications (Weitzman et al. 1990), a finding that confirms the clinically significant effects of ETS on children with asthma. Guidelines for the management of asthma all urge reduction of ETS exposure at home (USDHHS 1997).

Lung Growth and Development

During childhood, measures of lung function increase, more or less parallel to the increase in height. On the basis of the primarily cross-sectional data available at the time, the 1984 report of the Surgeon General (USDHHS 1984) concluded that the children of smoking parents in comparison with those of nonsmokers had small reductions of lung function, but the long-term consequences of these changes were regarded as unknown. In the 2 years between the 1984 and the 1986 reports, sufficient longitudinal evidence accumulated to support the conclusion in the 1986 report (USDHHS 1986) that involuntary smoking reduces the rate of lung function growth during childhood. Further cross-sectional studies have also been consistent with this conclusion (Samet and Wang 2000).

The effects of involuntary smoking on lung growth have been demonstrated in several longitudinal studies (Samet and Lange 1996). On the basis of cross-sectional data from a study of children in East Boston, Massachusetts, Tager and coworkers (1979) reported that the level of FEF_{25-75}, a spirometric forced expiratory flow rate sensitive to subtle effects on airways and parenchymal function, declined with an increasing number of smoking parents in the household. In 1983 in the first set of longitudinal data, this investigative group reported the results obtained on follow-up of these children over a 7-year period (Tager et al. 1983). Using a multivariate statistical technique, the investigators showed that both maternal smoking and active smoking by the child reduced the growth rate of the FEV_1. Lifelong exposure of a child to a smoking mother was estimated to reduce growth of the FEV_1 by 10.7, 9.5, and 7.0 percent after 1, 2, and 5 years of follow-up, respectively. Findings with additional follow-up were similar (Tager et al. 1985).

Longitudinal data from the study of air pollution in six U.S. cities also showed reduced growth of the FEV_1 in children whose mothers smoked cigarettes (Gold et al. 1996). The growth rate of the FEV_1 from ages 6 through 10 years was calculated for 7834 white children. The findings of a statistical analysis were that from ages 6 through 10 years, FEV_1 growth rate was reduced by 0.17 percent per pack of cigarettes smoked daily by the mother. This effect was somewhat smaller than that reported by Tager et al. (1983), although if it is extrapolated to age 20 years, a cumulative effect of 2.8 percent is predicted. In the most recent analysis of these data, Wang and colleagues (1994) modeled exposures in a time-dependent fashion, classifying exposure during the first 5 years of life and cumulative exposure up to the year before follow-up. Current maternal smoking was found to affect lung growth. Findings from other studies are consistent (Samet and Lange 1996).

TS and Middle-Ear Disease in Children

)titis media is one of the most frequent diseases diagnosed in children at outpatient facili-ies; forms of otitis media include acute, persistent, or recurrent disease as well as effusion ır fluid within the middle ear. There are now many reported studies on the association ıetween ETS exposure and otitis media in children. ETS exposure in these studies is ıssessed mostly by questionnaire or interview of the parents, but two studies assessed ETS :xposure objectively through the use of biomarkers (serum or salivary cotinine measure-nents in the children). Outcomes assessed in the studies vary from acute, persistent, and recurrent otitis media or middle-ear effusion, to consequences of otitis media such as hear-ing loss and ear surgery.

Positive associations between ETS and otitis media have been consistently demonstrated in studies of the cohort or prospective design, but not as consistently in the case-control studies. This difference may have arisen because the cohort studies include children from birth to age 2 years, the peak age of risk for middle-ear disease. Case-control studies, on the other hand, have been directed at older children who are not at peak risk for otitis media. Regardless of study type, however, increase in risk for middle-ear disease is demonstrated when the outcome assessed is recurring episodes of middle-ear effusion or otitis media, versus incident or single episodes of otitis media. In a 1997 metaanalysis, Strachan and Cook (1997) found a pooled odds ratio of 1.48 (95 percent CI: 1.08, 2.04) for recurrent otitis media if either parent smoked, 1.38 (95 percent CI: 1.23, 1.55) for middle-ear effusions, and 1.21 (95 percent CI: 0.95, 1.53) for outpatient or inpatient care for chronic otitis media or "glue ear."

The California EPA (Cal EPA 1997) and the United Kingdom Committee (Scientific Committee on Tobacco and Health, HSMO 1998) have reviewed the literature on ETS and middle-ear disease and concluded that there is a causal association with ETS exposure and otitis.

30.4 HEALTH EFFECTS OF INVOLUNTARY SMOKING IN ADULTS

Lung Cancer

In 1981, reports were published from Japan (Hirayama 1981) and Greece (Trichopoulos et al. 1981) that indicated increased lung cancer risk in nonsmoking women married to cigarette smokers. Subsequently, this controversial association has been examined in investigations conducted in the United States and other countries. The association of involuntary smoking with lung cancer derives biological plausibility from the presence of carcinogens in sidestream smoke and the lack of a documented threshold dose for respiratory carcinogens in active smokers (USDHHS 1982, IARC 1986). Moreover, genotoxic activity, the ability to damage DNA, has been demonstrated for many components of ETS (Lofroth 1989, Claxton et al. 1989, Weiss 1989), although several small studies have not found cytogenetic effects in passive smokers (Sorsa et al. 1985, 1989; Husgafvel-Pursiainen et al. 1987). Experimental exposure of nonsmokers to ETS leads to their excreting NNAL, a tobacco-specific carcinogen, in their urine (Hecht et al. 1993). Nonsmokers exposed to ETS also have increased concentrations of adducts of tobacco-related carcinogens (Maclure et al. 1989, Crawford et al. 1994).

Epidemiologists have directly tested the association between lung cancer and involuntary smoking utilizing conventional designs: the case-control and cohort studies. In a *case-*